CHAPTER 1

CROSS-COUPLING REACTIONS OF ORGANOTRIFLUOROBORATE SALTS

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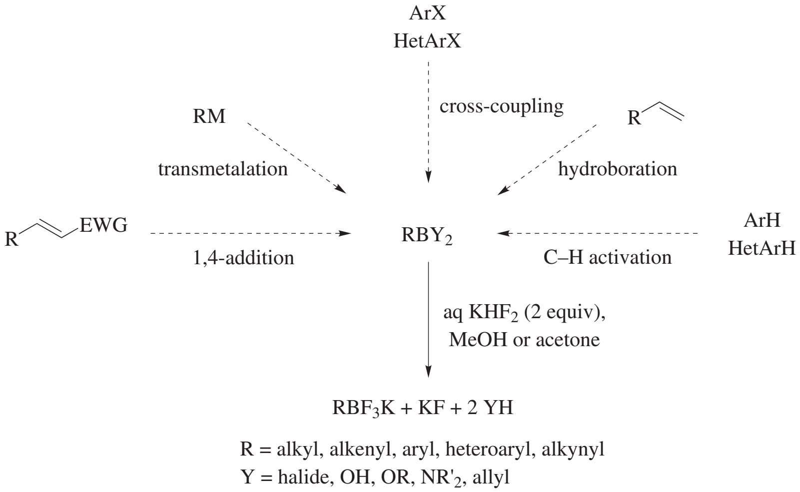
INTRODUCTION

The Suzuki-Miyaura cross-coupling reaction is widely recognized as one of the most powerful and broadly utilized synthetic methods available for carbon–carbon bond formation.[1–3] The importance of this coupling process has engendered a great deal of interest from practicing synthetic chemists both in academia and, because of the commercial importance of this reaction, in industry. Largely for historical reasons, boronic acids have become the standard reagents utilized for Suzuki-Miyaura cross-coupling reactions, and hundreds of these substances are now commercially available. Thousands of papers employing the reaction have been published, and many of these have been devoted to enhancements of the original procedure. Among the latter contributions, the vast majority of these important studies have dealt with improving the transformation by optimizing critical characteristics of the reaction such as the catalyst/ligand complex, the electrophile (aryl, heteroaryl, alkenyl, alkynyl, alkyl), the nucleofuge (chlorides, sulfonates, phosphates, esters), the solvent (e.g., water, ionic liquids[4–6]), the bases required, and the conditions of the reaction (e.g., by using sonication or microwaves[7,8]). Curiously, little effort was initially devoted to expand the scope of the reaction by altering the essential organoboron reagent. Organotrifluoroborates are one of several classes of organoboron reagents developed to provide a complementary suite of reagents for cross-coupling, affording alternatives to the classical boronic acid derivatives.

The first practical synthesis of organotrifluoroborates was reported in 1995, and involved the treatment of arylboronic acids with the inexpensive salt KHF_2.[9] It was subsequently determined that virtually any boronic acid could be converted to the corresponding organotrifluoroborate using the same protocol, and in fact nearly all organoboron reagents possessing an organic moiety and two labile groups (e.g., halides, $-OR$, $-NR_2$, allyl) could be transformed to the desired trifluoroborate salts. Consequently, organotrifluoroborates can be prepared by employing any of the well-known means of preparing organoboron compounds, with hydroboration, transmetalation, cross-coupling, C–H activation, and 1,4-addition being among the most important methods, followed by conversion to the salts (Scheme 1).

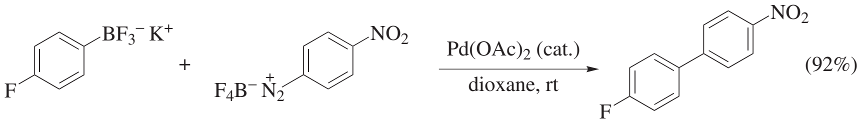


Scheme 1. Diverse approaches to organotrifluoroborates.

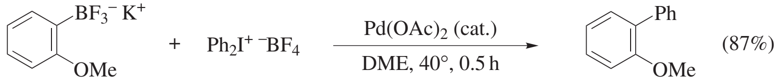
Owing to the commercial availability of KHF_2, the potassium salts of the trifluoroborates are the most conveniently prepared. The potassium counterion affords materials that reliably appear as crystalline solids or free-flowing powders. The cesium salts are also stable solids,[10] although the latter materials come at a greater cost both economically and in terms of their increased mass. Lithium organotrifluoroborates are somewhat unstable because of the strong thermodynamic driving force for formation of LiF, which leads to decomposition of the complex.[11] Alkali metal salts of the organotrifluoroborates have limited solubility in nonpolar organic solvents. For carrying out reactions in such media, the organotrifluoroborates can be readily converted to soluble tetraalkylammonium salts by treatment with tetraalkylammonium hydroxide (Eq. 1).[12] This conversion, however, incurs practical costs, including a loss of atom economy and, in some cases (e.g., alkyltrifluoroborate derivatives), a lack of crystallinity, creating difficulties in handling.

$$\mathrm{R^1BF_3^-\,K^+ \;+\; R^2{}_4N^+\,{}^-OH \longrightarrow R^1BF_3^{-\,+}NR^2{}_4 \;+\; KOH} \qquad \text{(Eq. 1)}$$

The first reported examples of organotrifluoroborates in Suzuki-type cross-coupling reactions employed highly reactive arenediazonium salts[13,14] and diaryliodonium salts[15] as electrophiles for the preparation of biaryls (Eqs. 2 and 3). Broader explorations were begun subsequently, using diverse organotrifluoroborates with a variety of electrophiles, and ongoing studies continue to expand the scope of the cross-coupling transformation.

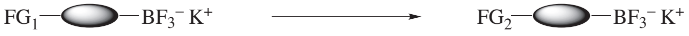


(Eq. 2)



(Eq. 3)

As a result of such investigations, several defining features have emerged as hallmarks of organotrifluoroborate chemistry. For example, the tetracoordinate organotrifluoroborates generally undergo stoichiometric coupling with a variety of organic halides and pseudohalides because competing protodeboronation is often nonexistent. Aside from the boronic acids, the trifluoroborates exhibit the best atom economy of any organoboron reagents used for cross-coupling. The byproducts of the coupling of organotrifluoroborates are relatively benign fluoride salts and boric acid, minimizing environmental concerns. Perhaps most importantly, the tetracoordinate nature of these materials, anchored by exceptionally strong boron-fluorine bonds, makes them inherently inert to many of the most common reagents utilized in organic synthesis. This property has some important consequences: (1) Several classes of organotrifluoroborates have demonstrated enhanced stability on storage as compared to other organoboron reagents. This feature is particularly relevant for heteroaryl, alkenyl, alkynyl, cyclopropyl, and cyclobutyl derivatives. (2) Organoboron reagents of unprecedented structure and functional group complexity, not accessible to tricoordinate boron species, can be prepared as their trifluoroborate salts, affording new opportunities for carbon–carbon bond-forming reactions. (3) Functional groups incorporated within the organotrifluoroborates can be selectively manipulated, leaving the boron-carbon bond intact (Scheme 2). Essentially, the trifluoroborates are a protected form of boronic acids,[16] with little or no penalty (and many benefits) being paid for the protection. As a result, one can initiate a synthetic sequence with a small, minimally functionalized organotrifluoroborate and build molecular complexity from this platform while retaining the key carbon–boron bond for future processing. In this manner, the organoboron species can be carried through several synthetic steps, with performance of the key coupling reaction taking place at a point more strategically convenient. The latter two features allow practitioners to expand the role of organoborons in their synthetic planning and fundamentally change retrosynthetic analyses involving boron-based processes.



Oxidations:
- epoxidation
- dihydroxylation
- ozonolysis
- Swern
- IBX
- Dess-Martin
- TPAP/NMO

Reductions:
- LAH
- $NaBH_4$
- H_2–Pd/C

Other:
- metal-halogen exchange
- Wittig
- Horner-Wadsworth Emmons
- Huisgen 1,3-dipolar cycloaddition
- carbonyl additions
- TosMIC condensations
- reductive amination

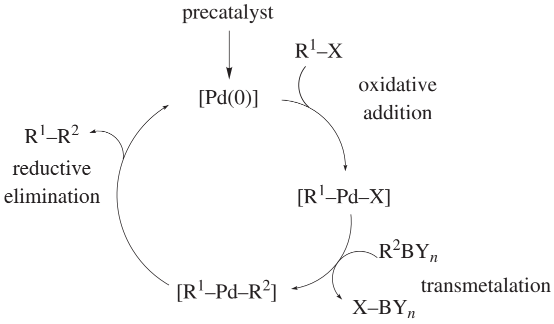
Scheme 2. Reactions tolerated by organotrifluoroborates.

This chapter outlines the scope and limitations of cross-coupling reactions employing organotrifluoroborates and comprehensively covers material published through August, 2009; the tables cover all references published through the middle of 2010. As a testament to their increasing importance, several review articles on various aspects of organotrifluoroborate chemistry have already appeared.[11,16–23]

MECHANISTIC CONSIDERATIONS

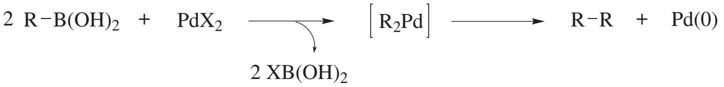
All available evidence suggests that the general mechanistic scheme for the cross-coupling of organotrifluoroborates is the same as that for cross-coupling with boronic acids and most other organometallic reagents.[24] Beginning with a Pd(II) precatalyst, reduction to the active Pd(0) species initiates the catalytic cycle. Oxidative addition of Pd(0) into the C–X bond of various electrophiles provides an organopalladium(II) species that subsequently undergoes transmetalation with an organoboron partner to generate a diorganopalladium intermediate. The diorganopalladium intermediate undergoes reductive elimination, completing the overall transformation with formation of the final product and regeneration of the Pd(0) species (Scheme 3).

At a more detailed level, however, important differences exist between transformations involving boronic acids, for example, and those involving the organotrifluoroborates. One such aspect is precatalyst activation. Although Pd(0) catalysts are sometimes used directly in cross-coupling reactions, their inherent instability to air oxidation makes them susceptible to decomposition if stored outside a glove box, and for this reason more stable Pd(II) precatalysts are preferred. Palladium(II) complexes are reduced in situ by any number of reductants,[25] including alcohols, amines, alkenes, and phosphines.[26] In cross-coupling reactions, the Pd(II) salts are often reduced by the organometallic reagent employed



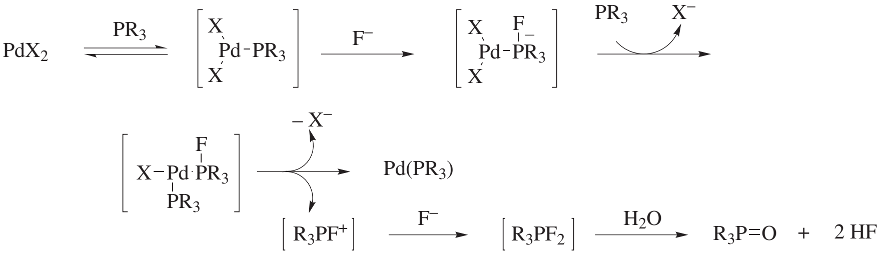
Scheme 3. General catalytic scheme for Suzuki-Miyaura cross-coupling.

in the reaction (Eq. 4). This process generates homocoupling products from the organometallic precursor.



$$2\ \mathrm{R{-}B(OH)_2} + \mathrm{PdX_2} \xrightarrow[\ 2\ \mathrm{XB(OH)_2}\ ]{} \left[\mathrm{R_2Pd}\right] \longrightarrow \mathrm{R{-}R} + \mathrm{Pd(0)} \qquad \text{(Eq. 4)}$$

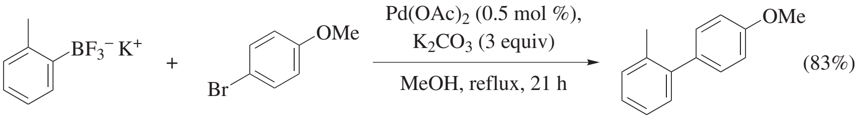
Mechanistic studies on organotrifluoroborates have shown that <0.1% of homocoupled products are generated when these reagents are employed with Pd(II) precatalysts, even when relatively high (5 mol %) catalyst loadings are used.[27] This implies that $PdCl_2(PPh_3)_2$ or related Pd(II) precatalysts are completely reduced prior to transmetalation from the trifluoroborate, and that fluoride catalyzes the reduction of the Pd(II) complex via a monophosphane Pd(0) complex (Scheme 4).[28–30]



Scheme 4. Fluoride-catalyzed reduction of Pd(II) to Pd(0).

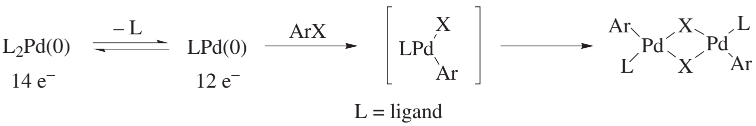
The oxidative addition step that takes place subsequent to precatalyst reduction appears to be independent of the organometallic reagent utilized, and thus to a large extent the factors that influence this step in other cross-coupling reactions will also play a significant role in organotrifluoroborate coupling reactions.[31–34] Depending on the reaction partners involved, the oxidative addition step can be the rate-determining step in cross-coupling reactions, and thus enormous efforts have been made to understand and improve this step. In fact, understanding the significant role that ligands play in the overall process constitutes one of the most important advances in cross-coupling protocols,[35–38] along with the design and development of ligands that have expanded the scope of the coupling reaction.[39–45]

The most common electrophiles for cross-coupling reactions are those containing Csp^2–X bonds. For reactive aryl bromides, there is little challenge in the oxidative addition step, and thus the cross-couplings can often be carried out under ligandless conditions with very low catalyst loadings in the presence of air (Eq. 5).[46]



(Eq. 5)

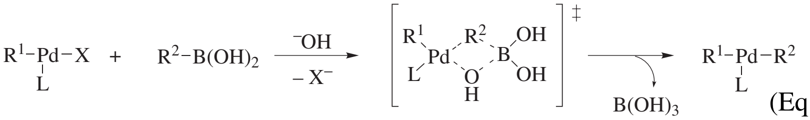
With less reactive aryl chloride electrophiles and challenging cross-coupling partners (e.g., sterically hindered systems and alkyltrifluoroborate nucleophiles), mono-ligated complexes incorporating sterically demanding, electron-rich phosphine ligands have consistently proven to be most effective catalysts.[43] These complexes have been engineered with design features tuned to optimal performance. Palladium(0) complexes with sterically encumbered ligands undergo oxidative addition with aryl halides by a dissociative mechanism through [LPd(0)] species. Bulky ligands shift the equilibrium toward formation of these highly reactive, monocoordinated, 12-electron organopalladium intermediates (Scheme 5).[32,47–50] The presence of large substituents on the phosphine ligand also increases the energy of the ground state in [L_2Pd(0)] complexes relative to that of the [L_2Pd(0)] species with smaller ligands, effectively lowering the energy of activation required to access the reactive [LPd(0)] intermediate, thus further facilitating the oxidative addition process.[34]



Scheme 5. Oxidative addition from L_2Pd(0) complexes using sterically encumbered ligands.

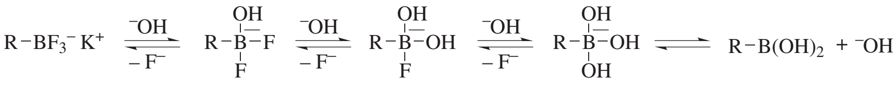
Electron-rich ligands may increase catalyst performance because the higher electron density on the metal lowers the energy of activation for oxidative addition. The development of ligands such as tricyclohexylphosphine and tri(*tert*-butyl)phosphine in cross-coupling reactions reflects this concept.[44,51] In addition to the more commonly used phosphine ligands, *N*-heterocyclic carbenes (NHCs) with similar attributes have been utilized with some success in organotrifluoroborate cross-coupling reactions.[52,53]

One of the more interesting aspects of the organotrifluoroborate variant concerns the nature of the organoboron species undergoing transmetalation. Mechanistic[54,55] as well as theoretical[56] studies concerning the Suzuki coupling reaction suggest that the weakly nucleophilic boronic acid derivatives undergo transmetalation via four-centered transition structures in which a bridging hydroxyl group facilitates the organic group transfer (Eq. 6).



(Eq. 6)

Except for the cross-coupling reactions with the highly reactive diazonium salts and iodonium salts mentioned above, organotrifluoroborates appear to require the presence of protic solvents under basic reaction conditions.[12,57] Early NMR and mass spectrometric studies on organotrifluoroborates under cross-coupling reaction conditions indicate that the reagents do not remain intact during the coupling, but a fluoride/hydroxy (alkoxy) exchange occurs, providing intermediates structurally similar to those generated in boronic acid couplings under basic conditions (Eq. 7).[46,58,59] A more detailed mechanistic evaluation, combined with theoretical calculations, subsequently revealed further details of the overall process and provides explanations for the superior performance of the organotrifluoroborates in many aspects of this reaction.[27] The study shows that the organotrifluoroborates undergo slow hydrolysis to the intermediates as shown in (Eq. 7). Importantly, both theoretical and experimental evidence indicate that fully hydrolyzed intermediates are involved in the critical transmetalation step. The organotrifluoroborates thus serve as stable precursors of cross-coupling reagents that, unlike the organotrihydroxyborate species, are resistant to hydrolytic carbon–boron bond cleavage.

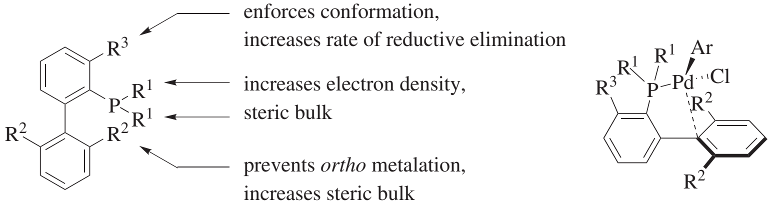


(Eq. 7)

In terms of the rate of transmetalation with respect to the organic halide (R–X) employed, the order is the reverse of that observed for the oxidative addition reaction, that is, Cl > Br > I, perhaps driven by the strength of the boron-halide bond formed in the final product. This reverse order complicates the determination of the rate-limiting step for any given pair of reactants, because either of these two steps can be the slower depending on the exact nature of the substrates.

As is the case with the oxidative addition reaction, the reductive elimination step appears to be independent of the boron species utilized. Here again, the more important component is the ligand about the metal center.[60] The two organic moieties to be bonded must be oriented *cis* about the metal for reductive elimination to occur, and bidentate ligands have the advantage of requiring the two organic substituents to be thus situated. In these systems the bite angle becomes an important factor; the observation has been made that a wider bite angle on the bidentate ligand (which necessarily brings the two organic subunits in closer proximity) leads to a faster rate of reductive elimination.[61,62] In bidentate as well as monodentate ligand systems, both steric and electronic effects play a role in the rate of reductive elimination. A decrease of the electron density about the metal facilitates reductive elimination,[63] and a relief of steric strain (i.e., using sterically encumbered ligands where the "cone angle" or "buried volume" is a measure of bulk) also facilitates the overall rate of collapse to product.

All of the above considerations explain why sterically demanding, electron-rich monodentate phosphines are among the most versatile, effective, and therefore broadly useful ligands in organotrifluoroborate cross-coupling protocols (Scheme 6).[40,43,45] Many of these ligands exhibit excellent stability in air, and their steric and electronic nature favors the [LPd(0)] form of the catalyst, providing them exceptional reactivity in the oxidative addition step of the catalytic cycle. Owing to the monodentate nature of the ligand, which frees up space about the metal center, transmetalation is also facilitated. Reductive elimination from the [LPd(II)R^1R^2] species is also faster than that from [L_2Pd(II)R^1R^2] species.[64,65] Sterically hindered dialkylbiarylphosphines incorporate other design features that recommend their use, including the non-phosphine bearing aryl group that stabilizes the Pd(0) catalyst, and the installation of substituents at the *ortho* position of this ring, which prevent unproductive cyclo-metalation and also increase the steric bulk of the ligand.

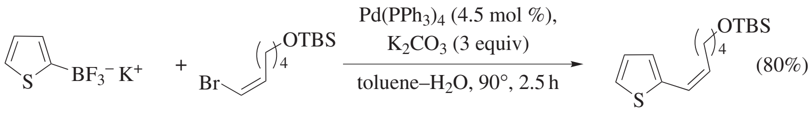


Scheme 6. Design elements in sterically hindered dialkylbiaryl phosphine ligands.

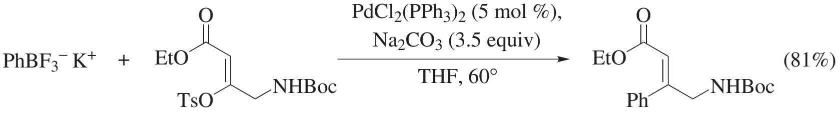
STEREOCHEMISTRY

To date, the best studied and most frequently applied stereochemical aspect in organotrifluoroborate cross-coupling is the stereochemistry at the alkenyl electrophiles and alkenytrifluoroborate nucleophiles. Strict stereochemical fidelity appears to be the norm for reported cross-couplings involving both alkenyl partners, but if conditions are not optimized, a loss of stereochemical control can occur.

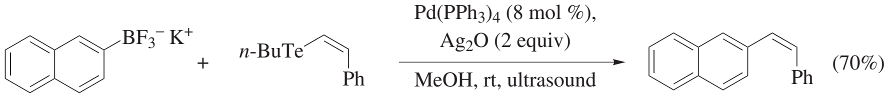
Bromides are the most commonly used alkenyl electrophiles in cross-coupling of aryl- and heteroaryltrifluoroborates, and complete stereospecificity has been observed in the cross-coupling of (*Z*)-alkenyl bromides with diverse aryltrifluoroborates (Eq. 8).[66] Complete stereospecificity has also been observed when alkenyl iodides,[67] enol tosylates (Eq. 9),[68] and alkenyl tellurides (Eq. 10)[69] are employed as electrophiles with aryl- and heteroaryltrifluoroborates.



(Eq. 8)

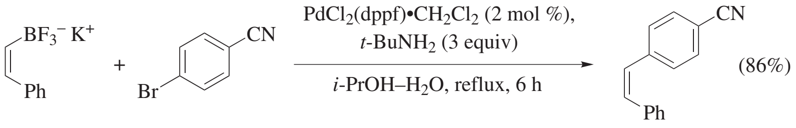


(Eq. 9)



(Eq. 10)

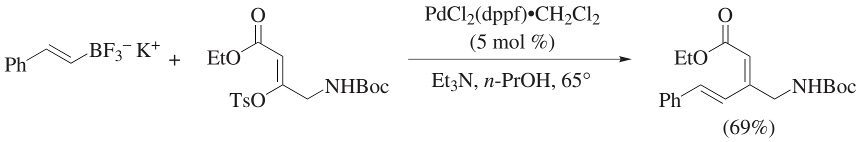
Although reaction conditions have been reported that lead to a deterioration of selectivity in coupling of stereodefined alkenyltrifluoroborates with aryl halides,[70] protocols have been developed wherein the configuration of the alkenyl component is retained (Eq. 11).[71]



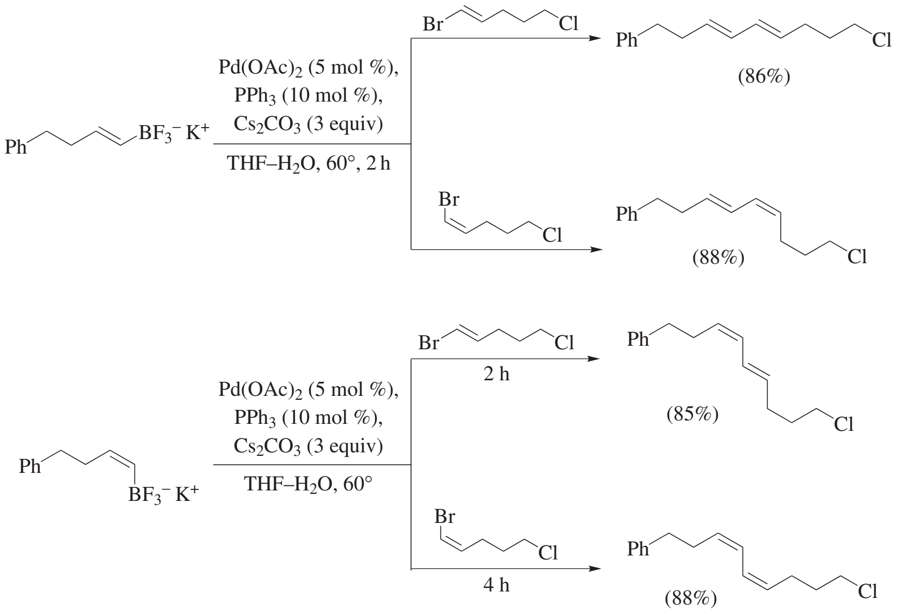
dppf = 1,1'-bis(diphenylphosphino)ferrocene

(Eq. 11)

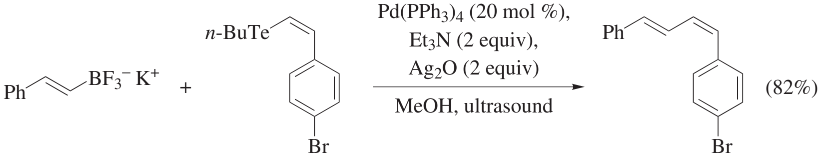
Most importantly, strict stereospecificity is maintained in both partners when conjugated dienes are prepared from alkenyltrifluoroborates and alkenyl bromides (Scheme 7).[72] Similar stereospecificities have been observed in cross-coupling of alkenyltrifluoroborates with enol tosylates (Eq. 12)[73] and alkenyl tellurides (Eq. 13).[68]



(Eq. 12)

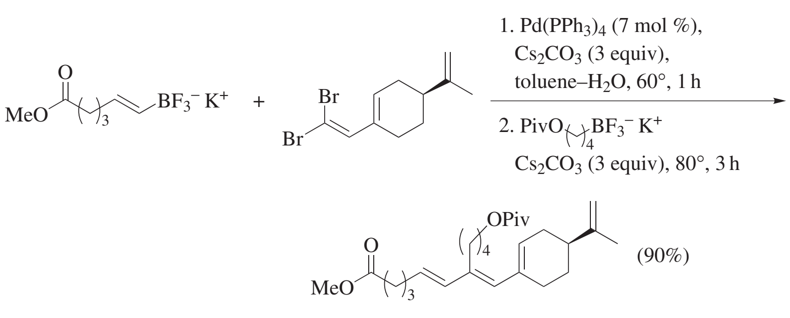


Scheme 7. Stereospecific synthesis of conjugated dienes.



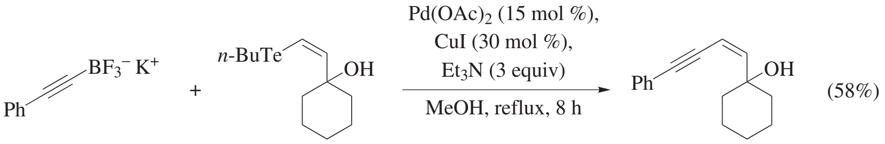
(Eq. 13)

The stereospecificity of the alkenyl cross-coupling process, combined with a chemoselectivity for the less hindered bromide in 1,1-disubstituted alkenes, allows an efficient two-step, one-pot construction of conjugated dienes.[74] Alkenyltrifluoroborates are used in the first step of the process, and alkyltrifluoroborates have been employed as the second nucleophilic partner (Eq. 14).



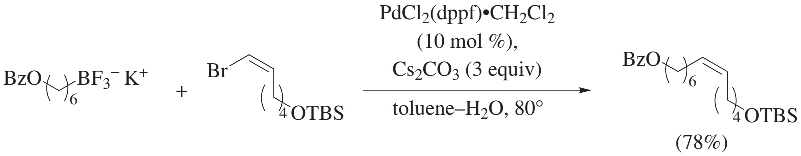
(Eq. 14)

Far fewer studies have been carried out on the cross-coupling of alkynyltrifluoroborates with stereodefined electrophiles, but examples employing alkenyl tellurides indicate that such transformations are readily accomplished in a stereocontrolled manner (Eq. 15).[75]

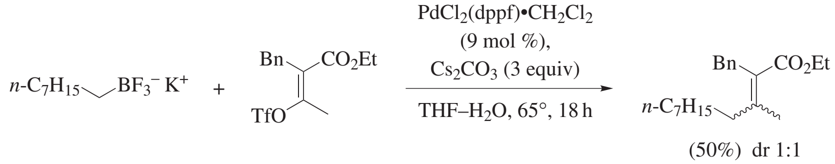


(Eq. 15)

Excellent stereochemical control can be achieved in the cross-coupling of alkyltrifluoroborates with alkenyl bromides (Eq. 16).[76] However, in one reported study concerning the use of enol triflate partners, a loss of stereochemical fidelity is observed in the transformation (Eq. 17).[58]

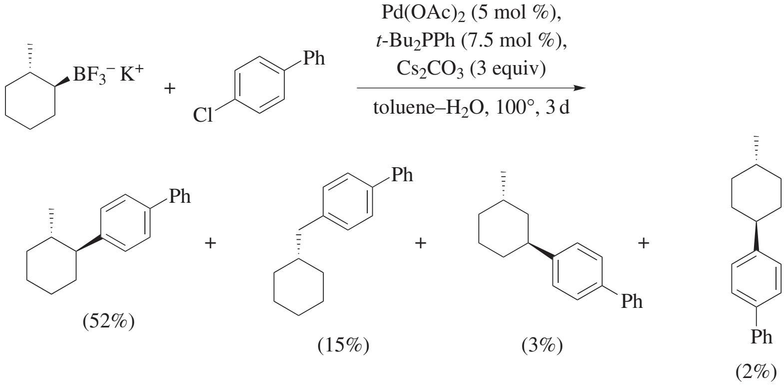


(Eq. 16)



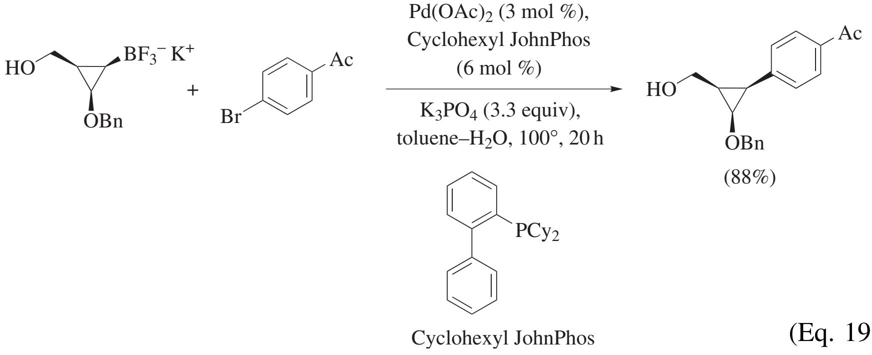
(Eq. 17)

Owing to the challenges involved in the transmetalation step of the catalytic cycle and the intervention of β-hydride elimination from the diorganopalladium(II) intermediate, the efficient cross-coupling of secondary alkyl organometallic reagents is rare. An important aspect of cross-coupling of secondary alkyltrifluoroborates is the stereochemical fidelity observed in those systems where the metal constitutes one of the substituents at a stereogenic center. Few examples of this process exist in organoboron chemistry,[77] but in one study involving organotrifluoroborates, complete stereochemical fidelity is observed in the transfer of the alkyl group.[78] Unfortunately, the intervention of the β-hydride elimination/isomerization process is rather extensive, leading to a mixture of constitutional isomers (Eq. 18).



(Eq. 18)

Cyclopropanes represent a special class of secondary alkyl organometallics. The hybridization of the carbon–boron bond is between that of alkyl- and alkenylboron compounds, thus making transmetalation more facile than that for alkylboron derivatives, and β-hydride elimination is undoubtedly inhibited by the strain encountered in a transition state that would lead to a cyclopropene. In reactions that are generally high yielding, numerous examples of stereospecific cross-couplings of cyclopropyltrifluoroborates have been reported (Eq. 19).[79–81]



(Eq. 19)

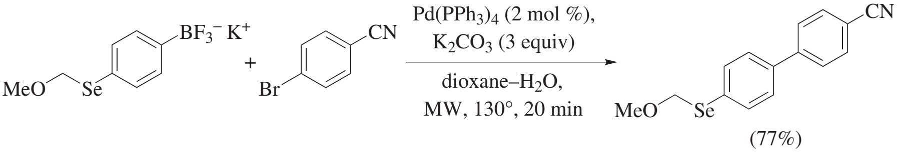
SCOPE AND LIMITATIONS

The Organotrifluoroborate

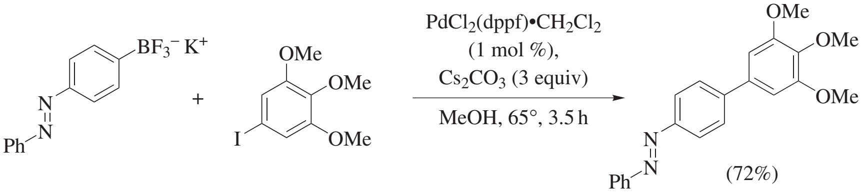
A wide range of organotrifluoroborates can be employed in cross-coupling reactions. The following section is a summary of the general reactivity pattern of the various reagents, focusing on those organotrifluoroborates that possess unique features.

Aryltrifluoroborates. Aryltrifluoroborates represent the class of organotrifluoroborates that is most often used in cross-coupling reactions. Virtually every substitution pattern and many functional groups have been incorporated in these systems, and for the most part acceptable cross-coupling conditions have been developed.

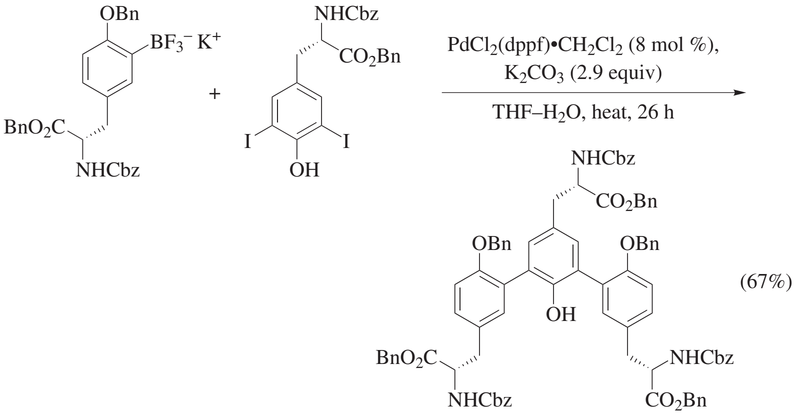
A variety of functional groups capable of surviving the subsequent cross-coupling step can be present within the aryltrifluoroborate substructure. In addition to the usual array of functional groups (e.g., ethers, halides, alcohols, aldehydes, ketones, esters, amines, amides, nitriles, nitro groups, and carboxylic acids), selenoethers,[82] selenoacetals (Eq. 20),[82] azo functional groups (Eq. 21),[83] protected α-amino acids (Eq. 22),[84] α,β-unsaturated Weinreb amides (Eq. 23),[85] and 1,2,3-triazoles (Eq. 24)[85] have all been incorporated as a part of the aryltrifluoroborates.



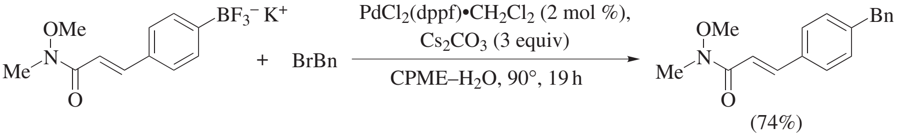
(Eq. 20)



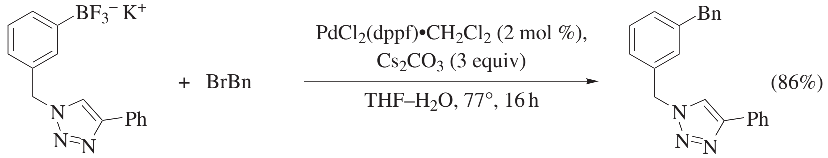
(Eq. 21)



(Eq. 22)

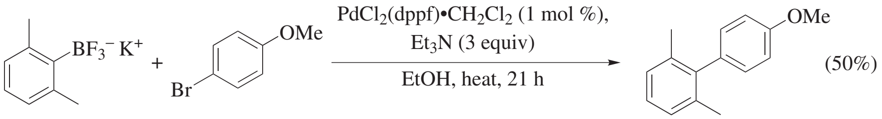


(Eq. 23)

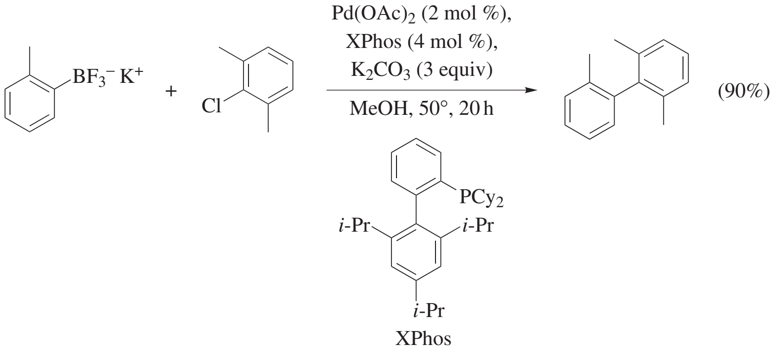


(Eq. 24)

Sterically encumbered aryltrifluoroborates have traditionally been difficult to cross-couple, particularly with electron-rich aryl chloride electrophiles. Although not yet tested in the most demanding situations, aryltrifluoroborates of reasonable steric demand have been prepared and reacted with aryl bromides and aryl chlorides, permitting the construction of sterically hindered biaryl products (Eqs. 25–26).[46,86,87]

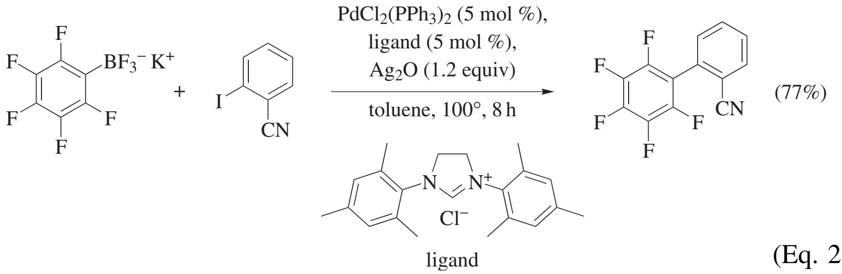


(Eq. 25)



(Eq. 26)

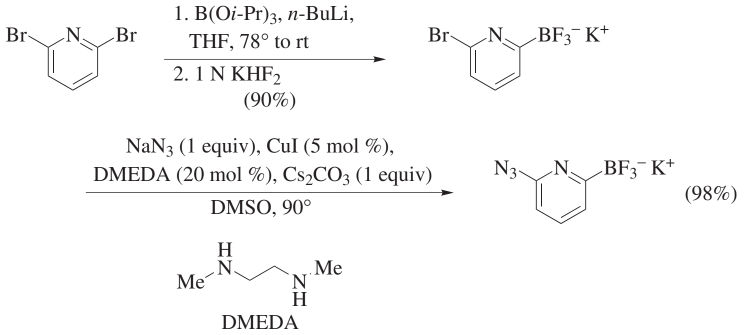
Another challenging class of arylboron compounds is that possessing an electron-deficient aromatic system. These reagents undergo facile protodeboronation. One of the advantageous features of the organotrifluoroborates is their ability to resist protodeboronation during Suzuki coupling, even in the most electron-deficient aromatic systems (Eq. 27).[88,89]



(Eq. 27)

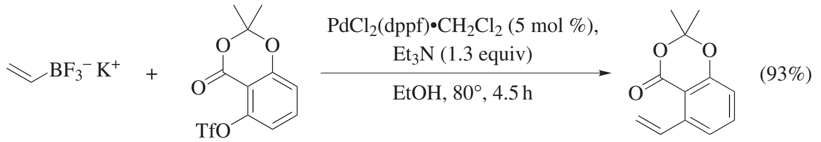
Heteroaryltrifluoroborates. Because of facile protodeboronation,[90] heteroarylboron species have proven extremely challenging to cross-couple in high yields.[91–93] In most cases, a large excess of the heteroarylboron species is required in developing cross-coupling protocols to compensate for protodeboronation. By contrast, heteroaryltrifluoroborates are relatively resistant to protodeboronation, and diverse heteroaryltrifluoroborates have been prepared and cross-coupled effectively with a variety of electrophiles. Trifluoroborate derivatives of substituted pyrazoles, pyrroles, furans, thiophenes, indoles, isoxazoles, quinolines, isoquinolines, pyrimidines, pyridazines, and pyridines have all been employed in these studies.[46,94,95]

Suzuki cross-couplings of 2-pyridylborons have proven to be particularly challenging,[94] but a number of protocols have been developed, providing solutions to this important problem.[90,96–101] Of note along these lines is the synthesis and copper-promoted reaction of the substituted 2-trifluoroboratopyridine shown in (Eq. 28).[102] This transformation indicates that such trifluoroborates are robust intermediates, but the development of their palladium-catalyzed cross-coupling has yet to be realized.

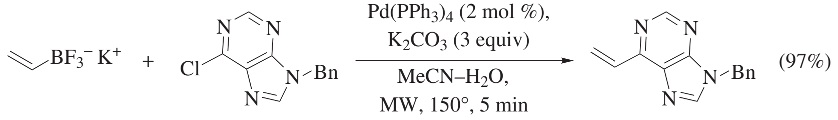


(Eq. 28)

Alkenyltrifluoroborates. Although diverse alkenyltrifluoroborates have been prepared and employed in cross-coupling reactions with a variety of electrophiles, perhaps the most important and certainly the most widely used reagent is the simplest: vinyltrifluoroborate. This vinylating agent has been used in a variety of cross-coupling reactions with a wide range of electrophiles, and it thus fills a useful niche among available vinylating agents (Eqs. 29 and 30).[72,103–105] Although with most electrophiles the vinylated materials can be isolated in high yields, with aryl chlorides homocoupling of the halide and Heck products can diminish the yield.[106]

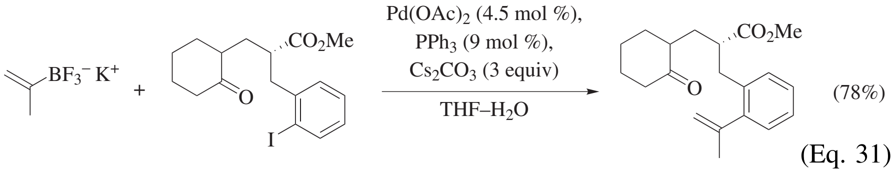


(Eq. 29)

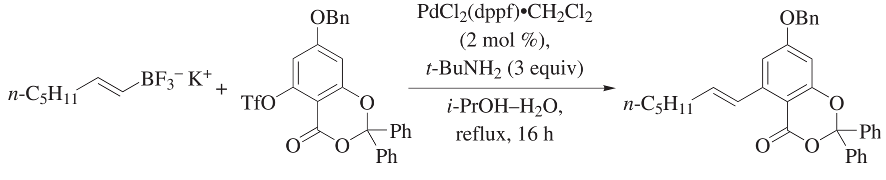


(Eq. 30)

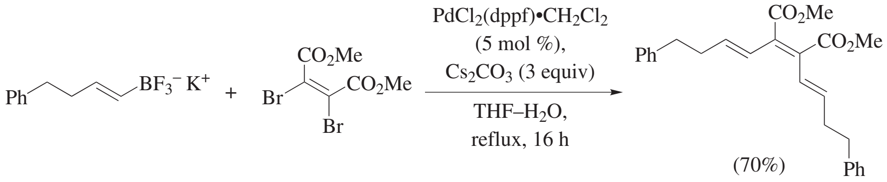
More highly elaborated alkenyltrifluoroborates, with diverse substitution patterns about the double bond, can also be effectively coupled (Eqs. 31–33).[72,107,108] Although these reactions are usually stereospecific (Eq. 11, Scheme 7), a loss of stereochemical integrity can result when reactions have not been suitably optimized.[70]



(Eq. 31)



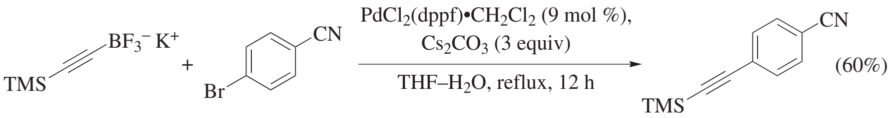
(Eq. 32)



(Eq. 33)

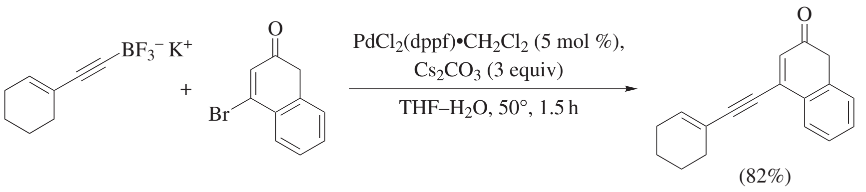
Alkynyltrifluoroborates. The cross-coupling of alkynyltrifluoroborates provides an alternative to the Sonogashira reaction for the incorporation of alkynes into organic substructures. Alkynyltrifluoroborates do not cross-couple effectively with aryldiazonium salts.[14] Instead, electron transfer from the trifluoroborate to the diazonium salt occurs, resulting in products of chemical reduction. However, other aryl electrophiles can be utilized quite effectively for cross-coupling, and for aryl triflates, catalyst loading can be extraordinarily low (<0.05 mol %).[109]

Ethynyltrifluoroborate has been prepared and is a stable, storable reagent, but attempts at utilizing it in cross-coupling procedures have resulted in coupling at both termini of the alkyne, forming symmetrical alkynes. (Trimethylsilyl)ethynyltrifluoroborate serves as a useful surrogate of ethynyltrifluoroborate (Eq. 34)[109] and allows the selective insertion of an ethynyl group into organic molecules upon cleavage of the trimethylsilyl protecting group.



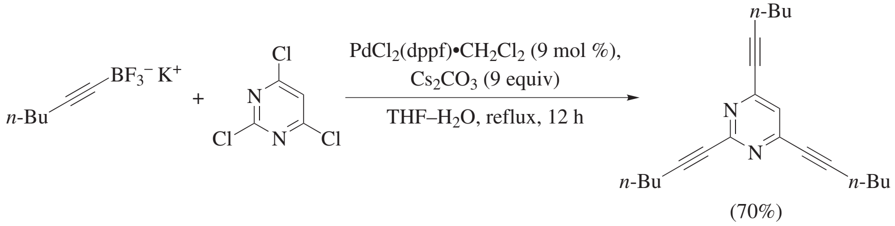
(Eq. 34)

More highly elaborated alkynyltrifluoroborates can be utilized in cross-coupling reactions with a variety of electrophiles, permitting alkynes to be prepared from diverse electrophilic precursors (Eq. 35).[110] All alkynyltrifluoroborates are more susceptible to protodeboronation than aryl- and alkenyltrifluoroborates,[109] and thus it is best to minimize the use of protic solvents in the cross-couplings. In some instances the palladium salts in the reaction mixture catalyze hydration of the triple bond forming ketones. This side reaction has been observed in substrates wherein neighboring groups such as aldehydes can participate in the hydration process.[109] Although unusual for organotrifluoroborates, anhydrous conditions are often effective for the alkynyl cross-coupling.

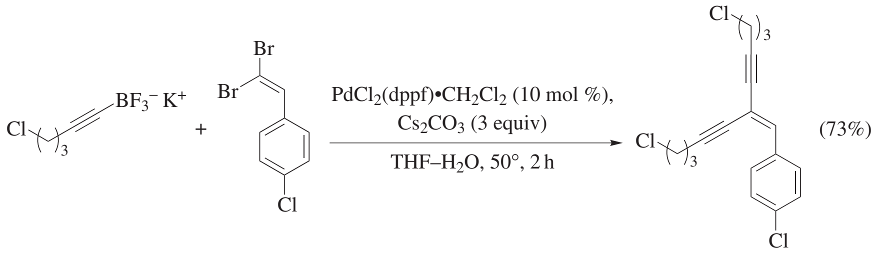


(Eq. 35)

Multiple cross-couplings can be effected on polyhalo-substituted substrates, allowing effective syntheses of diynes and triynes from relatively simple precursors (Eqs. 36–37).[109,111]

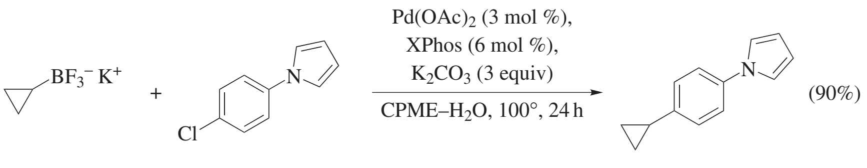


(Eq. 36)

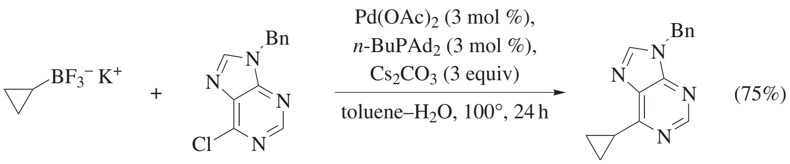


(Eq. 37)

Cyclopropyltrifluoroborates and Cyclobutyltrifluoroborates. The hybridization of the C−B bond in cyclopropyl- and cyclobutylmetallic reagents render them intermediate between alkenyl and alkyl systems in terms of their reactivity in cross-coupling reactions. In contrast to the corresponding boronic acids, both cyclopropyl- and cyclobutyltrifluoroborates resist protodeboronation, and thus are indefinitely stable and storable reagents. Conditions have been developed for the cross-coupling of cyclopropyltrifluoroborates with a variety of aryl- and heteroaryl bromides and chlorides (Eqs 38−39).[79−81,104,112] As pointed out previously (Eq. 19), these transformations are completely stereospecific.

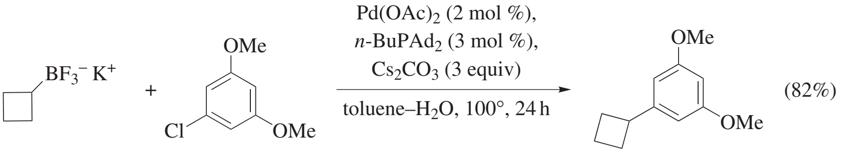


(Eq. 38)



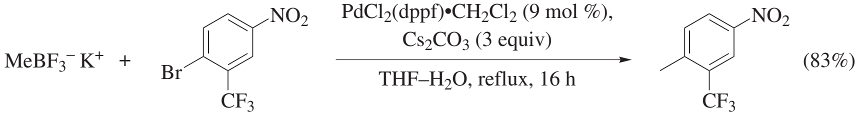
(Eq. 39)

Cross-couplings of cyclobutyl derivatives have been less widely explored.[112] The hybridization of the carbon−boron bond is closer to that of secondary alkylmetallic reagents, and the strain engendered in the β-hydride elimination process is not as high as that in the cyclopropyl system. Perhaps for these reasons, yields and reaction scope for cyclobutyltrifluoroborate cross-couplings are often lower than those of their cyclopropyl counterparts (see, however, Eq. 40).



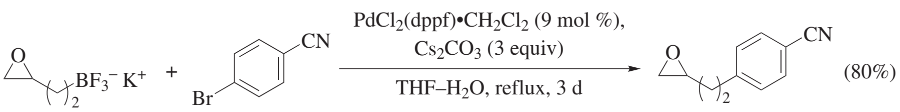
(Eq. 40)

Alkyltrifluoroborates. A diverse array of alkyltrifluoroborates has been developed for use in Suzuki-type cross-coupling reactions. Methyltrifluoroborate serves as a highly efficient and effective methylating agent. It is of value in cross-coupling with a variety of electrophiles (Eq. 41), including electron-rich aryl chlorides under appropriate conditions.[104,113–115]



(Eq. 41)

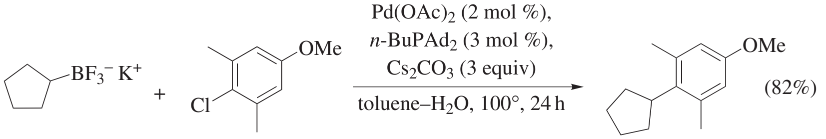
As in most Suzuki coupling reactions, primary alkyltrifluoroborates can be prepared and coupled with a diverse array of functional groups embedded within the nucleophilic partner. Alkenes, alkyl halides, alcohols, non-enolizable aldehydes, ketones, carboxylic acids, esters, amides, nitriles, thioethers, and sulfones have all demonstrated tolerance to the reaction conditions required for cross-coupling. Interestingly, epoxides can be present within the alkyltrifluoroborate, and this functional group remains intact during the cross-coupling event (Eq. 42).[116]



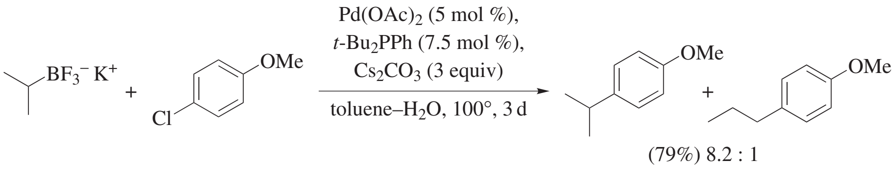
(Eq. 42)

Primary alkyltrifluoroborates couple highly effectively with a variety of aryl- and heteroaryl chlorides.[114] This protocol avoids the use of excess organoboron reagent, toxic thallium bases,[117] and reactive organolithium compounds[118] utilized in previously reported procedures. Because they undergo slow transmetalation and are susceptible to β-hydride elimination from the diorganopalladium intermediate, secondary organometallics pose greater challenges in cross-coupling than their primary organometallic relatives. Conditions have been developed that allow secondary alkyltrifluoroborates to undergo cross-coupling, even with highly hindered, electron-rich aryl chlorides (Eq. 43).[78] As described in the section "Side

Reactions", the coupling of secondary alkyltrifluoroborates results in the formation of isomerized products owing to processes involving competing β-hydride elimination, alkene reinsertion into the palladium–hydride bond with regiochemical reversal, and subsequent reductive elimination (Eq. 44).

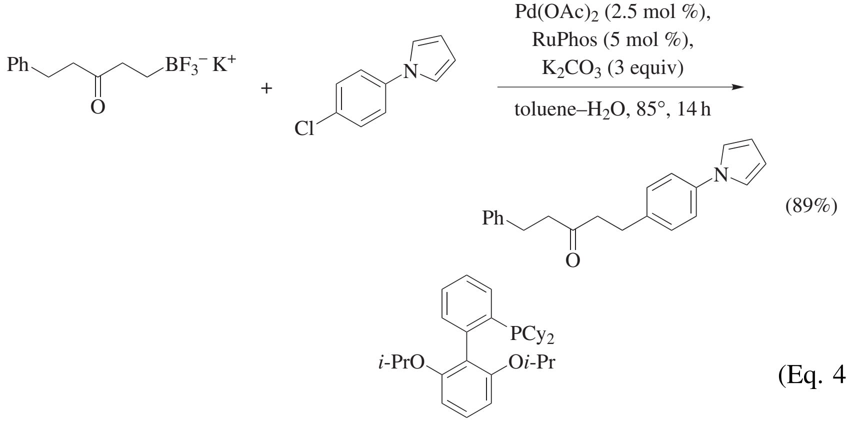


(Eq. 43)



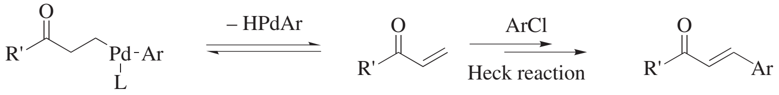
(Eq. 44)

β-Trifluoroboratocarbonyls. A useful and fairly unusual subset of alkyltrifluoroborate cross-coupling reagents are the β-trifluoroboratocarbonyls.[119] These reagents are readily prepared by conjugate addition reactions of bis(boronic) acid derivatives with α,β-unsaturated carbonyl precursors or by enolate alkylations of halomethylboron electrophiles. Ketone, hindered ester, and amide-based reagents all undergo cross-coupling with diverse aromatic and heteroaromatic halides (Eq. 45). β-Trifluoroboratoketones undergo cross-coupling quite effectively, and thus represent an unprecedented set of reagents for such transformations. Although small amounts (3–10%) of β-hydride elimination/Heck coupling products are formed with these reagents (Eq. 46),[119,120] virtually none of these types of byproducts are observed under conditions optimized for the β-ketoamide reagents.[121]



(Eq. 45)

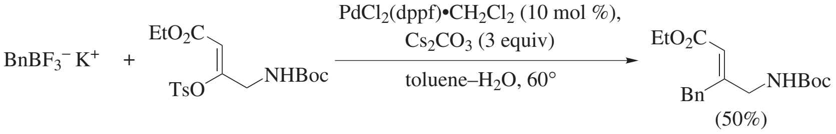
RuPhos



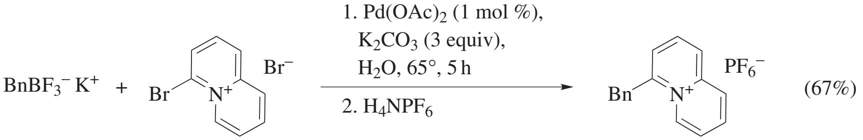
(Eq. 46)

Benzyltrifluoroborates and Crotyltrifluoroborates. Benzylic and allylic metallic species represent a special subset of alkylmetallic reagents because some of these species (allyllithium and allylmagnesium derivatives) are particularly prone to homocoupling during their formation, and as a class they are generally less reactive than alkyl- or arylmetallic reagents in cross-coupling. Benzylboron compounds are less readily available than other organoboron derivatives. They are obtained principally from transmetalation reactions involving organolithium and organomagnesium precursors. In addition to these features described for benzylmetallic reagents, the related allylmetallic compounds present challenges associated with site selectivity, stereoselectivity in double bond geometry, and enantioselectivity in more highly substituted systems.

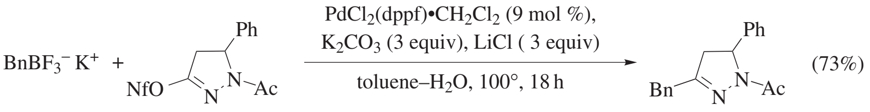
Perhaps owing to the lack of convenient synthetic approaches, few cross-couplings of benzyltrifluoroborates have been reported.[58,68,122,123] Although the scope of these transformations has not been fully delineated, a reasonably wide range of electrophilic partners has been explored (Eqs. 47–49).



(Eq. 47)



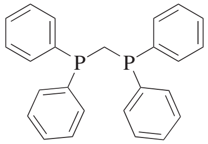
(Eq. 48)



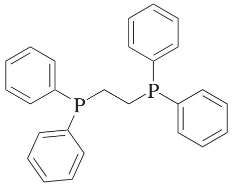
(Eq. 49)

The site selectivity observed in crotyltrifluoroborate systems is greatly influenced by the ligand array used in the coupling process. Using simple phosphine ligands such as PPh_3, dppm, dppe, and dppp, yields are low and/or carbon–carbon bond-formation is effected predominantly at the less substituted end of the allylic system.[124,125] Employing a D-*t*-BPF or CyPF-*t*-Bu ligand, the site selectivity is nearly 100% for the internally substituted carbon, and yields are high

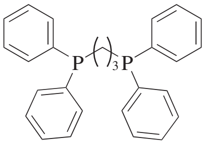
(Eq. 50).[124–126]



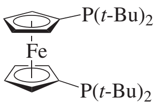
dppm



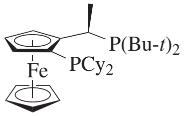
dppe



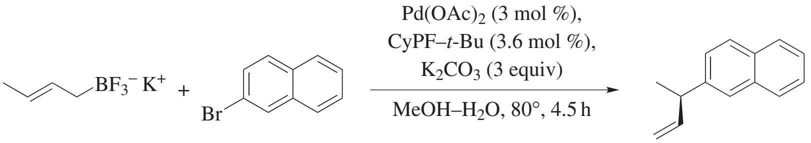
dppp



D-t-BPF



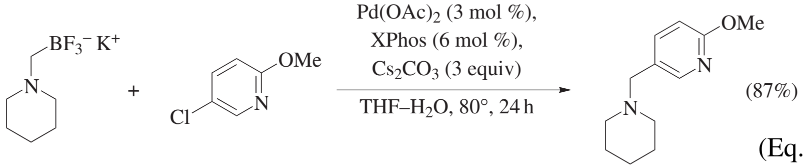
CyPF–t-Bu



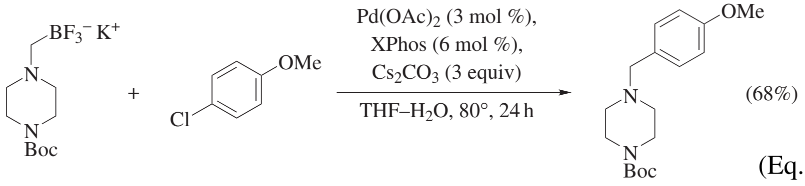
(90%) 88:12 regio, er 91.5:8.5

(Eq. 50)

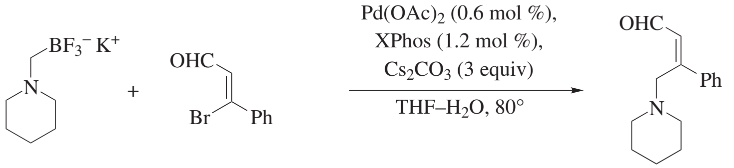
Aminomethyltrifluoroborates and Alkoxymethyltrifluoroborates. Aminomethyl- and alkoxymethyltrifluoroborates represent a class of alkylating agents that provides a convenient and unique access to useful organic molecules. The aminomethylation reaction is complementary to reductive amination for the installation of this valuable functional unit into aromatic and heteroaromatic systems. To date, only the syntheses of tertiary amines have been reported using this method.[127,128] The method appears to be quite general for a variety of aromatic and heteroaromatic bromides and chlorides (Eqs. 51–53).



(Eq. 51)



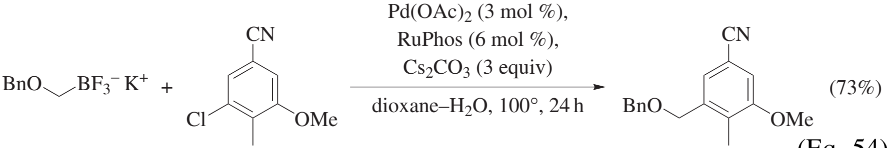
(Eq. 52)



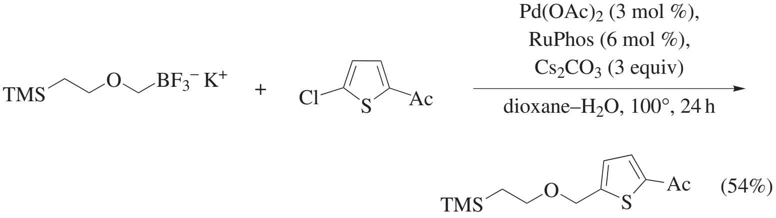
(67%)

(Eq. 53)

The analogous alkoxymethylation reaction also complements existing approaches to benzylic ethers and alcohols.[129] These ethers are commonly prepared by the Williamson ether synthesis, which requires access to benzylic electrophiles. A much more diverse collection of haloarenes or haloheteroarenes is available than their benzylic counterparts, and thus from a commodity chemical perspective the carbon−carbon bond-forming approach to the ethers is advantageous. By deprotection after alkoxymethylation, the cross-coupling also affords a route to benzylic alcohols. As in the aminomethylation reaction described above, diverse aryl chlorides and aryl bromides can be coupled with alkoxymethyltrifluoroborates to generate the desired target structures (Eqs. 54−55).

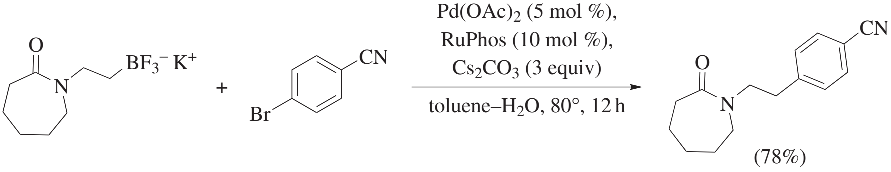


(Eq. 54)

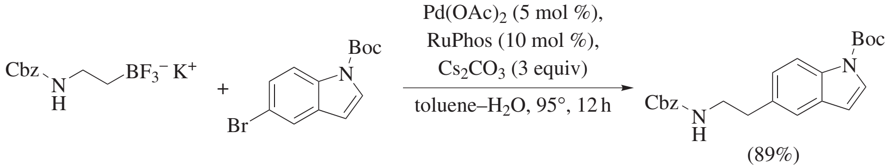


(Eq. 55)

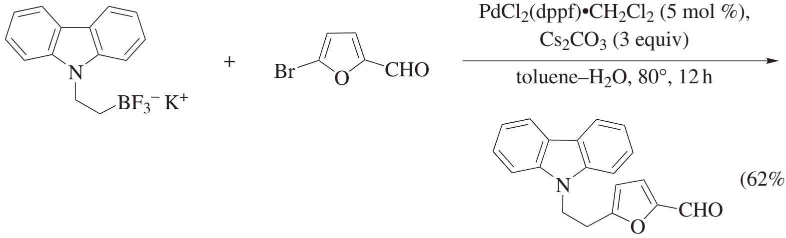
Aminoethyltrifluoroborates. Aminoethyltrifluoroborates comprise another relatively unique class of reagents for cross-coupling.[130,131] Generated by the hydroboration of enamines, enamides, and enecarbamates, these reagents permit facile incorporation of an aminoethyl subunit into aryl and heteroaryl platforms through cross-coupling. Although conditions exist for the cross-coupling of aminoethyltrifluoroborates with bromide, iodide, and triflate electrophiles (Eqs. 56−58), chlorides have thus far proven recalcitrant reaction partners.



(Eq. 56)



(Eq. 57)



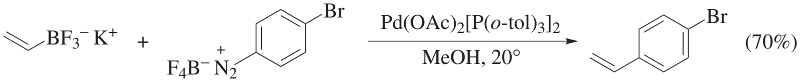
(Eq. 58)

The Electrophile

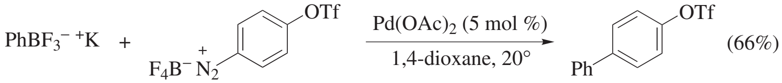
Many diverse electrophiles have been used in conjunction with organotrifluoroborates in cross-coupling reactions. Despite the large number of examples, generalizations are difficult to make on the suitability of individual electrophiles for cross-coupling. An attempt is made herein to outline the known scope and limitations of various reacting partners, but this task is not without some risk. In certain instances, yields may derive from subpar optimization, wherein a thorough exploration of catalysts and reaction conditions was not undertaken. Additionally, it is important to note that most synthetic methods are developed in an attempt to apply them across a wide spectrum of reacting partners. Inevitably, one discovers individual outliers for which the general procedure does not apply. It is likely that these substrates would react satisfactorily under slightly modified conditions. Thus, the yields and scope of reactivity often depend upon how much time is invested in seeking the best possible outcome. Most importantly, the success of many transformations, and especially Suzuki coupling reactions, is highly temporal. Substrates viewed as inert a few short years ago might now be coerced to react with ease on the basis of enhanced knowledge of the mechanistic details of the reaction and the development of high-performance catalytic systems.

Aryl and Heteroaryl Electrophiles. Aryl and heteroaryl groups represent the most broadly employed class of electrophilic partners for palladium-catalyzed organotrifluoroborate cross-coupling. A good outline of reactivity has been established, and the range of suitable nucleofuges is still expanding.

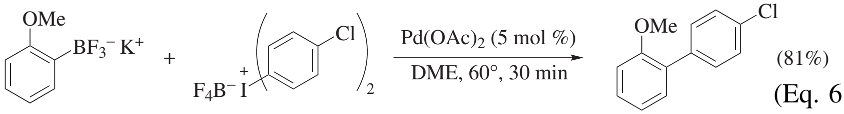
The seminal cross-coupling reactions of organotrifluoroborates focused on diazonium and iodonium salts.[13,15] These reactions take place under extremely mild conditions and afford cross-coupling products in high yields. One of the benefits of these leaving groups is the ability to conduct selective cross-couplings in the presence of reactive halides and triflates. Although yields are sometimes modest, diazonium salts can be selectively reacted in the presence of all halides (Eqs. 59–61).[13,15,132,133]



(Eq. 59)



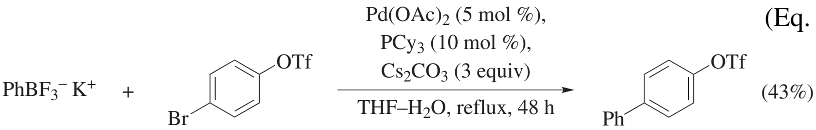
(Eq. 60)



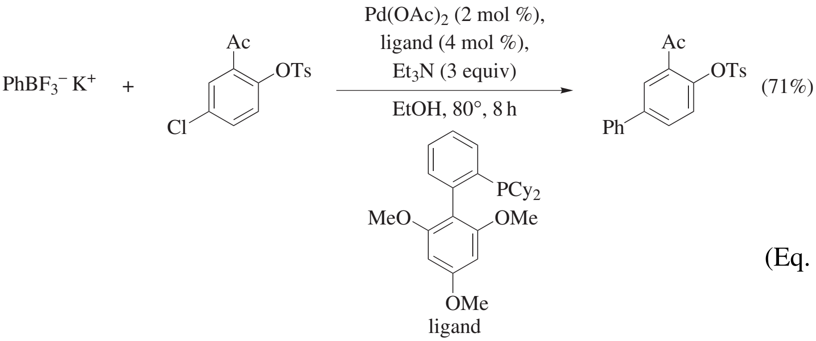
(Eq. 61)

Halides themselves are well represented as leaving groups among aryl and heteroaryl electrophiles. In the earliest studies, bromides and, to some extent, iodides dominated the substrates utilized because they are quite reactive in the oxidative addition step of the catalytic process. However, the commercial availability of a wider array of less expensive chlorides has provided impetus to finding conditions under which these partners can be coupled effectively. This endeavor has resulted in the development of catalyst systems that work very effectively with aryl and heteroaryl chlorides,[21] and nearly the full range of organotrifluoroborates perform effectively with these substrates.

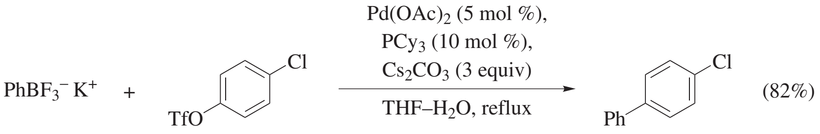
Selectivity issues can be important between and among the halides and other nucleofuges, and although some information on this subject is available,[134–136] rigorous rate studies and even extensive qualitative observations are lacking. Nevertheless, several trends emerge. For aryl nucleophiles, the reactivity appears to be in the order I > Br ≈ OTf > Cl > OTs (Eqs. 62–65).



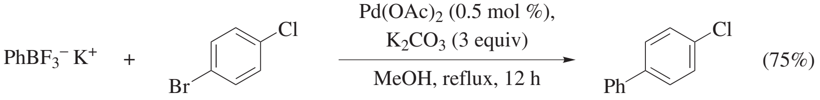
(Eq. 62)



(Eq. 63)



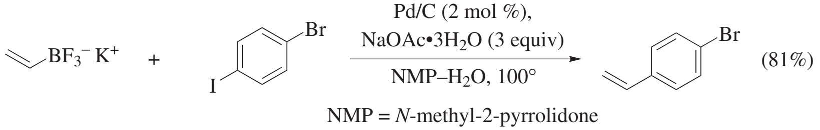
(Eq. 64)



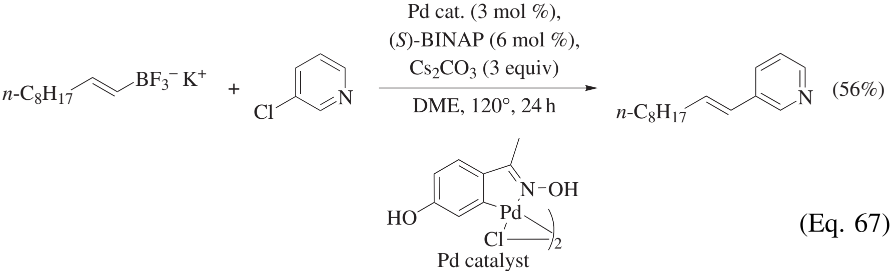
(Eq. 65)

A significant caveat arises in discussing the reactivity of aryl halide electrophiles; those protocols that are successfully developed for challenging reaction partners do not necessarily translate well to electrophiles that, a priori, one might view as more reactive. For example, successful cross-coupling conditions for aryl chlorides work abysmally when applied to aryl iodide substrates, indicating that the oxidative addition is not always the key step of the catalytic cycle.

Although some rigorous reactivity studies have been performed for the coupling of aryltrifluoroborate nucleophiles with aryl electrophiles, less information is available concerning the relative coupling rates of aryl electrophiles with alkenyltrifluoroborate nucleophiles (Eq. 66).[137] Among the halide electrophiles, aryl and heteroaryl bromides and iodides are the most common. Aryl and heteroaryl chlorides require more vigorous conditions (Eq. 67).[105]

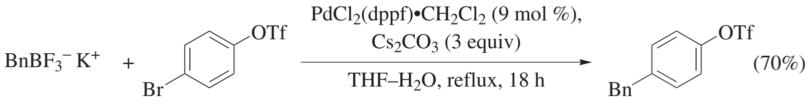


(Eq. 66)

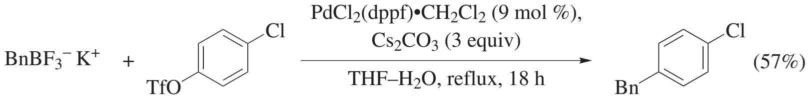


(Eq. 67)

In direct competition experiments, benzyltrifluoroborates have been observed to couple selectively with aryl electrophiles. The observed order of reactivity is Br > OTf > Cl (Eqs. 68–69).[58]

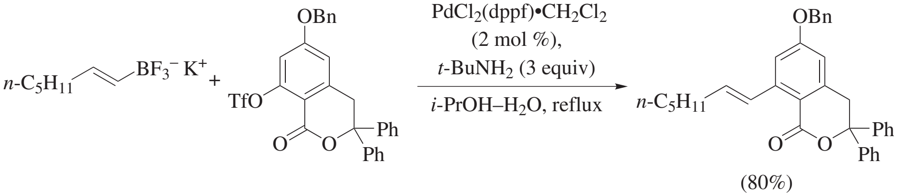


(Eq. 68)

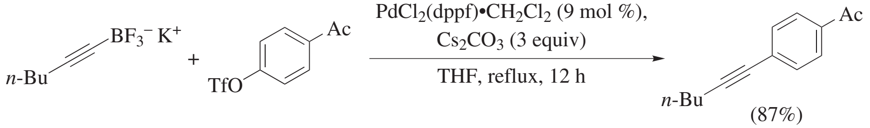


(Eq. 69)

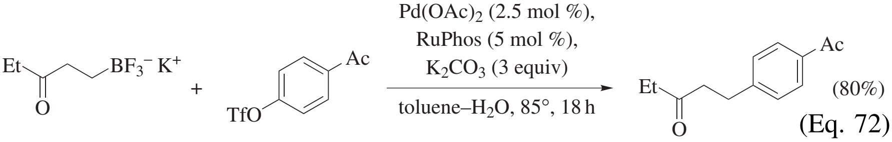
For various reasons, decidedly less effort has been devoted to an exploration of other nucleofuges in aryl electrophiles. Among these, triflates have received the most attention, providing good to excellent conversion to product with a broad range of organotrifluoroborates (Eqs. 70–73).[58,108,109,120,131]



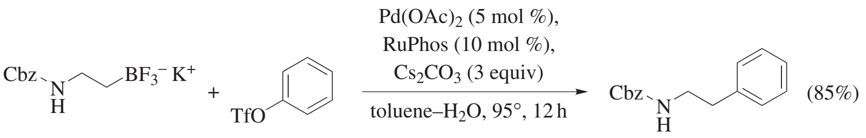
(Eq. 70)



(Eq. 71)

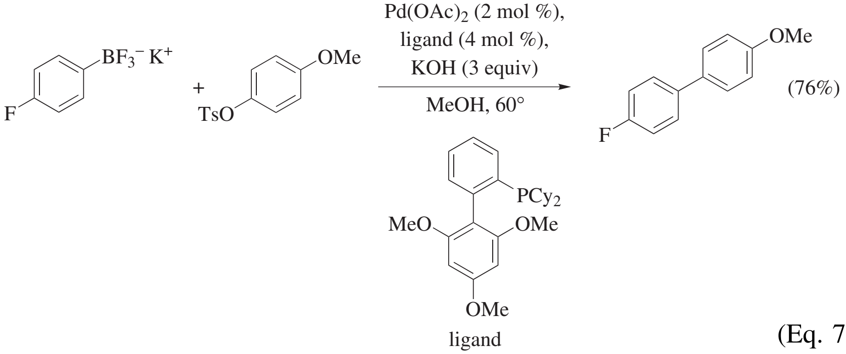


(Eq. 72)

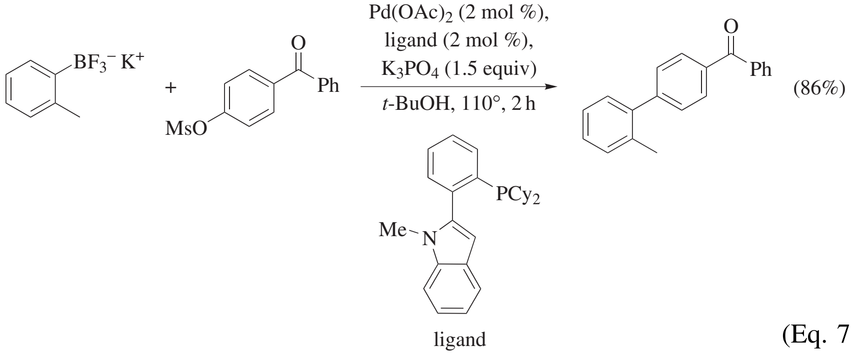


(Eq. 73)

Tosylates and mesylates have been explored to a much lesser extent, with successful examples reported only for aryltrifluoroborate nucleophiles (Eqs. 74–75).[108,135,138,139]

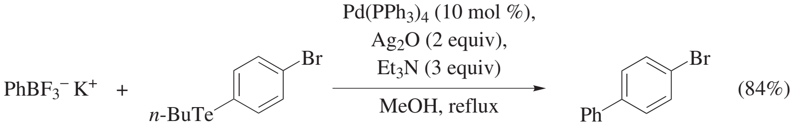


(Eq. 74)

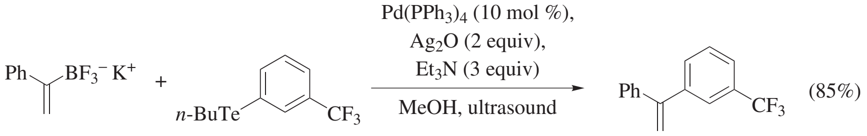


(Eq. 75)

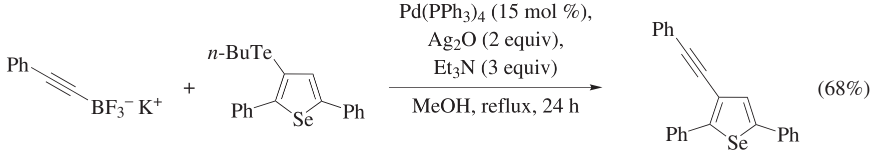
Tellurides and stiboranes[140] round out the classes of aryl nucleofuges that have been used in conjunction with organotrifluoroborates (Eqs. 76–79). The tellurides in particular serve as pseudohalides in numerous cross-coupling reactions, but the apparent requirement to employ two equivalents of silver salts as promoters in the reaction detracts from their appeal. Interestingly, the aryl tellurides appear to be more reactive than aryl bromides and aryl chlorides in the cross-coupling process, and tolerate a number of other functional groups as well.[141–144]



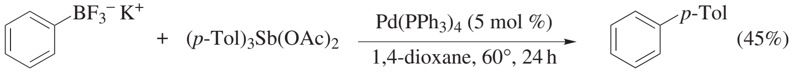
(Eq. 76)



(Eq. 77)



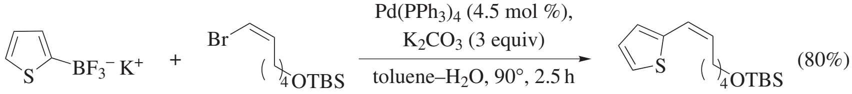
(Eq. 78)



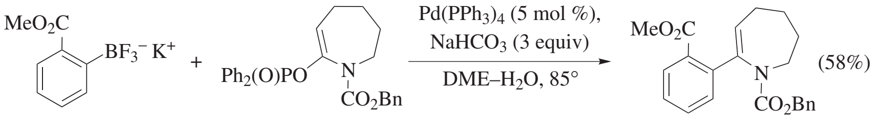
(Eq. 79)

Alkenyl Electrophiles. A significantly diminished range of nucleofuges have been utilized with electrophilic alkenyl coupling partners, and a more limited subset of organotrifluoroborates have been employed in these reactions. Nevertheless, it is evident that high yields can generally be achieved, and the reactions are stereospecific and chemoselective.

To date, alkenyl chlorides have not been employed as electrophilic alkenyl coupling partners. The most common leaving group in the alkenyl class of electrophiles is bromide. A number of functionalized aryl- and heteroaryltrifluoroborates react smoothly with alkenyl bromides, providing excellent yields of the desired products (Eq. 80).[66] The use of alkenyl iodides in reactions with aryl- and heteroaryl nucleophiles is rare.[12,67,83,145] An enol phosphate has also been employed in coupling with an aryltrifluoroborate (Eq. 81).[146]

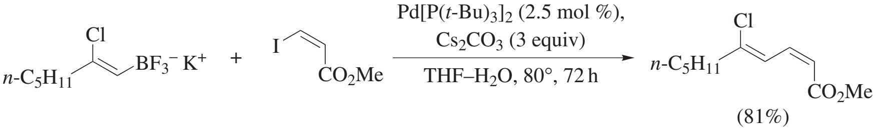


(Eq. 80)

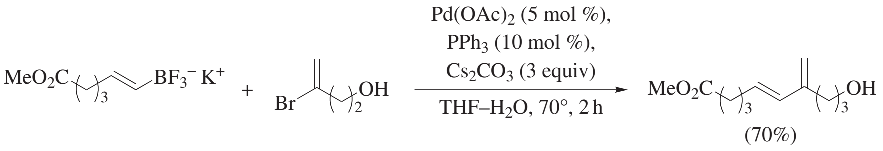


(Eq. 81)

Conjugated diene syntheses can be accomplished by cross-coupling of alkenyltrifluoroborates with alkenyl halides. Although a few alkenyl iodides have been employed (Eq. 82),[147,148] bromides dominate the scene (Eq. 83).[72] For both, the transformations are stereospecific and tolerant of a diverse array of functional groups.

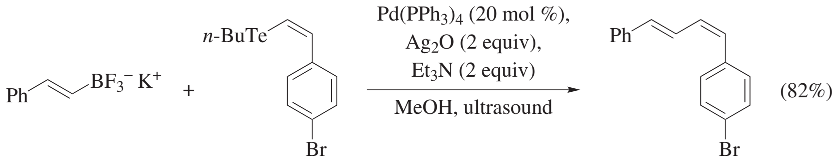


(Eq. 82)



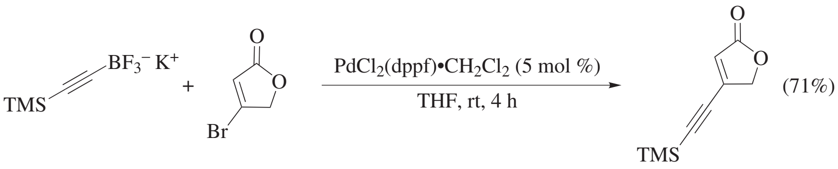
(Eq. 83)

Enol tosylates have rarely been used as electrophiles for alkenyltrifluoroborate cross-coupling,[68] but alkenyl tellurides are reasonably well represented (Eq. 84).[73] As is the case for aryl- and heteroaryltrifluoroborates, high catalyst loading and the necessity to use two equivalents of silver salts to promote the cross-coupling will undoubtedly prevent the widespread adoption of this protocol.

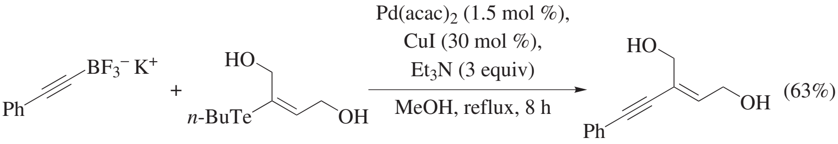


(Eq. 84)

Only bromide (Eq. 85)[110,111] and telluride (Eq. 86)[75,149] nucleofuges have been reported among alkenyl electrophilic partners for alkynyltrifluoroborates. A limited group of activated bromides (β-bromo α,β-unsaturated carbonyls) have been explored to date, but a wider range of alkenyl tellurides has been investigated. When compared to cross-coupling of aryl- and alkenyltrifluoroborates, reaction conditions for alkynyltrifluoroborate cross-coupling with alkenyltellurides are much more practical, as substoichiometric amounts of copper salts can be employed in place of superstoichiometric quantities of silver salts.

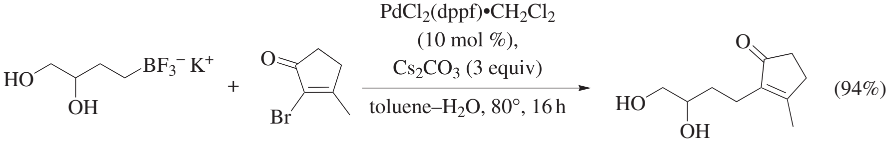


(Eq. 85)

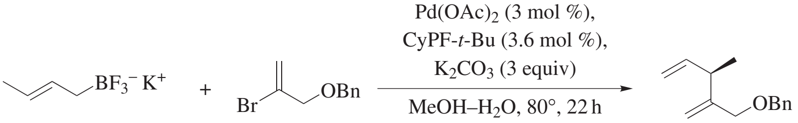


(Eq. 86)

Alkenyl bromides comprise the major electrophiles for coupling with sp^3-hybridized organotrifluoroborate nucleophiles (Eq 87).[76] Again, no alkenyl chloride or alkenyl iodide electrophiles appear to have been reported. In cross-coupling of a crotyltrifluoroborate with an alkenyl bromide in the presence of a chiral MandyPhos-type ligand, excellent site selectivity and modest enantioselectivity can be achieved (Eq. 88).[126]



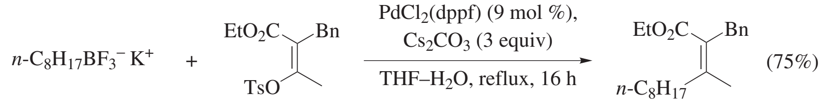
(Eq. 87)



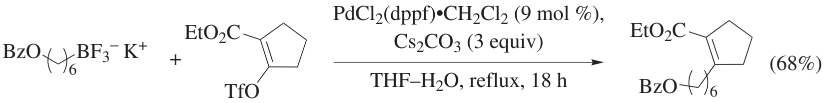
(76%) $\alpha/\gamma = 99{:}1$, 88.5:11.5 er

(Eq. 88)

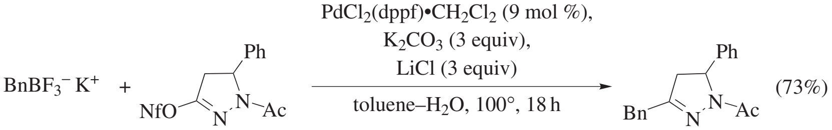
Although some sulfonates (Eqs. 89–91)[58,123] have been employed in cross-coupling with sp^3-hybridized organotrifluoroborate nucleophiles, this chemistry remains largely undeveloped. Yields among the few tosylates examined are modest; the triflates generally afford good yields, and the two nonaflates examined provide mixed results. More extensive studies will be required in this area to judge the practicality of the processes.



(Eq. 89)



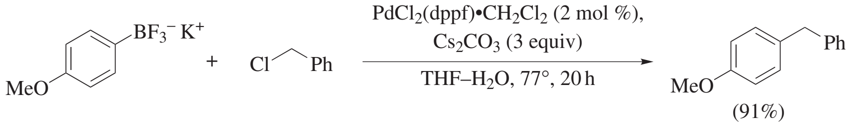
(Eq. 90)



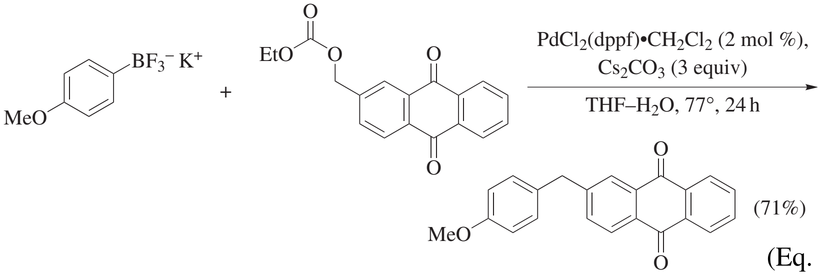
(Eq. 91)

Benzyl and Allyl Electrophiles. To date the only sp^3-type electrophiles employed with organotrifluoroborates have been the benzylic and allylic systems. The use of this class of electrophiles is further limited to aryl-, heteroaryl- and alkenyltrifluoroborates.

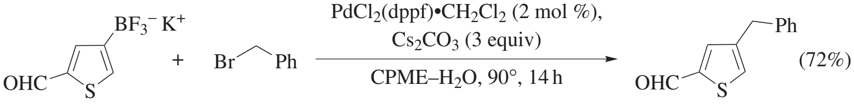
A variety of aryltrifluoroborates have been cross-coupled with benzylic halides (Eqs. 23, 24, and 92),[85] benzylic pseudohalides, and benzylic-type carbonates (Eq. 93). Benzyl iodides have not been explored, but benzyl chlorides and bromides couple satisfactorily. Only two heteroaryltrifluoroborates have been explored in conjunction with benzylic bromides, and both provide good yields (Eq. 94).[85] A limited number of allylic chlorides have also been partnered with phenyltrifluoroborate (Eq. 95).[150]



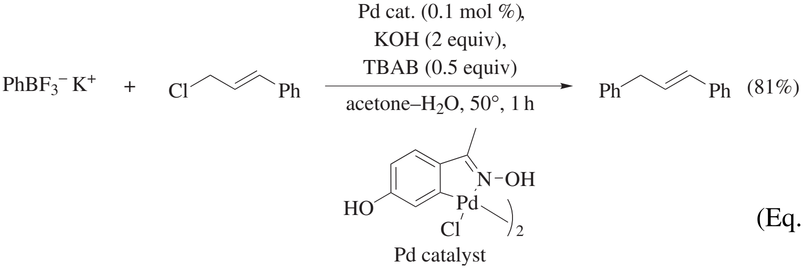
(Eq. 92)



(Eq. 93)

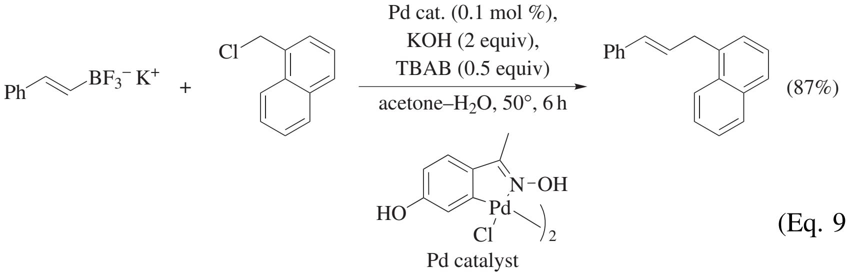


(Eq. 94)

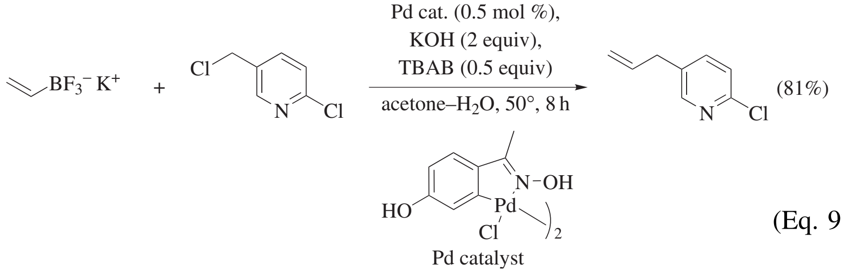


(Eq. 95)

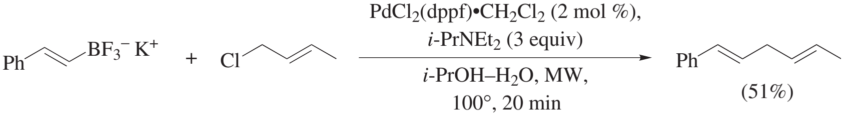
In cross-coupling with alkenyltrifluoroborates, chlorides have been the exclusive coupling partners in benzylic and pseudobenzylic systems (Eqs. 96–97).[70] Skipped dienes can be prepared by the reaction of alkenyltrifluoroborates with allylic halides (Eq. 98).[70,151] In limited studies, allyl chlorides, bromides, and iodides all appear equally effective.



(Eq. 96)



(Eq. 97)



(Eq. 98)

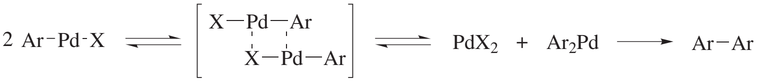
SIDE REACTIONS

For the most part, the same unwanted byproducts encountered in Kumada, Stille, Negishi, Hiyama, and other Suzuki-type cross-coupling transformations may be observed in cross-coupling reactions performed with organotrifluoroborates. In some cases, however, there are important differences between organotrifluoroborates and other reagents that prevent the formation of these materials. Additionally, a deeper mechanistic understanding of cross-coupling processes has led to reaction designs that mitigate many of the side reactions found in earlier versions of these reactions.

It is unfortunate that minor byproducts are often ignored and/or not reported and are simply separated away from the desired products. The following discussion outlines in general terms some of the side reactions one must be aware of, and cites specific cases where more detailed information is available.

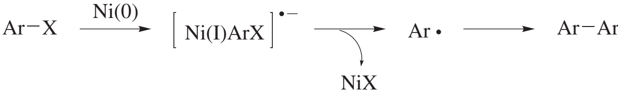
Homocoupling of the Organic Halide Electrophile

A byproduct found in many cross-coupling reactions is the dimer formed from homocoupling of the organic halide electrophile. This contaminant can have several origins, depending on the nature of the reaction being performed. In palladium-catalyzed reactions the most common source appears to be a metathesis reaction of the originally formed oxidative addition intermediate. The organopalladium halide disproportionates, thereby generating PdX_2 salts and diorganopalladiums, the latter of which reductively eliminate forming the homocoupled product (Eq. 99).[152] Because this process is kinetically second order in the palladium catalyst, and the desired cross-coupling reaction is typically first order in the catalyst, the amount of homocoupled product can often be minimized by simply lowering the catalyst loading in reactions of interest.



$$2\,\text{Ar{-}Pd{-}X} \rightleftharpoons \left[\begin{array}{c}\text{X{-}Pd{-}Ar}\\ \text{X{-}Pd{-}Ar}\end{array}\right] \rightleftharpoons \text{PdX}_2 + \text{Ar}_2\text{Pd} \longrightarrow \text{Ar{-}Ar} \qquad \text{(Eq. 99)}$$

Nickel-catalyzed reactions are prone to providing homocoupled products through electron-transfer reactions, forming radical species that subsequently dimerize (Eq. 100).[153]



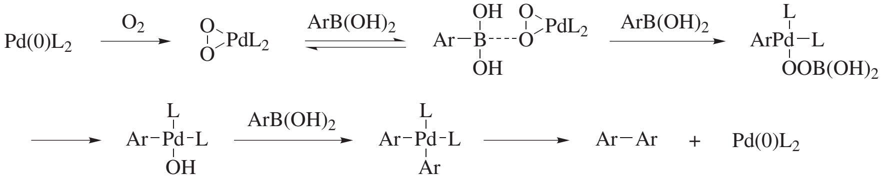
$$\text{Ar{-}X} \xrightarrow{\text{Ni(0)}} \left[\text{Ni(I)ArX}\right]^{\bullet -} \xrightarrow[\text{NiX}]{} \text{Ar}\bullet \longrightarrow \text{Ar{-}Ar} \qquad \text{(Eq. 100)}$$

Homocoupling of the Organoboron Reagent

Byproducts from homocoupling of organoborons in cross-coupling reactions can derive from several different processes. The first mode is associated with Pd(II) precatalyst reduction to Pd(0), which in most Suzuki reactions occurs by a double transmetalation reaction on the PdX_2 salt, followed by reductive elimination (Eq. 4).[27] This process generates a homocoupled product in proportion to the catalyst loading. By contrast, as outlined previously, catalyst activation in organotrifluoroborates appears to transpire through a fluoride-catalyzed hydrolytic reduction (Scheme 4) that avoids the formation of dimers when boronic acids are utilized. Cross-coupling using organotrifluoroborates thus minimizes homocoupled byproduct formation created through catalyst activation.

A related mode of organoboron homocoupling results from the metathesis reaction discussed previously (Eq. 99). This reaction generates homocoupled products derived from the electrophile, but also results in the formation of PdX_2 salts. The latter can react with organoborons, forming diorganopalladium species that reductively eliminate to yield homocoupled products derived from the nucleophilic component of the reaction. Because $<0.1\%$ of organoboron-derived homocoupling product is formed in organotrifluoroborate Suzuki-type reactions,[27] presumably any PdX_2 species formed by this process are reduced via the fluoride-catalyzed process described above (Scheme 4) prior to transmetalation with the organotrifluoroborate.

A third means by which organoboron reagents can lead to homocoupling products is via oxidative coupling. Mechanistic studies[27] suggest that the process transpires via formation of a palladium peroxo species, a process that is either reversible or boronic acid-mediated, and is sensitive to the concentration of the boronic acid (Scheme 8).[154] The reaction is reportedly slow under neutral conditions, but rapid under the aqueous basic conditions typically used in Suzuki cross-coupling reactions.[3,155] It has also been suggested that some of these homocoupled products arise upon workup of the reactions, wherein unreacted boronic acids undergo aerobic coupling in the presence of active catalyst. Organotrifluoroborates apparently do not facilitate palladium peroxo formation, and because they are only slowly (relative to catalytic turnover) hydrolyzed to boronic acids under the conditions utilized for cross-coupling, homocoupling resulting from this oxidative process is also minimized.



Scheme 8. Oxidative homocoupling of boronic acids.

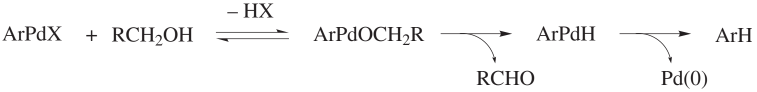
Protodeboronation

One of the banes of the Suzuki cross-coupling reaction is the formation of protodeboronated byproducts. Cross-coupling and protodeboronation occur competitively under conditions typically utilized for the Suzuki reaction with boronic acids, and consequently a significant excess of these reagents is employed in virtually every cross-coupling protocol involving these organoboron nucleophiles. The rate of protodeboronation is a function of both the reaction conditions and the structure of the organoboron reagent employed. For boronic acids, the presence of weak bases such as $KHCO_3$ inhibits boron–carbon bond cleavage,[156] and the use of anhydrous conditions with boronate ester nucleophiles is suggested to reduce the amount of protodeboronated material.[155] These conditions minimize the formation of trihydroxyborates [$RB(OH)_3^-$], the intermediates believed responsible for the protodeboronated products.[27]

Several structural classes of boronic acid are notorious for their facile protodeboronation. Some suffer boron–carbon bond cleavage during challenging cross-couplings under basic conditions (e.g., sterically hindered systems and electron-deficient aromatics).[155] As pointed out previously, trihydroxyborates are considered the critical intermediates responsible for protodeboronation under these conditions. However, several important classes of boronic acids are inherently unstable to protodeboronation, decomposing even upon simple benchtop storage (e.g., cyclopropyl-, cyclobutyl-, and some heteroarylboronic acids).[90] The corresponding organotrifluoroborates do not suffer protodeboronation even under strongly basic conditions at elevated temperatures for long periods of time, and nearly all can be stored on the shelf indefinitely. As discussed previously, the organotrifluoroborates serve as a stable reservoir of boronic acid derivatives, with slow fluoride–hydroxyl exchange leading to intermediates active in transmetalation.[46,58,59] This phenomenon, combined with the use of low concentrations of water used in the cross-coupling (reducing the concentration of trihydroxyborate), minimizes protodeboronation in the cross-coupling transformation.

Dehalogenation of Aryl Halides

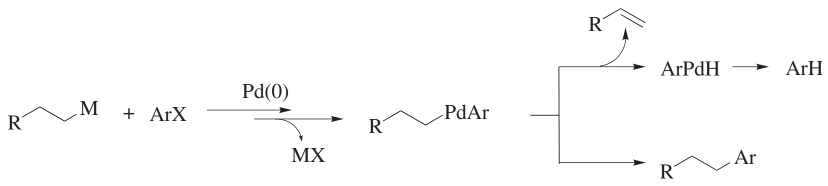
Dehalogenation of the halide electrophile is sometimes observed in organotrifluoroborate and other cross-coupling reactions, particularly when alcohol solvents are used. These products derive from an exchange of the halide on the palladium with alkoxide, with subsequent β-hydride elimination and reductive elimination (Eq. 101).[157] Analogous phenomena can be observed with amines present in the reaction mixture.



$$\mathrm{ArPdX} + \mathrm{RCH_2OH} \overset{-\,\mathrm{HX}}{\rightleftharpoons} \mathrm{ArPdOCH_2R} \xrightarrow[\mathrm{RCHO}]{} \mathrm{ArPdH} \xrightarrow[\mathrm{Pd(0)}]{} \mathrm{ArH}$$

(Eq. 101)

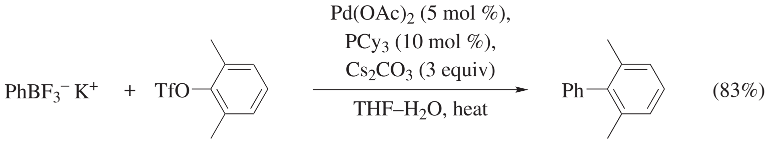
In the cross-coupling of alkylmetallic reagents the dehalogenated products may become more prevalent owing to the intervention of β-hydride elimination from the diorganopalladium intermediate (Scheme 9). This side reaction has been minimized by the development of highly effective catalyst/ligand combinations and high-throughput experimentation techniques leading to a more thorough optimization of the reaction conditions.[78,114]



Scheme 9. β-Hydride elimination.

Hydrolysis of Triflates

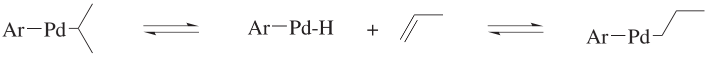
Early studies indicated that alkyltrifluoroborates cross-couple well with electron-deficient aryl triflates, but not with electron-rich electrophiles, which are more difficult to reduce.[58] Under the conditions first investigated for cross-coupling [MeOH solvent, $Pd(OAc)_2$ precatalyst, no ligand, K_2CO_3 base, reflux], competitive hydrolysis of the less reactive, electron-rich triflates occurs, leading to low yields of the final product. This phenomenon has been overcome by using catalyst systems and reaction conditions that facilitate the oxidative addition reaction [THF/H_2O solvent, $Pd(OAc)_2/PCy_3$ precatalyst, Cs_2CO_3 base, reflux], allowing efficient cross-coupling even with sterically encumbered and electron-rich reaction partners (Eq. 102).[134] With alkynyltrifluoroborate reagents, performing the cross-couplings under anhydrous conditions proves to be effective.[109]



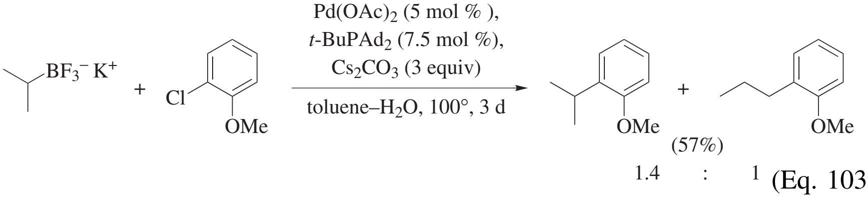
(Eq. 102)

β-Hydride Elimination/Isomerization

Cross-coupling of alkylmetallic reagents has always been a challenge because of the intervention of β-hydride elimination from the diorganopalladium intermediate (Scheme 10). As pointed out above, with the advent of effective ligands and access to high-throughput experimental techniques,[78] β-hydride elimination can largely be suppressed in reactions of primary organotrifluoroborates. It remains a significant problem, however, in the cross-coupling of secondary organometallics, and particularly for those reactions that involve sterically encumbered electrophiles. In these cases, β-hydride elimination followed by hydropalladation leads to an isomeric organopalladium intermediate that can reductively eliminate, leading to isomerized products (Eqs. 18, 44, and 103).



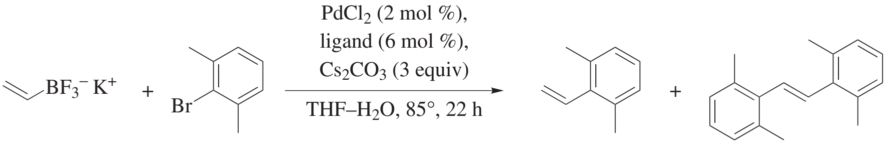
Scheme 10. Isomerization via β-hydride elimination/reinsertion.



(Eq. 103)

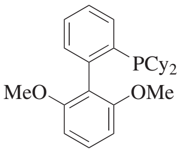
Heck-Type Coupling

Heck-type reactions can occur under conditions intended for vinyltrifluoroborate cross-coupling reactions, particularly with those substrates for which the initial cross-coupling is inherently difficult. This includes aryl chlorides and sterically encumbered aryl bromides.[106] To avoid unwanted Heck coupling, the ligand can be optimized so as to mitigate the formation of the alkene insertion products (Eq. 104). However, a Suzuki-Heck cascade can be used advantageously to build polymeric materials in an efficient, one-pot process.[158]



Ligand			
SPhos	3	:	1
XPhos	1	:	1
RuPhos	20	:	1

(Eq. 104)



SPhos

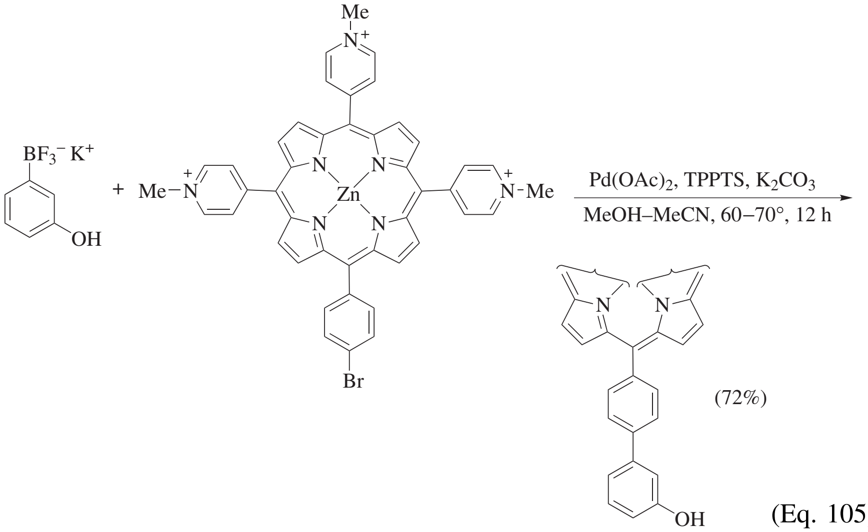
Phenol Formation

The inadvertent introduction of oxygen or the use of THF solvent containing tetrahydrofuran-2-hydroperoxide in cross-coupling reactions employing tricoordinate arylborons leads to the formation of phenol byproducts.[27] Oxidation of the aryltrifluoroborates to phenols is avoided under these conditions. The trifluoroborates appear to facilitate the decomposition of the tetrahydrofuran hydroperoxide by a mechanism that is not clear, but does not involve oxidation of the carbon–boron bond.

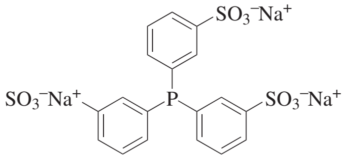
APPLICATIONS TO SYNTHESIS

Various organotrifluoroborates have been applied to the synthesis of molecules of interest in materials science, natural products chemistry, and the construction of molecules of biological or pharmacological interest. Some examples of these are outlined below.

Porphyrins constitute an extremely valuable class of molecules that find applications as therapeutics and photosensitizers, and are used in many areas of materials science. A method was reported that allowed the elaboration of cationic zinc porphyrins via cross-coupling with aryl- and vinyltrifluoroborates under aqueous conditions, allowing libraries of these target molecules to be constructed and analyzed for their physical and chemical properties (Eq. 105).[159]

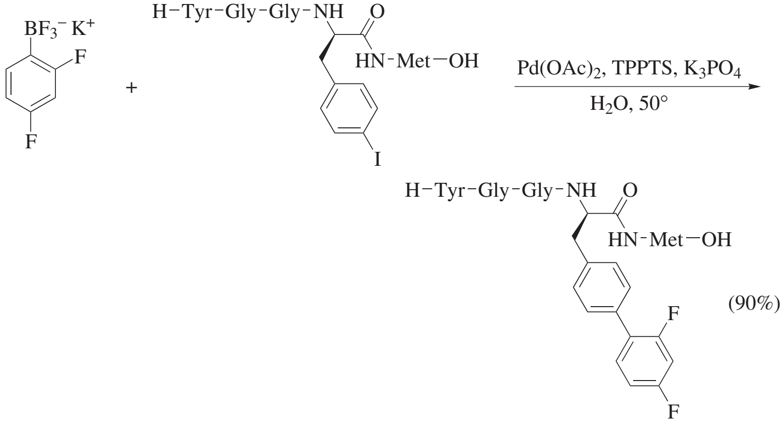


(Eq. 105)

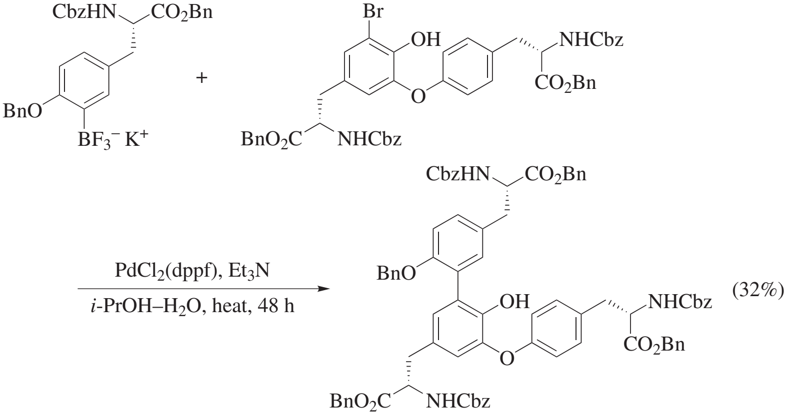


TPPTS

Aryltrifluoroborates have also been used to modify 4-iodophenylalanine residues of peptides through arylation (Eq. 106).[160] Additionally, diiodinated tyrosine derivatives have been doubly arylated under these and similar reaction conditions (Eq. 22).[84,160] The method was employed on thermally labile, hydrophilic peptides that mimic the nature of most biologically active peptides, allowing structure-activity relationship studies to be carried out rapidly on a variety of complex, water-soluble peptides without resorting to elaborate protection/deprotection schemes. Syntheses of dityrosine and pulcherosine (Eq. 107)[84] benefited from the use of aryltrifluoroborate technologies in assembling significant components of these naturally occurring amino acid derivatives, as other cross-coupling protocols for the desired transformation proved ineffective.

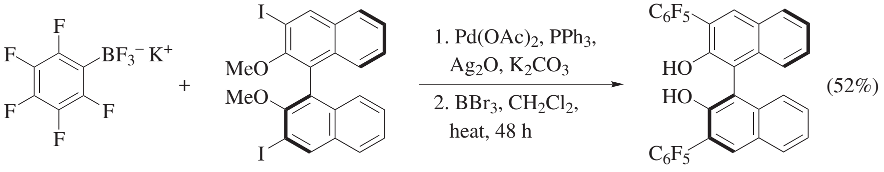


(Eq. 106)



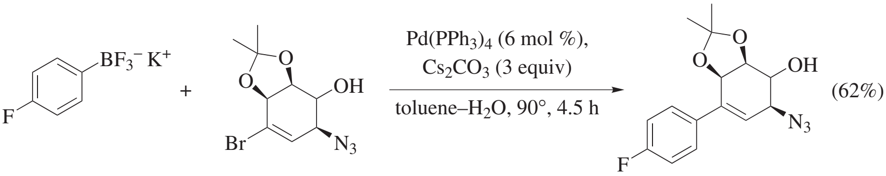
(Eq. 107)

A highly electron-deficient organotrifluoroborate, pentafluorophenyltrifluoroborate, was utilized for the construction of an enantiomerically enriched binaphthol derivative that was eventually incorporated into a molybdenum imido alkylidene catalyst used for olefin metathesis reactions (Eq. 108).[89] Neither Kumada- nor boronic acid Suzuki-type coupling reactions were suitable in this case.



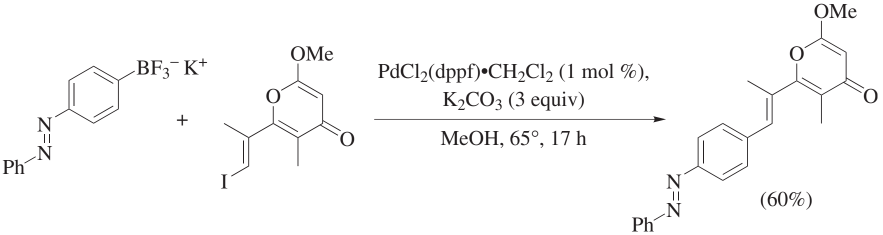
(Eq. 108)

The aryltrifluoroborate version of the Suzuki coupling reaction was utilized to derivatize cyclitol substructures incorporating the azide functional group (Eq. 109).[161] The latter could be utilized directly in Huisgen 1,3-dipolar cycloaddition reactions to generate triazoles, or reduced to amines to introduce amino acid moieties in the conduritol building block.



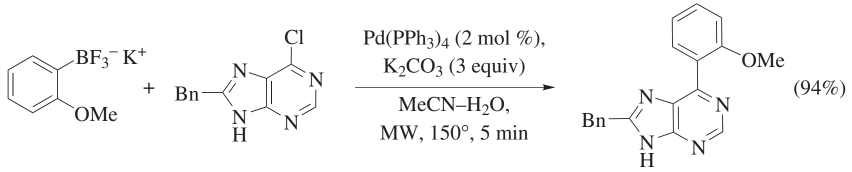
(Eq. 109)

Azobenzenes are valuable as photochromic ligands for the development of photoswitches used as protein agonists and antagonists. A novel approach to these structures employs aryltrifluoroborate coupling reactions (Eq. 110).[83] Arylboronates and arylboronic acids proved unsuitable for the desired transformations because they were either more difficult to access and/or provided low cross-coupling yields.

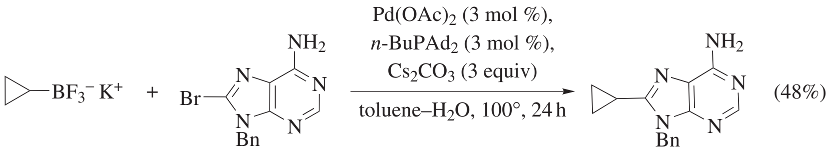


(Eq. 110)

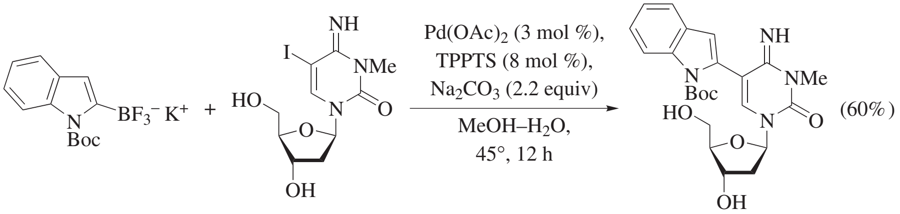
Organotrifluoroborates have been employed to generate families of modified purines. Both 6-chloropurine and 8-bromoadenine have been elaborated with aryl-, heteroaryl-, cyclopropyl-, and methyltrifluoroborates (Eqs. 111–113).[104,145]



(Eq. 111)

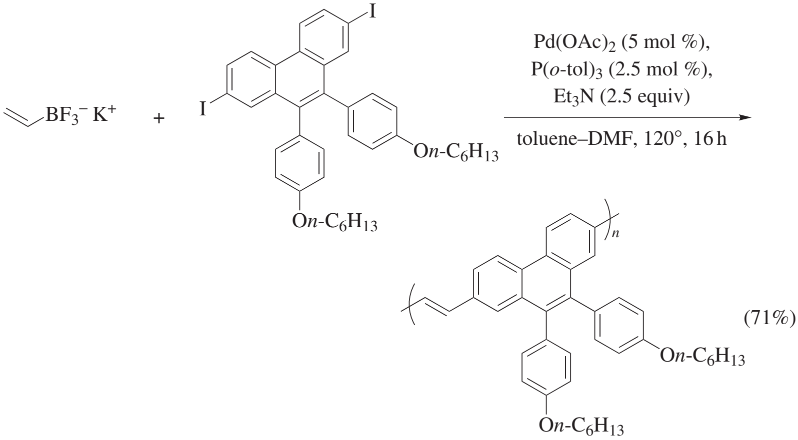


(Eq. 112)

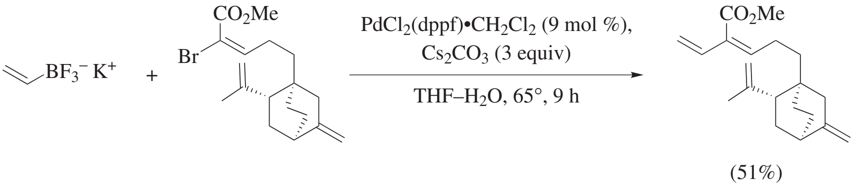


(Eq. 113)

Vinyltrifluoroborate is a shelf-stable reagent that has been employed in a variety of applications, including the synthesis of poly(2,7-phenanthrylenevinylenes), which are π-conjugated polymers of potential use in constructing organic light-emitting diodes (Eq. 114).[158] In this application, the initial cross-coupling reaction is followed by a subsequent Heck reaction, thereby forming the observed polymeric material. Vinyltrifluoroborate has also been incorporated into small molecule synthesis schemes. For example, it was used to generate a conjugated diene used in a subsequent Diels-Alder reaction to forge a key ring in the synthesis of the serofendic acids (Eq. 115).[162]

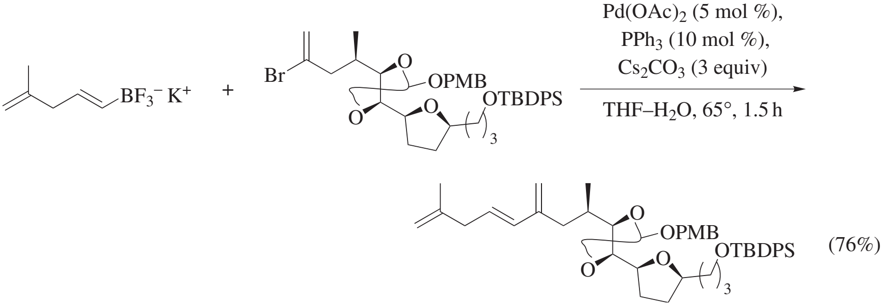


(Eq. 114)

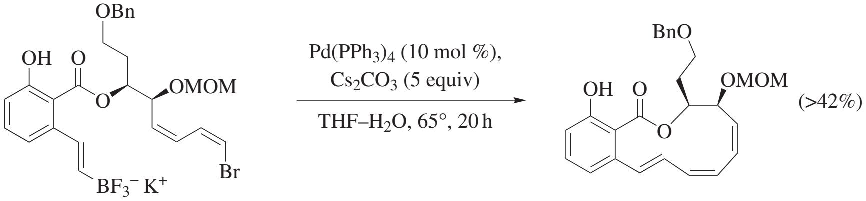


(Eq. 115)

Various alkenyltrifluoroborates have found their way into total synthesis efforts. For example, an alkenyltrifluoroborate cross-coupling was employed in the construction of a fragment of amphidinolide E (Eq. 116),[163] and an intramolecular cross-coupling to form a macrocyclic lactone was utilized to form the core of oximidine II (Eq. 117).[164] The latter reaction overcomes a great deal of strain in the formation of the 12-membered ring, which is composed of nine contiguous sp^2-hybridized carbon centers.



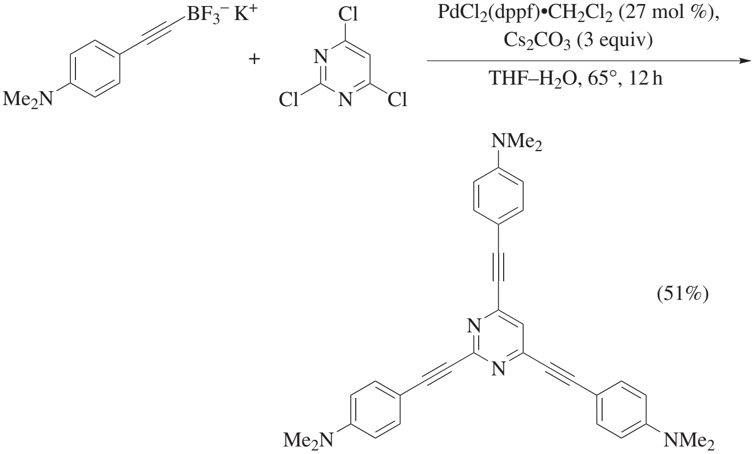
(Eq. 116)



(Eq. 117)

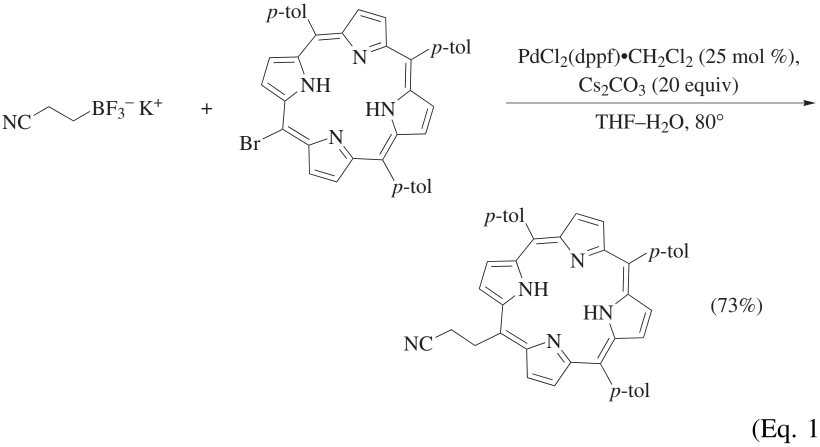
Air- and moisture-stable alkynyltrifluoroborates were utilized to generate tris(arylethynyl)pyrimidine species with potential interest as materials to be incorporated in a broad range of electronic and optoelectronic devices. The alkynyltrifluoroborates were used as a last resort when both Sonogashira and

Negishi protocols failed to produce the desired products in satisfactory yields (Eq. 118).[165]

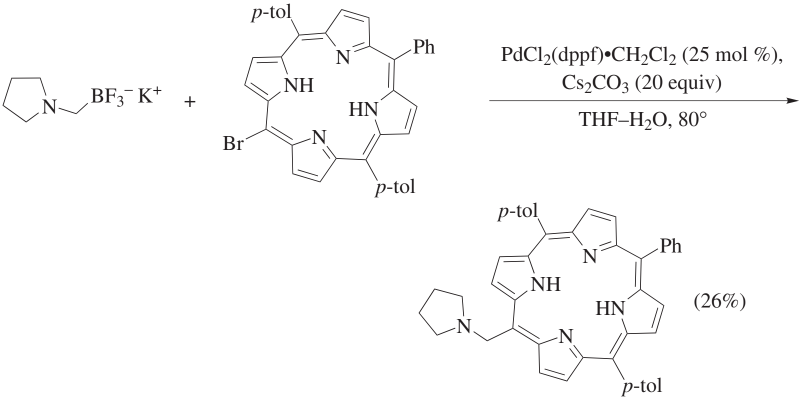


(Eq. 118)

Alkyltrifluoroborates have not been applied extensively to the synthesis of new materials, but in one important arena (porphyrins) they have proven to be practical reagents for the elaboration of organic substructures. As described previously, porphyrins have found practical utility in areas such as photodynamic therapy, nonlinear optical materials, and solar energy conversions. A variety of alkyltrifluoroborates (including aminomethyltrifluoroborates) have been utilized for the incorporation of functionalized alkyl groups into the porphyrin substructure (Eqs. 119–120).[115]



(Eq. 119)



(Eq. 120)

COMPARISON WITH OTHER METHODS

Direct comparison of cross-coupling reagents is problematic because no two reagents achieve their peak performance under the same conditions−each must be separately optimized using different protocols. Thus, any report of cross-coupling where two classes of reagents are examined under identical reaction parameters undoubtedly underestimates the results for at least one of the two reactants under comparison. Nevertheless, general trends emerge concerning various reagents. The Kumada, Negishi, Stille, Suzuki, and Hiyama coupling reactions all have important roles to play in modern organic synthesis, although among all of these protocols the Suzuki-Miyaura process has become the most widely used.

Kumada couplings[166] are highly effective owing to the high reactivity of the organomagnesium nucleophiles, but the process suffers because the reagents are air-sensitive and thus difficult to ship and store. Additionally, although tremendous inroads have been made in forming organomagnesium reagents with functional groups incorporated within the organometallic itself, these nucleophiles still have limited functional group tolerability for both reacting partners and must be converted to less nucleophilic reagents prior to cross-coupling in more highly elaborated systems.[167] The value in performing Kumada coupling derives from their relative environmental soundness, their economy, and their high reactivity. Thus, they are extremely valuable for cross-coupling of minimally functionalized systems.

Most organozinc reagents are also sensitive to moisture and oxygen, and in this manner suffer from some of the same limitations as organomagnesium reagents. However, they are more tolerant of functional groups than organomagnesium reagents, and Negishi cross-couplings can be carried out in more highly elaborated systems.[167] Additionally, some Negishi cross-couplings can be carried out in water without the formation of a discrete organozinc reagent, providing a further benefit.[168]

As a response to the need for air-stable, storable organometallic reagents capable of cross-coupling, organostannanes were developed and have been extensively employed. Their versatility, combined with their high reactivity and tolerance of diverse functional groups, has made the Stille coupling one of the most widely utilized protocols yet reported.[169] An additional advantage of the organostannanes is the relative strength and covalent character of the carbon–tin bond, which allows chemical manipulations of functional groups within the molecule while leaving the carbon–metal bond intact. However, toxicity is a major concern in the use of organostannanes. This feature of the reagents, in addition to a lack of atom economy (due to the incorporation of organic non-transferable ligands), and the difficulty of removing tin-containing by-products, has diminished the application of Stille couplings, particularly in the industrial setting.

Hiyama and related couplings employing organosilicon reagents are receiving more and more attention.[170–174b] These reagents are more environmentally sound than the tin reagents, particularly when fluoride-free versions of the process can be utilized. As with organostannanes, many functional groups embedded within the organosilanes can be chemically modified without cleaving the carbon–silicon bond. Other attractive features of the reagents include their relatively low cost, low toxicity, high chemical stability, and their tolerance of diverse functional groups.

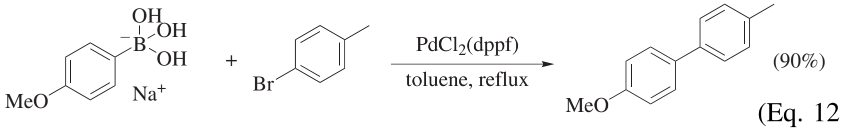
Cross-coupling reactions incorporating various organoboron reagents have come to dominate the landscape, and several different platforms have been utilized for these transformations. The availability of various trialkylboranes from diverse hydroborating reagents made them frequent partners in early Suzuki-Miyaura cross-coupling reactions. Although they have been employed extensively and effectively in this context, their scope is limited by the incompatibility of dialkylborane hydroborating reagents with a variety of functional groups. Being extremely air-sensitive reagents, the trialkylboranes must also be prepared and utilized in situ, making small-scale optimization onerous. They also lack the atom economy of other organoboron reagents.

Among the organoboron-based cross-coupling reagents, the boronic acids are now ubiquitous, with boronate esters playing a lesser role. Literally hundreds of boronic acids and boronate esters are currently commercially available. There is no question as to their value and importance in modern organic synthesis. However, the boronic acids are also known to possess rather significant practical limitations. The physico-chemical properties of the reagents make them less than ideal to handle. Boronic acids are often waxy solids that are difficult to purify. They exist as a mixture of the monomeric acids as well as trimeric anhydrides (boroxines), and in this sense they are inconvenient to assay and thus quantitate.[175] A close reading of the literature reveals that, largely because of competitive protodeboronation, boronic acids are almost always used in excess (20 to >100%), which is wasteful of precious and expensive material.

Boronate esters (in particular, the pinacolboronates) provide some advantages, but at a significant increase in cost. Thus, the monomeric pinacolboronates are more easily handled as solids and are more robust in general than the boronic acids. However, the boronates are less reactive in cross-coupling reactions, they have low atom economy, and the diols (especially pinacol) add considerable expense to the process, primarily because these reagents, like the boronic acids, are used in considerable excess in virtually all cross-coupling protocols.

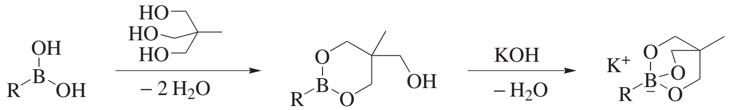
Additionally, both boronic acids and boronate esters possess the same inherent restriction: as tricoordinate boron species, their integrity can be compromised by a variety of the most useful, widely employed organic reagent classes, including acids, bases, nucleophiles, and oxidants. These reactivity patterns have the effect of limiting the manner in which these valuable reagents are employed in synthetic schemes. In the vast majority of cases, practitioners buy or make a boron substrate and immediately subject it to a cross-coupling protocol. Rarely are these reagents carried through several synthetic operations and then coupled at a point in a synthesis that might be more efficient or lead to higher convergency.

The aforementioned drawbacks have led to a surge in the development of boronic acid surrogates, or protected forms of boronic acids. As mentioned earlier, most organoboron-based cross-couplings do not readily proceed in the absence of a nucleophilic base. As a result of this observation, a number of preformed "ate" complexes have been prepared and investigated as coupling partners in the Suzuki-Miyaura reaction. In 2006, sodium trihydroxyborates were introduced as nucleophilic boronic acid surrogates.[176] These compounds are prepared by treatment of a toluene solution of boronic acid with sodium hydroxide. Once the "ate" complex is generated, it precipitates from solution and can be isolated easily by filtration as a free-flowing powder. However, these compounds are often difficult to obtain completely dry because they readily form hydrated complexes. When employed as a nucleophilic coupling partner, they can be used in excess to resolve the uncertain stoichiometry of the hydrated complexes. The anhydrous versions can be obtained by careful desiccation. Aryl trihydroxyborates undergo cross-coupling with aryl- and heteroaryl electrophiles to give the expected products in good yields (Eq. 121). Also, an alkyl version undergoes cross-coupling with an aryl bromide in good yield. Owing to the "ate" nature of the boron species, reactions employing trihydroxyborates can occur without the addition of a base. These are promising reagents, but to date they have not found extensive application.

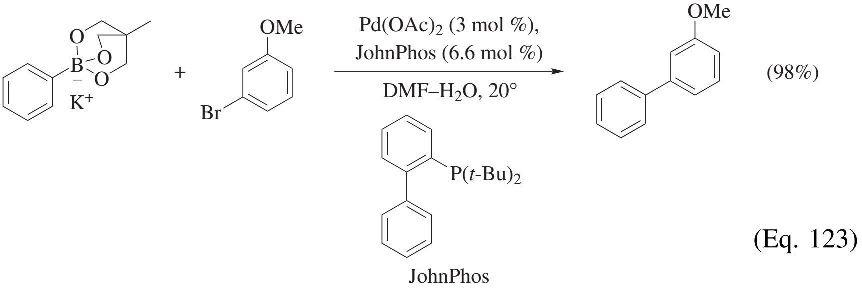


(Eq. 121)

Cyclic triolborates are another class of surrogates that have been developed for use in the Suzuki-Miyaura cross-coupling reaction.[177] Reaction of a boronic acid with a triol generates a hydroxymethyl-bound boronate ester. Upon subsequent treatment with KOH in toluene and removal of H_2O, the triol borate precipitates and can be isolated as a white solid (Eq. 122). These compounds can react at room temperature in Pd-catalyzed cross-coupling reactions with aryl bromides, aryl chlorides, and aryl triflates, in each case without the addition of a base (Eq. 123).

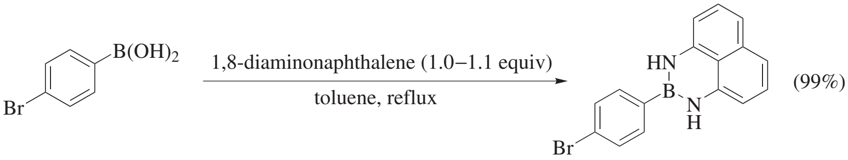


(Eq. 122)

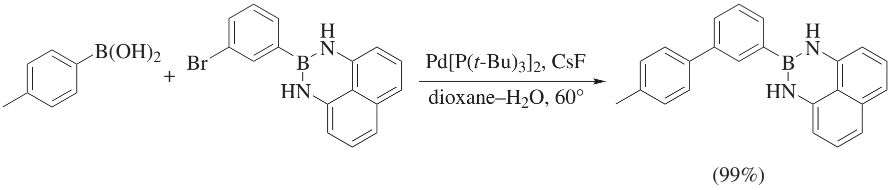


(Eq. 123)

Two other classes of protected boron derivatives have been recently introduced. The first are the "B(dan)" complexes, formed by the treatment of boronic acids with 1,8-diaminonaphthalene (Eq. 124).[178–180] This protecting group effectively lowers the Lewis acidity of the boron atom through donation of the lone pair from the nitrogen atoms into the vacant p-orbital of the boron, ultimately decreasing the overall reactivity of the boron center. Consequently, these diaminonaphthalene complexes are able to survive cross-coupling conditions used for boronic acids (Eq. 125), and they can be converted back to boronic acids in high yields by treatment with aqueous acids.

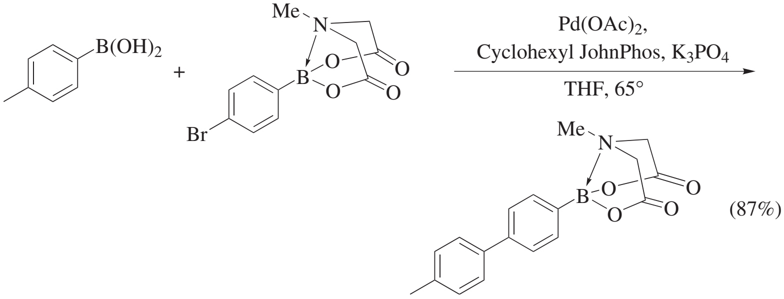


(Eq. 124)



(Eq. 125)

Treatment of boronic acids with *N*-methyliminodiacetic acid (MIDA) provides the second useful class of protected boronic acids. The MIDA rehybridizes the boron center from sp^2 to sp^3, generating a tetracoordinate boron species.[181–187] This rehybridization effectively renders the boron moiety inert to a variety of conditions that would affect tricoordinate organoborons, including oxidation and nucleophilic addition reactions. As in the case of the B(dan) compounds, anhydrous Pd-catalyzed cross-coupling reactions can be carried out in the presence of a MIDA boronate (Eq. 126). Another practical advantage of the MIDA boronates is that, unlike organotrifluoroborates, they may be isolated and purified by chromatography. They are also reported to be reliably solid materials and thus should be subject to purification by crystallization. When required, the MIDA protecting group can be readily removed to reveal the boronic acids by treatment under mild, aqueous basic reaction conditions.



(Eq. 126)

Although many of these boronic acid surrogates have been employed effectively to mask the boron atom in synthetic steps, as with any protecting group, there may be limitations associated with their use. The atom economy of the protecting groups is low, and sometimes (with B(dan) and MIDA complexes) two steps (a protection and deprotection) are required because the protected organoborons must be transformed back to the boronic acid before being employed in cross-coupling reactions. This essential unveiling of the boronic acid prior to the cross-coupling event leaves the boron moiety susceptible to the same protodeboronation issues associated with boronic acids, and an excess of these reagents is often used.

The organotrifluoroborates represent an alternative tetracoordinate boron species for cross-coupling, possessing their own strengths and limitations. As a class of reagents, the organotrifluoroborates are readily accessed from a variety of organoboron precursors by treatment with inexpensive KHF_2, which is 20 times less expensive than pinacol and more than 100 times less expensive than MIDA on a molar basis. As alluded to previously, this procedure[188] leads to isolable, tractable solids that are stable to air and moisture. As of this writing, nearly 1000 structurally diverse potassium organotrifluoroborates have been prepared, and virtually all of these are easily purified as monomeric, crystalline solids or well-defined powders. Aside from the boronic acids themselves, the organotrifluoroborates are the most atom-efficient organoboron reagents currently available. Perhaps most important is the behavior of the trifluoroborates in cross-coupling. In contrast to virtually all other organoborons, the relative resistance of organotrifluoroborates to protodeboronation under cross-coupling conditions allows them to be used frequently in stoichiometric quantities relative to their electrophilic partners.

These advantages are to be weighed against some of the weaknesses of organotrifluoroborate chemistry. Among these should be mentioned the necessity to utilize KHF_2 (a hazardous material that etches glass) in the preparation of the materials, and the presence of fluoride in the reagents and waste streams, which necessitates specialized reaction vessels and disposal for large-scale syntheses.

For small-scale preparations, the inability to chromatograph the organotrifluoroborates can create minor inconveniences, although their extraordinarily high propensity to form free-flowing powders or crystalline solids can mitigate these concerns. Finally, the potassium salts of the organotrifluoroborates are not highly soluble in non-polar solvents that might be required for chemical transformation of functional groups embedded within the organotrifluoroborates. However, the easily derived tetraalkylammonium salts are miscible in even the most non-polar solvents at low temperatures, and can be used when needed.

In addition to the general attributes of organotrifluoroborates, specific classes of these reagents have demonstrated features that recommend their use over that of boronic acids. As described previously, both electron-deficient aromatics[88,89] and many heteroaromatics[46,94,95] undergo competitive protodeboronation during cross-coupling events. This side reaction can be greatly minimized using the corresponding organotrifluoroborates.[27]

Potassium vinyltrifluoroborate is another valuable reagent that compares favorably with other available vinylating agents.[189] Its importance derives from the fact that vinylboronic acid readily polymerizes and cannot be isolated in pure form.[190] Vinyboron analogs such as the 2,4,6-trivinylcyclotriboroxane-pyridine complex can be employed,[191] but a 1:1 ratio of this trimer to the electrophilic coupling partner must be used, equating to three equivalents of the vinylating agent. Although vinylboronate esters have also been employed in cross-coupling reactions,[192] the diols used to prepare these reagents lead to low atom economy and add considerable expense to the overall procedure. Potassium vinyltrifluoroborate can be stored indefinitely at room temperature.[106]

The cross-coupling of more highly substituted alkenylboronic acids often requires superstoichiometric amounts of toxic thallium bases.[72,193–197] The use of alkenyltrifluoroborates alleviates the need for such bases, and affords cross-coupled products efficiently in high yield and with excellent stereospecificity.[71,72]

Although the Sonogashira reaction often provides a highly effective means for alkynylation, there are instances where this protocol fails to deliver the final product. In such instances, cross-coupling reactions with discrete alkynylmetallic reagents can provide an alternative entry to the desired products. Several alkynylborons have proven effective in this regard, but virtually all of these reagents are “ate” complexes generated and employed in situ.[198,199] Alkynyltrifluroborates represent a family of stable, storable reagents that are also highly effective in cross-coupling with a variety of aryl bromides and triflates.[109]

As is observed with many other boronic acids, cyclopropylboronic acid and cyclobutylboronic acid tend to undergo protodeboronation. This instability creates a significant safety hazard, because cyclopropane and cyclobutane can be generated in sealed bottles where these materials are stored. Cyclopropyltrifluoroborate and the cyclobutyl congener are indefinitely stable, providing storable reagents that are also highly effective in cross-coupling.[112]

Owing to the intervention of competitive β-hydride elimination, cross-coupling of alkylboronic acids with aryl and heteroaryl halides has always been problematic. One successful protocol employs excess silver oxide,[200] whereas other approaches require the use of toxic thallium bases or highly reactive organolithiums. The organotrifluoroborates provide a general solution to this challenge,[113] not only for primary alkyl systems,[114] but also for difficulties associated with methylation[200–204] and some secondary alkyl cross-couplings.[78]

The organotrifluoroborates provide solutions to problems encountered in a number of specialized cross-couplings as well. For example, although the cross-coupling of β-metallo esters[205] has been applied to the generation of amino acid derivatives,[206] there are limited examples of the corresponding ketone and amide derivatives.[207,208] The β-trifluoroborato ketones, esters, and amides thus serve as unique reagents for the construction of β-aryl and β-heteroaryl carbonyls via cross-coupling.[119–121]

In this same vein, alkoxymethyl-[129] and aminomethyltrifluoroborates[127,128] have been developed that expand the scope of cross-coupling reactions incorporating these valuable subunits, allowing more reactive alternatives to the less desirable organostannane versions of these reagents.[209–213]

EXPERIMENTAL CONDITIONS

The Organotrifluoroborate: Preparation and Handling

[Material Safety Data Sheet Potassium Bifluoride #333]

Caution! Potassium bifluoride (potassium hydrogen fluoride, KHF_2) is a hazardous material in terms of skin contact (corrosive, irritant, permeator), eye contact (irritant), ingestion, or inhalation. The amount of tissue damage depends on length of contact. Eye contact can result in corneal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to the gastrointestinal or respiratory tract, characterized by burning, sneezing, and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness, or death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

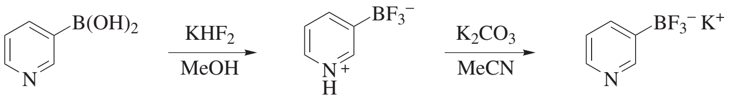
Chronic health problems can result from exposure to potassium bifluoride. The substance is toxic to lungs and mucous membranes. Repeated or prolonged exposure to the substance can result in target organ damage. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can cause local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degrees of respiratory irritation or lung damage.

As outlined previously, potassium organotrifluoroborates can be prepared from virtually any organoboron compound with two labile groups (Scheme 1). The syntheses of organotrifluoroborates from available boronic acids or boronate esters are typically carried out in methanol or acetone,[46,94] but other solvents can be used as well (e.g., Et_2O, MeCN).[58,72] For multistep transformations in which the boron is initially incorporated into substrates (e.g., by hydroboration, C–H activation, transmetalation, cross-coupling, etc.), the KHF_2 can be added directly to the reaction mixture. In either case, the KHF_2 can be added in two ways: (1) as a concentrated solution in water (∼4.5 M), or (2) as a solid, followed by the addition of water. Yields sometimes differ depending on the mode of addition. Since potassium bifluoride etches glass, it is often convenient to carry out the trifluoroborate synthesis in Nalgene vessels. The transformation from boron precursor to trifluoroborate appears in most cases to be complete in minutes, but reaction mixtures are often allowed to stir for periods of greater than one hour with no ill effects.

Upon completion of the trifluoroborate-generating reactions, the most convenient workup involves removal of all solvents, leaving a powder consisting of the organotrifluoroborate and KF. Two isolation procedures have proven most effective. Perhaps the easiest is to perform a continuous extraction of the powder using a Soxhlet extraction apparatus. Depending on the nature of the organotrifluoroborate, acetone, isopropyl acetate, or acetonitrile can be used as the solvent. The organotrifluoroborate will dissolve in these solvents, leaving the KF in the thimble of the extraction glassware. Upon cooling, the organotrifluoroborate may precipitate or crystallize out of solution. If not, a non-polar antisolvent such as hexane or Et_2O can be used to precipitate the desired product. The second isolation method involves simple trituration of the powder with hot acetone or acetonitrile, followed by crystallization or precipitation of the organotrifluoroborate.

Some assessment of the purity of the materials can be carried out by ^{1}H-NMR, ^{13}C-NMR, ^{11}B-NMR, and ^{19}F-NMR. However, none of these techniques will capture the presence of inorganic salts carried along in some multistep approaches to the organotrifluoroborates, and thus for a complete appraisal of purity elemental analysis is recommended.

There is a caveat in the use of KHF_2 to prepare organotrifluoroborates containing basic amines. As a strong acid, KHF_2 generates ammonium salts, which may lead to the generation of internal trifluoroborate salts. In most cases, these internal salts can be treated with base (e.g., K_2CO_3 in MeCN) to regenerate the amine (Eq. 127). Alternatively, the internal salt may be used directly in subsequent cross-coupling reactions.[94]



(Eq. 127)

The potassium salts of organotrifluoroborates are consistently solids in pure form. Tetraalkylammonium salts are less reliably so, and thus they may exist as difficult to handle syrups or glasses, depending on the ammonium salts employed and the structure of the organotrifluoroborate. No reliable chromatographic methods have been reported for the isolation or purification of any organotrifluoroborates.

Virtually all classes of organotrifluoroborates may be stored indefinitely on the shelf. They are air-stable, non-hygroscopic solids. The most sensitive materials appear to be the alkynyl- and allenyltrifluoroborates, which are best stored cold.

The Cross-Coupling

The execution of cross-coupling reactions with organotrifluoroborates is at its foundation no different than that employing other organometallic reagents.

Certainly, distinctions are noted among the protocols, which is to be expected of different classes of nucleophilic agents. The combination of ingredients in Suzuki couplings (reacting partners, precatalysts, ligands, solvents, bases, additives), along with added variables such as reaction temperature and time, as well as microwave[70,82,86,104,150,214–223] or ultrasound conditions,[69,73,149,224] afford a very large number of possible experimental combinations.

The following discussion provides a broad overview of the experimental details that have been employed for the cross-coupling of organotrifluoroborates. An important feature of these transformations should be kept in mind: reaction conditions vary widely among different substrate pairs, and indeed probably even among individual investigators that set out to optimize a reaction for any class of reacting substrates. In other words, no a priori "best" procedure exists for any given reaction pair, and satisfactory conditions are derived empirically by trial and error, increasingly with the aid of high-throughput experimentation.[78]

General Reaction Conditions. In general, the cross-couplings must be carried out in an inert atmosphere, but simple biaryl coupling reactions can be carried out in air.[46] With the exception of those transformations carried out with aryldiazonium ions,[13] diaryliodonium ions,[15] and cross-coupling of alkynyltrifluoroborates with activated bromides,[110] virtually all organotrifluoroborate coupling reactions require elevated temperatures (>65°), perhaps a reflection of the need for fluoride/hydroxide exchange to facilitate transmetalation (Eqs. 6 and 7).[27]

Choice of Catalyst or Precatalyst and Ligand. (*See catalyst and ligand charts preceding the Tabular Survey.*) Catalyst selection is key to the success of cross-coupling reactions, particularly when challenging reaction partners are involved. Both Pd(0) and Pd(II) catalysts can be employed in organotrifluoroborate cross-couplings, with the Pd(II) species being reduced to Pd(0) by the fluoride present in the reaction mixture (Scheme 4).[27] The use of Pd(II) precatalysts is often preferred, because Pd(0) species are air sensitive, and their integrity is difficult to assess quickly and accurately. Most conveniently, a large number of ligands are commercially available, and thus in screening efforts for reaction optimization many permutations can be examined without investing an inordinate amount of time in creating libraries of organometallic catalytic complexes.

As pointed out previously, in very simple systems (aryl bromide electrophiles with unhindered, electron-neutral or electron-rich aryltrifluoroborate nucleophiles), ligandless cross-coupling can be carried out using $Pd(OAc)_2$ as the catalyst (Eq. 5).[46,122,225] Supported catalysts, Pd/C and related species,[214,216,217,221,226,227] have also been used on a limited basis. Other popular catalysts for cross-coupling include $PdCl_2(dppf)\bullet CH_2Cl_2$, $Pd(PPh_3)_4$, and $PdCl_2(PPh_3)_2$, of which the former two have been used most extensively.

For more demanding cross-couplings, more sophisticated and elaborate systems must be employed. Besides dppf, dppb and XantPhos have been utilized as examples of chelating ligands. The most effective ligands, however, are sterically encumbered, electron-rich monodentate ligands such as P(*o*-tol)$_3$, PCy$_3$, P(*t*-Bu)$_3$, SPhos, RuPhos, XPhos, Cyclohexyl JohnPhos, *n*-BuPAd$_2$, and *t*-Bu$_2$PPh (Scheme 6).[21] These ligands facilitate cross-coupling with aryl chlorides, allow sterically demanding biaryl systems to be created, and permit transformations with alkyltrifluoroborates, including those at secondary carbon centers. In a similar manner, PEPPSI catalysts have proven effective for non-trivial couplings.[52,53] For those substrates exhibiting significant water solubility, TPPTS has been used to carry out the critical carbon–carbon bond-forming transformation.[104,159,160]

When reactions incorporating high-performance ligands are utilized, a Pd(II) precursor is employed to generate the active catalyst. The most commonly used salt is Pd(OAc)$_2$, but PdCl$_2$ and Pd(acac)$_2$ have also been used with success. Pd$_2$(dba)$_3$ is an effective source of Pd(0). As a point of interest, dba can serve as an active ligand in palladium-catalyzed reactions, and is thus not always an innocent bystander.[35–38,42] Sometimes dba can also control the rate of oxidative addition as well as the concentration of monocoordinated species in solution, which has an effect on transmetalation and reductive elimination rates as well. Consequently, profound differences in behavior may be seen between those processes employing Pd(OAc)$_2$ and cross-couplings incorporating Pd$_2$(dba)$_3$ as precatalysts.

Choice of Solvent. As discussed above, with the exception of diazonium salt and diaryliodonium salt electrophiles, a hydroxylic solvent or cosolvent must be utilized in organotrifluoroborate cross-coupling reactions to enable transmetalation. Aside from this requirement, there is no restriction on the solvents that may be employed, and numerous solvents have proven effective. The reaction mixtures are often biphasic as a result of the need to perform the reaction in the presence of a protic species (Eqs. 6 and 7). The reactions typically initiate as heterogeneous reaction mixtures as a result of the relative insolubility of the organotrifluoroborate in both protic and aprotic solvents, but become homogeneous as the reactions progress.

Solvents used in organotrifluoroborate cross-coupling include water, methanol, ethanol, *n*-propanol, 2-propanol, *tert*-butyl alcohol, THF, dioxane, DME, cyclopentyl methyl ether (CPME), toluene, DMF, *N*-methyl-2-pyrrolidone (NMP), and acetonitrile. The use of ionic liquids as solvents has also been explored.[132] The most common solvents are methanol, ethanol, THF, CPME, and toluene. Any of these solvents represents a good starting point for the examination of new coupling procedures.

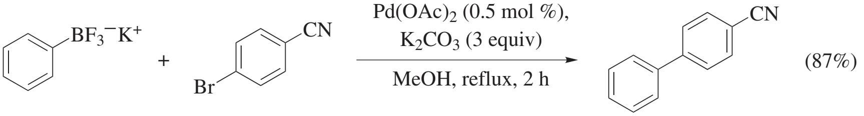
Although it is clearly not necessary that the solvents be anhydrous, for the most part they should be oxygen-free, at least for those reactions that are more challenging. Deoxygenation ensures that the active Pd(0) catalyst remains active, and also prevents deleterious oxidation of the phosphine ligands to phosphine oxides. Additionally, adventitious air can also induce oxidative coupling of the organoboron reagent (Scheme 8), reducing the availability of this reagent for cross-coupling and leading to byproducts that may be difficult to separate from the target molecule.

Choice of Base. Many bases have been utilized for organotrifluoroborate cross-couplings. When reactions are performed in ethereal or non-polar solvents such as toluene, bases such as NaOAc, K_2CO_3, Cs_2CO_3, Na_2CO_3, and K_3PO_4 appear to predominate, with the carbonates being the most effective. Factors such as cost and the ability to tolerate embedded functional groups play a major role in deciding which base to use. In hydroxylic solvents, amine bases seem to be most effective, with Et_3N, *i*-Pr_2NEt, and *t*-$BuNH_2$ all having been used. Bases used only occasionally include K_2HPO_4, LiOH, NaOH, and KOH. The alkoxides are less appealing because as strong bases they are less tolerant of sensitive functional groups, but for cross-couplings with minimally functionalized systems they are often quite effective.

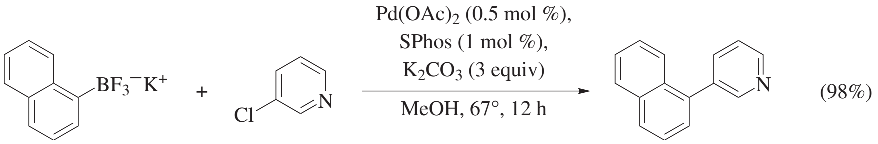
Additives. Very few additives are necessary or have been utilized in organotrifluoroborate cross-coupling reactions. Both CuI and silver salts[69,75,88,141–144,149,224] appear to be necessary when organotellurides are employed as electrophiles. Occasionally, TBAB has been used as a phase-transfer agent for various transformations, and this salt seems to be effective in this regard.[70,150,214,221,226,228] Both LiCl[123] and 18-crown-6[229] have been used in isolated cases, and thus their overall effectiveness cannot be accurately assessed.

Work-Up. No special considerations are required for isolating the products of cross-coupling using organotrifluoroborate nucleophiles. The byproducts of the reaction are boric acid and fluoride salts, which are easily removed from the reaction mixture by a simple aqueous workup. When necessary, much of the residual palladium can be removed by addition of small amounts of activated charcoal.

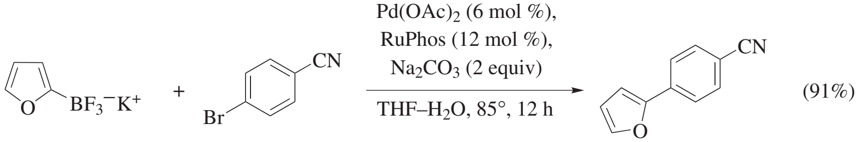
EXPERIMENTAL PROCEDURES



4-Phenylbenzonitrile [Cross-Coupling of an Aryltrifluoroborate with an Aryl Bromide Using $Pd(OAc)_2$].[46] To a suspension of potassium phenyltrifluoroborate (92.3 mg, 0.50 mmol), 4-bromobenzonitrile (91.01 mg, 0.50 mmol), and K_2CO_3 (0.2045 g, 1.50 mmol) in MeOH (0.75 mL) was added $Pd(OAc)_2$ (1.25 mL of a 2 mM solution in MeOH, 0.0025 mmol). The reaction mixture was heated at reflux for 2 h, then cooled to room temperature and diluted with H_2O (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 4 mL). The organic solution was washed with brine (10 mL) and dried ($MgSO_4$). The solution was then filtered through a short pad of silica gel, using a sequence of pentane and pentane/CH_2Cl_2. The solvents were removed under vacuum, and the residue was purified by chromatography on silica gel (elution with hexane) to yield 4-phenylbenzonitrile (77.9 mg, 87%): IR (neat) 2227, 1605, 1485, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76–7.68 (m, 4H), 7.60–7.58 (m, 2H), 7.52–7.43 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.6, 127.4, 118.9, 110.8. Anal. Calcd for $C_{13}H_9N$: C, 87.12; H, 5.06. Found: C, 87.04; H, 5.06.

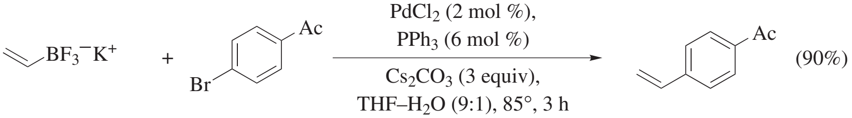


3-(Naphthalen-1-yl)pyridine [Cross-Coupling of an Aryltrifluoroborate with a Heteroaryl Chloride Using Pd(OAc)$_2$ and SPhos].[87] A threaded-top test tube containing a magnetic stir bar was charged with Pd(OAc)$_2$ (1.1 mg, 0.05 mmol), SPhos (4.1 mg, 0.01 mmol), potassium naphthyltrifluoroborate (257 mg, 1.1 mmol), and powdered anhydrous K$_2$CO$_3$ (415 mg, 3.0 mmol). The test tube was capped with a screw-top cap lined with a disposable Teflon septum, evacuated, and backfilled with argon (this process was repeated three times) through an 18-gauge needle. 3-Chloropyridine (114 mg, 1.0 mmol) was added via syringe through the septum, followed by addition of MeOH (2 mL). After the test tube was placed back under argon through the needle, the screw top cap was quickly removed and replaced with a new cap with an unpunctured septum. The reaction mixture was heated at 67° with vigorous stirring for 12 h. The reaction mixture was allowed to cool, diluted with EtOAc (10 mL), filtered through a thin pad of silica gel (eluting with 25% MeOH in EtOAc), and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (1:1 EtOAc/hexanes) to provide the title compound as a colorless oil (201 mg, 98%): ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.77 (d, $J = 2$ Hz, 1H), 8.70 (dd, $J = 2, 5$ Hz, 1H), 7.96–7.90 (m, 2H), 7.85–7.79 (m, 2H), 7.59–7.41 (m, 5H).

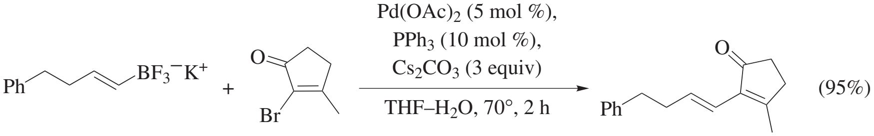


4-(Furan-2-yl)benzonitrile [Cross-Coupling of a Heteroaryltrifluoroborate with an Aryl Bromide Using Pd(OAc)$_2$ and RuPhos].[94] A Biotage microwave vial was charged with Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), RuPhos (14 mg, 0.03 mmol), 4-bromobenzonitrile (46.0 mg, 0.25 mmol), potassium furan-2-yltrifluoroborate (46.0 mg, 0.26 mmol), and Na$_2$CO$_3$ (53.0 mg, 0.5 mmol). The test tube was sealed with a cap lined with a disposable Teflon septum, evacuated, and purged with nitrogen (3 x). EtOH (1.4 mL) was added via syringe, and the reaction was conventionally heated at 85° for 12 h. The reaction mixture was allowed to cool to rt and filtered through a thin pad of silica gel (elution with 25% MeOH in EtOAc). The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography (7:1 hexane/EtOAc) to yield the pure product in 91% yield (38.49 mg, 0.23 mmol) as a white solid: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 (d, $J = 8.5$ Hz, 1H), 7.63 (d, $J = 8.5$ Hz, 1H), 7.52 (m, 1H), 6.80 (d, $J = 3.5$ Hz, 1H), 6.52 (dd, $J = 1.8, 3.4$ Hz, 1H);

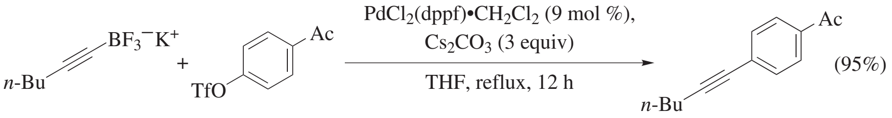
^{13}C NMR (125.8 MHz, $CDCl_3$) δ 152.1, 143.8, 134.8, 132.7, 124.1, 119.0, 112.3, 110.4, 108.3.



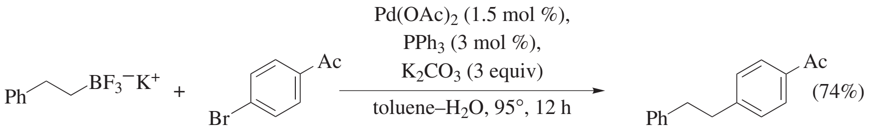
1-(4-Vinylphenyl)ethanone [Cross-Coupling of a Vinyltrifluoroborate with an Aryl Bromide Using $PdCl_2$ and PPh_3].[106] A solution of potassium vinyltrifluoroborate (134 mg, 1.00 mmol), $PdCl_2$ (3.5 mg, 0.02 mmol), PPh_3 (16 mg, 0.06 mmol), Cs_2CO_3 (978 mg, 3.00 mmol), and 1-(4-bromophenyl)ethanone (199 mg, 1.00 mmol) in THF/H_2O (9:1, 2 mL) was heated at 85° under a N_2 atmosphere in a sealed tube for 3 h, then was cooled to room temperature and diluted with H_2O (3 mL), followed by extraction with CH_2Cl_2 (3 × 10 mL). The solvent was removed under vacuum, and the crude product was purified by silica gel chromatography (20:1 *n*-pentane/Et_2O) to yield 1-(4-vinylphenyl)ethanone as a pale yellow solid (131.6 mg, 90%): mp 33–34°: IR 3054, 2987, 2306, 1681, 1605, 1422, 1359, 1265, 1181, 957, 922, 896, 847, 739, 705 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 6.76 (dd, J = 17.6, 10.9 Hz, 1H), 5.88 (dd, J = 17.6, 0.6 Hz, 1H), 5.39 (dd, J = 10.9, 0.6 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 142.3, 136.5, 136.2, 128.9, 126.5, 117.0, 26.8.



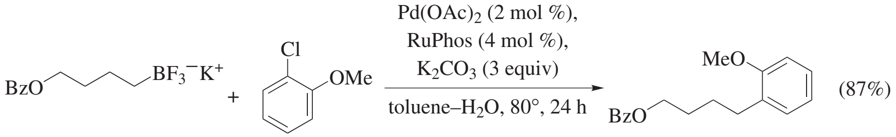
(*E*)-3-Methyl-2-(4-phenylbut-1-enyl)cyclopenten-2-one [Cross-Coupling of an Alkenyltrifluoroborate with an Alkenyl Bromide Using $Pd(OAc)_2$ and PPh_3].[72] To a mixture of potassium (*E*)-(4-phenylbut-1-enyl)-trifluoroborate (261.9 mg, 1.10 mmol), 2-bromo-3-methyl-cyclopent-2-enone (175.02, 1.00 mmol), Cs_2CO_3 (977 mg, 3.00 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and PPh_3 (26 mg, 0.1 mmol) was added THF/H_2O (10:1, 4 mL). The reaction mixture was heated at 70° with stirring under a nitrogen atmosphere for 2 h, cooled to rt, and diluted with H_2O (3 mL). The resulting mixture was extracted with Et_2O. The organic layers were combined and washed with 1 N HCl and brine, dried ($MgSO_4$), and filtered. The solvent was removed under vacuum, and the crude product was purified by silica gel chromatography (hexane) to afford the title compound (215.0 mg, 95%): IR (neat) 3025, 2918, 2852, 1625 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, J = 7.5 Hz, 2H), 7.20–7.15 (m, 3H), 6.75 (dt, J = 15.8, 6.7 Hz, 1H), 6.08 (d, J = 15.8 Hz, 1H), 2.75 (t, J = 7.3 Hz, 2H), 2.49–2.44 (m, 4H), 2.39–2.38 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 208.2, 169.6, 141.9, 135.3, 134.8, 128.4 (2C), 128.3 (2C), 125.8, 119.3, 35.9, 35.7, 34.8, 31.5, 17.5; HRMS–CI (m/z): M^+ calcd for $C_{16}H_{18}O$, 226.1357; found 226.1348.



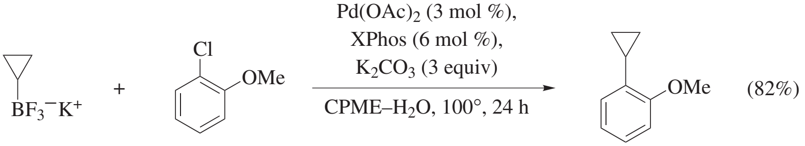
1-(4-Hex-1-ynyl)phenylethanone [Cross-Coupling of an Alkynyltrifluoroborate with an Aryl Sulfonate Using $PdCl_2(dppf)•CH_2Cl_2$].[109] Potassium (hex-1-ynyl)trifluoroborate (94 mg, 0.50 mmol), $PdCl_2(dppf)•CH_2Cl_2$ (36 mg, 0.045 mmol), and Cs_2CO_3 (489 mg, 1.50 mmol) were added to a flame-dried flask and dried under high vacuum for 2 h, after which time they were placed under argon. To this flask was added 4-acetylphenyl trifluoromethanesulfonate (134 mg, 0.50 mmol) and dry THF (5 mL). The solution was heated at reflux for 12 h. After this time the mixture was cooled, and 10 mL of H_2O was added to the flask. The resulting solution was then extracted with Et_2O. The combined organic extracts were washed with 1 M HCl and brine and then dried ($MgSO_4$). After the solid was removed by filtration, the solvent was removed under reduced pressure to leave a brown oil. The oil was purified by flash chromatography on silica gel (hexane) to afford the product as a clear oil (90.3 mg, 87%): R_f0.50; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dd, $J = 6.7$, 2.0 Hz, 2H), 7.47 (dd, $J = 6.7$, 1.9 Hz, 2H), 2.58 (s, 3H), 2.44 (t, $J = 7.1$ Hz, 2H), 1.62–1.59 (m, 2H), 1.50–1.47 (m, 2H), 0.95 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 135.6, 131.6, 129.2, 128.1, 94.4, 80.1, 30.6, 26.6, 22.0, 19.2, 13.6.



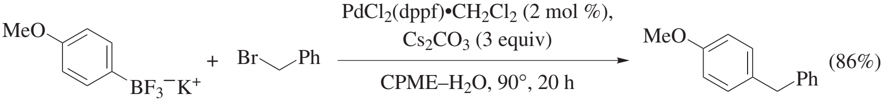
1-(4-Phenethylphenyl)ethanone [Cross-Coupling of an Alkyltrifluoroborate with an Aryl Bromide Using $Pd(OAc)_2$ and PPh_3].[230] A three-necked, 250-mL, round-bottomed flask, equipped with a reflux condenser, a rubber septum, a glass stopper, and a magnetic stirring bar, and connected to a vacuum-argon manifold, was charged sequentially with potassium 2-phenethyltrifluoroborate (7.77 g, 36.6 mmol), 1-(4-bromophenyl)ethanone (6.97 g, 35.0 mmol), K_2CO_3 (14.5 g, 105 mmol), PPh_3 (0.275 g, 1.05 mmol), and $Pd(OAc)_2$ (0.118 g, 0.53 mmol). The flask was evacuated and filled with dry argon three times. Toluene (105 mL) and H_2O (21 mL) were added, and the resulting two-phase mixture was stirred in a 95° oil bath for 12 h or until consumption of the 1-(4-bromophenyl)ethanone was indicated by GC analysis. The mixture was cooled to rt and then was transferred to a 250-mL separatory funnel. The flask was rinsed with toluene (20 mL) and H_2O (20 mL), and the resulting layers were shaken and separated. The organic layer was washed with 10% aqueous citric acid solution (20 mL) and saturated aqueous NaCl solution (20 mL). The organic layer was dried (Na_2SO_4, 0.780 g) and filtered through a medium-porosity glass-fritted funnel, and the drying agent was rinsed with toluene (20 mL). The resulting solution was concentrated (50° water bath, 9 mmHg) to give a light-yellow solid, which was crystallized from MeOH to give the title compound as a light tan solid (5.79 g, 74%): mp 68–72°; IR (KBr) 1676, 1601 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, $J = 8.3$ Hz, 2H), 7.30–7.15 (m, 7H), 3.01–2.92 (m, 4H), 2.58 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.7, 147.4, 141.0, 135.1, 128.7, 128.5, 128.4, 128.3, 126.1, 37.8, 37.3, 26.5; EIMS (70 eV) m/z: M^+ 224 (44), 209 (12), 181 (8), 133 (12), 105 (8), 91 (100), 65 (7). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found C, 85.59; H, 7.31.



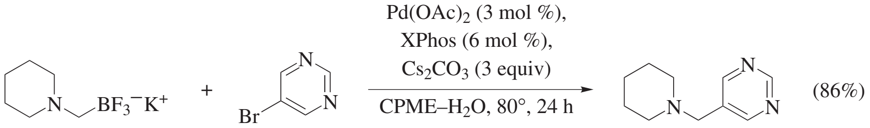
4-(2-Methoxyphenyl)butyl Benzoate [Cross-Coupling of an Alkyltrifluoroborate with an Aryl Chloride Using Pd(OAc)$_2$ and RuPhos].[114] A Biotage microwave vial was charged with $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), RuPhos (9.3 mg, 0.02 mmol), 2-chloroanisole (71.3 mg, 0.50 mmol), potassium 4-(benzoyloxy)butyltrifluoroborate (142 mg, 0.50 mmol), and K_2CO_3 (207 mg, 1.5 mmol). The test tube was sealed with a cap lined with a disposable Teflon septum, evacuated, and purged with N_2 (3 x). To the vial were added toluene (2.5 mL) and H_2O (0.25 mL), and then the reaction mixture was conventionally heated at 80° for 24 h. After the reaction mixture was allowed to cool to rt, GC/MS analysis showed complete conversion of the aryl chloride. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 1 mL). The resulting light yellow organic solution was concentrated and purified by silica gel column chromatography (99:1 hexane/EtOAc) to yield the product as a clear, colorless oil (124 mg, 87%): IR (neat) 3062, 2996, 2950, 2834, 1716, 1600, 1586, 1493, 1464, 1452, 1314, 1272, 1243, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.99–7.98 (d, $J = 7.6$ Hz, 2H), 7.50–7.48 (t, $J = 7.6$ Hz, 1H), 7.39–7.36 (t, $J = 7.8$ Hz, 2H), 7.12–7.08 (m, 2H), 6.83–6.78 (m, 2H), 4.31–4.28 (t, $J = 6.4$ Hz, 2H), 3.75 (s, 3H), 2.65–2.62 (t, $J = 7.4$ Hz, 2H), 1.78–1.68 (m, 4H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 166.7, 132.7, 130.6, 130.5, 129.8, 129.5, 128.3, 127.0, 120.4, 110.3, 64.9, 55.2, 29.8, 28.5, 26.2; HRMS–ESI (m/z): $[M + Na]^+$ calcd for $C_{18}H_{20}NaO_3$, 307.1310; found, 307.1306.



1-Cyclopropyl-2-methoxybenzene [Cross-Coupling of a Cyclopropyltrifluoroborate with an Aryl Chloride Using Pd(OAc)$_2$ and XPhos].[112] A Biotage microwave vial was charged with $Pd(OAc)_2$ (3.3 mg, 0.015 mmol), XPhos (14.3 mg, 0.03 mmol), potassium cyclopropyltrifluoroborate (74.7 mg, 0.505 mmol), and K_2CO_3 (210 mg, 1.5 mmol). The tube was sealed with a cap lined with a disposable Teflon septum, evacuated, and purged with N_2 (3 x). 2-Chloroanisole (71.3 mg, 0.5 mmol) and CPME/H_2O (10:1, 2 mL) were added by syringe, and the reaction mixture was stirred with conventional heating at 100° for 24 h, cooled to rt, and diluted with H_2O (1.5 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was dried (Na_2SO_4). The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography (99:1 hexane/EtOAc), yielding the product as a light yellow oil (75.2 mg, 82%): IR (neat) 3001, 1496, 1244 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14–7.10 (m, 1H), 6.88–6.82 (m, 3H), 3.86 (s, 3H), 2.18–2.15 (m, 1H), 0.92–0.89 (m, 2H), 0.66–0.62 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.6, 132.3, 126.5, 125.1, 120.8, 110.5, 55.8, 9.6, 7.8; HRMS–CI (*m/z*): $[M + H]^+$ calcd for $C_{10}H_{13}O$, 148.0888; found, 148.0879.

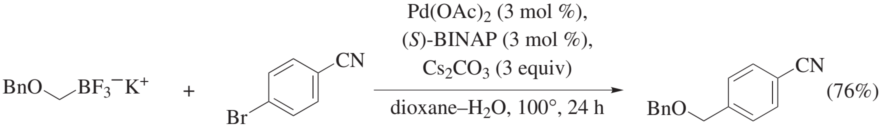


1-Benzyl-4-methoxybenzene [Cross-Coupling of an Aryltrifluoroborate with Benzyl Bromide Using $PdCl_2(dppf)•CH_2Cl_2$].[85] A solution of potassium 4-methoxyphenyltrifluoroborate (114.4 mg, 0.50 mmol), Cs_2CO_3 (489 mg, 1.50 mmol), $PdCl_2(dppf)•CH_2Cl_2$ (8 mg, 0.01 mmol), and benzyl bromide (90.6 mg, 0.50 mmol) in CPME/H_2O (10:1, 5 mL) was heated under a N_2 atmosphere in a sealed tube. The reaction mixture was stirred at 90° for 20 h, then was cooled to rt, diluted with H_2O (2 mL), and the product was extracted with CH_2Cl_2 (3 × 10 mL). The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography (100:1 *n*-pentane/Et_2O), yielding 1-benzyl-4-methoxybenzene as a clear, colorless oil (95.4 mg, 86%): ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.32 (t, $J = 7.3$ Hz, 2H), 7.29–7.24 (m, 3H), 7.18 (d, $J = 8.5$ Hz 2H), 6.86 (d, $J = 8.5$ Hz 2H), 3.96 (5, 2H), 3.81 (5, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 158.1, 141.4, 133.4, 130.0, 129.0, 128.6, 126.1, 114.0, 55.4, 41.2.

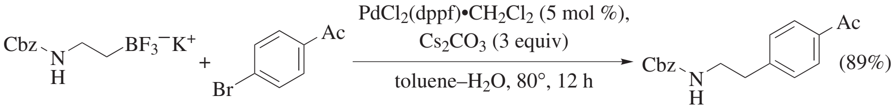


5-(Piperidin-1-ylmethyl)pyrimidine [Cross-Coupling of an Aminomethyltrifluoroborate with a Heteroaryl Bromide Using $Pd(OAc)_2$ and XPhos].[128] A solution of potassium 1-trifluoroboratomethylpiperidine (111 mg, 0.55 mmol), Cs_2CO_3 (489 mg, 1.50 mmol), $Pd(OAc)_2$ (3.5 mg, 0.015 mmol), XPhos (14.5 mg, 0.03 mmol), and 5-bromopyrimidine (79.5 mg, 0.50 mmol) in THF/H_2O (10:1, 2 mL) was heated under a N_2 atmosphere in a sealed tube. The reaction mixture was stirred at 80° for 24 h, then cooled to rt and diluted with H_2O (1 mL).

The reaction mixture was extracted with CH_2Cl_2 (3 × 2 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed under vacuum. The crude product was purified by silica gel chromatography (3.9:1:0.1 hexane/EtOAc/Et_3N), yielding the product as a pale-yellow oil (75 mg, 81%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.65 (s, 2H), 3.43 (s, 2H), 2.35 (br s, 4H), 1.56–1.52 (m, 4H), 1.41–1.40 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.7, 157.5, 132.0, 58.5, 54.5, 25.9, 24.2; HRMS–CI (m/z): M^+ calcd for $C_{10}H_{15}N_3$, 177.1266; found, 177.1257.



4-[(Benzyloxy)methyl]benzonitrile [Cross-Coupling of an Alkoxymethyltrifluoroborate with an Aryl Bromide Using Pd(OAc)$_2$ and (*S*)-BINAP].[129] A Biotage microwave vial was charged with potassium (benzyloxymethyl)trifluoroborate (125 mg, 0.55 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), (*S*)-BINAP (9.4 mg, 0.015 mmol), and Cs_2CO_3 (448 mg, 1.50 mmol). The test tube was sealed with a cap lined with a disposable Teflon septum, evacuated, and purged with nitrogen (3 x). 4-Bromobenzonitrile (91 mg, 0.50 mmol) and dioxane/H_2O (10:1, 2 mL) were added via syringe, and the reaction mixture was stirred with conventional heating at 100° for 24 h, then cooled to rt. The reaction mixture was extracted with EtOAc (3 × 3 mL), and the crude product was purified by silica gel column chromatography (15:1 hexane/EtOAc), yielding the product as a colorless oil (84.8 mg, 76%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, $J = 8.3$ Hz, 2H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.39–7.38 (m, 3H), 7.35–7.31 (m, 2H), 4.62 (s, 4H);^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.2, 137.8, 132.4, 128.7, 127.1, 119.0, 73.0, 71.3; HRMS–CI (m/z): $[M + H]^+$ calcd for $C_{15}H_{14}NO$, 224.1071; found, 224.1075.



Benzyl 4-Acetylphenethylcarbamate [Cross-Coupling of an Aminoethyltrifluoroborate with an Aryl Bromide Using PdCl$_2$(dppf)•CH$_2$Cl$_2$].[131] To a mixture of potassium β-aminoethyltrifluoroborate (69.1 mg, 0.242 mmol), 4-bromoacetophenone (47.8 mg, 0.240 mmol), Cs_2CO_3 (234.6 mg, 0.72 mmol), and $PdCl_2$(dppf)•CH_2Cl_2 (9.8 mg, 0.012 mmol) under N_2 was added toluene/H_2O (3:1, 1.5 mL). The reaction mixture was heated at 80° with stirring under a N_2 atmosphere in a sealed tube for 12 h and then cooled to rt. A saturated aqueous solution of NH_4Cl (4 mL) was added, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was dried ($MgSO_4$) and filtered. The solvent was removed under vacuum, and the crude product was purified by silica gel chromatography (3:7 EtOAc/hexane), affording the product as a white solid (63.5 mg, 89%): mp 84–85°; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.36–7.26 (m, 7H), 5.09 (s, 2H), 4.82 (br s, 1H), 3.50–3.46 (m, 2H), 2.88 (app t, J = 6.6 Hz, 2H), 2.57 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 197.8, 156.3, 144.6, 136.5, 135.6, 129.1, 128.7, 128.6, 128.2, 128.1, 66.7, 41.9, 36.2, 26.6.

TABULAR SURVEY

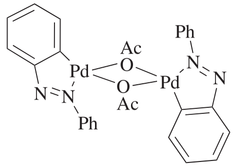
The tables cover all examples of the cross-coupling reactions of organotrifluoroborates from 1997 to the middle of 2010. The tables themselves are organized according to the nature of the organotrifluoroborate compound: aryltrifluoroborates (Table 1), heteroaryltrifluoroborates (Table 2), alkenyltrifluoroborates (Table 3), alkynyltrifluoroborates (Table 4), alkyltrifluoroborates (Table 5), cyclopropyltrifluoroborates (Table 6), benzyltrifluoroborates (Table 7), allyltrifluoroborates (Table 8), aminomethyltrifluoroborates (Table 9), alkoxymethyltrifluoroborates (Table 10), and aminoethyltrifluoroborates (Table 11). Table 12 summarizes the cross-coupling reactions of miscellaneous organotrifluoroborates, and finally, Table 13 presents carbonylative cross-coupling reactions of alkenyltrifluoroborates with aryl electrophiles.

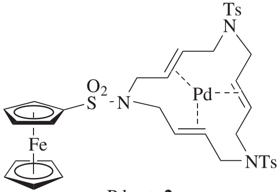
The tables are split into sub-tables according to the nature of the electrophiles employed (aryl electrophiles, heteroaryl electrophiles, alkenyltrifluoroborates, allylic and benzylic electrophiles, etc.). Entries within sub-tables are organized according to increasing carbon count, excluding protecting groups and counterions. Unreported yields are indicated by "(—)".

Charts 1 and 2 preceding the tables provide structures for the ligand and catalyst abbreviations and acronyms used in the tables. The following abbreviations, not including those found in the "*Journal of Organic Chemistry* Standard Abbreviations and Acronyms" list, are used in the tables:

Ad	adamantyl
CPME	cyclopentyl methyl ether
dan	1,8-diaminonaphthalene
dba	dibenzylideneacetone
Fc(*i*-Pr)$_2$	1,1′-bis(diisopropylphosphino)ferrocene
MW	microwave irradiation
Nf	perfluoro-1-butanesulfonate
NMP	*N*-methyl-2-pyrrolidone
PMP	*p*-methoxyphenyl
PTS	*p*-toluenesulfonic acid
TBDPS	*tert*-butyldiphenylsilyl
tol	tolyl, methylphenyl

CHART 1. ABBREVIATIONS AND ACRONYMS FOR Pd CATALYSTS APPEARING IN THE TABULAR SURVEY


Pd cat. **1**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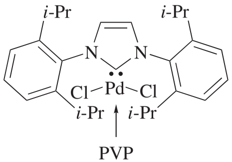
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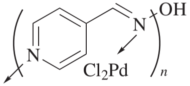
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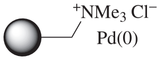
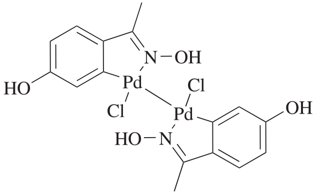
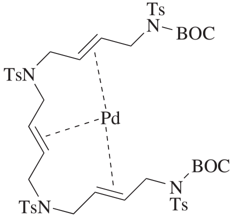
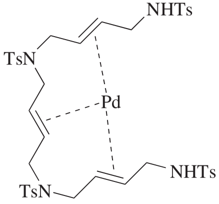
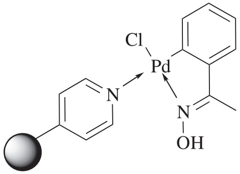
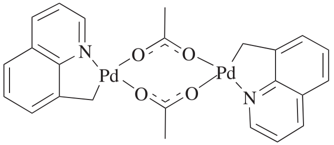

Pd cat. **5**

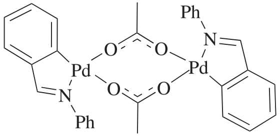

Pd cat. **6**

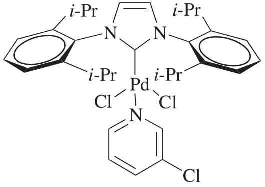

Pd cat. **7**

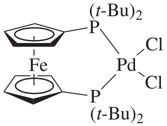

Pd cat. **8**

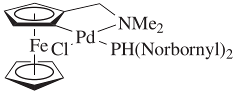

Pd cat. **9**


Pd cat. **10**


Pd cat. **11**


PEPPSI complex


Pd(dtbpf)Cl_2


SK-CC02-A

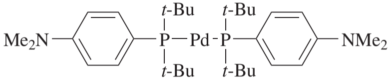
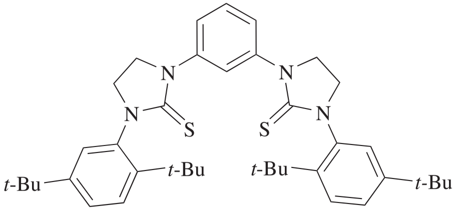
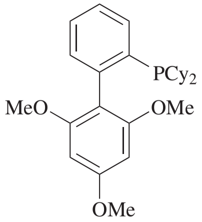

Pd(A-^{ta}Phos)$_2$$Cl_2$

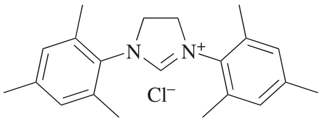
CHART 2. ABBREVIATIONS AND ACRONYMS FOR LIGANDS APPEARING IN THE TABULAR SURVEY



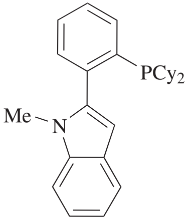
L1



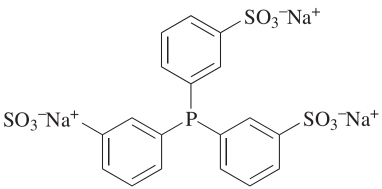
L2



L3

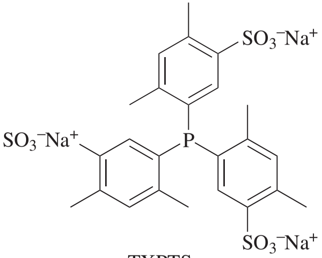


L4



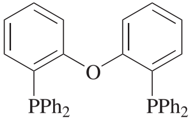
TPPTS

triphenylphosphine-3,3',3''-trisulfonic acid trisodium salt

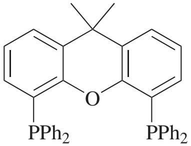


TXPTS

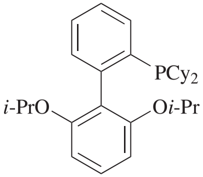
tri(4,6-dimethyl-3- sulfonatophenyl)phosphine trisodium salt



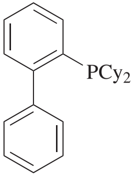
DPEPhos



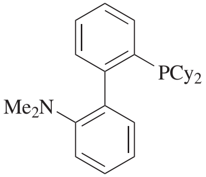
XantPhos



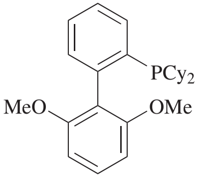
RuPhos



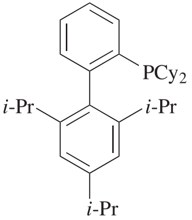
Cyclohexyl JohnPhos



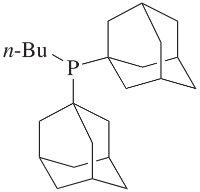
DavePhos



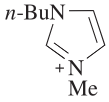
SPhos



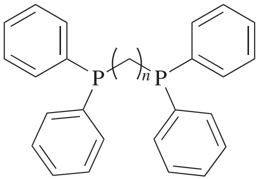
XPhos



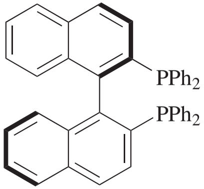
n-BuPAd$_2$
(cataCXium A)



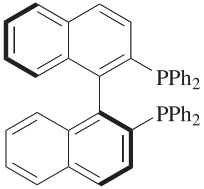
bmim
1-butyl-3-methylimidazolium ion



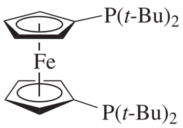
n		
1	dppm	1,4-bis(diphenyl)phosphinomethane
2	dppe	1,4-bis(diphenyl)phosphinoethane
4	dppb	1,4-bis(diphenyl)phosphinobutane



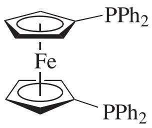
(*R*)-BINAP



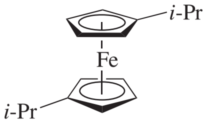
(*S*)-BINAP



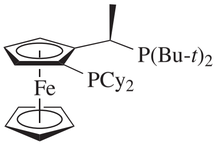
D-*t*-BPF
1,1'-di-*tert*-butylphosphinoferrocene



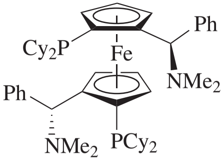
dppf
1,1'-bis(diphenylphosphino)ferrocene



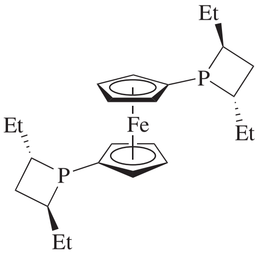
Fc(*i*-Pr$_2$)



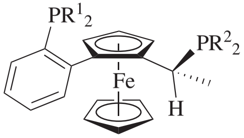
CyPF–*t*-Bu



L5

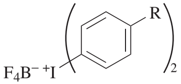
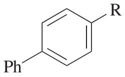
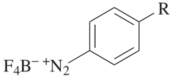
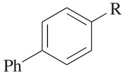
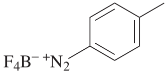
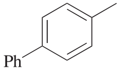
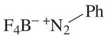
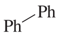
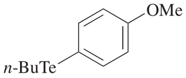
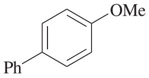


(*S,S*)-Et-FerroTANE



Walphos

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*				
C_6				
$PhBF_3^- K^+$		$Pd(OAc)_2$ (5%), DME, 60°, 30 min	 R H (99) Cl (92) Me (97)	15
		Pd cat. **1** (*x*%), $[bmim]^{+\,-}BF_4$–MeOH, rt	 R / *x* / Time (min) Br 4 180 (79) Cl 4 3 (95) OMe 2 180 (78) CO_2Et 2 5 (82)	132
		Pd cat., $[bmim]^{+\,-}BF_4$–MeOH, rt	 Pd cat. / Time (min) **10** 30 (65) **11** 10 (84)	132
		Pd cat. **2** (*x*%), 1,4-dioxane	 *x* / Temp (°) / Time (h) 5 rt 17 (63) 5 50 3 (45) 10 rt 22 (62)	231
		Catalyst (10%), additive (2 eq), Et_3N, MeOH, reflux Catalyst / Additive $Pd(acac)_2$ CuI (30) $Pd(acac)_2$ Ag_2O (55) $PdCl_2(dppf)•CH_2Cl_2$ Ag_2O (80) $Pd(PPh_3)_4$ Ag_2O (83)		142

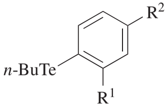
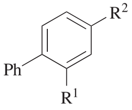
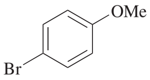
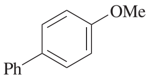
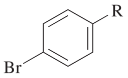
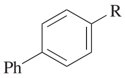
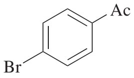
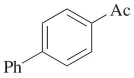
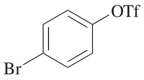
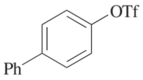
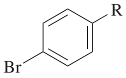
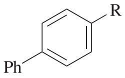
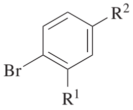
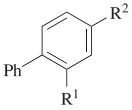
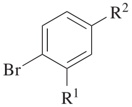
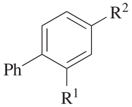
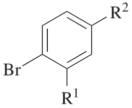
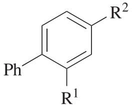
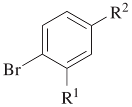
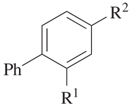
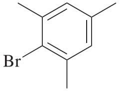
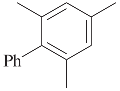
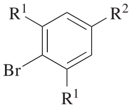
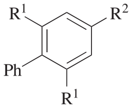
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux		R^1 R^2 H NO_2 (89) H I (42) H OH (92) H Cl (83) H Br (84) H Me (80) H Ac (80) H CO_2Me (83) Me H (74)	142
		$Pd(dtbpf)Cl_2$ (2%), Et_3N (3 eq), PTS–H_2O, rt, 2 h		(99)	232
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), H_2O, 2 h		R Temp (°) OH 65 (82) CO_2H rt (90) NHAc 65 (55)	136
		Pd cat. **3** (0.2%), Cs_2CO_3, MeOH, 60°, 1 d		(82)	233
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 48 h		(43)	134
$(PhBF_3^-)(n\text{-}Bu_4N^+)$		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 2 h		R NO_2 (98) OMe (78)	136
$PhBF_3^-$ K^+		$Pd(OAc)_2$ (1%), PPh_3 (1%), K_2CO_3 (3 eq), MeOH, reflux		R^1 R^2 Time (h) H NMe_2 14 (65) OMe OMe 18 (75)	46

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^-\ K^+$		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 R^1 R^2 H H (87) H OH (90) H NH_2 (97) H Me (95) H OMe (96) H Ac (95) Me H (24) CN H (93)	214
		$PdCl_2$ (1.2%), K_2CO_3 (3 eq), MeOH–H_2O, MW, 125°, 20 min	 R^1 R^2 H NO_2 (73) H OMe (99) H CN (73) H Ac (97) Me H (71)	215
		$PdCl_2$ (1.2%), K_2CO_3 (3 eq), MeOH, MW, 125°, 20 min	 R^1 R^2 H NO_2 (69) H OMe (79) H CN (55) H Ac (86) Me H (43)	215
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), Et_3N (3 eq), MeOH–THF, reflux, 15 h	 (70)	46



Pd/porous glass (0.45%),
Na$_2$CO$_3$ (4 eq), additive,
H$_2$O, MW, 150°, 10 min



R^1	R^2	Additive	Cycle: 1	2	3	4
H	OH	—	(96)	(95)	(98)	(95)
Me	Me	TBAB (1 eq)	(78)	(72)	(46)	(40)

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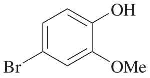
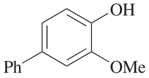
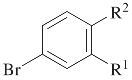


Pd/C (1%), aq. KOH (2 eq),
H$_2$O, MW, 120°

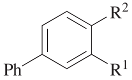


Time (min)	
15	(64)
30	(72)
60	(68)

217

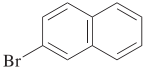


Pd(dba)$_2$ (0.1%), **L1** (0.1%)
K$_2$CO$_3$ (2 eq),
NMP–H$_2$O, 100°

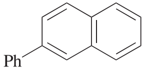


R^1	R^2	
NO$_2$	H	(99)
H	CHO	(87)

234

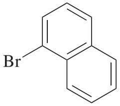


Pd(OAc)$_2$ (x%),
K$_2$CO$_3$ (3 eq),
MeOH, reflux

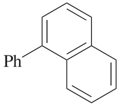


x	Time (h)	
0.5	2	(75)
2	2	(88)
0.2	9	(80)

136

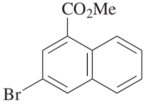


PdCl$_2$ (1.2%),
K$_2$CO$_3$ (3 eq),
MW, 125°, 20 min

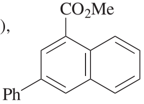


Solvent	
MeOH	(76)
MeOH–H$_2$O	(96)

215



Pd(OAc)$_2$ (10%), K$_2$CO$_3$ (3 eq),
DME–H$_2$O–EtOH,
MW, 110°, 7 min



(99)

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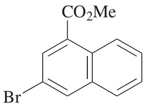
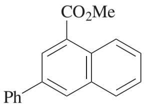
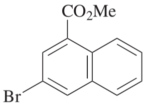
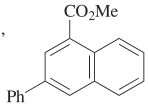
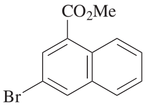
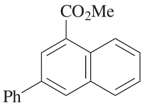
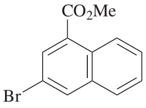
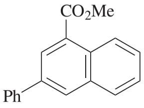
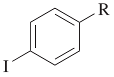
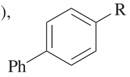
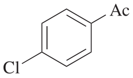
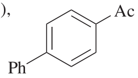
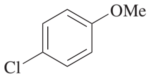
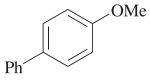
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
$PhBF_3^- K^+$		Pd(II)EnCat^{TM} (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		(40)	218
		Pd cat. **4** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		(99)	218
		Pd cat. **5** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		(10)	218
		Pd cat. **9** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		(0)	218
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min		R Me (86) OMe (93) Ac (98)	214
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min		(4)	214

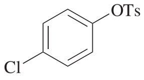


PEPPSI complex (2%),
base (3 eq), MeOH

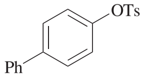


Base	Temp (°)	
K_2CO_3	60	(90)
K_2CO_3	rt	(86)
KOH	60	(91)
K_3PO_4	60	(84)

235

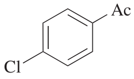


$Pd(OAc)_2$ (2%), **L2** (4%),
Et_3N (3 eq), EtOH, 80°, 6 h

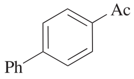


(84)

135

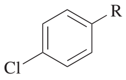


Pd source (0.01%),
K_2CO_3 (2 eq),
TBAB (0.5 eq), H_2O, 100°

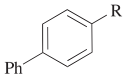


150

Pd Source		Time	
$Pd(OAc)_2$	—	20 h	(28)[a]
$Pd(OAc)_2$	MW	15 min	(19)[a]
$PdCl_2$	MW	15 min	(16)[a]



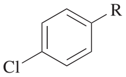
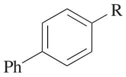
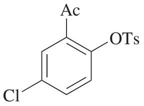
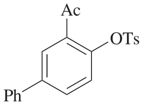
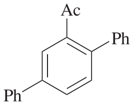
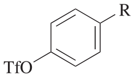
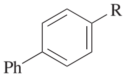
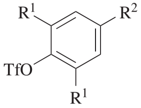
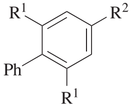
Pd cat. **6** (*x*%),
K_2CO_3 (2 eq),
TBAB (*y* eq), H_2O, 100°



150

R	*x*	*y*	Time (h)	
NH_2	1	1	10	(53)
OMe	1	1	6	(83)
Ac	0.01	0.5	20	(82)
Ac	0.05	0.5	7	(91)
CH_2CO_2H	1	0.5	4	(55)

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^-\ K^+$		Pd cat. **6** (*x*%), K_2CO_3 (2 eq), TBAB (*y* eq), H_2O, MW, 100° R, *x*, *y*, Time (min) NH_2 1 1 20 (71) OMe 1 1 20 (90) Ac 0.01 0.5 15 (87) CH_2CO_2H 1 0.5 15 (86)		150
		$Pd(OAc)_2$ (2%), **L2** (4%), Et_3N (3 eq), EtOH, 80°	 **I** +  **II** Time (h) 8 **I** (71) 18 **I** (38) + **II** (36)	135
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux	 R, Time (h) Cl 12 (50) Ac 1.5 (68)	136
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux	 R^1, R^2, Time (h) H NO_2 4 (65) H Cl 24 (82) H Me 22 (94) H OMe 20 (92) Me H 72 (83)	134

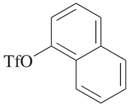
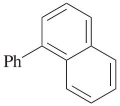
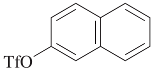
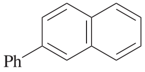
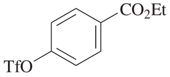
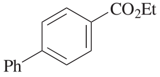
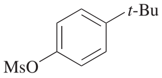
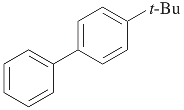
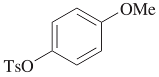
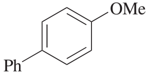
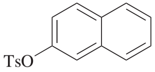
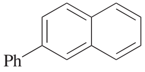
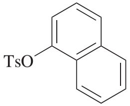
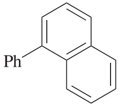
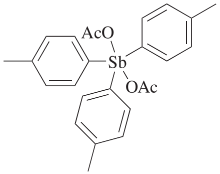
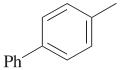
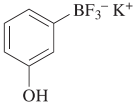
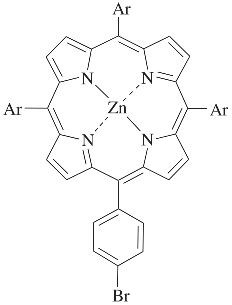
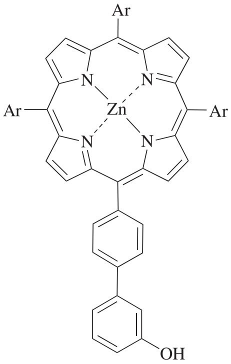
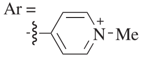
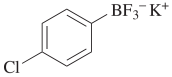
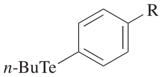
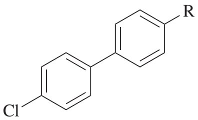
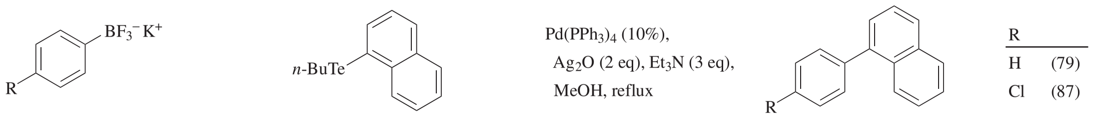
	Pd(OAc)$_2$ (5%), PCy$_3$ (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 22 h	 (86)	134
	Pd(OAc)$_2$ (5%), PCy$_3$ (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 20 h	 (92)	134
	PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), CsOAc (2 eq), THF–H$_2$O, reflux	 (99)	236
	Pd(OAc)$_2$ (2%), **L4** (2%), K$_3$PO$_4$ (1.5 eq), *t*-BuOH, 110°, 15 h	 (85)	138
	Pd(OAc)$_2$ (2%), **L2** (4%), base (3 eq), MeOH, 60°, 24 h	 Base K$_2$CO$_3$ (67) Cs$_2$CO$_3$ (88) KOH (98)	135
	Pd(OAc)$_2$ (2%), **L2** (4%), KOH (3 eq), MeOH, 60°	 (85)	135
	Pd(OAc)$_2$ (2%), **L2** (4%), KOH (3 eq), MeOH, 60°	 (85)	135

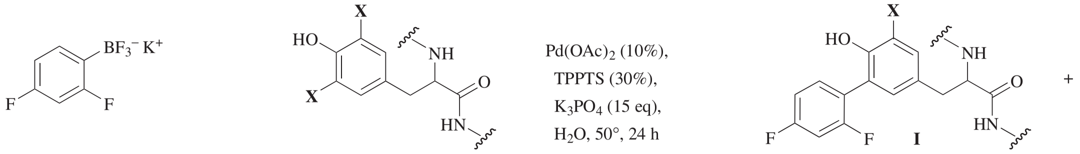
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^- K^+$		$Pd(PPh_3)_4$ (5%), 1,4-dioxane, 60°, 24 h	 (45)	140
		$Pd(OAc)_2$, TPPTS, K_2CO_3, $MeCN–H_2O$, 60–70°, 12 h	 (72) 	159
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux	 R H (59) Cl (94)	142



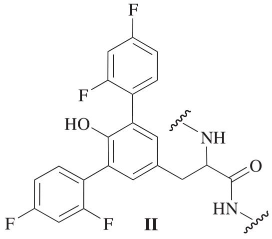
R	
H	(79)
Cl	(87)

142



I

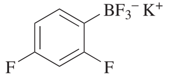
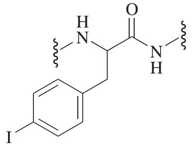
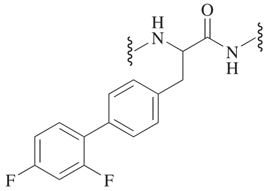
160



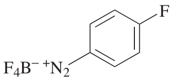
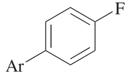
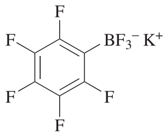
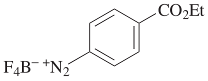
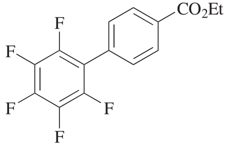
II

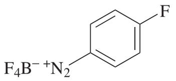
Peptide (X)	**I**	**II**
Ac-Phe-3,5-diiodo-Tyr-OH	(10)	(8)
H-3,5-diiodo-Tyr-Gly-Gly-Phe-Leu-OH	(25)	(28)
H-3,5-dibromo-Tyr-Gly-Gly-Phe-Leu-OH	(0)	(0)
H-3,5-diiodo-Tyr-Gly-Gly-Phe-Met-OH	(23)	(73)
H-3,5-diiodo-Tyr-D-Ala-Phe-Gly-Tyr-Pro-Ser-NH_2	(25)	(12)

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

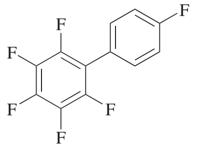
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(OAc)_2$ (5%), TPPTS (15%), K_3PO_4 (7.5 eq), H_2O, 50°		160

Peptide	Time (h)	
H-Tyr-Gly-Gly-4-iodo-Phe-Leu-OH	24	(98)
H-Gly-Gly-4-iodo-Phe-Leu-OH	3	(84)
For-Met-Leu-4-iodo-Phe-OH	3	(100)
H-Tyr-Gly-Gly-4-iodo-Phe-Met-OH	3	(90)
H-Tyr-D-Ala-4-iodo-Phe-Gly-Tyr-Pro-Ser-NH_2	3	(76)
H-Met-Glu-His-4-iodo-Phe-Arg-Trp-Gly-OH	24	(24)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
$ArBF_3^- K^+$		$Pd(PPh_3)_4$ (5%), DME, 20°	 Ar 2,3,4,5-C_6HF_4 (45)[b] 2,3,5,6-C_6HF_4 (23)[b] 2,3,4,6-C_6HF_4 (20)[b] 3,4,5-$C_6H_2F_3$ (27)[b]	237
		$Pd(OAc)_2$, dioxane, 20°	 (2)	237

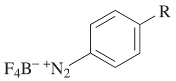


Pd source, solvent, 20°

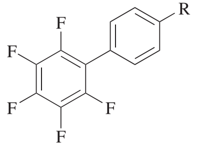


Pd cat.	Solvent	
Pd black	dioxane	(8)^{b}
Pd(PPh$_3$)$_4$	dioxane	(14)
Pd$_2$(μ-OAc)$_2$(P(*o*-tol)$_2$C$_6$H$_4$CH$_2$	dioxane	(4)^{b}
Pd$_2$(μ-OAc)$_2$(P(*o*-tol)$_2$C$_6$H$_4$CH$_2$	MeOH	(0)^{b}
Pd(PPh$_3$)$_4$	DMF	(3)^{b}
Pd(PPh$_3$)$_4$	DME	(32)

237

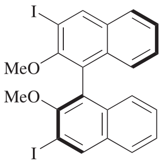


Pd(PPh$_3$)$_4$ (5%), DME, 20°

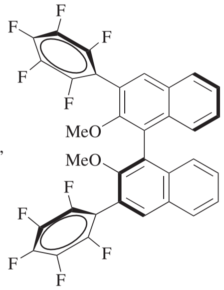


R	
H	(30)^{b}
NO$_2$	(13)
Me	(10)
OMe	(27)^{b}
CO$_2$Et	(46)

237



Pd(OAc)$_2$ (17%), PPh$_3$ (34%), Ag$_2$O (4 eq), K$_2$CO$_3$ (6.7 eq), toluene, 110°, 48 h



(—)

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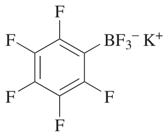
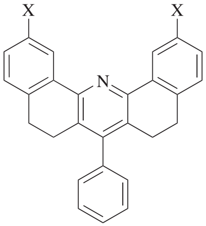
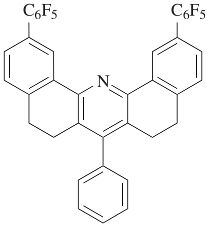
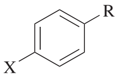
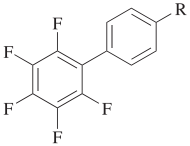
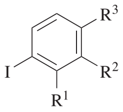
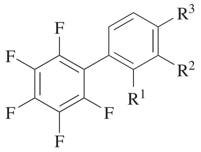
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(OAc)_2$ (0.1%), PPh_3 (0.2%), K_2CO_3, toluene, 100°	 X Br (0) I (20)	238
		$Pd(OAc)_2$ (10%), PPh_3 (20%), K_2CO_3 (2 eq), Ag_2O (1.2 eq), toluene, 100°	 X R Time (h) Br F 3 $(28)^b$ Br NO_2 5 $(36)^b$ Br NO_2 24 $(62)^b$ Br OMe 24 $(25)^b$ I H 3 (90) I NO_2 3 (81) I Me 3 (93) I CO_2Et 3 (82)	239

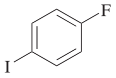


PdCl$_2$(PPh$_3$) (5%), **L3** (5%),
Ag$_2$O (1.2 eq),
toluene, 100°, 8 h

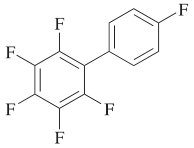


R^1	R^2	R^3	
H	H	H	(99)
H	H	F	(96)
H	H	NH$_2$	(3)
H	H	NO$_2$	(99)
H	H	Me	(91)
H	H	CN	(80)
H	H	CF$_3$	(80)
H	H	Ph	(86)
H	H	4-O$_2$NC$_6$H$_4$	(80)
H	CN	H	(96)
NO$_2$	H	H	(27)
Me	H	H	(49)
CN	H	H	(77)

88



Pd source (10%),
ligand (20%),
K$_2$CO$_3$ (2 eq),
Ag$_2$O (1.2 eq), toluene,
100°, 3 h



Pd Source	Ligand	
Pd(OAc)$_2$	none	(0)
Pd(OAc)$_2$	P(*o*-tol)$_3$	(67)
Pd(OAc)$_2$	PPh$_3$	(92)
Pd(PPh$_3$)$_4$	none	(71)

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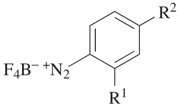
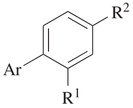
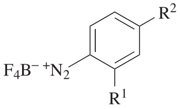
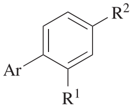
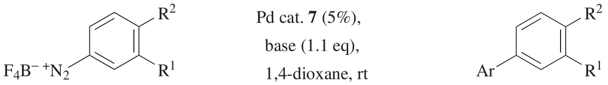
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

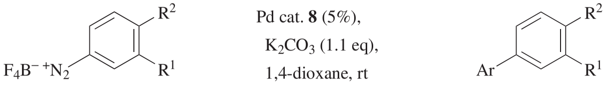
<table>
<tr><th>Aryltrifluoroborate</th><th>Electrophile</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_6</td><td></td><td></td><td></td><td></td></tr>
<tr><td>$ArBF_3^- K^+$</td><td></td><td>$Pd(OAc)_2$ (5%),
1,4-dioxane, 20°</td><td><table><tr><th>Ar</th><th>R^1</th><th>R^2</th><th>Time (h)</th><th></th></tr><tr><td>Ph</td><td>H</td><td>Me</td><td>3.7</td><td>(88)^c</td></tr><tr><td>Ph</td><td>H</td><td>OTf</td><td>1</td><td>(66)</td></tr><tr><td>Ph</td><td>OMe</td><td>OMe</td><td>6.5</td><td>(69)</td></tr><tr><td>4-FC_6H_4</td><td>H</td><td>NO_2</td><td>2.5</td><td>(92)</td></tr><tr><td>2,4-$Cl_2C_6H_3$</td><td>H</td><td>CO_2Et</td><td>72</td><td>(26)^c</td></tr></table></td><td>13</td></tr>
<tr><td></td><td></td><td>$Pd_2(\mu\text{-}OAc)_2$,
$(P(o\text{-}tol)_3)_2$ (5%),
MeOH, 20°</td><td><table><tr><th>Ar</th><th>R^1</th><th>R^2</th><th>Time (h)</th><th></th></tr><tr><td>Ph</td><td>H</td><td>I</td><td>22</td><td>(41)</td></tr><tr><td>2,4-$Cl_2C_6H_3$</td><td>H</td><td>CO_2Et</td><td>1.5</td><td>(73)</td></tr><tr><td>2,4-$Cl_2C_6H_3$</td><td>OMe</td><td>OMe</td><td>20</td><td>(trace)</td></tr><tr><td>3-$O_2NC_6H_4$</td><td>H</td><td>Br</td><td>8</td><td>(60)</td></tr></table></td><td>13</td></tr>
</table>



Pd cat. **7** (5%),
base (1.1 eq),
1,4-dioxane, rt

240

Ar	R^1	R^2	Base	Time (h)	
Ph	H	H	—	24	(0)
Ph	H	H	K_2CO_3	2.25	(64)
Ph	H	Me	K_2CO_3	24	(24)
Ph	H	Me	$CaCO_3$	25	(44)
Ph	H	OMe	K_2CO_3	16	(28)
Ph	Me	H	K_2CO_3	28	(53)
Ph	Me	H	$CaCO_3$	24	(38)
4-FC_6H_4	H	H	—	24	(0)
4-FC_6H_4	H	H	K_2CO_3	28	(55)
4-FC_6H_4	H	OMe	K_2CO_3	26	(91)

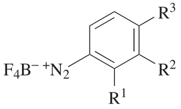
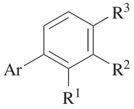
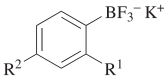
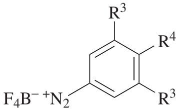
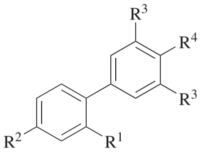


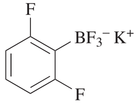
Pd cat. **8** (5%),
K_2CO_3 (1.1 eq),
1,4-dioxane, rt

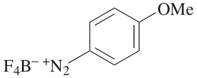
240

Ar	R^1	R^2	Time (h)	
Ph	H	H	22	(65)
Ph	H	Me	24	(53)
Ph	H	OMe	23	(54)
Ph	Me	H	24	(55)
4-FC_6H_4	H	H	24	(0)

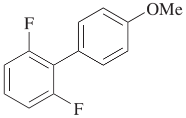
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

<table>
<tr><th>Aryltrifluoroborate</th><th>Electrophile</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_6</td><td></td><td></td><td></td><td></td></tr>
<tr><td>$ArBF_3^- K^+$</td><td> </td><td>Pd cat. **2** (5%),
1,4-dioxane</td><td>
<table>
<tr><th>Ar</th><th>R^1</th><th>R^2</th><th>R^3</th><th>Time (h)</th><th></th></tr>
<tr><td>Ph</td><td>H</td><td>H</td><td>NO_2</td><td>17</td><td>(69)</td></tr>
<tr><td>Ph</td><td>H</td><td>H</td><td>F</td><td>20</td><td>(35)</td></tr>
<tr><td>Ph</td><td>H</td><td>H</td><td>Me</td><td>19</td><td>(39)</td></tr>
<tr><td>Ph</td><td>H</td><td>H</td><td>OMe</td><td>17</td><td>(63)</td></tr>
<tr><td>Ph</td><td>H</td><td>H</td><td>*t*-Bu</td><td>16</td><td>(43)</td></tr>
<tr><td>Ph</td><td>H</td><td>Me</td><td>H</td><td>19</td><td>(30)</td></tr>
<tr><td>Ph</td><td>Me</td><td>H</td><td>H</td><td>19</td><td>(23)</td></tr>
<tr><td>4-FC_6H_4</td><td>H</td><td>H</td><td>H</td><td>17</td><td>(54)</td></tr>
<tr><td>4-FC_6H_4</td><td>H</td><td>H</td><td>OMe</td><td>17</td><td>(42)</td></tr>
</table></td><td>231</td></tr>
<tr><td> </td><td> </td><td>$Pd(OAc)_2$ (2%), *n*-PrOH,
MW, 40°, 5 min</td><td>
<table>
<tr><th>R^1</th><th>R^2</th><th>R^3</th><th>R^4</th><th></th></tr>
<tr><td>H</td><td>H</td><td>H</td><td>Me</td><td>(90)</td></tr>
<tr><td>H</td><td>H</td><td>H</td><td>OMe</td><td>(92)</td></tr>
<tr><td>H</td><td>H</td><td>Cl</td><td>H</td><td>(85)</td></tr>
<tr><td>F</td><td>H</td><td>H</td><td>Me</td><td>(87)</td></tr>
<tr><td>H</td><td>F</td><td>H</td><td>OMe</td><td>(97)</td></tr>
<tr><td>H</td><td>F</td><td>Cl</td><td>H</td><td>(99)</td></tr>
<tr><td>H</td><td>Cl</td><td>H</td><td>OMe</td><td>(86)</td></tr>
</table></td><td>241</td></tr>
</table>





Pd(OAc)$_2$ (2%), 2-PrOH,
MW, 75°, 10 min



(89)

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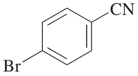
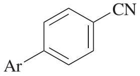
ArBF$_3^-$ K$^+$



PdCl$_2$(dppf)•CH$_2$Cl$_2$,
base (3 eq), reflux



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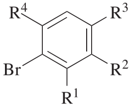
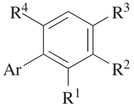
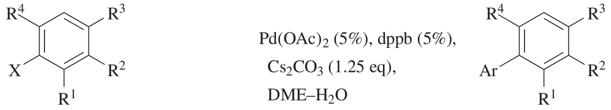
Ar	% Pd	Base	Time (h)	Solvent	
3-O$_2$NC$_6$H$_4$	0.5	Et$_3$N	12	EtOH	(89)
2,6-F$_2$C$_6$H$_3$	1	Et$_3$N	6	EtOH	(86)
2,3,4,5,6-F$_5$C$_6$	5	*i*-Pr$_2$NEt	36	MeOH–THF	(10)
2,3,4,5,6-F$_5$C$_6$	5	*i*-Pr$_2$NEt	36	THF	(38)

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$ArBF_3^- K^+$		$Pd(OAc)_2$ (x%), K_2CO_3 (3 eq), MeOH, reflux		

Ar	R^1	R^2	R^3	R^4	x	Time		Refs.
Ph	H	H	Cl	H	0.5	12 h	(75)	136
Ph	H	H	OH	H	0.5	36 h	(40)	136
Ph	H	H	NO_2	H	0.5	45 min	(>99)	136
Ph	H	H	CN	H	0.5	1 h	(87)	46
Ph	H	H	CO_2H	H	0.5	2 h	(96)	46
Ph	H	H	CF_3	H	0.5	1 h	(79)	136
Ph	H	H	OMe	H	0.5	2 h	(95)	136
Ph	H	H	CO_2H	H	0.5	2 h	(96)	46
Ph	H	H	NMe_2	H	0.5	24 h	(trace)	136
Ph	H	H	NHAc	H	0.5	18 h	(62)	136
Ph	H	H	COPh	H	0.5	45 min	(92)	136
Ph	H	CO_2Me	H	H	0.5	1 h	(87)	136
Ph	CHO	H	H	H	0.5	1 h	(89)	46
Ph	OMe	H	OMe	H	1	24 h	(50)	136
Ph	Me	H	Me	Me	2	12 h	(38)	136
Ph	Me	H	Me	Me	5	36 h	(52)	136
$4\text{-}FC_6H_4$	H	H	NO_2	H	1	2 h	(96)	136
$4\text{-}FC_6H_4$	H	H	CN	H	0.5	2 h	(96)	46

$(ArBF_3^-)\,(n\text{-}Bu_4N^+)$



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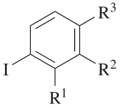
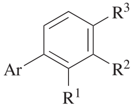
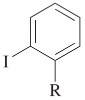
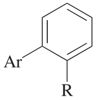
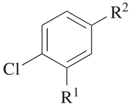
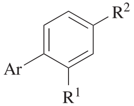
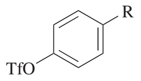
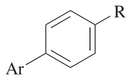
Ar	X	R^1	R^2	R^3	R^4	Time (h)	Temp (°)	
Ph	Br	H	H	NO_2	H	24	50	(79)
Ph	Br	H	H	Cl	H	12	50	(96)
Ph	Br	H	H	CN	H	12	rt	(93)
Ph	Br	H	H	OMe	H	24	50	(79)
Ph	Br	H	H	Ac	H	12	rt	(90)
Ph	Br	Me	H	Me	Me	24	50	(85)
Ph	I	H	H	H	H	12	rt	(100)
Ph	I	H	H	OMe	H	24	50	(82)
Ph	I	H	H	Ac	H	12	rt	(92)
Ph	I	H	NO_2	H	H	24	50	(76)
Ph	I	Me	H	H	H	12	rt	(97)
4-ClC_6H_4	Br	H	CHO	H	H	24	50	(60)
3-$O_2NC_6H_4$	Br	H	H	CHO	H	24	50	(78)
3-ClC_6H_4	Br	H	H	Ac	H	24	50	(92)

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)						Refs.
C_6									
$ArBF_3^- K^+$		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *i*-Pr_2NEt (3 eq), *i*-PrOH–H_2O, MW, 100°, 10 min		Ar	R^1	R^2	R^3		219
				Ph	H	H	Cl	(98)	
				Ph	H	H	F	(84)	
				Ph	H	H	OMe	(100)	
				Ph	H	H	Ac	(93)	
				Ph	H	NO_2	H	(98)	
				Ph	OMe	H	H	(100)	
				Ph	Me	H	Me	(77)	
				4-FC_6H_4	H	H	Ac	(96)	
				2,4,6-$F_3C_6H_2$	H	H	F	(50)	
		Pd/PVP (1%), K_2CO_3 (2 eq), H_2O, reflux, 4 h		Ar	R				221
				Ph	H			(91)	
				Ph	Me			(92)	
				4-BrC_6H_4	H			(93)	
				4-ClC_6H_4	H			(95)	
				4-FC_6H_4	H			(94)	
		Pd/C, TBAB (0.5 eq), NaOH (2.5 eq), H_2O, 100°, 2 h		Ar	R^1	R^2			226
				Ph	NO_2	H		(89)	
				4-FC_6H_4	H	NO_2		(98)	



Pd(OAc)$_2$ (1.2%),
MW, 95°, 15 min



Ar	R	
Ph	Ac	(90)
3-$O_2NC_6H_4$	H	(50)
4-ClC_6H_4	H	(98)
4-ClC_6H_4	Ac	(89)
4-ClC_6H_4	NO_2	(86)
4-ClC_6H_4	CN	(51)
4-FC_6H_4	CN	(99)
2,6-$F_2C_6H_3$	CN	(51)

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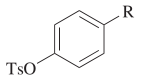
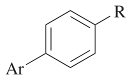


Pd(OAc)$_2$ (2%), **L2** (4%),
Et$_3$N (3 eq), EtOH,
80°, 0.5–6 h



Ar	R	
Ph	NO_2	(55)
Ph	CN	(93)
Ph	CHO	(86)
Ph	CF_3	(81)
Ph	OMe	(42)
Ph	Ac	(77)
Ph	CO_2Et	(99)
4-FC_6H_4	CN	(89)

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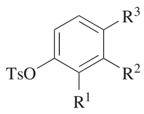
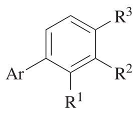


Pd(OAc)$_2$ (2%), **L2** (4%),
KOH (3 eq), MeOH,
60°, 0.5–6 h



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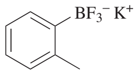
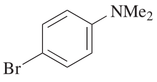
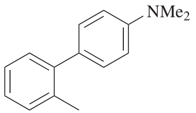
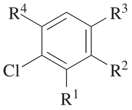
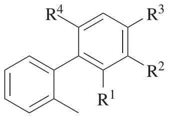
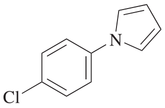
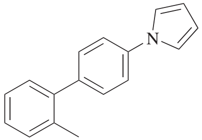
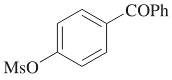
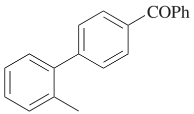
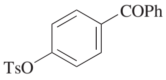
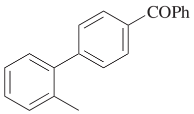
Ar	R^1	R^2	R^3	
Ph	H	H	H	(94)
Ph	H	H	Me	(90)
Ph	H	H	CHO	(trace)
Ph	H	H	CMe_2Et	(75)
Ph	Me	H	H	(82)
Ph	Me	Me	H	(80)
4-FC_6H_4	H	H	OMe	(76)

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd_2(dba)_3$ (0.5%), P(*t*-Bu)$_3$ (1.2%), THF, rt, 12 h	 (0)	57
		$Pd(OAc)_2$ (*x*%), SPhos (*y*%), K_2CO_3 (3 eq), MeOH		87

R^1	R^2	R^3	R^4	*x*	*y*	Temp (°)	Time (h)	
H	H	OMe	H	0.5	1	reflux	12	(89)
Me	H	H	Me	2	4	50	20	(92)
Me	Ph	H	H	0.5	1	reflux	12	(84)

		$Pd(OAc)_2$ (0.5%), SPhos (1%), K_2CO_3 (3 eq), MeOH, reflux, 12 h	 (96)	87
		$Pd(OAc)_2$ (2%), **L4** (2%), K_3PO_4 (1.5 eq), *t*-BuOH, 110°, 2 h	 (86)	138
		$Pd(OAc)_2$ (1%), **L4** (1%), $K_3PO_4•H_2O$ (3 eq), *t*-BuOH, 110°, 3 h	 (95)	284

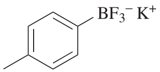
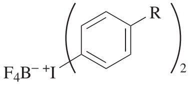
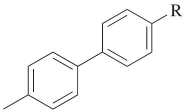
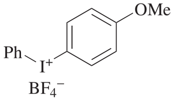
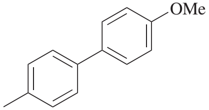
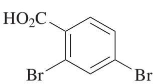
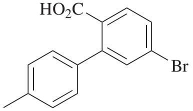
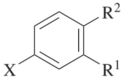
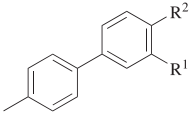
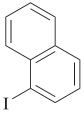
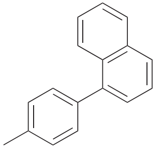
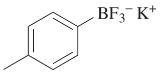
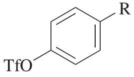
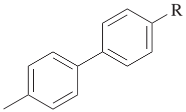
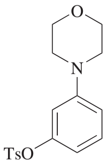
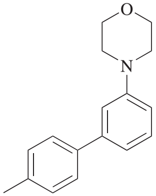
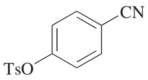
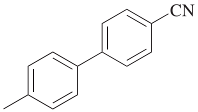
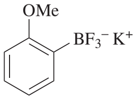
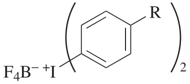
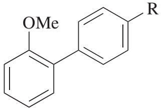
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min		R H (93) Cl (89) Me (95)	15
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min		(97)	15
		$Pd_2(dba)_3$•$CHCl_3$ (1.5%), LiOH (2.2 eq), NMP–H_2O, 65°, 36 h		(72)	242
		Pd/C (10%), K_2CO_3 (2 eq), EtOH–H_2O, 50°, 24 h		X R^1 R^2 Br H H (65) Br H NO_2 (85) Br H CN (65) Br Me H (63) I H Me (42)	227
		$PdCl_2(dppf)$•CH_2Cl_2 (2%), *i*-Pr_2NEt (3 eq), *i*-PrOH–H_2O, MW, 100°, 10 min		(85)	219

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(OAc)_2$ (1.2%), MW, 95°, 15 min	 R H (92) NO_2 (88) Me (63) CN (85) OMe (61) Ac (94)	86
		$Pd(OAc)_2$ (2%), **L2** (4%), KOH (3 eq), MeOH, 60°, 24 h	 (88)	135
		$Pd(OAc)_2$ (2%), **L2** (4%), Et_3N (3 eq), EtOH, 80°	 (98)	135
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min	 R H (87) Cl (81) Me (84)	15

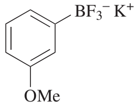
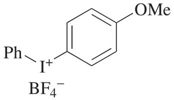
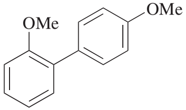
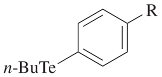
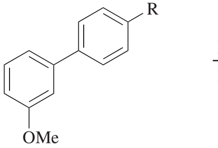
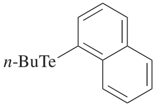
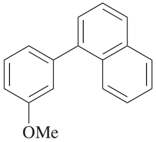
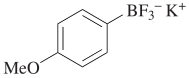
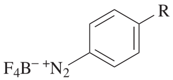
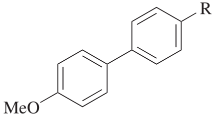
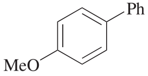
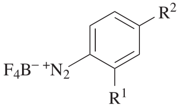
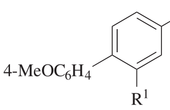
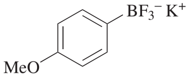
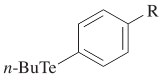
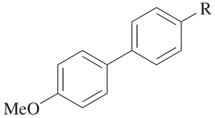
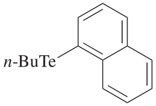
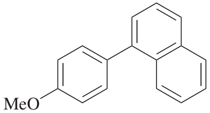
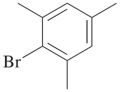
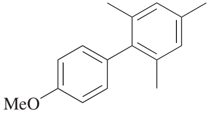
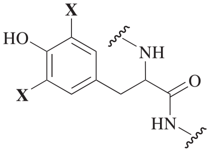
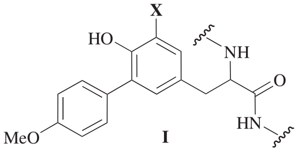
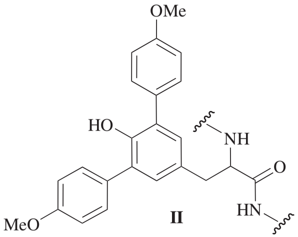
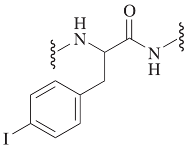
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min	 (87)	15
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux	 R H (78) Cl (80)	142
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux	 (79)	142
		Pd cat. **2** (5%), 1,4-dioxane	 R Time (h) H 19 (43) OMe 18 (40)	231
	$F_4B^{-}\ {}^{+}N_2Ph$	Pd cat. **7** (5%), K_2CO_3 (1.1 eq), 1,4-dioxane, rt, 24 h	 (85)	240
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 20°	 R^1 R^2 Time (h) H Me 4 (86) Ac H 1.7 (96)	13

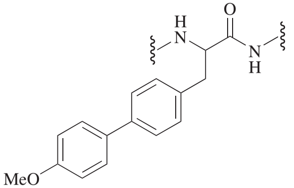
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux	 R — H (81) Cl (75)	142
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux	 (87)	142
		$Pd(OAc)_2$ (2%), PPh_3 (2%), K_2CO_3 (3 eq), MeOH, reflux, 24 h	 (52)	46
		$Pd(OAc)_2$ (10%), TPPTS (30%), K_3PO_4 (15 eq), H_2O, 50°, 24 h	 **I** +  **II**	160

Peptide (X)	**I**	**II**
Ac-Phe-3,5-diiodo-Tyr-OH	(0)	(92)
H-3,5-diiodo-Tyr-Gly-Gly-Phe-Leu-OH	(0)	(92)
H-3,5-dibromo-Tyr-Gly-Gly-Phe-Leu-OH	(0)	(0)
H-3,5-diiodo-Tyr-Gly-Gly-Phe-Met-OH	(17)	(83)
H-3,5-diiodo-Tyr-D-Ala-Phe-Gly-Tyr-Pro-Ser-NH_2	(8)	(40)

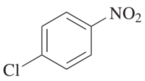


Pd(OAc)$_2$ (5%),
TPPTS (15%),
K_3PO_4 (7.5 eq), H_2O, 50°

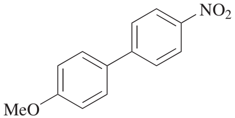


160

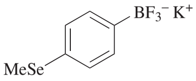
Peptide	Time (h)	
H-Tyr-Gly-Gly-4-iodo-Phe-Leu-OH	24	(26)
H-Gly-Gly-4-iodo-Phe-Leu-OH	3	(92)
For-Met-Leu-4-iodo-Phe-OH	3	(100)
H-Tyr-Gly-Gly-4-iodo-Phe-Met-OH	24	(52)
H-Tyr-D-Ala-4-iodo-Phe-Gly-Tyr-Pro-Ser-NH_2	24	(82)
H-Met-Glu-His-4-iodo-Phe-Arg-Trp-Gly-OH	24	(15)

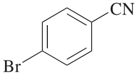


Pd/C, TBAB (0.5 eq),
NaOH (2.5 eq),
H_2O, 100°, 2 h

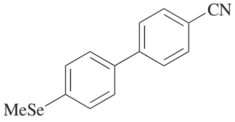


(97) 226



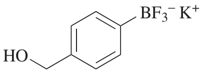
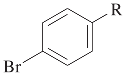
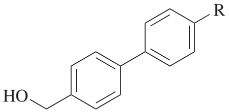
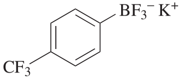
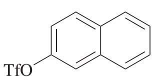
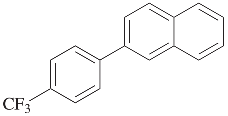
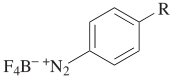
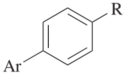


Pd(PPh$_3$)$_4$ (3%),
K_2CO_3 (3 eq),
1,4-dioxane–H_2O,
MW, 130°, 20 min



(61) 82

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(OAc)_2$ (5%), K_2CO_3 (3 eq), MeOH	 R / Time Me reflux 1 h (77) CN reflux 1 h (75) Me MW 5 min (92) CN MW 5 min (94)	222
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), $THF–H_2O$, reflux, 20 h	 (92)	134
$ArBF_3^- K^+$		$Pd_2(\mu\text{-}OAc)_2$, $(P(o\text{-}tol)_3)_2$ (5%), MeOH, 20°	 Ar / R / Time (h) $4\text{-}MeOC_6H_4$ Me 1 (83) $2\text{-}OHCC_6H_4$ F 4 (67)	13

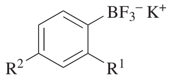
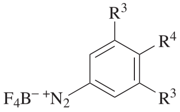
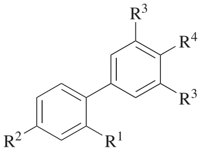
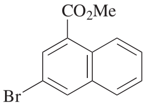
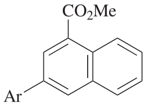
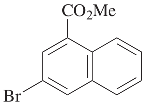
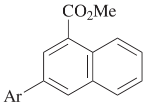
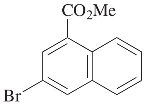
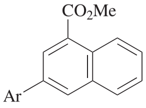
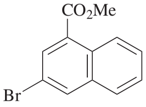
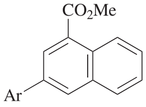
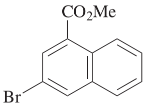
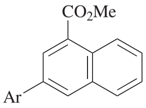
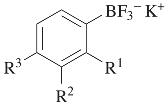
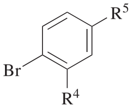
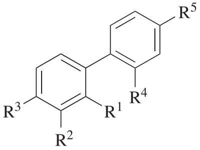
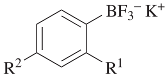
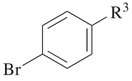
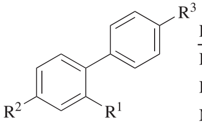
		$Pd(OAc)_2$ (2%), *n*-PrOH, MW, 40°, 5 min		R^1 R^2 R^3 R^4 H Me H Me (93) H Me H OMe (86) H Me Cl H (93) Me H H OMe (79)	241
$ArBF_3^-\ K^+$		$Pd(OAc)_2$ (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		Ar 4-$MeOC_6H_4$ (99) 4-NCC_6H_4 (81)	218
		Pd cat. **4** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		Ar 4-$MeOC_6H_4$ (99) 4-NCC_6H_4 (82)	218
		Pd(II)EnCat^{TM} (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		Ar 4-$MeOC_6H_4$ (50) 4-NCC_6H_4 (54)	218
		Pd cat. **5** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min		Ar 4-$MeOC_6H_4$ (35) 4-NCC_6H_4 (33)	218

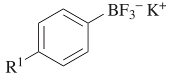
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

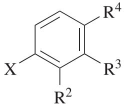
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
$ArBF_3^-\,K^+$		Pd cat. **9** (10%), K_2CO_3 (3 eq), DME–H_2O–EtOH, MW, 110°, 7 min	 Ar $4\text{-}MeOC_6H_4$ (58) $4\text{-}NCC_6H_4$ (0)	218
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux		

R^1	R^2	R^3	R^4	R^5	Time (h)		Refs.
H	H	OMe	H	CN	1	(99)	46
H	OMe	H	H	CN	3	(91)	46
Me	H	H	H	NO_2	12	(83)	136
Me	H	H	H	CN	5	(86)	46
Me	H	H	H	OMe	21	(83)	46
Me	H	H	CHO	H	12	(84)	46

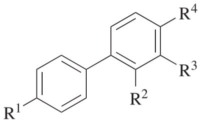
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min		214

R^1	R^2	R^3	
H	OMe	OMe	(96)
H	OMe	Me	(85)
Me	H	OMe	(82)
Me	H	Me	(85)





Pd (2.5 ppm),
Na_2CO_3 (3.7 eq),
TBAB (1 eq), $EtOH–H_2O$,
MW, 150°, 5 min



R^1	X	R^2	R^3	R^4	
Me	Br	H	H	H	(78)
Me	Br	H	H	Me	(67)
Me	Br	H	H	Ac	(82)
Me	I	H	H	H	(96)
Me	I	H	H	Me	(94)
Me	I	H	H	Ac	(95)
Me	I	H	F	H	(90)
Me	I	F	H	H	(93)
OMe	I	H	H	H	(90)

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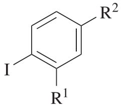
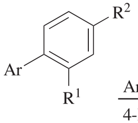
$ArBF_3^-\ K^+$



$PdCl_2(dppf)•CH_2Cl_2$ (2%),
i-Pr_2NEt (3 eq),
i-$PrOH–H_2O$,
MW, 100°, 10 min



Ar	R^1	R^2	
$4-MeC_6H_4$	H	F	(92)
$4-CF_3C_6H_4$	H	F	(98)
$4-CF_3C_6H_4$	H	Cl	(98)
$4-CF_3C_6H_4$	Me	H	(86)
$4-CF_3C_6H_4$	OMe	H	(94)

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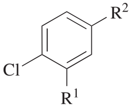
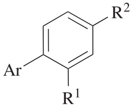
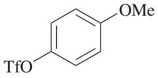
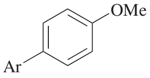
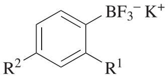
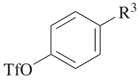
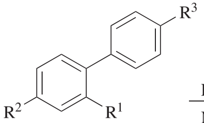
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
$ArBF_3^- K^+$		Pd cat. **6** (x%), K_2CO_3 (2 eq), TBAB (y eq), H_2O, 100°		150

x	y		Time	Ar	R^1	R^2	
0.05	0.5	—	8 h	4-$CF_3C_6H_4$	H	Ac	(78)
1	1	—	5 h	4-MeC_6H_4	CN	H	(85)
1	1	MW	20 min	4-MeC_6H_4	CN	H	(88)[a]
1	1	—	16 h	2-MeC_6H_4	CN	H	(73)
1	1	MW	20 min	2-MeC_6H_4	CN	H	(84)[a]

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 20 h	 Ar 4-MeC_6H_4 (66) 4-$CF_3C_6H_4$ (59) 4-$MeOC_6H_4$ (76)	134
		$Pd(OAc)_2$ (1.2%), MW, 95°, 15 min	 R^1 R^2 R^3 Me H Ac (85) H OMe H (95)	86

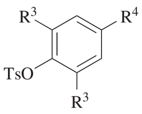
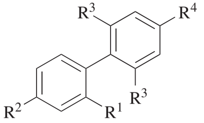
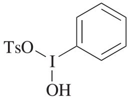
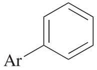
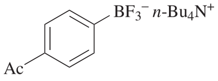
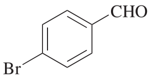
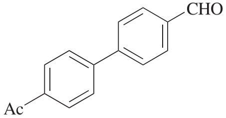
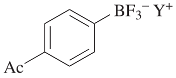
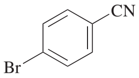
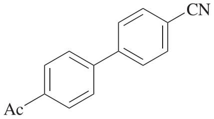
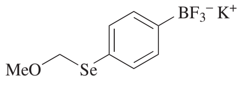
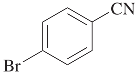
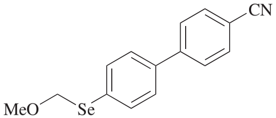
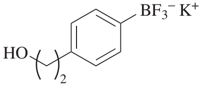
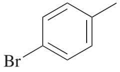
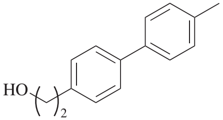
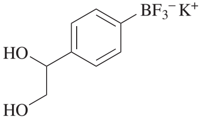
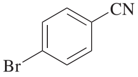
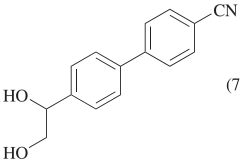
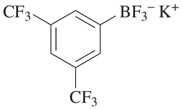
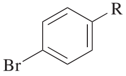
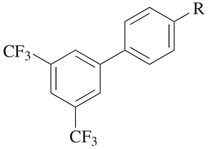
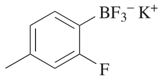
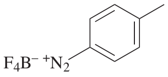
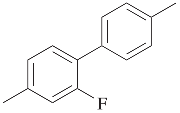
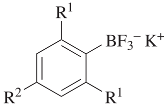
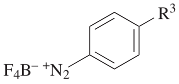
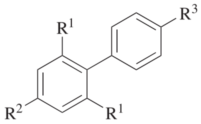
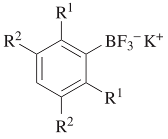
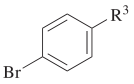
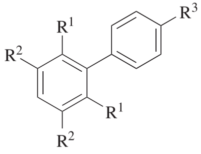
			$Pd(OAc)_2$ (2%), **L2** (4%), KOH (3 eq), MeOH, 60°, 0.5–6 h	 R^1 R^2 R^3 R^4 H Me H OMe (97) H Me H Ph (64) H Me Me H (32) H CF_3 H OMe (37) OMe H H OMe (53)	135
C_8	$ArBF_3^-\ K^+$		$Pd(OAc)_2$ (5%), DME, 60°, 30 min	 Ar 2-$MeOC_6H_4$ (87) 4-MeC_6H_4 (94)	15
			$Pd(OAc)_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O, 50°, 24 h	 (75)	12
			$Pd(OAc)_2$ (x%), PPh_3 (y%), K_2CO_3 (3 eq), MeOH, reflux, 16 h	 Y x y n-Bu_4N 5 10 (87) K 0.5 0.5 (70)	243 46

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 (77)	82
		$Pd(OAc)_2$ (5%), K_2CO_3 (3 eq), MeOH	 Time reflux 1 h (85) MW 5 min (88)	222
		$Pd(OAc)_2$ (0.6%), K_2CO_3 (3 eq), MeOH, reflux, 2 h	 (77)	244
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 R OMe (60) Me (87)	214

C_7			$Pd(OAc)_2$ (2%), *n*-PrOH, MW, 40°, 5 min	 (82)	241
			$Pd(OAc)_2$ (2%), 2-PrOH, MW, 75°, 10 min	 R^1 R^2 R^3 H Ac Me (57) H Ac OMe (51) Me H OMe (52)	241
			$PdCl_2(dppf)•CH_2Cl_2$ (*x*%), Et_3N (3 eq), EtOH, reflux		46

R^1	R^2	R^3	*x*	Time (h)	
H	CF_3	CN	0.5	12	(70)
Me	H	CN	0.5	16	(82)
Me	H	OMe	1	21	(50)

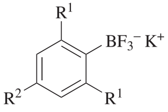
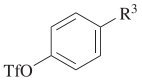
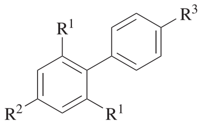
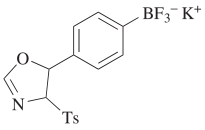
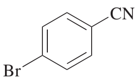
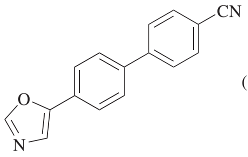
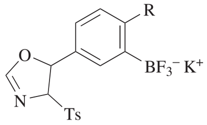
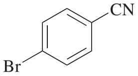
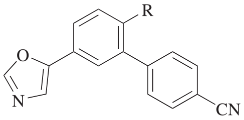
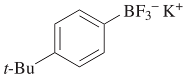
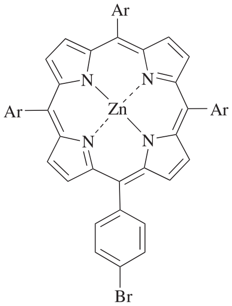
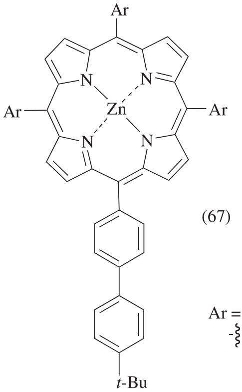
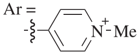
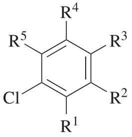
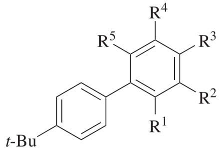
			$Pd(OAc)_2$ (1.2%), MW, 95°, 15 min	 R^1 R^2 R^3 H Ac H (60) Me H CN (56)	86
C_9					
			$Pd(OAc)_2$ (1%), DavePhos (2%), NEt_3 (3 eq), MeOH, 100°, 12 h	 (68)	245

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(OAc)_2$ (1%), DavePhos (2%), NEt_3 (3 eq), MeOH, 100°, 12 h	 R H (73) F (55)	245
C_{10}				
		$Pd(OAc)_2$, TPPTS, K_2CO_3, MeCN–H_2O, 60–70°, 12 h	 (67) 	159



$Pd(OAc)_2$ (*x*%),
SPhos (*y*%),
K_2CO_3 (3 eq), MeOH



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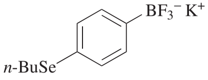
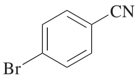
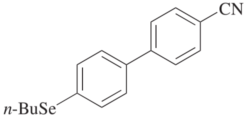
R^1	R^2	R^3	R^4	R^5	*x*	*y*	Temp (°)	Time (h)	
H	H	*n*-Bu	H	H	0.5	1	reflux	16	(90)
H	OMe	H	OMe	H	0.5	1	50	12	(93)
H	CO_2Me	H	H	H	0.5	1	50	12	(96)
Me	H	H	H	Me	1	2	50	12	(91)





$Pd(PPh_3)_4$ (3%),
K_2CO_3 (3 eq),
1,4-dioxane–H_2O,
MW, 130°, 20 min



(64)

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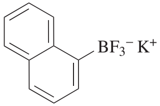
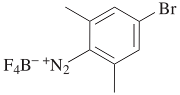
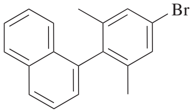




Pd catalyst (5%),
solvent, 20°



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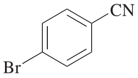
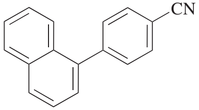
Pd cat.	Solvent	Time (h)	
$Pd(OAc)_2$	1,4-dioxane	24	(21)
$Pd_2(\mu\text{-}OAc)_2(P(o\text{-}tol)_3)_2$	MeOH	120	(10)[c]



$Pd(OAc)_2$ (0.5%),
K_2CO_3 (3 eq),
MeOH, reflux, 9 h



(60)

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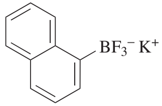
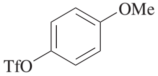
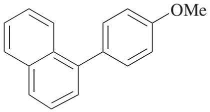
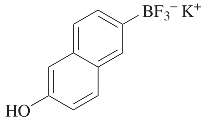
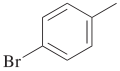
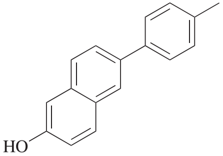
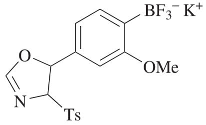
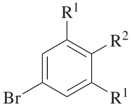
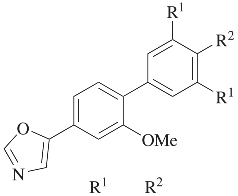
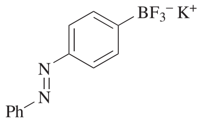
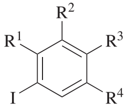
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

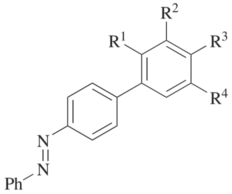
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 20 h	 (71)	134
		$Pd(OAc)_2$ (5%), K_2CO_3 (3 eq), MeOH Temp Time reflux 1 h (67) MW 5 min (83)		222
		$Pd(OAc)_2$ (1%), DavePhos (2%), NEt_3 (3 eq), MeOH, 100°, 12 h	 R^1 R^2 H CN (51) H OMe (51) OMe H (47)	245

C_{12}





$PdCl_2(dppf)\bullet CH_2Cl_2$ (1%), base (3 eq), MeOH, 65°



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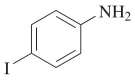
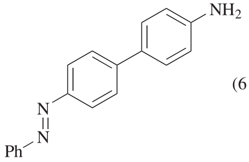
R^1	R^2	R^3	R^4	Base	Time (h)	
H	OMe	OMe	OMe	Cs_2CO_3	3.5	(72)
OH	OMe	H	CHO	Cs_2CO_3	4.7	(49)
H	H	Ac	H	K_2CO_3	2	(65)
H	H	NO_2	H	Cs_2CO_3	3.5	(66)
H	H	F	H	Cs_2CO_3	2	(47)
H	H	CH_2OH	H	*i*-Pr_2NEt	2	(61)



$Pd(OAc)_2$, PPh_3, K_2CO_3 (3 eq), MeOH, 65°, 14 h



(61)

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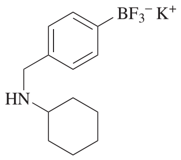
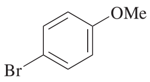
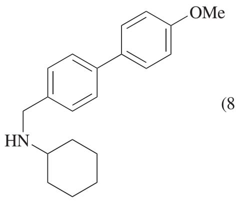
C_{13}





$Pd(OAc)_2$ (3%), K_2CO_3 (3 eq), MeOH, 75°, 3 h



(82)

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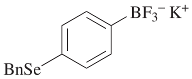
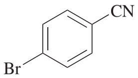
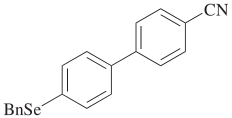
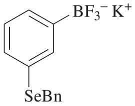
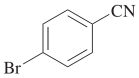
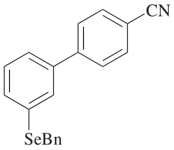
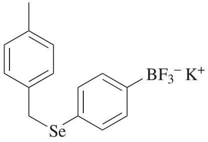
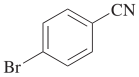
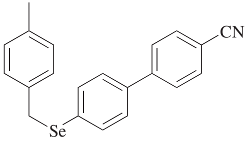
TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		Pd source (3%), base (3 eq), 1,4-dioxane–H_2O, MW	 Pd Source / Base / Temp (°) / Time $Pd(PPh_3)_4$ / K_2CO_3 / 100 / 1 h / (42) $Pd(PPh_3)_4$ / K_2CO_3 / 130 / 20 min / (87) $Pd(OAc)_2$ / Cs_2CO_3 / 130 / 30 min / (76) $PdCl_2(dppf)$ / Cs_2CO_3 / 130 / 30 min / (81)	82
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 (84)	82
C_{14}				
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 (87)	82

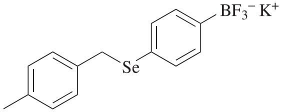
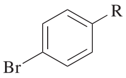
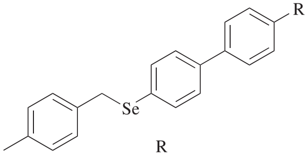
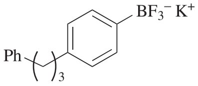
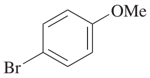
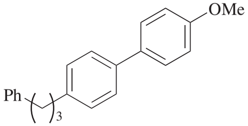
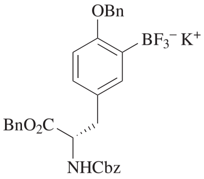
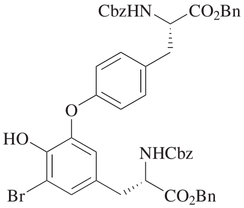
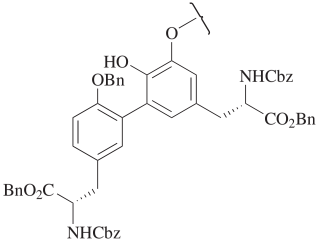
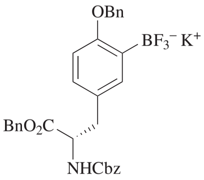
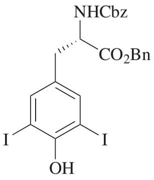
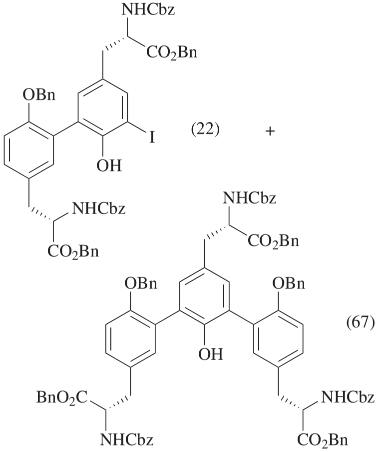
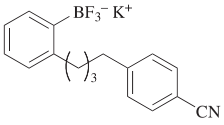
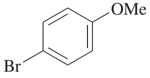
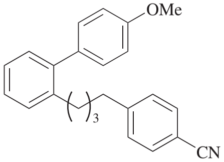
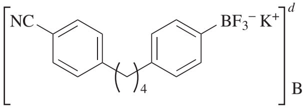
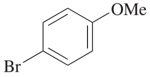
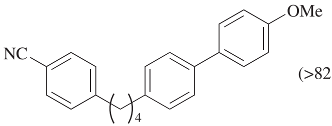
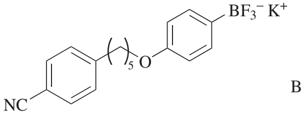
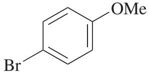
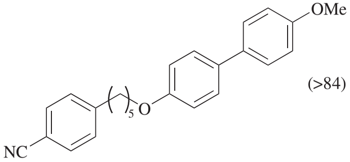
			Pd(PPh$_3$)$_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 R CHO (80) CF_3 (54)	82
C_{15}					
			Pd(OAc)$_2$ (0.5%), K_2CO_3 (3 eq), MeOH	 (>81)	225
C_{16}					
			PdCl$_2$(dppf)•CH_2Cl_2 (10%), Et_3N (6 eq), *i*-PrOH–H_2O, reflux, 48 h	 (32)	84

TABLE 1A. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}				
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (8%), K_2CO_3 (2.9 eq), $THF–H_2O$, reflux, 26 h	 (22) + (67)	84
C_{17}				
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, 65°, 2 h	 (>70)	225
[d]		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, 65°, 2 h	 (>82)	225

C_{18}						
			$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, 65°, 2 h		(>84)	225

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[a] The yield of the crude product was determined by ^1H NMR.

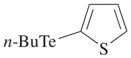
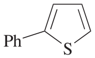
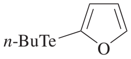
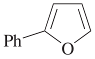
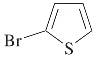
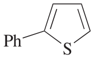
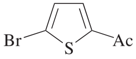
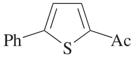
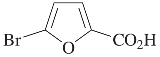
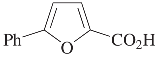
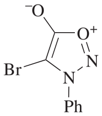
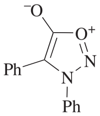
[b] The yield of the crude product was determined by ^{19}F NMR.

[c] The yield of the product was determined by GC analysis.

[d] The trifluoroborate derivative comes from the hydroboration/cross-coupling reaction of the corresponding 1,2-dibora species.

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^- K^+$		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux, 90 min	 (46)	142
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux, 90 min	 (63)	142
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 (78)	214
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 50 min	 (93)	46
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq) Solvent / Temp / Time (h) MeOH / reflux / 8 / (49) H_2O / 65° / 6 / (67)		46
		$PdCl_2(PPh_3)_2$ (5%), K_3PO_4 (3 eq), DME–H_2O, MW, 130°, 0.5 h	 (81)	247

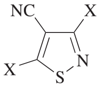
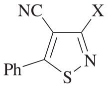
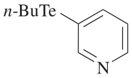
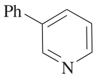
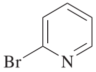
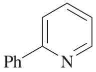
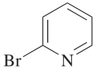
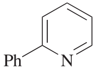
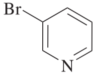
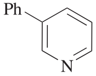
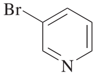
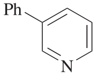
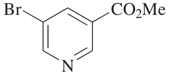
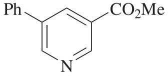
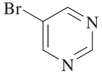
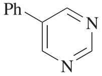
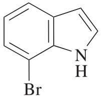
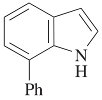
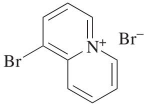
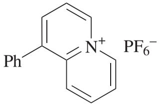
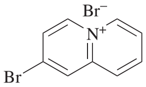
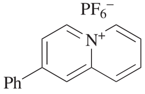
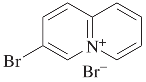
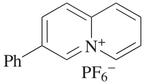
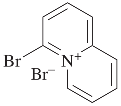
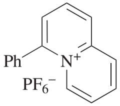
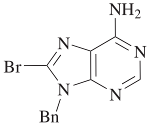
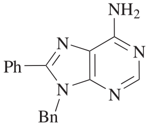
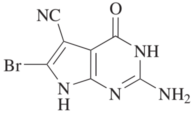
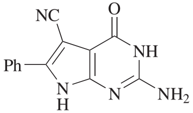
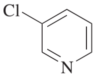
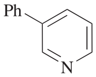
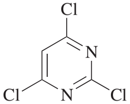
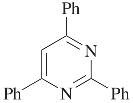
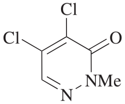
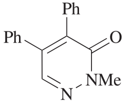
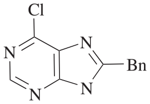
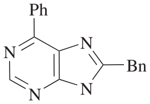
		Pd(OAc)$_2$ (5%), K_2CO_3 (1 eq), 18-crown-6 (0.5 eq), toluene, 110°		X Time (h) Br 18 (99) Cl 2 (99)	229
		Pd(PPh$_3$)$_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux		(65)	142
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min		(11)	214
		Pd(OAc)$_2$ (1%), K_2CO_3 (3 eq), MeOH, reflux, 5 h		(70)	46
		Pd(OAc)$_2$ (1%), K_2CO_3 (3 eq), MeOH, reflux, 2 h		(90)	46
($PhBF_3^-$) (n-Bu_4N^+)		Pd(OAc)$_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O, 50°, 24 h		(93)	12
$PhBF_3^-$ K^+		PdCl$_2$(dppf)•CH_2Cl_2 (5%), K_3PO_4 (4 eq), DMF–THF, 70°, 6 h		(85)	248
		Pd(OAc)$_2$ (1%), K_2CO_3 (3 eq), MeOH, reflux, 5 h		(92)	46

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^- K^+$		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 12 h	 (44)	46
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (93)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (76)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (74)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (24)	122
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 (96)	104

	$PdCl_2(PPh_3)_2$ (5%), *t*-$BuNH_2$ (3 eq), 2-propanol–H_2O, 85°, 4 d		(92)	249
	Pd cat. **6** (1%), K_2CO_3 (2 eq), TBAB (1 eq), H_2O, 100°		Time — 16 h (73) MW 20 min (68)	150
	Pd cat. **6** (1%), K_2CO_3 (2 eq), TBAB (1 eq), H_2O, 100°		Time — 8 h (79) MW 15 min (76)	150
	Pd cat. **6** (1%), K_2CO_3 (2 eq), TBAB (1 eq), H_2O, 100°		Time — 8 h (74) MW 15 min (82)	150
	$Pd(PPh_3)_4$ (2%), base (3 eq)			104

Base	Solvent		Temp (°)	Time	
K_2CO_3	THF–H_2O	—	80	18 h	(88)
Na_2CO_3	THF–H_2O	—	80	18 h	(73)
K_2CO_3	MeCN–H_2O	MW	150	5 min	(95)

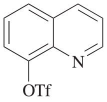
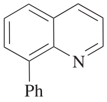
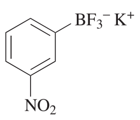
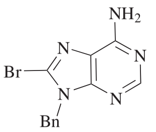
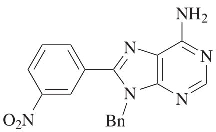
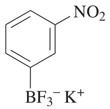
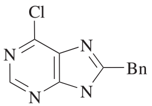
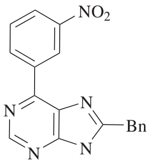
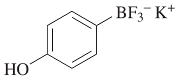
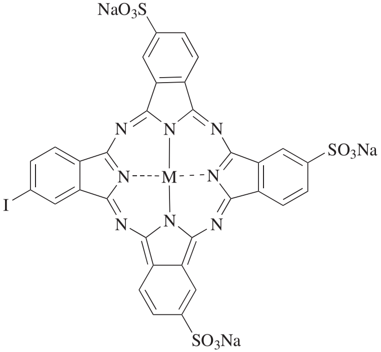
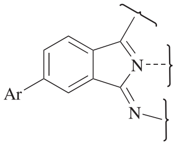
	$Pd(OAc)_2$ (5%), PCy_3(10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 24 h		(81)	134

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(PPh_3)_4$ (*x*%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 *x* 2 (53) 4 (90)	104
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 (79)	104
		$Pd(OAc)_2$, TXPTS, Na_2CO_3, MeCN–H_2O	 (—) Ar = 4-HOC_6H_4 M = GaOH	250

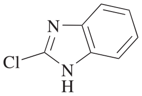
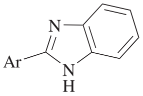
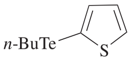
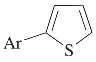
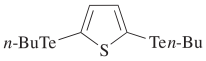
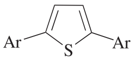
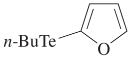
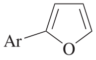
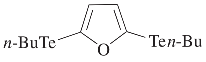
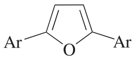
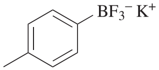
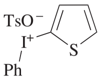
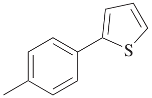
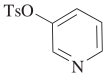
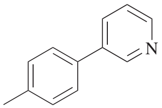
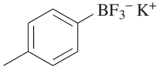
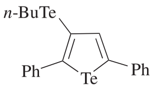
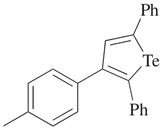
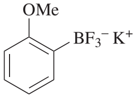
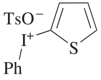
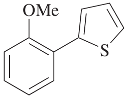
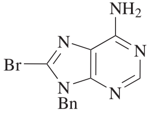
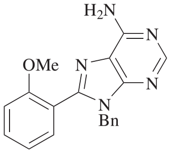
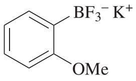
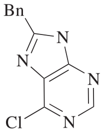
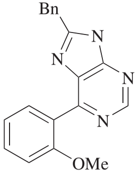
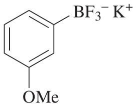
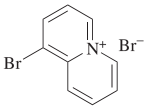
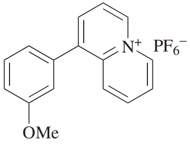
$ArBF_3^- K^+$		$PdCl_2(PPh_3)_2$ (10%), K_2CO_3, MeCN, MW, 150°, 30 min		Ar $4\text{-}ClC_6H_4$ (79) $4\text{-}FC_6H_4$ (68) $4\text{-}HOC_6H_4$ (0)	223
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h		Ar Ph (55) $3\text{-}H_2NC_6H_4$ (71) $4\text{-}FC_6H_4$ (56)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 2 h		Ar Ph (45) $3\text{-}H_2NC_6H_4$ (50) $4\text{-}FC_6H_4$ (32)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h		Ar Ph (68) $3\text{-}H_2NC_6H_4$ (50) $4\text{-}FC_6H_4$ (30)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h		Ar Ph (73) $3\text{-}H_2NC_6H_4$ (35) $4\text{-}FC_6H_4$ (55)	143
C_7					
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min		(91)	15
		$Pd(OAc)_2$ (2%), **L2** (4%), Et_3N (3 eq), EtOH, 80°, 5 h		(37)	135

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
		$Pd(PPh_3)_4$, Et_3N (3 eq), Ag_2O, MeOH, reflux		(86)	139
		$Pd(OAc)_2$ (5%), DME, 60°, 30 min		(83)	15
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(96)	104
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(94)	104
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(93)	122

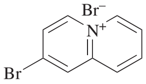
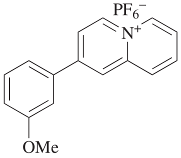
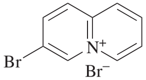
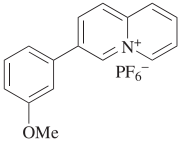
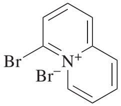
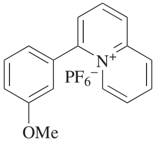
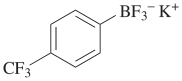
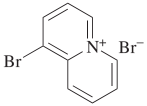
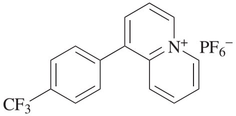
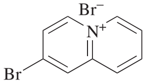
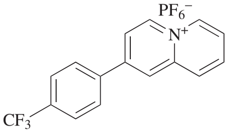
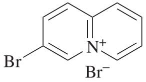
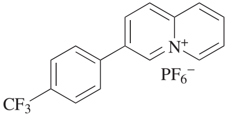
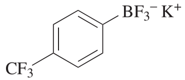
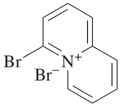
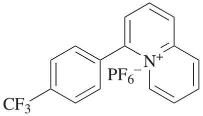
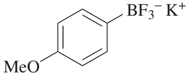
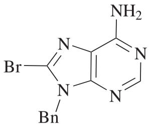
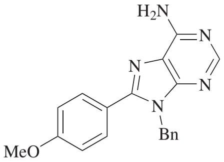
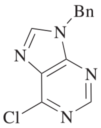
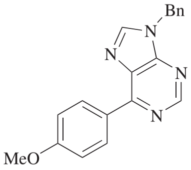
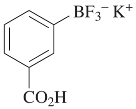
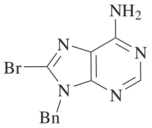
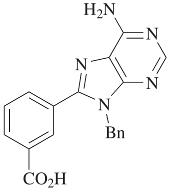
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(71)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(77)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(63)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(91)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(43)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(54)	122

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(40)	122
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(97)	104
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(95)	104
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(99)	104

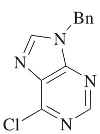
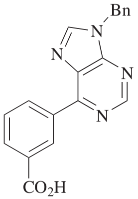
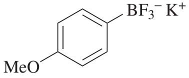
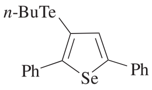
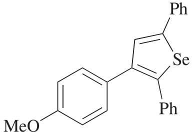
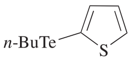
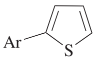
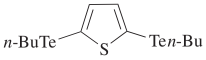
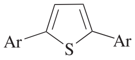
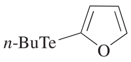
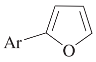
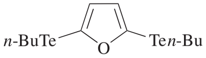
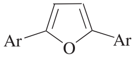
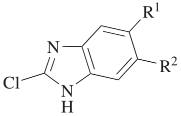
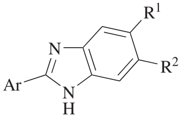
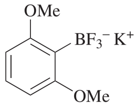
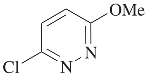
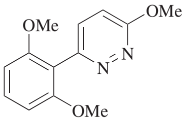
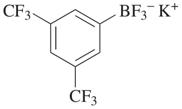
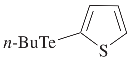
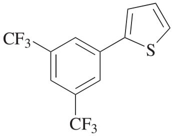
		Pd(PPh$_3$)$_4$ (2%), K$_2$CO$_3$ (3 eq), MeCN–H$_2$O, MW, 150°, 5 min	 (71)	104
		Pd(acac)$_2$ (10%), Et$_3$N, CuI (20%), MeOH, reflux, 4 h	 (68)	141
ArBF$_3^-$ K$^+$		Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h	 Ar 4-MeC$_6$H$_4$ (64) 4-MeOC$_6$H$_4$ (60) 4-HO$_2$CC$_6$H$_4$ (0)	143
		Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h	 Ar 4-MeC$_6$H$_4$ (15) 4-MeOC$_6$H$_4$ (55) 4-HO$_2$CC$_6$H$_4$ (0)	143
		Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h	 Ar 4-MeC$_6$H$_4$ (55) 4-MeOC$_6$H$_4$ (65) 4-HO$_2$CC$_6$H$_4$ (0)	143
		Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 2 h	 Ar 4-MeC$_6$H$_4$ (60) 4-MeOC$_6$H$_4$ (55) 4-HO$_2$CC$_6$H$_4$ (0)	143

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
$ArBF_3^- K^+$		$PdCl_2(PPh_3)_2$ (10%), K_2CO_3, MeCN, MW, 150°, 30 min		223

Ar	R^1	R^2	
$4-MeOC_6H_4$	H	H	(86)
$3-MeOC_6H_4$	H	H	(88)
$2-MeOC_6H_4$	H	H	(77)
$2-MeC_6H_4$	H	H	(72)
$4-CNC_6H_4$	H	H	(90)
$4-MeOC_6H_4$	F	H	(20)
$4-MeOC_6H_4$	OMe	H	(59)
$4-MeOC_6H_4$	CF_3	H	(69)
$4-MeOC_6H_4$	Me	Me	(69)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		PEPPSI complex (2%), K_2CO_3 (3 eq), MeOH, 6 h	 (92)	235
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143

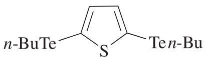
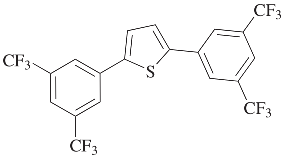
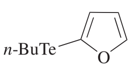
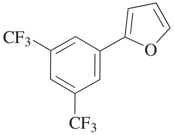
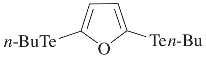
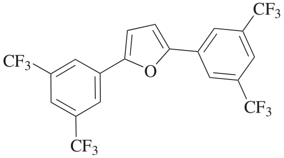
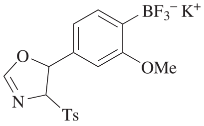
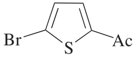
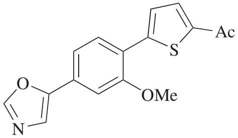
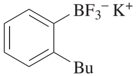
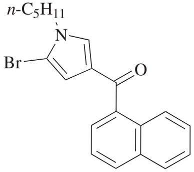
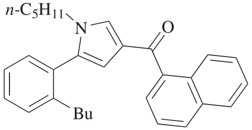
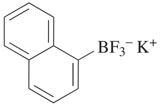
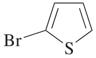
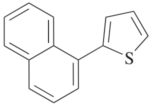
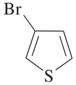
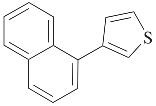
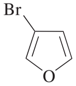
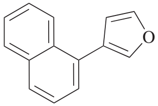
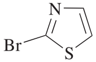
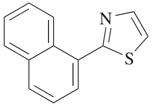
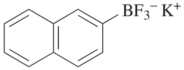
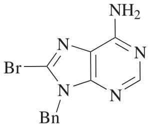
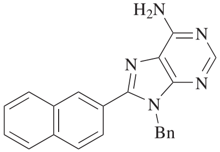
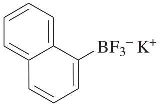
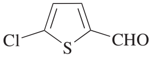
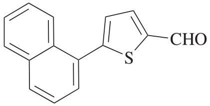
			Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h		(0)	143
			Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h		(0)	143
			Pd(OAc)$_2$ (10%), dppf (20%), Ag$_2$O (2 eq), MeOH, rt, 1.5 h		(0)	143
C$_{10}$			Pd(OAc)$_2$ (1%), DavePhos (2%), NEt$_3$ (3 eq), MeOH, 100°, 12 h		(44)	245
			Pd(PPh$_3$)$_4$, K$_2$CO$_3$, n-Bu$_4$NBr, toluene–H$_2$O, reflux, 24 h		(76)	228

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), K_2CO_3 (3 eq), EtOH, reflux, 13 h	 (83)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), K_2CO_3 (3 eq), EtOH, reflux, 13 h	 (72)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), K_2CO_3 (3 eq), EtOH, reflux, 9 h	 (68)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), K_2CO_3 (3 eq), EtOH, reflux, 13 h	 (80)	46
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 (97)	104
		$Pd(OAc)_2$ (1%), SPhos (2%), K_2CO_3 (3 eq), MeOH, reflux, 16 h	 (85)	87

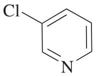
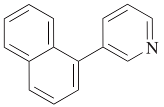
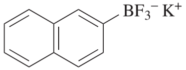
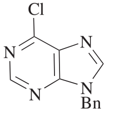
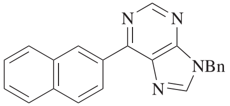
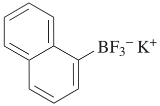
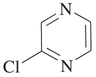
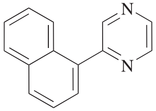
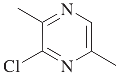
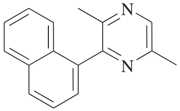
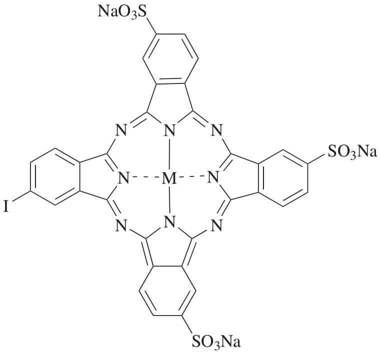
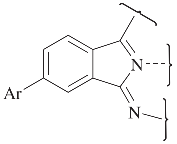
		$Pd(OAc)_2$ (0.5%), SPhos (1%), K_2CO_3 (3 eq), MeOH, reflux, 16 h	 (98)	87
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min	 (94)	104
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), K_2CO_3 (3 eq), EtOH, reflux, 9 h	 (85)	46
		$Pd(OAc)_2$ (0.5%), SPhos (1%), K_2CO_3 (3 eq), MeOH, 40°, 16 h	 (86)	87
C_{11}				
$ArBF_3^-\ K^+$		$Pd(OAc)_2$, TXPTS, Na_2CO_3, $MeCN–H_2O$	 Ar = 4-(*trans*-1-pentenyl)-C_6H_4 M = GaOH (—)	250

TABLE 1B. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

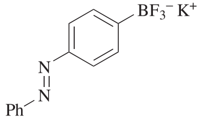
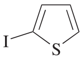
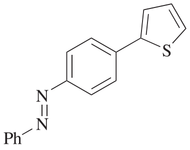
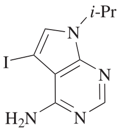
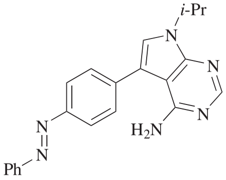
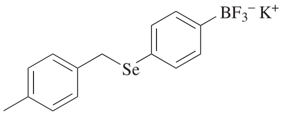
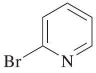
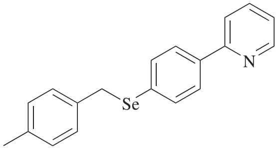
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}				
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), K_2CO_3 (3 eq), MeOH, 65°, 2 h	 (61)	83
		$PdCl_2(dppf)•CH_2Cl_2$, *i*-Pr_2NEt, EtOH, reflux	 (59)	83
C_{14}				
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 (91)	82

TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

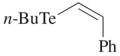
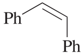
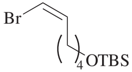
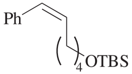
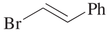
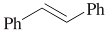
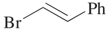
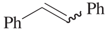
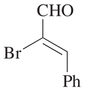
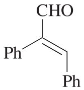
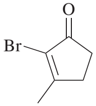
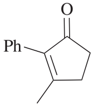
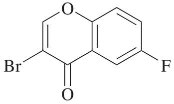
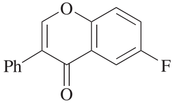
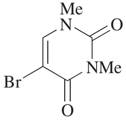
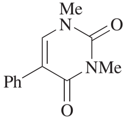
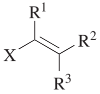
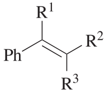
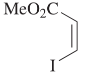
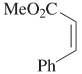
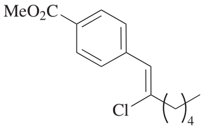
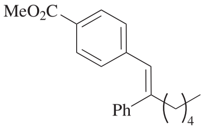
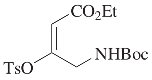
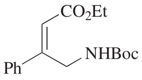
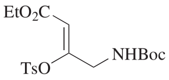
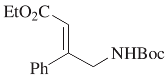
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^- K^+$		Pd source (x%), additive (2 eq), MeOH, rt, ultrasound, 40 min	 Pd Source, x, Additive $Pd(acac)_2$, 10, Ag_2O (10) $Pd(PPh_3)_4$, 10, Ag_2O (79) $Pd(PPh_3)_4$, 10, CuI (0) $Pd(PPh_3)_4$, 8, Ag_2O (82)	69
		$Pd(PPh_3)_4$ (x%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°	 x, Time 1.2, 5 h (92) 2, 35 min (97)	66
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 3 h	 (70)	136
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 (75) (Z)/(E) = 10:90	214
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 30 min	 (94)	66
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 1.8 h	 (87)	66
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 1 h	 (87)	66

TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$PhBF_3^- K^+$		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 3 h	 (88)	66
$(PhBF_3^-)$ $(n\text{-}Bu_4N^+)$		$Pd(OAc)_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O X R^1 R^2 R^3 Temp (°) Time (h) Br Me Me Me rt 12 I H H CO_2Et 50 24	 (91) (55)	12
$PhBF_3^- K^+$		$Pd(OAc)_2$ (4%), PPh_3 (9%), NaOH (4.7 eq), THF, 60°, 4 h	 (25)	67
		$Pd_2(dba)_3$ (2.5%), RuPhos (10%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 36 h	 (87)	148
		$Pd(PPh_3)_2Cl_2$ (5%), aq Na_2CO_3 (3.5 eq), THF, 60°	 (78)	68
		$Pd(PPh_3)_2Cl_2$ (5%), aq Na_2CO_3 (3.5 eq), THF, 60°	 (81)	68

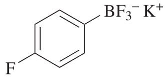
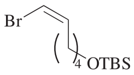
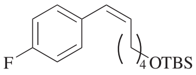
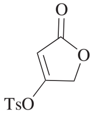
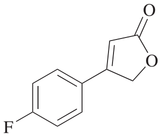
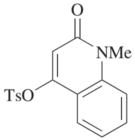
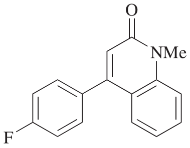
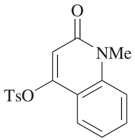
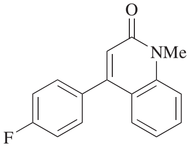
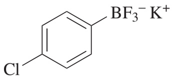
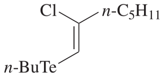
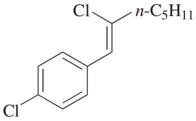
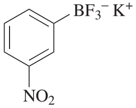
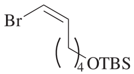
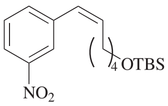
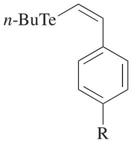
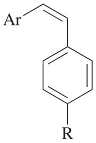
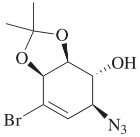
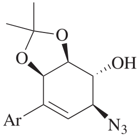
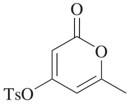
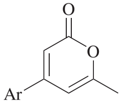
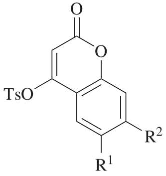
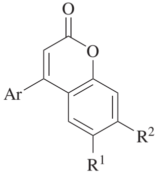
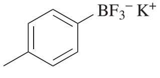
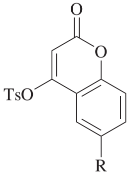
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 55 min		(95)	66
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h		(64)	251
		$Pd(PPh_3)_4$ (5%), Cs_2CO_3 (8 eq), toluene, 80°, 12 h		(48)	252
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h		(46)	251
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), Ag_2O (1 eq), MeOH, ultrasound, 60 min		(69)	224
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 55 min		(90)	66

TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

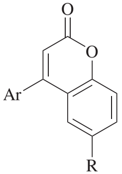
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
$ArBF_3^- K^+$		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), MeOH, rt, ultrasound	 Ar R Ph Me (76) Ph Br (78) 4-ClC_6H_4 H (70)	69
		$Pd(PPh_3)_4$ (6%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°	 Ar Time (h) Ph 2 (64) 4-FC_6H_4 4.5 (62)	161
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h	 Ar Ph (89) 4-FC_6H_4 (89)	251
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h	 Ar R^1 R^2 Ph H H (61) Ph F H (62) 4-FC_6H_4 H H (71) 4-FC_6H_4 F H (94) 4-FC_6H_4 Cl H (84) 4-FC_6H_4 Me H (75) 4-FC_6H_4 Me Me (63)	251

C_7



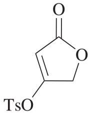


$Pd(PPh_3)_4$ (5%),
Cs_2CO_3 (8 eq),
toluene, 80°, 12 h

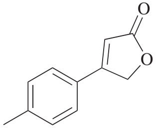


Ar	R	
Ph	H	(86)
Ph	Cl	(46)
Ph	F	(61)
Ph	Me	(58)
4-FC_6H_4	H	(80)
4-FC_6H_4	Cl	(92)
4-FC_6H_4	F	(86)
4-FC_6H_4	Me	(89)

252



$RhCl(PPh_3)_3$ (2%), dppf (2%),
K_2HPO_4 (4 eq),
toluene, 80°, 12 h



(66)

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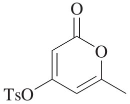
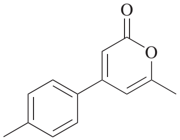
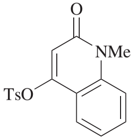


$RhCl(PPh_3)_3$ (2%), dppf (2%),
K_2HPO_4 (4 eq),
toluene, 80°, 12 h

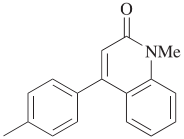


(99)

251



$Pd(PPh_3)_4$ (5%),
Cs_2CO_3 (8 eq),
toluene, 80°, 12 h



(68)

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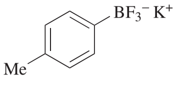
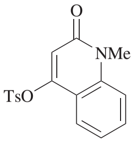
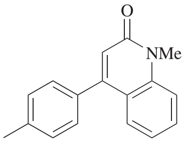
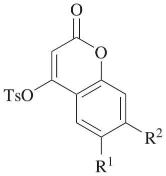
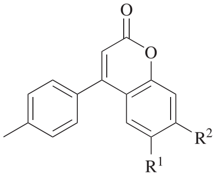
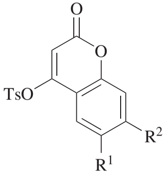
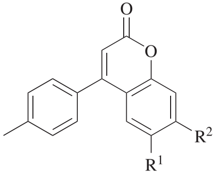
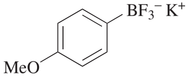
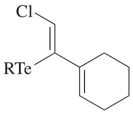
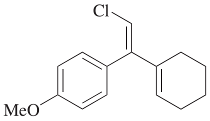
TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h		(42)	251
		$Pd(PPh_3)_4$ (5%), Cs_2CO_3 (8 eq), toluene, 80°, 12 h		R^1 R^2 H H (89) Cl H (87) F H (77) Me H (85) Me Me (86)	252
		$RhCl(PPh_3)_3$ (2%), dppf (2%), K_2HPO_4 (4 eq), toluene, 80°, 12 h		R^1 R^2 H H (75) Cl H (69) F H (92) Me H (67) Me Me (54)	251
		$Pd(PPh_3)_4$ (10%), Et_3N, Ag_2O, MeOH, ultrasound, 20 min		R *n*-Bu (85) Ph (72) 4-MeC_6H_4 (65)	224

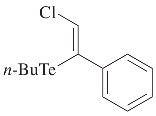
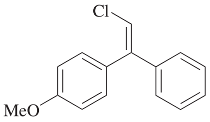
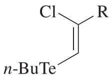
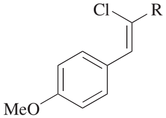
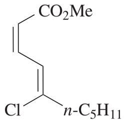
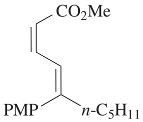
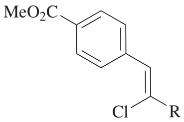
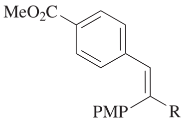
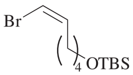
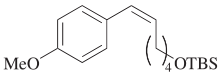
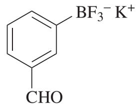
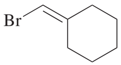
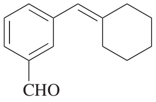
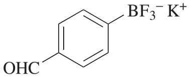
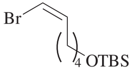
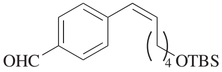
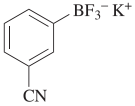
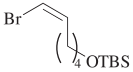
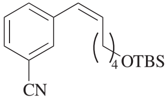
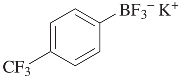
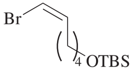
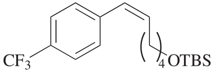
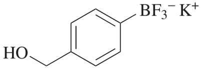
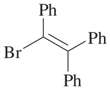
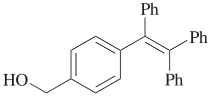
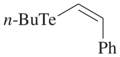
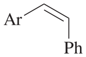
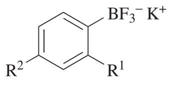
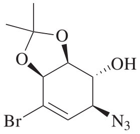
		Pd source (10%), Et$_3$N, Ag$_2$O, MeOH, ultrasound, 20 min	 Pd Source Pd$_2$(dba)$_3$ (40) Pd(OAc)$_2$ (44) Pd(PPh$_3$)$_4$ (60)	224
		Pd(PPh$_3$)$_4$ (10%), Et$_3$N (2 eq), Ag$_2$O (1 eq), MeOH, ultrasound	 R — Time (min) *n*-C$_5$H$_{11}$ 30 (82) Pr 60 (58) CH$_2$OMe 40 (73) C(Me)=CH$_2$ 40 (82) *t*-Bu 60 (74) Ph 20 (80)	224
		Pd$_2$(dba)$_3$ (2.5%), RuPhos (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 80°, 12–36 h	 (99)	148
		Pd$_2$(dba)$_3$ (2.5%), RuPhos (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 80°	 R *n*-C$_5$H$_{11}$ (89) Ph (84)	148
		Pd(PPh$_3$)$_4$ (2%), K$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 40 min	 (97)	66
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), K$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 1 h	 (85)	66

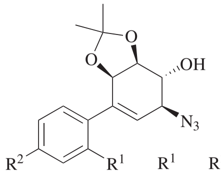
TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 3.5 h	 (89)	66
		$PdCl_2(dppf)•CH_2Cl_2$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 55°, 7.5 h	 (86)	66
		$Pd(PPh_3)_4$ (4.5%), P(*t*-Bu)$_3$ (9%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 3 h	 (89)	66
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH	 — Temp Time — reflux 1 h (75) MW — 5 min (94)	222
$ArBF_3^-\ K^+$		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), MeOH, rt, ultrasound, 40 min	 Ar 4-$MeOC_6H_4$ (60) 4-MeC_6H_4 (78) 2-MeC_6H_4 (62)	69



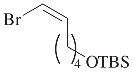


Pd(PPh_3)$_4$ (6%),
Cs_2CO_3 (3 eq),
toluene–H_2O, 90°

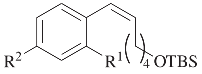


R^1	R^2	Time (h)	
H	Me	1.7	(70)
H	OMe	2	(71)
H	CF_3	6.5	(57)
H	CHO	3	(45)
H	CO_2H	9	(0)
Me	H	8	(60)

161

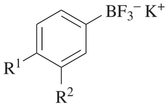


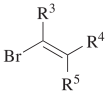
Pd(PPh_3)$_4$ (2%),
Cs_2CO_3 (3 eq),
toluene–H_2O, 90°



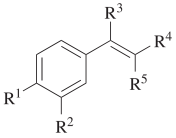
R^1	R^2	Time	
H	Me	25 min	(93)
Me	H	1.5 h	(91)

66





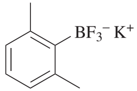
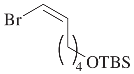
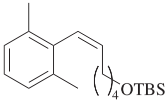
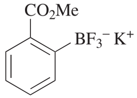
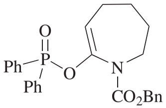
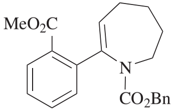
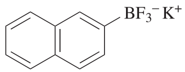
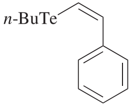
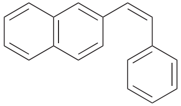
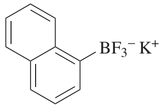
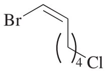
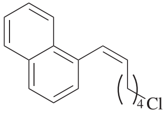
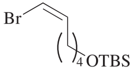
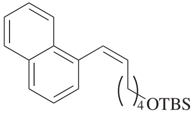
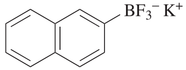
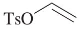
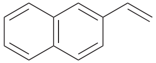
$PdCl_2$(dppf)•CH_2Cl_2 (2%),
K_2CO_3 (3 eq),
toluene–H_2O, 90°



R^1	R^2	R^3	R^4	R^5	Time (h)	
H	CHO	H	Me	Me	1.5	(96)
CHO	H	Me	Me	Me	2	(94)
CHO	H	Ph	H	H	3	(89)

66

TABLE 1C. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		Pd(PPh$_3$)$_4$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 2.8 h		(82)	66
		Pd(PPh$_3$)$_4$ (5%), $NaHCO_3$ (3 eq), DME–H_2O, 85°		(58)	146
C_{10}					
		Pd(PPh$_3$)$_4$ (8%), Ag_2O (2 eq), MeOH, ultrasound, rt		(70)	69
		Pd(PPh$_3$)$_4$ (2%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 1 h		(94)	66
		Pd(PPh$_3$)$_4$ (2%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 50 min		(>99)	66
		SK-CC02-A (5%), K_3PO_4 (2.7 eq), dioxane–H_2O, 100°		(55)	253

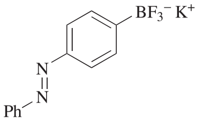
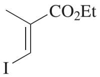
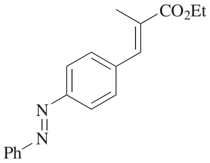
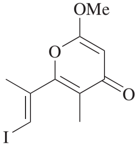
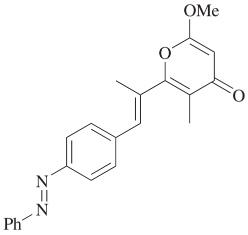
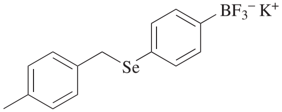
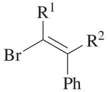
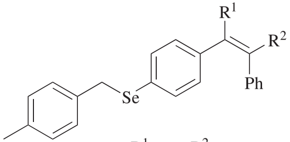
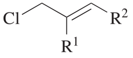
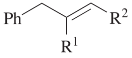
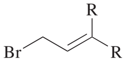
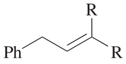
C_{12}				
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), Cs_2CO_3 (3 eq), MeOH, 65°, 4.7 h	 (41)	83
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), K_2CO_3 (3 eq), MeOH, 65°, 17 h	 (60)	83
C_{14}				
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), 1,4-dioxane–H_2O, MW, 130°, 20 min	 R^1 R^2 CHO H (74) Ph Ph (66)	82

TABLE 1D. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALLYLIC AND BENZYLIC ELECTROPHILES

<table>
<tr><th>Aryltrifluoroborate</th><th>Electrophile</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_6</td><td></td><td></td><td></td><td></td></tr>
<tr><td>$PhBF_3^- K^+$</td><td></td><td>Pd cat. **6** (0.1%),
KOH (2 eq),
TBAB (0.5 eq), acetone–H_2O</td><td>
<table>
<tr><th>R^1</th><th>R^2</th><th></th><th>Temp (°)</th><th>Time</th><th></th></tr>
<tr><td>H</td><td>H</td><td>—</td><td>rt</td><td>4 h</td><td>(72)</td></tr>
<tr><td>H</td><td>H</td><td>—</td><td>50</td><td>1.5 h</td><td>(96)[a]</td></tr>
<tr><td>H</td><td>Ph</td><td>—</td><td>rt</td><td>7 h</td><td>(69)</td></tr>
<tr><td>H</td><td>Ph</td><td>—</td><td>50</td><td>1 h</td><td>(81)</td></tr>
<tr><td>H</td><td>Ph</td><td>MW</td><td>50</td><td>10 min</td><td>(96)[a]</td></tr>
<tr><td>Cl</td><td>H</td><td>—</td><td>rt</td><td>14 h</td><td>(76)[a]</td></tr>
<tr><td>Cl</td><td>H</td><td>—</td><td>50</td><td>2 h</td><td>(98)[a]</td></tr>
<tr><td>Me</td><td>H</td><td>—</td><td>rt</td><td>14 h</td><td>(41)</td></tr>
<tr><td>Me</td><td>H</td><td>—</td><td>50</td><td>2 h</td><td>(65)</td></tr>
</table></td><td>150</td></tr>
<tr><td></td><td></td><td>$Pd(OAc)_2$ (5%),
1,4-dioxane, 100°</td><td>
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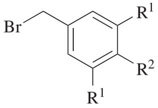
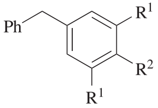
<tr><th>R</th><th>Time (h)</th><th></th></tr>
<tr><td>H</td><td>6</td><td>(96)[b]</td></tr>
<tr><td>Me</td><td>12</td><td>(95)[b]</td></tr>
</table></td><td>254</td></tr>
<tr><td></td><td></td><td>$PdCl_2(dppf)•CH_2Cl_2$ (2%),
Cs_2CO_3 (3 eq),
THF–H_2O, 77°</td><td>
<table>
<tr><th>R^1</th><th>R^2</th><th>Time (h)</th><th></th></tr>
<tr><td>H</td><td>H</td><td>23</td><td>(84)</td></tr>
<tr><td>H</td><td>Me</td><td>16</td><td>(80)</td></tr>
<tr><td>CF_3</td><td>H</td><td>12</td><td>(91)</td></tr>
</table></td><td>85</td></tr>
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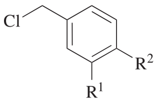
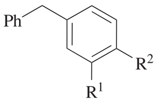
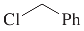


Pd cat. **6** (0.1%), KOH (2 eq), TBAB (0.5 eq), acetone–H_2O

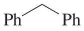


R^1	R^2	Temp (°)	Time (h)	
H	H	50	4	(81)
OMe	H	25	48	(71)[a]
OMe	H	50	2.5	(86)
H	Cl	50	2	(82)

150



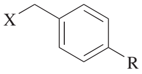
Pd(OAc)$_2$ (0.1%), KOH (2 eq), TBAB (0.5 eq), acetone–H_2O, 50°, 4 h



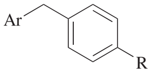
(64)

150

ArBF$_3^-$ K$^+$



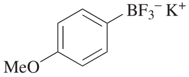
PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), Cs$_2$CO$_3$ (3 eq), CPME–H_2O, 90°

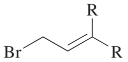


Ar	X	R	Time (h)	
Ph	Br	H	16	(85)
3-$O_2NC_6H_4$	Br	H	15	(69)
Ph	Cl	OMe	14	(78)

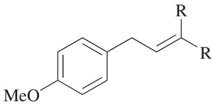
85

C_7



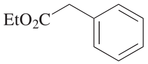


Pd(OAc)$_2$ (5%), 1,4-dioxane, 100°

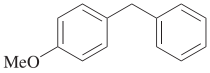


R	Time (h)	
H	6	(85)
Me	12	(87)

254



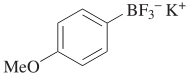
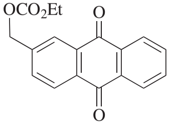
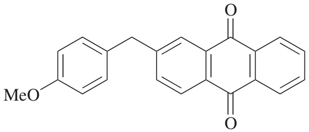
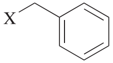
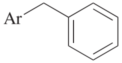
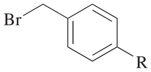
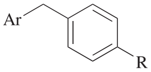
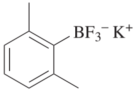
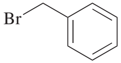
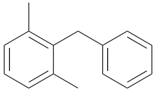
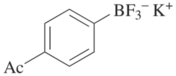
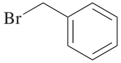
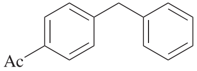
PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), Cs$_2$CO$_3$ (3 eq), THF–H_2O, 77°, 18 h



(91)

85

TABLE 1D. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALLYLIC AND BENZYLIC ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 24 h	 (71)	85
$ArBF_3^-\ K^+$		$PdCl_2$ (dppf)$\bullet CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°	 Ar — X — Time (h) 4-MeC$_6$H$_4$ — Br — 12 — (81) 4-MeOC$_6$H$_4$ — Cl — 20 — (91)	85
		$PdCl_2$ (dppf)$\bullet CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), CPME–H_2O, 90°	 Ar — R — Time (h) 4-MeOC$_6$H$_4$ — H — 20 — (86) 4-CF$_3$C$_6$H$_4$ — H — 18 — (87) 4-OHCC$_6$H$_4$ — H — 15 — (87) 4-MeOC$_6$H$_4$ — CN — 14 — (72)	85
C_8				
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 21 h	 (82)	85
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), CPME–H_2O, 90°, 15 h	 (80)	85

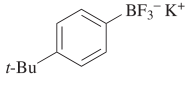
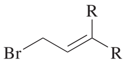
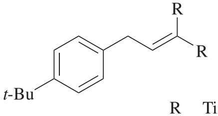
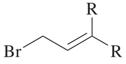
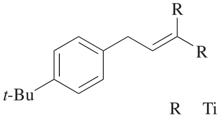
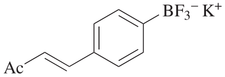
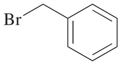
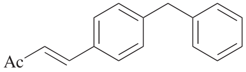
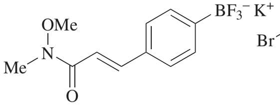
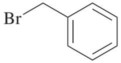
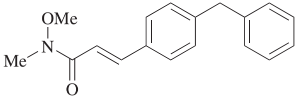
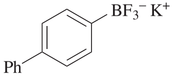
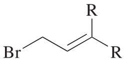
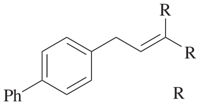
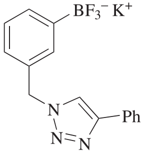
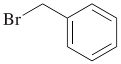
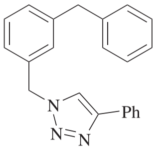
C_{10}					
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 100°	 R / Time (h) H / 6 / (84) Me / 12 / (71)		254
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 100°	 R / Time (h) H / 6 / (85) Me / 12 / (83)^b		254
		$PdCl_2$ (dppf)•CH_2Cl_2 (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 16 h		(70)	85
C_{11}					
		$PdCl_2$(dppf)•CH_2Cl_2 (2%), Cs_2CO_3 (3 eq), CPME–H_2O, 90°, 19 h		(74)	85
C_{12}					
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 100°	 R / Time (h) H / 6 / (72) Me / 12 / (65)		254

TABLE 1D. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH ALLYLIC AND BENZYLIC ELECTROPHILES (*Continued*)

Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
		$PdCl_2$ (dppf)•CH_2Cl_2 (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 16 h	 (86)	85

[a] The yield of the crude product was determined by ^1H NMR.

[b] The yield of the product was determined by GC analysis.

TABLE 1E. CROSS-COUPLING OF ARYLTRIFLUOROBORATES WITH MISCELLANEOUS ELECTROPHILES

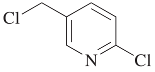
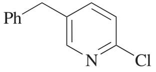
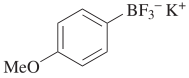
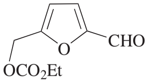
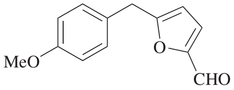
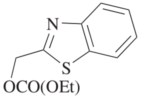
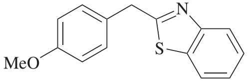
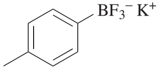
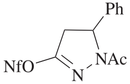
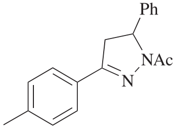
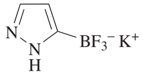
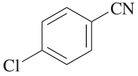
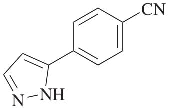
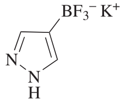
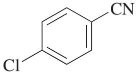
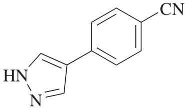
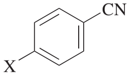
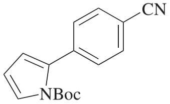
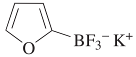
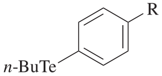
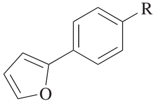
Aryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*				
C_6				
$PhBF_3^- K^+$	n-$C_6H_{13}Br$	Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	n-$C_6H_{13}Ph$ (0)	214
	^{11}MeI	$Pd_2(dba)_3$, P(o-tol)$_3$, K_2CO_3, DMF, 60°, 5 min	$^{11}MePh$ (13)	255
		Pd cat. **6** (0.1%), KOH (2 eq), TBAB (0.5 eq), acetone–H_2O, 50°, 9 h	 (77)	150
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 24 h	 (trace)	85
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, 77°, 24 h	 (trace)	85
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), K_2CO_3 (3 eq), LiCl (3 eq), toluene–H_2O, 100°, 18 h	 (87)	123

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*				
C_3				
		$Pd(OAc)_2$ (x%), RuPhos (y%), Na_2CO_3 (z eq), EtOH, 85°, 48 h	 x y z 1 2 2 (26) 5 10 3 (84)	94
		$Pd(OAc)_2$ (x%), RuPhos (y%), Na_2CO_3 (z eq), EtOH, 85°, 48 h	 x y z 1 2 2 (20) 5 10 3 (37)	94
C_4				
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 5 h	 X Br (90) Cl (52)	94
		$Pd(PPh_3)_4$ (10%), Ag_2O (2 eq), Et_3N (3 eq), MeOH, reflux, 90 min	 R Cl (52) H (40)	142

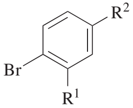
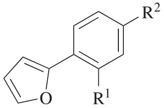
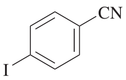
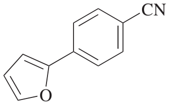
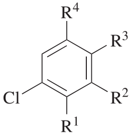
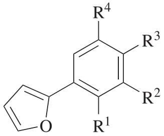
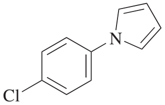
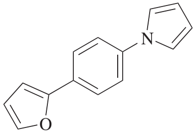
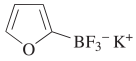
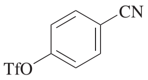
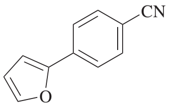
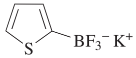
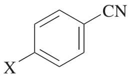
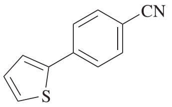
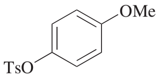
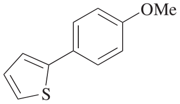
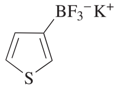
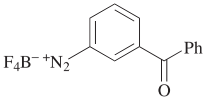
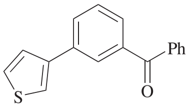
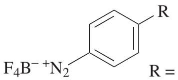
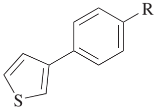
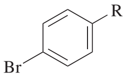
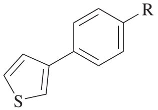
	$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8–36 h		R^1 R^2 H NO_2 (94) H CN (91) H OMe (85) H CHO (93) H Ac (89) H NHAc (91) H CO_2Me (92) Me H (94)	94
	$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8–36 h		(80)	94
	$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8–36 h	 R^1 R^2 R^3 R^4 H H CN H (84) H H OMe H (75) H H NO_2 H (75) H H CHO H (87) Me H H H (62) OMe OMe H CN (78)		94
	$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8–36 h		(99)	94

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8–36 h	 (82)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 2 h	 X: Br (98) Cl (83)	94
		$Pd(OAc)_2$ (2%), **L2** (4%), KOH (3 eq), MeOH, 60°, 5 h	 (27)	135
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 20°, 3 h	 (86)	13
	 R = H, OMe	Pd cat. **2** (5%), 1,4-dioxane, rt, 19 h	 (24)	231
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 R: OMe (8) Me (12) Ac (77)	214

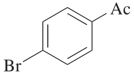
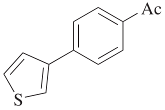
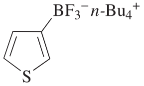
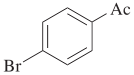
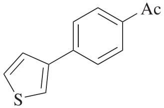
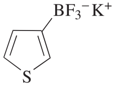
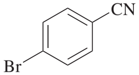
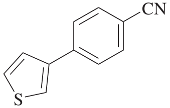
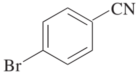
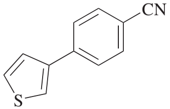
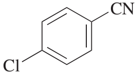
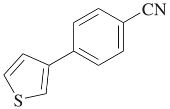
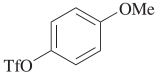
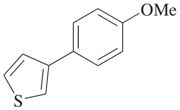
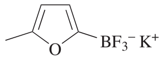
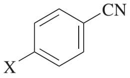
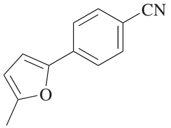
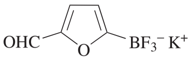
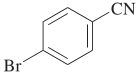
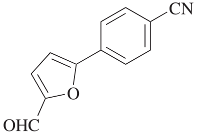
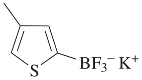
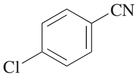
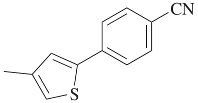
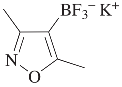
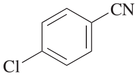
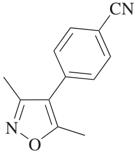
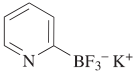
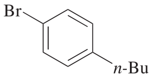
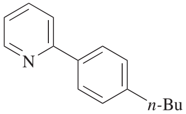
		$PdCl_2$ (1.2%), K_2CO_3 (3 eq), MW, 125°, 20 min		Solvent MeOH (57) MeOH–H_2O (79)	215
		$Pd(OAc)_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O, 50°, 24 h		(91)	12
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 5 h		(93)	46
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 5 h		(93)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 5 h		(96)	94
		$Pd(OAc)_2$ (5%), PCy_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 20 h		(79)	134

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8 h	 X Br (95) Cl (58)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 48 h	 (39)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 (74)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 (71)	94
		$Pd_2(dba)_3$ (1%), diphenylphosphine oxide (6%), base (3 eq), dioxane, 110°, 20 h	 Base KF (0)[a] NaO*t*-Bu (10)[a]	97

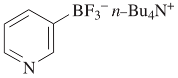
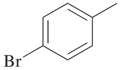
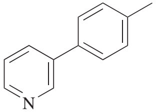
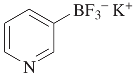
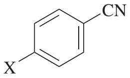
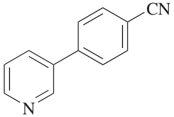
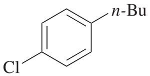
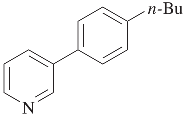
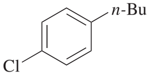
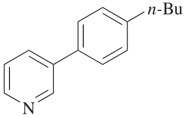
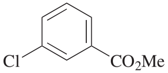
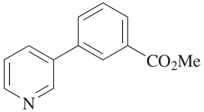
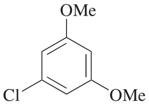
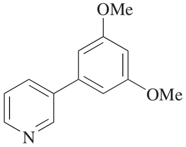
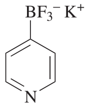
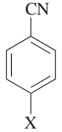
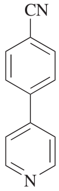
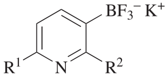
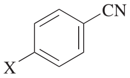
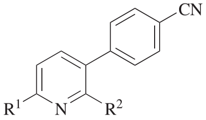
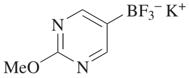
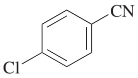
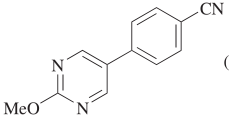
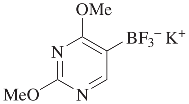
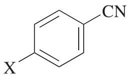
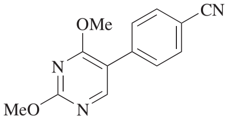
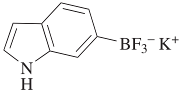
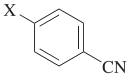
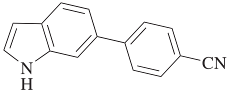
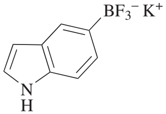
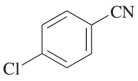
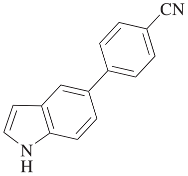
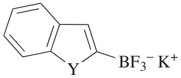
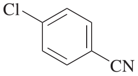
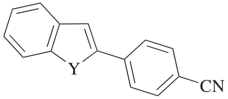
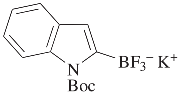
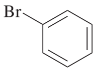
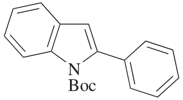
		$Pd(OAc)_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O, 50°, 24 h	 (69)	12
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 X Br (75) Cl (78)	94
		$Pd(OAc)_2$ (3%), SPhos (6%), K_2CO_3 (3 eq), EtOH, 72°, 22 h	 (73)	87
		$Pd_2(dba)_3$ (1%), PCy_3 (2.4%), K_3PO_4 (1.7 eq), dioxane–H_2O, 100°	 (85)	93
		$Pd(OAc)_2$ (3%), SPhos (6%), K_2CO_3 (3 eq), EtOH, 72°, 22 h	 (79)	87
		$Pd(OAc)_2$ (3%), SPhos (6%), K_2CO_3 (3 eq), EtOH, 72°, 22 h	 (82)	87

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 X Br (90) Cl (96)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 R^1 R^2 X H F Br (73) H F Cl (49) F H Br (61) F H Cl (77)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 (96)	94
C_6				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 X Br (88) Cl (86)	94

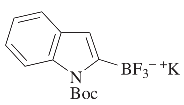
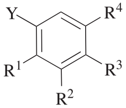
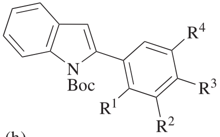
C_8

		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 8 h	 X Br (96) Cl (83)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°, 6 h	 (98)	94
		$Pd(OAc)_2$ (1%), RuPhos (2%), Na_2CO_3 (2 eq), EtOH, 85°		94
		Pd Source(x%), ligand (y%), Na_2CO_3 (3 eq), DME–H_2O		256

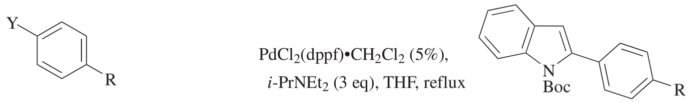
Y	Time (h)	
NBoc	6	(81)
S	7	(82)
O	12	(92)

Pd Source	x	Ligand	y	Temp (°)	Time (h)	
$Pd(OAc)_2$	5	PPh_3	10	90	1	(60)
$PdCl_2(PPh_3)_2$	10	none	—	90	1	(55)
$Pd(PPh_3)_4$	10	none	—	90	1	(92)
$Pd(PPh_3)_4$	10	none	—	50	4	(54)

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(PPh_3)_4$ (10%), Na_2CO_3 (3 eq), DME–H_2O, 90°		256

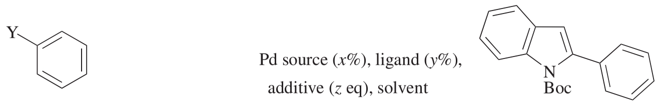
Y	R^1	R^2	R^3	R^4	Time (h)	
Br	H	H	F	H	5	(70)
Br	H	H	Me	H	4	(73)
Br	H	H	CF_3	H	4	(62)
Br	H	H	CN	H	6	(73)
Br	H	H	OMe	H	3	(76)
Br	H	OMe	H	H	4	(70)
Br	F	H	H	H	6	(63)
Br	CN	H	H	H	6	(36)
Br	OMe	H	H	H	4	(51)
Br	H	Me	H	Me	4	(77)
I	H	H	H	H	1	(90)
Cl	H	H	H	H	1	(0)
OTf	H	H	H	H	1	(64)
SMe	H	H	H	H	1	(0)
$BF_4^{-}{}^{+}N_2$	H	H	H	H	1	$(22)^b$



$PdCl_2(dppf) \cdot CH_2Cl_2$ (5%),
i-$PrNEt_2$ (3 eq), THF, reflux

256

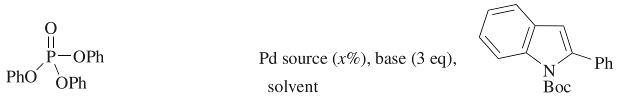
Y	R	Time (h)	
Br	NO_2	5	(65)
Cl	H	6	(13)[b]
OTf	H	1	(70)
OTf	H	6	(73)
SMe	H	1	(10)[b]
$BF_4^{-}\,^{+}N_2$	H	6	(14)[b]



Pd source (*x*%), ligand (*y*%),
additive (*z* eq), solvent

256

Y	Pd Source	*x*	Ligand	*y*	Additive	*z*	Solv	Temp	Time (h)	
Cl	$Pd(OAc)_2$	3	Xantphos	6	K_2CO_3	3	THF–H_2O	reflux	96	(36)
SMe	$Pd(PPh_3)_4$	5	none	—	Cu(I) salt	—	THF	reflux	1	(0)
$BF_4^{-}\,^{+}N_2$	$Pd(OAc)_2$	5	none	—	none	—	dioxane	rt	3	(0)

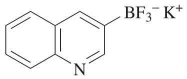
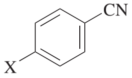
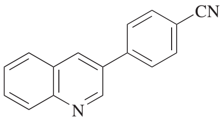
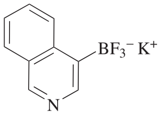
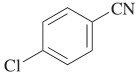
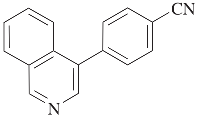


Pd source (*x*%), base (3 eq),
solvent

256

Pd Source	*x*	Base	Solvent	Temp	Time (h)	
$Pd(PPh_3)_4$	10	Na_2CO_3	DME–H_2O	90°	1	(31)[b]
$PdCl_2(dppf) \cdot CH_2Cl_2$	5	*i*-$PrNEt_2$	THF	reflux	6	(10)[b]

TABLE 2A. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_9					
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h		X Br (88) Cl (86)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 24 h		(85)	94

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[a] The yield of the product was determined by GC analysis.

[b] The yield of the crude product was determined by ^1H NMR.

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

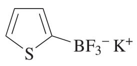
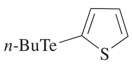
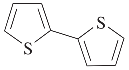
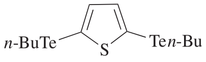
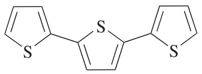
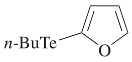
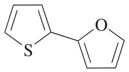
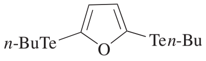
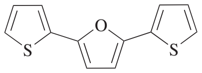
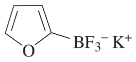
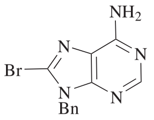
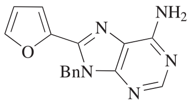
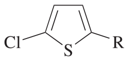
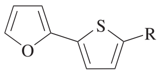
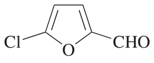
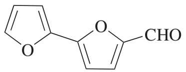
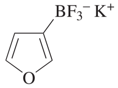
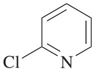
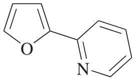
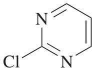
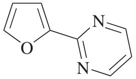
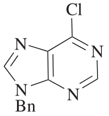
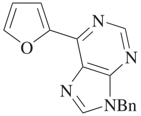
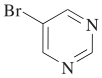
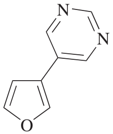
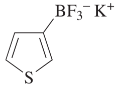
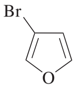
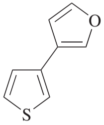
Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (34)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$Pd(PPh_3)_4$ (x%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 x 2 (51) 4 (73)	104
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 R Ac (77) CHO (64)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 (81)	94

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 28 h	 (67)	94
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 (92)	94
		$Pd(PPh_3)_4$ (x%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 x 2 (52) 4 (95)	104
		$PdCl_2(dppf)•CH_2Cl_2$ (0.5%), Et_3N (3 eq), EtOH, reflux, 18 h	 (72)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), Et_3N (3 eq), EtOH, reflux, 10 h	 (24)	46

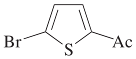
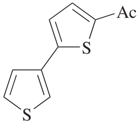
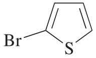
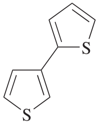
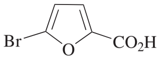
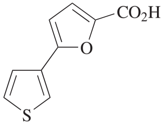
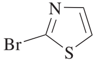
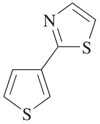
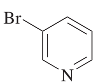
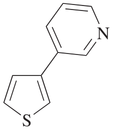
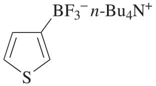
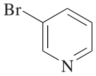
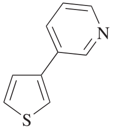
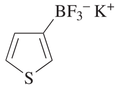
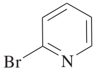
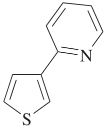
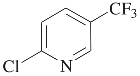
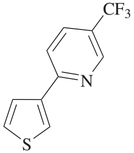
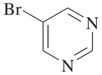
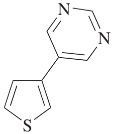
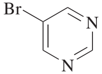
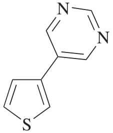
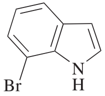
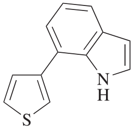
		Pd(OAc)$_2$ (2%), K_2CO_3 (3 eq), MeOH, reflux, 10 h	 (84)	46
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (0.5%), Et$_3$N (3 eq), EtOH, reflux, 13 h	 (63)	46
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (1%), K_2CO_3 (3 eq), EtOH, reflux, 10 h	 (70)	46
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), Et$_3$N (3 eq), EtOH, reflux, 14 h	 (67)	46
		Pd(OAc)$_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 7 h	 (68)	46
		Pd(OAc)$_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H$_2$O, 50°, 24 h	 (88)	12

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), MeOH, reflux, 15 h	 (60)	46
		Pd(A-^{ta}Phos)$_2$Cl$_2$ (2%), Et_3N (3 eq), PTS–H_2O, rt, 19 h	 (78)	257
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), MeOH, reflux, 7 h	 (64)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (0.5%), Et_3N (3 eq), EtOH, reflux, 18 h	 (75)	46
		$PdCl_2(dppf)•CH_2Cl_2$ (1%), Et_3N (3 eq), EtOH, reflux, 10 h	 (77)	46

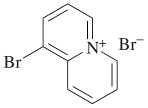
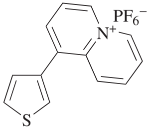
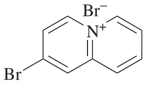
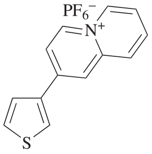
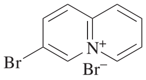
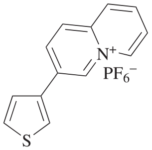
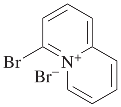
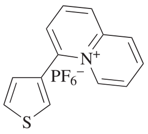
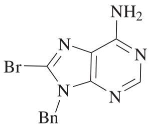
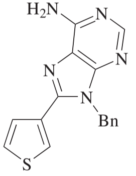
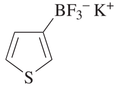
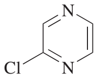
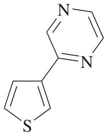
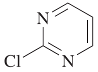
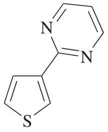
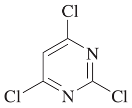
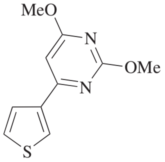
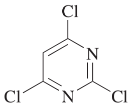
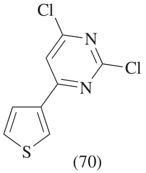
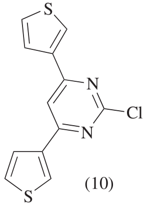
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(76)	122
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(98)	122
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(83)	122
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(56)	122
	$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min		(96)	104

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (1%), K_2CO_3 (3 eq), EtOH, reflux, 12 h	 (83)	46
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 12 h	 (52)	94
		$Pd(OAc)_2$ (2%), K_2CO_3 (3 eq), MeOH, reflux, 12 h	 (40)	46
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (1%), Et_3N (3 eq), EtOH, reflux, 9 h	 (70) +  (10)	46

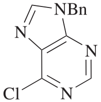
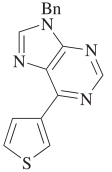
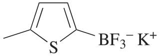
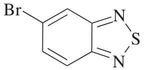
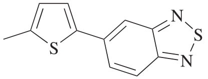
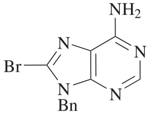
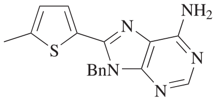
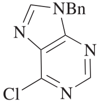
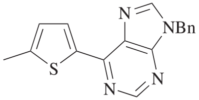
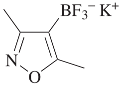
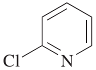
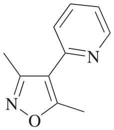
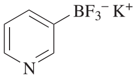
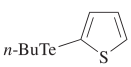
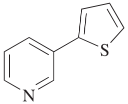
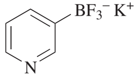
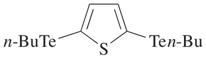
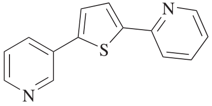
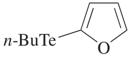
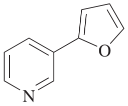
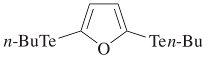
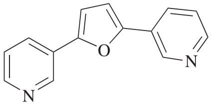
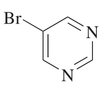
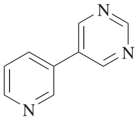
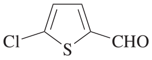
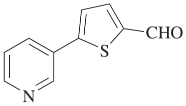
			$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min		(90)	104
C_5			PEPPSI complex (2%), K_2CO_3 (3 eq), MeOH 60°, 6 h		(98)	235
			$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min		(76)	104
			$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min		(91)	104
			$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h		(95)	94
			$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h		(0)	143

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$Pd(OAc)_2$ (10%), dppf (20%), Ag_2O (2 eq), MeOH, rt, 1.5 h	 (0)	143
		$PdCl_2(dppf)•CH_2Cl_2$ (0.5%), Et_3N (3 eq), EtOH, reflux, 18 h	 (64)	46
		$Pd(OAc)_2$ (3%), SPhos (6%), K_2CO_3 (3 eq), EtOH, 72°, 22 h	 (75)	87

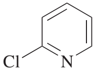
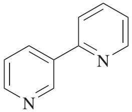
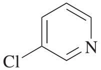
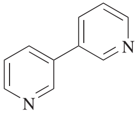
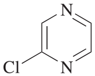
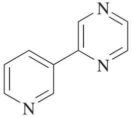
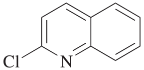
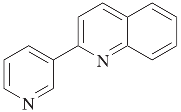
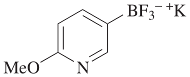
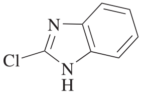
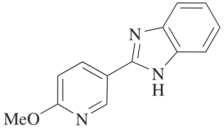
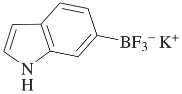
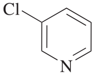
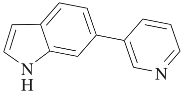
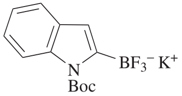
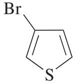
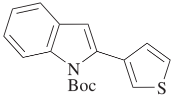
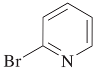
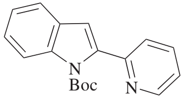
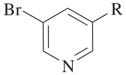
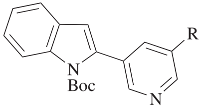
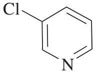
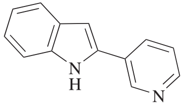
			Pd(OAc)$_2$ (3%), RuPhos (6%), Na$_2$CO$_3$ (2 eq), EtOH, 85°, 16 h	 (82)	94
			Pd(OAc)$_2$ (3%), SPhos (6%), K$_2$CO$_3$ (3 eq), EtOH, 72°, 22 h	 (75)	87
			Pd(OAc)$_2$ (3%), SPhos (6%), K$_2$CO$_3$ (3 eq), EtOH, 72°, 22 h	 (76)	87
			Pd(OAc)$_2$ (5%), SPhos (10%), K$_2$CO$_3$ (3 eq), EtOH, 72°, 22 h	 (81)	87
C$_6$			PdCl$_2$(PPh$_3$)$_2$ or PdCl$_2$(dppf)•CH$_2$Cl$_2$, K$_2$CO$_3$, MeCN, MW, 150°, 30 min	 (90)	223

TABLE 2B. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 (93)	94
		$Pd(PPh_3)_4$ (10%), Na_2CO_3 (3 eq), DME–H_2O, 90°, 3 h	 (95)	256
		$Pd(PPh_3)_4$ (10%), Na_2CO_3 (3 eq), DME–H_2O, 90°, 3 h	 (75)	256
		$Pd(PPh_3)_4$ (10%), Na_2CO_3 (3 eq), DME–H_2O, 90°, 3 h	 R Time (h) H 3 (77) Br 5 (80)	256
		$Pd(OAc)_2$ (3%), RuPhos (6%), Na_2CO_3 (2 eq), EtOH, 85°, 16 h	 (57)	94

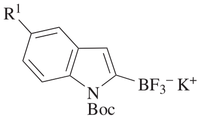
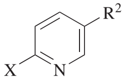
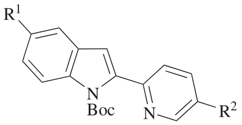
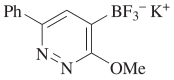
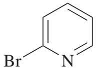
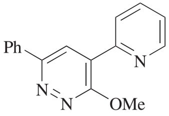
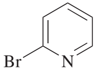
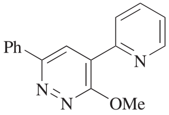
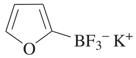
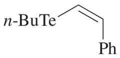
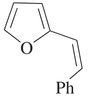
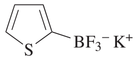
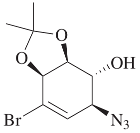
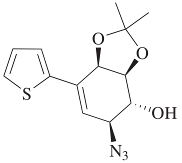
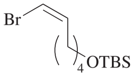
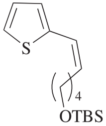
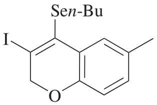
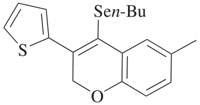
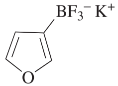
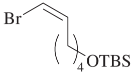
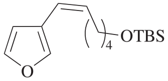
			$Pd(PPh_3)_4$ (10%), Na_2CO_3 (2.75 eq), DME–H_2O, 110°, 48 h	 R^1 X R^2 H Br Me (91) H Br OMe (85) H Br NMe_2 (86) OBn Br F (87) OBn Cl CF_3 (73)		258
C_{11}			$PdCl_2(dppf)\bullet CH_2Cl_2$, Et_3N, EtOH, reflux		(47)	95
			$Pd_2(dba)_3$, PCy_3, Et_3N, 1,4-dioxane, reflux		(33)	95

TABLE 2C. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), MeOH, rt, ultrasound, 40 min	 (0)	69
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 10 h	 (43)	161
		$Pd(PPh_3)_4$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 2.5 h	 (80)	66
		$PdCl_2(PPh_3)_2$ (5%), K_2CO_3 (2 eq), DMF–H_2O, 100°, 2 h	 (48)	259
		$Pd(PPh_3)_4$ (4.5%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 2.5 h	 (98)	66

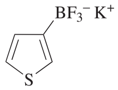
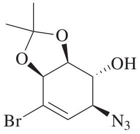
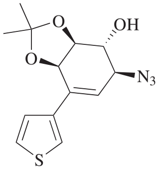
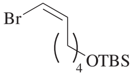
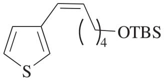
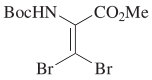
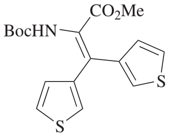
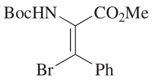
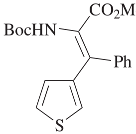
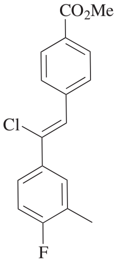
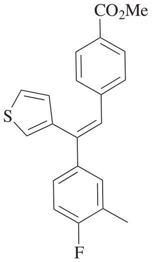
		$Pd(PPh_3)_4$ (6%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 5.5 h		(50)	161
		$Pd(PPh_3)_4$ (*x*%), K_2CO_3 (3 eq), toluene–H_2O, 90°, 50 min		*x* 4.5 (>99) 0.5 (93)	66
		$PdCl_2(dppf)•CH_2Cl_2$ (4%), K_2CO_3 (6 eq), toluene–H_2O, 90°, 3.5 h		(99)	260
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), K_2CO_3 (6 eq), toluene–H_2O, 90°, 3.5 h		(91)	260
		$Pd_2(dba)_3$ (2.5%), RuPhos (10%), Cs_2CO_3 (3 eq), THF–H_2O, 80°		(97)	148

TABLE 2C. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

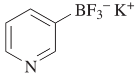
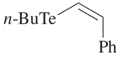
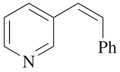
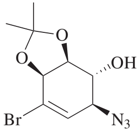
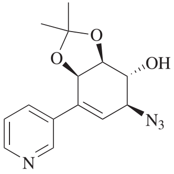
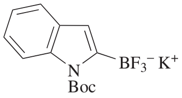
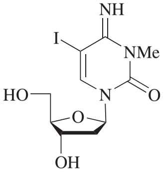
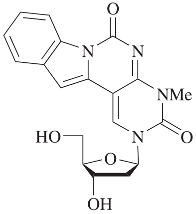
Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), MeOH, ultrasound, rt, 40 min	 (0)	69
		$Pd(PPh_3)_4$ (6%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 24 h	 (0)	161
C_8				
		$Pd(OAc)_2$ (3%), TPPTS (8%), Na_2CO_3 (2.2 eq), MeOH–H_2O, 45°, 12 h	 (60)	145

TABLE 2D. CROSS-COUPLING OF HETEROARYLTRIFLUOROBORATES WITH BENZYL ELECTROPHILES

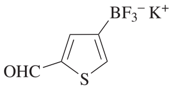
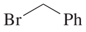
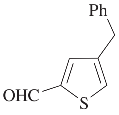
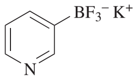
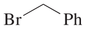
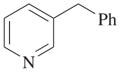
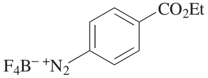
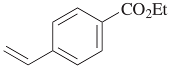
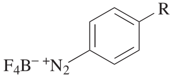
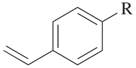
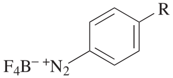
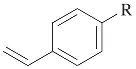
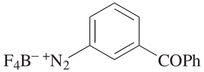
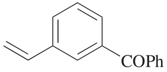
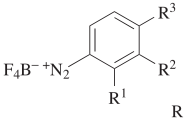
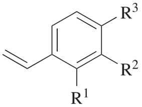
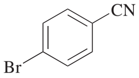
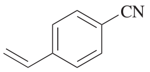
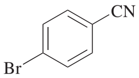
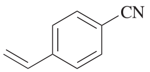
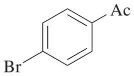
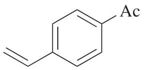
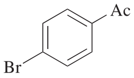
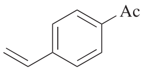
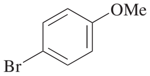
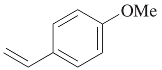
Heteroaryltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), CPME–H_2O, 90°, 14 h	 (72)	85
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), CPME–H_2O, 90°, 22 h	 (67)	85

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 20°, 1 h	 (65)	13
		Pd cat. **1** (0.1%), [bmim]BF_4–MeOH, rt 10 min	 R: H (80) R: Me (83)	132
		Pd cat. **2** (5%), 1,4-dioxane, rt	 R / Time (h) NO_2 3 (60) Me 3.5 (36) OMe 3 (41) *t*-Bu 3.5 (43)	231
		$Pd(OAc)_2$ (5%), 1,4-dioxane, 20°, 5 min	 (86)	133
		$Pd_2(\mu\text{-}OAc)_2(P(o\text{-}tol)_3)_2$ (x%), MeOH, 20°		133

R^1	R^2	R^3	x	Time (min)	
H	H	Br	0.1	30	(70)
H	H	OMe	1	20	(81)
H	H	CO_2Et	0.1	120	(88)
H	H	OTf	0.5	60	(75)
H	COPh	H	5	instantaneous	(81)
H	COPh	H	1	10	(86)
Me	H	H	0.5	20	(78)

	$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (3 eq), *i*-PrOH–H_2O, reflux, 6 h		(76)	71
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6 h		(69)	261
	$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), MeOH, reflux, 3 h		(90)	261
	$Pd(OAc)_2$ (1%), TBAB, K_2CO_3, H_2O, 120°		Time — 20 h (82) MW 20 min (89)	70
	Pd cat. (2%), ligand (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°			106

Pd cat.	Ligand	Time (h)	
$PdCl_2(dppf)•CH_2Cl_2$	—	22	(63)
$Pd(PPh_3)_4$	—	40	(62)
$Pd(OAc)_2$	PPh_3	45	(72)
$PdCl_2$	PPh_3	22	(72)

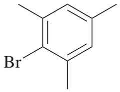
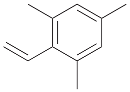
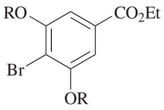
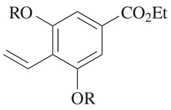
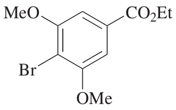
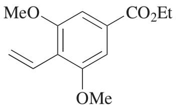
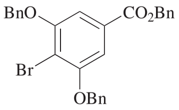
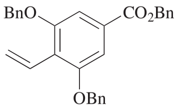
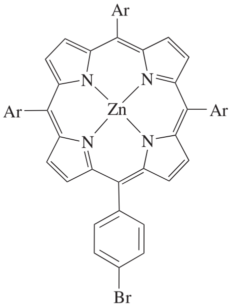
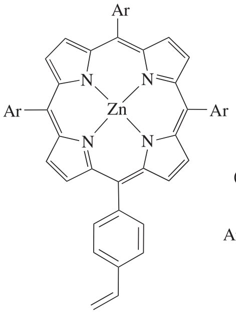
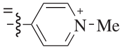
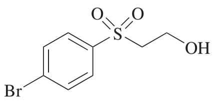
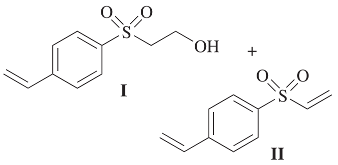
	$PdCl_2(dppf)•CH_2Cl_2$ (18%), Cs_2CO_3 (3 eq), THF–H_2O, 90°, 4 d		(32)	262
	$PdCl_2(dppf)•CH_2Cl_2$ (18%), Cs_2CO_3 (3 eq), THF–H_2O, 90°, 2 d		R H (24) TBS (18)	262

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$PdCl_2(dppf)•CH_2Cl_2$ (18%), Cs_2CO_3 (3 eq), THF–H_2O, 90°, 7 d	 (53)	262
		$PdCl_2(dppf)•CH_2Cl_2$ (18%), Cs_2CO_3 (3 eq), THF–H_2O, 90°, 4 d	 (87)	262
		$Pd(OAc)_2$, TPPTS, K_2CO_3, MeCN–H_2O, 60–70°, 12 h	 (56) Ar = 	159



$Pd(OAc)_2$ (2%), PPh_3 (4–5%), base, solvent



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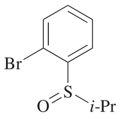
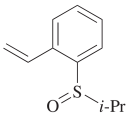
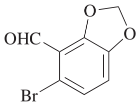
Base	Solvent	Temp (°)	**I + II**	**I/II**
NaOH (4 eq)	THF–H_2O (10:1)	70	(95)	6:1
NaOH (2 eq) + KF (1 eq)	THF–H_2O (7.5:1)	70	(95)	10:1
K_2CO_3 (3 eq)	toluene–H_2O (6:1)	80	(97)	22:1
K_2CO_3 (1 eq) + NaOAc (2 eq)	toluene–H_2O (4:1)	80	(90)	1:0



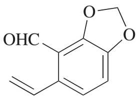
$Pd(PPh_3)_2Cl_2$, THF–H_2O, 85°, 22 h



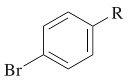
(70) 264



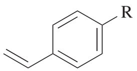
$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 3 h



(96) 147



$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°



R	Time (h)	
Cl	4	(81)
Me	7	(79)
CF_3	5	(62)
Ac	3	(90)

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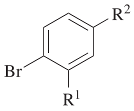
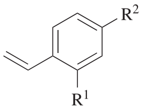


$PdCl_2(dppf)\cdot CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h



R^1	R^2	
H	CN	(68)
CHO	H	(65)

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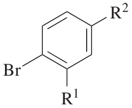
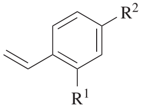
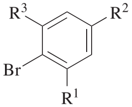
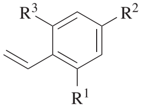
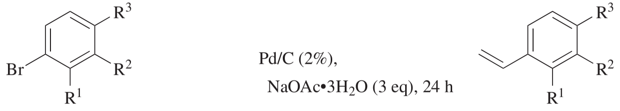
TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°	 R^1 R^2 Time H CN — 14 h (82) H OMe — 24 h (67) H OMe MW 20 min (63) H Ac — 2 h (93) H Ac — 3 h (72) H Ac MW 20 min (92) H CO_2Et — 8 h (71) Me H — 14 h (65) Me H MW 30 min (68)	70
		$PdCl_2$ (2%), RuPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 R^1 R^2 R^3 H NMe_2 H (93) Me Me Me (81)	106



Pd/C (2%),
NaOAc•3H_2O (3 eq), 24 h

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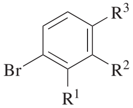
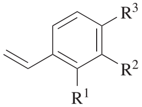
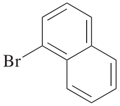
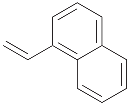
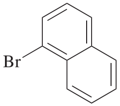
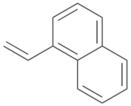
R^1	R^2	R^3	Solvent	Temp (°)	
H	H	NO_2	NMP	100	(78)
H	H	CN	NMP	100	(46)[a]
H	H	CN	NMP–H_2O	100	(9)[a]
H	H	Ac	NMP	100	(44)[a]
H	H	OBn	NMP	140	(28)[a]
H	H	OBn	NMP–H_2O	140	(26)[a]
H	NO_2	H	NMP	100	(88)[a]
NO_2	H	H	NMP	100	(53)[a]
NO_2	H	H	NMP–H_2O	100	(18)[a]

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 R^1 R^2 R^3 H H Cl (77) H H NO_2 (84) H H Me (76) H H CN (83) H H CF_3 (64) H H CHO (83) H H OMe (72) H H CH_2OH (82) H H Ac (85) H H CO_2Me (87) H H NHAc (78) H H COPh (85) H CN H (78) H OMe H (74) H Ac H (79) Me H H (82) CN H H (82) OMe H H (71) Ac H H (92)	106
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h	 (75)	261
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6 h	 (68)	261

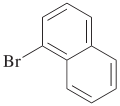
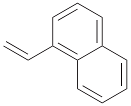
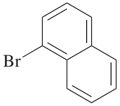
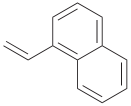
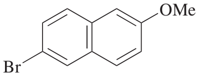
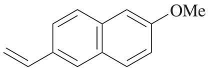
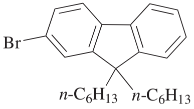
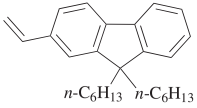
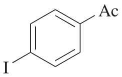
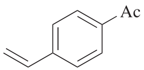
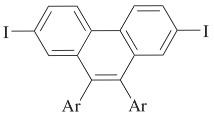
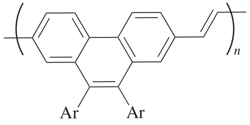
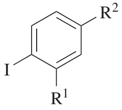
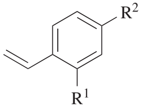
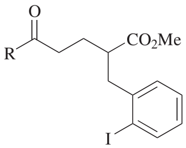
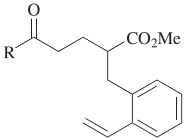
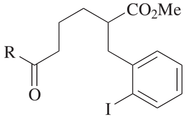
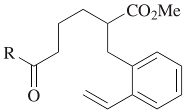
	$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°		Time (h) 22 (82) 8 (81)	106
	Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°		Time — 10 h (74) MW 20 min (78)	70
	Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°		Time — 14 h (57) MW 30 min (68)	70
	$PdCl_2(dppf)•CH_2Cl_2$ (5%), Et_3N (1 eq), *n*-PrOH, reflux, 4 h		(62)	265
	$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h		(73)	261
 Ar = n-$C_6H_{13}OC_6H_4$-4	$Pd(OAc)_2$ (5%), P(*o*-tol)$_3$ (2.5%), Et_3N (2.5 eq), toluene–DMF, 120°, overnight		(71)	158

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 BF_3^- K^+		Pd/C (2%), NaOAc•3 H_2O (3 eq), 24 h		137

R^1	R^2	Solvent	Temp (°)	
H	NO_2	NMP	80	(90)^a
H	Br	NMP	100	(68)^a
H	Br	NMP–H_2O	100	(81)^a
H	OMe	NMP	100	(58)^a
H	OMe	NMP–H_2O	100	(69)
NO_2	H	NMP	100	(75)^a
NO_2	H	NMP–H_2O	100	(73)
OH	H	NMP	100	(67)
Me	H	NMP	100	(40)^a
Me	H	NMP–H_2O	100	(79)^a
OBn	H	NMP	100	(60)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		Pd(OAc)$_2$ (5%), PPh$_3$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 4 h	 R: Me (72) R: *i*-Pr (74)	107
		Pd(OAc)$_2$ (5%), PPh$_3$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 4 h	 R: Me (64) R: *i*-Pr (92)	107

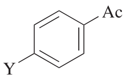
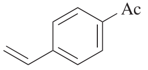
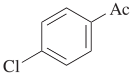
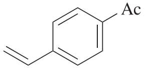
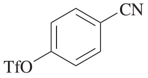
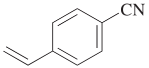
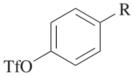
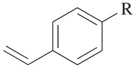
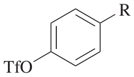
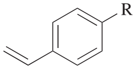
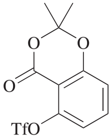
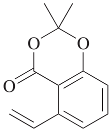
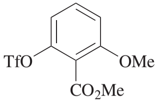
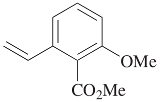
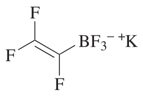
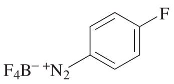
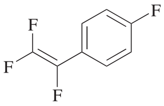
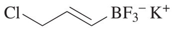
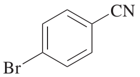
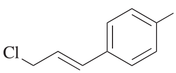
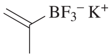
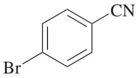
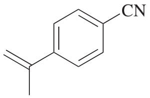
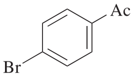
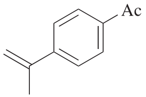
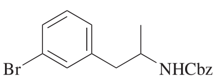
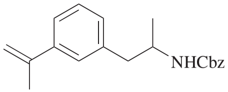
	$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h		Y OTf (82) I (89) Cl (0)	106
	$PdCl_2$ (2%), RuPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h		(65)	106
	$PdCl_2(dppf)•CH_2Cl_2$ (5%), *i*-Pr_2NEt (3 eq), *i*-PrOH–H_2O, MW, 100°, 15 min		(90)	220
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6 h		R NO_2 (72) Ac (84)	261
	$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h		R NO_2 (82) OMe (64) Ac (95)	261
	$PdCl_2(dppf)•CH_2Cl_2$ (5%), Et_3N (1.3 eq), EtOH, 80°, 4.5 h		(93)	103
	$PdCl_2(dppf)•CH_2Cl_2$, Et_3N (1.3 eq), MeOH, 50°, 10 h		(91)	266

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		Pd source (5%), solvent, 20°		237
		Pd Source / Solvent		
		$Pd_2(\mu\text{-OAc})_2(P(o\text{-tol})_2C_6H_4CH_2)$ MeOH	$(0)^b$	
		$Pd(PPh_3)_4$ MeOH	$(14)^b$	
		$Pd(OAc)_2$-bipy MeOH	$(0)^b$	
		$Pd(PPh_3)_4$ dioxane	$(40)^b$	
C_3				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), t-$BuNH_2$ (3 eq), i-PrOH–H_2O, reflux, 24 h	 (0)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), t-$BuNH_2$ (3 eq), i-PrOH–H_2O, reflux, 5 h	 (70)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), n-PrOH, reflux, 5 h	 (81)	261
		$PdCl_2(dppf)$ (1%), i-Pr_2NH (2%), K_2CO_3, n-PrOH, 90°	 (80)	267

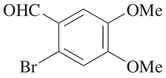
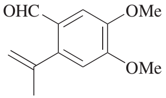
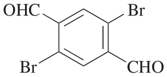
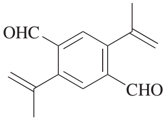
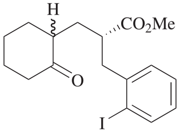
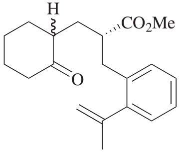
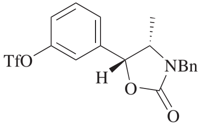
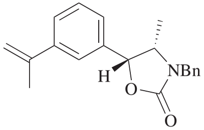
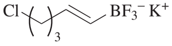
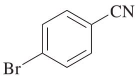
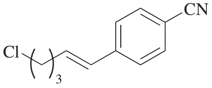
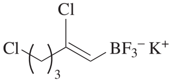
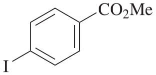
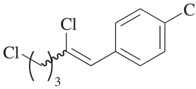
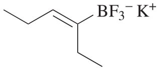
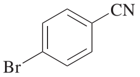
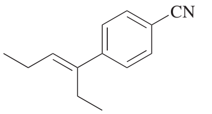
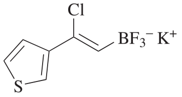
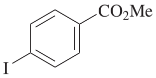
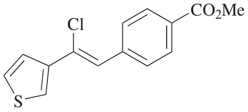
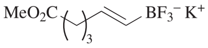
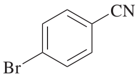
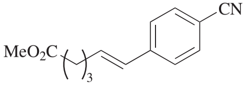
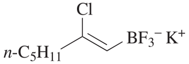
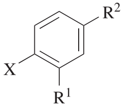
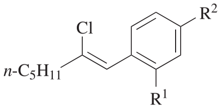
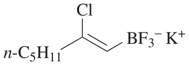
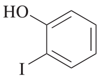
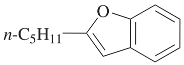
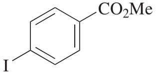
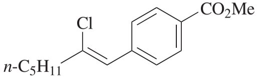
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 3 h		(>99)	147
		$Pd(OAc)_2$ (10%), PPh_3 (20%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 h		(84)	147
		$Pd(OAc)_2$ (4.5%), PPh_3 (9%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 5 h		(78)	107
		$PdCl_2(dppf)$ (1%), *i*-Pr_2NH (2%), K_2CO_3, *n*-PrOH, 90°		(95)	267
C_5					
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 6 h		(52)	71
		$Pd_2(dba)_3$ (1.5%), P(*t*-Bu)$_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (*Z*)/(*E*) = 62:38	(50)	148

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 7 h	 (70)	71
		$Pd_2(dba)_3$ (1.5%), P(*t*-Bu)$_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (36)	148
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 14 h	 (33)	71
		$Pd_2(dba)_3$ (1.5%), P(*t*-Bu)$_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°		148

X	R^1	R^2	Time (h)	
Br	H	H	12	(70)
Br	H	NO_2	12	(46)
Br	H	OMe	36	(56)
Br	H	CO_2Me	48	(63)
I	NH_2	H	12	(74)
Cl	OH	H	12	(0)

		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h		(58)	148
		Pd cat. (x%), ligand (y%), Cs_2CO_3 (3 eq), THF–H_2O			148

Pd cat.	x	Ligand	y	Temp (°)	Time (h)	
$Pd_2(dba)_3$	1.5	XantPhos	6	90	20	(85)
$PdCl_2$	5	$P(t\text{-}Bu)_3$•HBF_4	10	reflux	60	(72)
$Pd_2(dba)_3$	2.5	$P(t\text{-}Bu)_3$•HBF_4	5	reflux	90	(81)
$Pd_2(dba)_3$	1.5	$P(t\text{-}Bu)_3$•HBF_4	3	120	12	(92)

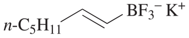
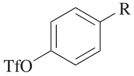
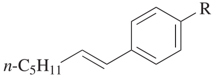
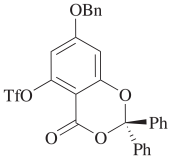
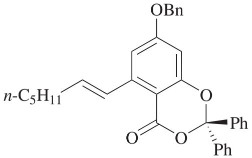
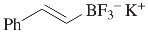
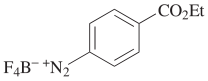
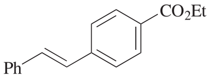
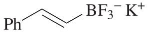
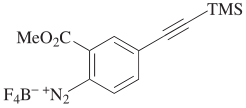
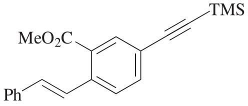
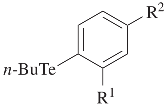
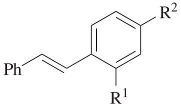
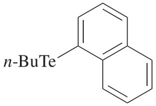
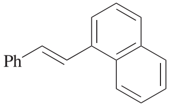
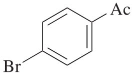
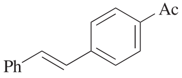
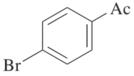
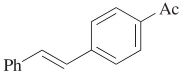
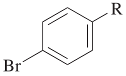
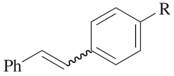
		$PdCl_2(dppf)$•CH_2Cl_2 (5%), $i\text{-}Pr_2NEt$ (3 eq), i-PrOH–H_2O, MW, 100°, 15 min		R NO_2 (82) OMe (61)	220
		$PdCl_2(dppf)$•CH_2Cl_2 (2%), $t\text{-}BuNH_2$ (3 eq), i-PrOH–H_2O, reflux, overnight		(80)	108
C_8					
		$Pd_2(\mu\text{-}OAc)_2$- $(P(o\text{-}tol)_3)_2$ (5%), MeOH, 20°, 1–2 min		(96)	133

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(OAc)_2$, 1,4-dioxane, rt, 19 h	 (58)	268
		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), K_2CO_3 (2 eq), MeOH, rt, ultrasound, 40 min	 R^1 R^2 H H (90) Me H (91) H Cl (77) H Br (91) H I (71) H Me (83) H OMe (75) H CO_2Me (72)	69
		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), K_2CO_3 (2 eq), MeOH, rt, ultrasound	 (87)	69
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 8 h	 (91)	261
		$Pd(OAc)_2$ (1%), TBAB, K_2CO_3, H_2O, 120°	 Time — 24 h $(88)^c$ MW 20 min $(92)^c$	70
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 R (*Z*)/(*E*) Me 19:81 (77) Ac 13:87 (87)	214

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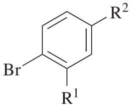
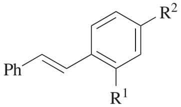
<tr><td> </td><td>Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°</td><td>
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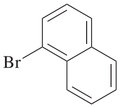
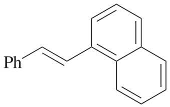
<tr><th>R^1</th><th>R^2</th><th></th><th>Time</th><th></th></tr>
<tr><td>H</td><td>CN</td><td>—</td><td>14 h</td><td>(84)</td></tr>
<tr><td>H</td><td>OMe</td><td>—</td><td>14 h</td><td>(78)</td></tr>
<tr><td>H</td><td>OMe</td><td>MW</td><td>20 min</td><td>(75)[c]</td></tr>
<tr><td>H</td><td>Ac</td><td>—</td><td>3 h</td><td>(91)</td></tr>
<tr><td>H</td><td>Ac</td><td>MW</td><td>20 min</td><td>(93)[c]</td></tr>
<tr><td>H</td><td>CO_2Et</td><td>—</td><td>8 h</td><td>(81)</td></tr>
<tr><td>Me</td><td>H</td><td>—</td><td>14 h</td><td>(88)</td></tr>
<tr><td>Me</td><td>H</td><td>MW</td><td>20 min</td><td>(92)</td></tr>
</table></td><td>70</td></tr>
<tr><td> </td><td>Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°</td><td>
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<tr><td>—</td><td>14 h</td><td>(83)</td></tr>
<tr><td>MW</td><td>20 min</td><td>(90)</td></tr>
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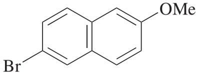
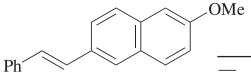
<tr><td> </td><td>Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O</td><td>
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<tr><td>MW</td><td>20 min</td><td>(79)[c]</td></tr>
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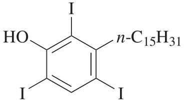
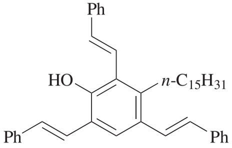
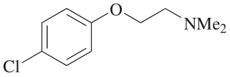
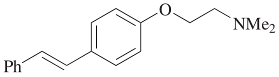
<tr><td> </td><td>$Pd(OAc)_4$ (5%), K_3PO_4 (6 eq), n-Bu_4NBr (0.5%), EtOH, 80°, 24 h</td><td> (61)</td><td>269</td></tr>
<tr><td> </td><td>$PdCl_2(dppf)\bullet CH_2Cl_2$, Et_3N, i-PrOH–H_2O</td><td> (—)</td><td>270</td></tr>
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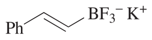
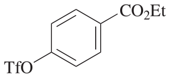
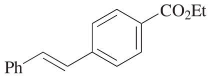
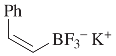
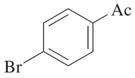
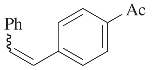
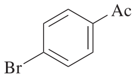
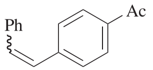
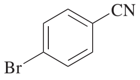
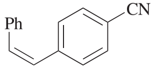
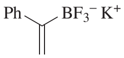
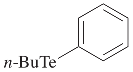
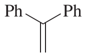
TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (2%), CsOAc (2 eq), $THF–H_2O$, reflux	 (95)	236
		$Pd(OAc)_2$ (1%), TBAB, K_2CO_3, H_2O, 120°, 14 h	 (79)[c] (*Z*)/(*E*) = 80:20	70
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°, 14 h	 (55) (*Z*)/(*E*) = 80:20	70
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-$PrOH–H_2O$, reflux, 6 h	 (86)	71
		$Pd(PPh_3)_4$ (10%), base (3 eq), additive (2 eq), MeOH, ultrasound	 Base / Additive Cs_2CO_3 AgOAc (81) Et_3N AgOAc (84) Et_3N Ag_2O (61) K_2CO_3 Ag_2O (60)	144

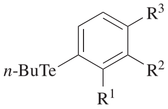
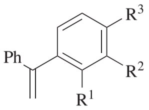
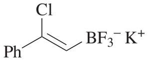
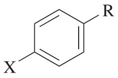
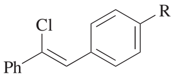
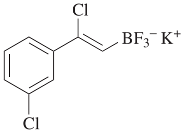
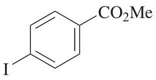
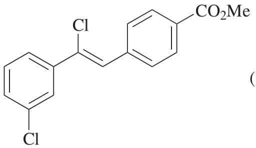
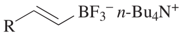
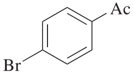
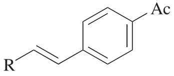
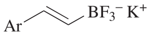
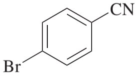
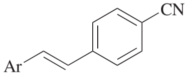
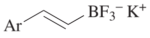
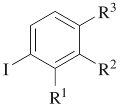
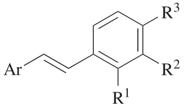
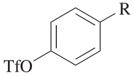
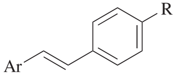
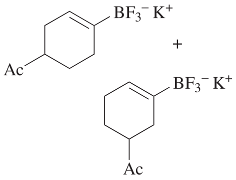
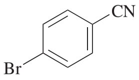
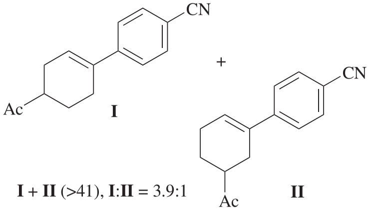
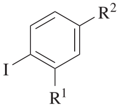
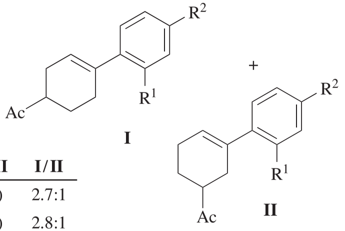
		$Pd(PPh_3)_4$ (10%), Et_3N (3 eq), AgOAc (2 eq), MeOH, ultrasound		R^1 R^2 R^3 Time (min) H H H 20 (80) H H Br 20 (91) H H Cl 20 (80) H H F 20 (79) H H OH 20 (87) H H Me 20 (82) H H OMe 20 (83) H CF_3 H 20 (85) Me H H 30 (76) Me H F 30 (74)	144
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h		X R Br H (70) Br NO_2 (46) I CO_2Me (80)	148
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h		(81)	148
		$Pd(OAc)_2$ (5%), dppb (5%), Cs_2CO_3 (1.25 eq), DME–H_2O, 50°, 24 h		R Ph (55) $n\text{-}C_6H_{13}$ (87)	12
		$PdCl_2(dppf)$•CH_2Cl_2 (2%), $t\text{-}BuNH_2$ (3 eq), $i\text{-}PrOH–H_2O$, reflux, 6 h		Ar Ph (80) $4\text{-}FC_6H_4$ (73)	71

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *i*-$PrNEt_2$, *i*-PrOH–H_2O, MW, 100°, 10 min	 Ar | R^1 | R^2 | R^3 | Ph | H | H | H | (67) Ph | H | H | F | (61) Ph | H | H | Cl | (99) Ph | H | H | Ac | (91) Ph | H | NO_2 | H | (76) Ph | OMe | H | H | (79) Ph | Me | H | Me | (96) Ph | Me | H | H | (92) 4-ClC_6H_4 | H | NO_2 | H | (87) 4-ClC_6H_4 | H | H | OMe | (85)	271
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), *i*-Pr_2NEt (3 eq), *i*-PrOH–H_2O, MW, 100°, 15 min	 Ar | R | Ph | NO_2 | (92) 4-ClC_6H_4 | H | (75)	220
		$Pd(OAc)_2$ (1.5%), K_2CO_3 (3 eq), EtOH, reflux, 5 h	 **I** + **II** (>41), **I**:**II** = 3.9:1	272, 273



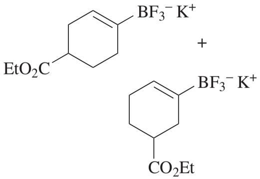
Pd(OAc)$_2$ (0.5%),
K$_2$CO$_3$ (3 eq), EtOH,
reflux, 5 h

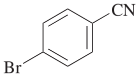


R^1	R^2	**I + II**	**I/II**
H	H	(56)	2.7:1
H	CF$_3$	(57)	2.8:1
OMe	H	(48)	5.1:1

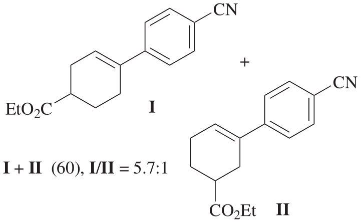
272, 273

C$_9$



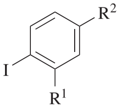


Pd(OAc)$_2$ (1.5%),
K$_2$CO$_3$ (3 eq), EtOH,
reflux, 5 h

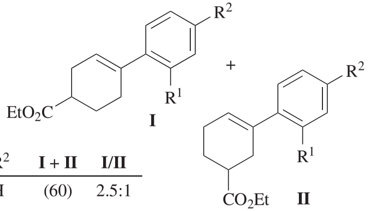


I + II (60), **I/II** = 5.7:1

272



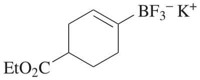
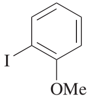
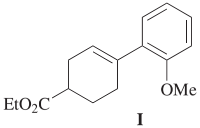
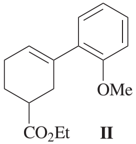
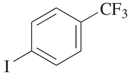
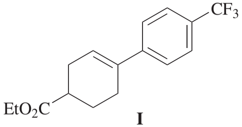
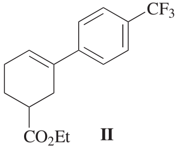
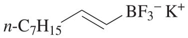
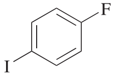
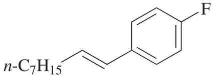
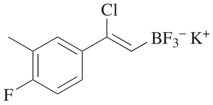
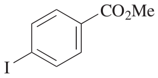
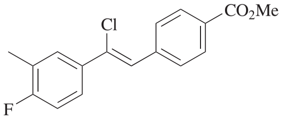
Pd(OAc)$_2$ (0.5%),
K$_2$CO$_3$ (3 eq), EtOH,
reflux, 5 h



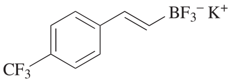
	R^1	R^2	**I + II**	**I/II**
—	H	H	(60)	2.5:1
—	H	CF$_3$	(62)	2.9:1
MW	H	CF$_3$	(64)	3.1:1
—	OMe	H	(50)	3.9:1

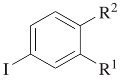
272

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

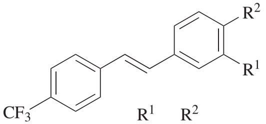
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), EtOH, reflux	 **I** +  **II** **I** + **II** (53), **I**/**II** = 2.3:1	272
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), EtOH, reflux	 **I** +  **II** **I** + **II** (73), **I**/**II** = 4.4:1	273
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), i-$PrNEt_2$, i-PrOH–H_2O, MW, 100°, 10 min	 (91)	271
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3•HBF_4$ (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (79)	148

C$_{10}$



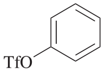


PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%),
i-PrNEt$_2$, *i*-PrOH–H$_2$O,
MW, 100°, 10 min

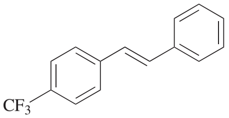


R^1	R^2	
H	Cl	(92)
H	Ac	(95)
NO$_2$	H	(81)

271

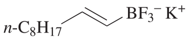


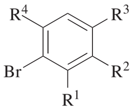
PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%),
i-PrNEt$_2$, *i*-PrOH–H$_2$O,
MW, 100°, 10 min



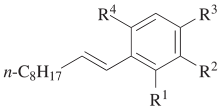
(90)

220





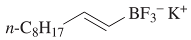
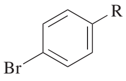
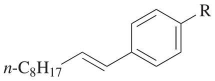
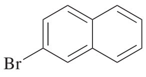
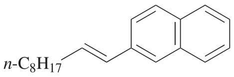
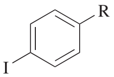
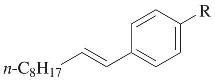
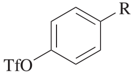
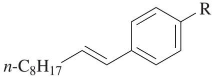
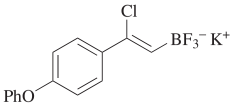
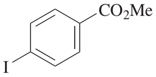
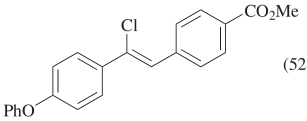
PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%),
base (3 eq), *i*-PrOH–H$_2$O,
reflux

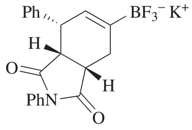
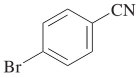
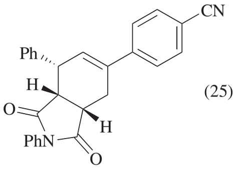


R^1	R^2	R^3	R^4	Base	Time (h)	
H	H	F	H	Et$_3$N	14	(59)
H	H	NO$_2$	H	*t*-BuNH$_2$	2	(71)
H	H	CN	H	*t*-BuNH$_2$	6	(87)
H	H	CF$_3$	H	*t*-BuNH$_2$	10	(65)
H	H	Ac	H	*t*-BuNH$_2$	6	(69)
H	OMe	H	H	*t*-BuNH$_2$	6	(61)
CN	H	H	H	*t*-BuNH$_2$	6	(75)
Me	H	Me	Me	Et$_3$N	14	(38)
Ac	H	H	H	*t*-BuNH$_2$	14	(63)

71

TABLE 3A. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°, 14 h	 R — Time OMe — 22 h (81) OMe MW 20 min (91)^c Ac — 3 h (93) Ac MW 20 min (89)	70
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), t-$BuNH_2$ (3 eq), i-PrOH–H_2O, reflux, 10 h	 (78)	106
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), t-$BuNH_2$ (3 eq), i-PrOH–H_2O, reflux	 R Time (h) OMe 6 (60) Ac 2 (65)	106
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), t-$BuNH_2$ (3 eq), i-PrOH–H_2O, reflux	 R Time (h) NO_2 3 (76) Ac 8 (60)	106
C_{14}				
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3•HBF_4$ (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (52)	148

C_{20}				
		$PdCl_2(dppf)$ (2.5%), Cs_2CO_3 (3 eq), CH_2Cl_2–H_2O, reflux, 4 h	 (25)	273

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[a] The yield of the product was determined by GC analysis.

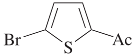
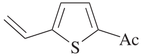
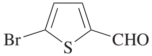
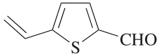
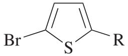
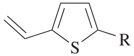
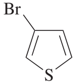
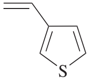
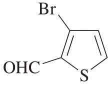
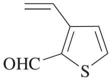
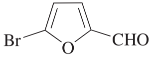
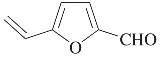
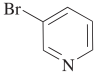
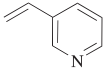
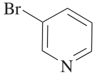
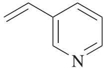
[b] The yield of the crude product was determined by ^{19}F NMR.

[c] The yield of the crude product was determined by ^{1}H NMR.

[d] The trifluoroborate derivative was prepared by a Diels-Alder reaction and was not isolated. The indicated yield is a two-step yield.

[e] The trifluoroborate derivative was prepared by a Diels-Alder reaction and was not isolated. The indicated yield is a multi-step yield.

TABLE 3B. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h	 (60)	261
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°	 Time — 14 h (75) MW 20 min (86)	70
		$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 R H (64) Ac (66)	106
		$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 (70)	106
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 3 h	 (82)	147
		$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 (70)	106
		$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h	 (71)	106
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°	 Time — 14 h (52) MW 30 min (81)	70

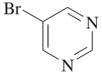
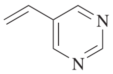
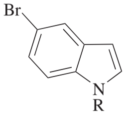
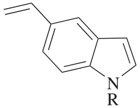
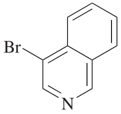
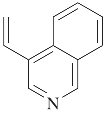
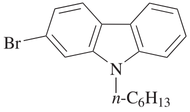
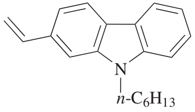
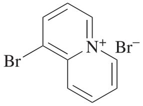
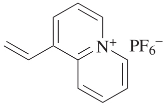
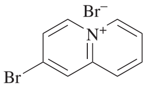
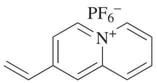
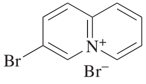
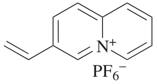
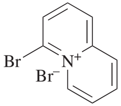
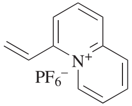
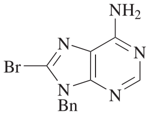
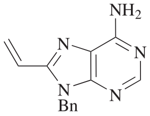
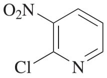
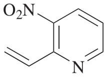
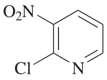
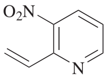
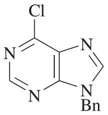
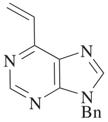
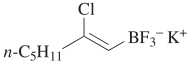
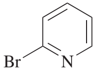
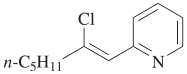
	$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h		(79)	106
	$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h		R H (38) Ts (88) Boc (77) Bn (71)	106
	$PdCl_2$ (2%), PPh_3 (6%), Cs_2CO_3 (3 eq), THF–H_2O, 85°, 22 h		(88)	106
	$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 14 h		(41)	265
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(72)	122
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(71)	122
	1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6		(70)	122

TABLE 3B. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (53)	122
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 (0)	104
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (1 eq), *n*-PrOH, reflux, 3 h	 (62)	261
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6 h	 (64)	261
		$Pd(PPh_3)_4$ (2%), K_2CO_3 (3 eq), MeCN–H_2O, MW, 150°, 5 min	 (97)	104
C_7				
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3•HBF_4$ (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (25)	148

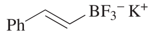
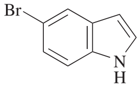
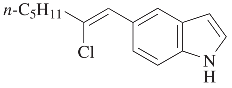
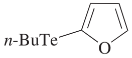
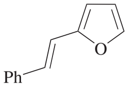
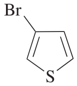
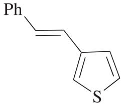
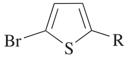
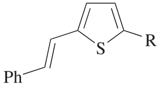
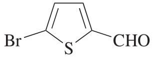
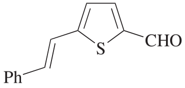
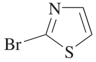
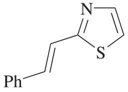
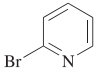
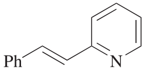
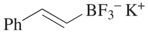
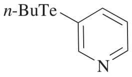
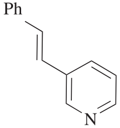
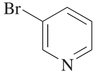
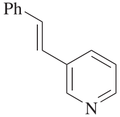
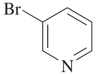
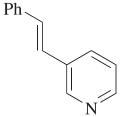
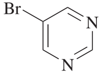
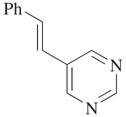
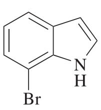
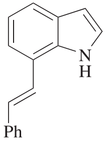
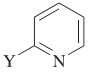
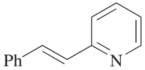
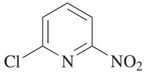
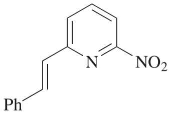
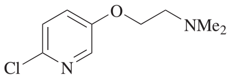
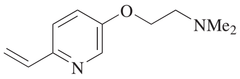
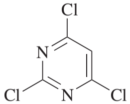
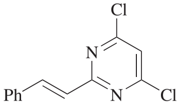
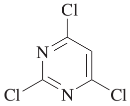
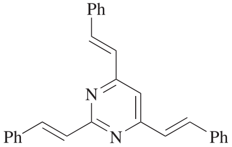
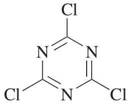
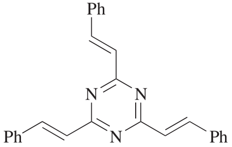
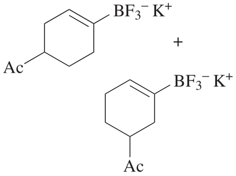
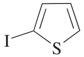
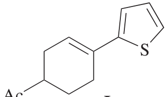
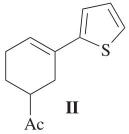
C_8			$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3 \bullet HBF_4$ (3%), Cs_2CO_3 (3 eq), $THF–H_2O$, 120°, 36 h	 (77)	148
			$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), K_2CO_3 (2 eq), MeOH, rt, ultrasound	 (59)	69
			$PdCl_2(dppf) \bullet CH_2Cl_2$ (2%), $t\text{-}BuNH_2$ (3 eq), $i\text{-}PrOH–H_2O$, reflux, 5 h	 (80)	71
			$PdCl_2(dppf) \bullet CH_2Cl_2$ (2%), $t\text{-}BuNH_2$ (3 eq), $i\text{-}PrOH–H_2O$, reflux, 3 h	 R H (69) Ac (91)	71
			Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°	 Time — 12 h (80) MW 20 min (82)	70
			$PdCl_2(dppf) \bullet CH_2Cl_2$ (2%), Et_3N (3 eq), $i\text{-}PrOH–H_2O$, reflux, 3 h	 (83)	71
			$PdCl_2(dppf) \bullet CH_2Cl_2$ (2%), Et_3N (1 eq), $n\text{-}PrOH$, reflux, 8 h	 (83)	261

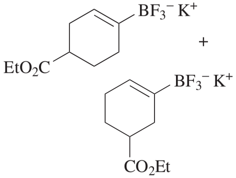
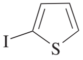
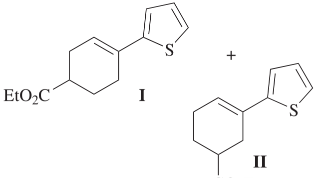
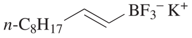
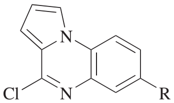
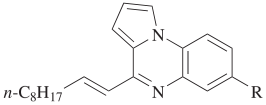
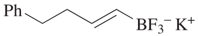
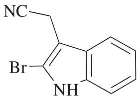
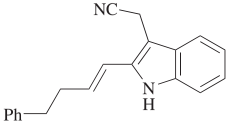
TABLE 3B. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(PPh_3)_4$ (8%), Ag_2O (2 eq), K_2CO_3 (2 eq), MeOH, rt, ultrasound	 (69)	69
		Pd cat. **6** (1%), TBAB, K_2CO_3, H_2O, 120°	 Time — 14 h (79) MW 20 min (86)	70
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 4 h	 (57)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 6 h	 (73)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux, 9 h	 (70)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *t*-$BuNH_2$ (3 eq), *i*-PrOH–H_2O, reflux	 Y Time (h) Br 4 (70) OTf 18 (41)	71

		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (3 eq), *i*-PrOH–H_2O, reflux, 18 h		(51)	71
		$PdCl_2(dppf)•CH_2Cl_2$, Et_3N, *i*-PrOH–H_2O		(—)	270
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (3 eq), *i*-PrOH–H_2O, reflux, 5 h		(55)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (3 eq), *i*-PrOH–H_2O, reflux, 7 h		(72)	71
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Et_3N (3 eq), *i*-PrOH–H_2O, reflux, 8 h		(64)	71
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), EtOH, 5 h	 **I** +  **II**		272, 273

	I + II	I/II
reflux	(50)	5.2:1
MW	(54)	4.8:1

TABLE 3B. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(OAc)_2$ (0.5%), K_2CO_3 (3 eq), EtOH, reflux, 5 h	 **I** + **II** (55), **I**/**II** = 3.8:1	272
C_{10}				
		$PdCl_2(dppf)•CH_2Cl_2$, Cs_2CO_3, THF–H_2O, reflux	 R: H (66) R: OMe (69)	274
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 3 h	 (90)	72

[a] The trifluoroborate derivative was prepared by a Diels-Alder reaction and was not isolated. The indicated yield is a two-step yield.

TABLE 3C. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

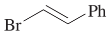
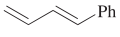
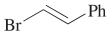
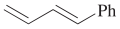
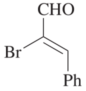
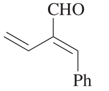
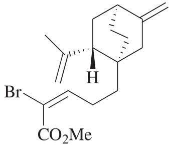
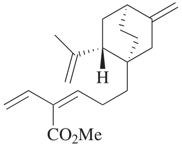
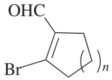
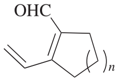
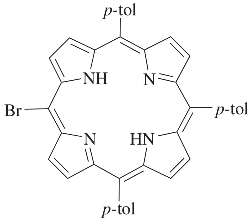
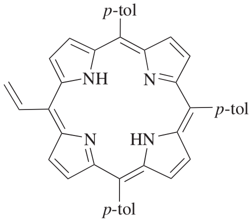
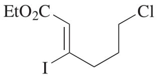
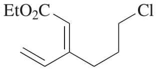
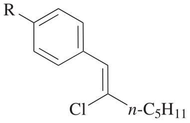
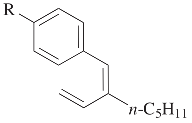
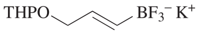
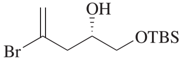
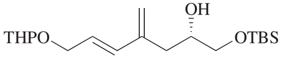
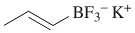
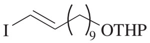
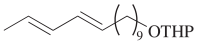
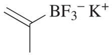
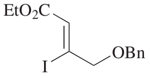
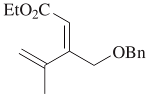
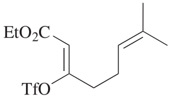
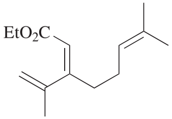
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (9%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 6 h	 (72)	261
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), Et$_3$N (1 eq), *n*-PrOH, reflux, 3 h	 (74)	261
		Pd(OAc)$_2$ (5%), PPh$_3$ (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 70°, 2.5 h	 (73)	72
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (9%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 9 h	 (51)	162
		Pd(OAc)$_2$ (5%), PPh$_3$ (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 50°	 *n* Time (h) 1 3 (92) 3 2 (—)	147
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (25%), Cs$_2$CO$_3$ (20 eq), THF–H$_2$O, 80°, overnight	 (61)	115

TABLE 3C. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 60°, 12 h	 (73)	147
		$Pd_2(dba)_3$ (2.5%), RuPhos (10%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18-36 h	 R — (Z)/(E) CO_2Me (87) — NO_2 (69) 85:15	148
C_3				
		$Pd(OAc)_2$ (10%), dppf (10%), *t*-$BuNH_2$, THF, reflux	 (84)	275
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 24 h	 (91)	276
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 24 h	 (70)	147
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, rt, 15 h	 (56)	147

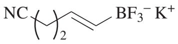
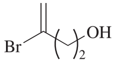
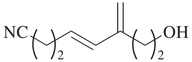
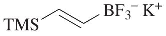
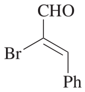
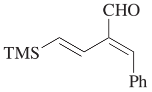
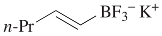
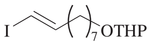
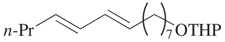
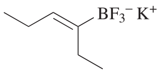
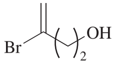
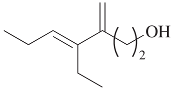
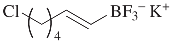
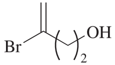
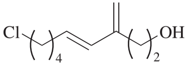
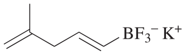
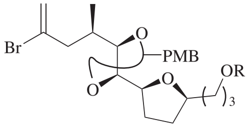
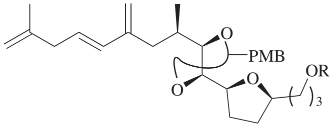
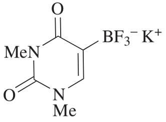
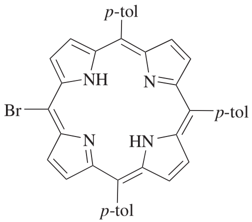
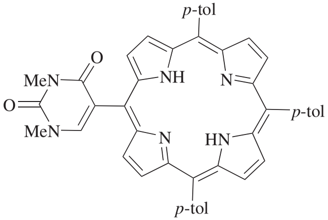
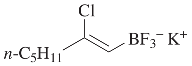
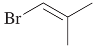
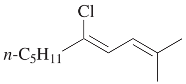
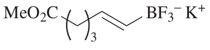
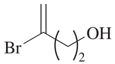
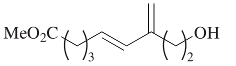
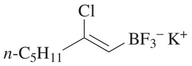
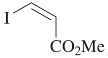
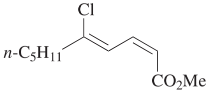
C_5						
			$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h		(80)	72
			$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h		(82)	72
			$PdCl_2(dppf)•CH_2Cl_2$ (2%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 24 h		(82)	276
C_6						
			$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h		(66)	72
			$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 4 h		(72)	72

TABLE 3C. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 R = TBDPS	$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 1.5 h	 (76) R = TBDPS	163
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), THF–H_2O, 80°, overnight	 (75)	115
C_7				
		$Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3•HBF_4$ (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h	 (70)	148
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h	 (70)	72
		$Pd(P(t\text{-}Bu)_3)_2$ (2.5%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 72 h	 (81)	148

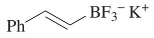
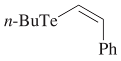
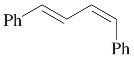
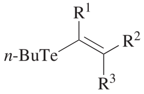
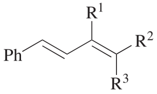
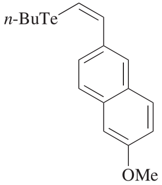
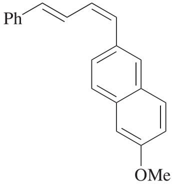
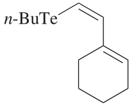
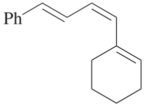
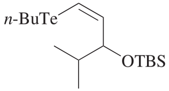
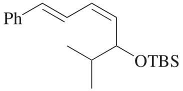
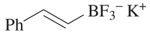
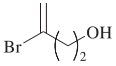
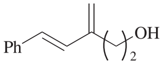
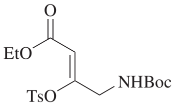
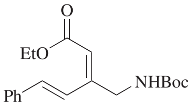
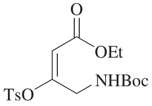
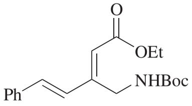
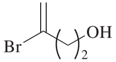
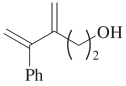
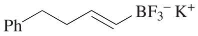
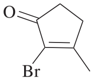
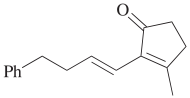
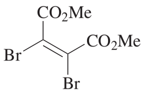
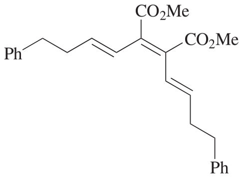
C_8 		$Pd(PPh_3)_4$ (20%), base (2 eq), additive (2 eq), MeOH, ultrasound, 20 min	 Base / Additive K_2CO_3 / Ag_2O (65) Cs_2CO_3 / Ag_2O (67) Et_3N / Ag_2O (66) Et_3N / AgOAc (84)	73
		$Pd(PPh_3)_4$ (20%), Et_3N (2 eq), AgOAc (2 eq), MeOH, ultrasound, 20 min	 R^1 / R^2 / R^3 H / H / 4-BrC_6H_4 (82) H / H / *t*-Bu (70) H / Ph / H (85) Me / Ph / Cl (82) CH_2OH / H / H (57)	73
		$Pd(PPh_3)_4$ (20%), Et_3N (2 eq), AgOAc (2 eq), MeOH, ultrasound, 20 min	 (67)	73
		$Pd(PPh_3)_4$ (20%), Et_3N (2 eq), AgOAc (2 eq), MeOH, ultrasound, 20 min	 (48)	73
		$Pd(PPh_3)_4$ (20%), Et_3N (2 eq), AgOAc (2 eq), MeOH, ultrasound, 20 min	 (79)	73

TABLE 3C. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

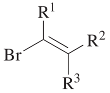
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h	 (70)	72
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Et_3N (1 eq), *n*-PrOH, 65°	 (69)	68
		$PdCl_2(PPh_3)_2$ (5%), aq Na_2CO_3 (3.5 eq), THF, 60°, 14 h	 (67)	68
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 12 h	 (60)	72
C_{10}				
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 8 h	 (95)	72



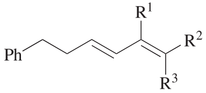
PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%)
Cs$_2$CO$_3$ (3 eq),
THF–H$_2$O, 70°, 5 h



(70) 72

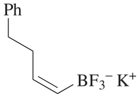


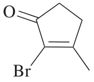
Pd(OAc)$_2$ (5%),
PPh$_3$ (10%),
Cs$_2$CO$_3$ (3 eq),
THF–H$_2$O, 70°



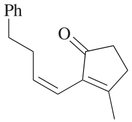
72

R^1	R^2	R^3	Time (h)	
H	Me	Me	4	(70)
H	H	$(CH_2)_3CN$	2	(78)
Me	Me	Me	6	(95)
CHO	H	Ph	2	(88)
$(CH_2)_2OH$	H	H	2	(79)
$(CH_2)_2OTIPS$	H	H	2	(85)
$(CH_2)_2OTBS$	H	H	2	(80)
$(CH_2)_2OTES$	H	H	2	(80)





Pd(OAc)$_2$ (5%),
PPh$_3$ (10%),
Cs$_2$CO$_3$ (3 eq),
THF–H$_2$O, 70°, 12 h



(94) 72

TABLE 3C. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

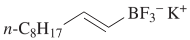
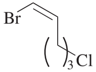
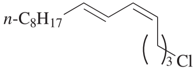
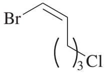
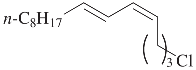
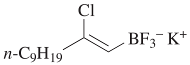
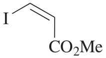
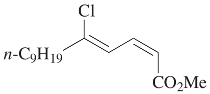
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Pd source (9%), ligand (18%), base (3 eq), THF–H_2O, reflux, 14 h	 Pd Source / Ligand / Base / ds $Pd(PPh_3)_4$ / — / Cs_2CO_3 / >99 / (81) $Pd(OAc)_2$ / PPh_3 / Cs_2CO_3 / >99 / (87) $Pd(OAc)_2$ / PPh_3 / K_2CO_3 / 98 / (67) $Pd(OAc)_2$ / PCy_3 / Cs_2CO_3 / 95 / (33)	72
		$Pd(OAc)_2$ (5%), PPh_3 (10%), Cs_2CO_3 (3 eq), THF–H_2O, 70°, 2 h	 (85)	72
C_{11}				
		$Pd_2(dba)_3$, $P(t\text{-}Bu)_3\cdot HBF_4$, Cs_2CO_3, THF–H_2O, 80°	 (76)	148

TABLE 3D. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALLYLIC AND BENZYLIC ELECTROPHILES

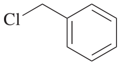
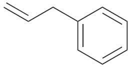
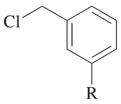
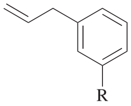
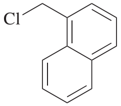
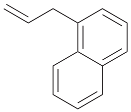
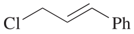
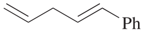
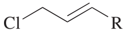
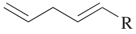
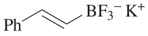
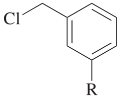
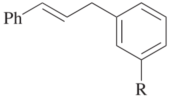
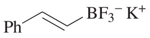
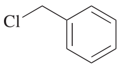
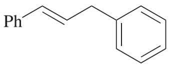
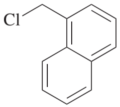
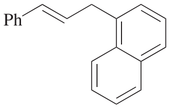
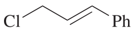
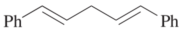
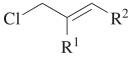
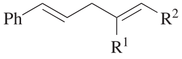
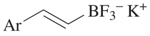
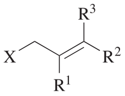
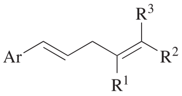
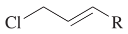
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(OAc)_2$ (0.1%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 (51)[a]	70
		Pd cat. **6** (*x*%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 R *x* H 0.1 (75) OMe 1 (59)	70
		Pd cat. **6** (0.1%), TBAB, KOH, acetone–H_2O, 50°, 8 h	 (83)	70
		$Pd(OAc)_2$ (0.1%), TBAB (0.5 eq), KOH (2 eq), acetone–H_2O, 50°, 14 h	 (66)[a]	70
		Pd cat. **6** (0.1%), TBAB (0.5 eq), KOH (2 eq), acetone–H_2O, 50°, 14 h	 R H (61) Ph (84)	70
C_8				
		Pd cat. **6** (0.1%), TBAB, KOH, acetone–H_2O, 50°	 R Time (h) H 14 (85) OMe 8 (89)	70

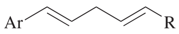
TABLE 3D. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ALLYLIC AND BENZYLIC ELECTROPHILES (*Continued*)

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(OAc)_2$ (0.1%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 (78)[a]	70
		Pd cat. **6** (0.1%), TBAB, KOH, acetone–H_2O, 50°, 6 h	 (87)	70
		$Pd(OAc)_2$ (0.1%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 (93)[a]	70
		Pd cat. **6** (0.1%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 R^1 R^2 H H (79) H Me (77) Ph H (68)	70
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), *i*-$PrNEt_2$ (3 eq), *i*-PrOH–H_2O, MW, 100°, 20 min	 Ar X R^1 R^2 R^3 Ph Br H H H (65) Ph I H H H (55) Ph Cl H H H (81) Ph Cl H Ph H (46) Ph Cl H Me Me (54) Ph Cl Me H H (64) Ph Cl H Me H (51) 4-ClC_6H_4 Cl H H H (71)	151

$C_{8–9}$



$PdCl_2(dppf)•CH_2Cl_2$ (2%),
i-$PrNEt_2$ (3 eq),
i-PrOH–H_2O,
MW, 100°, 20 min



Ar	R	
4-FC_6H_4	H	(89)
4-FC_6H_4	Ph	(75)
4-MeC_6H_4	H	(79)
4-MeC_6H_4	Me	(81)

151

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[a] The yield of the crude product was determined by ^1H NMR.

TABLE 3E. CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH MISCELLANEOUS ELECTROPHILES

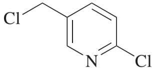
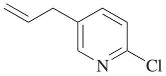
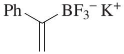
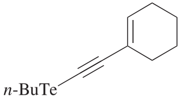
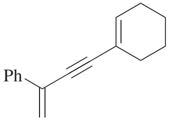
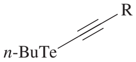
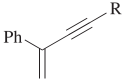
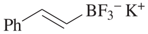
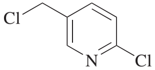
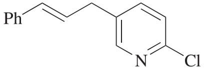
Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		Pd cat. **6** (0.5%), TBAB, KOH, acetone–H_2O, 50°, 8 h	 (81)	70
C_8				
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (74)	149
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 R: Ph (73) n-C_5H_{11} (68) n-C_6H_{13} (71)	149
		Pd cat. **6** (0.1%), TBAB, KOH, acetone–H_2O, 50°, 14 h	 (81)	70

TABLE 4A. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

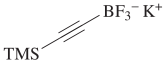
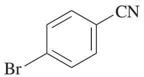
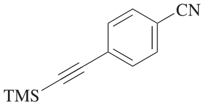
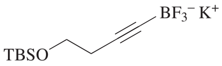
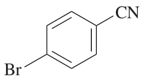
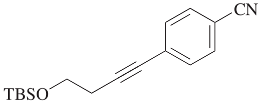
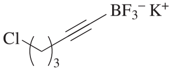
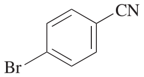
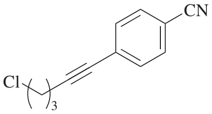
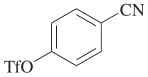
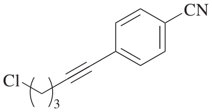
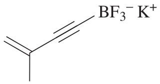
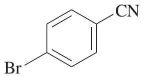
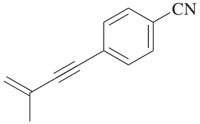
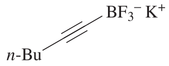
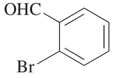
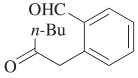
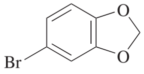
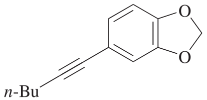
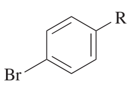
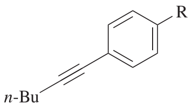
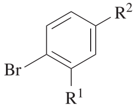
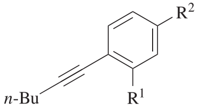
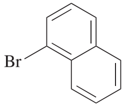
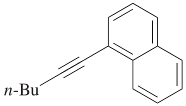
Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (60)	109
C_4				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (88)	109
C_5				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (85)	109
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), *i*-Pr_2NEt (3 eq), *i*-PrOH–H_2O, MW, 100°, 15 min	 (94)	220
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (87)	109

TABLE 4A. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (53)	109
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), solvent, reflux, 12 h	 Solvent THF–H_2O (44) THF (75)	109
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 R OH (48) Me (trace) CN (98) CH_2OH (76) CO_2H (73) NMe_2 (61)	109
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF, reflux, 12 h	 R^1 R^2 H OH (trace) H Me (36) H NMe_2 (33) CHO H (89)	109
		Pd source (9%), base (3 eq) THF–H_2O (*x*/*y*), reflux, 12 h See subtable on p.215.		109

Pd Source	Base	*x*/*y*	
$PdCl_2(dppf)•CH_2Cl_2$	Cs_2CO_3	20:1	(87)
$PdCl_2(PPh_3)_2$	Cs_2CO_3	10:1	(22)
$PdCl_2(dppf)•CH_2Cl_2$	K_2CO_3	10:1	(40)
$PdCl_2(dppf)•CH_2Cl_2$	K_3PO_4	10:1	(42)
$PdCl_2(dppf)•CH_2Cl_2$	Cs_2CO_3	10:1	(43)
$PdCl_2(dppf)•CH_2Cl_2$	K_2CO_3	20:1	(87)

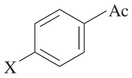
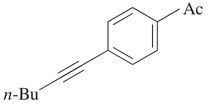
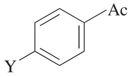
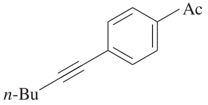
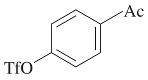
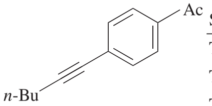
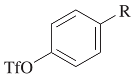
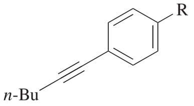
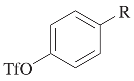
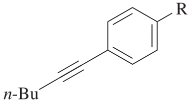
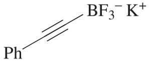
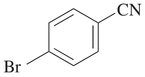
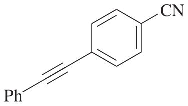
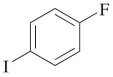
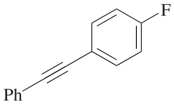
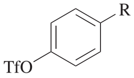
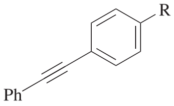
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h		X I (48) Cl (29)	109
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF, reflux, 60 h		Y I (30) OTs (0) OMs (0) Cl (40)	109
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), solvent, reflux, 12 h		Solvent THF–H_2O (10:1) (68) THF–H_2O (20:1) (73) THF (87)	109
	$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF, reflux, 12 h		R NO_2 (98) Me (55) OMe (78) Ac (87)	109

TABLE 4A. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), i-Pr_2NEt (3 eq), i-PrOH–H_2O, MW, 100°, 15 min	 R CN (90) Me (79) OMe (65)	220
C_8				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (69)	109
		$PdCl_2(dppf)•CH_2Cl_2$ (2%), i-$PrNEt_2$, i-PrOH–H_2O, MW, 100°, 10 min	 (60)	220
		Pd source, base (3 eq), i-PrOH–H_2O, MW, 100°, 15 min		220

Pd Source	R	Base	
$PdCl_2(dppf)•CH_2Cl_2$ (5%)	NO_2	i-Pr_2NEt	(96)
$Pd_2dba_3•CH_2Cl_2$	CN	Cs_2CO_3	(50)
$Pd_2dba_3•CH_2Cl_2$	CN	K_2CO_3	(60)
$PdCl_2(dppf)•CH_2Cl_2$ (5%)	CN	i-Pr_2NEt	(91)

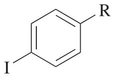
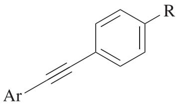
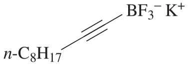
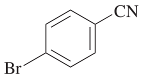
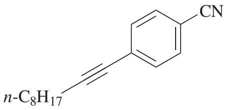
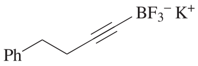
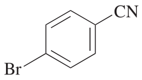
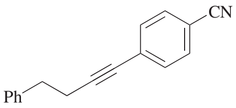
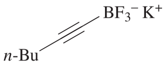
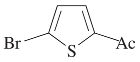
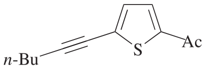
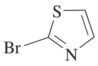
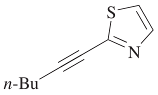
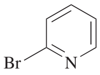
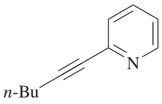
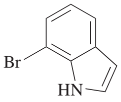
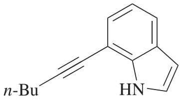
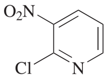
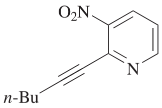
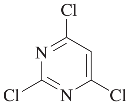
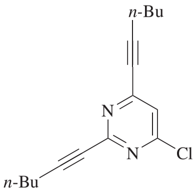
C_9					
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (2%), *i*-PrNEt$_2$, *i*-PrOH–H$_2$O, MW, 100°, 10 min		Ar R 4-MeC$_6$H$_4$ Cl (65) 4-MeOC$_6$H$_4$ Cl (68) 4-MeOC$_6$H$_4$ Br (72) 4-MeOC$_6$H$_4$ Ac (69) 4-NCC$_6$H$_4$ Ac (52)	271
C_{10}					
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (9%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 12 h		(91)	109
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (9%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, reflux, 12 h		(92)	109

TABLE 4B. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), solvent, reflux, 12 h	 Solvent THF–H_2O (47) THF (88)	109
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (78)	109
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (30)	109
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), solvent, reflux, 12 h	 Solvent THF–H_2O (46) THF (97)	109
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (85)	109
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (9%), Cs_2CO_3 (6 eq), THF–H_2O, reflux, 12 h	 (62)	109

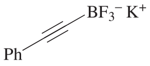
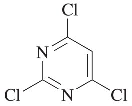
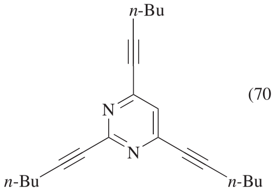
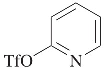
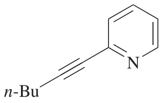
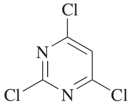
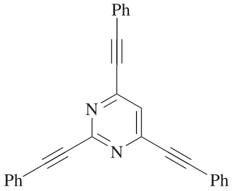
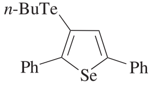
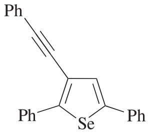
C_8			$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (9 eq), THF–H_2O, reflux, 12 h	 (70)	109
			$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF, reflux, 12 h	 (31)	109
			$PdCl_2(dppf)•CH_2Cl_2$ (27%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (74)	165
			$Pd(PPh_3)_4$ (15%), Et_3N, Ag_2O, MeOH, reflux, 24 h	 (71)	141

TABLE 4B. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

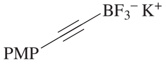
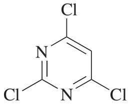
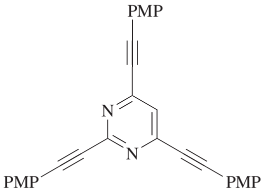
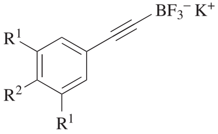
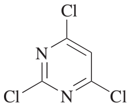
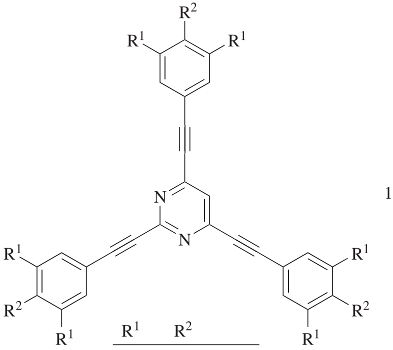
Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$PdCl_2(dppf)•CH_2Cl_2$ (27%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 (35)	165
C_{10}				
		$PdCl_2(dppf)•CH_2Cl_2$ (27%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 12 h	 R^1 R^2 H NMe_2 (51) OMe OMe (45)	165

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

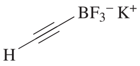
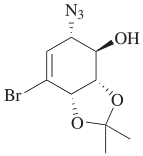
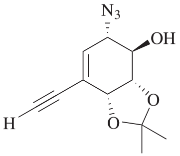
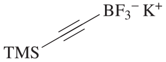
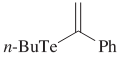
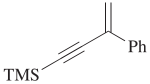
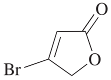
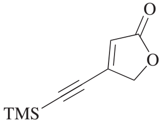
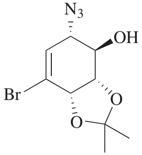
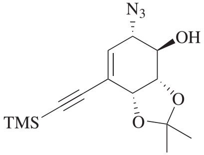
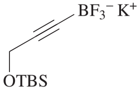
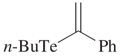
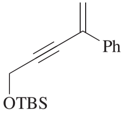
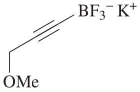
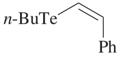
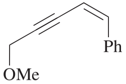
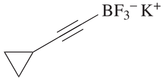
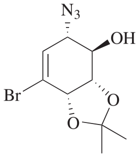
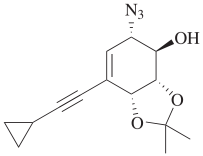
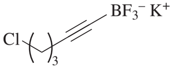
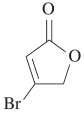
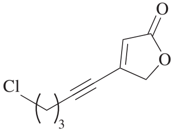
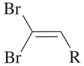
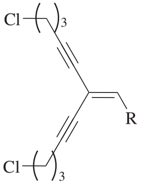
Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 24 h	 (0)	277
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (77)	149
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), THF, rt, 4 h	 (71)	110
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 24 h	 (0)	277
C_3				
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (70)	149

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h	 (28)	75
C_5				
		Pd(PPh$_3$)$_4$ (10%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 24 h	 (47)	277
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), THF, rt, 3 h	 (89)	110
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (10%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 50°, 2 h	 R Ph (82) 4-ClC$_6$H$_4$ (73) 4-MeC$_6$H$_4$ (76) 2-MeC$_6$H$_4$ (66) 1-naphthyl (82) 4-O$_2$NC$_6$H$_4$ (64)	111

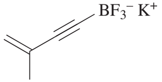
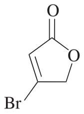
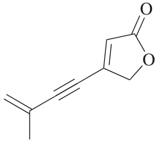
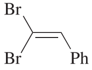
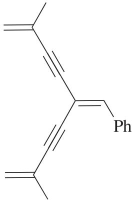
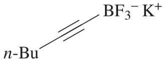
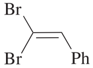
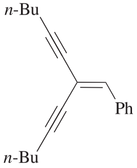
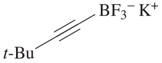
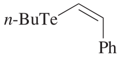
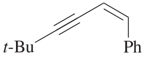
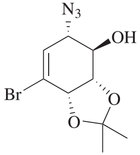
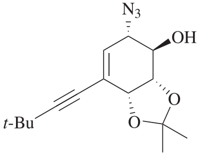
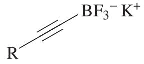
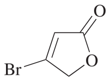
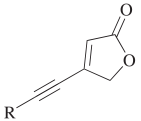
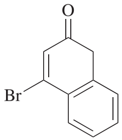
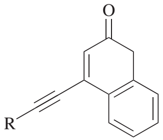
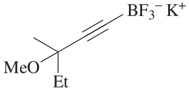
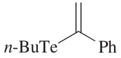
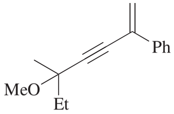
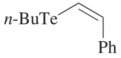
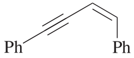
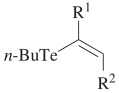
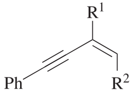
			$PdCl_2(dppf)•CH_2Cl_2$ (5%), THF, rt, 3 h		(88)	110
			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 2 h		(74)	111
C_6						
			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 2 h		(85)	111
			$Pd(acac)_2$ (15%), CuI (30%), Et_3N (3 eq), MeOH, reflux, 8 h		(61)	75
			$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 4 h		(74)	277

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$PdCl_2(dppf) \cdot CH_2Cl_2$ (5%), THF, rt	 R Time (h) *t*-Bu 3 (95) *n*-Bu 4 (95)	110
		$PdCl_2(dppf) \cdot CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), $THF–H_2O$, 50°	 R Time (h) *t*-Bu 1 (97) *n*-Bu 1.5 (91)	110
C_7				
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (74)	149
C_8				
		Pd source (15%), CuI (30%), Et_3N (3 eq), MeOH, reflux, 8 h	 Pd Source $Pd(OAc)_2$ (55) $Pd(acac)_2$ (77) $[Pd(allyl)Cl]_2$ (68) $PdCl_2(C_6H_5CN)_2$ (66)	75
		$Pd(acac)_2$ (15%), CuI (30%), Et_3N (3 eq), MeOH, reflux, 8 h	 R^1 R^2 H CH_2OH (58) CH_2OH H (51) CH_2OH CH_2OH (63)	75

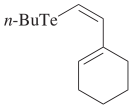
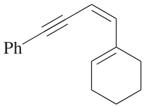
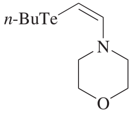
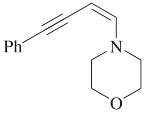
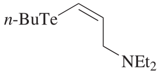
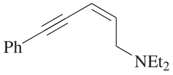
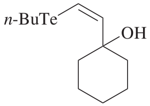
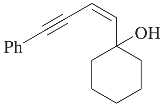
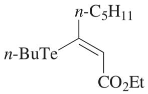
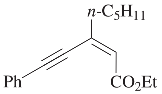
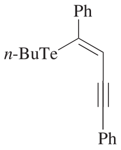
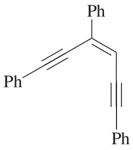
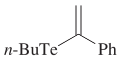
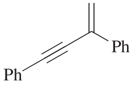
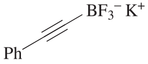
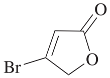
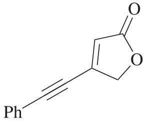
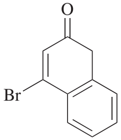
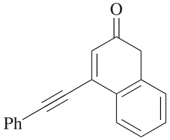
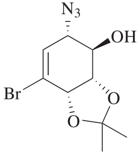
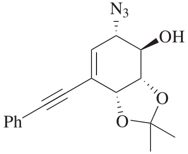
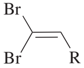
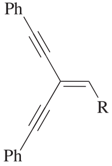
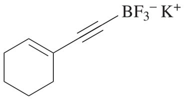
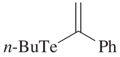
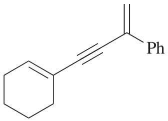
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(68)	75
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(0)	75
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(0)	75
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(58)	75
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(65)	75
	Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(68)	75
	Pd(PPh$_3$)$_4$ (10%), Et$_3$N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min		(79)	149

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), THF, rt, 6 h	 (91)	110
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 2 h	 (92)	110
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 8 h	 (69)	277
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 50°, 2 h	 R Ph (73) 4-ClC_6H_4 (81) *n*-C_8H_{17} (75)	111
		$Pd(PPh_3)_4$ (10%), Et_3N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (79)	149

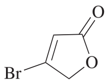
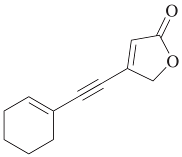
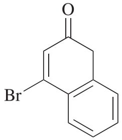
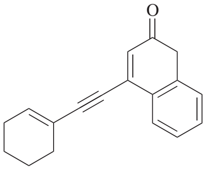
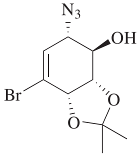
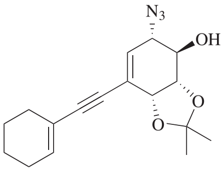
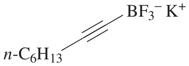
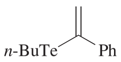
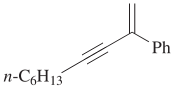
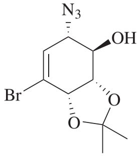
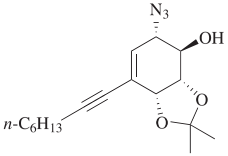
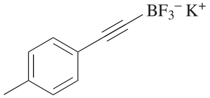
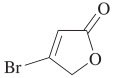
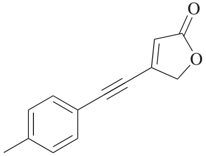
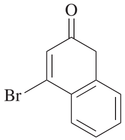
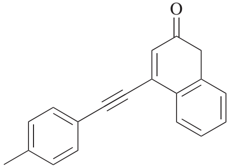
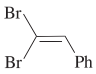
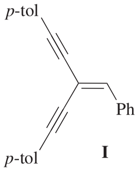
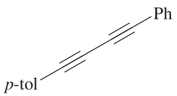
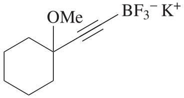
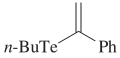
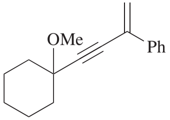
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), THF, rt, 5 h		(80)	110
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 50°, 1.5 h		(82)	110
		Pd(PPh$_3$)$_4$ (10%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 5.5 h		(56)	277
		Pd(PPh$_3$)$_4$ (10%), Et$_3$N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min		(73)	149
		Pd(PPh$_3$)$_4$ (10%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 4 h		(55)	277

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), THF, rt, 6 h	 (87)	110
		PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 50°, 2 h	 (85)	110
		Pd source (x%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 50°	 **I** +  **II**	111

Pd Source	x	Time (h)	**I**	**II**
PdCl$_2$(dppf)•CH$_2$Cl$_2$	5	4	(52)	(16)
PdCl$_2$(dppf)•CH$_2$Cl$_2$	10	2	(76)	(8)
Pd(OAc)$_2$	10	16	(23)	(26)

		Pd(PPh$_3$)$_4$ (10%), Et$_3$N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min	 (74)	149

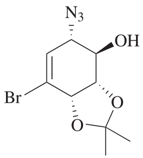
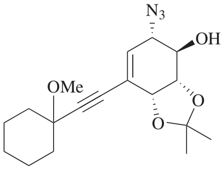
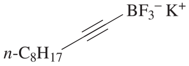
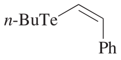
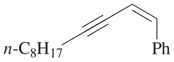
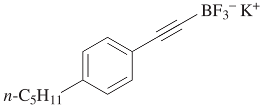
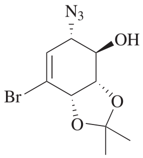
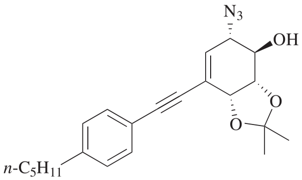
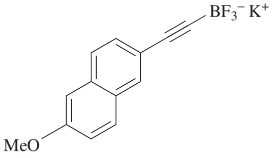
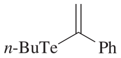
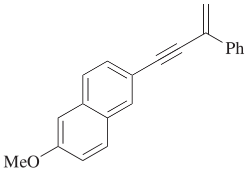
		Pd(PPh$_3$)$_4$ (10%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 10 h		(54)	277
C$_{10}$					
		Pd(acac)$_2$ (15%), CuI (30%), Et$_3$N (3 eq), MeOH, reflux, 8 h		(73)	75
C$_{13}$					
		Pd(PPh$_3$)$_4$ (10%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 90°, 3 h		(70)	277
		Pd(PPh$_3$)$_4$ (10%), Et$_3$N (2 eq), AgOAc (1 eq), MeOH, ultrasound, 20 min		(85)	149

TABLE 4C. CROSS-COUPLING OF ALKYNYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

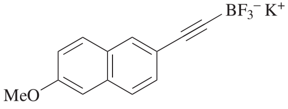
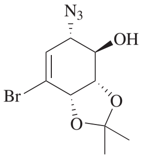
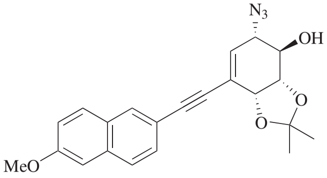
Alkynyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 90°, 3 h	 (60)	277

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

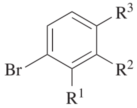
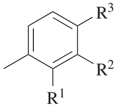
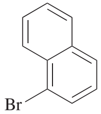
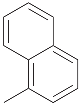
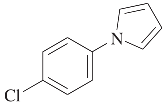
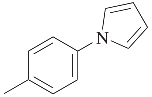
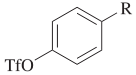
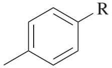
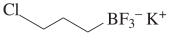
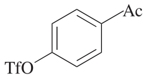
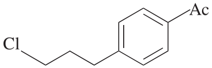
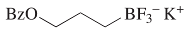
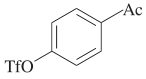
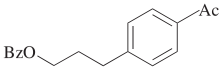
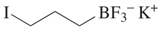
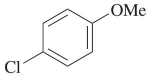
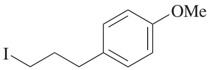
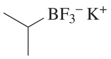
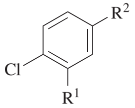
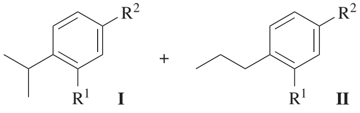
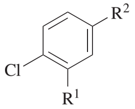
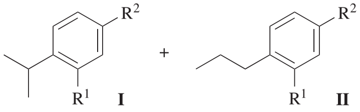
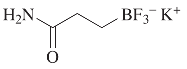
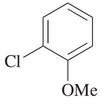
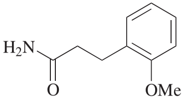
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
$MeBF_3^- K^+$		$PdCl_2(dppf) \bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 16–18 h	 R^1 R^2 R^3 H H NO_2 (77) H H CN (68) H H Ac (80) H H NHAc (67) H H COPh (92) H CO_2Me H (57) CN H H (60) CF_3 H NO_2 (83) Ac H H (61)	113
		$PdCl_2(dppf) \bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 16–18 h	 (85)	113
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h	 (72)	114
		$PdCl_2(dppf) \bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 16–18 h	 R NO_2 (85) Ac (85)	113
C_3				
		$PdCl_2(dppf) \bullet CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 d	 (72)	113

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 d	 (70)	113
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (0)	114
		$Pd(OAc)_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 72 h	 **I** + **II** R^1 / R^2 / **I + II** / **I:II** H / OMe / (77) / 3.5:1 OMe / H / (78) / 1:6	78
		$Pd(OAc)_2$ (5%), *t*-Bu$_2$PPh (7.5%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 72 h	 **I** + **II** R^1 / R^2 / **I + II** / **I:II** H / OMe / (79) / 8.2:1 OMe / H / (57) / 1.4:1	78
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (0)	121

C_4

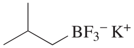
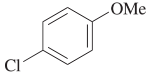
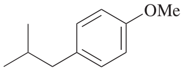
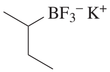
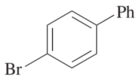
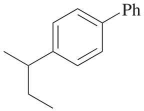
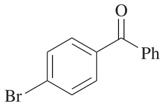
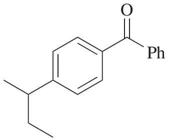
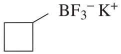
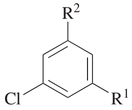
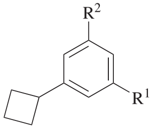
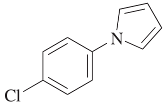
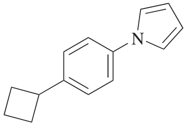
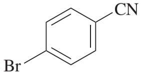
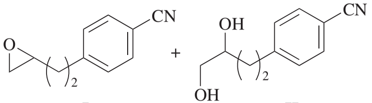
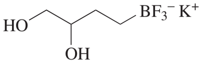
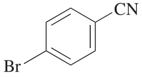
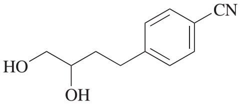
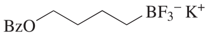
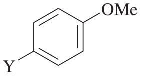
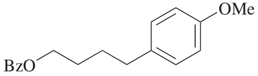
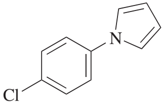
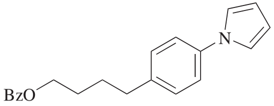
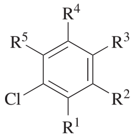
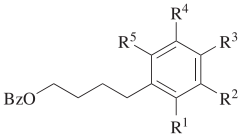
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h		(77)	114
		$Pd(OAc)_2$ (7.5%), RuPhos (15%), K_3PO_4 (3 eq), toluene–H_2O, 115°, 72 h		(45)	278
		$Pd(OAc)_2$ (7.5%), RuPhos (15%), K_3PO_4 (3 eq) Solvent Temp (°) Time (h) toluene–H_2O 115 110 (51) xylene–H_2O 130 24 (30)		(51)	278
		$Pd(OAc)_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h		R^1 R^2 OMe OMe (82) CO_2Me H (63)	112
		$Pd(OAc)_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h		(74)	112

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), $THF–H_2O$ (*x*/*y*), reflux	 **I** + **II** *x*/*y* Time **I** **II** 10:1 8 h — (74) 40:1 3 d (80) —	116
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), $THF–H_2O$, reflux, 21 h	 (65)	244
		$Pd(OAc)_2$ (2%), RuPhos (4%), base (3 eq), $toluene–H_2O$, 80°, 36 h	 Y Base Br K_2CO_3 (88) I Cs_2CO_3 (80) Cl K_2CO_3 (92) OTf K_2CO_3 (75)	114
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), $toluene–H_2O$, 80°, 24 h	 (94)	114

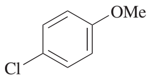


Pd(OAc)$_2$ (2%), RuPhos (4%), K$_2$CO$_3$ (3 eq), toluene–H$_2$O, 80°, 24 h

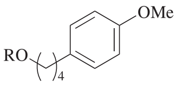


R^1	R^2	R^3	R^4	R^5	
H	H	H	H	H	(81)
H	H	NO$_2$	H	H	(96)
H	H	CF$_3$	H	H	(90)
H	H	CN	H	H	(87)
H	H	CHO	H	H	(90)
H	H	Me	H	H	(82)
H	H	Ac	H	H	(87)
H	H	COPh	H	H	(89)
H	CO$_2$Me	H	H	H	(91)
H	OMe	H	OMe	H	(89)
OMe	H	H	H	H	(87)
Me	H	H	H	Me	(95)
Me	H	OMe	H	Me	(92)
OMe	OMe	H	CN	H	(80)

114



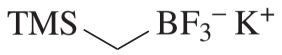
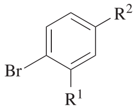
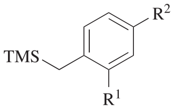
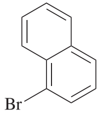
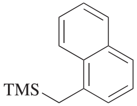
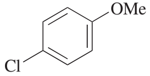
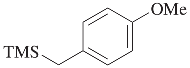
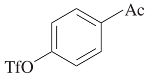
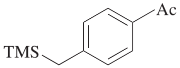
Pd(OAc)$_2$ (2%), RuPhos (4%), K$_2$CO$_3$ (3 eq), toluene–H$_2$O, 80°, 36 h



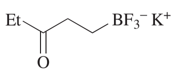
R	
Piv	(82)
TBS	(71)

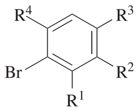
114

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

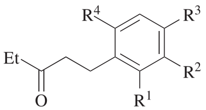
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6–8 h	 R^1 R^2 H Ac (65) H COPh (60) H NHAc (53) H CN (55) CN H (51)	113
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6–8 h	 (77)	113
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h	 (71)	114
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 6–8 h	 (70)	113

C_5



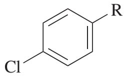


$Pd(OAc)_2$ (2.5%),
RuPhos (5%), K_2CO_3 (3 eq),
toluene–H_2O, 85°

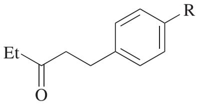


R^1	R^2	R^3	R^4	Time (h)	
H	CN	H	H	18	(87)
H	OMe	H	H	24	(87)
H	Ac	H	H	18	(87)
H	H	NO_2	H	18	(93)
H	H	Me	H	24	(75)
H	H	CN	H	18	(88)
H	H	CHO	H	18	(78)
H	H	OMe	H	24	(86)
H	H	Ac	H	83	(83)
H	H	CO_2Me	H	18	(89)
H	H	NHAc	H	24	(78)
Me	H	Me	Me	24	(76)

120

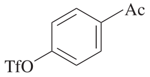


$Pd(OAc)_2$ (2.5%),
RuPhos (5%), K_2CO_3 (3 eq),
toluene–H_2O, 85°, 18 h

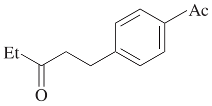


R	
CN	(85)
OMe	(77)

120



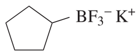
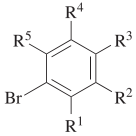
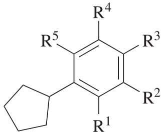
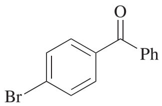
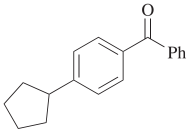
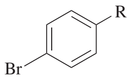
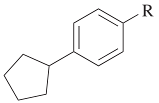
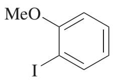
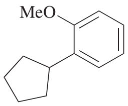
$Pd(OAc)_2$ (2.5%),
RuPhos (5%), K_2CO_3 (3 eq),
toluene–H_2O, 85°, 18 h

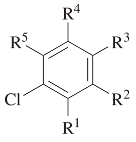
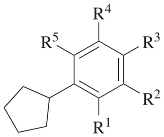


(80)

120

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_5$				
		Pd(OAc)$_2$ (2%), *n*-BuPAd$_2$ (3%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 100°, 24 h	 R^1 R^2 R^3 R^4 R^5 H H NO$_2$ H H (86) H H CN H H (—) H H Ac H H (49) H CO$_2$Me H H H (93) H OMe H OMe H (81) OMe H H H H (83) Me H OMe H Me (77)	78
		Pd(OAc)$_2$ (7.5%), RuPhos (15%), K$_3$PO$_4$ (3 eq), toluene–H$_2$O, 115°, 44 h	 (70)	278
		Pd(OAc)$_2$ (7.5%), RuPhos (15%), K$_3$PO$_4$ (3 eq), toluene–H$_2$O, 115°	 R Time (h) NO$_2$ 20 (58) CN 67 (62) CF$_3$ 90 (85) 43 (53)	278
		Pd(OAc)$_2$ (2%), *n*-BuPAd$_2$ (3%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 100°, 72 h	 (70)	78

		$Pd(OAc)_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h		78

R^1	R^2	R^3	R^4	R^5	
H	H	NO_2	H	H	(89)
H	H	CN	H	H	(—)
H	H	CF_3	H	H	(82)
H	H	OMe	H	H	(88)
H	H	Ac	H	H	(51)
H	CO_2Me	H	H	H	(89)
H	OMe	H	OMe	H	(92)
OMe	H	H	H	H	(87)
Me	H	OMe	H	Me	(82)

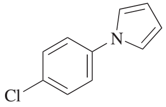
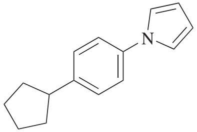
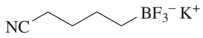
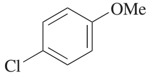
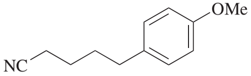
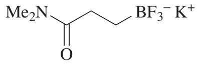
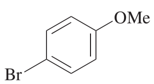
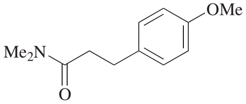
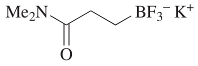
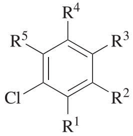
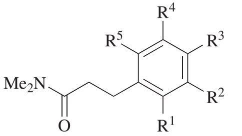
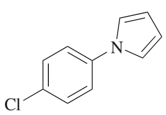
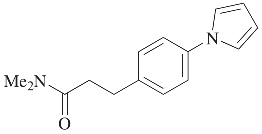
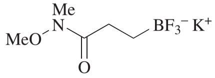
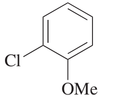
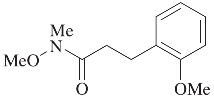
		$Pd(OAc)_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h		(94)	78
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h		(80)	114
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 24 h		(50)	120

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		121

R^1	R^2	R^3	R^4	R^5	
H	H	H	H	H	(75)
H	H	NO_2	H	H	(85)
H	H	CF_3	H	H	(76)
H	H	CN	H	H	(81)
H	H	CHO	H	H	(87)
H	H	OMe	H	H	(86)
H	H	Ac	H	H	(94)
H	OMe	H	OMe	H	(78)
H	CO_2Me	H	H	H	(81)
CN	H	H	H	H	(83)
Me	H	H	H	H	(75)
OMe	H	H	H	H	(79)
Me	H	H	H	Me	(76)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (71)	121
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (—)	121

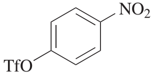
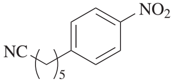
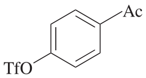
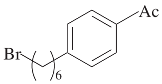
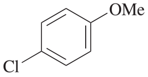
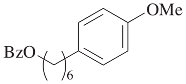
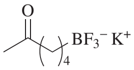
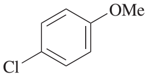
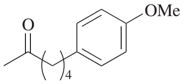
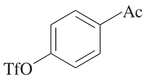
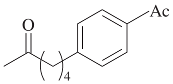
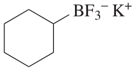
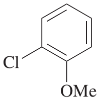
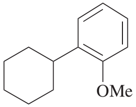
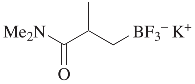
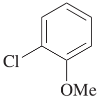
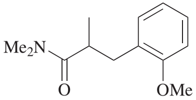
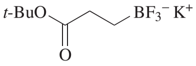
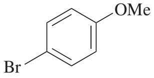
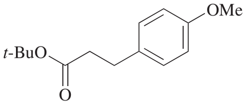
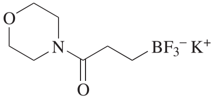
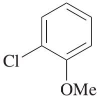
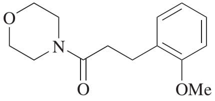
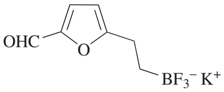
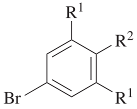
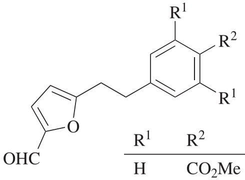
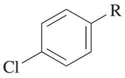
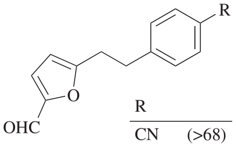
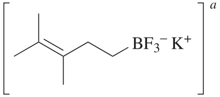
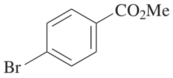
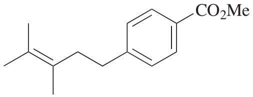
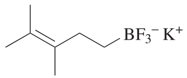
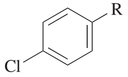
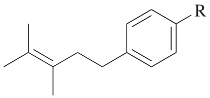
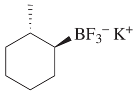
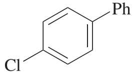
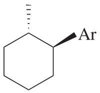
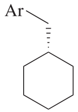
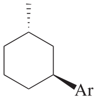
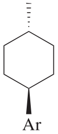
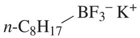
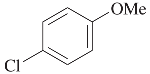
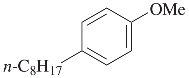
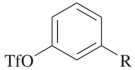
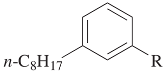
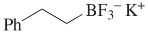
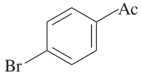
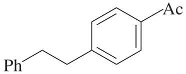
C_6						
			$PdCl_2(dppf){\bullet}CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h		(73)	58
			$PdCl_2(dppf){\bullet}CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h		(61)	58
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(91)	114
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h		(78)	114
			$PdCl_2(dppf){\bullet}CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h		(79)	58
			$Pd(OAc)_2$ (5%), *n*-$BuPAd_2$ (7.5%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 72 h		(79)	78
			$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		(60)	121

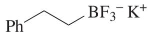
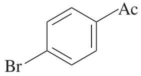
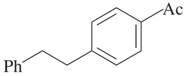
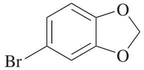
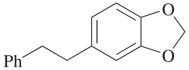
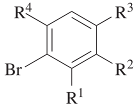
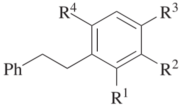
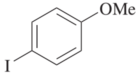
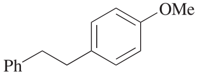
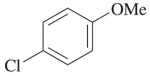
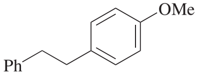
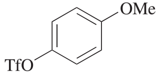
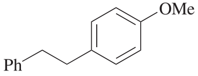
TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 24 h	 (70)	120
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (65)	121
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R^1 R^2 H CO_2Me (>69) OMe H (>62)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R CN (>68) CHO (>72)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>80)	279

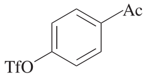
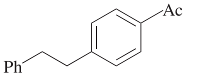
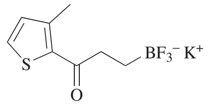
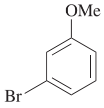
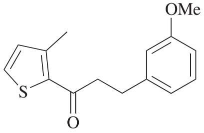
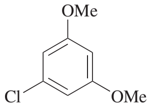
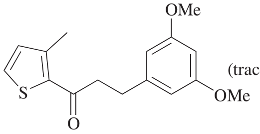
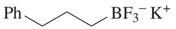
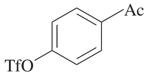
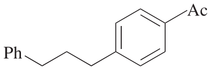
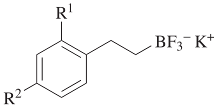
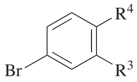
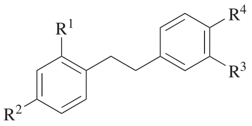
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R OMe (>62) CHO (>62)	279
		$Pd(OAc)_2$ (5%), ligand (7.5%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 72 h	 **I** +  **II** +  **III** +  **IV** Ar = 4-PhC_6H_4	78
C8				
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h	 (82)	114
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 R CN (65) CF_3 (59)	58
		$Pd(OAc)_2$ (1.5%), PPh_3 (3%), K_2CO_3 (3 eq), toluene–H_2O, 95°	 (74)	230

Ligand	**I + II + II + IV**	**I/II/III/IV**
n-$BuPAd_2$	(80)	4.4:1.4:1:2
t-Bu_3P	(48)	16:6:1:1
PhP*t*-Bu_2	(72)	27.7:8.1:1.6:1

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

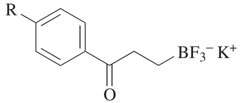
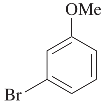
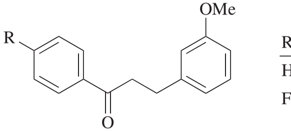
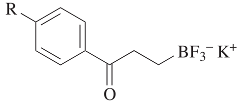
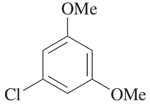
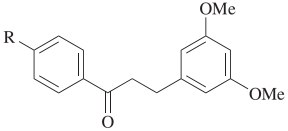
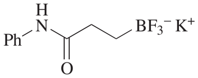
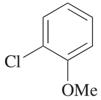
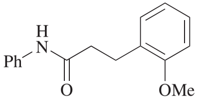
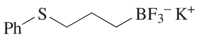
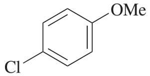
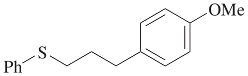
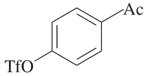
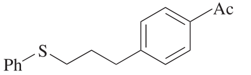
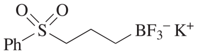
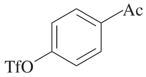
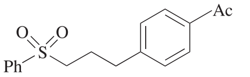
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		Pd (2.5 ppm), Na_2CO_3 (3.7 eq), TBAB (1 eq), EtOH–H_2O, MW, 150°, 5 min	 (0)	214
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h to 3 d	 $(25)^b$	113
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h to 3 d	 R^1 R^2 R^3 R^4 H H OH H (trace) H H OMe H (45) H OMe H H (86) H H NMe_2 H (0) Me H H H (82) Me H Me Me (68)	113
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h to 3 d	 (0)	113
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (87)	114
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h to 3 d	 $(12)^b$	113

C$_9$

		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (96)	58
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (55)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (trace)	119
		$PdCl_2(dppf){\bullet}CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (84)	58
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		279

R^1	R^2	R^3	R^4	
H	CN	H	OMe	(>71)
H	CN	H	Ac	(>77)
H	CN	CO_2Me	H	(>82)
H	CF_3	H	CO_2Me	(>76)
H	OMe	CO_2Me	H	(>72)
Me	H	H	OMe	(>59)

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 R H (55) F (64)	119
 R = H, F		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (trace)	119
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (84)	121
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 24 h	 (0)	114
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 d	 (66)	113
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 d	 (70)	113

C_{10}

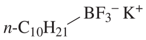
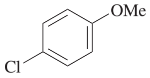
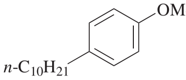
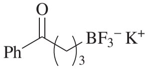
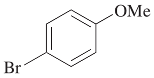
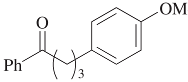
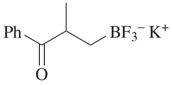
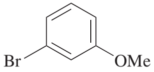
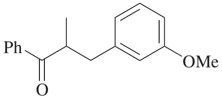
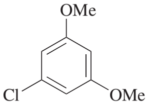
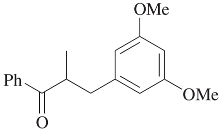
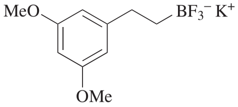
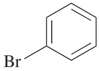
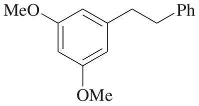
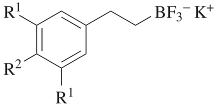
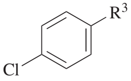
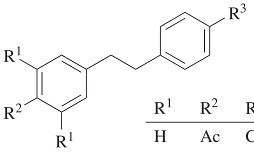
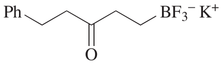
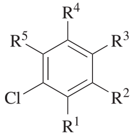
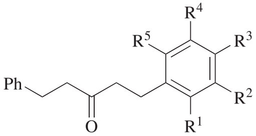
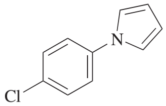
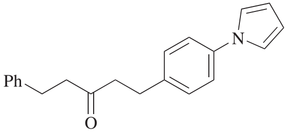
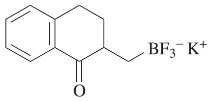
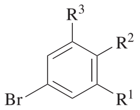
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 36 h		(70)	114
		$Pd(OAc)_2$ (5%), RuPhos (10%), K_2CO_3, toluene–H_2O, 80°, 23 h		(74)	280
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		(60)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		(60)	119
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>73)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R^1 R^2 R^3 H Ac CHO (>79) OMe H OMe (>75) OMe H CHO (>81) OMe H Ac (>78)		279

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

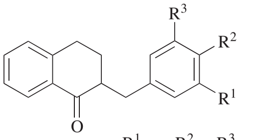
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (89)	119

R^1	R^2	R^3	R^4	R^5	
H	H	H	H	H	(83)
H	H	NO_2	H	H	(75)
H	H	CN	H	H	(73)
H	H	CHO	H	H	(94)
H	H	CF_3	H	H	(82)
H	H	OMe	H	H	(78)
H	H	Ac	H	H	(80)
H	OMe	H	OMe	H	(89)
H	CO_2Me	H	H	H	(89)
CN	H	H	H	H	(81)
Me	H	H	H	H	(70)
OMe	H	H	H	H	(88)
Me	H	H	H	Me	(67)



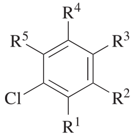


Pd(OAc)$_2$ (2.5%),
RuPhos (5%),
K_2CO_3 (3 eq),
toluene–H_2O, 85°, 14 h

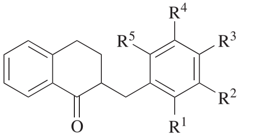


R^1	R^2	R^3	
H	CN	H	(75)
OMe	H	H	(68)
OMe	H	OMe	(74)

119

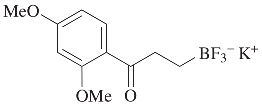


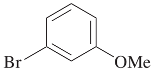
Pd(OAc)$_2$ (2.5%),
RuPhos (5%),
K_2CO_3 (3 eq),
toluene–H_2O, 85°, 14 h



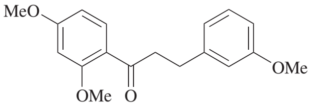
R^1	R^2	R^3	R^4	R^5	
H	H	CN	H	H	(72)
H	OMe	H	H	H	(trace)
Me	H	H	H	Me	(trace)
H	OMe	H	OMe	H	(trace)

119



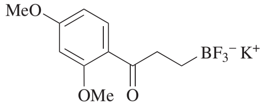
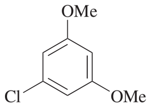
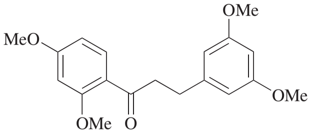
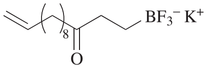
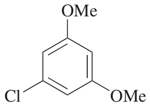
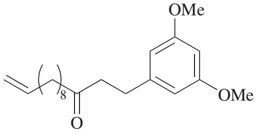


Pd(OAc)$_2$ (2.5%),
RuPhos (5%),
K_2CO_3 (3 eq),
toluene–H_2O, 85°, 14 h



(79) 119

TABLE 5A. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (87)	119
C_{13}				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (81)	119

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[a] The trifluoroborate derivative comes from the hydroboration/cross-coupling reaction of the corresponding 1,2-dibora species.

[b] The yield of the product was determined by GC analysis.

TABLE 5B. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

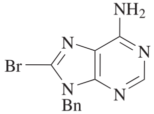
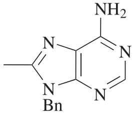
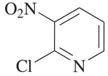
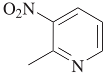
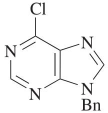
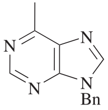
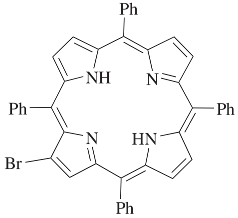
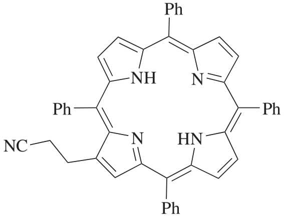
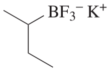
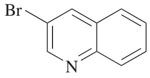
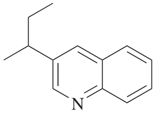
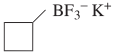
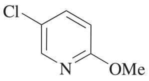
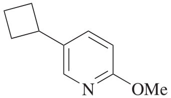
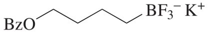
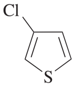
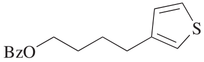
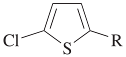
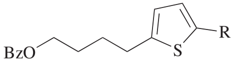
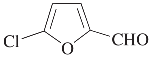
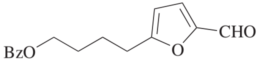
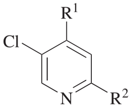
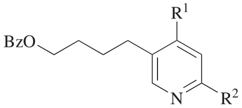
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*				
C_1				
$MeBF_3^- K^+$		$Pd(OAc)_2$ (10%), TPPTS, Cs_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min	 (0)	104
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), $THF–H_2O$, reflux, 16–18 h	 (32)	113
		$Pd(OAc)_2$ (10%), TPPTS, Cs_2CO_3 (3 eq), $MeCN–H_2O$, MW, 150°, 5 min	 (44)	104
C_3				
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), $THF–H_2O$, 80°	 (70)	115
C_4				
		$Pd(OAc)_2$ (7.5%), RuPhos (15%), K_3PO_4 (3 eq), toluene–H_2O, 115°, 48 h	 (37)	278

TABLE 5B. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		Pd(OAc)$_2$ (2%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (45)	112
		Pd(OAc)$_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (81)	114
		Pd(OAc)$_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R H (96) Ac (76) CHO (71)	114
		Pd(OAc)$_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (83)	114
		Pd(OAc)$_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 R^1 R^2 H H (93) H F (73) H OMe (97) CHO H (85)	114

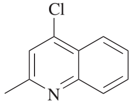
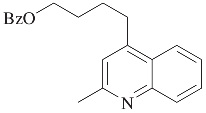
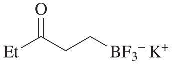
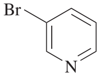
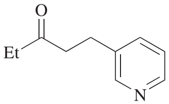
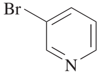
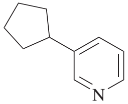
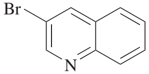
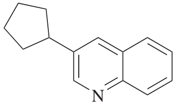
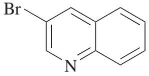
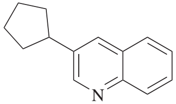
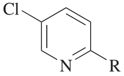
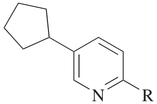
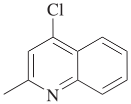
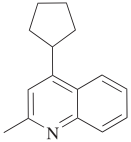
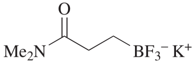
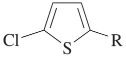
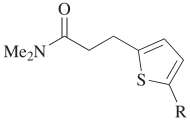
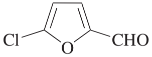
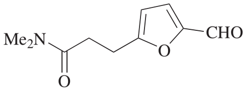
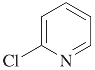
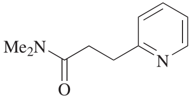
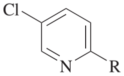
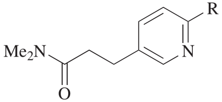
		Pd(OAc)$_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(91)	114
C_5					
		Pd(OAc)$_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene-H_2O, 85°, 18 h		(73)	120
		Pd(OAc)$_2$ (x%), ligand (2x%), K_3PO_4 (3 eq), toluene–H_2O, 115°		x Ligand 7.5 RuPhos (40) 20 SPhos (15)	278
		Pd(OAc)$_2$ (x%), RuPhos (2x%), K_3PO_4 (3 eq), toluene–H_2O, 115°, 88 h	 x Ligand Time (h) 7.5 RuPhos 20 (40) 7.5 RuPhos 88 (60) 20 SPhos 20 (25)	(60)	278
		Pd(OAc)$_2$ (2%), n-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h		(72)	78

TABLE 5B. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 R H (57) F (77) OMe (92)	78
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (88)	78
		$Pd(OAc)_2$ (2.5%), SPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 R H (79) CHO (66)	121
		$Pd(OAc)_2$ (2.5%), SPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (73)	121
		$Pd(OAc)_2$ (2.5%), SPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (trace)	121
		$Pd(OAc)_2$ (2.5%), SPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 R H (50) F (60) OMe (87)	121

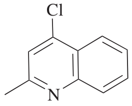
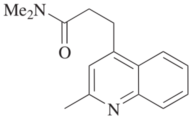
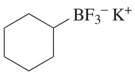
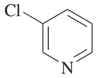
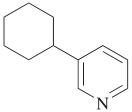
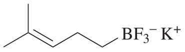
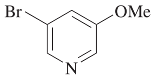
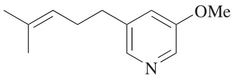
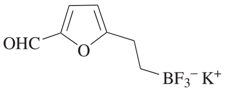
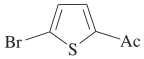
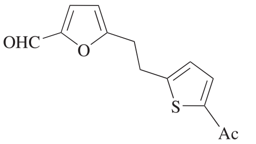
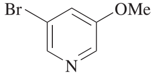
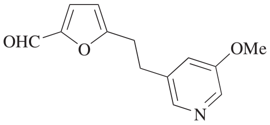
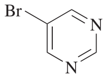
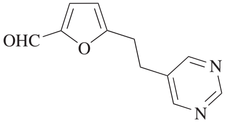
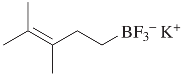
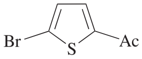
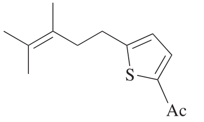
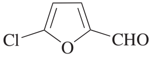
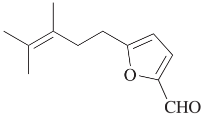
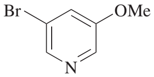
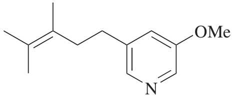
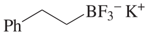
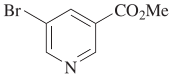
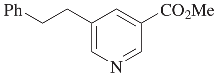
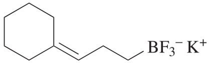
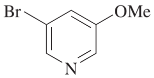
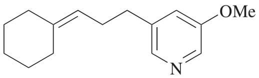
			$Pd(OAc)_2$ (2.5%), SPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h		(72)	121
C_6			$Pd(OAc)_2$ (5%), *n*-$BuPAd_2$ (7.5%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 72 h		(87)	78
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>69)	279
C_7						
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>75)	279
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>56)	279
			$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>60)	279

TABLE 5B. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>79)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>79)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>80)	279
C_8				
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), K_3PO_4 (4 eq), DMF–THF, 70°, 6 h	 (60)	161
C_9				
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>81)	279

C_{10}

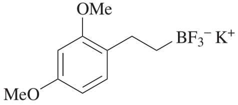
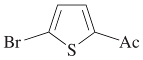
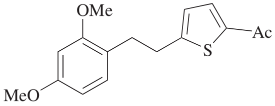
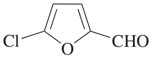
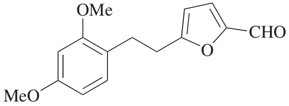
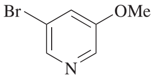
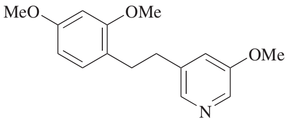
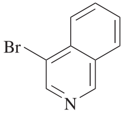
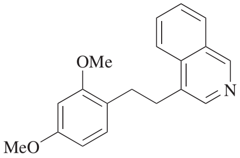
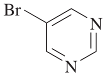
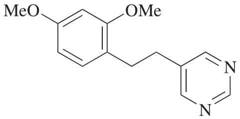
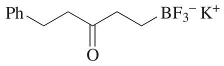
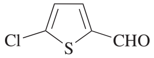
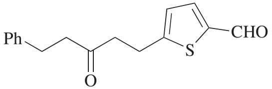
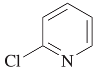
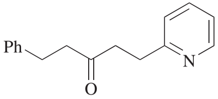
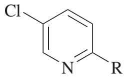
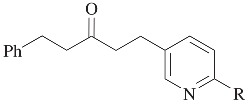
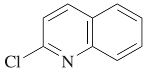
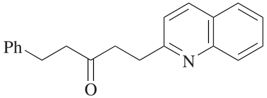
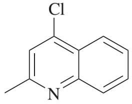
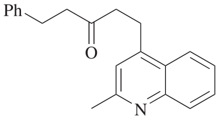
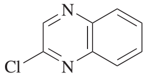
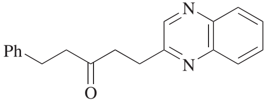
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>83)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>84)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>82)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>72)	279
		$Pd(OAc)_2$ (2%), RuPhos (4%), K_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h		(>75)	279

TABLE 5B. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (60)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (0)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 R H (72) F (73) OMe (87)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (60)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (65)	119
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 14 h	 (43)	119

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[a] The trifluoroborate derivative comes from the hydroboration/cross-coupling reaction of the corresponding 1,2-dibora species.

TABLE 5C. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

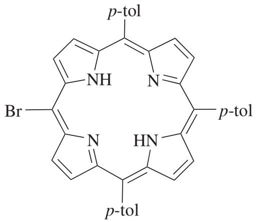
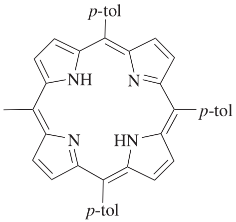
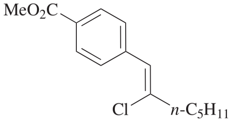
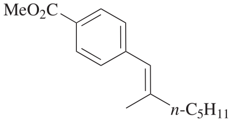
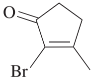
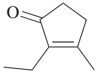
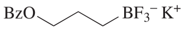
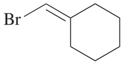
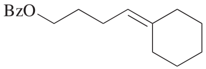
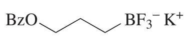
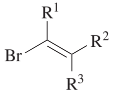
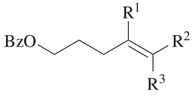
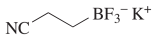
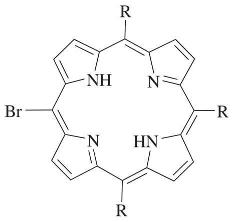
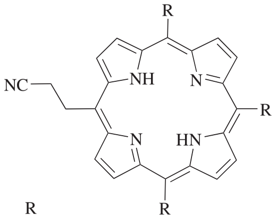
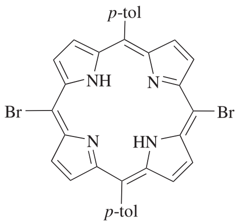
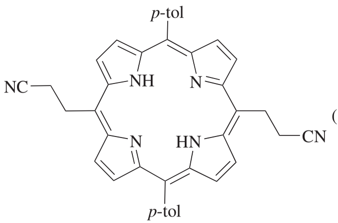
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
$MeBF_3^- K^+$		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), THF–H_2O, 80°, overnight	 (29)	115
		$Pd_2(dba)_3$ (2.5%), RuPhos (10%), Cs_2CO_3 (3 eq), THF, 80°, 18–36 h	 (67)	148
C_2				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 4 h	 (83)	76
C_3				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 5 h	 (82)	76

TABLE 5C. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°	 R^1 R^2 R^3 Time (h) CHO H Ph 12 (69) Ph H H 3 (54) Ph Ph Ph 3 (91)	76
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), THF–H_2O, 80°, overnight	 R 4-MeC_6H_4 (73) *c*-C_6H_{11} (25)	115
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (40 eq), THF–H_2O, 80°, overnight	 (35)	115

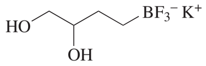
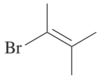
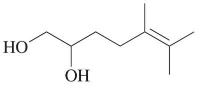
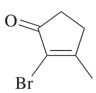
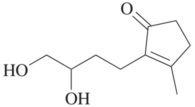
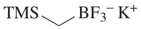
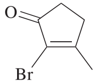
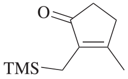
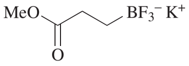
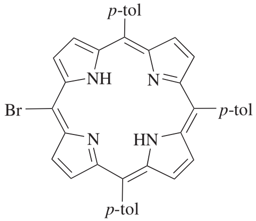
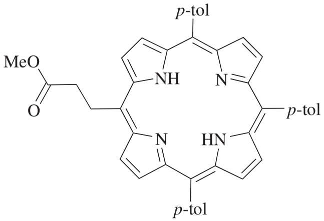
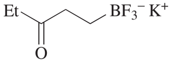
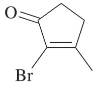
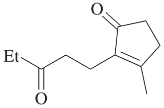
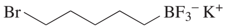
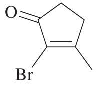
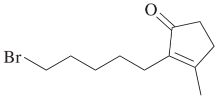
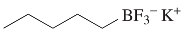
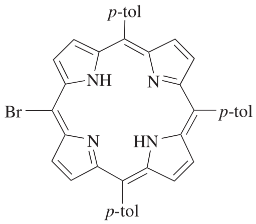
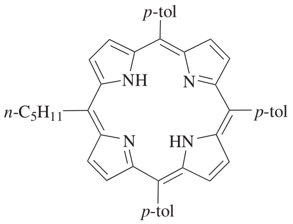
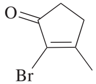
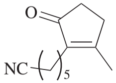
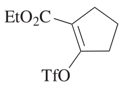
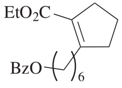
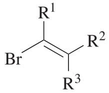
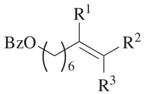
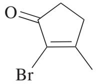
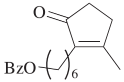
C_4					
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–pH 9 buffer, 90°, 19 h		(60)	244
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 16 h		(94)	76
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 8 h		(95)	76
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), THF–H_2O, 80°		(16)	115
C_5					
		$Pd(OAc)_2$ (2.5%), RuPhos (5%), K_2CO_3 (3 eq), toluene–H_2O, 85°, 18 h		(78)	120
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 22 h		(69)	76

TABLE 5C. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), $THF–H_2O$, 80°, overnight	 (21)	115
C_6				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), $toluene–H_2O$, 80°, 7 h	 (86)	76
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), $THF–H_2O$, reflux, 18 h	 (68)	58
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), $toluene–H_2O$, 80°	 R^1 R^2 R^3 Time (h) Me Me Me 3 (93) H H $(CH_2)_4OTBS$ 2 (78)	76
		$PdCl_2(dppf)•CH_2Cl_2$ (*x*%), base (3 eq), $toluene–H_2O$, 80°	 *x* Base Time (h) 10 Cs_2CO_3 7 (74) 5 Cs_2CO_3 24 (68) 10 K_2CO_3 7 (39)	76

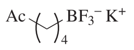
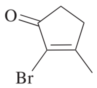
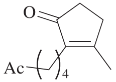
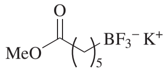
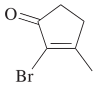
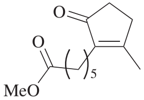
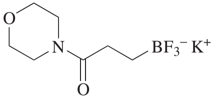
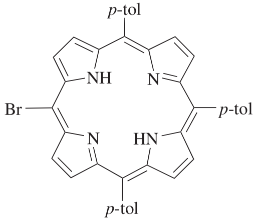
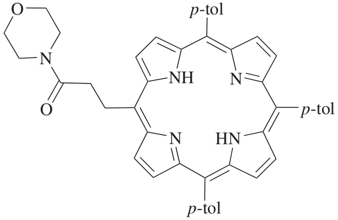
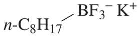
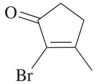
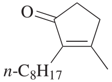
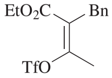
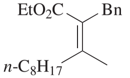
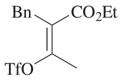
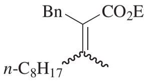
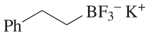
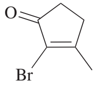
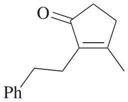
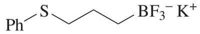
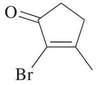
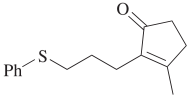
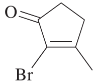
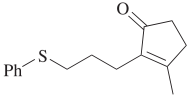
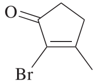
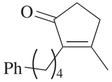
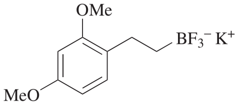
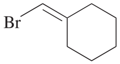
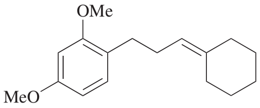
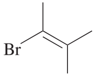
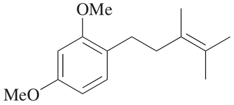
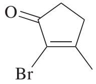
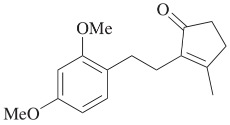
C_7			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 11 h	 (87)	76
			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 18 h	 (63)	76
			$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), THF–H_2O, 80°, overnight	 (21)	115
C_8			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 8 h	 (53)	76
			$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (75)	58
			$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (50) (Z)/(E) = 1:1	58
			$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 9 h	 (92)	76

TABLE 5C. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (41)	76
		$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (90)	76
C_{10}				
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 18 h	 (63)	76
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>74)	279
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>72)	279
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 24 h	 (>32)	279

[a] The trifluoroborate derivative comes from the hydroboration/cross-coupling reaction of the corresponding 1,2-dibora species.

TABLE 5D. CROSS-COUPLING OF ALKYLTRIFLUOROBORATES WITH IMIDOYL ELECTROPHILES

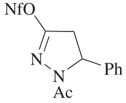
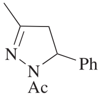
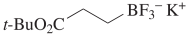
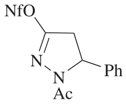
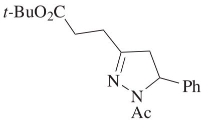
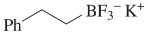
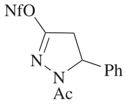
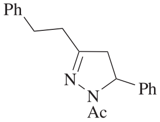
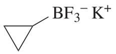
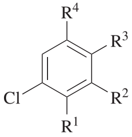
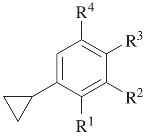
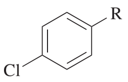
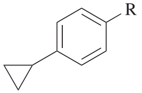
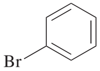
Alkyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
$MeBF_3^- K^+$		$PdCl_2(dppf)•CH_2Cl_2$ (9%), K_2CO_3 (3 eq), LiCl (3 eq), toluene–H_2O, 100°, 18 h	 (0)	123
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), K_2CO_3 (3 eq), LiCl (3 eq), toluene–H_2O, 100°, 18 h	 (32)	123
C_8				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), K_2CO_3 (3 eq), LiCl (3 eq), toluene–H_2O, 100°, 18 h	 (55)	123

TABLE 6A. CROSS-COUPLING OF CYLCOPROPYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Cyclopropyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$Pd(OAc)_2$ (3%), XPhos (6%), K_2CO_3 (3 eq), CPME–H_2O, 100°		112
		$Pd(OAc)_2$ (3%), XPhos (6%), K_2CO_3 (3 eq), THF–H_2O, 80°, 24 h	 R: CN (76) R: COPh (80)	112
C_4				
		$Pd(PPh_3)_4$ (5%), K_3PO_4 (3 eq), toluene–H_2O, 100°	 (66)	79

R^1	R^2	R^3	R^4	Time (h)	
H	H	OMe	H	24	(75)
H	OMe	H	OMe	24	(94)
H	CO_2Me	H	H	48	(82)
H	H	1-pyrrolyl	H	24	(90)
OMe	H	H	H	24	(82)
OMe	OMe	H	CN	24	(96)

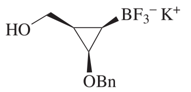
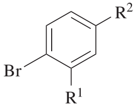
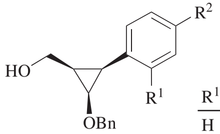
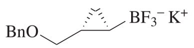
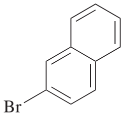
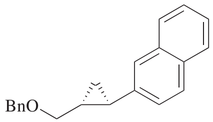
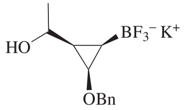
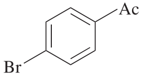
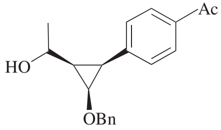
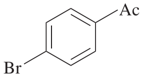
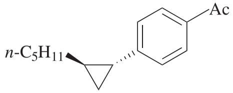
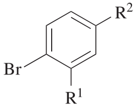
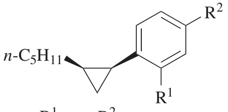
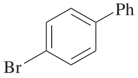
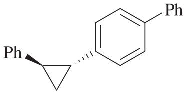
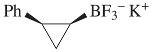
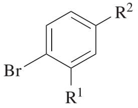
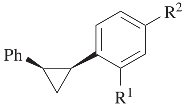
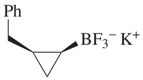
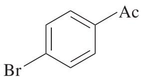
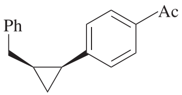
			$Pd(OAc)_2$ (3%), Cyclohexyl JohnPhos (6%), K_3PO_4 (3.3 eq), toluene–H_2O, 100°, 20 h	 R^1 R^2 H NO_2 (47) H CN (62) H Ac (88) H Ph (84)[a] OMe H (69)[b]	80
			$Pd(PPh_3)_4$ (5%), K_3PO_4 (3 eq), toluene–H_2O, 100°	 (85)	79
C_5			$Pd(OAc)_2$ (3%), Cyclohexyl JohnPhos (6%), K_3PO_4 (3.3 eq), toluene–H_2O, 100°, 20 h	 (89)	80
C_8			$Pd(PPh_3)_4$ (2%), K_3PO_4•$3H_2O$ (3 eq), toluene–H_2O, reflux, 20 h	 (86)	81

TABLE 6A. CROSS-COUPLING OF CYLCOPROPYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Cyclopropyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Pd(PPh_3)_4$ (2%), K_3PO_4•$3H_2O$ (3 eq), toluene–H_2O, reflux, 20 h	 R^1 R^2 H Ac (87) OMe H (79)	81
C_9				
		$Pd(PPh_3)_4$ (2%), K_3PO_4•$3H_2O$ (3 eq), toluene–H_2O, reflux, 20 h	 (83)	81
		$Pd(PPh_3)_4$ (2%), K_3PO_4•$3H_2O$ (3 eq), toluene–H_2O, reflux, 20 h	 R^1 R^2 H Ac (88) H Ph (80) OMe H (76)	81
C_{10}				
		$Pd(PPh_3)_4$ (2%), K_3PO_4•$3H_2O$ (3 eq), toluene–H_2O, reflux, 20 h	 (91)	81

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[a] These products were isolated as a 12:88 ratio between the protodeboronated cyclopropane and the desired product.

[b] These products were isolated as a 22:78 ratio between the protodeboronated cyclopropane and the desired product.

TABLE 6B. CROSS-COUPLING OF CYLCOPROPYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

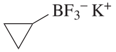
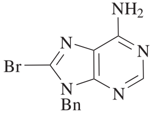
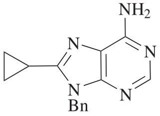
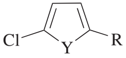
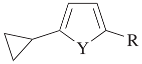
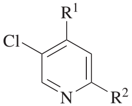
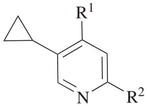
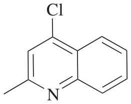
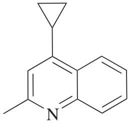
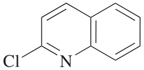
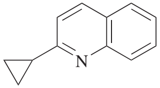
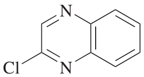
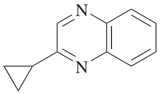
Cyclopropyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$Pd(OAc)_2$ (3%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (48)	104
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 Y R S CHO (99) S Ac (90) O CHO (78)	112
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 R^1 R^2 H OMe (85) CHO H (52)	112
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (95)	112
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (70)	112
		$Pd(OAc)_2$ (2%), *n*-$BuPAd_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (79)	112

TABLE 6B. CROSS-COUPLING OF CYLCOPROPYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

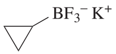
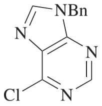
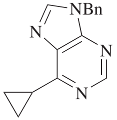
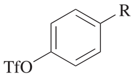
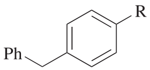
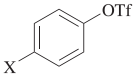
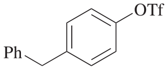
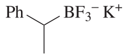
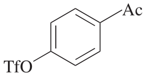
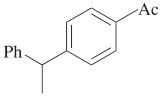
Cyclopropyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$Pd(OAc)_2$ (3%), *n*-BuPAd$_2$ (3%), Cs_2CO_3 (3 eq), toluene–H_2O, 100°, 24 h	 (75)	104

TABLE 7A. CROSS-COUPLING OF BENZYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Benzyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$PdCl_2(dppf)\cdot CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 R H (91)[a] Ac (96) NO_2 (89) Cl (57)	58
		$PdCl_2(dppf)\cdot CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 X Br (70) I (16)	58
C_8				
		$PdCl_2(dppf)\cdot CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (4)	58

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[a] The yield of the product was determined by GC analysis.

TABLE 7B. CROSS-COUPLING OF BENZYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

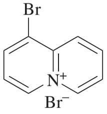
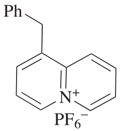
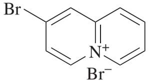
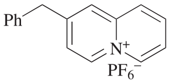
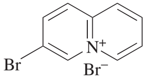
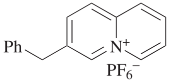
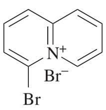
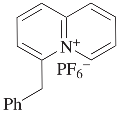
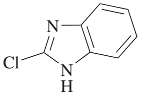
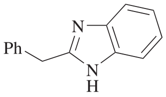
Benzyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (48)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (64)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (39)	122
		1. $Pd(OAc)_2$ (1%), K_2CO_3 (3 eq), H_2O, 65°, 5 h 2. H_4NPF_6	 (67)	122
		$PdCl_2(PPh_3)_2$ (10%), K_2CO_3, MeCN, MW, 150°, 30 min	 (0)	223

TABLE 7C. CROSS-COUPLING OF BENZYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

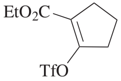
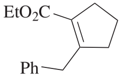
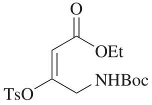
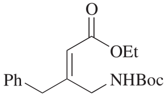
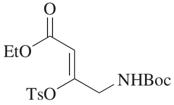
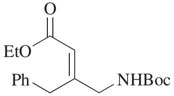
Benzyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 18 h	 (89)	58
		$Pd(PPh_3)_2Cl_2$ (5%), aq Na_2CO_3 (3.5 eq), THF, 60°	 (31)	68
		$PdCl_2(dppf)•CH_2Cl_2$ (10%), Cs_2CO_3 (3 eq), THF–H_2O, 60°	 (50)	68

TABLE 7D. CROSS-COUPLING OF BENZYLTRIFLUOROBORATES WITH IMIDOYL ELECTROPHILES

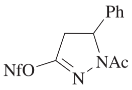
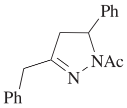
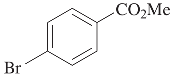
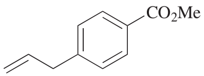
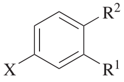
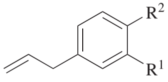
Benzyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$PdCl_2(dppf)•CH_2Cl_2$ (9%), K_2CO_3 (3 eq), LiCl (3 eq), toluene–H_2O, 100°, 18 h	 (73)	123

TABLE 8A. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$Pd(OAc)_2$ (3%), Walphos (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 (99)	125
		$PdCl_2$(D-*t*-BPF) (3%), K_2CO_3 (3 eq), *i*-PrOH–H_2O, MW 120°		281

X	R^1	R^2	Time (min)	
Br	Cl	H	30	(71)
Br	H	Cl	20	(94)
I	Br	H	40	(71)
I	Cl	H	45	(84)
I	H	H	35	(77)
I	H	I	50	(95)
I	H	Cl	40	(79)
I	H	Br	30	(95)
I	H	F	30	(85)
I	H	CF_3	50	(77)
I	H	CN	30	(81)
I	H	Me	20	(95)

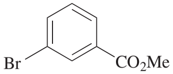
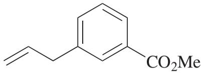
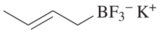
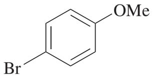
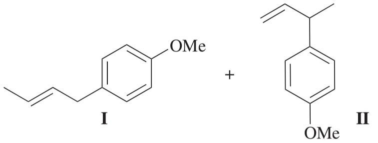
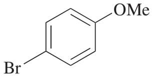
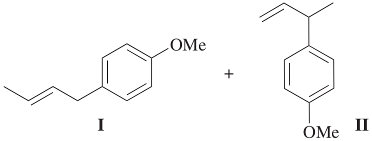
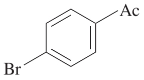
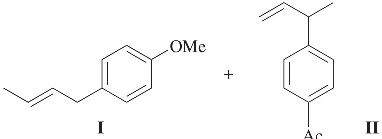
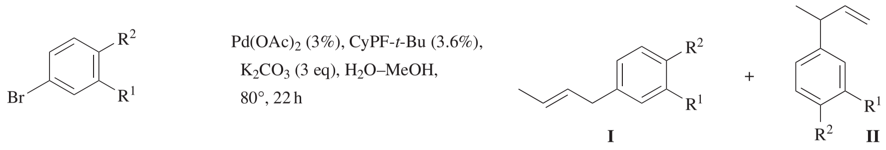
Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF, reflux, 22 h	 (38)	124

TABLE 8A. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

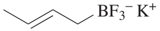
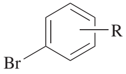
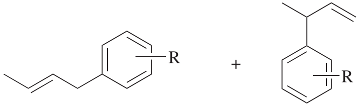
Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (3%), ligand (3%), K_2CO_3 (3 eq), THF–H_2O, 20 h, reflux	 Ligand — **I/II** dppm — 22:78 — (35)[a] dppe — 63:37 — (17)[a] dppf — <1:99 — (68)[a] D-*t*-BPF — <1:99 — (87)	124
		$Pd(PPh_3)_4$ (3%), K_2CO_3 (3 eq), THF–H_2O, 20 h, reflux	 **I/II** = 22:78 (42)[a]	124
		$Pd(OAc)_2$ (3%), CyPF-*t*-Bu (3.6%), K_2CO_3 (3 eq), MeOH–H_2O, 80°, 4.5 h	 **I/II** = 9:91 **II** = (97) 80% ee	126



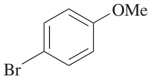
126

R^1	R^2	**I/II**	**II**	% ee **II**
H	CF$_3$	10:90	(70)	90
H	CO$_2$Me	7:93	(93)	82
H	*i*-Bu	16:84	(86)	80
H	*t*-Bu	16:84	(86)	86
H	Ph	11:89	(95)	85
H	PhO	16:84	(99)	79
CO$_2$Me	H	11:89	(85)	79

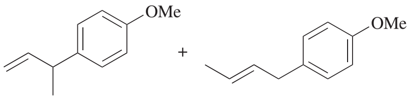
TABLE 8A. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF, reflux, 22 h	 **I** **II**	124

R	**I + II**	**I/II**
4-NH_2	(80)	<1:99
4-NHBz	(96)	<1:99
4-MeO	(90)	<1:99
3-MeO	(85)	<1:99
2-MeO	(84)	<1:99
4-*t*-Bu	(88)	2:98
2,6-Me	(87)	<1:99
4-CO_2Me	(92)	<1:99
3-CO_2Me	(92)	<1:99
2-CO_2Me	(92)	<1:99
4-CN	(77)	<1:99
4-CF_3	(83)	<1:99
4-O_2N	(80)	<1:99
4-Ac	(94)^b	<1:99
2-naphthyl	(93)	<1:99
4-*i*-Bu	(91)	0:100



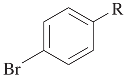
Pd(OAc)$_2$ (3%), ligand (3%),
K$_2$CO$_3$ (3 eq), THF–H$_2$O,
reflux, 20 h



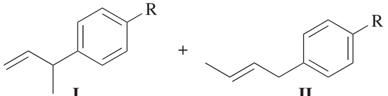
I **II**

125

Ligand	**I + II**	**I/II**
PPh$_3$	(42)^a	78:22
dppm	(35)^a	78:22
dppe	(17)^a	37:63
dppp	(37)^a	>99:1
dppf	(68)^a	>99:1
DPEphos	(21)^a	>99:1
Xantphos	(10)^a	>99:1
DBFPhos	(10)^a	>99:1
D-*t*-BPF	(87)	>99:1



Pd(OAc)$_2$ (3%), D-*t*-BPF (3.6%),
K$_2$CO$_3$ (3 eq), THF
reflux, 22 h

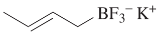
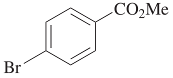
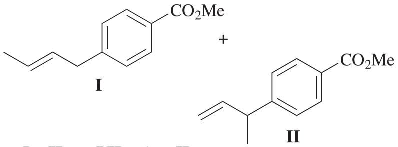


I **II**

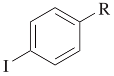
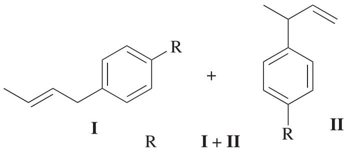
125

R	**I/II**	
OMe	>99:1	(85)
CO$_2$Me	>99:1	(99)

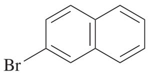
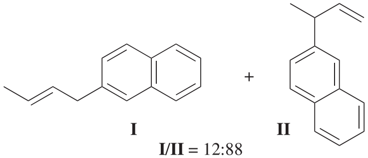
TABLE 8A. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (3%), ligand (3.6%), K_2CO_3 (3 eq), solvent, reflux, 22 h		125

Ligand	Solvent	I + II	I/II	% ee II	
(*R*)-BINAP	THF	(86)	32:68	3	—
(*S*,*S*)-Et-FerroTANE	THF	(84)	69:31	12	—
L5	THF	(98)	7:93	31	(*R*)
(*R*,*S*)-CyPF-*t*-Bu	THF	(96)	8:92	63	(*R*)
(*R*,*S*)-CyPF-*t*-Bu	$THF–H_2O$	(93)	5:95	82	(*R*)
(*R*,*S*)-CyPF-*t*-Bu	$MeOH–H_2O$	(93)	7:93	82	(*R*)

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		$PdCl_2$(D-*t*-BPF) (3%), K_2CO_3 (3 eq), *i*-$PrOH–H_2O$, MW, 120°		281

R	I + II
Cl	(54)
Br	(41)
Me	(77)

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Pd(OAc)_2$ (3%), CyPF-*t*-Bu (3.6%), K_2CO_3 (3 eq), $H_2O–MeOH$, 80°, 4.5 h	 **I/II** = 12:88 **II** = (90) 83% ee	126

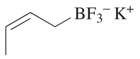
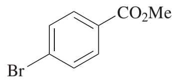
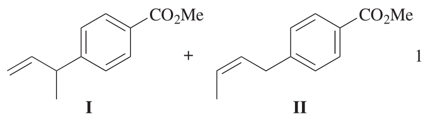
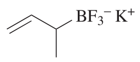
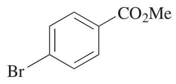
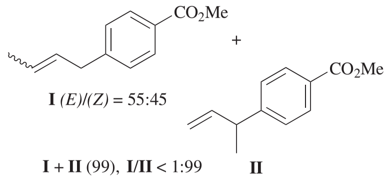
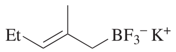
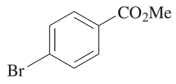
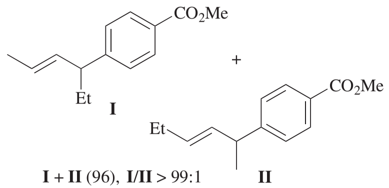
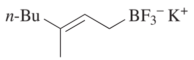
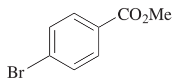
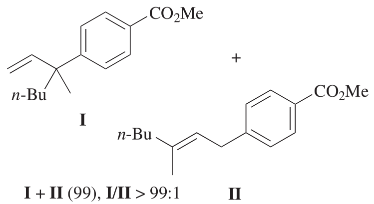
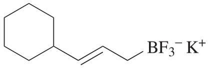
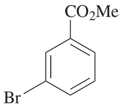
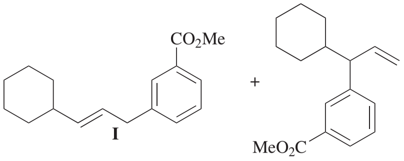
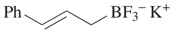
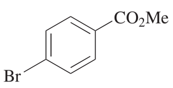
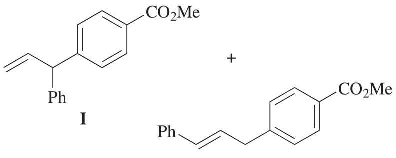
			Pd(OAc)$_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 **I** + **II** (91), **I/II** > 99:1	125
			Pd(OAc)$_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 **I** (*E*)/(*Z*) = 55:45 **I** + **II** (99), **I/II** < 1:99	125
C_6					
			Pd(OAc)$_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 **I** + **II** (96), **I/II** > 99:1	125
C_8					
			Pd(OAc)$_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 **I** + **II** (99), **I/II** > 99:1	125

TABLE 8A. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF, reflux, 22 h	 **I** + **II** (98), **I**/**II** < 1:99 **II** **I** *(Z)*/*(E)* = 80:20	124
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF reflux, 22 h	 **I** + **II** (98), **I**/**II** > 99:1 (99)	125

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[a] The yield of the crude product was determined by ^1H NMR.

[b] This yield was obtained under optimized conditions.

TABLE 8B. CROSS-COUPLING OF ALLYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

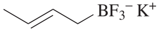
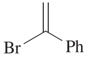
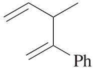
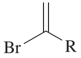
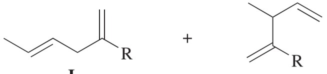
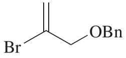
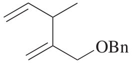
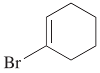
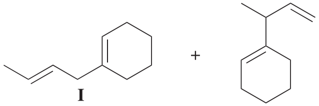
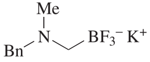
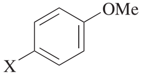
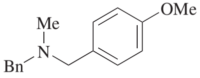
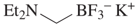
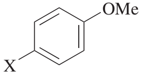
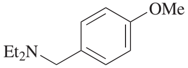
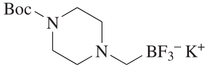
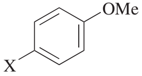
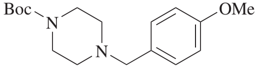
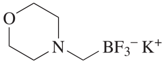
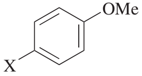
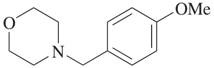
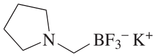
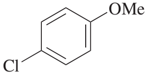
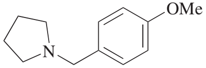
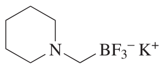
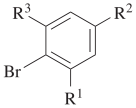
Allyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(OAc)_2$ (3%), CyPF-*t*-Bu (3.6%), K_2CO_3 (3 eq), H_2O–MeOH, 80°, 22 h	 (47)	126
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF, reflux, 22 h	 **I** + **II** R — **I + II** — **I/II** Ph — (75) — <1:99 CH_2OCH_2Bn — (66) — <1:99	124
		$Pd(OAc)_2$ (3%), CyPF-*t*-Bu (3.6%), K_2CO_3 (3 eq), H_2O–MeOH, 80°, 22 h	 (76)	126
		$Pd(OAc)_2$ (3%), D-*t*-BPF (3.6%), K_2CO_3 (3 eq), THF, reflux, 22 h	 **I** + **II** **I + II** (98), **I/II** < 1:99	124

TABLE 9A. CROSS-COUPLING OF AMINOMETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

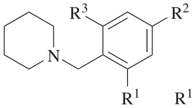
Aminomethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		X Br (81) Cl (95)	 128 127
C_5					
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		X Br (85) Cl (84)	 128 127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		X Br (72) Cl (74)	 128 127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		X Br (81) Cl (75)	 128 127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		(82)	127

C_6



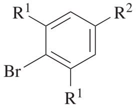


Pd(OAc)$_2$ (3%), XPhos (6%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 80°, 22–24 h

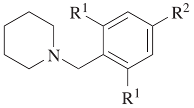


R^1	R^2	R^3	
H	NO_2	H	(68)
H	CN	H	(83)
H	CHO	H	(66)
H	OMe	H	(80)
H	CO_2Me	H	(83)
H	NMe_2	H	(72)
H	NHAc	H	(80)
H	COPh	H	(72)
Me	Me	Me	(69)
OMe	OMe	H	(75)

128

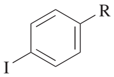


Pd(OAc)$_2$ (3%), XPhos (6%), Cs$_2$CO$_3$ (3 eq), CPME–H$_2$O, 95°, 12–18 h

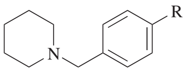


R^1	R^2	
H	NO_2	(75)
H	CHO	(73)
H	COPh	(76)
H	NMe_2	(82)
Me	Me	(77)

128



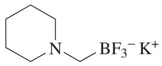
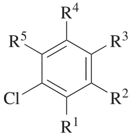
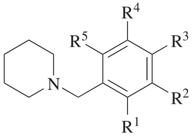
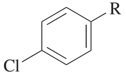
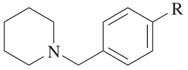
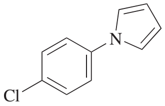
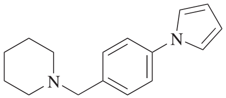
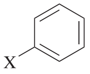
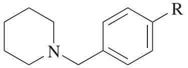
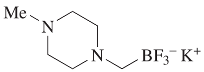
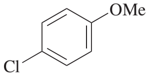
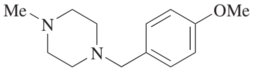
Pd(OAc)$_2$ (3%), XPhos (6%), Cs$_2$CO$_3$ (3 eq), THF–H$_2$O, 80°, 18–24 h

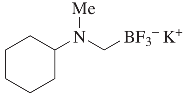
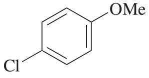
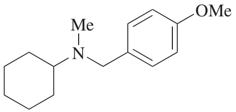
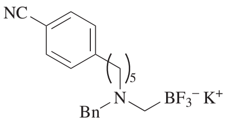
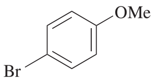
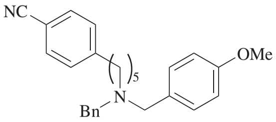


R	
H	(83)
Ac	(82)

127

TABLE 9A. CROSS-COUPLING OF AMINOMETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aminomethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 R^1 R^2 R^3 R^4 R^5 H H H H H (85) H H OMe H H (94) H OMe H OMe H (99) H CO_2Me H H H (91) Me H H H H (63) Me H H H Me (66)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), CPME–H_2O, 95°, 18–24 h	 R Ac (92) CN (92) CHO (83)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (92)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 X OTf (65) OTs (0)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (68)	127

C_7					
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		(75)	127
C_{13}					
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 24 h		(>71)	225

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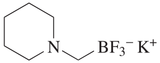
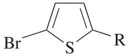
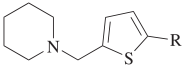
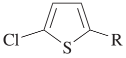
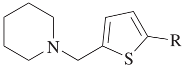
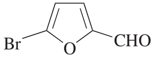
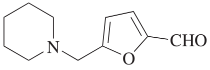
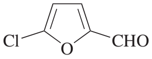
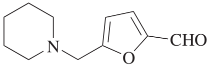
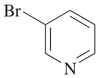
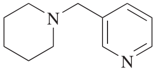
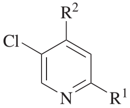
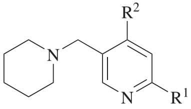
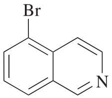
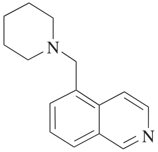
[a] The trifluoroborate derivative comes from the hydroboration/cross-coupling of a dibora species.

TABLE 9B. CROSS-COUPLING OF AMINOMETHYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

Aminomethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 R H (62) Ac (77)	128
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 R H (65) CHO (78) Ac (93)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (80)	128
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (82)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (63)	128
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 R^1 R^2 H H (77) H CHO (60) OMe H (87)	127
		$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h	 (76)	128

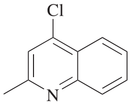
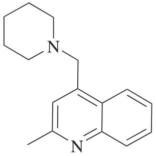
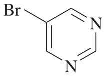
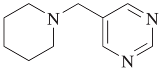
	$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		(97)	127
	$Pd(OAc)_2$ (3%), XPhos (6%), Cs_2CO_3 (3 eq), THF–H_2O, 80°, 18–24 h		(84)	128

TABLE 9C. CROSS-COUPLING OF AMINOMETHYLTRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

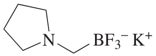
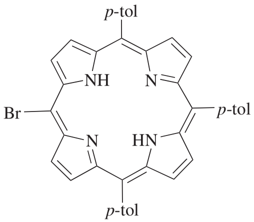
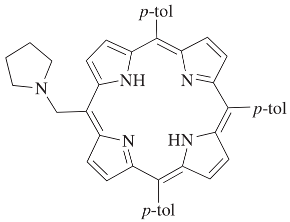
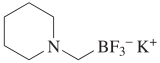
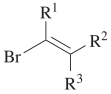
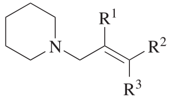
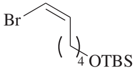
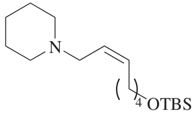
Aminomethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		$PdCl_2(dppf)•CH_2Cl_2$ (25%), Cs_2CO_3 (20 eq), $THF–H_2O$, 80°, overnight	 (26)	115
C_6				
		$Pd(OAc)_2$ (0.6%), XPhos (1.2%), Cs_2CO_3 (3 eq), $THF–H_2O$, 80°, 48 h	 R^1 R^2 R^3 H Ph H (78) Ph H H (80) Ph H CHO (67)	127
		$Pd(OAc)_2$ (1%), XPhos (2%), Cs_2CO_3 (3 eq), $THF–H_2O$, 80°, 24 h	 (63)	127

TABLE 10A. CROSS-COUPLING OF ALKOXYMETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

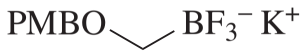
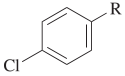
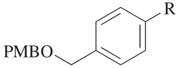
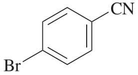
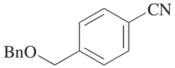
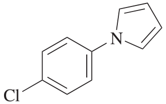
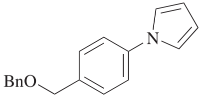
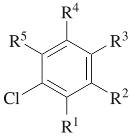
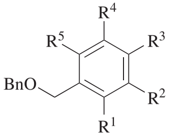
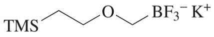
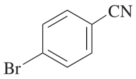
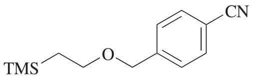
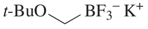
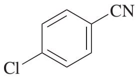
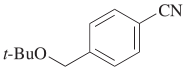
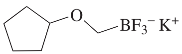
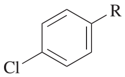
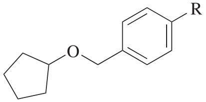
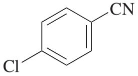
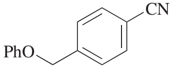
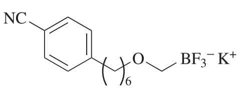
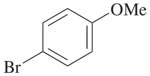
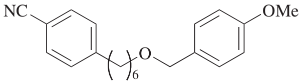
Alkoxymethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_1					
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h		R — CN (72) R — OMe (74)	129
		$Pd(OAc)_2$ (3%), ligand, Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h		Ligand: RuPhos (6%) (76) SPhos (6%) (58) (*S*)-BINAP (3%) (76) DPEPhos (3%) (68) Fc(*i*-Pr)$_2$ (3%) (73)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h		(85)	129

TABLE 10A. CROSS-COUPLING OF ALKOXYMETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Alkoxymethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 R^1 R^2 R^3 R^4 R^5 H H H H H (74) H H CN H H (75) H H OMe H H (77) H OMe H OMe H (75) H CO_2Me H H H (72) Me H H H H (86) Me H H H Me (72) OMe OMe H CN H (73)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (80)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (67)	129
C_6				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 R CN (67) OMe (60)	129

C_7					
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h		(48)	129
C_{14}					
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h		(>50)	225

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[a] The trifluoroborate derivative comes from the hydroboration/cross-coupling of a dibora species.

TABLE 10B. CROSS-COUPLING OF ALKOXYMETHYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

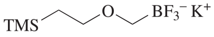
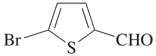
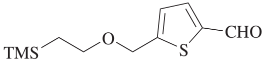
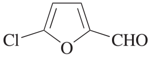
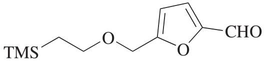
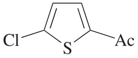
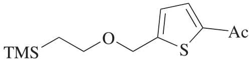
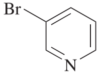
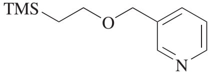
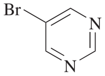
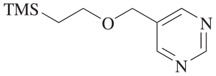
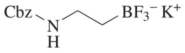
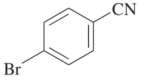
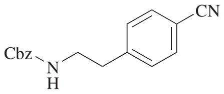
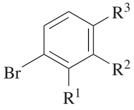
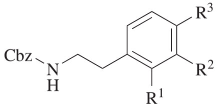
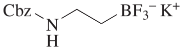
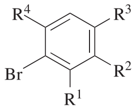
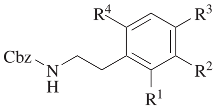
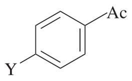
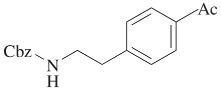
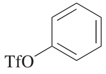
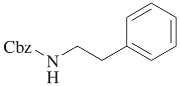
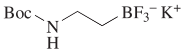
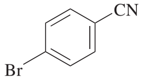
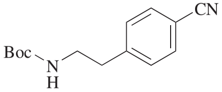
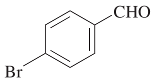
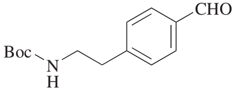
Alkoxymethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (40)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (50)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (54)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (70)	129
		$Pd(OAc)_2$ (3%), RuPhos (6%), Cs_2CO_3 (3 eq), dioxane–H_2O, 100°, 24 h	 (51)	129

TABLE 11A. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (71)	130
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h		131

R^1	R^2	R^3	
H	H	NO_2	(84)
H	H	Cl	(70)
H	H	Me	(71)
H	H	CF_3	(88)
H	H	CN	(75)
H	H	CHO	(87)
H	H	Ac	(89)
H	H	CO_2Me	(86)
H	Ac	H	(91)
CN	H	H	(70)
OMe	H	OMe	(55)

TABLE 11A. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 R^1 R^2 R^3 R^4 H H H H (86) H H H Me (82) H H Me H (75) H H OMe H (80) H H NHAc H (46) H H OMe OMe (79) H OMe H H (86) Me H Me Me (85)	131
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 Y I (60) OTf (82)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (85)	131
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (73)	130
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (79)	131

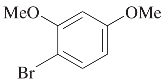
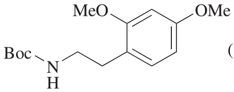
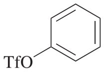
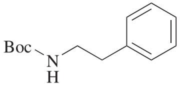
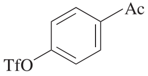
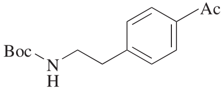
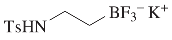
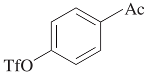
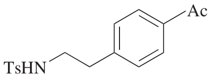
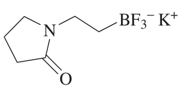
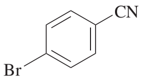
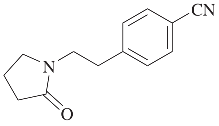
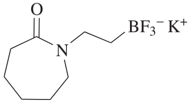
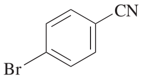
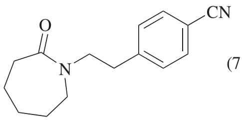
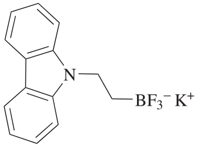
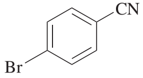
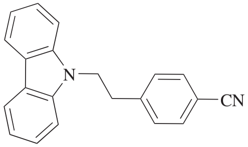
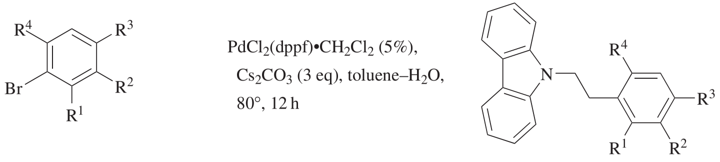
			$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h		(86)	131
			$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h		(78)	131
			$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h		(72)	131
			$PdCl_2(dppf)•CH_2Cl_2$ (9%), Cs_2CO_3 (3 eq), THF–H_2O, reflux, 3 d		(75)	113
C_6			$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h		(71)	130
C_8			$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h		(78)	130

TABLE 11A. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
		Pd source (5%), ligand (10%), base (3 eq), toluene–H_2O, 80°, 12 h		130

Pd Source	Ligand	Base	
$PdCl_2(dppf)•CH_2Cl_2$	—	Cs_2CO_3	(90)
$PdCl_2(dppf)•CH_2Cl_2$	—	K_2CO_3	(69)
$Pd(OAc)_2$	PPh_3	Cs_2CO_3	(78)
$PdCl_2$	PPh_3	Cs_2CO_3	(56)



PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%),
Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O,
80°, 12 h

R^1	R^2	R^3	R^4	
H	H	H	H	(89)
H	H	Cl	H	(73)
H	H	NO$_2$	H	(79)
H	H	Me	H	(81)
H	H	CF$_3$	H	(74)
H	H	CHO	H	(84)
H	H	OMe	H	(70)
H	H	Ac	H	(82)
H	H	NHAc	H	(73)
H	H	COPh	H	(79)
H	OMe	H	H	(68)
H	Ac	H	H	(79)
H	H	CO$_2$Me	H	(84)
Me	H	H	H	(79)
CN	H	H	H	(85)
Me	H	Me	Me	(88)

130

TABLE 11A. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES (*Continued*)

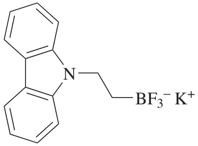
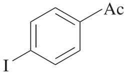
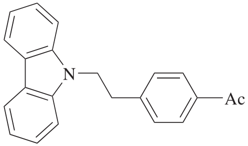
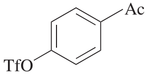
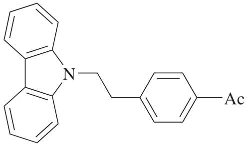
Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (79)	130
		$PdCl_2(dppf)\bullet CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (77)	130

TABLE 11B. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

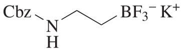
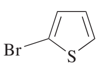
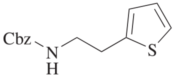
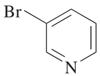
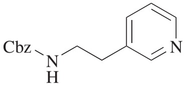
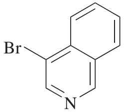
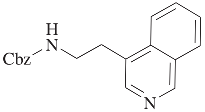
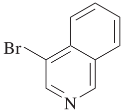
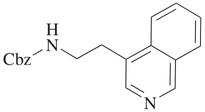
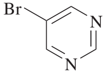
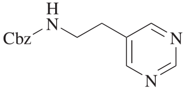
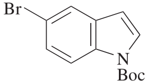
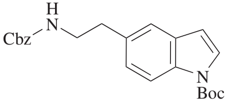
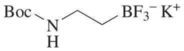
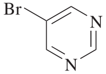
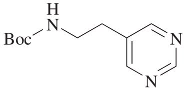
Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (79)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (81)	131
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (74)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (84)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (80)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (89)	131
		$Pd(OAc)_2$ (5%), RuPhos (10%), Cs_2CO_3 (3 eq), toluene–H_2O, 95°, 12 h	 (83)	131

TABLE 11B. CROSS-COUPLING OF AMINOETHYLTRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES (*Continued*)

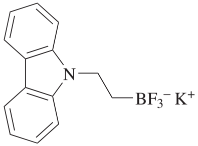
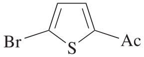
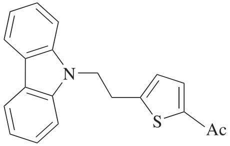
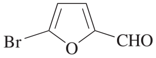
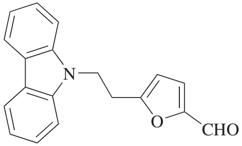
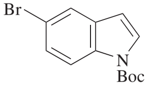
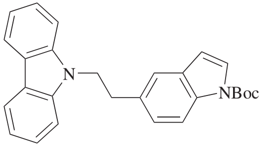
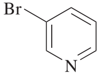
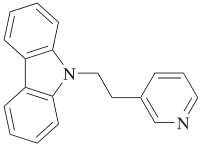
Aminoethyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
		$Pd(OAc)_2$ (2%), RuPhos (4%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (71)	130
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (62)	130
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (63)	130
		$PdCl_2(dppf)•CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), toluene–H_2O, 80°, 12 h	 (69)	130

TABLE 12A. CROSS-COUPLING OF MISCELLANEOUS TRIFLUOROBORATES WITH HETEROARYL ELECTROPHILES

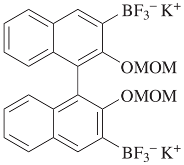
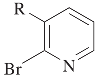
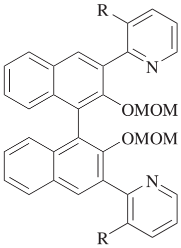
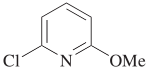
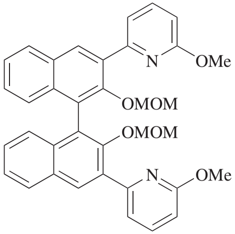
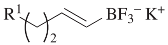
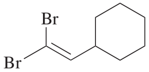
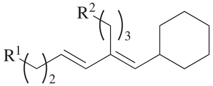
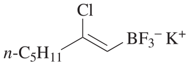
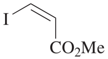
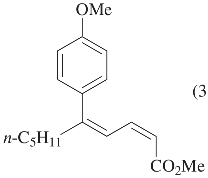
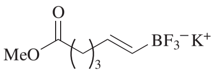
Trifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20}				
		$Pd(PPh_3)_4$ (10%), K_2CO_3, DMF–H_2O, MW, 150°, 15 min	 R H (97) HO (—) *n*-BuO (56) *n*-$C_6H_{13}O$ (64) BnO (51) TsO (27)	282
		$Pd(PPh_3)_4$ (10%), K_2CO_3, DMF–H_2O, MW, 150°, 15 min	 (63)	282

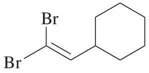
TABLE 12B. CROSS-COUPLING OF MISCELLANEOUS TRIFLUOROBORATES WITH ALKENYL ELECTROPHILES

Trifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-10}				
		1. $Pd(PPh_3)_4$ (7%), Cs_2CO_3 (3 eq), toluene–H_2O, $temp_1$, $time_1$ 2. $R^2(CH_2)_3BF_3^-K^+$, $PdCl_2(dppf){\bullet}CH_2Cl_2$ (5%), Cs_2CO_3 (3 eq), 80°, $time_2$		74

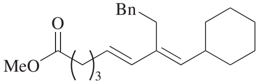
R^1	R^2	$Temp_1$ (°)	$Time_1$ (h)	$Time_2$ (h)	
$NCCH_2$	$PivOCH_2$	60	2	2.5	(91)
$NCCH_2$	$AcCH_2$	60	2	3.5	(87)
$ClCH_2$	$PivOCH_2$	60	2	2.5	(90)
$ClCH_2$	$AcCH_2$	60	2	4	(89)
Ph	$PivOCH_2$	60	1	2.5	(90)
Ph	$AcCH_2$	60	1	5	(89)
n-C_6H_{13}	$PivOCH_2$	80	5	2.5	(90)
n-C_6H_{13}	$AcCH_2$	80	5	5	(87)
n-C_6H_{13}	Ph	80	5	1	(85)

Trifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		1. $Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3{\bullet}HBF_4$ (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h 2. 4–$MeOC_6H_4BF_3^-K^+$, $Pd_2(dba)_3$ (2.5%), $P(t\text{-}Bu)_3{\bullet}HBF_4$ (3%), 100°, 48 h	 (33)	148



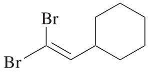


1. Pd(PPh$_3$)$_4$ (7%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, temp$_1$, time$_1$
2. Cs$_2$CO$_3$ (3 eq), BnCH$_2$BF$_3$$^-K^+$, 80°, time$_2$

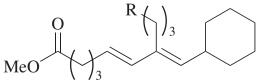


Temp$_1$ (°)	Time$_1$ (h)	Time$_2$ (h)	
80	1.25	1	(85)
60	2	2.5	(84)
60	2	2.5	(89)

74

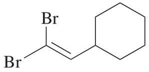


1. Pd(PPh$_3$)$_4$ (7%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 60°, 2 h
2. R(CH$_2$)$_3$BF$_3$$^-K^+$, Cs$_2CO_3$ (3 eq), 80°, time$_2$

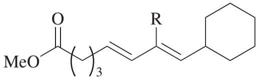


R	Time$_2$ (h)	
PivOCH$_2$	2	(89)
BzOCH$_2$	2	(90)
NCCH$_2$	3	(89)
MeCOCH$_2$	3	(89)
PhS	1.5	(90)

74



1. Pd(PPh$_3$)$_4$ (7%), Cs$_2$CO$_3$ (3 eq), toluene–H$_2$O, 60°, 2 h
2. PdCl$_2$(dppf)•CH$_2$Cl$_2$ (5%), Cs$_2$CO$_3$ (3 eq), RBF$_3$$^-$ K$^+$, 80°, time$_2$



R	Time$_2$ (h)	
Me	2.5	(84)
Et	25	(82)
CH$_2$CH(CH$_2$)$_3$	1	(83)

74

TABLE 12B. CROSS-COUPLING OF MISCELLANEOUS TRIFLUOROBORATES WITH ALKENYL ELECTROPHILES (*Continued*)

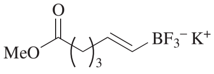
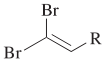
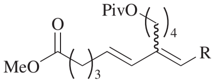
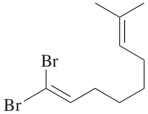
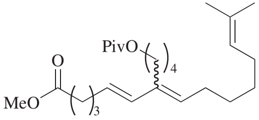
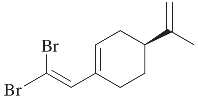
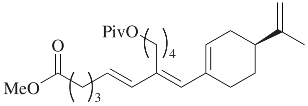
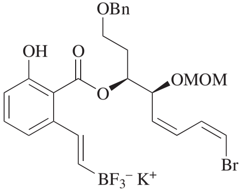
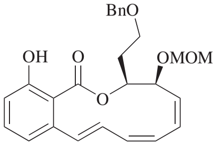
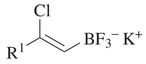
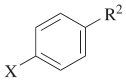
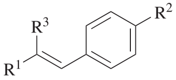
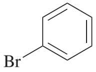
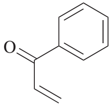
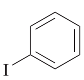
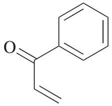
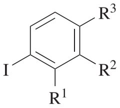
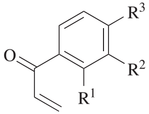
	Trifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			1. $Pd(PPh_3)_4$ (7%), Cs_2CO_3 (3 eq), toluene–H_2O, 60°, 1 h 2. $PivO(CH_2)_4BF_3^-K^+$, Cs_2CO_3 (3 eq), 80°, 3 h	 R — (*E,E*)/(*E,Z*) *n*-C_7H_{15} — 92:8 — (85) $Ph(CH_2)_2$ — 94:6 — (87)	74
			1. $Pd(PPh_3)_4$ (7%), Cs_2CO_3 (3 eq), toluene–H_2O, 60°, 1 h 2. $PivO(CH_2)_4BF_3^-K^+$, Cs_2CO_3 (3 eq), 80°, 3 h	 (86) (*E,E*)/(*E,Z*) = 92:8	74
			1. $Pd(PPh_3)_4$ (7%), Cs_2CO_3 (3 eq), toluene–H_2O, 60°, 1 h 2. $PivO(CH_2)_4BF_3^-K^+$, Cs_2CO_3 (3 eq), 80°, 3 h	 (90)	74
C_{17}		intramolecular coupling	$Pd(PPh_3)_4$ (10%), Cs_2CO_3 (5 eq), THF–H_2O, reflux, 20 h	 (42)	164

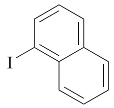
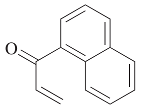
TABLE 12C. CROSS-COUPLING OF MISCELLANEOUS TRIFLUOROBORATES WITH ARYL ELECTROPHILES

Trifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-9}				
		1. $Pd_2(dba)_3$ (1.5%), $P(t\text{-}Bu)_3$•HBF_4 (3%), Cs_2CO_3 (3 eq), THF–H_2O, 120°, 12 h 2. $R^3BF_3^-K^+$, $Pd_2(dba)_3$ (2.5%), $P(t\text{-}Bu)_3$•HBF_4 (3%), 100°, 48 h		148

X	R^1	R^2	R^3	
Br	n-C_5H_{11}	NO_2	CH=CH_2	(56) (*Z*)/(*E*) = 60:40
I	n-C_5H_{11}	CO_2Me	CH=CH_2	(42)
I	n-C_5H_{11}	CO_2Me	Me	(—)
I	n-C_5H_{11}	CO_2Me	Ph	(26)
I	n-C_5H_{11}	CO_2Me	4-$MeOC_6H_4$	(38)
I	Ph	CO_2Me	4-$MeOC_6H_4$	(44)
I	3-Me-4-FC_6H_3	CO_2Me	3-thienyl	(43)

TABLE 13. CARBONYLATIVE CROSS-COUPLING OF ALKENYLTRIFLUOROBORATES WITH ARYL ELECTROPHILES

Alkenyltrifluoroborate	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		CO (20 bar), $Pd(OAc)_2$ (2%), PPh_3 (6%), Na_2CO_3 (1.1 eq), THF, 80°, 20 h	 (0)	283
		CO (20 bar), $Pd(OAc)_2$ (2%), PPh_3 (6%), base (1.1 eq), solvent, 80°, 20 h	 Base / Solvent K_2CO_3 THF (32)[a] K_2CO_3 toluene (0)[a] K_2CO_3 DMF (22)[a] K_2CO_3 dioxane (21)[a] Na_2CO_3 THF (59)[a] NaOAc THF (34)[a] KF THF (8)[a] KO*t*-Bu THF (0)[a]	283
		CO (20 bar), $Pd(OAc)_2$ (2%), PPh_3 (6%), Na_2CO_3 (1.1 eq), THF, 80°, 20 h	 R^1 R^2 R^3 H H Br (45) H H Cl (42) H Cl Cl (60) Me H H (40) H Me H (70) H H Me (72) H H Ac (40) H H CO_2Et (68)	283

	CO (20 bar), Pd(OAc)$_2$ (2%), PPh$_3$ (6%), Na$_2$CO$_3$ (1.1 eq), THF, 80°, 20 h		(35)	283

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[a] The yield of the product was determined by GC analysis.

REFERENCES

[1] Wolfe, J. P.; Nakhla, J. S. In *Name Reactions for Homologations (Part 1)*; Li, J. J., Ed.; Wiley-VCH: Weinheim, 2009, pp 163–184.

[2] Littke, A. F. In *Modern Arylation Methods*; Ackermann, L., Ed.; Wiley-VCH: Weinheim, 2009, pp 25–67.

[3] Miyaura, N. *Cross-Coupling Reactions*; Springer-Verlag: Berlin, 2002.

[4] Bai, L.; Wang, J.-X. *Curr. Org. Chem.* **2005**, *9*, 535.

[5] Singh, R.; Sharma, M.; Mamgain, R.; Rawat, D. S. *J. Braz. Chem. Soc.* **2008**, *19*, 357.

[6] Liu, Y.; Wang, S.-S.; Liu, W.; Wan, Q.-X.; Wu, H.-H.; Gao, G.-H. *Curr. Org. Chem.* **2009**, *13*, 1322.

[7] Singh, B. K.; Kaval, N.; Tomar, S.; Van der Eycken, E.; Parmar, V. S. *Org. Proc. Res. Dev.* **2008**, *12*, 468.

[8] Leadbeater, N. E. *Chem. Commun.* **2005**, 2881.

[9] Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.

[10] Matteson, D. S.; Maliakal, D.; Pharazyn, P. S.; Kim, B. J. *Synlett* **2006**, 3501.

[11] Darses, S.; Genet, J.-P. *Chem. Rev.* **2008**, *108*, 288.

[12] Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.

[13] Darses, S.; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393.

[14] Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875.

[15] Xia, M.; Chen, Z.-C. *Synth. Commun.* **1999**, *29*, 2457.

[16] Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275.

[17] Darses, S.; Genet, J. P. *Eur. J. Org. Chem.* **2003**, 4313.

[18] Molander, G.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49.

[19] Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623.

[20] Doucet, H. *Eur. J. Org. Chem.* **2008**, *2008*, 2013.

[21] Molander, G.; Canturk, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9240.

[22] Molander, G.; Sandrock, D. L. *Curr. Opin. Drug Discovery Dev.* **2009**, *12*, 811.

[23] Molander, G. A.; Jean-Gérard, L. *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine,* 2nd ed.; Wiley-VCH: Weinheim, 2011.

[24] Echavarren, A. M.; Cardenas, D. G. In *Metal-Catalyzed Cross-Coupling Reactions,* 2nd ed.; Wiley-VCH: Weinheim, 2004.

[25] Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules,* 2nd ed.; University Science Books: Sausalito, CA, 1999.

[26] Amatore, C.; Carre, E.; Jutand, A.; M'Barki, M. A. *Organometallics* **1995**, *14*, 1818.

[27] Butters, M.; Harvey, J.; Jover, J.; Lennox, A.; Lloyd-Jones, G.; Murray, P. *Angew. Chem., Int. Ed.* **2010**, *49*, 5156.

[28] Mason, M. R.; Verkade, J. G. *Organometallics* **1990**, *9*, 864.

[29] Mason, M. R.; Verkade, J. G. *Organometallics* **1992**, *11*, 2212.

[30] McLaughlin, P. A.; Verkade, J. G. *Organometallics* **1998**, *17*, 5937.

[31] Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434.

[32] Hartwig, J. F.; Paul, F. *J. Am. Chem. Soc.* **1995**, *117*, 5373.

[33] Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030.

[34] Hartwig, J. F. *Synlett* **2006**, 1283.

[35] Amatore, C.; Jutand, A. *Coord. Chem. Rev.* **1998**, *178–180*, 511.

[36] Amatore, C.; Broeker, G.; Jutand, A.; Khalil, F. *J. Am. Chem. Soc.* **1997**, *119*, 5176.

[37] Fairlamb, I. J. S.; Kapdi, A. R.; Lee, A. F. *Org. Lett.* **2004**, *6*, 4435.

[38] Macé, Y.; Kapdi, A. R.; Fairlamb, I. J. S.; Jutand, A. *Organometallics* **2006**, *25*, 1795.

[39] Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.

[40] Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366.

[41] Altman, R. A.; Buchwald, S. L. *Nat. Protoc.* **2007**, *2*, 3115.

[42] Biscoe, M. R.; Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 6686.

[43] Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.

[44] Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555.

[45] Fleckenstein, C. A.; Plenio, H. *Chem. Soc. Rev.* **2010**, *39*, 694.

[46] Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

[47] Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969.

[48] Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046.

[49] Barrios-Landeros, F.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 6944.

[50] Galardon, E.; Ramdeehul, S.; Brown, J. M.; Cowley, A.; Hii, K. K. *Angew. Chem., Int. Ed.* **2002**, *41*, 1760.

[51] Shen, W. *Tetrahedron Lett.* **1997**, *38*, 5575.

[52] Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2768.

[53] Organ, M. G.; Chass, G. A.; Fang, D.-C.; Hopkinson, A. C.; Valente, C. *Synthesis* **2008**, 2776.

[54] Smith, G. B.; Dezeny, G. C.; Hughes, D. L.; King, A. O.; Verhoeven, T. R. *J. Org. Chem.* **1994**, *59*, 8151.

[55] Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.

[56] Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Maseras, F. *J. Am. Chem. Soc.* **2005**, *127*, 9298.

[57] Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020.

[58] Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.

[59] Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899.

[60] Brown, J. M.; Cooley, N. A. *Chem. Rev.* **1988**, *88*, 1031.

[61] Brown, J. M.; Guiry, P. J. *Inorg. Chim. Acta* **1994**, *220*, 249.

[62] Marcone, J. E.; Moloy, K. G. *J. Am. Chem. Soc.* **1998**, *120*, 8527.

[63] Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398.

[64] Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936.

[65] Barder, T. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 12003.

[66] Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743.

[67] Grosjean, C.; Novakovic, K.; Scott, S. K.; Whiting, A.; Willis, M. J.; Wright, A. R. *J. Mol. Cat. A: Chem.* **2008**, *284*, 33.

[68] Steinhuebel, D.; Baxter, J. M.; Palucki, M.; Davies, I. W. *J. Org. Chem.* **2005**, *70*, 10124.

[69] Cella, R.; Stefani, H. A. *Tetrahedron* **2006**, *62*, 5656.

[70] Alacid, E.; Nájera, C. *J. Org. Chem.* **2009**, *74*, 2321.

[71] Molander, G. A.; Bernardi, C. R. *J. Org. Chem.* **2002**, *67*, 8424.

[72] Molander, G. A.; Felix, L. A. *J. Org. Chem.* **2005**, *70*, 3950.

[73] Cella, R.; Orfão, A. T. G.; Stefani, H. A. *Tetrahedron Lett.* **2006**, *47*, 5075.

[74] Molander, G. A.; Yokoyama, Y. *J. Org. Chem.* **2006**, *71*, 2493.

[75] Stefani, H. A.; Cella, R.; Dörr, F. A.; Pereira, C. M. P.; Zeni, G.; Gomes, M., Jr. *Tetrahedron Lett.* **2005**, *46*, 563.

[76] Molander, G. A.; Ham, J.; Seapy, D. G. *Tetrahedron* **2007**, *63*, 768.

[77] Crudden, C. M.; Glasspoole, B. W.; Lata, C. J. *Chem. Commun.* **2009**, 6704.

[78] Dreher, S. D.; Dormer, P. G.; Sandrock, D. L.; Molander, G. A. *J. Am. Chem. Soc.* **2008**, *130*, 9257.

[79] Hohn, E.; Pietruszka, J.; Solduga, G. *Synlett* **2006**, 1531.

[80] Charette, A.; Mathieu, S.; Fournier, J.-F. *Synlett* **2005**, 1779.

[81] Fang, G. H.; Yan, Z. J.; Deng, M. Z. *Org. Lett.* **2004**, *6*, 357.

[82] Ahn, H. R.; Cho, Y. A.; Kim, D.-S.; Chin, J.; Gyoung, Y.-S.; Lee, S.; Kang, H.; Ham, J. *Org. Lett.* **2009**, *11*, 361.

[83] Harvey, J. H.; Butler, B. K.; Trauner, D. *Tetrahedron Lett.* **2007**, *48*, 1661.

[84] Skaff, O.; Jolliffe, K. A.; Hutton, C. A. *J. Org. Chem.* **2005**, *70*, 7353.

[85] Molander, G. A.; Elia, M. D. *J. Org. Chem.* **2006**, *71*, 9198.

[86] Kabalka, G. W.; Zhou, L.-L.; Naravane, A. *Tetrahedron Lett.* **2006**, *47*, 6887.

[87] Barder, T. E.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 2649.

[88] Adonin, N. Y.; Babushkin, D. E.; Parmon, V. N.; Bardin, V. V.; Kostin, G. A.; Mashukov, V. I.; Frohn, H.-J. *Tetrahedron* **2008**, *64*, 5920.

[89] Singh, R.; Czekelius, C.; Schrock, R. R.; Muller, P.; Hoveyda, A. H. *Organometallics* **2007**, *26*, 2528.

[90] Knapp, D. M.; Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2009**, *131*, 6961.

[91] Billingsley, K.; Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 3484.

[92] Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358.
[93] Kudo, N.; Perseghini, M.; Fu, G. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1282.
[94] Molander, G. A.; Canturk, B.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 973.
[95] Clapham, K. M.; Batsanov, A. S.; Greenwood, R. D. R.; Bryce, M. R.; Smith, A. E.; Tarbit, B. *J. Org. Chem.* **2008**, *73*, 2176.
[96] Yang, D. X.; Colletti, S. L.; Wu, K.; Song, M.; Li, G. Y.; Shen, H. C. *Org. Lett.* **2008**, *11*, 381.
[97] Billingsley, K. L.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4695.
[98] Deng, J. Z.; Paone, D. V.; Ginnetti, A. T.; Kurihara, H.; Dreher, S. D.; Weissman, S. A.; Stauffer, S. R.; Burgey, C. S. *Org. Lett.* **2008**, *11*, 345.
[99] Ackermann, L.; Potukuchi, H. K. *Synlett* **2009**, 2852.
[100] Yamamoto, A.; Takizawa, M.; Yu, X. Q.; Miyaura, N. *Heterocycles* **2010**, *80*, 359.
[101] Gütz, C.; Lützen, A. *Synthesis* **2010**, 85.
[102] Cho, Y. A.; Kim, D.-S.; Ahn, H. R.; Canturk, B.; Molander, G. A.; Ham, J. *Org. Lett.* **2009**, *11*, 4330.
[103] Clemens, R. T.; Jennings, M. P. *Chem. Commun.* **2006**, 2720.
[104] Hasník, Z.; Pohl, R.; Hocek, M. *Synthesis* **2009**, 1309.
[105] Alacid, E.; Nájera, C. *J. Org. Chem.* **2009**, *74*, 8191.
[106] Molander, G. A.; Brown, A. R. *J. Org. Chem.* **2006**, *71*, 9681.
[107] Saadi, J.; Lentz, D.; Reissig, H.-U. *Org. Lett.* **2009**, *11*, 3334.
[108] Garcia-Fortanet, J.; Debergh, J. R.; DeBrabander, J. K. *Org. Lett.* **2005**, *7*, 685.
[109] Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* **2002**, *67*, 8416.
[110] Kabalka, G. W.; Dong, G.; Venkataiah, B. *Tetrahedron Lett.* **2004**, *45*, 5139.
[111] Kabalka, G. W.; Dong, G.; Venkataiah, B. *Tetrahedron Lett.* **2005**, *46*, 763.
[112] Molander, G. A.; Gormisky, P. E. *J. Org. Chem.* **2008**, *73*, 7481.
[113] Molander, G. A.; Yun, C. S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534.
[114] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626.
[115] Horn, S.; Cundell, B.; Senge, M. O. *Tetrahedron Lett.* **2009**, *50*, 2562.
[116] Molander, G. A.; Ribagorda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148.
[117] Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, *18*, 1405.
[118] Zou, G.; Falck, J. R. *Tetrahedron Lett.* **2001**, *42*, 5817.
[119] Molander, G. A.; Jean-Gérard, L. *J. Org. Chem.* **2009**, *74*, 1297.
[120] Molander, G. A.; Petrillo, D. E. *Org. Lett.* **2008**, *10*, 1795.
[121] Molander, G. A.; Jean-Gérard, L. *J. Org. Chem.* **2009**, *74*, 5446.
[122] Cañeque, T.; Cuadro, A. M.; Alvarez-Builla, J.; Vaquero, J. J. *Tetrahedron Lett.* **2009**, *50*, 1419.
[123] Grimm, J. B.; Wilson, K. J.; Witter, D. J. *J. Org. Chem.* **2009**, *74*, 6390.
[124] Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 704.
[125] Yamamoto, Y.; Takada, S.; Miyaura, N.; Iyama, T.; Tachikawa, H. *Organometallics* **2009**, *28*, 152.
[126] Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 1368.
[127] Molander, G. A.; Gormisky, P. E.; Sandrock, D. L. *J. Org. Chem.* **2008**, *73*, 2052.
[128] Molander, G. A.; Sandrock, D. L. *Org. Lett.* **2007**, *9*, 1597.
[129] Molander, G. A.; Canturk, B. *Org. Lett.* **2008**, *10*, 2135.
[130] Molander, G. A.; Vargas, F. *Org. Lett.* **2007**, *9*, 203.
[131] Molander, G. A.; Jean-Gérard, L. *J. Org. Chem.* **2007**, *72*, 8422.
[132] Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Paolillo, R.; Taccardi, N. *Eur. J. Inorg. Chem.* **2005**, 582.
[133] Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045.
[134] Molander, G. A.; Petrillo, D. E.; Landzberg, N. R.; Rohanna, J. C.; Biolatto, B. *Synlett* **2005**, 1763.
[135] Zhang, L.; Meng, T.; Wu, J. *J. Org. Chem.* **2007**, *72*, 9346.
[136] Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867.
[137] Joucla, L.; Cusati, G.; Pinel, C.; Djakovitch, L. *Tetrahedron Lett.* **2008**, *49*, 4738.
[138] So, C. M.; Lau, C. P.; Kwong, F. Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 8059.
[139] Stein, A. L.; Alves, D.; da Rocha, J. T.; Nogueira, C. W.; Zeni, G. *Org. Lett.* **2008**, *10*, 4983.

[140] Qin, W.; Yasuike, S.; Kakusawa, N.; Sugawara, Y.; Kawahata, M.; Yamaguchi, K.; Kurita, J. *J. Organomet. Chem.* **2008**, *693*, 109.

[141] Alves, D.; Prigol, M.; Nogueira, C. W.; Zeni, G. *Synlett* **2008**, 914.

[142] Cella, R.; Cunha, R. L. O. R.; Reis, A. E. S.; Pimenta, D. C.; Klitzke, C. F.; Stefani, H. A. *J. Org. Chem.* **2006**, *71*, 244.

[143] Botteselle, G. V.; Hough, T. L. S.; Venturoso, R. C.; Cella, R.; Vieira, A. S.; Stefani, H. A. *Aust. J. Chem.* **2008**, *61*, 870.

[144] Singh, F. V.; Milagre, H. M. S.; Eberlin, M. N.; Stefani, H. A. *Tetrahedron Lett.* **2009**, *50*, 2312.

[145] Mizuta, M.; Seio, K.; Miyata, K.; Sekine, M. *J. Org. Chem.* **2007**, *72*, 5046.

[146] Guo, J.; Harling, J. D.; Steel, P. G.; Woods, T. M. *Org. Biomol. Chem.* **2008**, *6*, 4053.

[147] Yoshida, K.; Takahashi, H.; Imamoto, T. *Chem.–Eur. J.* **2008**, *14*, 8246.

[148] Guinchard, X.; Bugaut, X.; Cook, C.; Roulland, E. *Chem.–Eur. J.* **2009**, *15*, 5793.

[149] Singh, F. V.; Weber, M.; Guadagnin, R. C.; Stefani, H. A. *Synlett* **2008**, 1889.

[150] Alacid, E.; Nájera, C. *Org. Lett.* **2008**, *10*, 5011.

[151] Kabalka, G. W.; Dadush, E.; Al-Masum, M. *Tetrahedron Lett.* **2006**, *47*, 7459.

[152] Ozawa, F.; Hidaka, T.; Yamamoto, T.; Yamamoto, A. *J. Organomet. Chem.* **1987**, *330*, 253.

[153] Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 6319.

[154] Adamo, C.; Amatore, C.; Ciofini, I.; Jutand, A.; Lakmini, H. *J. Am. Chem. Soc.* **2006**, *128*, 6829.

[155] Miyaura, N. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2004.

[156] Scheidel, M.-S.; Briehn, P.; Bäuerle, P. *J. Organomet. Chem.* **2002**, *653*, 200.

[157] Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972.

[158] Grisorio, R.; Suranna, G. P.; Mastrorilli, P.; Nobile, C. F. *Org. Lett.* **2007**, *9*, 3149.

[159] Tremblay-Morin, J.-P.; Ali, H.; van Lier, J. E. *Tetrahedron Lett.* **2006**, *47*, 3043.

[160] Vilaró, M.; Arsequell, G.; Valencia, G.; Ballesteros, A.; Barluenga, J. *Org. Lett.* **2008**, *10*, 3243.

[161] Bellomo, A.; Gonzalez, D.; Stefani, H. A. *J. Organomet. Chem.* **2008**, *693*, 1136.

[162] Toyota, M.; Asano, T.; Ihara, M. *Org. Lett.* **2005**, *7*, 3929.

[163] Esteban, J.; Costa, A. M.; Vilarrasa, J. *Org. Lett.* **2008**, *10*, 4843.

[164] Molander, G. A.; Dehmel, F. *J. Am. Chem. Soc.* **2004**, *126*, 10313.

[165] Achelle, S.; Ramondenc, Y.; Dupas, G.; Plé, N. *Tetrahedron* **2008**, *64*, 2783.

[166] Fuchter, M. J. In *Name Reactions for Homologations* (*Part 1*); Li, J. J., Ed.; Wiley: Hoboken, 2009.

[167] Piller, F.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 6802.

[168] Krasovskiy, A.; Duplais, C.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2009**, *131*, 15592.

[169] Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. Reac.* **1997**, *50*, 1.

[170] Yet, L. In *Name Reactions for Homologations* (*Part 1*); Li, J. J., Ed.; Wiley: Hoboken, 2009.

[171] Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, *41*, 1486.

[172] Denmark, S. E.; Baird, J. D. *Chem.–Eur. J.* **2006**, *12*, 4954.

[173] Denmark, S. E.; Sweis, R. F. In *Metal-Catalyzed Cross-Coupling Reactions,* 2nd ed.; De Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weiheim, 2004.

[174] Denmark, S. E.; Ober, M. H. *Aldrichimica Acta* **2003**, *36*, 75.

[174b] Chang, W.-T. T.; Smith, R. C.; Regens, C. S.; Bailey, A. D.; Werner, N. S.; Denmark, S. E. *Org. React.* **2011**, *75*, 213.

[175] Hall, D. G., Ed. *Boronic Acids*; Wiley-VCH: Weinheim, 2005.

[176] Cammidge, A. N.; Goddard, V. H. M.; Gopee, H.; Harrison, N. L.; Hughes, D. L.; Schubert, C. J.; Sutton, B. M.; Watts, G. L.; Whitehead, A. J. *Org. Lett.* **2006**, *8*, 4071.

[177] Yamamoto, Y.; Takizawa, M.; Yu, X. Q.; Miyaura, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 928.

[178] Noguchi, H.; Hojo, K.; Suginome, M. *J. Am. Chem. Soc.* **2007**, *129*, 758.

[179] Noguchi, H.; Shioda, T.; Chou, C.-M.; Suginome, M. *Org. Lett.* **2008**, *10*, 377.

[180] Iwadate, N.; Suginome, M. *Org. Lett.* **2009**, *11*, 1899.

[181] Mancilla, T.; Contreras, R.; Wrackmeyer, B. *J. Organomet. Chem.* **1986**, *307*, 1.

[182] Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2007**, *129*, 6716.

[183] Lee, S. J.; Gray, K. C.; Paek, J. S.; Burke, M. D. *J. Am. Chem. Soc.* **2007**, *130*, 466.

[184] Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 14084.

[185] Uno, B. E.; Gillis, E. P.; Burke, M. D. *Tetrahedron* **2009**, *65*, 3130.

[186] Dick, G. R.; Knapp, D. M.; Gillis, E. P.; Burke, M. D. *Org. Lett.* **2010**, *12*, 2314.

[187] Struble, J. R.; Lee, S. J.; Burke, M. D. *Tetrahedron* **2010**, *66*, 4710.

[188] Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460.

[189] Denmark, S. E.; Butler, C. R. *Chem. Commun.* **2009**, 20.

[190] Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.

[191] Kerins, F.; O'Shea, D. F. *J. Org. Chem.* **2002**, *67*, 4968.

[192] Lightfoot, A. P.; Twiddle, S. J. R.; Whiting, A. *Synlett* **2005**, 529.

[193] Uenishi, J.; Beau, J. M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756.

[194] Kobayashi, S.; Mori, K.; Wakabayashi, T.; Yasuda, S.; Hanada, K. *J. Org. Chem.* **2001**, *66*, 5580.

[195] Scheidt, K. A.; Bannister, T. D.; Tasaka, A.; Wendt, M. D.; Savall, B. M.; Fegley, G. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 6981.

[196] Pazos, Y.; Iglesias, B.; de Lera, A. R. *J. Org. Chem.* **2001**, *66*, 8483.

[197] Mergott, D. J.; Frank, S. A.; Roush, W. R. *Org. Lett.* **2002**, *4*, 3157.

[198] Soderquist, J. A.; Matos, K.; Rane, A.; Ramos, J. *Tetrahedron Lett.* **1995**, *36*, 2401.

[199] Fürstner, A.; Seidel, G. *Tetrahedron* **1995**, *51*, 11165.

[200] Zou, G.; Reddy, Y. K.; Falck, J. R. *Tetrahedron Lett.* **2001**, *42*, 7213.

[201] Mu, Y.; Gibbs, R. A. *Tetrahedron Lett.* **1995**, *36*, 5669.

[202] Zhou, X.; Tse, M. K.; Wan, T. S. M.; Chan, K. S. *J. Org. Chem.* **1996**, *61*, 3590.

[203] Enguehard, C.; Renou, J.-L.; Collot, V.; Hervet, M.; Rault, S.; Gueiffier, A. *J. Org. Chem.* **2000**, *65*, 6572.

[204] Gray, M.; Andrews, I. P.; Hook, D. F.; Kitteringham, J.; Voyle, M. *Tetrahedron Lett.* **2000**, *41*, 6237.

[205] Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056.

[206] Rilatt, I.; Caggiano, L.; Jackson, R. F. W. *Synlett* **2005**, 2701.

[207] Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1988**, *110*, 3296.

[208] Fujimura, T.; Aoki, S.; Nakamura, E. *J. Org. Chem.* **1991**, *56*, 2809.

[209] Majeed, A. J.; Antonsen, Ø.; Benneche, T.; Undheim, K. *Tetrahedron* **1989**, *45*, 993.

[210] Férézou, J. P.; Julia, M.; Li, Y.; Liu, L. W.; Pancrazi, A. *Synlett* **1991**, 53.

[211] Kosugi, M.; Sumiya, T.; Ohhashi, K.; Sano, H.; Migita, T. *Chem. Lett.* **1985**, 997.

[212] Falck, J. R.; Patel, P. K.; Bandyopadhyay, A. *J. Am. Chem. Soc.* **2007**, *129*, 790.

[213] Jensen, M. S.; Yang, C.; Hsiao, Y.; Rivera, N.; Wells, K. M.; Chung, J. Y. L.; Yasuda, N.; Hughes, D. L.; Reider, P. J. *Org. Lett.* **2000**, *2*, 1081.

[214] Arvela, R. K.; Leadbeater, N. E.; Mack, T. L.; Kormos, C. M. *Tetrahedron Lett.* **2006**, *47*, 217.

[215] Harker, R. L.; Crouch, R. D. *Synthesis* **2007**, 25.

[216] Schmöger, C.; Szuppa, T.; Tied, A.; Schneider, F.; Stolle, A.; Ondruschka, B. *ChemSusChem* **2008**, *1*, 339.

[217] Freundlich, J. S.; Landis, H. E. *Tetrahedron Lett.* **2006**, *47*, 4275.

[218] Schön, U.; Messinger, J.; Eichner, S.; Kirschning, A. *Tetrahedron Lett.* **2008**, *49*, 3204.

[219] Kabalka, G. W.; Al-Masum, M. *Tetrahedron Lett.* **2005**, *46*, 6329.

[220] Kabalka, G. W.; Naravane, A.; Zhao, L. L. *Tetrahedron Lett.* **2007**, *48*, 7091.

[221] Lei, W. *Chin. J. Chem.* **2006**, *24*, 770.

[222] Park, Y. H.; Ahn, H. R.; Canturk, B.; Jeon, S. I.; Lee, S.; Kang, H.; Molander, G. A.; Ham, J. *Org. Lett.* **2008**, *10*, 1215.

[223] Savall, B. M.; Fontimayor, J. R. *Tetrahedron Lett.* **2008**, *49*, 6667.

[224] Guadagnin, R. C.; Suganuma, C. A.; Singh, F. V.; Vieira, A. S.; Cella, R.; Stefani, H. A. *Tetrahedron Lett.* **2008**, *49*, 4713.

[225] Molander, G. A.; Sandrock, D. L. *J. Am. Chem. Soc.* **2008**, *130*, 15792.

[226] Lysén, M.; Köhler, K. *Synthesis* **2006**, 692.

[227] LeBlond, C. R.; Butler, K. M.; Ferrington, M. W.; Browe, M. A. *Synth. Commun.* **2009**, *39*, 636.

[228] Huffman, J. W.; Padgett, L. W.; Isherwood, M. L.; Wiley, J. L.; Martin, B. R. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5432.

[229] Christoforou, I. C.; Koutentis, P. A.; Rees, C. W. *Org. Biomol. Chem.* **2003**, *1*, 2900.

[230] Molander, G. A.; Petrillo, D. E. *Org. Synth.* **2007**, *84*, 317.

[231] Masllorens, J.; González, I.; Roglans, A. *Eur. J. Org. Chem.* **2007**, 158.

[232] Lipshutz, B. H.; Petersen, T. B.; Abela, A. R. *Org. Lett.* **2008**, *10*, 1333.

[233] Mennecke, K.; Kirschning, A. *Synthesis* **2008**, 3267.

[234] Chen, W.; Li, R.; Han, B.; Li, B.-J.; Chen, Y.-C.; Wu, Y.; Ding, L.-S.; Yang, D. *Eur. J. Org. Chem.* **2006**, 1177.

[235] O'Brien, C. J.; Kantchev, E. A. B.; Valente, C.; Hadei, N.; Chass, G. A.; Lough, A.; Hopkinson, A. C.; Organ, M. G. *Chem.–Eur. J.* **2006**, *12*, 4743.

[236] Bing, W.; Hui-Xia, S.; Zhi-Hua, S. *Eur. J. Org. Chem.* **2009**, 3688.

[237] Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *J. Fluorine Chem.* **2002**, *117*, 115.

[238] Korenaga, T.; Kosaki, T.; Kawauchi, Y.; Ema, T.; Sakai, T. *J. Fluorine Chem.* **2006**, *127*, 604.

[239] Frohn, H. J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *Tetrahedron Lett.* **2002**, *43*, 8111.

[240] Dachs, A.; Masllorens, J.; Pla-Quintana, A.; Roglans, A.; Farjas, J.; Parella, T. *Organometallics* **2008**, *27*, 5768.

[241] Kabalka, G. W.; Zhou, L.-L.; Naravane, A. *Lett. Org. Chem.* **2007**, *4*, 325.

[242] Houpis, I. N.; Huang, C.; Nettekoven, U.; Chen, J. G.; Liu, R.; Canters, M. *Org. Lett.* **2008**, *10*, 5601.

[243] Molander, G. A.; Petrillo, D. E. *J. Am. Chem. Soc.* **2006**, *128*, 9634.

[244] Molander, G. A.; Figueroa, R. *Org. Lett.* **2006**, *8*, 75.

[245] Molander, G. A.; Febo-Ayala, W.; Jean-Gérard, L. *Org. Lett.* **2009**, *11*, 3830.

[246] Molander, G. A.; Cooper, D. J. *J. Org. Chem.* **2008**, *73*, 3885.

[247] Browne, D. L.; Taylor, J. B.; Plant, A.; Harrity, J. P. A. *J. Org. Chem.* **2009**, *74*, 396.

[248] Huang, J.; Orac, C. M.; McKay, S.; McKay, D. B.; Bergmeier, S. C. *Bioorg. Med. Chem.* **2008**, *16*, 3816.

[249] Gibson, C. L.; Huggan, J. K.; Kennedy, A.; Kiefer, L.; Lee, J. H.; Suckling, C. J.; Clements, C.; Harvey, A. L.; Hunter, W. N.; Tulloch, L. B. *Org. Biomol. Chem.* **2009**, *7*, 1829.

[250] Ali, H.; St-Jean, O.; Tremblay-Morin, J.-P.; van Lier, J. E. *Tetrahedron Lett.* **2006**, *47*, 8275.

[251] Wu, J.; Zhang, L.; Luo, Y. *Tetrahedron Lett.* **2006**, *47*, 6747.

[252] Wu, J.; Zhang, L.; Xia, H.-G. *Tetrahedron Lett.* **2006**, *47*, 1525.

[253] Gøgsig, T. M.; Søbjerg, L. S.; Lindhardt, A. T.; Jensen, K. L.; Skrydstrup, T. *J. Org. Chem.* **2008**, *73*, 3404.

[254] Gerbino, D. C.; Mandolesi, S. D.; Schmalz, H. G.; Podestá, J. C. *Eur. J. Org. Chem.* **2009**, 3964.

[255] Hisashi, D.; Ikuya, B.; Akihito, N.; Kengo, S.; Chunxiang, K.; Takamitsu, H.; Hideo, T.; Masaaki, S. *Chem.–Eur. J.* **2009**, *15*, 4165.

[256] Kassis, P. l.; Bénéteau, V.; Mérour, J.-Y.; Routier, S. *Synthesis* **2009**, 2447.

[257] Lipshutz, B. H.; Abela, A. R. *Org. Lett.* **2008**, *10*, 5329.

[258] Pagano, N.; Maksimoska, J.; Bregman, H.; Williams, D. S.; Webster, R. D.; Xue, F.; Meggers, E. *Org. Biomol. Chem.* **2007**, *5*, 1218.

[259] Godoi, B.; Neto, J. S. S.; Sperança, A.; Acker, C. I.; Nogueira, C. W.; Zeni, G. *Tetrahedron Lett.* **2009**, *50*, 5326.

[260] Queiroz, M. J. R. P.; Abreu, A. S.; Calhelha, R. C.; Carvalho, M. S. D.; Ferreira, P. M. T. *Tetrahedron* **2008**, *64*, 5139.

[261] Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107.

[262] Carter, R. R.; Wyatt, J. K. *Tetrahedron Lett.* **2006**, *47*, 6091.

[263] Grosjean, C.; Henderson, A. P.; Hérault, D.; Ilyashenko, G.; Knowles, J. P.; Whiting, A.; Wright, A. R. *Org. Proc. Res. Dev.* **2009**, *13*, 434.

[264] Szadkowska, A.; Makal, A.; Wozniak, K.; Kadyrov, R.; Grela, K. *Organometallics* **2009**, *28*, 2693.

[265] Grisorio, R.; Piliego, C.; Fini, P.; Cosma, P.; Mastrorilli, P.; Gigli, G.; Suranna, G. P.; Nobile, C. F. *J. Phys. Chem. C* **2008**, *112*, 7005.

[266] Li, M.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 6087.

[267] Achmatowicz, M.; Chan, J.; Wheeler, P.; Liu, L.; Faul, M. M. *Tetrahedron Lett.* **2007**, *48*, 4825.

[268] Armitt, D. J.; Crisp, G. T. *Tetrahedron* **2006**, *62*, 1485.

[269] Arcadi, A.; Attanasi, O. A.; Berretta, S.; Bianchi, G.; Filippone, P. *Synthesis* **2006**, 2523.

[270] Ragab, H. M.; Kim, J. S.; Dukat, M.; Navarro, H.; Glennon, R. A. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4283.

[271] Kabalka, G. W.; Al-Masum, M.; Mereddy, A. R.; Dadush, E. *Tetrahedron Lett.* **2006**, *47*, 1133.

[272] De, S.; Welker, M. E. *Org. Lett.* **2005**, *7*, 2481.

[273] De, S.; Day, C.; Welker, M. E. *Tetrahedron* **2007**, *63*, 10939.

[274] Guillon, J.; Forfar, I.; Desplat, V.; Fabre, S. B.; Thiolat, D.; Massip, S.; Carrie, H.; Mossalayi, D.; Jarry, C. *J. Enzyme Inhib. Med. Chem.* **2007**, *22*, 541.

[275] Fürstner, A.; Larionov, O.; Flügge, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5545.

[276] Wu, C.-Y.; Hsien, M.-F.; Yen, Y.-P. *Lett. Org. Chem.* **2008**, *5*, 514.

[277] Bellomo, A.; Weber, M.; Gonzalez, D.; Stefani, H. A. *Catal. Commun.* **2009**, *10*, 1647.

[278] van den Hoogenband, A.; Lange, J. H. M.; Terpstra, J. W.; Koch, M.; Visser, G. M.; Visser, M.; Korstanje, T. J.; Jastrzebski, J. T. B. H. *Tetrahedron Lett.* **2008**, *49*, 4122.

[279] Molander, G. A.; Sandrock, D. L. *Org. Lett.* **2009**, *11*, 2369.

[280] Sumida, Y.; Yorimitsu, H.; Oshima, K. *J. Org. Chem.* **2009**, *74*, 3196.

[281] Al-Masum, M.; Alam, S. *Tetrahedron Lett.* **2009**, *50*, 5201.

[282] Goldys, A.; McErlean, C. S. P. *Tetrahedron Lett.* **2009**, *50*, 3985.

[283] Pirez, C.; Dheur, J.; Sauthier, M.; Castanet, Y.; Mortreux, A. *Synlett* **2009**, 1745.

[284] So, C. M.; Lau, C. P.; Chan, A. S. C.; Kwong, F. Y. *J. Org. Chem.* **2008**, *73*, 7731.

CHAPTER 2

ASYMMETRIC TRANSFORMATIONS BY DEPROTONATION USING CHIRAL LITHIUM AMIDES

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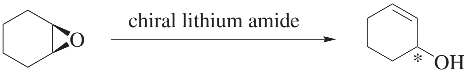
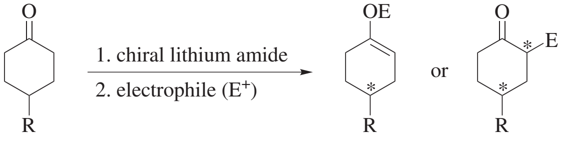
INTRODUCTION

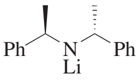
Over the past 25 years or so, chiral lithium amide bases have seen significant application in reactions that can be broadly described as asymmetric deprotonations. Several reviews provide an overview of particular facets of the chiral lithium amide base repertoire.[1–13] Developments in the methodology, including design and exploration of novel bases, moves toward catalysis, and applications to new types of substrates have increased the scope of the chemistry considerably. Chiral lithium amides are used successfully in several classes of asymmetric reactions, including (1) the rearrangement of symmetrical epoxides into allylic alcohols (Eq. 1), (2) the conversion of prochiral cyclic ketones into chiral enolates and the reactions thereof (Eq. 2), and (3) aromatic and benzylic functionalization of tricarbonyl(η^6-arene)chromium(0) complexes. The desymmetrization of prochiral cyclic ketones has become a well-established strategy in organic synthesis, and has seen significant application in target-oriented synthesis. Typical chiral bases employed in asymmetric deprotonation processes are, for the most part, lithium amides **1**–**8**.



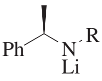
(Eq. 1)



(Eq. 2)



(*R*,*R*)-**1**



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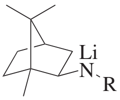

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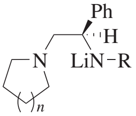

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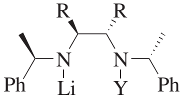
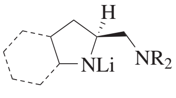


5 (Y = H, Li)



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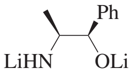

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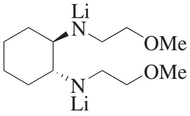

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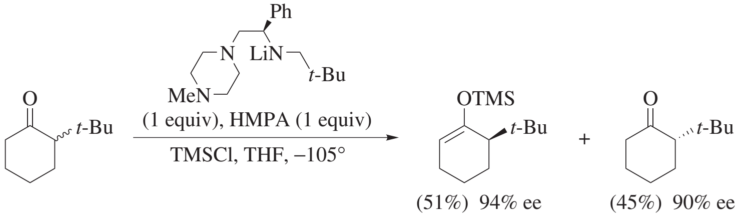
In addition to the popular strategy of desymmetrizing conformationally biased prochiral cyclohexanones, the chiral base approach is often used with oxa-, aza-, and thiabicyclo[3.2.1]octan-3-ones as substrates. Mono-protected *cis*-bicyclo[3.3.0]octane-3,7-diones, which are conformationally constrained prochiral cyclopentanones, are popular as substrates for desymmetrization by a chiral base since the products are chiral intermediates in the synthesis of carbacyclins. Cyclic imides are also excellent substrates for the chiral base-enolization approach and the products provide an attractive entry for the synthesis of enantiomerically enriched alkaloids. The chiral base method is also useful in metalations at bridgehead positions, in which the enolate structure can be more carbanion-like. A few kinetic resolution processes involving chiral lithium amide bases are also known, where a deficiency of base or an incomplete reaction time is employed to convert the fast-reacting enantiomer present in the mixture into a product, while the slow-reacting enantiomer is recovered (e.g., Eq. 3).[14]



(Eq. 3)

In this chapter, the use of chiral lithium amides as bases for enantioselective deprotonation will be covered. For the deprotonation of prochiral cyclic ketones, the data in the Tabular Survey are divided into two tables, the first describing transformations involving the formation of silyl enol ethers (Table 2), and the second describing transformations of lithium enolates without silylation (Table 3). The products shown in the Tabular Survey are compounds in which the enantiomeric excess corresponding to the deprotonation event is first determined. In accord with this approach, the "Conditions" column details all of the steps required for the conversion of the shown starting material into the shown product, and not simply the conditions of the enantioselective deprotonation. Mechanistically unrelated processes, such as the use of lithium amides in mixed aggregates for asymmetric aldehyde addition, or as nucleophiles in asymmetric aza-Michael reactions, are not included in this chapter.

The stereoselective preparation of (*E*)- or (*Z*)-enolates of α-branched esters using chiral lithium amides, and its use in combination with the Ireland-Claisen rearrangement,[15–19] has been omitted from the scope of this review because the enolization does not involve the selection between enantiotopic protons, nor is it an enantioselective process.

MECHANISM AND STEREOCHEMISTRY

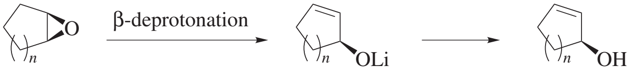
General

A common theme of most enantioselective deprotonations using chiral lithium amides is the formation of a reactive carbon nucleophile by a metalation process involving desymmetrization of a prochiral starting material. Asymmetric induction is accomplished as a result of incorporating at least one stereogenic element into the base, which is sited at either or both of the two α-carbons adjacent to the nitrogen of the amide group. The solution structure of lithium dialkylamides can be rather complex, owing to their propensity to self-associate into higher aggregated species.[20] In this context, coordinating solvent molecules play an important role because they function not only as the reaction media but also as ligands. Any model of the solution structure of a chiral lithium amide is complicated further when additives that are often present in enantioselective deprotonation reactions, such as lithium chloride and hexamethylphosphoric triamide (HMPA), are considered.

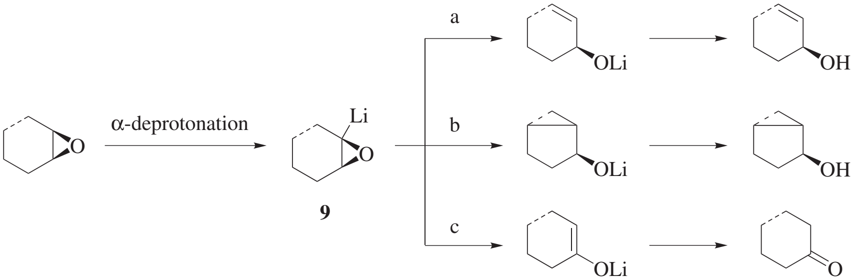
For the purpose of rationalizing the stereochemical outcome of many enantioselective deprotonations it is usually sufficient to treat the chiral lithium amide as its monomer form. This species undergoes precoordination with an appropriate substrate in a fashion where the nitrogen atom of the amide is poised to abstract a proton and the lithium can be donated to a nearby heteroatom. In most cases, the heteroatom is an oxygen atom leading to the formation of a lithium alkoxide or lithium enolate. Steric interactions between the chiral base and substrate are predominantly implicated as the key factor for discrimination between various transition states corresponding to deprotonation. Unsurprisingly, the observed enantioselectivity is generally higher when the reaction is performed at lower temperatures. Tricarbonyl(η^6-arene)chromium(0) complexes are somewhat distinguished as these undergo directed metalation of the aromatic ring (or a benzylic position) to afford a C–Li bond that is not stabilized by a heteroatom resonance. The "Mechanism and Stereochemistry" section includes a discussion of enantioselective deprotonation for the following classes of substrate: (1) epoxides, (2) prochiral cyclic ketones, and (3) tricarbonyl(η^6-arene)chromium(0) complexes. These three categories are the main pillars of this field of research and they have each received considerable attention with regard to the reaction mechanism.

Epoxides

The non-enantioselective base-promoted rearrangement of epoxides is a well-investigated process that has been reviewed previously.[21,22] The type of rearrangement that takes place depends upon the structure of the epoxide, as well as various other factors including the nature of the base, the choice of solvent, and the temperature used. A β-deprotonation results in rearrangement of the epoxide to provide an allylic alcohol (Eq. 4), whereas α-deprotonation can lead to one or a mixture of the following: (a) rearrangement to an allylic alcohol, (b) insertion into a nearby C−H bond, or (c) rearrangement to generate an enolate or ketone (Scheme 1). In certain cases the intermediate carbenoid **9** may also be trapped using electrophiles.

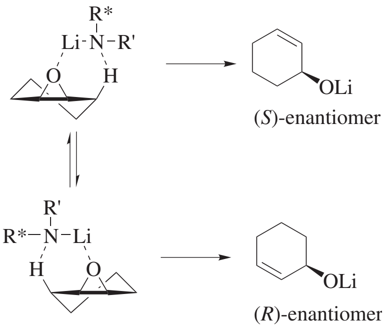


(Eq. 4)



Scheme 1

The enantioselective rearrangement of epoxides to allylic alcohols using chiral lithium amides has been the particular subject of some reviews.[3,8,23] When the base is a chiral lithium amide and the epoxide is prochiral, a selective rearrangement occurs to afford an enantiomerically enriched allylic alcohol. Deuterium-labeling studies have demonstrated that cyclohexene oxide, with or without a substituent, undergoes *syn* β-hydrogen removal in the presence of lithium dialkylamides, such as Et_2NLi or LDA (lithium diisopropylamide).[24,25] The lithium amide precoordinates to a lone pair on the epoxide oxygen, and it is the formation of a complex between epoxide and base that is assumed to promote *syn*-elimination. This implies for the enantioselective version of the same transformation that a *syn* β-elimination pathway is also involved with a preference for the removal of an enantiotopic proton (Scheme 2).[8] For cyclic epoxides, the enantiotopic protons should therefore occupy a pseudo-axial orientation in the substrate. Evidence for *syn* β-elimination of cyclohexene oxide promoted by chiral lithium amides is provided by ^2H NMR spectroscopy at natural abundance levels of deuterium.[26] In the study, cyclohexene oxide exhibits a primary kinetic isotope effect upon its partial deprotonation by lithium amides, resulting in a modest relative enrichment of deuterium at the β_{syn}-position.



Scheme 2

The possible intermediacy of the epoxide-lithium amide complex has been explored further in the particular context of using proline-derived chiral lithium amides.[27–29] Thus, four plausible reaction intermediate complexes are identified for the conversion of cyclohexene oxide into cyclohex-2-en-1-ol using the model base lithium (*S*)-2-[(pyrrolidin-1-yl)methyl]pyrrolidide (**10**, Fig. 1). The cyclohexene oxide can approach the base from either its top or bottom face, which differ because chelation of the pyrrolidine ring to the lithium cation affords the base a concave and a convex face. In both cases, there are enantiotopic β-hydrogen atoms in the substrate that give, upon deprotonation, either the (*R*)- or (*S*)-enantiomer of the allylic alcohol product.

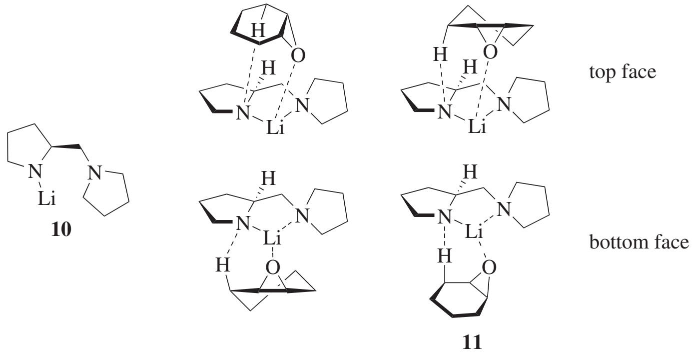


Figure 1. Plausible intermediate complexes for the conversion of cyclohexene oxide into cyclohex-2-en-1-ol using the model base lithium (*S*)-2-[(pyrrolidin-l-yl)methyl]pyrrolidide (**10**).

With a view to evaluating these reaction intermediates by computational methods, an optimized transition-state structure has been proposed of $LiNH_2$ and propene oxide using MP2/6-31+G* ab initio calculations.[29] The reaction intermediates have been added to this initial structure and molecular mechanics (MM3) calculations were carried out to determine their optimized geometries and conformational energies. For a series of eight proline-derived lithium amides based on lithium (*S*)-2-[(pyrrolidin-1-yl)methyl]pyrrolidide, the reaction intermediate complex of the type **11** (correctly leading to formation of the (*S*)-isomer of cyclohex-2-en-1-ol) is identified as the most energetically favored. A quite good linear correlation is found between the populations calculated from the conformational energies of reaction intermediates leading to (*S*)- or (*R*)-cyclohex-2-en-1-ol and the experimentally reported % ee values. The MM3 force-field approach appears promising for a theoretical evaluation of the enantioselectivity of this asymmetric process and may prove useful in the design of new chiral lithium amide reagents. In a separate endeavor, a series of isopinocamphenyl-based chiral lithium amides have also been evaluated by computational methods.[30]

Significant rate accelerations for the non-enantioselective rearrangement of epoxides to allylic alcohols can be achieved using a mixed base system of LDA with potassium *tert*-butoxide.[31] In parallel to the deprotonation of epoxides using lithium dialkylamides, these reactions appear to follow a *syn*-periplanar stereochemical course.[32] It is speculated that the increased reaction rates may arise from a push-pull mechanism (Fig. 2). Thus chiral bases featuring both lithium amide and lithium alkoxide functionalities in the same molecule have been developed, such as the dilithiated amino alcohols of the ephedrine and norephedrine family (e.g. **7**).[33,34] These chiral bases are very effective reagents for the enantioselective deprotonation of epoxides.[35,36]

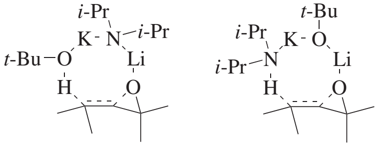
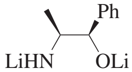


Figure 2. Push-pull mechanism for deprotonation of epoxides.



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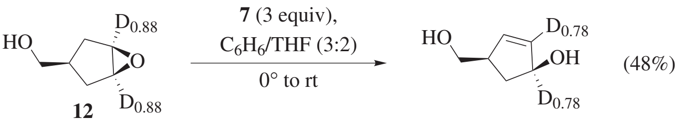
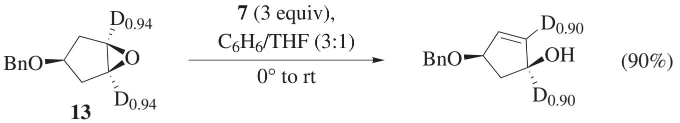
Isotopic labeling of epoxide substrates, in particular the use of deuterium atoms, can be employed to study the mechanism of their rearrangement using chiral lithium amides. For instance, partial reversible deprotonation (loss of deuterium) at the α-position is observed for the deprotonation of 4-substituted cyclopentene oxide **12**, possessing a free hydroxyl group, by base **7** (Eq. 5).[37,38] The structurally related epoxide **13** gives efficient β-elimination under essentially the same reaction conditions (Eq. 6).



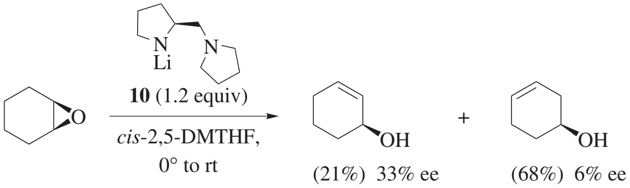
(Eq. 5)



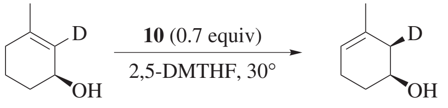
13

(Eq. 6)

Lithium (*S*)-2-[(pyrrolidin-1-yl)methyl]pyrrolidide (**10**) deprotonates cyclohexene oxide in THF to give (*S*)-cyclohex-2-en-1-ol in 79% ee.[39,40] When the solvent is changed from THF to a more sterically demanding solvent such as 2,5-dimethyltetrahydrofuran (2,5-DMTHF), the allylic lithium alkoxide isomerizes to the homoallylic lithium alkoxide, affording the homoallylic alcohol after quenching (Eq. 7).[41] The process is intramolecular and completely stereospecific with regard to the stereogenic center that bears the hydroxyl group.[42] The erosion of enantiomeric excess of both products in Eq. 7 is explained by further 1,3-proton transfers. To probe the stereochemical course of this 1,3-proton transfer in more detail, deuterium-labeled substrate **14** (>99.5% ee), prepared using an enantioselective reduction as the key asymmetric step, is subjected to the reaction conditions (Eq. 8).[43] In this reaction, a methyl group present at C-3 is sufficient to prevent further 1,3-proton transfers of the homoallylic alkoxide intermediate and racemization is therefore avoided. The (1*S*,2*R*)-configuration in homoallylic alcohol product **15** (47% yield after HPLC) shows that the 1,3-proton transfer delivers the proton *anti* with respect to the oxygen.



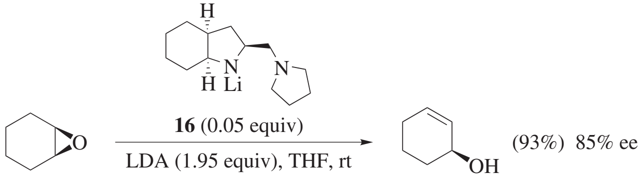
(Eq. 7)



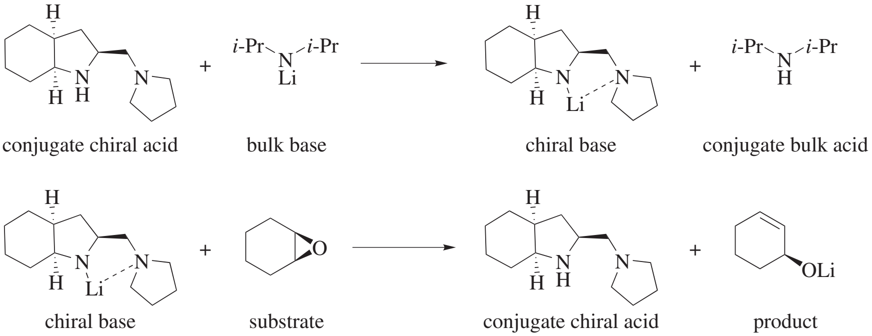
14 **15** (47%)

(Eq. 8)

The rearrangement of epoxides to allylic alcohols can be carried out using substoichiometric quantities of chiral lithium amide.[3,23] For example, cyclohexene oxide is converted into (*S*)-cyclohex-2-en-1-ol using 0.05 equivalents of lithium amide **16** in 93% yield and 85% ee (Eq. 9).[44] In this reaction, LDA (1.95 equivalents) is included as a bulk base in order to regenerate the chiral reagent after it becomes protonated to give the corresponding chiral amine. In general, an efficient catalytic enantioselective deprotonation reaction requires the rate of reaction between the bulk base and substrate (i.e. the racemic background reaction) to be substantially slower than (1) the rate of regeneration of the chiral base and (2) the enantioselective deprotonation reaction itself (Scheme 3).



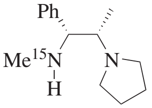
(Eq. 9)



Scheme 3

The choice of bulk base to use with a particular chiral lithium amide can have a significant effect on the outcome of a catalytic enantioselective deprotonation reaction. Bulk bases used in stoichiometric quantities for the catalytic deprotonation of epoxides include LDA, lithiated imidazoles such as 2-lithio-1-methylimidazole, and even methyllithium in a rare case.[45,46] When the most common base LDA is employed, it is often necessary to add an excess of 1,8-diazabicycloundec-7-ene (DBU) to increase the rate of reaction and obtain optimal enantioselectivities. DBU is assumed to cause solvation of lithium amides favoring more reactive aggregates, although an additional role has been observed. Thus, LDA in THF reversibly deprotonates DBU at the 6-position to afford lithiated DBU (**17**) where the lithium is coordinated to the azaallylic system (Eq. 10).[47] The lithiated DBU can function as a base but it also forms heterodimers with chiral lithium amides as observed by ^{6}Li NMR spectroscopy of a mixture of [^{6}Li]-**17** in the presence of [^{15}N]-labeled chiral amine **18**.

(Eq. 10)



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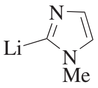

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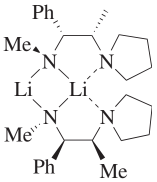


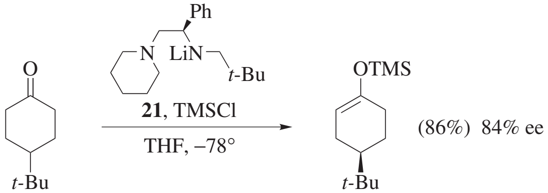
20

Such heterodimers may be the active species for catalytic enantioselective deprotonation, although it is noteworthy that the reaction in Eq. 9 is very effective in the absence of DBU. Calculations at the pBP86/DN*//PM3 level of theory suggest that the heterodimer prefers to be mono-solvated (compared to no solvation or being di-solvated) and that DBU is better at solvating it than THF.[47]

Lithiated 1-methylimidazole (**19**) forms heterodimers with chiral lithium amides that promote enantioselective deprotonations of cyclohexene oxide in up to 96% ee.[48,49] Evidence for the heterodimer is similarly provided by ^{6}Li NMR spectroscopy of a mixture of [^{6}Li]-**19** together with [^{15}N]-labeled chiral amine **18**. In a separate experiment, lithiation of chiral amine **18** affords the corresponding chiral lithium amide as its homodimer **20**.[50] This homodimer is not basic enough to deprotonate DBU (it becomes solvated by DBU instead), but it is able to deprotonate 1-methylimidazole to produce **19**, which proceeds to form the same heterodimer as before with the excess lithium amide. A calibrated quench-extraction-gas chromatography procedure has been used to determine initial rates and reaction orders of an enantioselective deprotonation reaction.[51] Using this approach, the rate-limiting activated complex for the enantioselective deprotonation of cyclohexene oxide by lithium (1*R*,2*S*)-*N*-methyl-1-phenyl-2-pyrrolidinylpropanamide, with or without **19**, has been proposed. Thus, in the absence of **19**, the activated complex consists of a lithium amide dimer, one molecule of cyclohexene oxide, and one molecule of THF.[50] Addition of **19** serves to break up the lithium amide dimer so that the transition state structure now consists of one molecule each of lithium amide, **19**, epoxide, and THF.[52]

Prochiral Cyclic Ketones

One of the first reports of the desymmetrization of prochiral cyclic ketones to give chiral enolates concerned the asymmetric deprotonation of *cis*-2,6-dimethylcyclohexanone.[53] However, the conversion of 4-*tert*-butylcyclohexanone into the corresponding silyl enol ether quickly has become the benchmark reaction for examining chiral base efficacy (Eq. 11).[54−56] In conformationally biased cyclohexanones, such as 4-*tert*-butylcyclohexanone, a stereoelectronic preference exists for removal of the axial protons, and chiral lithium amides are able to discriminate between the enantiotopic protons. When phenylglycine-derived chiral bases such as **21** are used, it is sometimes necessary to add HMPA to the reaction mixture to achieve optimal asymmetric induction.



(Eq. 11)

Solvent-dependent changes in the aggregation state of lithium amide **21** have been monitored through a combination of ^{6}Li and ^{15}N NMR spectroscopy.[55] In d_8-THF, the ^{6}Li NMR spectrum of [^{6}Li,^{15}N$_2$]-**21** shows a doublet of doublets indicative of lithium coupling to two neighboring ^{15}N nuclei. The corresponding ^{15}N NMR spectrum shows two sets of triplets (1:1:1) to reveal that each nitrogen atom couples to one neighboring ^{6}Li nucleus. Therefore, lithium amide **21** in this solvent exists as a monomer possessing a five-membered chelate structure. In d_8-toluene, the ^{6}Li NMR spectrum of $[^{6}Li,^{15}N_2]$-**21** shows a doublet of triplets, indicative of coupling to three neighboring ^{15}N nuclei. The corresponding ^{15}N NMR spectrum displays a triplet (1:1:1) and a quintet (1:2:3:2:1), indicating that one nitrogen atom couples to one neighboring lithium while the other nitrogen couples to two neighboring lithiums. These observations support the conclusion that lithium amide **21** exists as a homodimer in this solvent, and the structure of this dimer has been verified by X-ray crystallography.[55] The core of the homodimer is a Li–N–Li–N four-membered ring, and a five-membered chelate is formed in each base subunit present in the dimer (Fig. 3). The conformation of each lithium amide unit in the homodimer is very similar to that of the neopentyl group on the amide nitrogen fixed *trans* to the phenyl group. This indicates that the lone pair on the amide nitrogen is fixed *cis* to the phenyl group and the dimer is formed by coordination of this lone pair to a vacant orbital on lithium from the other molecule in the dimer.

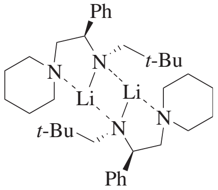
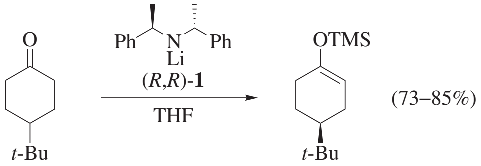


Figure 3. Homodimer of lithium amide **21**.

The addition of two equivalents of HMPA to the homodimer in d_8-toluene changes the situation dramatically and the ^{6}Li and ^{15}N NMR spectra now resemble the spectra of the chelated monomer previously observed in d_8-THF. Hence it appears that HMPA is highly effective in dissociating the dimeric form of lithium amide **21** to generate a monomeric species that is presumably more reactive and more selective. This assumption is reflected by the performance of **21** in deprotonations of 4-*tert*-butylcyclohexanone using toluene as the solvent. Whereas the yield and enantioselectivity of this reaction are low in the absence of HMPA (12% yield, 58% ee), the addition of two equivalents of HMPA results in a substantial improvement (87% yield, 82% ee).[55]

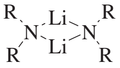
In general, the highest enantioselectivities in chiral base-mediated ketone deprotonations are obtained by trapping the lithium enolates as silyl enol ethers using the internal quench protocol.[57] These ketone deprotonation reactions are usually more effective if the electrophile TMSCl (trimethylsilyl chloride) is premixed with the base before addition of the ketone (internal quench conditions, IQ), rather than added to the enolate formed by exposure of the ketone to the base (external quench conditions, EQ). Another important observation is that the enantioselectivities under external quench conditions are often enhanced by the addition of lithium chloride (Eq. 12).[58–61] It subsequently has become clear that lithium chloride is also responsible for the improved efficacy of the internal quench conditions, since under these conditions rapid trapping of the enolate by TMSCl leads to delivery of lithium chloride to the lithium amide during the course of the deprotonation reaction. Another pathway for the formation of lithium chloride under internal quench conditions is indicated by the fact that TMSCl is not fully compatible with lithium dialkylamides and lithium chloride is generated to some extent even at low temperatures.[62] Otherwise, lithium chloride can either be added as a solid to a lithium amide or it can be generated in situ by treatment of the amine hydrochloride salt precursor to the base with two equivalents of *n*-butyllithium. A related beneficial effect is encountered using zinc(II) chloride as an additive.[63] In contrast, the use of lithium bromide as an additive under external quench conditions gives improved enantioselectivities only when it is present in excess (∼3 equivalents), and lithium iodide is ineffective in improving enantioselectivities.



(Eq. 12)

Conditions	% ee
TMSCl, −78° (IQ)	69
−78°; then TMSCl (EQ)	23
LiCl (0.5 equiv), −78°; then TMSCl	83

The impact of lithium chloride on the solution structure of chiral lithium amides (*R*,*R*)-**1** and **21** has been studied by ^{6}Li and ^{15}N NMR spectroscopy in an attempt to rationalize the improved enantioselectivities when these bases are employed. In the absence of lithium halide, chiral base (*R*,*R*)-**1** in d_8-THF exists almost entirely as the homodimer **22**, which is represented by a triplet in its ^{6}Li NMR spectrum and a quintet (1:2:3:2:1) in its ^{15}N NMR spectrum.[60] The homodimer has been independently characterized by X-ray crystallography and found to be solvated by two molecules of THF.[64] When lithium chloride is added to the mixture, two new species are identified. These are mixed dimer **23** and trimer **24** in which lithium chloride is incorporated into the solution structures. Mixed dimer **23** is the major component when more than 0.5 equivalent of lithium chloride is added, which might suggest that this species is responsible for the highly enantioselective deprotonation of ketones. The analogous mixed dimer formed between chiral base **21** and lithium chloride has also been observed using the same NMR techniques.[65,66]



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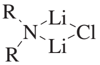

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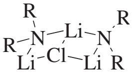
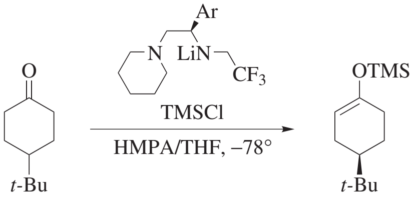


24

R = (*R*)-1-phenylethyl

Phenylglycine-derived bases possessing a fluorine-containing alkyl group, such as compound **25**, are superior lithium amides compared to their corresponding unfluorinated analogs, in a fashion that is not ascribable simply to the difference in bulkiness of the alkyl group on the amide nitrogen.[67,68] The ^{6}Li, ^{15}N, and ^{19}F NMR spectra of amide **25** in d_8-THF show that this lithium amide exists as a chelated monomeric form, with spectra resembling those of lithium amide **21** in this solvent. It can therefore be concluded that a fluorine atom does not form an additional chelate ring to the lithium. It is speculated that the beneficial effect of incorporating fluorine atoms into the alkyl group arises from an electrostatic interaction between fluorine and lithium, although this is unproven.[67] Chiral bases of this type with a bulky group other than phenyl on the stereogenic carbon have been assessed for their performance in deprotonation reactions of 4-substituted cyclohexanones.[65,66] Changing the phenyl group to a more bulky substituent does not lead to an improvement in selectivity and, on the contrary, can lead to an erosion in enantioselectivity (Eq. 13).

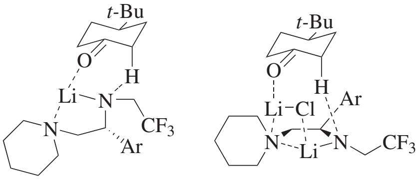


(Eq. 13)

Ar	Yield (%)	% ee
Ph (**25**)	82	85
1-naphthyl	91	87
2-naphthyl	85	78
3,5-$Me_2C_6H_3$	85	57
3,5-(t-Bu)$_2C_6H_3$	54	~0

On the basis of these results and of what is known for the solution structure of this type of base in the presence of lithium chloride, the proposed mechanism for the reaction has been revised. Rather than proceeding through a six-membered (Ireland-type) transition state, it seems likely that this transformation involves an eight-membered cyclic transition state **26** which includes lithium chloride (Fig. 4). As stated previously, under the internal quench conditions, a small quantity of lithium chloride is generated from trapping of the intermediate enolate with TMSCl. The revised transition state model **26** places the aryl group (Ar) of the base considerably closer to the *tert*-butyl substituent in the substrate and better explains the effect of increasing the steric bulk of Ar on the enantioselectivity of the reaction.

Concentration-dependent effects have been observed, in particular for the deprotonation of the substrate 8-thiabicyclo[3.2.1]octan-3-one (TBON) using chiral base **27**.[69] Thus, treatment of TBON with lithium amide **27** followed by addition of benzaldehyde gives mono-aldol product **28** as the major product and the bis-aldol product **29** typically in 10–15% yield (Eq. 14). The formation of a product where two aldol reactions have taken place on the same

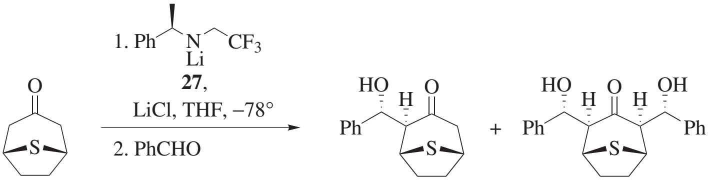


Ireland-type

26

Figure 4. Cyclic transition state **26** better supports the enantioselectivity observed in Eq. 13 than the Ireland-type model.

molecule is unprecedented with closely related substrates that possess oxa- and azabicyclo[3.2.1]octan-3-one frameworks. In the case of TBON, the enantiopurity of mono-aldol product **28** increases as the reaction mixture is made more dilute. Even though it is possible to speculate that the formation of bis-aldol product **29** may be responsible for these variations in enantioselectivity, perhaps through a kinetic resolution process, no correlation between the enantiomeric purity of **28** and the quantity of **29** formed is found.



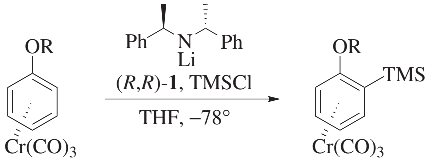
TBON **28** **29** (Eq. 14)

TBON [M]	**28**/**29**	Yield **28** (%)	% ee
0.12	86:14	55	46
0.10	88:12	61	53
0.05	80:20	65	63
0.035	84:16	72	71

Tricarbonyl(η^6-arene)chromium(0) Complexes

Functionalization of tricarbonylchromium(0) complexes of arenes has received considerable attention in organometallic chemistry.[70,71] Complexation of an arene ring to tricarbonylchromium(0) results in an increase in acidity of both the *ortho*-hydrogens bonded to the aromatic ring, and any benzylic hydrogens associated with the arene. This makes tricarbonyl(η^6-arene)chromium complexes excellent substrates for deprotonation by strong bases such as *n*-butyllithium and LDA.[7] Complexes with heteroatom-containing substituents can be deprotonated at the *ortho* position by chiral lithium amides to generate desymmetrized lithiated arenes, which undergo quenching by electrophiles. Otherwise, chiral lithium amides can differentiate between enantiotopic protons at the benzylic sites of chromium arenes or they can differentiate between enantiotopic methyl groups at the 2- and 6-positions of some atropisomeric benzamide and anilide complexes.[72–74] For example, anisole complex **30** is deprotonated by chiral base

(R,R)-**1** and the resulting aryllithium species reacts with TMSCl under internal quench conditions to afford the silylated product in 83% yield and 84% ee (Eq. 15).[75–79] In this reaction, lithium chloride is generated in situ, but in circumstances where other electrophiles are used it has been shown that lithium chloride is a critical additive for achieving good yields of product and good levels of asymmetric induction.[75,80] This situation arises because unless the anisole complex **30** is completely metalated, reactions involving an external quench are undermined by a rapid racemization process involving non-stereoselective proton transfer between the aryllithium species and the remaining starting material. Evidence for the rapid racemization process is provided by transmetalation experiments involving an enantiomerically enriched tin derivative.[75,80] In the absence of lithium chloride, complete metalation of **30**, by (R,R)-**1** requires 3 h at −78°, whereas in the presence of lithium chloride (ca. 0.5 equivalent) metalation is complete within 2 minutes at the same temperature.[75,80] Lithium chloride accelerates the rate of metalation of **30**, presumably because a mixed lithium amide-lithium chloride aggregate is much more reactive toward the substrate.

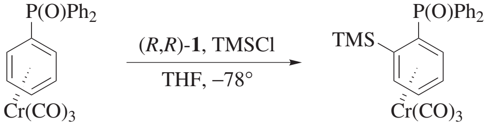


R	Yield (%)	% ee
Me (**30**)	83	84
Et	82	81
i-Pr	65	90
t-Bu	0	—
MOM	76	80

(Eq. 15)

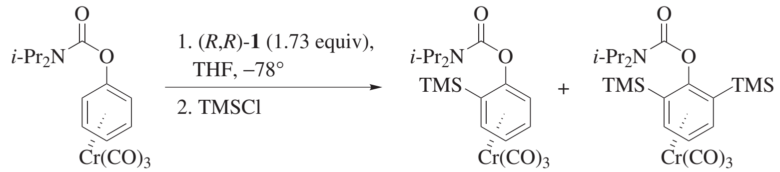
In this well-studied system, there is very little effect of changing the O-alkyl group from methyl to ethyl but an isopropyl group results in a decrease in chemical yield and a slight improvement in enantioselectivity. The use of a *tert*-butyl group completely stops the reaction, presumably because chelation of the base to the ether oxygen is precluded on steric grounds and without this interaction the reaction does not proceed. Even though a methoxymethyl (MOM) group possesses an additional metal-coordination site, this substituent proves to be of no benefit and the result is close to that for anisole complex **30**.

Subjecting phosphine oxide complex **31** to identical conditions of silylation gives the aryl silane product in 90% yield and 72% ee (Eq. 16).[81,82] Significantly, the sense of asymmetric induction in this reaction (as revealed by X-ray crystallography) is opposite to that seen with the anisole substrate. This is very likely a consequence of contrasting transition-state geometries for the directed metalation of an aryl ether complex versus a phosphine oxide complex. In the anisole system, coordination to oxygen in an unhindered environment promotes deprotonation via a six-membered transition state. In contrast, phosphine oxide **31** is considerably more hindered, and, assuming that coordination to oxygen is important, a seven-membered arrangement would be required.



31 (90%) 72% ee (Eq. 16)

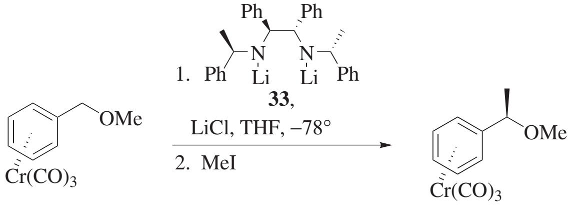
For the asymmetric metalation of a phenyl carbamate complex involving an external TMSCl quench, an excess of base is essential to prepare the corresponding mono-silylated product with optimal enantiomeric enrichment (67% ee).[83] Thus, deprotonation using 1.15 equivalents of (*R*,*R*)-**1** affords exclusively the mono-silylated product **32** but in racemic form (2% ee), whereas the use of 1.73 equivalents of base gives **32** in 67% ee together with the bis-silylated product in a 1:1 ratio (Eq. 17). Several hypotheses can be proposed to explain the correlation between excess amounts of base and the observed enantioselectivity of **32**. A kinetic resolution involving deprotonation of *rac*-**32** by excess amounts of base after the addition of TMSCl seems highly unlikely since it cannot be reproduced by treating a sample of *rac*-**32** with (*R*,*R*)-**1** and TMSCl. Instead, a deuteration experiment reveals that dilithiation of the starting material is important. The result in Eq. 17 can thus be rationalized: in the absence of TMSCl, the mono-lithiated species deprotonates the remaining starting material, leading to rapid racemization (compare to the reactivity of anisole complex **30**). The racemic *o*-lithiated complex then undergoes a second lithiation, with the (1*S*)-enantiomer reacting more rapidly than the (1*R*)-enantiomer. This leads to the observed product distribution upon quenching with TMSCl.



32 (44%) 67% ee (46%) (Eq. 17)

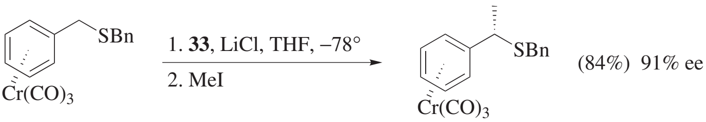
Deprotonation at the benzylic site of tricarbonyl(η^6-arene)chromium complexes produces an anionic complex that consists of a pentadienyl anion fragment η^5-coordinated to the metal along with an exocyclic π-bond. Stabilization is provided by the change in coordination and by localization of the negative charge onto the chromium tricarbonyl moiety.[84] The bis(lithium amide) base **33** is a very effective reagent for the enantioselective deprotonation of chromium arenes at the benzylic positions. For example, enantioselectivities observed for the functionalization of (alkyl benzyl ether)tricarbonylchromium complexes such as **34** using this base are often excellent (Eq. 18).[85–87] Curiously, functionalization of the closely related tricarbonylchromium complexes of benzyl sulfides using the same enantiomer of the base proceeds in the opposite stereochemical sense

(Eq. 19).[88] To the best of our knowledge, the origin of this reversal in stereochemical outcome has not yet been satisfactorily explained.



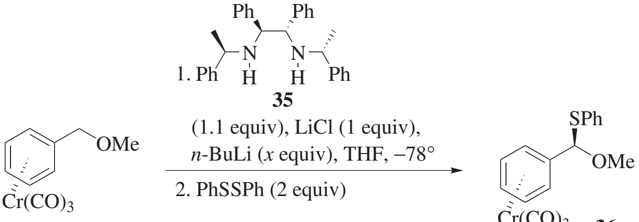
34

(Eq. 18)



(Eq. 19)

Several studies have been carried out to examine in more detail the mechanism of these highly stereoselective reactions involving deprotonation of chromium arenes by chiral base **33**.[7,89] Thus, treatment of methyl ether complex **34** first with *n*-butyllithium (1.1 equivalents), followed by chiral diamine **35** and lithium chloride (both 1.1 equivalents) and finally by diphenyl disulfide (2 equivalents) affords the sulfur derivative **36** in 79% yield but in racemic form. Therefore, the racemic anion formed by the action of *n*-butyllithium does not undergo an asymmetric electrophilic quench under control of diamine **35** in the reaction mixture. The effect of *n*-butyllithium stoichiometry has also been investigated for the enantioselective version of this reaction (Eq. 20). As expected, a correlation is found below 1.1 equivalents between the number of equivalents of *n*-butyllithium and the chemical yield. Gradually decreasing the number of equivalents from 2.2 to 0.28, however, does not affect the excellent enantioselectivity.



34 **36**

(Eq. 20)

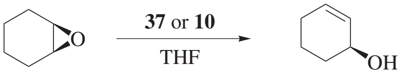
x	Yield **36** (%)	% ee	Recovered **34** (%)
2.2	95	98	0
1.1	96	95	0
0.55	60	92	40
0.28	21	96	67

A short structure-reactivity study involving bases that possess just some of the structural components of bis(lithium amide) **33** has also been conducted.[89] Removal of the backbone phenyl groups, or removal of the side-arm chirality, or methylation of one of the amide sites to give a tertiary amine, all significantly reduce the enantioselectivities for the conversion of **34** to **36** (to 5–40% ee) even though the yields remain high (80–93%). The last result suggests that the bis(lithium amide) **33** is a much more selective species with respect to complex **34** than the corresponding mono-lithiated base. Therefore, the outcome presented in Eq. 20 can be ascribed to a ready exchange of lithium cations between all the nitrogen sites in the system and that the di-lithiated base **33** is the most reactive species with respect to complex **34**.

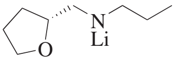
SCOPE AND LIMITATIONS

Epoxides

The first report of a chiral lithium amide-mediated desymmetrization reaction involves rearrangement of cyclohexene oxide to cyclohex-2-en-1-ol.[90] With chiral bases such as **37**, only modest enantioselectivities are obtained (Eq. 21). Much improved enantioselectivities for the same transformation are observed using lithium (*S*)-2-[(pyrrolidin-1-yl)methyl]pyrrolidide (**10**).[39,40]



Conditions	Yield (%)	% ee
37, reflux	76	21
10, –78° to rt	78	77



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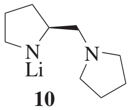
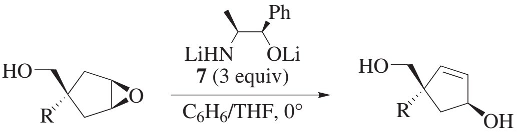


10

(Eq. 21)

Dilithiated amino alcohols of the ephedrine and norephedrine family such as **7** are very effective reagents for the base-mediated desymmetrization of epoxides.[33,34] These chiral bases allow access to either enantiomer of allylic alcohols in good yields and enantioselectivities using commercially available amino alcohols. The method shows improved results with epoxy alcohols **38** as the substrates (Eq. 22),[35,36] and evidence suggests that the stereocenter bearing nitrogen in the amino alcohol dominates the enantioselection.[8]

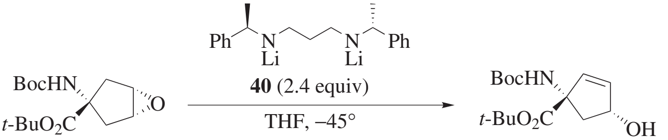


38

R	Yield (%)	% ee
H	65	>95
Me	63	99
Bu	67	96
$BnOCH_2$	76	89

(Eq. 22)

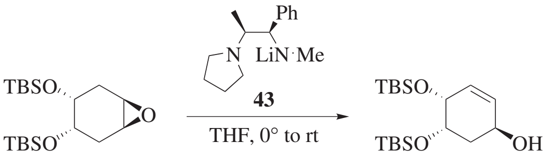
A desymmetrization of a symmetrical epoxide has been studied in the synthesis of the metabatropic glutamate receptor agonist LY459477.[91] Thus, treatment of epoxide **39** (3 kg scale) with 2.4 equivalents of chiral bis(lithium amide) **40** affords the allylic alcohol **41** in good yield with essentially complete enantioselectivity (Eq. 23). A bidentate chelation model is proposed for this efficient asymmetric process, which involves deprotonation of the carbamate N–H and chelation of the base to both the lithiated carbamate and the epoxide. This example neatly illustrates the applicability of chiral lithium amides for industrial synthesis.



39 **41** (74–79%) 99.6% ee

(Eq. 23)

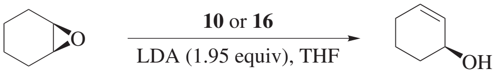
The chiral-base route from a 4,5-bis(silyloxy)cyclohexene oxide to an allylic alcohol can provide useful intermediates for the synthesis of cyclic polyols. For example, enantioselective rearrangement of epoxide **42** on a multigram scale using base **43** gives the allylic alcohol **44** in 93% yield and >95% ee (Eq. 24).[92,93] The product **44** is useful for the asymmetric synthesis of aminodeoxyconduritols and conduritol F.



42 **44** (93%) >95% ee

(Eq. 24)

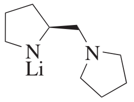
Other types of substrates that have been investigated for their rearrangement to allylic alcohols include 4-hydroxycyclopentene oxides,[33,34,94,95] 4-aminocyclopentene oxides,[96–98] 4,5-dimethylcyclohexene oxides,[99,100] 4,5-bis(silyloxymethyl)cyclohexene oxides,[101] and aziridinocyclohexene oxides.[102,103] The asymmetric rearrangement of epoxides using chiral lithium amides has been the subject of several reviews,[3,8,23] and this reaction class is the most effective when using the base in substoichiometric quantities. For this transformation to proceed under conditions of catalysis, a second lithium amide, usually LDA, is present as a bulk base for regeneration of the chiral lithium amide. The first successful account of such an enantioselective deprotonation process involves the proline-derived base **10**.[104] A number of structurally more complex diamines provide improvements to the performance of this catalytic epoxide rearrangement.[44] For example, using chiral diamine **16** as the base (0.05 equivalents) results in a considerable enhancement both in terms of the yield and enantioselectivity for the rearrangement of cyclohexene oxide (Eq. 25). The performance of the latter base also makes DBU no longer essential as an additive to promote the reaction.



10 or **16**

LDA (1.95 equiv), THF

Conditions	Yield (%)	% ee
10 (0.05 equiv), DBU (6 equiv), 0° to rt	65	59
16 (0.05 equiv), rt	93	85



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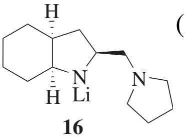
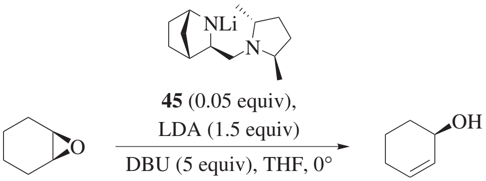


16

(Eq. 25)

Exceptional yields and enantioselectivities are achieved using chiral lithiated 3-aminomethyl-2-azabicyclo[2.2.1]heptanes such as **45** to isomerize epoxides to allylic alcohols (Eq. 26).[105–107] The presence of excess DBU (5 equivalents) in the catalytic reaction leads to a more rapid conversion of the epoxide and improved enantioselectivities. The role of DBU in catalytic enantioselective deprotonations of this kind appears to be rather complex; lithiated DBU may participate in the reaction process (see Eq. 10 in the section "Mechanism and Stereochemistry").[108] Particularly impressive with this catalytic system are successful rearrangements of notoriously difficult substrates, such as cyclopentene oxide and (*Z*)-4-octene oxide. Also, this type of base has proven to be very effective in the rearrangement of a silacyclopentene oxide.[109]



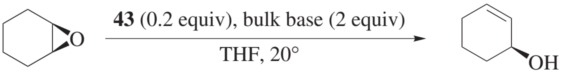
45 (0.05 equiv),
LDA (1.5 equiv)

DBU (5 equiv), THF, 0°

(95%) >98% ee

(Eq. 26)

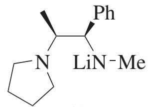
The catalytic deprotonation of cyclohexene oxide has been performed using novel bulk bases, which include lithiated imidazoles.[48,49,110] Using lithium amide **43** as the chiral reagent (0.2 equivalent), bulk bases **19** or **46** exhibit significantly enhanced performance compared to LDA with respect to the enantioselectivity of the reaction (Eq. 27). This improvement occurs either through suppression of the competitive non-stereoselective deprotonation by the bulk base to yield racemic product or by changing the nature of the active species. Extension of the substrate scope of this system to functionalized cyclopentene and cyclohexene oxides, such as **42**, reveals some undesired reaction manifolds not previously noted for cyclohexene oxides.[111] These troublesome side-reactions, such as nucleophilic ring-opening of the epoxide by the bulk base, can be circumvented by changing the bulk base from **46** to lithiated imidazole **47** (Eq. 28).



43 (0.2 equiv), bulk base (2 equiv)

THF, 20°

Bulk base	Yield (%)	% ee
19	96	92
46	96	92
LDA	90	22



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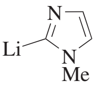

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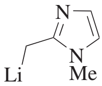
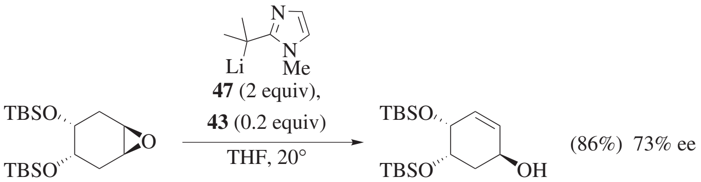


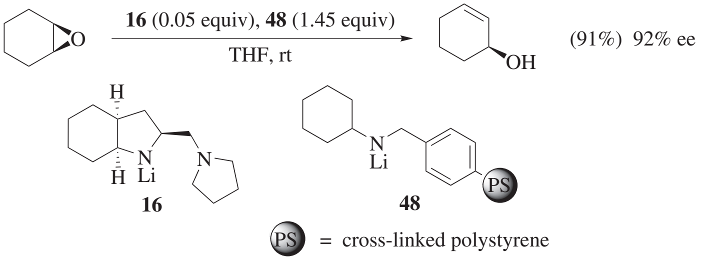
46

(Eq. 27)



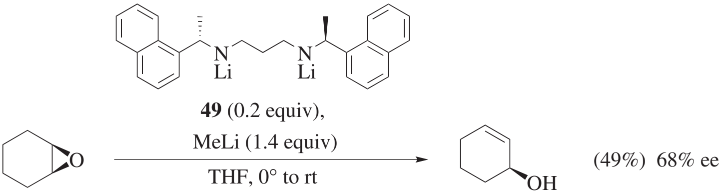
(Eq. 28)

The bulk base for catalytic enantioselective deprotonation of epoxides can also be a polymer-bound lithium amide.[112,113] Treatment of a range of symmetrical epoxides with chiral lithium amide **16** (0.05 equivalents) and polymer-bound lithium amide **48** (1.45 equivalents) in THF affords the corresponding allylic alcohols in good yields and enantioselectivities (e.g., Eq. 29). The enantioselectivities are higher than those obtained in the corresponding solution-state version using LDA as the bulk base.[44] This enhancement is attributed to a lower reactivity of solid-supported lithium amides, which makes the non-enantioselective background reaction less favored.



(Eq. 29)

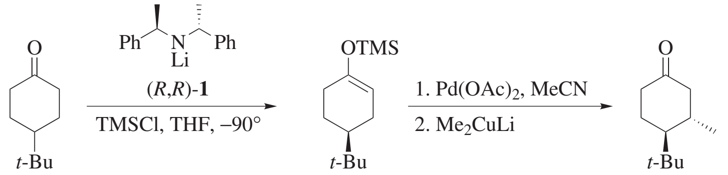
Catalytic enantioselective deprotonation of epoxides has been carried out using chiral bis(lithium amide) bases such as **49** (Eq. 30).[45,46] In general, the yields and enantioselectivities for this class of bases are only moderate; it is worth noting that *n*-butyllithium or methyllithium is used as the bulk base and that the mixture of reagents is compatible with cyclohexene oxide at room temperature. In addition, there are reports of α-pinene-based chiral lithium amides for the catalytic enantioselective deprotonation of cyclohexene oxide.[30,114] The reactions operate at 0° using 0.2 equivalents of the chiral base with LDA (1.25 equivalents) as the bulk base. A maximum selectivity of 94% ee is obtained for the rearrangement of cyclohexene oxide using the lithium amide derived from (−)-*N*,*N*-diisopinocamphenylamine.



(Eq. 30)

Prochiral Cyclic Ketones

Transformations Involving Silyl Enol Ethers. In conformationally biased cyclohexanones, such as 4-*tert*-butylcyclohexanone, a stereoelectronic preference exists for removal of the axial protons, and chiral lithium amides are able to discriminate between enantiotopic protons in enolization reactions (Eq. 31).[54,56,115,116] Therefore, it is possible to generate preferentially one enantiomer of the corresponding silyl enol ether by trapping with TMSCl (usually in excess, ~5 equivalents). It is worth noting that the values of % ee for silyl enol ether products obtained using a series of bases had been overestimated because of extrapolation from ee values determined for only moderately enantioenriched products.[54] These values have subsequently been corrected, and the maximum rotation for (*R*)-4-*tert*-butyl-1-trimethylsilyloxycyclohex-1-ene is considered to be $[\alpha]_{365}^{25}$ +237 (benzene).[116,117] The absolute configuration of the (*S*)-product is determined by chemical correlation to the known compound **50**, as depicted in Eq. 31.

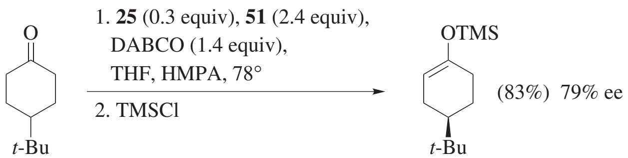


(66%) 88% ee

50 (56–73%)

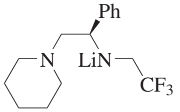
(Eq. 31)

Only a single report of an enantioselective deprotonation of 4-substituted cyclohexanones is on record that employs a substoichiometric quantity of chiral lithium amide.[118,119] Deprotonation of 4-*tert*-butylcyclohexanone with a combination of chiral lithium amide **25** (0.3 equivalents) and bulk base **51** (2.4 equivalents) in THF in the presence of HMPA and 1,4-diazabicyclo[2.2.2]octane (DABCO) gives the silyl enol ether upon addition of TMSCl (Eq. 32). In light of the advances made with epoxides, it is somewhat surprising that this remains the only successful implementation of catalytic asymmetric deprotonation of cyclic ketones using lithium amides.

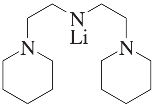


(83%) 79% ee

(Eq. 32)



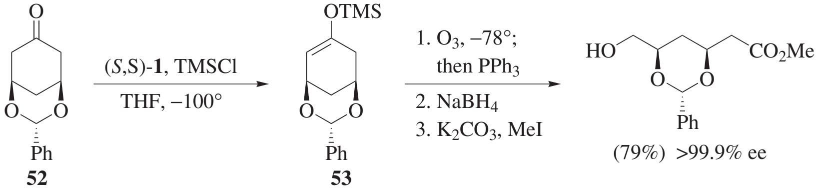
25



51

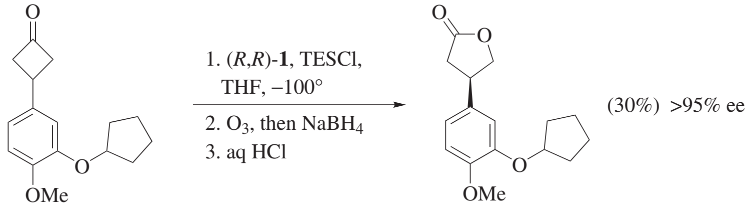
An enantiomerically enriched silyl enol ether is converted into the corresponding 2-enone upon treatment under the conditions of the Saegusa-Ito oxidation (i.e., palladium(II) acetate in acetonitrile).[120] The reaction proceeds via an oxo-allylpalladium intermediate that is frequently used to prepare a more suitable derivative for the determination of enantiomeric excess at the deprotonation step. Enantiomerically enriched 2-enones can also be prepared by treatment of the silyl enol ether intermediates with singlet oxygen and triphenylphosphine, and this conversion occurs at an early stage in a total synthesis of the fungal metabolite penitrem D (see Eq. 83 in the section "Applications to Synthesis").[121] Alternatively, the transformation is accomplished by treatment with phenylselenyl chloride followed by hydrogen peroxide.[122]

Silyl enol ethers obtained by enantioselective deprotonation may be ring-opened using the conditions for ozonolysis. For example, ozonolysis is a key step in a formal synthesis of the antiobesity agent (−)-tetrahydrolipstatin using the rigid bicyclic cyclohexanone **52** as the substrate (Eq. 33).[123] The deprotonation of **52** affords its silyl enol ether **53** with a higher enantiomeric excess (>99.9% ee) compared to the reaction with 3,5-di(benzyloxy)cyclohexanone as the substrate (74% ee). In this case, the improvement can be attributed to an increased rigidity in the bicyclic compound. Silyl enol ether ozonolysis is used similarly as a key step for the synthesis of intermediates toward bafilomycin A_1,[124] pseudomonic acid B,[125] reiswigin A,[126] and some archaebacterial lipids.[127,128] It is an established route to *cis*-2,6-disubstituted piperidines,[129−131] and the method has been applied to a total synthesis of (+)-monomorine.[132]



(Eq. 33)

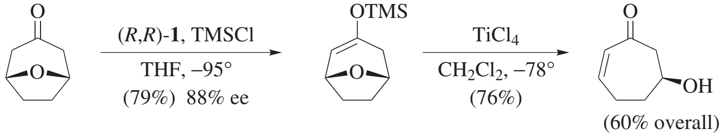
Unconventional substrates for desymmetrization using a chiral lithium amide include 3-substituted cyclobutanones such as **54**. This substrate has similarly been ring-cleaved using an enolization-ozonolysis approach. Thus, enantioselective deprotonation of **54** followed by ozonolysis, reduction, and cyclization affords an intermediate that allows access to the antidepressant rolipram (Eq. 34).[133] Other chiral β-substituted γ-butyrolactones have been prepared using this approach, facilitating the synthesis of some lignan lactones, such as (−)-hinokinin and (−)-savinin.[134−136] Enantioselective deprotonation-ozonolysis of a 3-arylcyclobutanone has been used to prepare (−)-baclofen, which is a selective $GABA_B$ agonist used as an antispastic agent.[137] The oxidative bond cleavage of a silyl enol ether may otherwise be performed using molybdenyl acetylacetonate and *tert*-butyl hydroperoxide. This reaction has been implemented during a formal synthesis of (+)-α-cuparenone.[138]



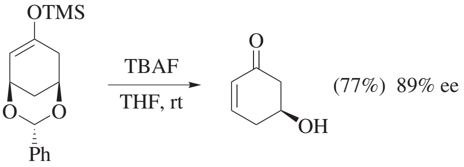
54

(Eq. 34)

Ring-opening processes involving β-elimination have been effected with some β-oxygenated enol silanes. For example, 8-oxabicyclo[3.2.1]octan-3-one is desymmetrized by chiral base (*R*,*R*)-**1** in 88% ee, and exposure of its silyl enol ether to titanium(IV) chloride affords (*S*)-6-(hydroxy)cyclohept-2-enone in 60% overall yield (Eq. 35).[139] This kind of framework can otherwise be ring-opened under reducing conditions with DIBAL-H and 5 M lithium perchlorate in diethyl ether.[140] Silyl enol ether **53** similarly undergoes desilylation with concomitant elimination of an alkoxy group upon treatment with tetrabutylammonium fluoride (TBAF).[141] In this instance, partial racemization is observed (Eq. 36).



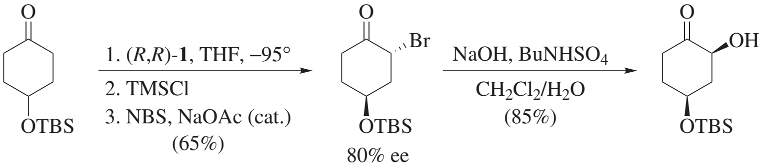
(Eq. 35)



53 95% ee

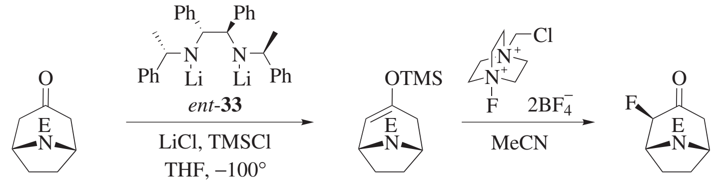
(Eq. 36)

Despite the high synthetic potential of α-halo ketones, there are not many examples where the chiral base-enolization method has been used in conjunction with an electrophilic halogenation reagent, such as *N*-chlorosuccinimide (NCS).[142] An important example of α-chlorination using NCS as the electrophile is shown in Eq. 84 (see the section “Applications to Synthesis”). Bromination of a silyl enol ether using *N*-bromosuccinimide (NBS), in the presence of buffering sodium acetate, has been examined as the starting point for a synthesis of the enyne A-ring synthon of the 1α-hydroxy vitamins D (Eq. 37).[143] The product α-bromo ketone is converted into the corresponding α-hydroxy ketone (with inversion of configuration) when combined with NaOH under phase-transfer conditions. The substrate *cis*-2,6-dimethylcyclohexanone has similarly been desymmetrized using chiral lithium amides and brominated with NBS.[53] The analogous iodination using *N*-iodosuccinimide (NIS) has been utilized for synthesis. α-Iodo ketones prepared in this way have been shown to participate in an Et_3B-mediated Reformatsky-type reaction toward the synthesis of FR901483 (see Eq. 85 in the section "Applications to Synthesis")[144] and to undergo radical allylations toward the synthesis of (+)-phorbol.[145]



(Eq. 37)

The enantiomerically enriched α-fluoro ketone **56**, which functions as an asymmetric epoxidation catalyst, can be accessed through an α-fluorination reaction.[146] Deprotonation of *N*-acylated tropinone **55** using bis(lithium amide) *ent*-**33** and exposure of its silyl enol ether to Selectfluor® leads to **56** in 55% yield and ~60% ee (Eq. 38). The relatively modest enantioselectivities in the enolization of *N*-acylated tropinones compared to *N*-methylated variants is well known.[147] The enantiopurity in this case can be enhanced to >98% ee by recrystallization of the product.

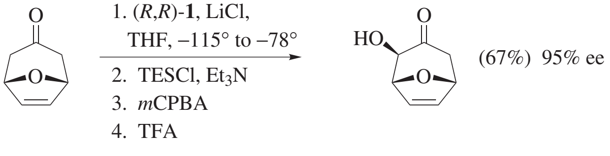


55
E = CO_2Et

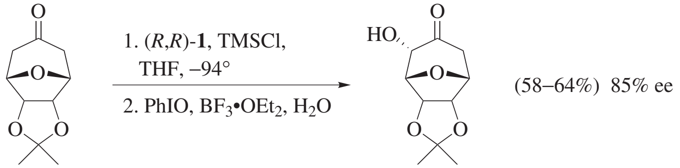
56
(55%) ~60% ee

(Eq. 38)

The chiral base method can be used to introduce a hydroxyl group by reaction of the silyl enol ether intermediate with *m*CPBA. An α-hydroxy ketone prepared in this way is an intermediate in short syntheses of the lactones (5*S*,6*S*)-aeginetolide and (5*S*)-dihydroactinidolide.[148] Likewise, α-hydroxylation of 8-oxabicyclo[3.2.1]oct-6-en-3-one is a key step during a synthesis of the C(38)–C(44) segment of spongistatin 1 (Eq. 39).[149] A similar chiral-base method facilitates the preparation of a full set of hydroxymethyl *C*-glycosides.[150] In other reactions, hydroxyl substituents are introduced successfully using dimethyldioxirane (DMDO)[122,151] or a mixture of iodosylbenzene and BF_3•OEt_2 in water (Eq. 40).[139] In the latter case, an α-hydroxy ketone product is obtained with the opposite configuration (*endo*) since the initial *exo*-approach of PhIO (giving an α-iodo ketone) is followed by a substitution with water that occurs with inversion.

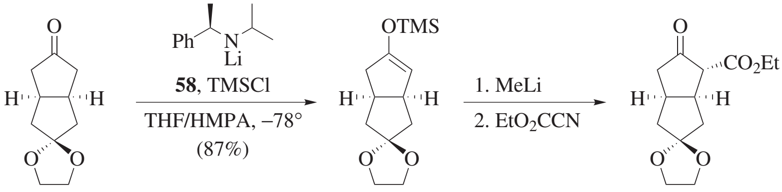


(Eq. 39)



(Eq. 40)

Acylations can also be performed, and an early example of this construction is found in some work toward the carbacyclins.[152] Thus, deprotonation of mono-protected *cis*-bicyclo[3.3.0]octane-3,7-dione **57** using lithium amide **58** and TMSCl in THF/HMPA gives silyl enol ether **59** in good yield but moderate enantiomeric excess (Eq. 41). The lithium enolate is subsequently regenerated by treating **59** with methyllithium, and trapping of this species with ethyl cyanoformate leads to installation of the ethyl ester moiety. A β-keto ester is obtained with an identical level of enantiomeric purity relative to the starting silyl enol ether. Some alkylations of a mono-protected *cis*-bicyclo[3.3.0]octane-3,7-dione are similarly carried out by treating the silyl enol ether with methyllithium followed by an alkylating reagent.[153]



57

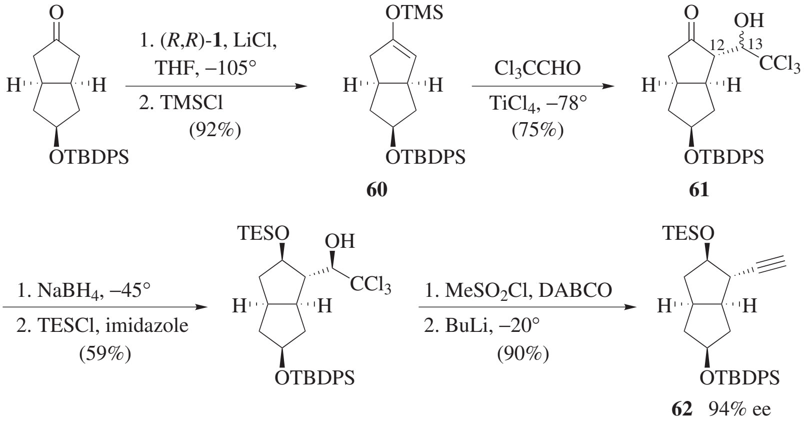
59 71% ee

71% ee

(Eq. 41)

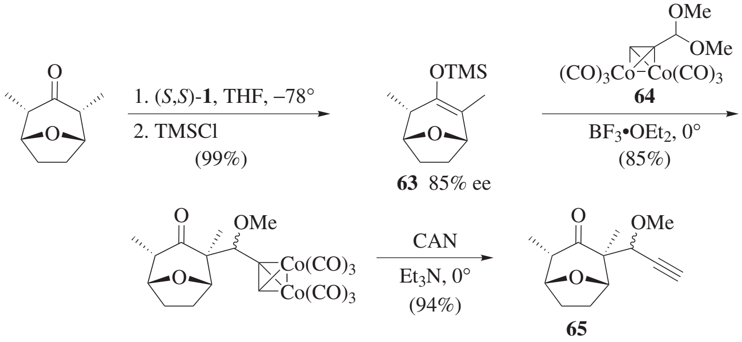
It is also possible to perform aldol reactions with chiral silyl enol ethers by promotion with a suitable Lewis acid. In this regard, a stepwise method for the ethynylation of enol ethers based on the facile conversion of trichlorocarbinol groups into triple bonds has been developed.[154] Aldol reaction of silyl enol ether **60** with chloral in the presence of titanium tetrachloride gives β-keto alcohol **61** in ≥98% de with respect to C(12) and in 60% de with respect to C(13) (Scheme 4). This intermediate is converted into alkyne **62** with an ee value of 94% in four additional steps. Alkyne **62** is used as an intermediate for the preparation of the potent antimetastatic prostacyclin analog cicaprost and its isomer isocicaprost.[154] Related aldol reactions using (*E*)-oct-2-en-1-al as the electrophile and either titanium tetrachloride or BF_3•OEt_2 as the Lewis acid are reported.[155] A TBAF-promoted aldol reaction followed by acetylation and elimination to the *exo*-olefin forms part of a formal synthesis of (−)-methylenolactocin.[134]

The Nicholas reaction has also been performed using a chiral base-generated silyl enol ether as nucleophile.[156,157] In the presence of BF_3•OEt_2, chiral silyl



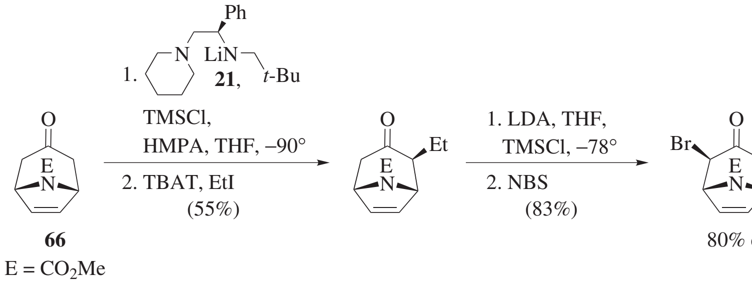
Scheme 4

enol ether **63** undergoes coupling with the dicobalt-stabilized propargylic cation derived from **64** to afford alkyne **65** upon oxidative demetalation (Scheme 5). Alkyne **65** is subsequently elaborated into a *trans*-fused bicyclo[5.3.0]decane system as a precursor to the pseudoguaiane carbon framework.



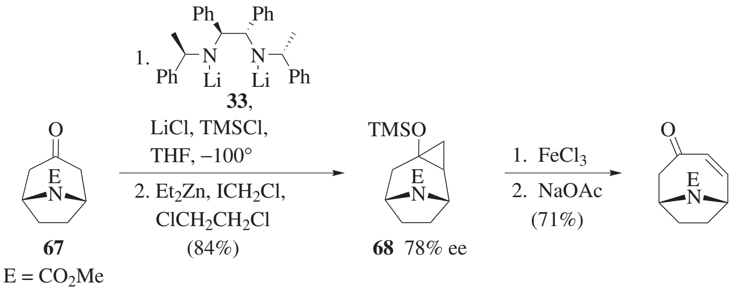
Scheme 5

Direct *C*-alkylation of ketone metal enolates with carbon electrophiles (e.g., iodomethane or allyl bromide) tends to provide low enantioselectivities when the enolization is mediated by a chiral lithium amide.[53,158] Better selectivities are achieved via the silyl enol ether using tetrabutylammonium triphenyldifluorosilicate (TBAT) as the source of fluoride, as has been demonstrated in a synthesis of (+)-ibogamine.[159] Thus, whereas it appears to not be possible to alkylate the lithium enolate of tropenone **66** using ethyl iodide, treatment of the silyl enol ether of **66** with TBAT and ethyl iodide successfully installs the ethyl group (Eq. 42). Bromination of the product reveals an 80% enantiomeric excess.

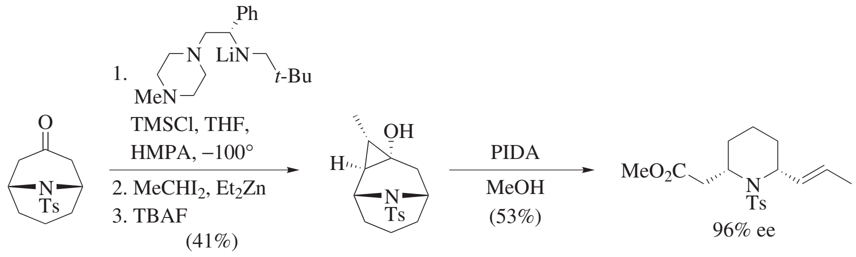


(Eq. 42)

The chiral base-enolization approach in conjunction with the Simmons-Smith reaction leads to chiral 1-silyloxybicyclo[n.1.0]alkanes, which can undergo further reactions such as ring expansion or oxidative bond cleavage. For example, desymmetrization of tropinone **67** by bis(lithium amide) base **33** and cyclopropanation of the resulting silyl enol ether using modified conditions for the Simmons-Smith reaction (diethylzinc and chloroiodomethane in 1,2-dichloroethane) gives **68** in high yield and satisfactory enantioselectivity (Eq. 43).[147] As part of a concise route towards (−)-anatoxin A, this intermediate undergoes a radical-based ring expansion upon exposure to iron(III) chloride[160] to afford a 2-cycloalkenone. A similar chiral base-mediated desymmetrization and cyclopropanation approach is a key feature of syntheses of (−)-pinidine and (+)-indolizidine 223AB.[161,162] Instead of performing a ring expansion, the cyclopropane derivatives are made to undergo an oxidative bond cleavage using hypervalent λ^n-iodanes, such as phenyliodine(III) diacetate (PIDA) in a protic solvent (Eq. 44).

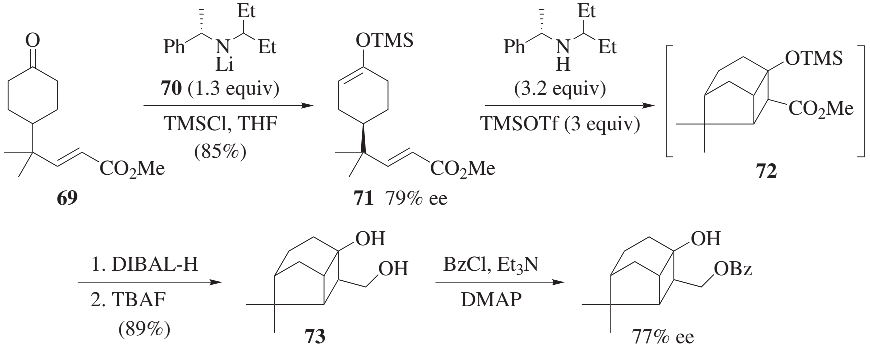


(Eq. 43)



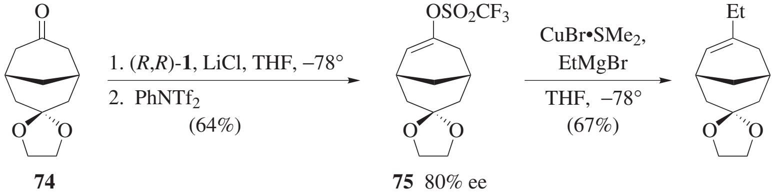
(Eq. 44)

Silyl enol ethers obtained using the chiral base-enolization approach have been made to react intramolecularly through a Michael addition-aldol sequence.[163] Thus, enantioselective deprotonation of cyclohexanone **69** using chiral base **70** generates silyl enol ether **71** in 85% yield and 79% ee (Scheme 6). Treatment of **71** with the chiral amine precursor to **70** and TMSOTf leads to rapid assembly of the tricyclic cyclobutane derivative **72**. Conversion of **72** into diol **73** requires two further steps (89% overall yield); the enantiomeric excess, determined upon benzoylation of **73**, is 77%. Using the more conventional base (*R*,*R*)-**1**, the enantioselective conversion of **69** into *ent*-**71** is reported to proceed in 88% yield and 61% ee.[163]



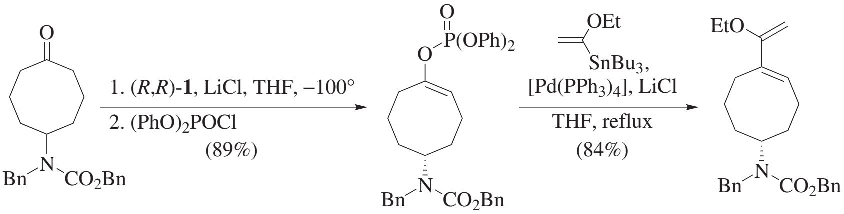
Scheme 6

Transformations Involving Other Enol Ethers. Chiral lithium enolates can be acylated at oxygen using acetic anhydride to form the corresponding enol acetates, and the enantiomeric excess of these compounds can be conveniently determined by ^{1}H NMR spectroscopy using a chiral shift reagent.[53,69,115,164,165] Alternatively, *O*-triflation generates an enol triflate; this has been used for the preparation of a tacrine-huperzine A hybrid.[166] Thus, enantioselective deprotonation and exposure of the resulting lithium enolate to *N*-phenyltriflimide converts ketone **74** into enol triflate **75** (Eq. 45). Enol triflate **75** successfully participates in a copper-mediated cross-coupling reaction with ethylmagnesium bromide. In addition, a Pd-catalyzed carbonylation reaction converts a related enol triflate into its corresponding homologated ester.[167] (*S*)-4-*tert*-Butylcyclohex-1-enyl nonaflate, obtained using nonafluorobutanesulfonyl fluoride as the electrophile, is an effective substrate for a range of Heck coupling reactions.[168] Other Pd-catalyzed cross-coupling strategies with enol sulfonates prepared using chiral lithium amides are known.[169,170]



(Eq. 45)

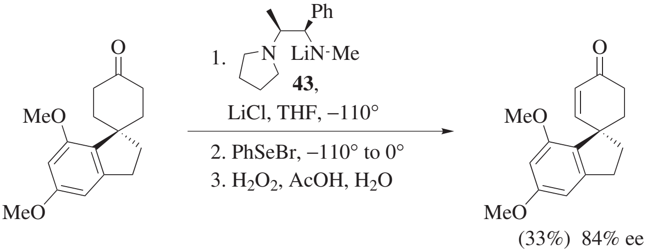
O-Phosphorylation is used in a formal synthesis of (−)-anatoxin A.[171] Here, the lithium enolate of **76** is captured using diphenyl chlorophosphate to generate enol phosphate **77** (Eq. 46). This compound successfully participates in a Stille coupling with 1-ethoxy-1-tributylstannylethene.



76 **77** 88% ee

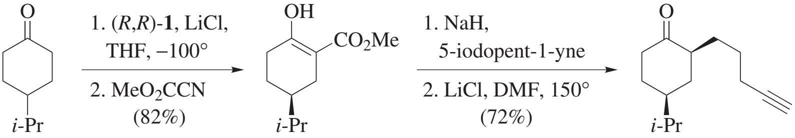
(Eq. 46)

Direct Transformations of Lithium Enolates. In many instances, the lithium enolate obtained using a chiral base is combined directly with an electrophile without the need for the formation of the silyl enol ether intermediate. For example, the lithium enolate can be converted into its corresponding enone by the sequence of selenation, oxidation, and spontaneous elimination (Eq. 47).[172] This transformation, albeit low-yielding in this case, nicely complements the Saegusa-Ito oxidation which requires silyl enol ethers as substrates.



(Eq. 47)

Direct *C*-acylation of a lithium enolate takes place in a total synthesis of (−)-erythrodiene.[173] Enantioselective deprotonation of 4-isopropylcyclohexanone using chiral base (*R*,*R*)-**1** and quenching of the resulting lithium enolate with methyl cyanoformate gives β-keto ester **78**, which is isolated as the enol form (Eq. 48). β-Keto ester **78** is an intermediate for an overall alkylation of 4-isopropylcyclohexanone with 5-iodopent-1-yne that takes advantage of the Krapcho decarboxylation. A similar sequence, albeit via the silyl enol ether, occurs in a short formal synthesis of (−)-indolizidine 223AB.[174] Enantioselective acylation with methyl cyanoformate as the electrophile is used for the synthesis of 8-oxa-analogs of norcocaine,[175,176] the tropane alkaloid (+)-anhydroecgonine,[177] and the C(18)-C(24) unit of lasonolide A.[178] Similarly, trifluoroacetylation of a cyclohexanone is reported using 2,2,2-trifluoroethyl trifluoroacetate as the electrophile (see Eq. 87 in the section "Applications to Synthesis").[179]

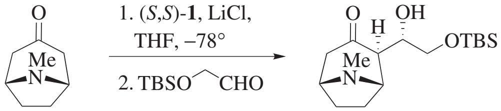


78 ≥94% ee

96% ee

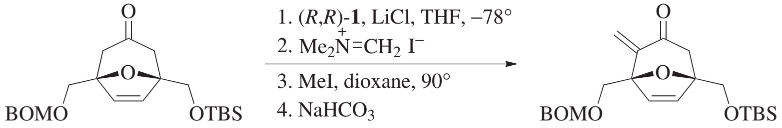
(Eq. 48)

Simple aldehydes, especially benzaldehyde and cyclohexanecarboxaldehyde, are widely used as electrophiles in methodology studies of aldol reactions in which the enolization is executed using a chiral lithium amide. Typical substrates for this aldol reaction are azabicyclo[3.2.1]octan-3-ones,[58,59,61,180–182] thiabicyclo[3.2.1]octan-3-ones,[183,184] 1,3-dioxan-5-ones,[61,185–187] and *cis*-3,5-dimethylcyclohexanone.[165] The extension of enantioselective deprotonation-aldol reactions to synthesis, however, is surprisingly rare. One example is a synthesis of unnatural (*S*)-(+)-cocaine by a route that includes deprotonation using chiral base (*S*,*S*)-**1** as part of an aldol process (Eq. 49).[188] In this example, the resulting β-keto alcohol is obtained as a single diastereoisomer in 72% yield. The asymmetric benzoylation of a tropinone allows for a synthesis of the tropane alkaloid ferrugine.[189] Aldol reactions based on lithium enolates derived from the *cis*-bicyclo[3.3.0]octane-3-one framework have also been investigated.[155,190]



(72%) 90–92% ee (Eq. 49)

The analogous Mannich reaction is not well known, although a Mannich reaction with Eschenmoser's reagent has been carried out to prepare **79**, which is an intermediate for the formal synthesis of the potent tumor promoter (+)-phorbol (Eq. 50).[145] In this example, the starting bridged ketone is chiral by virtue of non-equivalent alcohol protecting groups, and is enantiomerically enriched (80% ee). Subsequent methylation of the dimethylamino group, followed by elimination, installs an *exo*-methylene group adjacent to the ketone.



80% ee

79 (70%) >97% ee

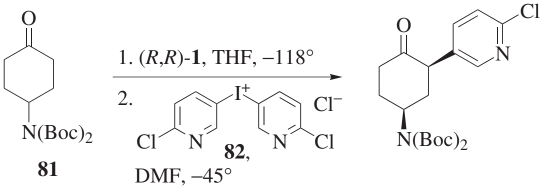
(Eq. 50)

The lithium enolate of tropinone undergoes ring opening upon treatment with a chloroformate to yield a substituted cyclohept-2-enone.[181,182,191–194] Optimal enantioselectivities for this transformation are achieved using (*S*,*S*)-**1** in the presence of lithium chloride (≥0.5 equivalent) and the products, such as **80**, are used to prepare some chiral tropane alkaloids (Eq. 51). For example, cyclohept-2-enone **80**, prepared using benzyl chloroformate, can be converted into the natural alkaloid physoperuvine in four additional steps.[191,194] The enantioselective deprotonation and ring-opening of tropinone has been investigated using polymeric chiral lithium amide reagents.[181,182]

80 (85%) 95% ee

(Eq. 51)

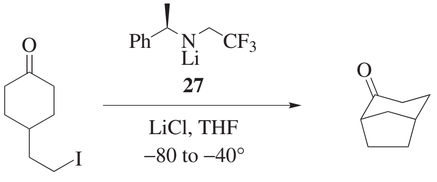
Diaryl iodonium(III) salts are an attractive class of electrophilic reagents that undergo coupling with enolates. The enantioselective α-arylation of cyclohexanones using diaryl iodonium salts has been developed and applied to a synthesis of (−)-epibatidine.[195] Thus, cyclohexanone **81** is deprotonated using chiral base (*R*,*R*)-**1** and arylated by dipyridyl iodonium salt **82** to afford the α-arylated ketone with high diastereo- and enantioselectivity (Eq. 52).



(41%) 94% ee
>90% de

(Eq. 52)

As mentioned previously, the chiral base enolization of prochiral cyclic ketones and then direct intermolecular *C*-alkylation of the corresponding lithium enolates usually leads to poor enantioselectivities.[53,158] However, the intramolecular S_N2 reaction of lithium enolates is rather more promising, and can be effected by asymmetric deprotonation with good enantioselectivity.[196] For example, exposure of cyclohexanone **83**, which has an iodoethyl group at C(4), to lithium amide **27** results in the formation of bicyclic ketone **84** in 70% yield and 80% ee (Eq. 53). In a related transformation, a lithium enolate is able to participate in a transannular C–C bond forming process involving epoxide ring-opening.[197]



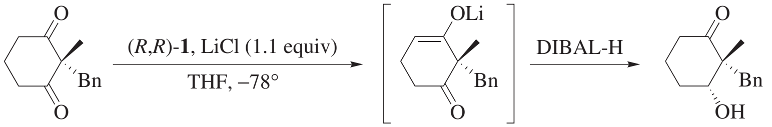
83

84 (70%) 80% ee

(Eq. 53)

In a recent entry into the repertoire of transformations that can be performed using a chiral lithium amide, it is possible to carry out selective enolizations of certain prochiral diketones so that the enolized ketone is effectively protected from the action of a second reagent. For example, cyclic 1,3-diketone **85** is combined with chiral base (*R*,*R*)-**1** to generate the lithium enolate (Eq. 54).[198]

The remaining ketone is reduced in situ using DIBAL-H to afford β-keto alcohol **86** in 77% yield, 95% de, and 99% ee. A conceptually similar approach involving selective enolization (and silylation) of *meso*-1,9-diketones has been described with potential for synthesizing hexapropionate synthons.[199]



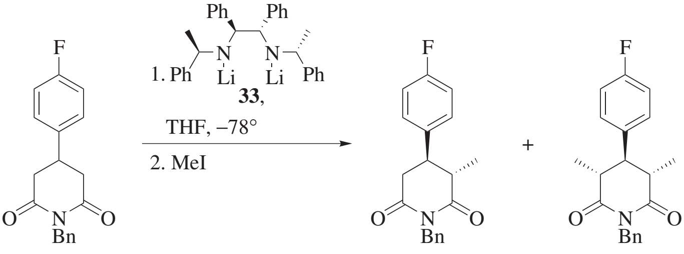
85 **86**

(77%) 99% ee, 95% de

(Eq. 54)

Cyclic Imides

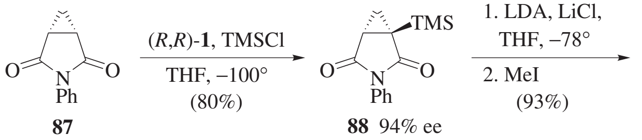
Application of the chiral base-enolization method to cyclic imides is a potentially attractive entry to chiral alkaloids. Certain 4-arylglutarimides undergo asymmetric deprotonation with high levels of selectivity using chiral bis(lithium amide) bases.[200−202] Thus, 4-fluorophenylglutarimides are deprotonated using bis(lithium amide) base **33** and alkylated with a variety of reagents (Eq. 55). The levels of asymmetric induction depend on the electrophile employed and, generally, in circumstances where an appreciable quantity of a dialkylated product is formed, the enantiomeric purity of the desired monoalkylated product is enhanced. This outcome is attributed to a favorable kinetic resolution process in which the minor enantiomer of the product is consumed in a fast second alkylation. This asymmetric desymmetrization process has been applied to the asymmetric synthesis of the selective serotonin reuptake inhibitor (−)-paroxetine.[200,201]



(65%) 97% ee (14%)

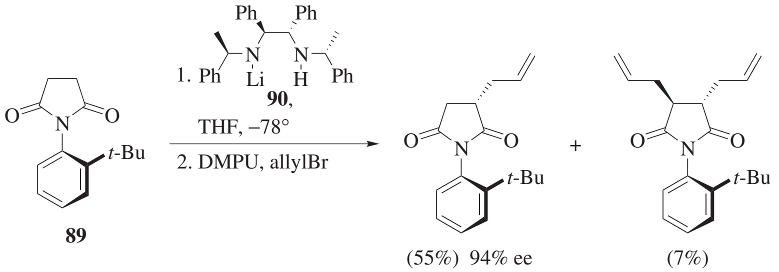
(Eq. 55)

The desymmetrization of cyclopropylane-fused succinimides constitutes another entry into the range of reactions that can be carried out using chiral lithium amide bases.[203,204] For example, treatment of imide **87** with chiral base (*R*,*R*)-**1** in the presence of TMSCl gives mono-silylated product **88** in good yield and excellent enantioselectivity (Eq. 56). The product **88** can be further elaborated in a number of ways. For example, further deprotonation using LDA–lithium chloride and trapping with a variety of electrophiles gives products in 57–93% yields. Silyl imide **88** also undergoes highly regioselective reduction and thionation reactions using DIBAL-H or Lawesson's reagent, respectively.



(Eq. 56)

The deprotonation of imide **89** is an unusual example of a chiral base-mediated enantioselective enolization, in which position-selective enolization generates an atropisomeric enolate intermediate that reacts with electrophiles in a face-selective fashion to give a chiral imide product (Eq. 57).[205] For the successful implementation of this strategy, the use of monolithiated base **90** is necessary for the deprotonation, while alkylation requires the use of reactive alkyl halides in the presence of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU). This procedure gives monoalkylated succinimides in reasonable yields and excellent enantioselectivities. When the di-lithiated base is employed, however, the dialkylated product (predominantly as the *trans* isomer) is obtained as the major product in an almost racemic form. In a similar fashion to the above glutarimide work, the enantiomeric purity of the monoalkylated product appears to be slightly enhanced in reactions where some dialkylation is evident. Again, this may be a consequence of a kinetic resolution of the first-formed product being superimposed on the initial asymmetric deprotonation. The related deprotonation and mono-alkylation of **89** using piperonyl bromide as the electrophile (in 40% yield, 95% ee) provides a novel entry into the lignan lactone (+)-hinokinin.[205]

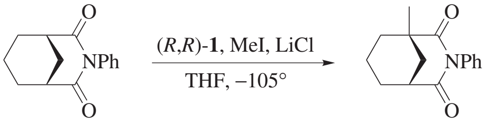


(Eq. 57)

The asymmetric deprotonation of ring-fused imides is valuable for the synthesis of bioactive target molecules that include the erythrinan alkaloids.[206] For example, the chiral-base approach allows the preparation of the erythrinan alkaloid (+)-erysotramidine in a highly enantiomerically enriched form (see Scheme 7 in the section "Applications to Synthesis").[207,208] In addition, the proposed structure of the alkaloid jamtine *N*-oxide has been prepared using similar methods.[200,202,209] As a result, the original assignment for the structure of this natural product was found to be incorrect.

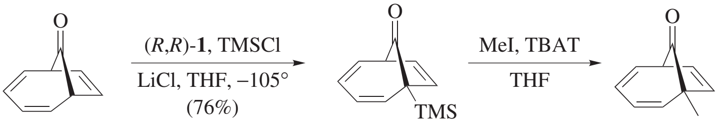
Deprotonation at Bridgehead Carbons

Previous sections have illustrated asymmetric variants of rather conventional enolization reactions. However, the chiral base method is also useful in metalations at bridgehead positions, in which the enolate structure may be more carbanion-like.[210] A small number of these somewhat surprising asymmetric metalation-substitution reactions have been achieved. For example, addition of chiral base (*R*,*R*)-**1** to a mixture of imide **91** in the presence of an appropriate electrophile (internal quenching conditions) enables an enantioselective silylation, alkylation, or acylation at the bridgehead position (Eq. 58).[211]



91 (57%) 97% ee (Eq. 58)

The enantioselective generation of bridgehead carbanions is also possible starting from bridged ketones. For example, ketone **92** is deprotonated using chiral lithium amide (*R*,*R*)-**1**, and trapping with TMSCl under internal quench conditions results in the formation of mono-silylated bridged ketone **93** in 98% ee (Eq. 59).[210,212] Unfortunately, the internal quench approach with this system is incompatible with other electrophiles; indirect access to products with other bridgehead substituents, such as **94**, is possible using the silyl exchange reaction with TBAT.

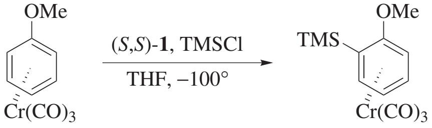


92 **93** 98% ee **94** (42%) (Eq. 59)

The total synthesis of (+)-clusianone has been achieved by enantioselective deprotonation at a bridgehead carbon, and in this case the reaction is carried out in the kinetic resolution mode (see Eq. 89 in the section “Applications to Synthesis”).[213]

Tricarbonyl(η^6-arene)chromium(0) Complexes

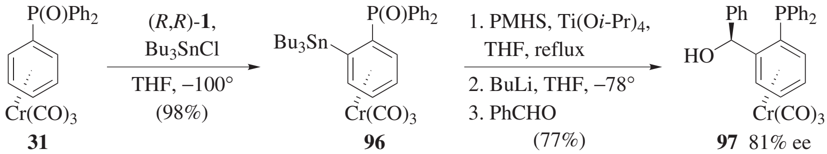
Enantioselective deprotonation of anisole complex **30** and silylation affords the corresponding arylsilane **95** (Eq. 60),[75–80,214,215] which has utility in the synthesis of the marine natural product (+)-ptilocaulin (see Scheme 8 in the section “Applications to Synthesis”).[78,79] Complex **95** has also been shown to participate in a dearomatizing asymmetric propargylation/allylation/Pauson-Khand cyclization sequence.[214]



30 **95** (87%) 87% ee (Eq. 60)

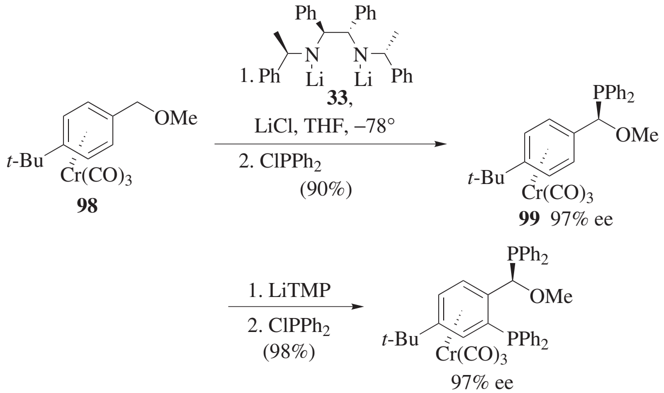
The type of reaction illustrated by conversion of **30** into **95** is also possible for prochiral complexes having other substituents, including carbon, nitrogen, and halogen types, but the yields and levels of asymmetric induction are variable.[75–77,216] The presence of an oxygen-containing function, presumably to ensure efficient coordination of lithium, appears to be a prerequisite to ensure at least workable levels of asymmetric induction.

The synthesis of enantiomerically enriched phosphines using the chiral-base approach is of considerable interest owing to their potential as chiral ligands for asymmetric catalysis. For example, phosphine oxide **31** is deprotonated using chiral base (*R*,*R*)-**1** and stannylated with tributyltin chloride to afford arylstannane **96** in 98% yield (Eq. 61).[81,82] The phosphine oxide can be reduced to the corresponding phosphine using polymethylhydrosiloxane (PMHS) and titanium tetraisopropoxide. At this point, transmetalation of the tin group for lithium and electrophilic trapping with benzaldehyde affords chiral phosphine **97** as a single diastereomer in 81% ee.



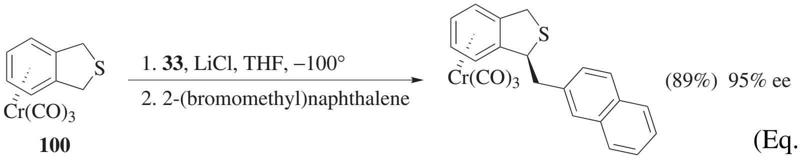
(Eq. 61)

Additional phosphine complexes have been prepared by asymmetric deprotonation at the benzylic sites of tricarbonyl(η^6-arene)chromium complexes.[87,217,218] In general, for deprotonation at benzylic positions, better enantioselectivites are observed when bis(lithium amide) base **33** is used rather than **1**. Treatment of benzyl ether complex **98** with base **33** and electrophilic trapping with chlorodiphenylphosphine affords phosphine **99** in 90% yield and 97% ee (Eq. 62). A second phosphine substituent is introduced selectively using lithium tetramethylpiperidide (LiTMP) and chlorodiphenylphosphine to prepare the novel diphosphine (−)-hasiphos.



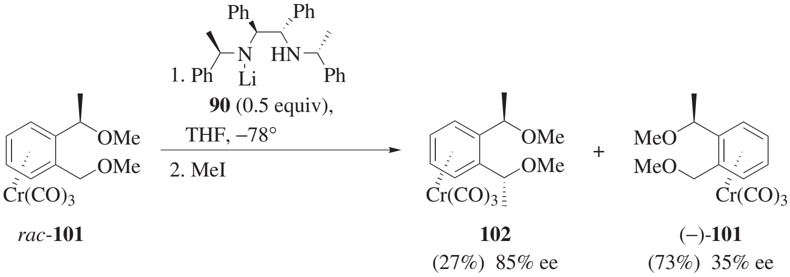
(Eq. 62)

The asymmetric deprotonations of benzylic ethers,[85–87,89,219–223] benzylic thioethers,[82,88,224] and benzylamine derivatives[225] of (η^6-arene)chromium complexes have been investigated in some detail. For example, conformationally constrained (η^6-1,3-dihydroisobenzothiophene)chromium complex **100** is deprotonated and reacted with a variety of electrophiles in excellent yield and enantioselectivity (Eq. 63).[82,224] The enantioselective deprotonation-methylation of a benzyl allyl ether complex has been utilized in syntheses of gossonorol and boivinianin B.[223]



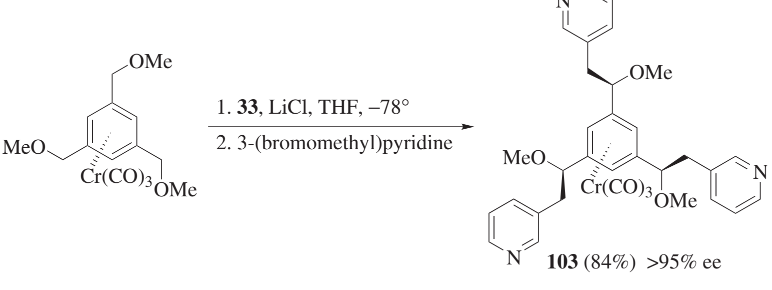
(Eq. 63)

In the quest for new ligand motifs with potential as active, economic, and environmentally friendly catalysts, chiral-base chemistry has been used to prepare novel C_2- and C_3-symmetric molecules. For example, a kinetic resolution procedure is performed upon the racemic starting material *rac*-**101** to give methylated **102**, which leads to a C_2-symmetric product after oxidative removal of the tricarbonylchromium(0) unit (Eq. 64).[226] In this reaction decomplexation has been achieved in 91% yield using ceric ammonium nitrate (CAN).



(Eq. 64)

In a synthesis of enantiomerically pure C_3-symmetric ligands, a 1,3,5-trisubstituted complex is trifunctionalized by reaction with three equivalents of bis(lithium amide) **33** and trapping with 3-(bromomethyl)pyridine.[217,218] This transformation results in the production of C_3-symmetric complex **103** in 84% yield and ≥95% ee (Eq. 65).



(Eq. 65)

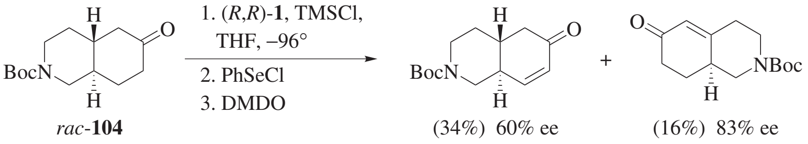
Site-Selective Enolizations and Kinetic Resolutions

Chiral lithium amide base enolization can also be a powerful tool in reactions involving chiral substrates in either racemic or non-racemic form. In the case of enantiomerically pure (or substantially enriched) substrates, the chiral base can be used to control the site selectivity of an otherwise poorly regiocontrolled enolization, whereas in the case of racemic substrates a kinetic resolution can result.

An example of site-selective enolization of a ketone was presented earlier in Eq. 50 where the starting bridged ketone is chiral and enantiomerically enriched (80% ee).[145] Other site-selective enolizations that are known include the enolization of some 3-keto steroids,[227,228] or of an unsymmetrical (−)-quinic acid-derived ketone.[229] Stereoselective deprotonation of a *cis*-bicyclo[3.3.0]octane-3-one bearing an *exo*-olefin at the 7-position plays an important part in a total synthesis of (+)-3-oxacarbacyclin.[190] Related selective enolizations mediated by chiral lithium amides occur in a synthesis of 4-deoxyverrucarol,[230] as well as in syntheses of the antifungal natural products chlorotetaine, bacilysin, and anticapsin (see Eq. 87 in the section "Applications to Synthesis").[179,231]

In the case of racemic substrates, chiral lithium amides frequently lend themselves well to effective kinetic resolutions. Typically, a deficiency of base or a shortened reaction time is employed so that one enantiomer of the substrate reacts preferentially, leading to enantiomeric enrichment of both the starting material and the product. Examples of kinetic resolutions using chiral lithium amides are shown in Eqs. 3, 64, and 89, where the starting material is a 2-substituted cyclohexanone, a tricarbonyl(η^6-arene)chromium(0) complex, and a bridged ketone, respectively.[14,213,226] Other substrate types include cyclic epoxides,[106,232–235] acyclic alkoxy epoxides,[236] bicyclic ketones,[237] an imidazolidinone,[238] and a β-lactam.[239] In a number of other processes discussed elsewhere, it appears that unplanned kinetic resolution may be superimposed on an initial desymmetrization process, and thus contribute to the overall level of selectivity (Eqs. 55, 57, and 67).

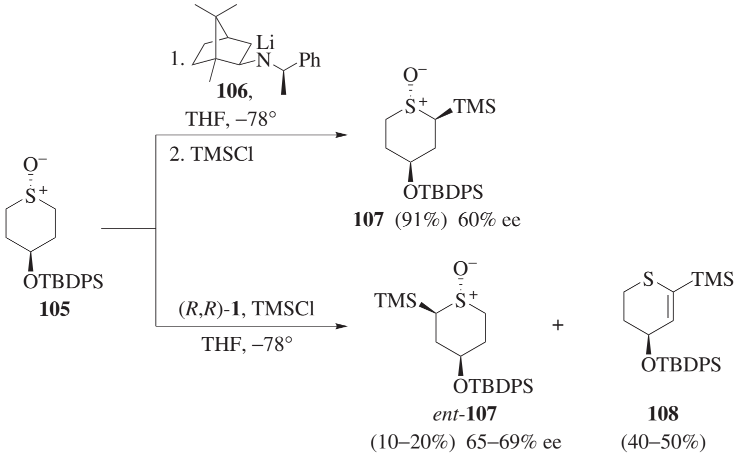
A novel regiodivergent resolution has been developed for the bicyclic ketone *rac*-**104** (Eq. 66).[240,241] In this process, reagent control by the base (*R*,*R*)-**1** at −96° results in the two enantiomers of *rac*-**104** being converted selectively into different enolate constitutional isomers. The crude mixture of silyl enol ethers is converted into the corresponding 2-enones by the sequence of selenation, oxidation, and spontaneous elimination. The resulting isolated constitutionally isomeric enones are of the opposite absolute configuration (ee values of 60% and 83%), thereby confirming that a novel kinetic resolution takes place under these circumstances. A regiodivergent resolution has also been carried out using a racemic *cis*-bicyclo[3.3.0]octan-3-one as the substrate.[190]



(Eq. 66)

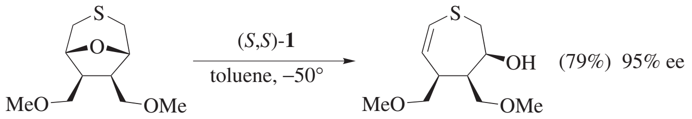
Deprotonation Adjacent to Sulfur

A variety of chiral base-mediated deprotonations have been reported that involve deprotonation adjacent to sulfur at various oxidation states. Substrates include 4-substituted thiane oxides, which undergo deprotonation and electrophilic quenching with good diastereocontrol. For example, the anions derived from such sulfoxides undergo methylation *trans* to the S^+-O^- bond with good to excellent stereoselectivities.[242,243] In the arena of chiral-base chemistry, treatment of *trans*-sulfoxide **105** with camphor-derived base **106** followed by TMSCl affords α-silyl sulfoxide **107** in 91% yield with an enantiomeric excess of ca. 60% (Eq. 67).[244,245] Analogous reactions involving the use of (*R*,*R*)-**1** as the base yield interesting results; using an external quench with this base, only racemic **107** is obtained whereas using an internal quench affords a mixture of *ent*-**107** (10–20%, 65–69% ee) and **108** (40–50%) along with the starting sulfoxide. This reaction is difficult to reproduce precisely owing to polysilylation of *ent*-**107**, and the proportions of the various products depend upon the rate at which the sulfoxide is added to the mixture of base and TMSCl. Vinyl sulfide **108** is generated via a TMSCl-mediated Pummerer-type reaction of **107** which occurs at surprisingly low temperatures. Further examination suggests that the improved level of asymmetric induction under the internal quench conditions using (*R*,*R*)-**1** arises from this reaction initially producing racemic **107** and an in situ kinetic resolution subsequently taking place to preferentially convert **107** into **108**.[244,245]



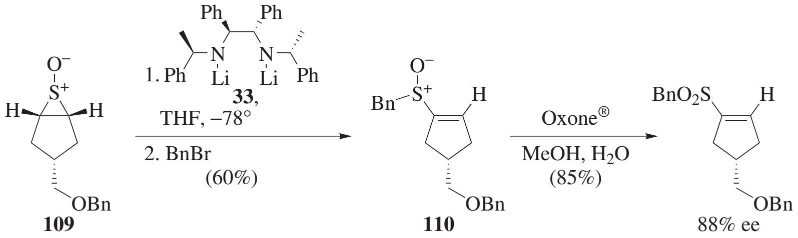
(Eq. 67)

Certain types of oxabicyclic frameworks can be converted into unsaturated alcohols by ring opening, in a fashion akin to the conversion of epoxides into allylic alcohols. For example, thiaoxa[3.2.1]- and -[3.3.1]bicycles are ring-opened using the chiral base (*S*,*S*)-**1** to provide allylic alcohols (Eq. 68).[246] As part of a project aimed at the asymmetric synthesis of polysubstituted *cis*-decalins, this method has been extended to a more complex pentacyclic dioxa-bridged system.[247]



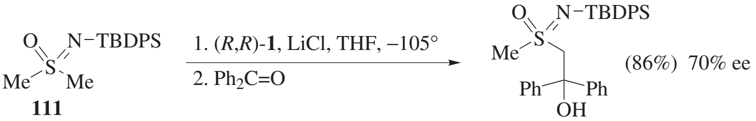
(Eq. 68)

For a limited range of substrates, episulfoxides can be converted into alkenyl sulfoxides using chiral lithium amides.[248,249] For example, episulfoxide **109** is deprotonated using chiral bis(lithium amide) **33** to form an intermediate alkenyl sulfenic acid anion, which can be alkylated with methyl iodide or benzyl bromide (Eq. 69). Before determining the extent of asymmetric induction, the alkenyl sulfoxide product **110** is first converted into its corresponding sulfone using potassium peroxymonosulfate (Oxone®). The chiral-base approach is moderately selective with a small group of such episulfoxides, which include norbornene derivatives.[248,249]



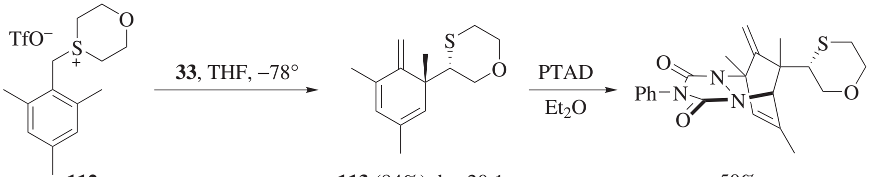
(Eq. 69)

The desymmetrization of *N*-trialkylsilyl dimethyl sulfoximines generates enantiomerically enriched sulfoximines, which are *S*-stereogenic compounds.[250] Thus, dimethyl sulfoximine **111** is deprotonated using chiral base (*R*,*R*)-**1**, and the resulting carbanion can be captured with a variety of electrophiles (Eq. 70). Chiral sulfoximines of this type are not readily available by other approaches, although at present the variable yields and levels of selectivity require further development of the chiral-base method.



(Eq. 70)

An interesting process for dearomatizing a benzene ring is the [2,3]-sigmatropic rearrangement of benzylsulfonium ylides (thia-Sommelet rearrangement). This reaction can be performed enantioselectively (up to 50% ee) using chiral lithium amides.[251] Treatment of benzylsulfonium salt **112** with bis(lithium amide) **33** results in the generation of a benzylsulfonium ylide that rearranges to give cyclohexa-1,3-diene **113** in 84% yield (Eq. 71). The enantiomeric excess is determined after Diels–Alder adduct formation using 4-phenyl-[1,2,4]triazole-3,5-dione (PTAD). No enantioselection is observed when bases (*R*,*R*)-**1** or **10** are used instead of **33**, although the product **113** is obtained in 76% and 33% yield, respectively. The presence of the ether oxygen in substrate **112** appears to be critical for enantioselectivity; the corresponding carbacyclic analog (replacing O by CH_2) shows no enantioselectivity in the presence of chiral bases. The importance of the ether group supports the idea that lithium-oxygen coordination plays a key role in this process.

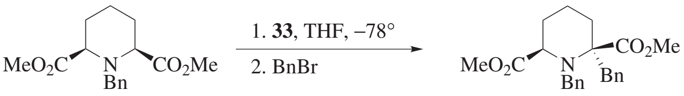


112 **113** (84%) dr >20:1 50% ee

(Eq. 71)

Miscellaneous Transformations

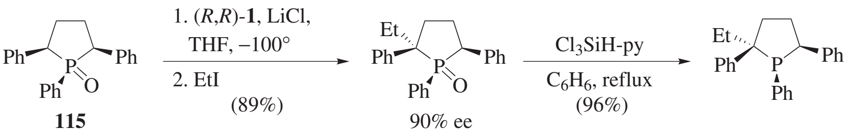
The deprotonation of *meso*-piperidine diesters can be carried out with excellent enantioselectivity using bis(lithium amide) base **33**.[252] Thus, deprotonation of piperidine diester **114** followed by addition of electrophiles produces alkylated piperidine diesters in good yields and ≥98% ee in all cases (Eq. 72). A combination of this desymmetrization procedure with ring-closing metathesis plays a key part in synthetic routes toward chiral azaspirocycles.[253,254] Unfortunately, with this system, in the case of asymmetric allylation using allyl bromide as the electrophile, the enantioselectivity is sensitive to the scale of the reaction, with larger scale reactions (~5 g) delivering poorer selectivities (down to 67% ee).[254]



114 (78%) >98% ee

(Eq. 72)

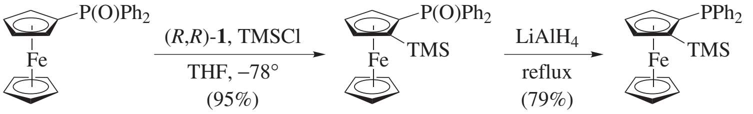
Prochiral cyclic phosphine oxides are good substrates for the chiral base-mediated asymmetric deprotonation reaction.[255,256] Thus, lithium amide (*R*,*R*)-**1** can discriminate between the two benzylic sites of phosphine oxide **115**, and the resulting organolithium species is functionalized by a range of electrophiles (Eq. 73). The phosphine oxide products are reduced to give the corresponding chiral phosphines using the mixture of trichlorosilane and pyridine in benzene.



115 90% ee

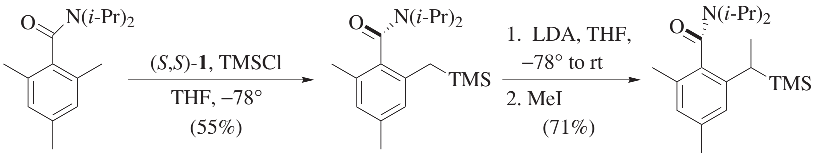
(Eq. 73)

The metalation of ferrocene derivatives is generally much less facile than metalation of tricarbonyl(η^6-arene)chromium complexes. This characteristic is reflected by their very poor reactivity with chiral lithium amides. Many ferrocene derivatives do not undergo appreciable deprotonation with either LDA or a chiral lithium amide base, even in the presence of lithium chloride or TMSCl.[257] Failures include hydroxymethyl ferrocene, its methyl and MOM ethers, and related phosphine and sulfide derivatives. Sulfone and carboxamide derivatives do undergo conversion into their corresponding silylated ferrocenes but only in racemic form. Unique among the range of ferrocenes tested, phosphine oxide **116** undergoes silylation using chiral base (*R*,*R*)-**1** to give a non-racemic silane (95% yield, 54% ee, Eq. 74). This phosphine oxide is subsequently reduced using lithium aluminum hydride to afford the corresponding phosphine derivative.



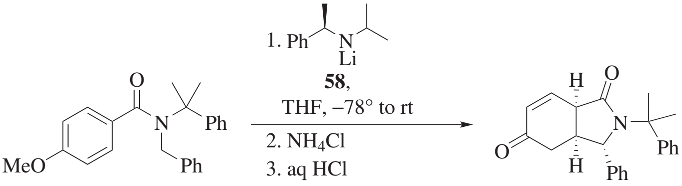
116 54% ee (Eq. 74)

Enantiomerically enriched atropisomeric amides are accessed by the desymmetrization of *N*,*N*-dialkylmesitamides.[258] *N*,*N*-Diisopropylmesitamide **117** is deprotonated by chiral lithium amide (*S*,*S*)-**1**, and trapping with TMSCl gives **118** in 88% ee (Eq. 75). Hindered tertiary aromatic amide **118** exhibits atropisomerism about the Ar–CO bond. This species undergoes a site-selective lithiation using LDA to afford a methylated product as a single constitutional isomer.



117 **118** 88% ee (Eq. 75)

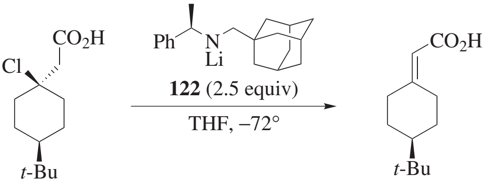
Chiral lithium amides are also employed in a dearomatizing cyclization reaction that delivers chiral, saturated isoindolones.[259–262] This reaction involves the formation of an enantiomerically enriched benzylic organolithium compound that has found application in the syntheses of (−)-isodomic acid C (see Scheme 9 in the section "Applications to Synthesis")[260] and (−)-kainic acid.[262] Thus, deprotonation of *N*-benzylanisamide **119** at its benzylic site using base **58** leads to cyclization upon warming of the reaction mixture (Eq. 76). An aqueous quench and acidic work-up furnishes the enone **120** in 62% yield and 86% ee.[262]



(Eq. 76)

119 **120** (62%) 86% ee

Chiral lithium amides promote the enantioselective dehydrohalogenation of the prochiral acid **121** leading to an axially chiral product (Eq. 77).[263–265] Optimal enantioselectivites for this transformation are achieved using 2.5 equivalents of the 1-adamantyl-substituted chiral base **122**. The requirement for more than 1 equivalent of base arises from the presence of a carboxylic acid in the starting material. This kind of transformation is more effective when chiral alkoxides are employed as the reagents.[266]

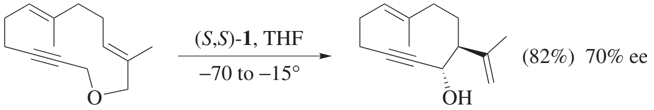


121

(84%) 82% ee

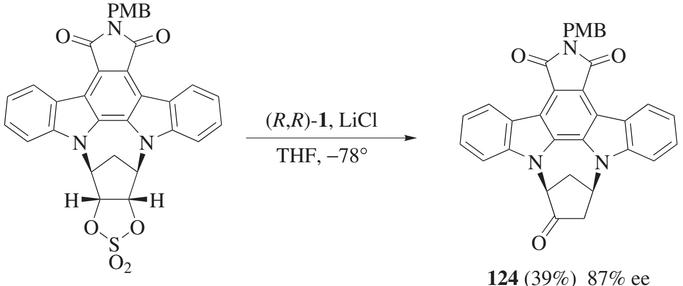
(Eq. 77)

Wittig [2,3]-sigmatropic rearrangements of macrocyclic allylic propargylic ethers lead to ring-contracted carbocycles constituting a viable strategy for the construction of 10- and 14-membered isoprenoid systems. A natural extension of the work is to use chiral lithium amides as bases, and moderate enantioselectivities are obtained for the asymmetric version of this process (Eq. 78).[267–269]



(Eq. 78)

A functionalized indolocarbazole, related to the natural product K-252a, is prepared by rearrangement of a cyclic sulfate.[270,271] Thus, addition of substrate **123** to a solution of lithium amide (*R*,*R*)-**1** and lithium chloride (4 equivalents) at −78° provides ketone **124** in moderate-to-low yield but good enantioselectivity (Eq. 79).

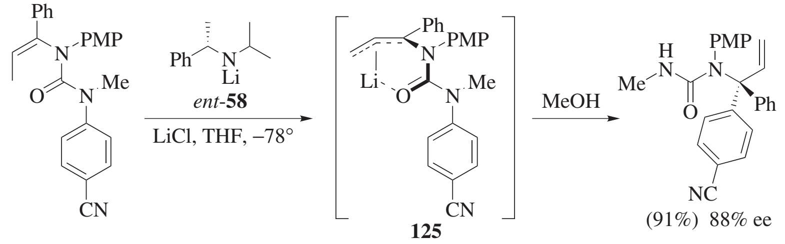


123

124 (39%) 87% ee

(Eq. 79)

Asymmetric lithiation of a series of achiral vinyl ureas using lithium amides is a viable route toward enantiomerically enriched amine derivatives bearing a tertiary substituent.[272] The transformation involves enantioselective lithiation of the vinyl urea to generate a planar chiral allyllithium species, such as **125**, which then undergoes an N to C aryl migration (Eq. 80). Studies indicate that the configuration of the product originates from stereoselective formation of the allyllithium species itself and not from a stereoselective reaction of a configurationally unstable allyllithium species under control of the associated chiral amine. It appears to be an example of the enantioselective formation of an organolithium species by a chiral lithium amide that does not involve deprotonation of one of a pair of enantiotopic protons.



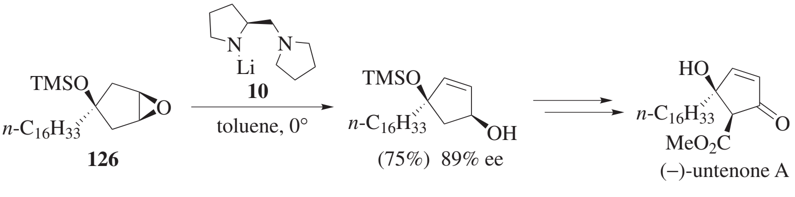
(Eq. 80)

APPLICATIONS TO SYNTHESIS

The potential of asymmetric enolization and metalation processes mediated by chiral lithium amides to deliver chiral intermediates for target synthesis will be evident from applications mentioned throughout the section “Scope and Limitations.” In many cases, the development of a new role for the chiral lithium amide, and its application to target molecule syntheses, especially of natural products, are inextricably linked.

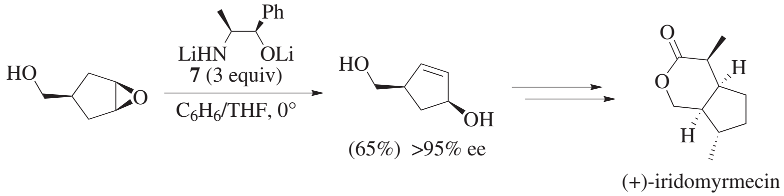
In this section we highlight selected total syntheses that underscore the scope of the lithium amide desymmetrization approach.

Applications of the rearrangement of epoxides using chiral lithium amides include the preparation of both the (*R*)- and (*S*)-enantiomers of 4-hydroxycyclopent-2-enone (useful for the synthesis of prostaglandins and various cyclopentanoid natural products),[273–275] as well as the ant-derived terpenes lasiol[99] and faranal.[100] (*S*)-Cyclohex-2-en-1-ol, prepared by enantioselective deprotonation, has been used to prepare some conformationally restricted nor-LTD$_4$ analogs[276] and to prepare methyl (5*S*)-(benzoyloxy)-6-oxohexanoate, which is an intermediate in leukotriene synthesis.[277] Extension of the desymmetrization method to a protected tertiary alcohol-containing cyclopentene oxide **126** allows for a concise asymmetric synthesis of (−)-untenone A, which is considered to be a key intermediate in the biosynthetic path of the manzamenones (Eq. 81).[278]



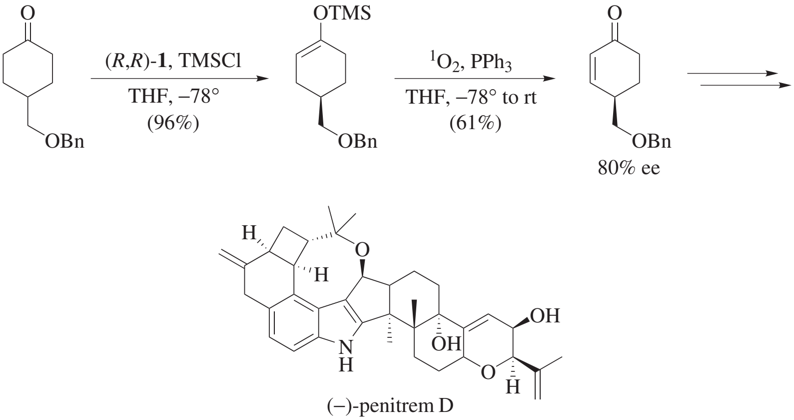
(Eq. 81)

The desymmetrization of epoxides using dilithiated amino alcohol **7** has been applied to the synthesis of carbocyclic nucleosides in the shape of a formal synthesis of carbovir[279,280] and the cyclopentene core of nucleoside Q.[281] The insecticidal iridoid (+)-iridomyrmecin and a precursor to the prostaglandins have been prepared using the combination of enantioselective epoxide rearrangement with a subsequent Ireland-Claisen rearrangement (Eq. 82).[37,282]



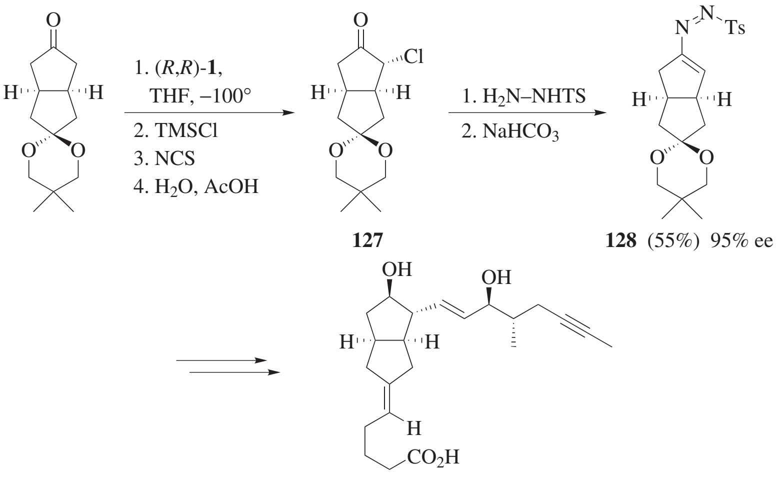
(Eq. 82)

The Saegusa–Ito oxidation has been used in conjunction with enantioselective deprotonation of conformationally biased cyclic ketones toward the synthesis of 4-deoxyverrucarol[230] and brasilenol.[283] A series of potential MetAP-2 reversible inhibitors have also been prepared using the same process at an early stage of the synthesis.[284,285] A related transformation, involving treatment of the silyl enol ether intermediate with singlet oxygen and triphenylphosphine, occurs at an early stage in a total synthesis of the fungal metabolite penitrem D (Eq. 83).[121]



(Eq. 83)

Enantioselective deprotonation of mono-protected *cis*-bicyclo[3.3.0]octane-3,7-dione frameworks affords products that function as chiral intermediates toward the synthesis of carbacyclins. A significant example of this chemistry involves the preparation of α-chloro ketone **127** by chlorination of a silyl enol ether derivative using NCS, en route to azoalkene **128** (Eq. 84).[286] Azoalkene **128** is a valuable intermediate for synthesis of carbacyclin and 3-oxacarbacyclin,[287] (*E*,*Z*)-13,14-dinor-*inter*-*p*-phenylene carbacyclin,[142] the prostacyclin analogs (16*S*)-iloprost and (16*S*)-3-oxa-iloprost,[286] as well as 3-oxa-15-deoxy-16-(*m*-tolyl)-17,18,19,20-tetranorisocarbacyclin and 15-deoxy-16-(*m*-tolyl)-17,18,19,20-tetranorisocarbacyclin.[288]



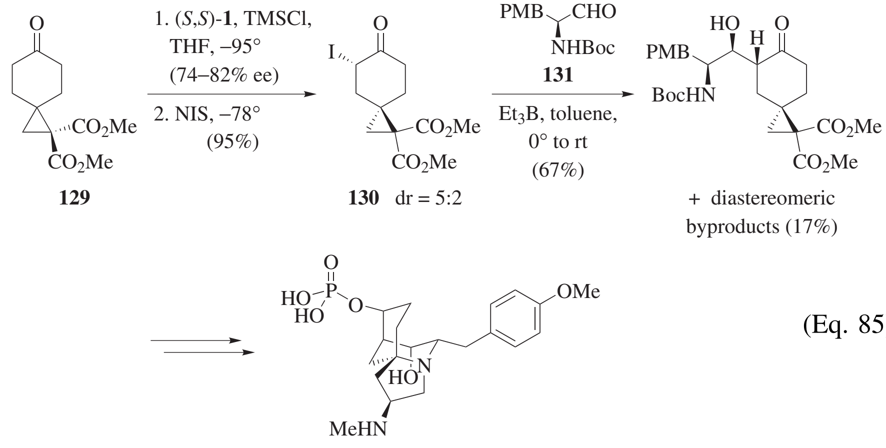
127

128 (55%) 95% ee

(Eq. 84)

16*S*-iloprost

The analogous α-iodination of a cyclic ketone using NIS plays an important part in a total synthesis of FR901483, which is an inhibitor of purine biosynthesis.[144] Thus, deprotonation of spiro[2.5]octan-6-one **129** in the standard fashion and iodination affords α-iodo ketone **130** in excellent yield and satisfactory enantioselectivity (Eq. 85). A Et_3B-mediated Reformatsky-type reaction allows subsequent coupling of **130** with aldehyde **131** to provide the corresponding β-keto alcohol with an acceptable degree of selectivity (67% yield, containing 17% of minor diastereomeric byproducts).



129

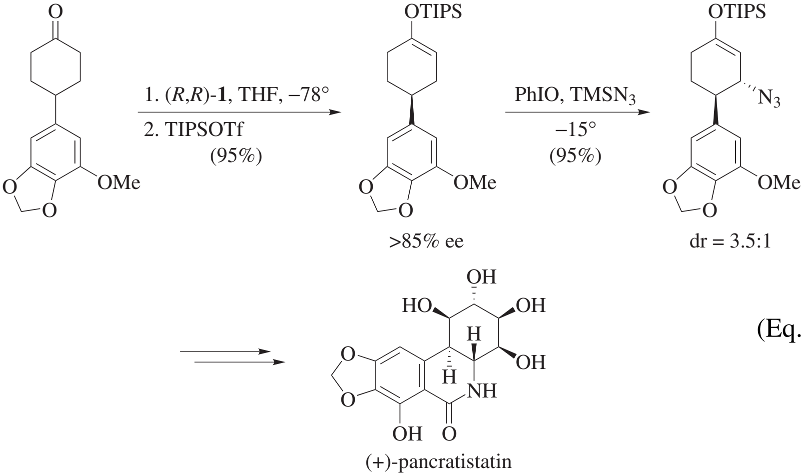
130 dr = 5:2

+ diastereomeric
byproducts (17%)

(Eq. 85)

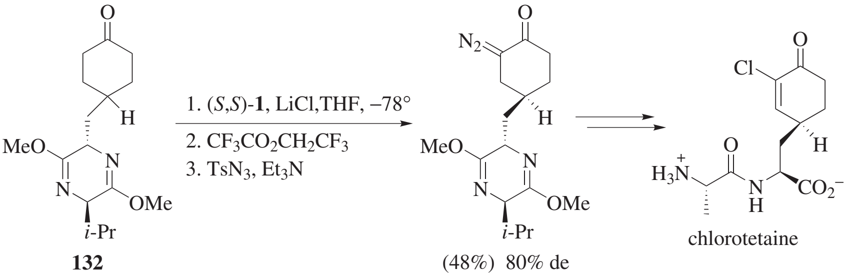
FR901483

In a novel transformation, triisopropylsilyl enol ethers are converted into β-azido triisopropylsilyl enol ethers by reaction with the combination of iodosylbenzene and trimethylsilyl azide.[289] This transformation is used in conjunction with the chiral base-enolization technique in the synthesis of the antitumor alkaloid (+)-pancratistatin (Eq. 86),[290,291] as well as the core structure of lycorane type alkaloids.[292]



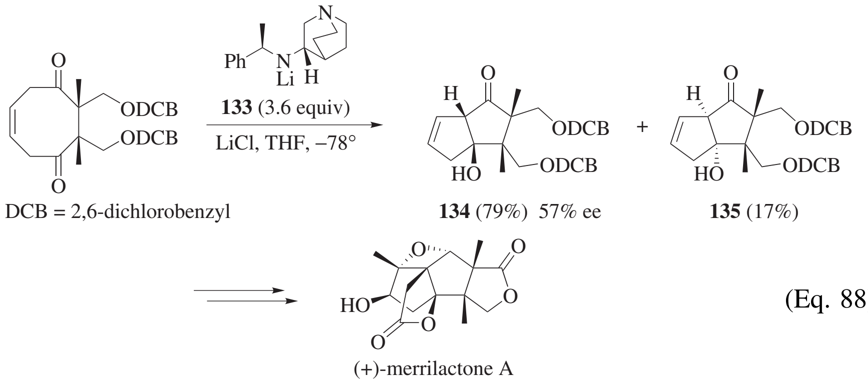
(Eq. 86)

The antifungal natural product chlorotetaine has been prepared by a sequence that includes site-selective enolization of diastereomerically pure cyclohexanone **132** and trifluoroacetylation using 2,2,2-trifluoroethyl trifluoroacetate as the electrophile (Eq. 87).[179,231] Treatment of the crude β-keto ester with *p*-tosyl azide facilitates the formation of an α-diazo ketone with a diastereomeric purity of 80%. The synthetic target is accomplished in eight additional steps. The related natural products bacilysin and anticapsin have been synthesized using a site-selective enolization of **132** combined with the Saegusa-Ito oxidation as an important step.[179]



(Eq. 87)

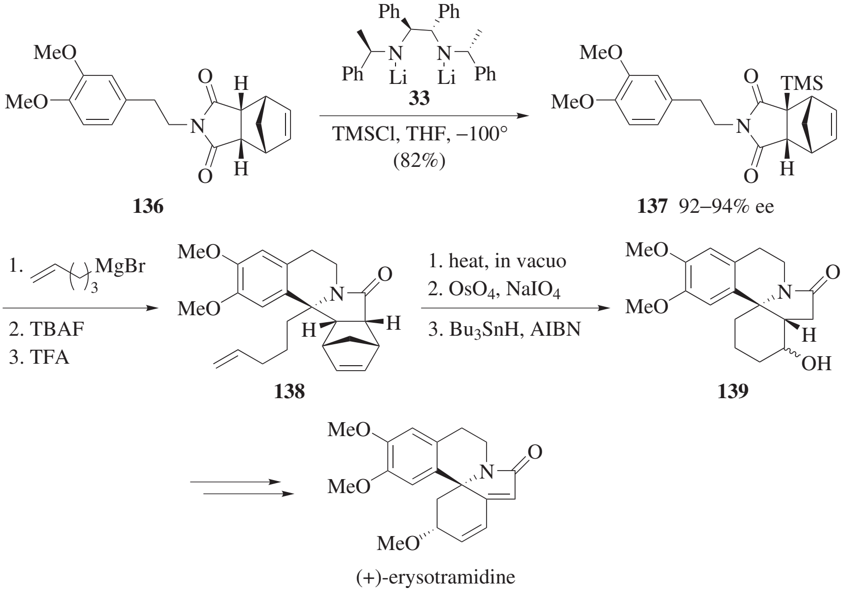
A novel chiral base-induced transannular desymmetrization has been employed as the key step in a synthesis of (+)-merrilactone A, which has potent neurotrophic factor-like activity.[293] The key step involves the transannular aldol reaction of an eight-membered *meso*-1,4-diketone, and this can be performed asymmetrically using chiral lithium amides, such as **133** (Eq. 88). A high steric bulk of the hydroxyl protecting group in the substrate (here it is 2,6-dichlorobenzyl) appears to be necessary to direct the formation of the desired diastereoisomer **134** over undesired product **135**. Even under optimized conditions involving the novel base **133**, the enantioselectivity of this reaction is only moderate (57% ee), although recrystallization of the product leads to enantiomeric enrichment (to 99% ee). In contrast, the enantiomeric purity of the desired diastereoisomer obtained using the more conventional base (*S*,*S*)-1 is low (31% ee).



(Eq. 88)

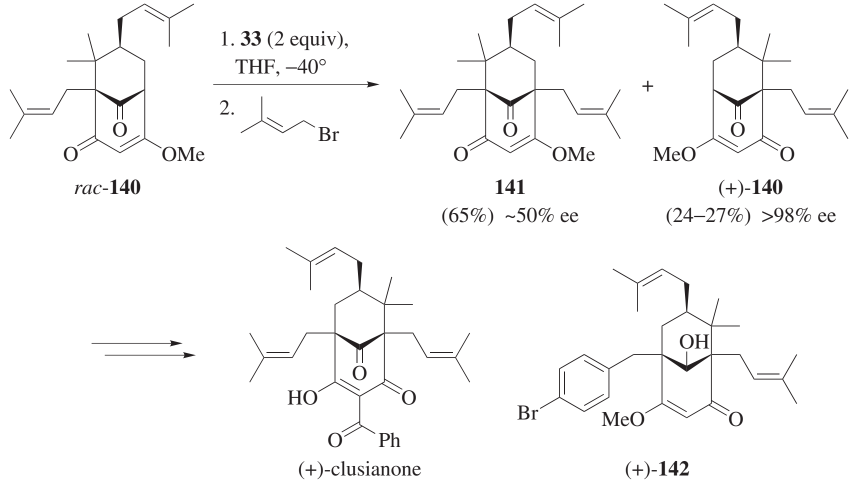
For the synthesis of the erythrinan alkaloid (+)-erysotramidine, the ring-fused imide **136** is treated with bis(lithium amide) **33** in the presence of TMSCl to give silylated imide **137** in 82% yield and very high enantioselectivity (Scheme 7).[207,208] Assembly of the core structure of erysotramidine is achieved following the enantioselective deprotonation step through a six-step sequence. First, a pent-4-enyl Grignard reagent undergoes addition to the imide with complete regiocontrol. Desilylation of the resulting adduct using TBAF, followed by an *N*-acyliminium mediated ring closure, gives **138** in excellent yield and as a single diastereoisomer. A retro-Diels–Alder gives the desired unsaturated lactam, the side chain of which is then cleaved under standard oxidative conditions to produce an aldehyde. A reductive cyclization under free-radical conditions leads efficiently to hydroxylactam **139** as a mixture of diastereomers at the newly formed carbinol center (~3:1 ratio). The synthesis of the target natural product is accomplished from this point in four additional steps.

The total synthesis of (+)-clusianone provides an example of enantioselective deprotonation at a bridgehead carbon that is carried out in the kinetic resolution mode.[213] Thus, racemic bridged ketone **140** is treated with two equivalents of bis(lithium amide) **33** followed by prenyl bromide (Eq. 89). Under these conditions, the prenylated product **141** is isolated in 65% yield and with an ee of



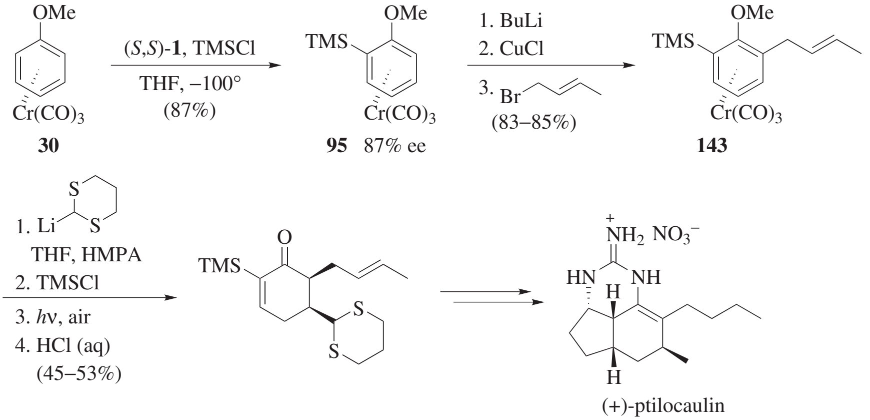
Scheme 7

about 50%. The recovered starting material (+)-**140** is isolated in 24–27% yield in an enantiomerically enriched form (>98% ee). The assignment of the absolute configuration of (+)-**140** has been determined by derivatization to alcohol (+)-**142**, which affords suitable crystals for X-ray structure determination. Conversion of (+)-**140** into clusianone establishes the absolute configuration of this natural product, which had not been previously assigned, to be the (+)-isomer.



(Eq. 89)

The enantioselective deprotonation of anisole complex **30** and silylation to give **95** has found application to the synthesis of (+)-ptilocaulin, which is an antimicrobial and cytotoxic marine metabolite.[78,79] A key transformation involves nucleophilic addition of 2-lithio-1,3-dithiane to bis-*ortho*-substituted (η^6-anisole)chromium complex **143** under specific conditions that suppress competing *tele*-substitution pathways (Scheme 8).

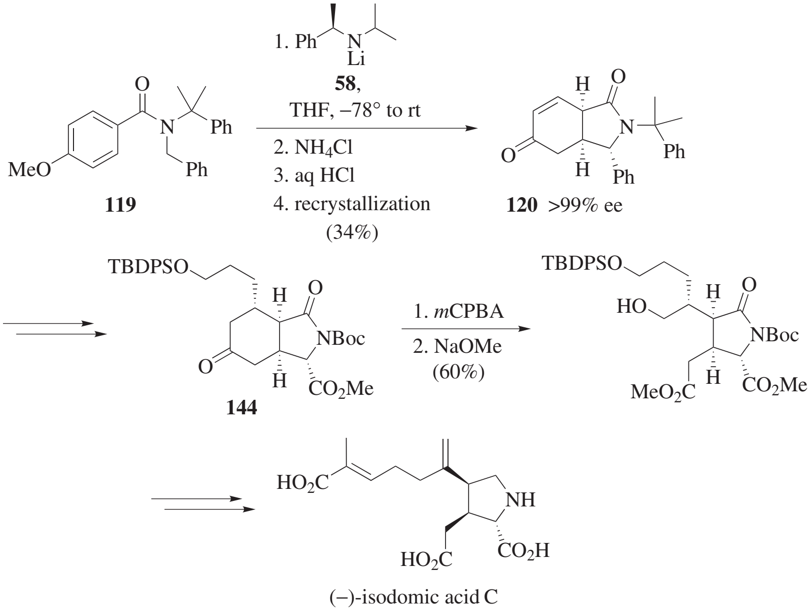


Scheme 8

The benzylic deprotonation of *N*-benzyl anisamides using chiral lithium amides and their transformation to afford chiral, saturated isoindolones (see Eq. 76) has been utilized to prepare natural products such as the neuroactive algal metabolites (−)-isodomic acid C[260] and (−)-kainic acid.[262] In the former example, (−)-isodomic acid C is prepared over eighteen steps following the asymmetric dearomatizing cyclization (Scheme 9). A key step involves a regioselective Baeyer–Villiger oxidation of ketone **144**, and this step is followed by careful methanolysis with slow addition of sodium methoxide. Overall, this method enables cleavage of the six-membered ring while avoiding epimerization of the C(3),C(4)-*cis* stereochemistry.

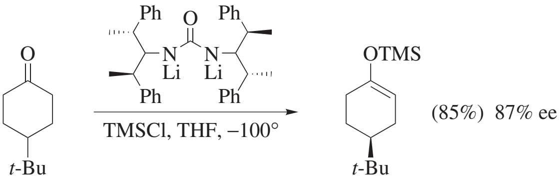
COMPARISON WITH OTHER METHODS

Substrates that do not feature electrophilic sites such as carbonyl groups may be deprotonated enantioselectively using either a chiral alkyllithium reagent, such as menthyllithium,[294,295] or, more usually, an alkyllithium that is coordinated to a chiral ligand, such as the well-investigated butyllithium-(−)-sparteine combination.[296] This reagent is sometimes assessed in parallel with chiral lithium amides.[73,74,246,250,258,272,297–302] The combination of butyllithium with chiral diamines is a less satisfactory reagent than chiral lithium amides for the enantioselective *ortho*-lithiation of tricarbonyl(η^6-arene)chromium complexes.[303] By careful consideration of the pK_a of the enantiotopic protons in the substrate, an assessment can usually be made between situations where a chiral lithium amide



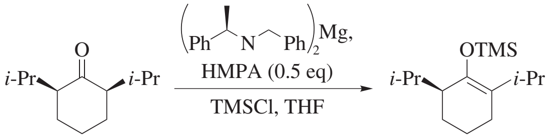
Scheme 9

or an alkyllithium reagent is the more effective base. For example, whereas chiral lithium amides react very poorly in the directed *ortho* metalation of ferrocene complexes, the use of butyllithium-(−)-sparteine for the same process has met with some success.[304,305] Somewhat closer in overall character to chiral lithium amides are chiral lithiated urea derivatives, which are able to transform prochiral cyclic ketones into silyl enol ethers in good yields and 83–88% ee (Eq. 90).[306,307]



(Eq. 90)

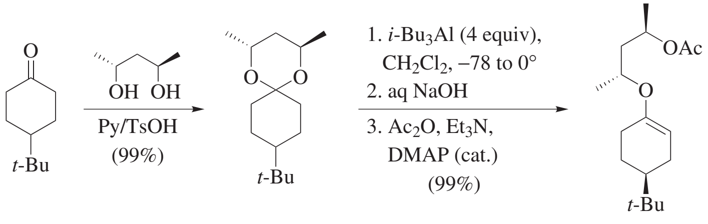
Chiral magnesium bis(amides) have emerged as alternative bases to chiral lithium amides and their utility has been demonstrated for the enantioselective deprotonation of prochiral cyclic ketones.[308–314] Low conversions of cyclic ketones into silyl enol ethers are observed when chiral magnesium bis(amides) are used in the absence of either HMPA or DMPU as additive (~0.5 equivalents). Nonetheless, these bases are effective reagents for this transformation and good to excellent enantioselectivities have been reported. Other than for 4-substituted cyclohexanones as substrates, chiral magnesium bis(amides) seem particularly suited to enantioselective deprotonation of *cis*- and *trans*-2,6-disubstituted cyclohexanones (Eq. 91).[310–312] These bases function rather well with ketones even at room temperature.



Temp (°)	Yield (%)	% ee
−60	66	99
−40	90	98
rt	94	82

(Eq. 91)

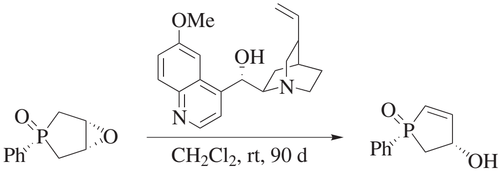
The diastereoselective enol borination of cyclic ketones using chlorobis(isopinocamphenyl)borane in the presence of a chiral diamine is another method for the desymmetrization of prochiral cyclic ketones.[315] This approach exploits the strategy of double stereodifferentiation to prepare enol boranes with good selectivities, and further transformations lead to enantiomerically enriched products. For example, upon treatment of the enol borane of 4-*tert*-butylcyclohexanone, prepared using this method in 75% yield and 89% de, with phenylselenyl chloride followed by oxidation, (*R*)-4-*tert*-butyl-2-cyclohexen-l-one is prepared in 51% yield and 89% ee. Another desymmetrization process that is applicable to conformationally biased cyclohexanones is formation of a chiral acetal with (*R*,*R*)-2,4-pentanediol, followed by a highly diastereoselective cleavage of the acetal group using triisobutylaluminum (TRIBAL).[122,316,317] After subsequent acetylation, this process affords a desymmetrized vinyl ether with a diastereomeric purity of ca. 80% (Eq. 92).



78% de

(Eq. 92)

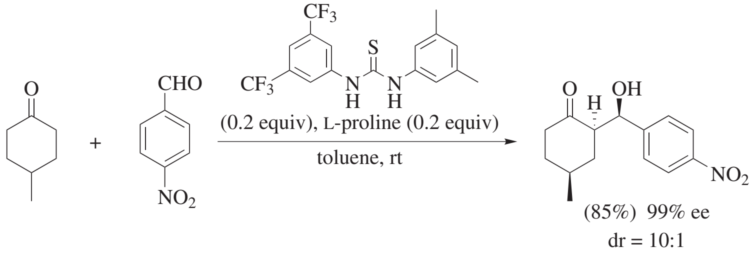
The rearrangement of a diastereomerically pure cyclic phospholene epoxide into the corresponding allylic alcohol proceeds in good chemical yield but with no asymmetric induction using chiral lithium amides or BuLi-(−)-sparteine.[318,319] However, the rearrangement is achieved in up to 52% ee using *Cinchona* alkaloids such as quinidine, but in a reaction time of 90 days (Eq. 93). These bases coordinate to the P=O functional group to promote an *anti*-β-proton abstraction for this substrate. *Cinchona* alkaloids can function as alternatives to chiral lithium amides under very restricted circumstances.



(41%) 52% ee

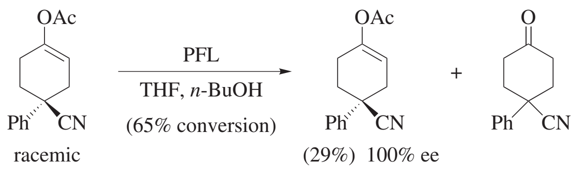
(Eq. 93)

Ongoing developments in the field of organocatalysis include the realization of desymmetrization processes that are akin to those achieved using chiral lithium amides. For example, 4-substituted cyclohexanones undergo enantioselective aldol reactions with aromatic aldehydes promoted by a substoichiometric mixture of L-proline and a thiourea cocatalyst (65–86% yield, 7:2:1 to 1:0:0 dr, ≥94% ee, Eq. 94).[320] Toluene is used as the solvent and hydrogen-bonding interactions between the various components are a very important feature of the reaction mechanism, not least in the initial formation of a proline-thiourea complex that is considerably more soluble in organic solvents than L-proline itself. Other desymmetrizations of 4-substituted cyclohexanones include the use of modified proline organocatalysts for the aldol reaction.[321] Examples of chiral ionic liquids as organocatalysts for processes such as α-alkylation are on record.[322]



(Eq. 94)

Enantioselective desymmetrizations can otherwise be accomplished using asymmetric transition-metal catalysts[323] or enzymes.[324,325] For example, planar chiral tricarbonyl(η^6-arene)chromium complexes are prepared by catalytic asymmetric desymmetrization processes based on palladium or gold catalysis.[326–328] The enol acetates of some 4,4-disubstituted cyclohexanones are resolved using the enzyme *Pseudomonas fluorescens* lipase (PFL).[325,329] Thus, the prochiral ketone 4-cyano-4-phenylcyclohexanone is converted into its racemic enol acetate that is resolved using PFL to give unreacted enantiomerically pure (100% ee) (*S*)-enol acetate (Eq. 95). By comparison, deprotonation of 4-cyano-4-phenylcyclohexanone using (*S*,*S*)-**1** at −78° with acetic anhydride as an external quench affords the (*R*)-enol acetate in 54% ee (50% yield). Therefore, the enzymatic approach has value in the preparation of highly enantiomerically enriched materials for use in synthesis, although the major limitation is the exceptional specificity of the enzyme toward its substrate. For example, in this case PFL reacts poorly and exhibits long reaction times with 4-phenylcyclohexanone or 4-cyanocyclohexanone,[330] illustrating a requirement for both an aromatic and a cyano group in the 4-position in the substrate.



(Eq. 95)

EXPERIMENTAL CONDITIONS

Some chiral amine precursors to chiral lithium amides are commercially available but it is not uncommon for the synthetic organic chemist to prepare the required amine from simpler and cheaper starting materials, such as enantiomerically enriched α-methylbenzylamine, which is used to prepare non-racemic bis(1-phenylethyl)amine (**1**). New or optimized methods for the synthesis of chiral amines continue to be developed, and the recent literature (January 2000–May 2009) has been reviewed.[331] A thorough survey of the chemical literature is therefore advised before embarking on the preparation of a particular chiral amine, as a more practicable or efficient synthesis may be readily available.

Starting-point synthetic procedures for the chiral amine precursors to the following bases can be identified from their associated references: proline-derived bases **10** and related,[39] phenylglycine-derived bases,[94] chelated diamine bases **21** and related,[68,116,332–334] norephedrine-derived base **43**,[335] *O*-acetyl mandelic acid-derived chelated bases,[336] α-methylbenzylamine-derived base **1** and related,[337–340] and bis(lithium amide) base **33**.[341] Although far from comprehensive, this list of bases and their associated references cover the key chiral lithium amides for enantioselective deprotonation.

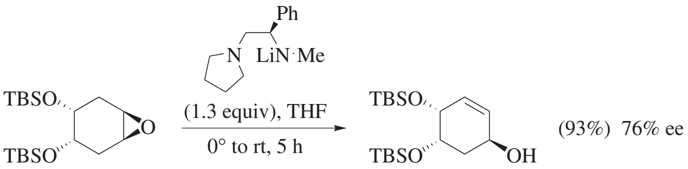
A solution of the chiral lithium amide is invariably prepared by treatment of the corresponding chiral amine precursor with *n*-butyllithium in a dry, aprotic solvent (e.g., THF, dried by refluxing over sodium/benzophenone) at a low temperature (ranging from 0 to −110°). If *n*-butyllithium is added to the amine at −78° or lower, it is not uncommon to warm the cold mixture to 0° for a short duration and then re-cool to the intended reaction temperature to ensure complete formation of the lithium amide. The precursor to the base can be either the free amine or the corresponding amine hydrochloride salt. In the latter case, two equivalents of *n*-butyllithium are required since one equivalent of this reagent is consumed in generating the free amine and lithium chloride. This approach may be advantageous, since lithium chloride has been shown to be a beneficial additive for enantioselective deprotonations.[58,59,61,80]

For asymmetric deprotonation reactions involving an external electrophilic quench, a solution of the substrate is introduced to the cold solution of the base via syringe or cannula transfer, and the mixture is stirred at low temperature for between 10 minutes to 3 hours. If required, an electrophile is then added and the reaction mixture is stirred with monitoring by TLC until formation of the desired product is complete. The reaction mixture is then quenched by the addition of an appropriate aqueous solution of either saturated NH_4Cl or $NaHCO_3$. The product can be isolated by extraction into an organic solvent and purified by distillation or column chromatography. For asymmetric deprotonation reactions involving an internal electrophilic quench, the electrophile (usually TMSCl) is added to either the solution containing the base or the solution containing the substrate, before the two components are mixed. The reactions are then treated in the same fashion as previously described.

It is important to recognize that some types of substrate are sensitive to excess amounts of chiral bases, and will over-react under the standard conditions.

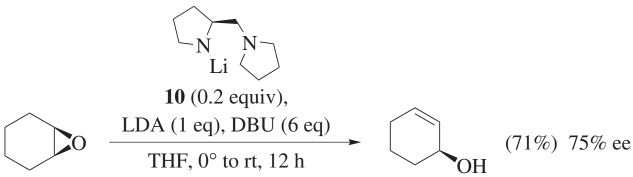
Examples of such substrates include cyclic imides, bridged imides, bridged ketones, and some substrates intended for kinetic resolution processes. To limit exposure of the substrate to excess amounts of base, the sequence of additions is inverted and the solution of the chiral lithium amide is added to a cold solution of the substrate dropwise via syringe or cannula transfer.

EXPERIMENTAL PROCEDURES

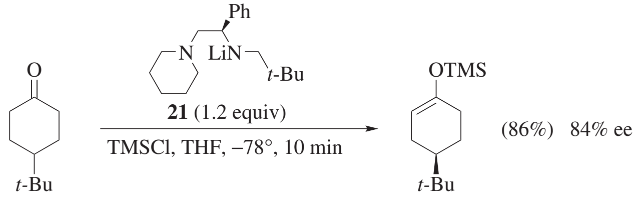


(1*S*,4*R*,5*S*)-4,5-bis(*tert*-Butyldimethylsilyloxy)cyclohex-2-en-1-ol (Enantioselective Rearrangement of a *meso*-Epoxide to an Allylic Alcohol Using a Chiral Lithium Amide).[342] *n*-Butyllithium (0.7 mL of a 1.5 M solution in hexane, 1.05 mmol) was added dropwise to a stirred solution of (*R*)-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (206 mg, 1.0 mmol) in THF (2.5 mL) at 0° under nitrogen. After 30 min at 0°, a solution of (1*S**,2*R**,4*R**,5*S**)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohexene oxide (280 mg, 0.8 mmol) in THF (5 mL) was added dropwise by means of a cannula, and the resulting solution was allowed to warm to rt over 4 h. After the mixture had been stirred at rt for 1 h, saturated aqueous NH_4Cl solution (3 mL) and Et_2O (20 mL) were added, and the layers were separated. The aqueous layer was diluted with H_2O (10 mL) and then extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with 2% HCl (15 mL), H_2O (15 mL), and then brine (15 mL), dried (Na_2SO_4), and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by column chromatography (petroleum ether/EtOAc, 5:1) afforded (1*S*,4*R*,5*S*)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohex-2-en-1-ol (261 mg, 93%, 76% ee) as white crystals: mp 60–62°; R_f 0.4 (petroleum ether/EtOAc, 4:1); $[\alpha]_D$ −87.1 (*c* 0.6 in $CHCl_3$); IR ($CHCl_3$) 3606, 1601, 835 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.75 (m, 1H), 5.65 (dddd, *J* = 10.0, 3.0, 1.0, 1.0 Hz (appearing as a double double triplet), 1H), 4.45 (m, 1H), 4.13 (dddd, *J* = 3.0, 3.0, 1.0, 1.0 Hz (appearing as a triplet of triplets), 1H), 4.07 (ddd, *J* = 8.0, 3.0, 2.0 Hz (appearing as a doublet of triplets), 1H), 2.25 (dddd, *J* = 13.0, 8.0, 5.0, 0.5 Hz, 1H), 1.55 (ddd, *J* = 13.0, 6.0, 2.2 Hz, 1H), 0.90 (s, 9H), 0.89 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H) and 0.07 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 131.1, 130.3, 69.7, 68.8, 65.9, 37.5, 26.0, 25.9, 18.4, 18.3, −4.4 (x 2), −4.6, −4.9; LRMS (CI, NH_3) *m/z* (% relative intensity, ion): 359 (25, $[M + H]^+$), 341 (10, $[M - OH]^+$), 301 (10, $[M - CMe_3]^+$, 227 (100, $[M - OSi\textit{t}\text{-}BuMe_2]^+$). Anal. Calcd for $C_{18}H_{38}O_3Si_2$: C, 60.3; H, 10.7. Found: C, 60.5; H, 10.7.

For the determination of enantiomeric excess, the allylic alcohol was converted into the corresponding Mosher esters. (*R*)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (10 μL, 0.05 mmol; 98% ee) was added dropwise to a stirred solution of the allylic alcohol (13 mg, 0.04 mmol), Et_3N (10 μL, 0.07 mmol), and DMAP (1 mg) in CH_2Cl_2 (2 mL) at rt under nitrogen. After 16 h, H_2O (5 mL) and Et_2O (10 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with 2% HCl (10 mL) and H_2O (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure to give the crude product (21 mg, 100%) as a colorless oil. (1*S*,2′*S*,4*S*,5*R*)-4,5-bis(*tert*-Butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate: R_f 0.5 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.43–7.35 (m, 3H), 5.91 (ddd, *J* = 10.0, 5.0, 1.5 Hz, 1H), 5.73 (ddd, *J* = 10.0, 2.5, 1.0, 1H), 5.52 (m, 1H), 4.02 (m, 1H), 3.66 (ddd, *J* = 11.5, 3.0, 3.0 Hz (appearing as a doublet of triplets), 1H), 3.56 (q, *J* = 1.0 Hz, 3H), 2.12 (ddd, *J* = 11.5, 11.5, 9.0 Hz (appearing as a triplet of doublets), 1H), 1.99 (m, 1H), 0.89 (s, 9H), 0.86 (s, 9H), 0.08 (s, 3H), 0.06 (s, 6H) and 0.04 (s, 3H). (1*R*,2′*S*,4*R*,5*S*)-4,5-bis(*tert*-Butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate: R_f 0.5 (petroleum ether/EtOAc, 10:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.43–7.35 (m, 3H), 5.87 (ddd, *J* = 10.5, 5.0, 1.5 Hz, 1H), 5.59 (ddd, *J* = 10.5, 2.5, 1.0 Hz, 1H), 5.52 (m, 1H), 4.02 (m, 1H), 3.67 (ddd, *J* = 11.5, 3.0, 3.0 Hz (appearing as a doublet of triplets), 1H), 3.57 (q, *J* = 1.0 Hz, 3H), 2.20 (ddd, *J* = 11.5, 11.5, 9.5 Hz (appearing as a triplet of doublets), 1H), 2.03 (m, 1H), 0.90 (s, 9H), 0.85 (s, 9H), 0.09 (s, 3H), 0.07 (s, 6H), 0.05 (s, 3H). ^{1}H NMR analysis of the mixture of Mosher esters indicated that the allylic alcohol product was obtained with an enantiomeric excess of 76%.

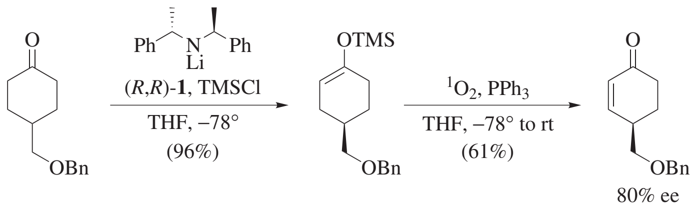


(*S*)-Cyclohex-2-en-1-ol (Enantioselective Rearrangement of Cyclohexene Oxide Using a Substoichiometric Quantity of an Asami-Type Chiral Lithium Amide).[104] *n*-Butyllithium (1.6 mL of a 1.5 M solution in hexane, 2.4 mmol) was added to a mixture of (*S*)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (62 mg, 0.4 mmol) and diisopropylamine (202 mg, 2.0 mmol) in THF (10 mL) at 0° under an argon atmosphere. The reaction mixture was stirred at 0° for 30 min before a solution of DBU (1.815 g, 12 mmol) in THF (6 mL) was added. After the mixture was stirred at 0° for 30 min, cyclohexene oxide (196 mg, 2.0 mmol) in THF (6 mL) was added at 0°. The reaction mixture was warmed to rt and stirring was continued at this temperature for 12 h. Saturated aqueous NH_4Cl solution and Et_2O were then added, and the organic layer was washed successively with 1 M HCl and brine, and then was dried ($MgSO_4$). The solvent was removed at atmospheric pressure, and the resulting crude cyclohex-2-en-1-ol was benzoylated with benzoyl chloride (3.4 mmol) and pyridine (3.4 mmol) in CH_2Cl_2 (10 mL) for 2 h. After addition of H_2O and Et_2O, the organic layer was washed with 1 M HCl and brine, and then was dried ($MgSO_4$). After the solvent was removed under reduced pressure, the oily substance was purified by column chromatography (hexane/ether, 10:1) to give cyclohex-2-en-1-yl benzoate (288 mg, 71%, 75% ee)[39]: IR (neat) 3070, 3040, 2940, 1710, 1650, 1600, 1585, 1490, 1450, 1315, 1270, 1175, 1110, 1070, 1050, 1025, 1010, 920, 710 cm^{-1}; ^1H NMR (CCl_4) δ 8.3–7.6 (m, 2H), 7.6–6.9 (m, 3H), 6.1–5.6 (m, 2H), 5.6–5.1 (m, 1H), 2.5–1.3 (m, 6H). The resulting cyclohex-2-en-1-yl benzoate was hydrolyzed with NaOH (0.4 g, 10 mmol) in MeOH (10 mL) by stirring overnight at rt. After removal of the MeOH at atmospheric pressure, Et_2O and H_2O were added to the mixture. The organic layer was washed with H_2O and brine, then dried ($MgSO_4$). The solvent was removed at atmospheric pressure, and the resulting crude cyclohex-2-en-1-ol[343] was purified by bulb-to-bulb distillation (150°, 20 mmHg): $[\alpha]_D^{25}$ −97.3 (*c* 0.96, $CHCl_3$) (lit.[344] $[\alpha]_D$ +130.6 (*c* 1.21 $CHCl_3$) for (*R*)-cyclohex-2-en-1-ol, >99% ee); ^1H NMR ($CDCl_3$) δ 5.91–5.53 (m, 2H), 4.26–3.72 (m, 1H), 2.81–1.30 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 131.0, 130.3, 65.4, 32.0, 25.1, 19.1. An enantiomeric excess of 75% was determined by comparison of the specific rotations.



(*R*)-4-*tert*-Butyl-1-trimethylsilyloxycyclohex-1-ene (Enantioselective Enolization and Silylation of a 4-Substituted Cyclohexanone Using a Koga-Type Chiral Lithium Amide).[345] Under an argon atmosphere, *n*-butyllithium (0.93 mL of a 1.61 M solution in hexane, 1.50 mmol) was added to a solution of (*R*)-*N*-neopentyl-1-phenyl-2-(1′-piperidino)ethylamine (432 mg, 1.58 mmol) in THF (18 mL) at rt, and the mixture was stirred at −78° for 5 min. A solution of 4-*tert*-butylcyclohexanone (194 mg, 1.25 mmol) and TMSCl (0.79 mL, 6.3 mmol) in THF (2 mL) was added during 90 s, and the mixture was stirred at −78° for 10 min. After addition of Et_3N (2 mL) and saturated aqueous $NaHCO_3$ solution (6 mL), the reaction mixture was allowed to warm to rt, and was extracted with hexane (200 mL in total). The organic extract was washed successively with 0.1 M aqueous citric acid (5 × 50 mL, until the pH of the aqueous washings was nearly 4), H_2O (20 mL), saturated aqueous $NaHCO_3$ solution (20 mL), and brine (20 mL), and then dried (Na_2SO_4).

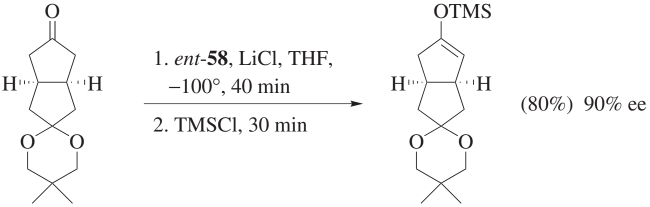
Evaporation of the solvent gave a pale yellow oil, which was purified by column chromatography (hexane) followed by bulb-to-bulb distillation to give (*R*)-4-*tert*-butyl-1-trimethylsilyloxycyclohex-1-ene (244 mg, 86%, 84% ee)[115] as a colorless oil: bp 160° (5 mmHg); $[\alpha]_{365}{}^{25}$ +198.5 (*c* 1.01, benzene) (lit.[117] $[\alpha]_{365}{}^{25}$ +237 (benzene) for the maximum rotation); IR 3040, 2960, 2870, 1675 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.84 (m, 1H), 2.25–1.95 (m, 3H), 1.88–1.73 (m, 2H), 1.34–1.12 (m, 2H), 0.87 (s, 9H), 0.18 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 150.4, 104.1, 44.1, 32.2, 31.1, 27.5, 25.2, 24.5, 0.44; LRMS *m*/*z*: 226.2 (M^+), 211.2 ($[M - Me]^+$), 169.1, 142.1, 127.1; HRMS *m*/*z*: M^+ calcd for $C_{13}H_{26}OSi$, 226.1753: found, 226.1752. An enantiomeric excess of 84% was determined by comparison of the specific rotations.



(*R*)-4-[(Benzyloxy)methyl]cyclohex-2-en-l-one (Enantioselective Enolization and Silylation of a 4-Substituted Cyclohexanone Using the Overberger Base and Conversion of the Silyl Enol Ether into the Corresponding 2-Enone).[121] A solution of (*S*,*S*)-bis(1-phenylethyl)amine (36.4 g, 162 mmol) in THF (500 mL) was cooled to −78°, *n*-butyllithium (60 mL of a 2.5 M solution in hexane, 150 mmol) was added dropwise over 10 min, and the violet solution was stirred for a further 30 min. After the introduction of TMSCl (78.7 mL, 620 mmol) dropwise over 10 min, the solution became colorless. After an additional 10 min, a solution of 4-[(benzyloxy)methyl]cyclohexanone (27.1 g, 124 mmol) in THF (30 mL) was added dropwise over 30 min. The mixture was stirred for 10 min and then was treated with Et_3N (173 mL, 1.24 mol) at −78° followed by saturated aqueous $NaHCO_3$ solution (150 mL) below −20°. After extraction with hexane (3 × 150 mL), the combined organic layers were washed with 3 N citric acid (1 × 200 mL), 1 N citric acid (2 × 130 mL), 0.6 N citric acid (7 × 130 mL, or until all of the amine byproduct was removed as determined by TLC and ninhydrin stain), saturated aqueous $NaHCO_3$ solution, and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Distillation through a short-path Widmer column gave the silyl enol ether intermediate (34.5 g, 96%) as a colorless oil: bp 135–140° (0.5–1 mmHg); $[\alpha]_{Hg365}{}^{25}$ +103 (*c* 2.09, benzene); IR ($CHC1_3$) 3005, 2920, 2860, 1670, 1365, 1250, 1180, 1110, 880, 840 cm^{-1}; ^{1}H NMR (250 MHz, $CDC1_3$) δ 7.35–7.25 (m, 5H), 4.85–4.80 (m, 1H), 4.50 (s, 2H), 3.45–3.30 (m, 2H), 2.20–2.00 (m, 3H), 2.00–1.70 (m, 3H), 1.50–1.30 (m, 1H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, $CDC1_3$) δ 150.2, 138.7, 128.3, 127.5, 127.4, 103.0, 74.8, 73.0, 33.8, 29.1, 27.1, 26.1, 0.3; HRMS (CI, NH_3) m/z: $[M + H]^+$ calcd for $C_{17}H_{26}O_2Si$, 291.1730; found, 291.1721.

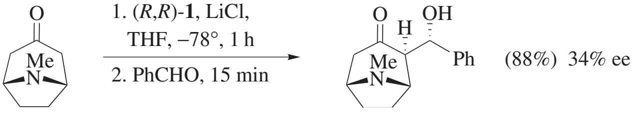
The chiral amine was recovered by neutralization of the acidic aqueous layer with 25% NaOH solution and extraction with CH_2Cl_2 (3 × 150 mL). The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Distillation through a short-path Widmer column afforded (*S*,*S*)-bis(1-phenylethyl)amine (34.6 g, 95% recovery) as a colorless oil: bp 98–100° (0.5 mmHg); $[\alpha]_D^{25}$ −171 (*c* 2.04, $CHCl_3$) (lit.[337] $[\alpha]_D^{25}$ −196.3).

At −78°, oxygen was bubbled through a solution of the silyl enol ether (347.8 g, 1.197 mol) and Rose Bengal (725 mg) in THF (2 L) with irradiation by a 1000 W Hg lamp through a 2% aqueous $K_2Cr_2O_7$ filter solution. After 8 h, triphenylphosphine (329.8 g, 1.257 mol) was added at −78°, and the resultant mixture was allowed to warm to rt overnight. MeOH (150 mL) was then added and the mixture was concentrated. The residue was taken up in 1:1 Et_2O/EtOAc (3 L), and any undissolved material was removed by filtration. After concentration and column chromatography (12.5% EtOAc in hexane), distillation afforded (*R*)-4-[(benzyloxy)methyl]cyclohex-2-en-l-one (158.0 g, 61%, 80% ee) as a colorless oil (the percent ee was determined by comparison of the specific rotations): bp 140–145° (0.5–1 mmHg); $[\alpha]_D^{25}$ +103.7 (*c* 1.89, MeOH) (lit.[121,346] $[\alpha]_D^{25}$ −129.3 (*c* 1.8, MeOH) for the enantiomer); UV–Vis (EtOH) λ_{max} 211 nm (ε 16000); IR ($CHCl_3$) 3000, 2860, 1680, 1450, 1390, 1360, 1230, 1110, 835, 690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.30–7.10 (m, 5H), 6.80 (br d, $J = 10$ Hz, 1H), 6.40 (dd, $J = 10, 3$ Hz, 1H), 4.40 (s, 2H), 3.40–3.30 (m, 2H), 2.65–2.55 (m, 1H), 2.45–2.15 (m, 2H), 2.05–1.90 (m, 1H), 1.75–1.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 151.5, 137.9, 130.0, 128.4, 127.7, 127.5, 73.2, 72.4, 36.9, 36.6, 25.8; HRMS (CI, NH_3) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}O_2$, 217.1228; found 217.1231.

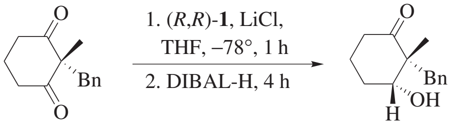


((3a′*R*,6a′*S*)-5,5-Dimethyl-3′,3a′,4′,6a′-tetrahydro-1′*H*-spiro[[1,3]dioxane-2,2′-pentalene]-5′-yloxy)trimethylsilane (Enantioselective Enolization and Silylation of a Mono-Protected *cis*-Bicyclo[3.3.0]octane-3,7-dione Using a Chiral Lithium Amide).[142] *n*-Butyllithium (90 mL of a 1.55 M solution in hexane, 140.95 mmol) was added dropwise to a suspension of (*R*,*R*)-bis(1-phenylethyl)amine hydrochloride (18.45 g, 70.47 mmol) in THF (300 mL) at −78°. The mixture was gradually warmed to rt, whereby a clear yellow solution was formed. The solution was subsequently cooled to −100°, and a solution of the mono-protected *cis*-bicyclo[3.3.0]octane-3,7-dione (10.00 g, 44.58 mmol) in THF (120 mL) was added over a period of 30 min. After the mixture was stirred at −100° for 40 min, TMSCl (9.70 g, 89.17 mmol) was added dropwise, and the reaction mixture was stirred at this temperature for 30 min. The cooling bath was then removed, and saturated aqueous $NaHCO_3$ solution (6 mL) was added. The mixture was warmed to rt within 45 min and $MgSO_4$ was added. After stirring for 30 min, the mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was diluted with pentane (200 mL), at which point the hydrochloride salt of the chiral amine precipitated and was removed by filtration. The filtrate was concentrated in vacuo and the residue was purified by column chromatography (hexane/EtOAc, 9:1) to give the title product (10.40 g, 80%, 90% ee) as a colorless oil: R_f0.66 (hexane/EtOAc, 1:1); $[\alpha]_D$ +16.7 (*c* 1.00, acetone); IR (neat) 2955, 2904, 2852, 1644 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.61 (m, 1H), 3.48 (s, 2H), 3.45 (s, 2H), 3.12–3.05 (m, 1H), 2.68–2.50 (m, 2H), 2.40–2.25 (m, 2H), 2.05–1.96 (m, 1H), 1.60–1.52 (m, 2H), 0.97 (s, 3H), 0.95 (s, 3H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 108.9, 107.3, 72.8, 71.5, 43.2, 41.2, 40.2, 40.0, 35.6, 30.1, 22.6, 0.00; LRMS (EI) m/z: 296 (33, M$^+$), 224 (24), 209 (66), 206 (51), 181 (28), 168 (28), 167 (100), 154 (24), 128 (92), 75 (30), 74 (25), 73 (86), 69 (43). Anal. Calcd for $C_{16}H_{28}O_3Si$: C, 64.82; H, 9.52. Found: C, 64.99; H, 9.53. The enantiomeric excess was determined to be 90% by NMR shift studies using Ag(fod) (1 equiv) and (+)-Pr(tfc)$_3$ (1 equiv): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.38 (4H, minor), 4.44 (4H, major).

The chiral amine hydrochloride salt was recovered by washing the silica gel used in the purification of the title compound with THF (1 L). The washings were concentrated under reduced pressure, and the residue was combined with the sample of amine hydrochloride obtained during isolation of the title compound. The resulting mixture was suspended in 0.5 M aqueous HCl (200 mL), and the mixture was heated at reflux until a clear solution was obtained. Subsequently, the solution was cooled first to rt and then to 0°, whereby a white solid precipitated. Recrystallization of the solid from water gave (*R*,*R*)-bis(1-phenylethyl)amine hydrochloride (12.95 g, 70%).

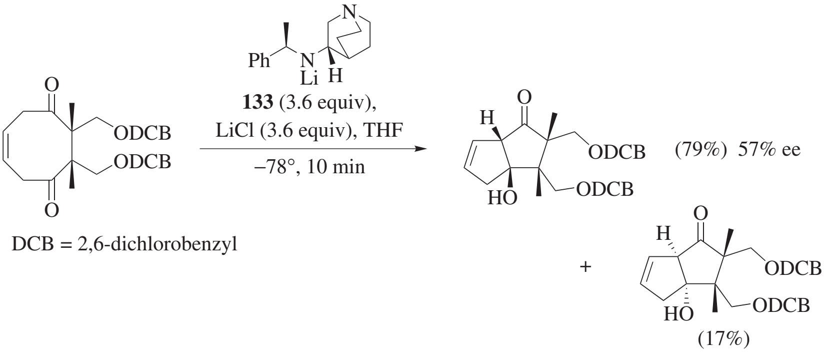


(1*S*,2*R*,1′*S*)-2-(1′-Hydroxybenzyl)-8-methyl-8-azabicyclo[3.2.1]octan-3-one (Enantioselective Enolization of Tropinone Using a Chiral Lithium Amide and Aldol Reaction with Benzaldehyde).[177,347] *n*-Butyllithium (0.48 mL of a 2.3 M solution in hexane, 1.1 mmol) was added to a solution of (*S*)-*N*-isopropyl-1-phenylethyl)amine hydrochloride (0.180 g, 1.1 mmol) in THF (3.2 mL) at 0°. The mixture was stirred at 0° for 25 min and then was cooled to −78°. A solution of tropinone (0.139 g, 1.0 mmol) in THF (2 mL) was added dropwise, and the reaction mixture was stirred for 45 min at −78°. Benzaldehyde (0.13 mL, 1.2 mmol) was then added and the mixture was stirred at −78° for 15 min followed by quenching with saturated aqueous NH_4Cl solution (2 mL). The mixture was warmed to rt and extracted with Et_2O (3 × 10 mL). The combined extracts were washed with water, dried ($MgSO_4$), and the solvents were removed under reduced pressure. After the residue was dissolved in CH_2Cl_2 (1 mL), the solution was diluted with hexane (20 mL), which caused the product to precipitate. The crude mixture was dried under vacuum for two days to afford (1*S*, 2*R*,1′*S*)-2-(1′-hydroxybenzyl)-8-methyl-8-azabicyclo[3.2.1]octan-3-one (0.215 g, 88%, 34% ee) as a yellow solid: mp 132–133°, $[\alpha]_D^{25}$ +19.7 (*c* 1.20, MeOH); IR (KBr) 3399, 3086, 2954, 2880, 2807, 1711, 1491, 1452, 1077, 760, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.19 (m, 5H), 5.21 (d, $J = 3.1$ Hz, 1H), 3.57 (d, $J = 6.6$ Hz, 1H), 3.48–3.43 (m, 1H), 2.84 (ddd, $J = 15.6, 4.6, 1.5$ Hz, 1 H), 2.44 (s, 3H), 2.42–2.39 (m, 1H), 2.30 (ddd, $J = 15.7, 2.0, 2.0$ Hz, 1H), 2.25–2.07 (m, 2H), 1.65–1.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.0, 141.7, 128.0, 127.3, 125.2, 76.5, 67.1, 63.8, 61.5, 51.6, 40.5, 26.3, 26.1; LRMS (CI, NH_3) m/z: 247 (18), $[M + H]^+$ 246 (100), 140 (52), 82 (20). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.50; H, 8.06; N, 5.70. The enantiomeric excess was determined to be 34% by ^1H NMR with (+)-Eu(tfc)$_3$ added to the sample in $CDCl_3$ solution. The product was recrystallized from hexane/$CHCl_3$ several times to afford yellow crystals, mp 132–133°, $[\alpha]_D^{20}$ + 23 (*c* 1.73, $CHCl_3$).



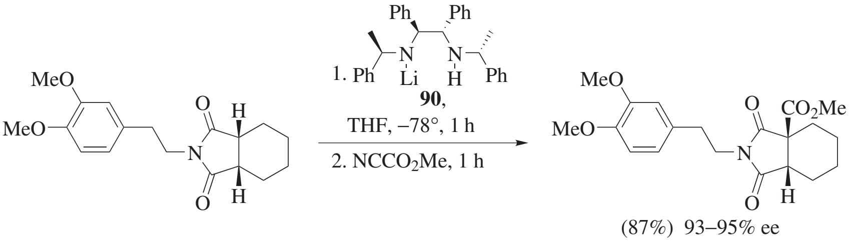
(77%) 99% ee, 95% de

(2*R*,3*R*)-2-Benzyl-3-hydroxy-2-methylcyclohexanone (Selective Enolization of a Cyclic 1,3-Diketone Using the Overberger Base and Subsequent Reduction with DIBAL-H).[198] (*R*,*R*)-bis(1-Phenylethyl)amine hydrochloride (73 mg, 0.28 mmol) was suspended in dry THF (2 mL), cooled to −78°, and *n*-butyllithium (0.26 mL of a 2.11 M solution in hexane, 0.55 mmol) was added. The mixture was stirred at rt for 10 min. 2-Benzyl-2-methylcyclohexane-1,3-dione (50 mg, 0.23 mmol) was dissolved in dry THF (2 mL) and cooled to −78°. The base was cooled to −78° and added to the diketone via cannula transfer. The mixture was stirred at −78° for 1 h, and then DIBAL-H (0.45 mL of a 1.7 M solution in THF, 0.77 mmol) was added. After the mixture was stirred at −78° for 4 h, the reaction was quenched by the addition of 1 M aqueous HCl (2 mL). The reaction mixture was diluted with EtOAc (20 mL) and water (3 mL), and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic phases were washed with 1 M aqueous HCl (3 × 3 mL) and brine (3 × 3 mL), and then dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (petroleum ether/EtOAc, 3:1) to give (2*R*,3*R*)-2-benzyl-3-hydroxy-2-methylcyclohexanone (39 mg, 77%, 99% ee, 95% de) as a white solid: mp 78–79°; R_f 0.23 (petroleum ether/EtOAc, 3:1); HPLC (Chiralcel OD, hexane/*i*-PrOH, 95:5, 0.5 mL min^{-1}) t_R 41.6 min (major), 54.9 min (minor), and 27.0 min and 38.1 min (minor); $[\alpha]_D$ −25 (*c* 0.5 in CH_2Cl_2); IR (CH_2Cl_2) 3687, 3603, 2942, 2685, 2410, 2302, 1705, 1604, 1516, 1494, 1373, 1065, 992, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.14 (m, 5H), 3.77 (dd, $J = 7$, 3 Hz, 1H), 3.11 (d, $J = 14$ Hz, 1H), 2.97 (d, $J = 14$ Hz, 1H), 2.59–2.51 (m, 2H), 2.19–1.98 (m, 2H), 1.91–1.72 (m, 2H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.8, 137.5, 130.6, 128.0, 126.3, 75.7, 54.5, 37.7, 37.3, 28.5, 20.7, 20.4; LRMS (EI, 180°) *m*/*z*: 218 (M^+, 62), 159 (14), 147 (19), 127 (16), 117 (12), 99 (11), 91 (100), 71 (8); HRMS (EI, 180°) *m*/*z*: M^+ calcd for $C_{14}H_{18}O_2$, 218.1307; found, 218.1307.



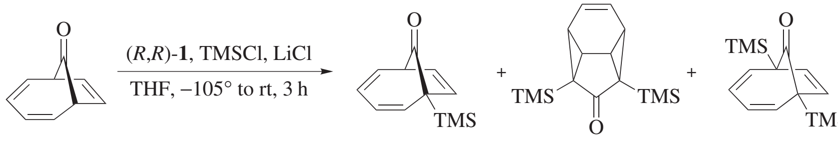
(2*S*,3*S*,3a*S*,6a*S*)-3,3a,4,6a-Tetrahydro-2,3-bis[((2′,6′-dichlorophenyl) methoxy)methyl]-2,3-dimethyl-3a-hydroxy(2*H*)-pentalen-1-one (Enantioselective Transannular Aldol Reaction of an Eight-Membered *meso*-1,4-Diketone Mediated by a Chiral Lithium Amide).[293] (1′*R*,3*S*)-*N*-(1′-Phenylethyl)-1-azabicyclo[2.2.2]octan-3-amine (4.12 g, 17.9 mmol) and LiCl (759 mg, 17.9 mmol) were dissolved in THF (70 mL). To this solution at −78° was added *n*-butyllithium (11.4 mL of a 1.57 M solution in hexane, 17.9 mmol), and the mixture was allowed to warm to rt. After 20 min, the solution was re-cooled to −78° and stirred for 1 h. In a separate flask, (2*R**,3*S**)-2,3-bis[[(2′,6′-dichlorophenyl) methoxy]methyl]-2,3-dimethyl-6-cyclooctene-1,4-dione (2.73 g, 5.02 mmol) was dissolved in THF (100 mL) and cooled to −78°. The solution of the lithium amide was transferred to the solution of the *meso*-1,4-diketone, and the reaction mixture was stirred for 10 min at −78° before quenching with saturated aqueous NH_4Cl solution. The aqueous phase was extracted twice with EtOAc, and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated.

The residue was purified by column chromatography (hexane/EtOAc, 10:1–2:1) to give the desired title compound (2.16 g, 79%, 57% ee), along with an undesired diastereoisomer (473 mg, 17%). Recrystallization (hexane/EtOAc, 1:1) gave the enantiopure title product (1.15 g, 53%, 99% ee) as colorless crystals: mp 150–151°; R_f 0.40 (hexane/EtOAc, 3:1); HPLC (Chiralcel OD, hexane/*i*-PrOH, 85:15, 1.0 mL min^{-1}) t_R 9 min (major), 15 min (minor); $[\alpha]_D^{26}$ +208.7 (*c* 1.00, $CHCl_3$); IR (film) 2928, 2359, 1737, 1564, 1437, 1199, 1100, 768 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.33 (m, 4H), 7.21 (m, 2H), 5.58 (dd, J = 5.5, 2.5 Hz, 1H), 5.55 (dd, J = 5.5, 2 Hz, 1H), 4.70 (s, 2H), 4.66 (d, J = 11 Hz, 1H), 4.62 (d, J = 11 Hz, 1H), 4.11 (d, J = 9 Hz, 1H), 3.48 (d, J = 10 Hz, 1H), 3.46 (d, J = 10 Hz, 1H), 3.19 (d, J = 2.5 Hz, 1H), 3.10 (d, J = 9 Hz, 1H), 2.95 (dd, J = 18.5, 2 Hz, 1H), 2.45 (d, J = 18.5 Hz, 1H), 2.44 (br s, 1H), 1.14 (s, 3H), 1.09 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 215.4, 137.0, 136.7, 133.2, 133.0, 131.4, 130.0, 128.4, 128.4, 126.6, 86.9, 75.0, 73.2, 67.4, 67.2, 65.9, 60.4, 59.7, 50.2, 47.8, 19.1, 17.4; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{26}Cl_4O_4Na$, 565.0477; found, 565.0477. Characterization data relating to the undesired diastereoisomer can be found in the original paper.[293]



(3a*S*,7a*S*)-2-[2′-(3″,4″-Dimethoxyphenyl)ethyl]-1,3-dioxooctahydroisoindole-3a-carboxylic Acid Methyl Ester (Enantioselective Deprotonation of a Cyclic Imide Using a Chiral Lithium Amide and Acylation with Methyl Cyanoformate).[202] *n*-Butyllithium (8.50 mL of a 2.5 M solution in hexanes, 21.3 mmol) was added dropwise via syringe over 25 min to a solution of (1*S*,2*S*)-*N*,*N*′-bis[(*R*)-1-phenylethyl]-1,2-diphenylethanediamine (8.79 g, 20.9 mmol) in THF (50 mL) at −78°, maintaining the internal temperature between −78° and −75°. The resulting pink solution was allowed to warm to rt and stirred at this temperature for 30 min. The solution was re-cooled to −78° and transferred over 2 h via cannula to a solution of 2-[2′-(3″,4″-dimethoxyphenyl)ethyl]-1,3-dioxooctahydroisoindole (6.00 g, 18.9 mmol) in THF (80 mL) at −78°, maintaining the internal temperature at −78°. The reaction mixture was stirred at −78° for 1 h, and then a solution of methyl cyanoformate (3.00 mL, 37.8 mmol) in THF (10 mL) was added dropwise via cannula over 15 min. The resulting yellow solution was stirred at −78° for 1 h before the cooling bath was removed and saturated aqueous $NaHCO_3$ solution (80 mL) was slowly added, followed by H_2O (20 mL). The phases were separated, and the aqueous phase was extracted with EtOAc

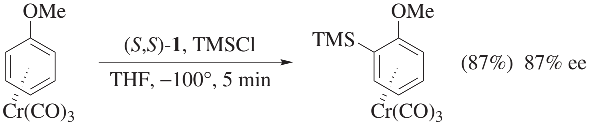
(3 × 50 mL). The combined organic phases were washed with brine (50 mL), and then dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude solid residue was purified by column chromatography (petroleum ether/EtOAc, 7:3–1:1). This afforded both the recovered diamine (8.40 g, 96%) as small white crystals and (3a*S*,7a*S*)-2-[2′-(3″,4″-dimethoxyphenyl)ethyl]-1,3-dioxooctahydroisoindole-3a-carboxylic acid methyl ester (6.20 g, 87%, 93–95% ee) as a colorless oil: HPLC (OD column, hexane/EtOH, 9:1, 0.6 mL min^{-1}) t_R 35 min (major), 47 min (minor); $[\alpha]_D^{25}$ −62.0 (*c* 1.1, $CHCl_3$); R_f 0.4 (petroleum ether/CH_2Cl_2/EtOAc, 2:2:1); IR ($CHCl_3$) 2940, 1742, 1701, 1515, 1349, 1234, 1026, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.75–6.69 (m, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 3.73 (m, 2H), 3.72 (s, 3H), 3.19 (dd, $J = 6.5$, 3.7 Hz, 1H), 2.86 (app. td, $J = 7.7$, 2.2 Hz, 2H), 2.26 (m, 1H), 1.98 (ddd, $J = 14.2$, 8.5, 4.2 Hz, 1H), 1.60–1.48 (m, 2H), 1.37–1.30 (m, 3H), 1.10 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 176.1, 170.2, 148.9, 147.8, 129.9, 121.1, 112.0, 111.1, 56.0, 55.9, 54.1, 53.3, 43.8, 39.8, 32.7, 28.5, 21.4, 20.8, 20.5; MS (FAB) *m/z* (% relative intensity, ion): 375 (100, M^+), 164 (90, $[C_{10}H_{12}O_2]^+$), 151 (35, $[C_9H_{11}O_2]^+$); HRMS (FAB) *m/z*: M^+ calcd for $C_{20}H_{25}NO_6$, 375.1682; found, 375.1683. Anal. Calcd for $C_{20}H_{25}NO_6$: C, 63.99; H, 6.71; N, 3.73. Found: C, 63.69; H, 6.75; N, 3.65.



(76%) 98% ee **I** **I** + **II** (23%) **II**

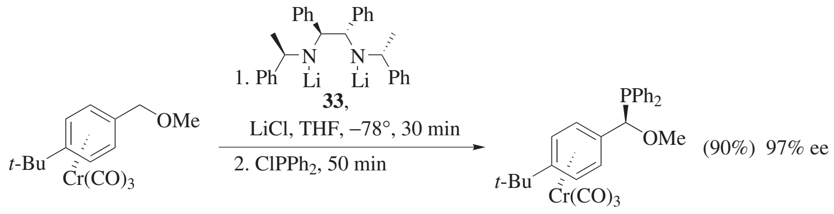
1-(Trimethylsilyl)bicyclo[4.2.1]nona-2,4,7-trien-9-one (Enantioselective Deprotonation at a Bridgehead Position and Silylation Using a Chiral Lithium Amide).[210,212] A solution of chiral lithium amide and LiCl was prepared by treatment of a suspension of (*R*,*R*)-bis(1-phenylethyl)amine hydrochloride (864 mg, 3.3 mmol) in THF (15 mL) at −78° with *n*-butyllithium (4.17 mL of a 1.45 M solution in hexanes, 6.05 mmol). The solution was allowed to warm to rt, and after 10 min was re-cooled to −105°. The solution was cannulated dropwise into a solution of bicyclo[4.2.1]nona-2,4,7-trien-9-one (396 mg, 3 mmol) and TMSCl (1.2 mL, 9 mmol) in THF (30 mL) at −105° over 45 min to maintain the internal temperature. The resulting solution was allowed to warm slowly to rt over 3 h, quenched with aqueous NH_4Cl solution (20 mL), and diluted with Et_2O (50 mL). The two phases were separated, and the organics washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and evaporated to afford a pale yellow solid. Purification by flash column chromatography (4% Et_2O in petroleum ether) gave 1-(trimethylsilyl)bicyclo[4.2.1]nona-2,4,7-trien-9-one as a white crystalline solid (464 mg, 76%, 98% ee): mp 87–89°; HPLC (Chiralcel OD, hexane, 0.1 mL min^{-1}) t_R 61 min (minor), 67 min (major); $[\alpha]_D^{26}$ −182° (*c* 0.99 in $CHCl_3$); IR (solid) 2951, 1732, 1250, 1243, 1151, 1060, 1031, 839, 752, 679 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.97–5.84 (m, 3H), 5.71–5.69 (dd, $J = 6.8$, 2.3 Hz, 1H), 5.66–5.62 (m, 2H), 3.14 (dd, $J = 7.5$, 2.2 Hz, 1H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 218.3, 130.5, 129.3, 127.0, 125.7, 124.6, 122.2, 54.6, 51.6, −3.7; HRMS (EI) m/z: M^{+} calcd for $C_{12}H_{16}OSi$, 204.0970; found, 204.0988. Anal. Calcd for $C_{12}H_{16}OSi$: C, 70.53; H, 7.89. Found: C, 70.52; H, 7.79.

Further elution gave a mixture of undesired 1,6-bis(trimethylsilyl)bicyclo [4.2.1]nona-2,4,7-trien-9-one and 7,9-bis(trimethylsilyl)tetracyclo[4.3.0.0.^{2,9}0.^{5,7}] nona-3-en-8-one (63 mg, 23%). Characterization data relating to these byproducts can be found in the original paper.[210]

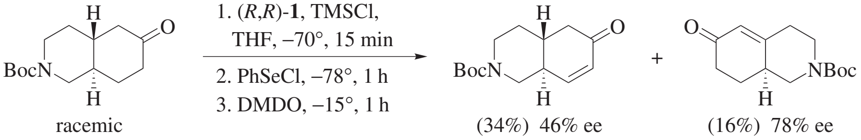


(2*S*)-Tricarbonyl(η^6-2-trimethylsilylanisole)chromium(0) (Enantioselective *ortho*-Metalation and Silylation of a Tricarbonyl(η^6-arene)chromium(0) Complex Using a Chiral Lithium Amide).[79] A stirred solution of (*S*,*S*)-bis(1-phenylethyl)amine (608 mg, 2.70 mmol) in THF (60 mL) was cooled to −70°, and a solution of *n*-butyllithium (1.78 mL of a 1.6 M solution in hexane, 2.85 mmol) was added dropwise. After 45 min, the solution was cooled to −100°. Under vigorous stirring, TMSCl (1.86 mL, 14.7 mmol) and a solution of tricarbonyl(η^6-anisole)chromium(0) (600 mg, 2.46 mmol) in THF (5 mL) were injected consecutively and very rapidly. After 5 min, the mixture was diluted with MTBE and washed with 2 N HCl (150 mL). The hydrochloride salt of the chiral amine was observed to precipitate from the aqueous layer upon standing. The organic layer was washed with saturated aqueous NaHCO$_3$ solution and brine, and then was dried (K$_2$CO$_3$). After the solvent was removed under reduced pressure, purification of the residue by column chromatography (hexane/EtOAc, 4:1) gave the title compound (673 mg, 87%, 87 ±2% ee) as a greenish-yellow powder. A sample of the product (3.40 g, 82% ee; combined product of several experiments) was recrystallized from hexane (250 mL) at 4° and subsequently at −18° to afford (2*S*)-tricarbonyl(η^6-2-trimethylsilylanisole)chromium(0) (2.38 g, 70%, ≥99% ee): mp 108°; HPLC (Chiralcel OJ, hexane/*i*-PrOH, 9:1, 0.8 mL min^{-1}) t_R 13.0 min, 16.9 min; $[\alpha]_D^{20}$ −236.8 (*c* 1.105, CHCl$_3$); IR (KBr) 1942, 1885, 1865, 1842, 1517, 1458, 1408, 1262, 844, 666 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.68 (app. dt, $J_t = 6$ Hz, $J_d = 1.5$ Hz, 1H), 5.57 (dd, $J = 6$, 1.5 Hz, 1H), 4.97 (d, $J = 7$ Hz, 1H), 4.79 (t, $J = 6$ Hz, 1H), 3.73 (s, 3H), 0.31 (s, 9H); ^{13}C NMR (67.5 MHz, CDCl$_3$) δ 233.2, 147.5, 101.8, 95.9, 88.8, 85.0, 73.4, 55.3, −0.7; LRMS (EI, 70 eV) m/z: 316 (M^{+}, 18), 260 (10), 232 (100), 201 (9), 187

(11), 180 (4), 135 (31), 52 (100). Anal. Calcd for $C_{13}H_{16}O_4Cr$: C, 49.39; H, 5.10. Found: C, 49.26; H, 5.14.

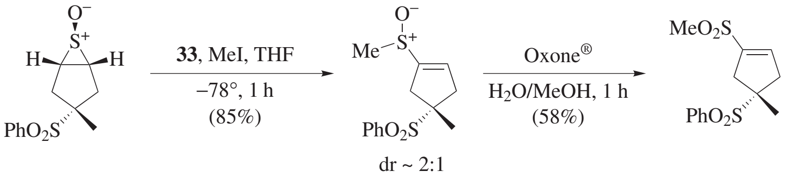


(*R*)-Tricarbonyl[η^6-1-(1′-diphenylphosphino-1′-(methoxy)methyl)-4-*tert*-butylbenzene]chromium(0) (Enantioselective Deprotonation at a Benzylic Site of a Tricarbonyl(η^6-arene)chromium(0) Complex Using a Chiral bis-(Lithium Amide) Base and Reaction with Chlorodiphenylphosphine).[87] *n*-Butyllithium (1.33 mL of a 1.84 M solution in hexane, 2.45 mmol) was added dropwise to a stirred solution of *N*,*N*′-bis[(*R*)-1-phenylethyl]-2*S*,3*S*-butanediamine (515 mg, 1.22 mmol) in THF (12 mL) at −78°. The solution was allowed to reach rt over 30 min. The resulting deep pink solution of the chiral diamide was then re-cooled to −78°, and a solution of heat-gun-dried LiCl (52 mg, 1.22 mmol) in THF (8 mL) was added via a cannula. Stirring was continued for a further 5 min before a solution of tricarbonyl(η^6-1-methoxymethyl-4-*tert*-butylbenzene)chromium(0) (350 mg, 1.11 mmol) in THF (5 mL) at −78° was added dropwise (∼2 min) via a short cannula. After the orange solution was stirred at −78° for 30 min, chlorodiphenylphosphine (0.6 mL, 3.33 mmol) was added in one portion, resulting in a color change of the solution to yellow. Stirring was continued for a further 50 min before MeOH (1 mL) was added and the solvent was removed under reduced pressure. Column chromatography (hexane/CH_2Cl_2, 10:0–7:3) of the residue gave (*R*)-tricarbonyl[η^6-1-(1′-diphenylphosphino-1′-(methoxy)methyl)-4-*tert*-butylbenzene]chromium(0) (500 mg, 90%, 97% ee) as a yellow solid: mp 143–144°; HPLC (Chiralcel AD, hexane/*i*-PrOH, 98:2, 0.6 mL min^{-1}) t_R 13.5 min (minor); 18.0 min (major); $[\alpha]_D^{20}$ +66.1 (*c* 0.75, CH_2Cl_2); IR (CH_2Cl_2) 1960, 1882 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.39–7.28 (m, 8H), 5.27 (s, 2H), 5.14 (d, J = 7.0 Hz, 1H), 4.79 (d, J = 7.0 Hz, 1H), 4.76 (d, J = 4.0 Hz, 1H), 3.57 (s, 3H), 1.24 (s, 9H); ^{31}P NMR (146 MHz, $CDCl_3$) δ 11.3; ^{13}C NMR (90 MHz, $CDCl_3$) δ 233.7, 134.5 (d, J = 14.1 Hz), 134.1 (d, J = 1.5 Hz), 133.9 (d, J = 2.2 Hz), 133.5 (d, J = 15.4 Hz), 129.3 (d, J = 2.3 Hz), 128.4, 128.3, 128.2, 123.9, 108.9 (d, J = 16.5 Hz), 90.3 (d, J = 6.3 Hz), 90.1 (d, J = 3.6 Hz), 89.9, 89.5, 83.2 (d, J = 14.3 Hz), 60.0 (d, J = 4.2 Hz), 33.8, 30.8; LRMS (EI) *m*/*z*: M^+ 498 (3), $[M - CO]^+$ 470 (16), $[M - 2CO]^+$ 442 (9), $[M - 3CO]^+$414 (100), 384 (38), 306 (14), $[M - 2CO - PPh_2]^+$ 257 (6), $[M - Cr(CO)_3 - PPh_2]^+$ 177 (99). Anal. Calcd for $C_{27}H_{27}CrO_4P$: C, 65.06; H, 4.46. Found: C, 64.97; H, 4.43.



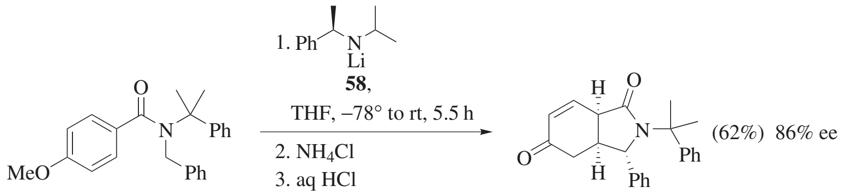
(4a*R*-*trans*)-3,4,4a,5,6,8a-Hexahydro-6-oxo-2-(1*H*)isoquinolinecarboxylic Acid 1′,1′-Dimethylethyl Ester and (8a*S*)-3,4,6,7,8,8a-Hexahydro-6-oxo-2-(1*H*)isoquinolinecarboxylic Acid 1′,1′-Dimethylethyl Ester (Regiodivergent Resolution of a Racemic Bicyclic Ketone into its Silyl Enol Ethers Using a Chiral Lithium Amide Followed by Conversion of the Products to the Corresponding 2-Enones by Selenation, Oxidation, and Elimination).[240,241] A solution of the chiral lithium amide was prepared by treatment of (*R*,*R*)-bis(1-phenylethyl)amine (0.51 g, 2.32 mmol) in THF (30 mL) at −70° (±2°) under a nitrogen atmosphere with *n*-butyllithium (1.45 mL of a 1.6 M solution in hexane, 2.32 mmol). The solution was allowed to warm to rt to ensure complete formation of the lithium amide, and then after 5 min was re-cooled to −70° (±2°). TMSCl (0.96 g, 7.74 mmol) was added slowly to the mixture and, after 2 min, was followed by a solution of (4a*R*-*trans*)-octahydro-6-oxo-2-(1*H*)isoquinolinecarboxylic acid 1′,1′-dimethylethyl ester (0.40 g, 1.55 mmol) in THF (15 mL), added dropwise over a period of 10 min to maintain a constant temperature of −70° (±2°). After the mixture had been held at this temperature for 15 min, triethylamine (6 mL) was added, followed by saturated aqueous $NaHCO_3$ solution, (45 mL). The mixture was extracted with petroleum ether (2 × 60 mL), and the combined extracts were washed with saturated aqueous NH_4Cl solution (60 mL) and saturated aqueous $NaHCO_3$ solution (45 mL), dried (Na_2SO_4), and evaporated under reduced pressure. This gave the crude enol silanes (0.42 g, 85%) in a 59:41 ratio of Δ6,7 to Δ5,6 isomers. Data of the mixture: IR ($CHCl_3$) 3624, 2929, 1671, 1367, 1162, 1127, 892, 863 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.81 (ddd, $J = 5, 2, 2$ Hz, 1H, Δ6,7); 4.66 (br s, 1H, Δ5,6), 4.14–4.03 (m, 4H, Δ6,7 and Δ5,6), 2.69 (ddd, $J = 13, 13, 3$ Hz, 1H, Δ5,6), 2.66 (ddd, $J = 13, 13, 3$ Hz, 1H, Δ6,7), 2.33 (dd, $J = 13, 11$ Hz, 1H, Δ5,6), 2.30 (dd, $J = 13, 11$ Hz, 1H, Δ6,7), 2.23 (m, 1H, Δ6,7), 2.28–2.17 (m, 2H, Δ5,6), 2.04–1.94 (m, 2H, Δ6,7), 1.99 (m, 1H, Δ5,6), 1.78 (m, 2H, Δ6,7 and Δ5,6), 1.66–1.58 (m, 4H, Δ6,7 and Δ5,6), 1.47 (s, 9H, Δ5,6), 1.45 (s, 9H, Δ6,7), 1.43–1.11 (m, 4H, Δ6,7 and Δ5,6), 0.17 (s, 9H, Δ5,6), 0.16 (s, 9H, Δ6,7); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 154.7 (Δ6,7 and Δ5,6), 149.3 (Δ6,7 and Δ5,6), 108.1 (Δ5,6), 102.6 (Δ6,7), 79.3 (Δ6,7 and Δ5,6), 49.0 (Δ6,7 and Δ5,6), 43.9 (Δ6,7 and Δ5,6), 39.6 (Δ5,6), 39.4 (Δ5,6), 37.3 (Δ6,7), 36.6 (Δ6,7), 32.4 (Δ5,6), 29.8 (Δ5,6), 28.5 (Δ6,7 and Δ5,6), 27.8 (Δ6,7), 26.5 (Δ5,6), 0.30 (Δ6,7 and Δ5,6); HRMS (EI) *m/z*: $[M - C_4H_8]^+$ calcd for $C_{17}H_{31}NO_3Si$, 269.1447; found, 269.1437. Anal. Calcd for $C_{17}H_{31}NO_3Si$: C, 62.93; H, 9.60; N, 4.30. Found: C, 62.7; H, 9.8; N, 4.2.

The crude mixture of Δ6,7 and Δ5,6 enol silanes (1.55 mmol) was dissolved in CH_2Cl_2 (20 mL) under a nitrogen atmosphere, and the solution was cooled to −78°. A solution of phenylselenyl chloride (0.30 g, 1.55 mmol) in CH_2Cl_2 (10 mL) was added to the reaction mixture, which was then stirred at −78° for 1 h before being quenched with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), and the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/EtOAc, 4:1) afforded a mixture of stereoisomeric selenides (0.57 g, 91%), which was used immediately in the next step. Selected data for the mixture of selenides: LRMS (FAB) *m/z*: $[M (^{80}Se) + H]^+$ 409 (27), $[M (^{78}Se) + H]^+$ 407 (16). The mixture of selenides (1.4 mmol) was dissolved in CH_2Cl_2 (20 mL), and the solution was cooled to −15° under a nitrogen atmosphere. Dimethyldioxirane (2.7 mmol) in acetone was added slowly to the reaction mixture, which was then stirred for 1 h before being diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (2 × 20 mL). After the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure, the residue was purified by column chromatography (petroleum ether/EtOAc, 4:1). This gave firstly, the Δ7,8 enone (0.12 g, 34% yield, 46% ee), followed by the Δ4a,5 enone (0.06 g, 16% yield, 78% ee), both as white solids. Percent ee for both isomers was determined from chiral shift NMR results using TFAE. Characterization data for the Δ7,8 enone: $[\alpha]_D^{25}$ −22.5 (*c* 0.4 in $CHCl_3$) [lit.[348] $[\alpha]_D^{26}$ −55.6 (*c* 1.2 in $CHCl_3$); IR (KBr) 1702, 1697, 1412, 1366, 1267, 1255, 1159 cm^{-1}; ^1H NMR (300 MHz, DMSO, 300 K) δ 6.80 (dd, $J = 10, 3$ Hz, 1H), 5.91 (ddd, $J = 10, 3, 1$ Hz, 1H), 4.14 (dddd, $J = 12, 4, 4, 2$ Hz, 1H), 4.12 (ddd, $J = 14, 4, 2$ Hz, 1H), 2.65 (ddd, $J = 13, 12, 3$ Hz, 1H), 2.47 (dd, $J = 12, 12$ Hz, 1H), 2.19 (dd, $J = 16, 13$ Hz, 1H), 2.16 (m, 1H), 2.14 (dd, $J = 16, 6$ Hz, 1H), 1.81 (m, 1H), 1.60 (m, 1H), 1.42 (s, 9H), 1.30 (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 197.0, 154.8, 150.2, 130.9, 80.0, 47.3, 44.9, 43.7, 40.9, 40.4, 31.5, 28.4. Characterization data for the Δ4a,5 enone: $[\alpha]_D^{25}$ +52.0° (*c* 0.3 in $CHCl_3$); IR (KBr) 1697, 1687, 1679, 1425, 1241, 1166 cm^{-1}; ^1H NMR (300 MHz, DMSO, 300 K) δ 5.92 (s, 1H), 4.05 (m, 1H), 3.99 (m, 1H), 2.86 (ddd, $J = 14, 12, 4$ Hz, 1H), 2.55 (dd, $J = 10, 10$ Hz, 1H), 2.51 (m, 1H), 2.46–2.24 (m, 4H), 2.02 (m, 1H), 1.53 (m, 1H), 1.43 (s, 9H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 196.5, 161.4, 152.8, 123.9, 78.1, 47.8, 42.3, 35.3, 34.9, 32.2, 27.1, 24.3; HRMS (EI) *m/z*: $[M - C_4H_8]^+$ calcd for $C_{14}H_{21}NO_3$, 195.0895; found 195.0869. Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.9; H, 8.6; N, 5.3.

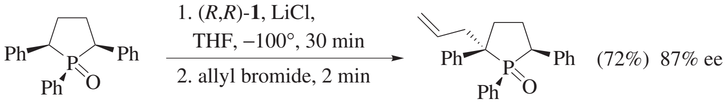


(1*S*)-([1-Methyl-3-(methylsulfonyl)cyclopent-3-en-1-yl])sulfonylbenzene (Enantioselective Rearrangement of an Episulfoxide Using a Chiral Lithium Amide and Alkylation with Iodomethane, Followed by Oxidation of the Sulfoxide Product to the Sulfone).[248,249] A solution of the chiral bis(lithium amide) was prepared by the addition of *n*-butyllithium (1.74 ml of a 1.4 M solution in hexane, 2.44 mmol) to a solution of (1*S*,2*S*)-*N*,*N*′-bis[(*R*)-1-phenylethyl]-1,2-diphenylethanediamine (555 mg, 1.32 mmol) in THF (3 mL) at −78° followed by warming to rt for 10 min. After the resulting solution was cooled to −78°, a solution of (1α,3β,5α,6α)-3-methyl-3-(phenylsulfonyl)-6-thiabicyclo [3.1.0]-hexane 6-oxide (300 mg, 1.11 mmol) and iodomethane (0.66 mL, 10.6 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 1 h and then was quenched with saturated aqueous NH_4Cl solution (20 mL), warmed to rt, and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried ($MgSO_4$), the solvents were removed under reduced pressure, and the residue was subjected to column chromatography (EtOAc) to give a 2:1 mixture of diastereomers of (1*S*)-([1-methyl-3-(methylsulfinyl)cyclopent-3-en-1-yl]sulfonyl)benzene (267 mg, 85%) as a colorless oil: HPLC (OD column, hexane/*i*-PrOH, 4:1) major diastereoisomer t_R 20.1 min (major), 23.4 min (minor), minor diastereoisomer t_R 27.8 min (minor), 29.3 min (major); IR ($CHCl_3$) 2933, 2851, 1621, 1586, 1459, 1378, 1308, 1142, 1122, 1089, 990, 959 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.95−7.86 (m, 2H + 2H), 7.75−7.54 (m, 3H + 3H), 6.24 (s, 1H + 1H), 3.52−3.40 (m, 2H + 2H), 2.65−2.35 (m, 5H + 5H), 1.49 (s, 3H), 1.48 (s, 3H); LRMS (EI) *m/z*: M^+ 284 (6), 188 (4), 159 (3), 143 (100), 142 (79), 127 (46), 95 (95), 79 (80), 77 (80); HRMS (EI) *m/z*: M^+ calcd for $C_{13}H_{16}O_3S_2$, 284.0541; found 284.0534.

A solution of Oxone® (521 mg, 0.85 mmol) in H_2O (5 mL) was added to a solution of the sulfoxides (241 mg, 0.85 mmol) in MeOH (5 mL), and the mixure was stirred for 1 h. The reaction mixture was diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The extracts were dried ($MgSO_4$), and the solvent was removed under reduced pressure. Purification by chromatography (EtOAc/petroleum ether, 3:2) gave (1*S*)-([1-methyl-3-(methylsulfonyl)cyclopent-3-en-1-yl]sulfonyl)benzene (147 mg, 58%) as a white solid. Recrystallization from *i*-PrOH/hexane, and then *i*-PrOH gave optically pure material for X-ray analysis: mp 124−125°; $[\alpha]_D$ −24 (*c* 0.4, $CHCl_3$); IR ($CHCl_3$); 2929, 2853, 1629, 1586, 1318, 1140 and 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.5 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 2H), 6.60 (s, 1H), 3.57 (d, *J* = 18.0 Hz, 1H), 3.61−3.49 (m, 1H), 2.93 (s, 3H), 2.63 (d, *J* = 17.0 Hz, 1H), 2.52 (d, *J* = 18.5 Hz, 1H), 1.51 (s, 3H); LRMS (CI) *m/z*: $[M + H]^+$301 (12), 283 (10), 209 (13), 203 (11), 171 (15), 159 (100), 143 (37), 125 (77), 97 (57), 79 (71); HRMS (CI) m/z: $[M + H]^+$ calcd for $C_{13}H_{16}O_4S_2$, 301.0568; found 301.0578. Anal. Calcd for $C_{13}H_{16}O_4S_2$: C, 51.98; H, 5.37; S, 21.35. Found: C, 51.85; H, 5.48; S, 21.12.



(3*S*,3a*S*,7a*R*)-2,3,3a,4-Tetrahydro-3-phenyl-2-(2′-phenylpropan-2′-yl)-(7a*H*)-isoindol-1,5-dione (Enantioselective Deprotonation and Dearomatizing Cyclization of an *N*-Benzyl-*N*-cumyl Anisamide Using a Chiral Lithium Amide).[260,262] To a suspension of (*R*)-*N*-isopropyl-1-phenylethylamine (2.8 g, 13.93 mmol) in THF (150 mL) at −78° was added dropwise *n*-butyllithium (11.14 mL of a 2.5 M solution in hexane, 27.86 mmol). The resulting mixture was allowed to warm to rt over 15 min, resulting in a clear yellow solution. This was then re-cooled to −78°, and a solution of *N*-benzyl-*N*-(1′-methyl-1′-phenylethyl)-4-methoxybenzamide (2.5 g, 6.96 mmol) in THF (50 mL) was added dropwise. The mixture was stirred at −78° for 30 min before being slowly warmed to rt over 5 h. The reaction was quenched with NH_4Cl, the layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic fractions were washed with 3 M aqueous HCl and brine, dried with $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (petroleum ether/EtOAc, 5:1) gave the title compound (1.50 g, 62%, 86% ee) as a white solid: mp 127−129°. Recrystallization from EtOAc afforded (3*S*,3a*S*,7a*R*)-2,3,3a,4-tetrahydro-3-phenyl-2-(2′-phenylpropan-2′-yl)-(7a*H*)-isoindol-1,5-dione (0.820 g, 34%, >99% ee): HPLC (Regis β-GEM, hexane/*i*-PrOH, 7:3) t_R 7.96 min, 8.57 min; $[\alpha]_D^{26}$ −224.0 (*c* 1.05, $CHCl_3$); IR (film) 2956, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.5−7.2 (m, 10H), 6.94 (dd, $J = 10, 5$ Hz, 1H), 6.17 (dd, $J = 10, 2$ Hz, 1H), 4.48 (d, $J = 2.5$ Hz, 1H), 3.70 (m, 1H), 2.83−2.52 (m, 3H), 1.86 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 171.9, 145.9, 144.7, 141.8, 130.6, 129.4, 128.5, 127.3, 126.2, 125.6, 67.6, 60.3, 42.7, 41.8, 39.4, 28.6, 27.5; LRMS (CI) m/z: $[M + H]^+$346 (20), 176 (100); HRMS m/z: M^+ calcd for $C_{23}H_{23}NO_2$, 345.1729; found 345.1732.



(1*S*,2*S*,5*S*)-2-(Prop-2′-enyl)-1,2,5-triphenylphospholane-1-oxide (Enantioselective Deprotonation of a Phospholane Using a Chiral Lithium Amide and Electrophilic Quench with Allyl Bromide).[255,256] A solution of the chiral lithium amide containing an equimolar amount of LiCl was prepared by treatment of a suspension of (*R*,*R*)-bis(1-phenylethyl)amine hydrochloride (287 mg, 1.1 mmol) in THF (5 mL), under N_2 at about −100°, with *n*-butyllithium (1.6 M in hexanes, 1.34 mL, 2.15 mmol). The suspension was allowed to warm to rt over a period of 20 min, during which time all the solid dissolved and the solution turned pale yellow. The solution was re-cooled to −100° ±2° (ethanol/N_2) and a solution of 1,2,5-triphenylphospholane-1-oxide (332 mg, 1.0 mmol) in THF (9 mL) was added dropwise over a period of 30 min, maintaining the temperature at −100° ±2°. After the deep orange/red solution was stirred at −100° for a further 30 min, freshly distilled allyl bromide (0.87 mL, 10 mmol) was added. Stirring of the yellow/orange solution was continued for 2 min before the addition of saturated aqueous NH_4Cl solution (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure, leaving a yellow oil. Purification by column chromatography (Et_2O) yielded (1*S*,2*S*,5*S*)-2-(prop-2′-enyl)-1,2,5-triphenylphospholane-1-oxide (269 mg, 72%, 87% ee) as a white solid: mp 183–189°; HPLC (Chiralcel OD, hexane/*i*-PrOH, 7:3, 1 mL min^{-1}) t_R 4.8 min (major), 7.0 min (minor); $[\alpha]_D^{23}$ +92 (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 2975, 1638, 1600, 1495, 1450, 1158, 1106 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.19–6.77 (m, 15H), 5.32 (m, 1H), 5.02 (d, J = 17.1 Hz, 1H), 4.97 (d, J = 10.1 Hz, 1H), 3.93 (app. dt, J = 23.5, 9.1 Hz, 1H), 3.10 (m, 1H), 2.86 (ddd, J = 14.2, 8.8, 5.5 Hz, 1H), 2.74–2.31 (m, 4H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 140.1, 136.2, 132.9, 132.7–125.2 (aromatic CH), 129.3, 118.4, 49.1 (d, J = 61 Hz), 46.5 (d, J = 59 Hz), 42.1, 30.7 (d, J = 15 Hz), 24.3 (d, J = 12 Hz); LRMS (EI) m/z: M$^+$ 372 (100), 331 (27), 268 (13), 205 (9), 129 (19), 91 (38); HRMS (EI) m/z: M$^+$ calcd for $C_{25}H_{25}OP$, 372.1643; found, 372.1639. Anal. Calcd for $C_{25}H_{25}OP$: C, 80.61; H, 6.77. Found: C, 80.46; H, 6.58.

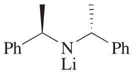
TABULAR SURVEY

An effort has been made to tabulate all reported examples of asymmetric transformations involving deprotonation using chiral lithium amide bases. A guide to the lithium amide bases used in the Tables is provided in Charts 1 and 2 preceding the Tables. It is important to note that the numbering of the bases in the Charts and the Tables is different from the numbering of the compounds for the text portion of this Chapter. The organization of the entries in all of the tables is by ascending order of the carbon count of the substrate. Protecting groups are not included in the carbon count. For organometallic complexes, the carbon count is applied only to the coordinating fragment that undergoes the asymmetric transformation. Unless stated, the quantity of TMSCl in the conditions is 5 equivalents. Isolated yields of the products are included in parentheses, and a dash (—) indicates that no yield was reported.

The following abbreviations (excluding those listed in “The *Journal of Organic Chemistry* Standard Abbreviations and Acronyms”) have been used in the tables:

DCB	2,6-dichlorobenzyl
diast.	diastereoisomer
DMM	dimethoxymethane
2,5-DMTHF	2,5-dimethyltetrahydrofuran
DNB	3,5-dinitrobenzoyl
eq	equivalents
EQ	external quench
LiTMP	lithium tetramethylpiperidide
Mes	mesityl
n.d.	not determined
NIS	*N*-iodosuccinimide
Np	naphthyl
Oxone®	potassium peroxymonosulfate, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$
PCC	pyridinium chlorochromate
PIDA	phenyliodine diacetate
PMHS	polymethylhydrosiloxane
PMP	*p*-methoxyphenyl
TBAT	tetrabutylammonium triphenyldifluorosilicate
TBDPS	*tert*-butyldiphenylsilyl

CHART 1. CHIRAL LITHIUM AMIDE BASES AND AMINES USED IN THE TABLES



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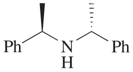

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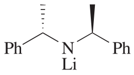

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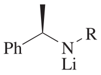
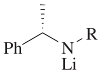
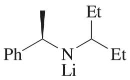


	R
3a	Me
3b	Et
3c	*n*-Pr
3d	*i*-Pr
3e	*t*-Bu
3f	CH_2*i*-Pr
3g	$(CH_2)_2$*t*-Bu
3h	$(CH_2)_2F$
3i	CH_2CHF_2
3j	$CH_2CF_2CF_3$
3k	$(CH_2)_2NMe_2$
3l	*c*-C_6H_{11}
3m	Ph
3n	Bn
3o	Tr



	R
4a	H
4b	Me
4c	Et
4d	CH_2*t*-Bu
4e	TBS
4f	*c*-C_6H_{11}
4g	*n*-C_6H_{13}
4h	4-ClC_6H_4
4i	2-Ad



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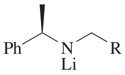
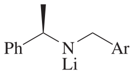
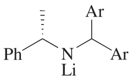


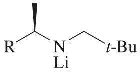
	R
6a	CF_3
6b	*t*-Bu
6c	1-Ad



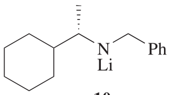
	Ar
7a	4-FC_6H_4
7b	4-$MeOC_6H_4$



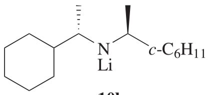
	Ar
8a	Ph
8b	Bn
8c	1-Np



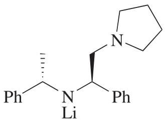
	R
9a	*c*-C_6H_{11}
9b	1-Np



10a



10b



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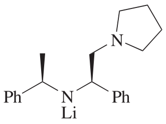

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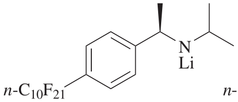

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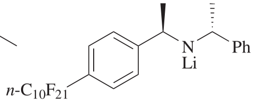

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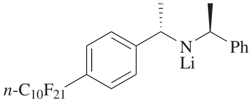

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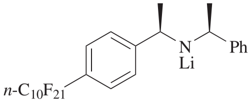

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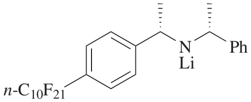

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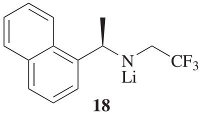
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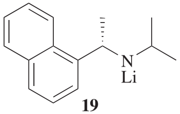
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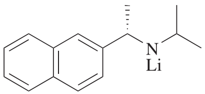
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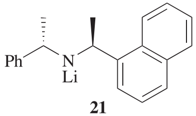
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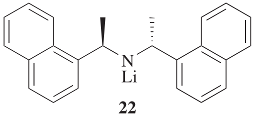
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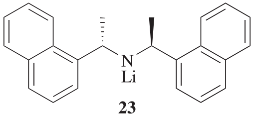
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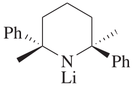
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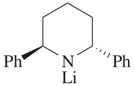
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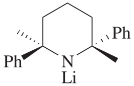
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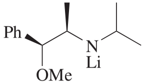
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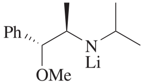
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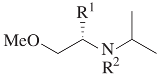
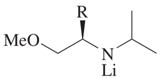
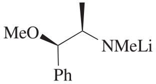


	R^1	R^2
29a	*i*-Pr	H
29b	Bn	Li
29c	*i*-Pr	Li



	R
30a	*t*-Bu
30b	Ph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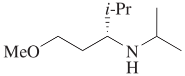
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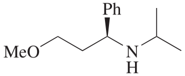
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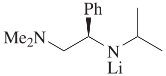
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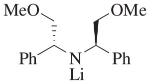
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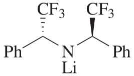
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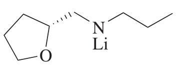
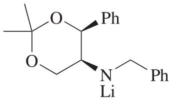

37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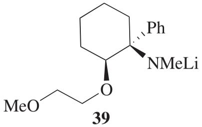
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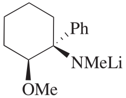
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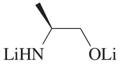
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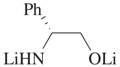
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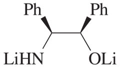
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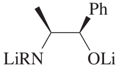
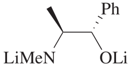


	R
44a	H
44b	Me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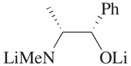
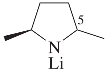
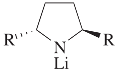

46

CHART 1. CHIRAL LITHIUM AMIDE BASES AND AMINES USED IN THE TABLES (*Continued*)

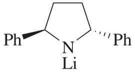


47

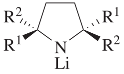
(config. at C5 not specified)



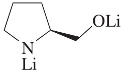
	R
48a	Me
48b	Ph



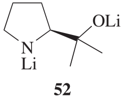
49



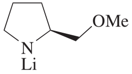
	R^1	R^2
50a	Me	Ph
50b	Ph	Me



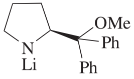
51



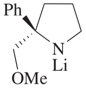
52



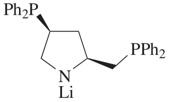
53



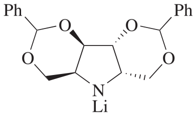
54



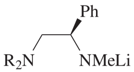
55



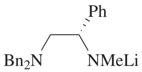
56



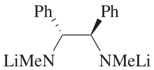
57



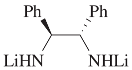
	R
58a	Me
58b	Et



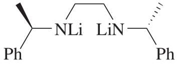
59



60

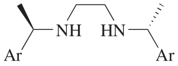


61

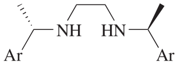


62

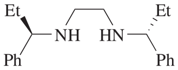
63



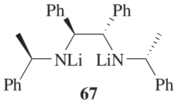
	Ar
64a	Ph
64b	2-$MeOC_6H_4$



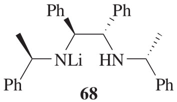
	Ar
65a	Ph
65b	1-Np
65c	2-Np



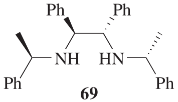
66



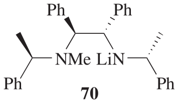
67



68



69



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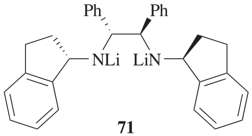
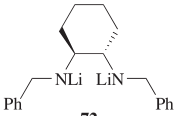
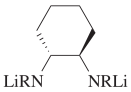


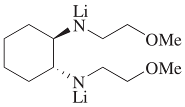
71



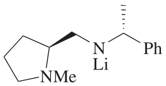
72



	R
73a	Me
73b	*i*-Pr



74



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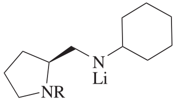
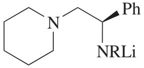
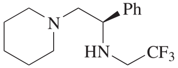


	R
76a	Me
76b	Et
76c	*i*-Pr
76d	CH$_2$*i*-Pr
76e	CH$_2$*t*-Bu



	R
77a	Me
77b	Et
77c	*n*-Pr
77d	*i*-Pr
77e	*t*-Bu
77f	CH$_2$*i*-Pr
77g	CH(*i*-Pr)$_2$
77h	CH$_2$*t*-Bu
77i	CH$_2$F
77j	(CH$_2$)$_2$F
77k	CH$_2$CHF$_2$
77l	CH$_2$CF$_3$
77m	CH$_2$CF$_2$CF$_3$



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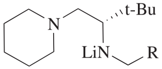
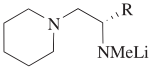
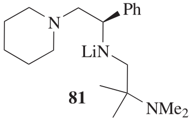


	R
79a	*t*-Bu
79b	CF$_3$



	R
80a	*c*-C$_6$H$_{11}$
80b	Ph
80c	4-PhC$_6$H$_4$



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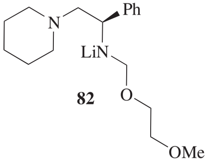

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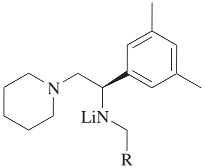
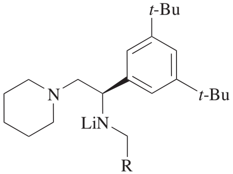
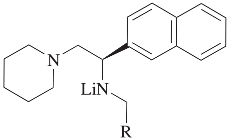


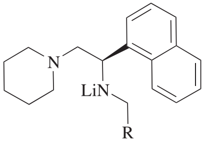
	R
83a	*t*-Bu
83b	CF$_3$



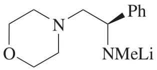
	R
84a	*t*-Bu
84b	CF$_3$



	R
85a	*t*-Bu
85b	CF$_3$



	R
86a	*t*-Bu
86b	CF$_3$



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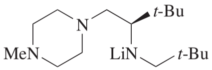

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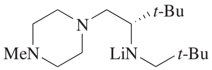

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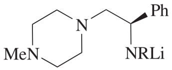
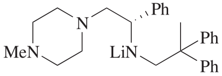


	R
90a	*i*-Pr
90b	CH$_2$*t*-Bu
90c	CH$_2$CF$_3$
90d	Bn
90e	(CH$_2$)1-Ad



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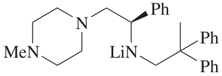

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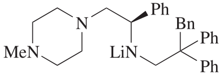
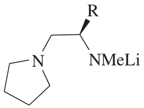
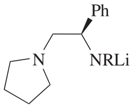


93

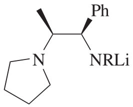
CHART 1. CHIRAL LITHIUM AMIDE BASES AND AMINES USED IN THE TABLES (*Continued*)



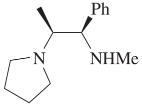
	R
94a	*i*-Pr
94b	*t*-Bu



	R
95a	H
95b	Me
95c	*i*-Pr
95d	*t*-Bu
95e	Bn



	R
96a	H
96b	Me
96c	CH_2CF_3



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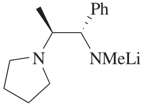

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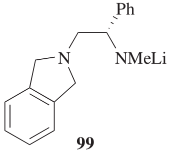

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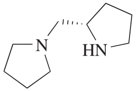

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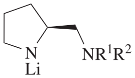
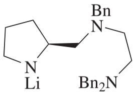


	R^1	R^2
101a	Et	Et
101b	Me	Ph
101c	*i*-Pr	Et
101d	*i*-Pr	*i*-Pr



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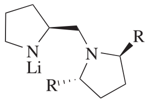
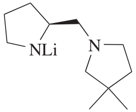


	R
103a	H
103b	Me



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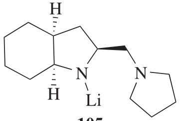

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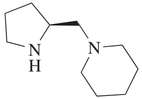

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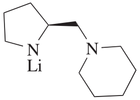

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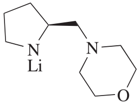

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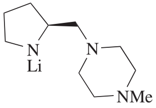

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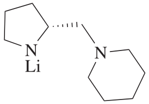

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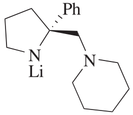

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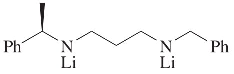

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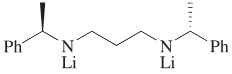

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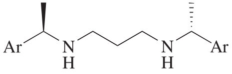
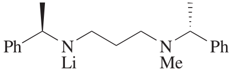


	Ar
114a	Ph
114b	2-MeOC$_6$H$_4$



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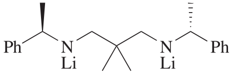

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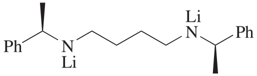

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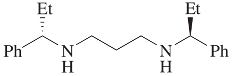
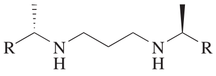
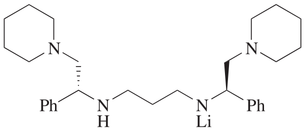


118



	R
119a	*t*-Bu
119b	1-Np



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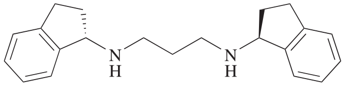
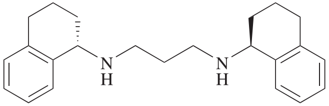
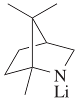


121



122

CHART 1. CHIRAL LITHIUM AMIDE BASES AND AMINES USED IN THE TABLES (*Continued*)



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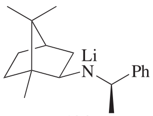

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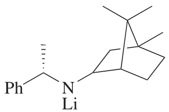

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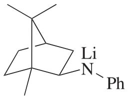

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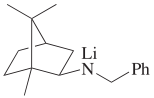

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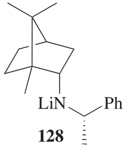

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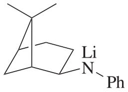

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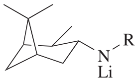
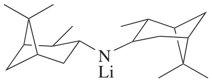


	R
130a	*i*-Pr
130b	c-C_6H_{11}
130c	Ph



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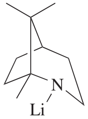

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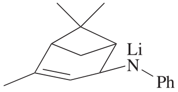

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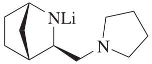

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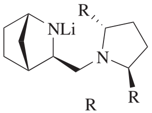
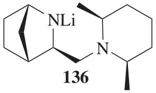


	R
135a	Me
135b	Et



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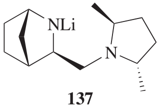

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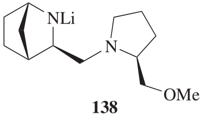

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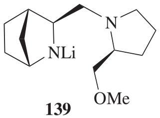

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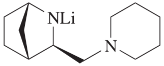

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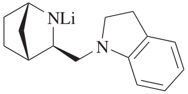

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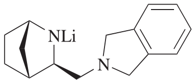
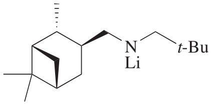
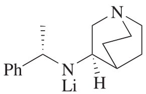


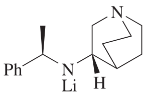
142



143



144



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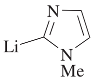

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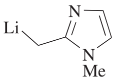
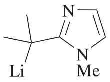
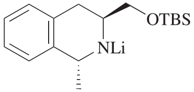


147



148

lithiated imidazoles used as bases



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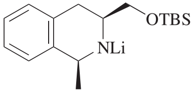
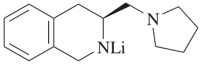
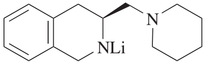


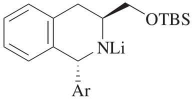
150



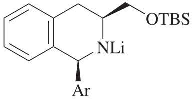
151



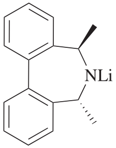
152



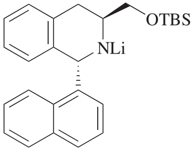
	Ar
153a	Ph
153b	Mes



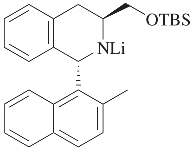
	Ar
154a	Ph
154b	Mes



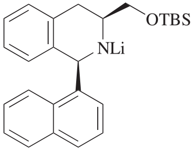
155



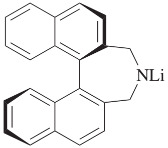
156



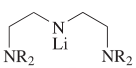
157



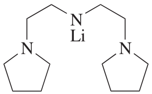
158



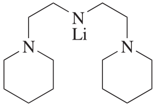
159



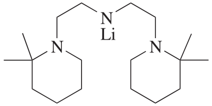
	R
160a	Et
160b	*n*-Pr



161



162



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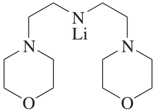
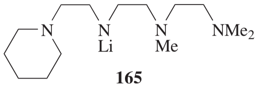
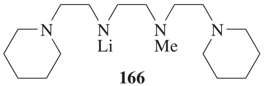


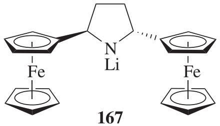
164



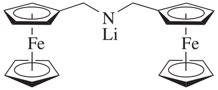
165



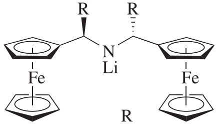
166



167



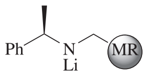
168



	R
169a	Me
169b	Ph

CHART 2. POLYMER-SUPPORTED LITHIUM AMIDE BASES USED IN TABLES

MR = Merrifield resin SP = soluble polymer PS = cross-linked polystyrene
copolymer of styrene and 4-chloromethylstyrene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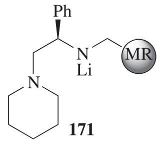
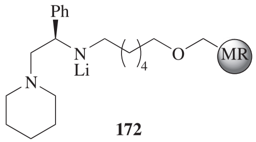
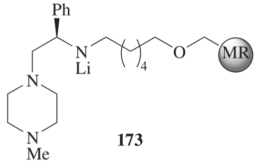

171


172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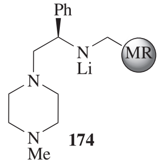
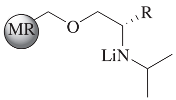
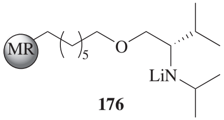
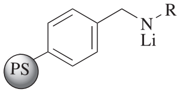

174

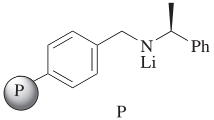


	R
175a	Me
175b	*i*-Pr
175c	Bn

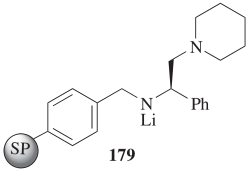

176

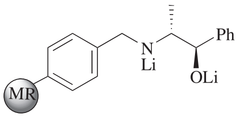


	R
177a	*i*-Pr
177b	*c*-C_6H_{11}



	P
178a	MR
178b	SP


179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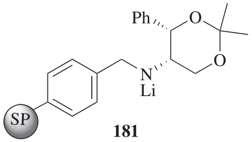
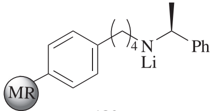
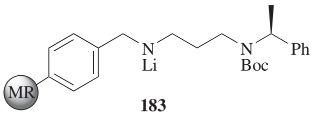
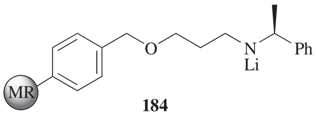

181


182



183



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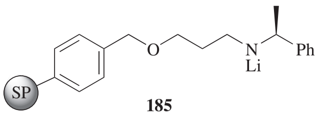
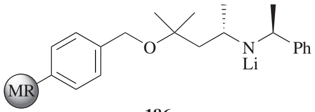


185



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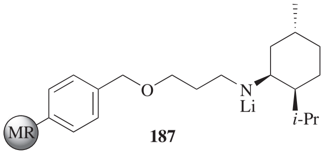
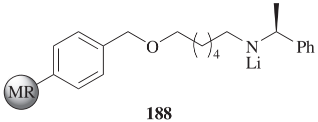
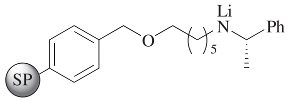


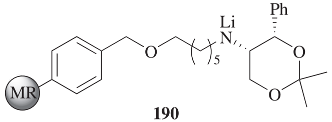
187



188



189



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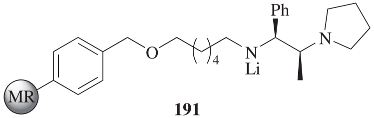

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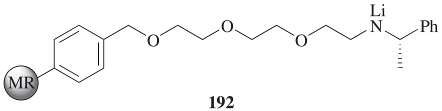
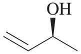
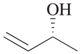
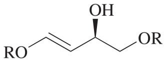
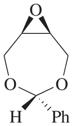
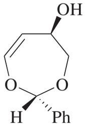
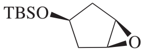
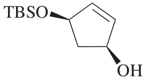


192

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*			
C_4 	**103a** (1.5 eq), DBU (1.5 eq), THF, rt, overnight	 (60)[a] 70–72% ee	39, 349
	76b (1.5 eq), HMPA (1.65 eq), THF, rt, overnight	 (58)[a] 62% ee[b]	349
	**103a** (1.5 eq), DBU (1.5 eq), THF, rt, overnight	 R / % ee[b] Bn (74) 40 MOM (80) 40	350
	**103a** (1.5 eq), DBU (1.5 eq), THF, rt, overnight	 (95) 76% ee[b]	350
C_5 	**103a** (1.6 eq), 4°, 3 h	 Solvent / % ee[c] THF (76) 66	274, 273, 275
		Et_2O (83) 70–72	274, 273, 275
		benzene (92) 90	274, 273, 275
		toluene (84) 84	274, 273
		hexane (91) 88–90	274, 273, 275

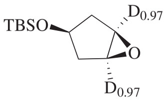
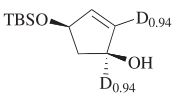
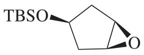
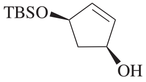
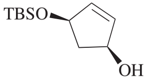
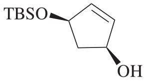
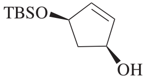
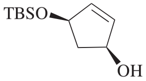
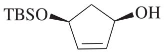
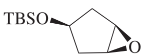
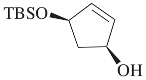
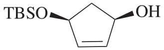
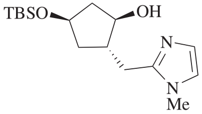
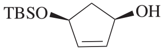
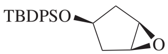
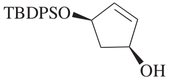
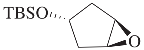
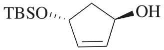
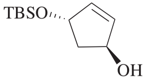
	**103a** (3 eq), benzene, 0° to rt, 2 h		(50) —% ee	38, 37
	**108** (1.6 eq), 4°, 3 h		Solvent — % ee[c] THF (65) 26 benzene (78) 89	274, 273
	95b (1.1 eq), 0° to rt, 10 h		Solvent — % ee[d] THF (65) 74 benzene (40) 88 Et_2O (65) 82	95, 94
	77a (1.1 eq), benzene, 0° to rt, 30 h		(66) 97% ee[d]	94
	87 (1.1 eq), benzene, 0° to rt, 30 h		(60) 94% ee[d]	94
	44a (3.5 eq), THF, −78° to rt, 16 h		(70) 58% ee[e]	34
	ent-**44a** (3.5 eq), THF, −78° to rt, 16 h		(77) 70% ee[e]	34

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	**44b** (4 eq), THF, −78° to rt, 16 h	 (90) 40% ee[e]	34
	46 (4 eq), THF, −78° to rt, 16 h	 (90) 22% ee[e]	34
	96b (0.2 eq), **147** (1.8 eq), THF, 0° to rt, 28 h	 (59) ~10% ee	111
	134 (*x* eq), LDA (2 eq), DBU (5 eq), THF, 0°, 4 h	 *x* — % ee 1.2 (85) 95 0.05 (60) 67	106
	**96b**, THF, 0° to rt, 26 h	 (54) 85% ee[d]	281
	**103a** (1.5 eq), hexane, reflux, 3.5 h	 (58) 17% ee	273
	103a (1.5 eq), DBU (1.65 eq), hexane, rt, overnight	 (93) 73% ee	273

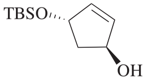
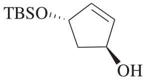
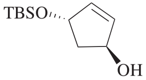
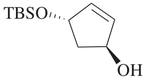
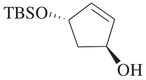
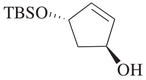
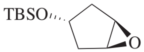
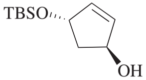
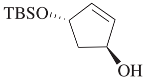
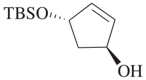
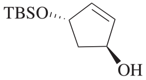
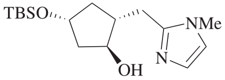
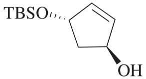
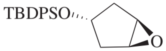
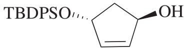
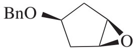
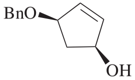
103a (1.5 eq), benzene, rt, overnight		(65) 1% ee				273
103a (1.5 eq), reflux, 1–3.5 h		Solvent			% ee	273
		Et$_2$O		(73)	27	
		DMM		(75)	42	
		DME		(57)	49	
		THF		(78)	58	
		THF/py		(93)	57	
103a (1.5 eq), additive (1.65 eq), THF, rt		Additive	Time (h)		% ee	
		Et$_3$N	2	(78)	62	273
		TMEDA	overnight	(82)	61	273
		HMPA	1	(91)	62	273
		DBN	overnight	(59)	68	273
		DBU	overnight	(97)	74	273, 275
108 (1.5 eq), DBU (1.65 eq), THF, rt, overnight		(86) 71% ee				273
107 (1.5 eq), DBU (1.65 eq), THF, rt, 3 h		(64) 53% ee				273
109 (1.5 eq), THF, rt, overnight		(81) 52% ee				273

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	**95b** (1.1 eq), Et_2O, 0° to rt, 24 h	 (38) 55% ee^d	95, 94
	77a (1.1 eq), Et_2O, 0° to rt, 24 h	 (35) 68% ee^d	94
	44b (4 eq), THF, −78° to rt, 16 h	 (38) 36% ee^f	34
	96b (0.2 eq), **147** (1.8 eq), THF, 0° to rt, 28 h	 (15) 72% ee^d +  (53) ~10% ee	111
	96b (0.2 eq), **148** (1.8 eq), THF, 0° to rt, 28 h	 (43) 68% ee^d	111
	*ent*-**96b**, THF, 0° to rt, 26 h	 (76) 88% ee^d	281
	**44a** (3 eq), −78 to 0°, 16 h	 Solvent / % ee^{e,f}	
		THF (91) 86	33, 34, 37
		benzene/THF (3:1) (98) 80	33

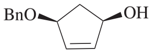
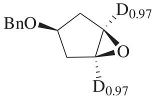
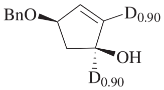
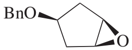
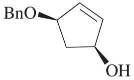
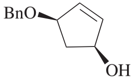
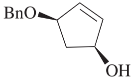
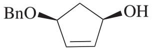
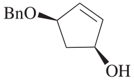
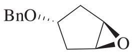
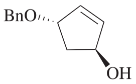
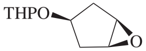
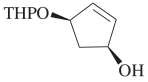
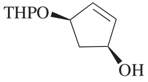
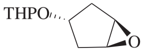
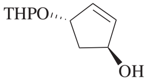
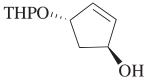
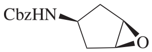
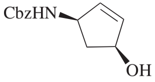
	ent-**44a** (3 eq), −78 to 0°, 16 h	 Solvent / % ee^e THF (92) 80 benzene/THF (3:1) (96) 74	33, 34 33
	**44a** (3 eq), benzene/THF (3:1), 0° to rt, 2 h	 (90) —% ee	38, 37
	**41** (3 eq), THF, −78 to 0°, 16 h	 (40) 0% ee^d	33
	42 (3 eq), THF, −78 to 0°, 16 h	 (60) 0% ee^d	33
	44b (3 eq), THF, −78 to 0°, 16 h	 (51) 14% ee^d	33
	45 (3 eq), THF, −78 to 0°, 16 h	 (96) 22% ee^d	33
	95b, 0° to rt, 10 h	 Solvent / % ee^d THF (70) 43 benzene (78) 25 Et_2O (70) 36	95

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	**44b** (4 eq), THF, −78° to rt, 16 h	 (38) 36% ee[f]	34
	**103a** (1.6 eq), 4°, 3 h	 Solvent — % ee THF (89)[a] 62 benzene (77)[a] 89	274, 273
	95b, 0° to rt, 10 h	 Solvent — % ee[d] THF (50) 46 benzene (30) 29 Et_2O (50) 47	95
	**95b** (1.1 eq), Et_2O, 0° to rt, 24 h	 (40–50) 59% ee[d]	95, 94
	77a (1.1 eq), Et_2O, 0° to rt, 24 h	 (52) 21% ee[d]	95, 94
	**103a** (3 eq), DBU (*x* eq), 20°, 4–7.5 h	 Solvent *x* — % ee toluene 0 (19) 41 THF 0 (61) 74 THF 3.3 (59) 83	96

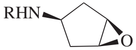
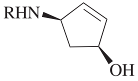
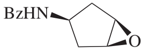
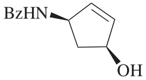
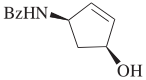
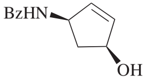
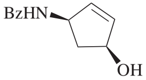
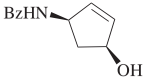
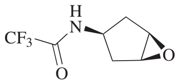
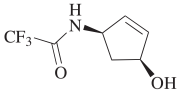
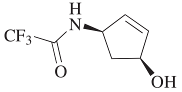
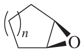
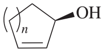
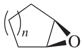
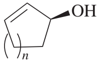
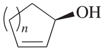
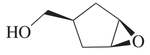
	**105** (3 eq), THF, 0°, 20 h		R — % ee Cbz (69) 90 Bz (82) 90	96
	**95b** (3 eq), THF, 0° to rt, 20 h		(73) 60% ee	98, 351, 97
	96b (3 eq), THF, 0° to rt, 20 h		(51) 92% ee	97, 351
	103a (0.2 eq), **177b** (1.8 eq), DBU (3.3 eq), THF, 16 h		(83) 81% ee	113
	105 (0.1 eq), c-$C_6H_{11}NBnLi$ (2.9 eq), THF, −15°, 12 h		(87) 67% ee	113
	105 (*x* eq), **177b** (2.8–2.9 eq), DBU (3.3 eq), THF		*x* Temp (°) Time (h) — % ee 0.2 0 12 (87) 94 0.2 −15 16 (89) 97 0.2 −30 48 (86) 97 0.15 −15 24 (81) 95 0.1 −15 36 (84) 94	113

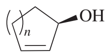
TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	**95b** (3 eq), THF, 0° to rt, 20 h	 (52) 46% ee[d]	351, 97
	96b (3 eq), THF, 0° to rt, 20 h	 (73) 88% ee[d]	351, 97
C_{5-7} 	**135a** (0.05 eq), LDA (1.5 eq), DBU (5 eq), THF, 6–24 h		105
		n Temp (°) % ee	
		1 rt (81) 96	
		2 0 (95) 99	
		3 0 (93) >99	
C_{5-8} 	**103a** (1.5 eq), DBU (1.5 eq), THF		
		n Temp Time % ee[b]	
		1 reflux 1.5–4 h (49)[a] 31	349
		1 reflux 2 h (53)[a] 41	39
		4 rt overnight (45)[a] 58	349, 39
		4 reflux 2 h (84)[a] 50	349, 39
	76b (1.5 eq), HMPA (1.65 eq), THF		349
		n Temp Time % ee[b]	
		1 reflux 1.5–4 h (48)[a] 15	
		2 rt overnight (80)[a] 67[m]	
		4 rt overnight (56)[a] 42	
		4 reflux 1.5–4 h (61)[a] 34	

C$_6$

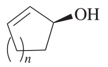


134 (*x* eq), LDA (2 eq), DBU (5 eq), THF, 0°



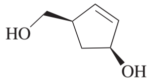
n	*x*	Time (h)		% ee	
1	1.2	24	(78)	95	107, 106
1	0.15	24	(67)	49	107, 106
2	1.2	6	(87)	97	107
2	0.05	6	(91)	96	107, 106
3	1.2	6	(93)	98	107
3	0.05	6	(89)	96	107, 106
4	1.2	36	(84)	81	107
4	0.05	36	(81)	78	107, 106

105 (*x* eq), **177b** (1.45–1.8 eq), THF



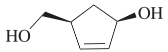
n	*x*	Temp	Time (h)		% ee^c	
1	0.2	rt	24	(50)	77	113
1	0.05	rt to 55°	50	(48)	69	113
2	0.2	rt	12	(89)	94	112, 113
2	0.05	rt	36	(91)	92	112, 113
3	0.05	rt	72	(54)	94	112, 113
4	0.2	55°	12	(87)	52	113

44a (3 eq),
benzene/THF (2:1),
0° to rt, 24 h

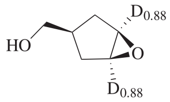


(66) 95% ee^d 280, 282

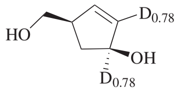
ent-**44a** (3 eq),
benzene/THF (2:1),
0° to rt, 24 h



(57) 95% ee^d 280, 282

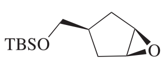
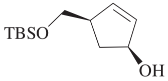
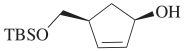
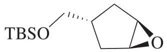
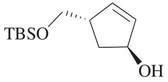
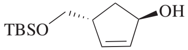
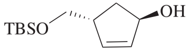
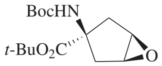


44a (3 eq), benzene/THF (3:2), 0° to rt, 13 h



(48) ~95% ee 38, 37

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6				
	**103a** (1.5 eq), DBU (1.5 eq), THF, rt, 48 h		(28) 72% ee^d	279
	ent-**95b** (2 eq), solvent, 0°, 48 h		Solvent — % ee^d THF (20) 80 benzene (14) 40	352, 336
	**103a** (1.8 eq), DBU (1.8 eq), THF, rt, 48 h		(74) 83% ee^d	279
	134 (0.2 eq), LDA (2 eq), DBU (5 eq), THF, rt, 48 h		(42) 95% ee	106
	ent-**95b** (2 eq), THF, 0°, 48 h		(—) 27% ee^d	336
	Lithium amide (3 eq), THF, 0° to rt, 18 h		Lithium Amide — % ee^g **95b** (57) 25 **134** (46) 42 **1a** (60) 52 **3n** (47) 26 **67** (48) 93	91
	43 (3 eq), THF, 0° to rt, 18 h		(10) 42% ee^g	91

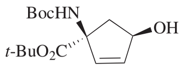
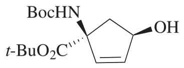
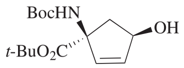
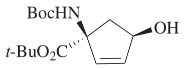
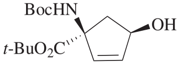
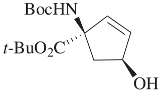
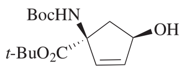
62 (3 eq), THF, 0° to rt, 18 h		(25) 78% ee[g]	91
67 (*x* eq), LDA (*y* eq), THF, 0°, 18–22 h		*x* *y* % ee 2.2 0 (75) 97 1.1 0 (46) 83 1.1 1.1 (64) 89 0.2 2.2 (6) 66	91
67 (1.1 eq), 2-lithio-1,3- dimethoxybenzene (3.3 eq), THF, 0°, 19 h		(70) 90% ee	91
62 (2.2 eq), THF		Temp (°) Time (h) % ee 0 4 (66) 86 −10 1.25 (71) 89 −40 14 (79) 95 −55 18 (80) 97 −78 7 (76) 98	91
62 (1.1 eq), THF, 0°, 18 h		(40) 75% ee	91
1. NaH (1.5 eq), THF, 22°, 1 h 2. **62** (1.1 eq), 0°, 7 h		(61) 32% ee	91
64a (2.2 eq), *n*-BuLi (3.3 eq), THF, 0°, 7 h		(75) 62% ee	91

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	**113** (2.2 eq), THF, −10°, 1.25 h	 (76) 93% ee	91
	117 (2.2 eq), THF, −10°, 2 h	 (52) 4% ee	91
	115 (2.2 eq), THF, −10°, 3 h	 (63) 6% ee	91
	112 (2.2 eq), THF, −10°, 1 h	 (12) 50% ee	91
	116 (2.2 eq), THF, −10°, 3 h	 (68) 84% ee	91
	113 (2.2 eq), THF/MTBE/hexanes	 Temp (°) Time (h) % ee –5 1 (78) 93 –25 3 (84) 96 –45 6 (85) 98–99 –78 7 (80) 99	91

113 (2.2 eq),
solvent/hexanes (6:1),
THF (*x* eq), −5°, 1.5 h



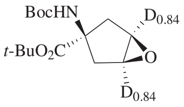
Solvent	x		% ee	
THF	—	(64)	94	
MTBE	0	(73)	84	
MTBE	4.4	(73)	88	
MTBE	22	(77)	88	
toluene	0	(39)	35	*ent*-product
toluene	4.4	(53)	90	
toluene	22	(65)	92	

91

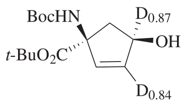
113 (2.2 eq), additive (5 eq),
THF/hexanes (6:1),
−5°, 1.5 h

Additive		% ee
—	(75)	92
LiOH	(77)	91
LiCl	(76)	84
LiO*t*-Bu	(69)	75
NaO*t*-Bu	(39)	12

91

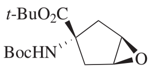


113 (2.2 eq), THF,
0°, 1.5 h

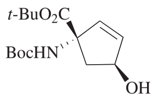


(63) 93% ee

91



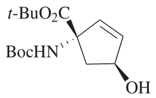
67 (2.2 eq), THF,
0°, 16 h



(36) 61% ee

91

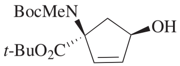
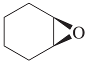
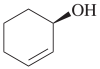
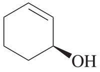
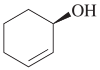
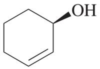
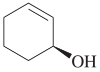
113 (2.2 eq), THF,
−45°, 1.25 h



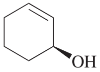
(3) 48% ee

91

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

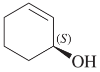
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	**67** (1.2 eq), THF, 0°, 5 h	 (54) 85% ee	91
	**47** (2 eq), THF, 0° to reflux, 2 h	 (44) 3% ee	90
	4a (2 eq), THF, 0° to reflux, 2 h	 (51) 3% ee	90
	4c (2 eq), THF, 0° to reflux, 2 h	 (69) 13% ee	90
	Lithium amide (2 eq), THF, 0° to reflux, 2 h	 Lithium amide % ee *ent*-**3d** (95) 10 **2**^{h} (65) 36	90
	37 (2 eq), THF, 0° to reflux, 2 h	 (76) 21% ee	90

103a (1.5 eq), overnight

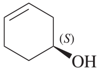


Solvent	Temp (°)		% ee	
THF	−78 to rt	$(78)^a$	77	40, 39
THF	0 to rt	$(75–77)^a$	$79–82^d$	40, 39, 353
THF	0	$(60)^a$	67^d	276
Et_2O	−78 to rt	$(71)^a$	48	39
DME	−78 to rt	$(72)^a$	68	39
benzene	reflux (2 h)	$(29)^a$	19	39

103a (1.2 eq), 0–20°



I +

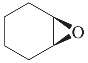
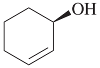
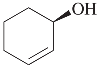
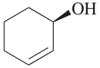
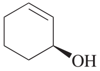
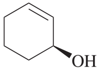
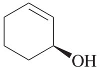


II

41

Solvent	Time (h)	$\mathbf{I}^i$	% ee **I**	$\mathbf{II}^i$	% ee **II**
THF	24	(98)	80	(0)	—
THF (20°)	48	(89)	70	(0)	—
DMTHF (*cis*/*trans*= 52:48)	10	(23)	43	(55)	8
DMTHF (*cis*/*trans*= 52:48)	24	(21)	24	(64)	3
DMTHF (99:1 *cis*)	12	(35)	66	(42)	19
DMTHF (99:1 *cis*)	24	(21)	33	(68)	6
DMTHF (99:1 *cis*)	72	(17)	29	(74)	5
DMTHF (2:98 *trans*)	10	(21)	33	(59)	4
DMTHF (2:98 *trans*)	20	(21)	13	(68)	3
DMTHF (2:98 *trans*)	48	(15)	7	(73)	1
5% THF in DMTHF(*cis*/*trans* = 52:48)	24	(34)	65	(41)	23
5% THF in DMTHF (99:1*cis*)	12	(66)	69	(19)	51
5% THF in DMTHF (99:1 *cis*)	24	(42)	66	(51)	25
5% THF in DMTHF (99:1 *cis*)	72	(30)	60	(63)	21
2.5% THF in DMTHF (99:1 *cis*) (20°)	12	(47)	78	(30)	43
2.5% THF in DMTHF (99:1 *cis*) (20°)	24	(33)	67	(45)	34
2.5% THF in DMTHF (99:1 *cis*) (20°)	120	(17)	47	(62)	24
MTHF	24	(77)	71	(14)	39
TMTHF	12	(31)	36	(5)	35
TMTHF	24	(25)	27	(32)	6
Et_2O	12	(22)	64	(23)	4
Et_2O	24	(17)	20	(53)	3 (*R*)
DME (20°)	12	(42)	76	(31)	16
DME (20°)	24	(26)	52	(59)	9

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	**76a** (1.5 eq), additive (1.65 eq), THF, rt, overnight	 Additive — % ee^m — (85)^a 45 HMPA (85)^a 53 pyridine (78)^a 46 Et_3N (80)^a 45 TMEDA (81)^a 45 DBU (81)^a 42	349
	75 (1.5 eq), HMPA (*x* eq), THF, rt, overnight	 *x* — % ee^m 0 (66)^a 50 2 (80)^a 33	349
	76c (1.5 eq), HMPA (1.65 eq), THF, rt, overnight	 (75)^a 49% ee^m	349
	Lithium amide (1.5 eq), HMPA (1.65 eq), THF, rt, overnight	 Lithium Amide — % ee^m **76d** (63)^a 33 **76e** (77)^a 53	349
	104 (1.2 eq), THF, 0° to rt	 (88) 78% ee	354
	107 (1.5 eq), THF, −78° to rt, overnight	 (71)^a 69% ee^m	40, 39, 49, 350

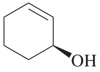
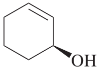
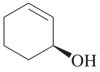
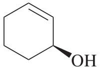
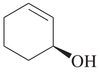
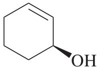
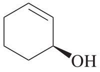
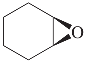
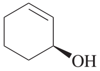
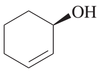
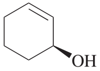
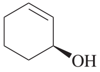
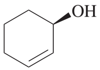
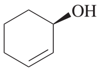
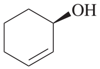
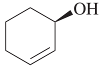
108 (1.5 eq), THF, overnight		Temp (°) | % ee^m −78 to rt | (70)^a | 73 0 to rt | (72)^a | 76	40, 39, 350 40
109 (1.5 eq), THF, −78° to rt, overnight		(67)^a 58% ee^m	40, 39, 350
Lithum amide (1.5 eq), THF, −78° to rt, overnight		Lithium Amide | % ee^m **101a** | (69)^a | 71 **101b** | (55)^a | 41	40, 39, 350
Lithium amide (1 eq), THF, 0°, 16 h		Lithium Amide | % ee^d **101c** | (75) | 70 **101d** | (66) | 40	353
102 (1 eq), THF, 0°, 16 h		(40) 20% ee^d	353
95b (1.1 eq), additive, 0° to rt, 16 h		Solvent | Additive | % ee^d THF | — | (60) | 77 Et_2O | — | (55) | 65 benzene | — | (50) | 63 THF | LiCl | (58) | 65 THF | *t*-BuOLi | (65) | 73	94, 355, 49 94 94 94 94
Lithium amide (1.1 eq), THF, 0° to rt, 16 h		Lithium Amide | % ee **94a** | (58) | (60)^d **94b** | (55) | (58)^d	355, 94 94

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	Lithium amide (1.1 eq), THF, 0° to rt, 16 h	 Lithium Amide — % ee **95a** (60) 0^d **95e** (52) 31^d **95c** (50) 13^d **77a** (60) 80^d	94
	80b (2 eq), THF, 0° to rt, 24 h	 (92) 79% ee	356
	87 (1.1 eq), THF, 0° to rt, 16 h	 (60) 77% ee^d	94
	96b (1 eq), THF, rt, 25 h	 (96)^i 93% ee	50, 49, 48, 357
	ent-**96b** (1 eq), THF, rt, 25 h	 (96)^i 93% ee	50
	Lithium amide (2 eq), THF, 0° to rt	 Lithium Amide — Time (h) — % ee **80c** 60 (35) 60 **80a** 48 (60) 70	356
	ent-**95b** (1 eq), alkali metal reagent (1 eq), Et_2O, rt	 (—) Alkali Metal Reagent — % ee *n*-BuLi 70 *n*-BuNa 37 *n*-BuLi/*n*-BuNa (1:1) 10	358

33 (2 eq),
alkali metal reagent (2 eq),
20°, 10 min

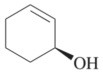


(—) <15% conv

Alkali Metal Reagent	Solvent	% ee
n-BuLi	THF	46
n-BuLi	Et_2O	27
n-BuNa	THF	24
n-BuNa	Et_2O	17
n-BuLi/*n*-BuNa (1:1)	THF	25
n-BuLi/*n*-BuNa (1:1)	Et_2O	9

359

32 (2 eq),
alkali metal reagent (2 eq),
20°, 10 min

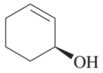


(—) <15% conv

Alkali Metal Reagent	Solvent	% ee
n-BuLi	THF	48
n-BuLi	Et_2O	3
n-BuNa	THF	30
n-BuNa	Et_2O	19
n-BuLi/*n*-BuNa (1:1)	THF	27
n-BuLi/*n*-BuNa (1:1)	Et_2O	19

359

29a (2 eq),
alkali metal reagent (2 eq),
20°, 10 min

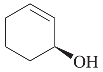


(—) <15% conv

Alkali Metal Reagent	Solvent	% ee
n-BuLi	THF	33
n-BuLi	Et_2O	4
n-BuNa	THF	25
n-BuNa	Et_2O	22
n-BuLi/*n*-BuNa (1:1)	THF	23
n-BuLi/*n*-BuNa (1:1)	Et_2O	8

359

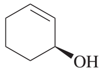
4b, THF, 20°, 22 h



(—) 47% conv, 19% ee

357

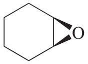
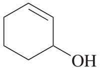
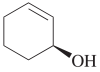
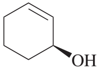
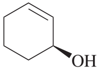
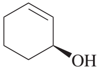
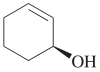
4a, THF, 20°, 5 h



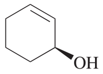
(—) 37% conv, 5% ee

357

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	**96a**, THF, 20°, 6.5 h	 (—) 15% conv, 0% ee	357
	4g, THF, 20°, 22 h	 (—) 43% conv, 21% ee	357
	103a (1.5 eq), DBU (1.65 eq), THF, rt, 12 h	 (80)^a 81% ee	104
	103a (0.5 eq), lithium amide (1.5 eq), THF, rt, 12 h	 Lithium Amide % ee Et$_2$NLi (81)^a 37 lithium pyrrolidide (59)^a 37 LDA (63)^a 48 (c-C_6H_{11})$_2$NLi (38)^a 4 LiTMP (72)^a 2	 104 104 104, 113 104 104
	103a (0.5 eq), LDA (1.5 eq), additive (2 eq), THF, rt, 12 h	 Additive % ee TMEDA (67)^a 43 HMPA (63)^a 54	104
	103a (0.5 eq), LDA (1.5 eq), DBU (x eq), THF, rt, 12 h	 x % ee 2 (71)^a 61 4 (79)^a 68 6 (81)^a 72 10 (82)^a 74	104

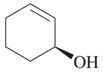
103a (*x* eq), LDA (*y* eq), DBU (6 eq), THF, rt, 12 h



x	y		% ee
0.33	1.67	$(83)^a$	73
0.2	1.8	$(69)^a$	68
0.1	1.9	$(76)^a$	68
0.05	1.95	$(65)^a$	59
0.2	1.0	$(71)^a$	75
0.12	1.08	$(75)^a$	69
0.06	1.14	$(61)^a$	59

104

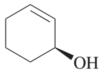
105 (1.5 eq), THF, rt, 6 h



$(86)^a$ 89% ee^c

44

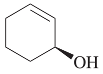
105 (*x* eq), LDA (1.8–2.0 eq), THF, rt



x	Time (h)		% ee^c
0.2	6	$(95)^a$	88
0.1	12	$(97)^a$	88
0.05	12	$(93)^a$	85
0.03	18	$(92)^a$	79
0.01	18	$(74)^a$	60

44

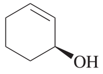
105 (0.2 eq), LDA (1.8 eq), additive (2 eq), THF, rt, 6 h



Additive		% ee^c
HMPA	$(66)^a$	76
DBU	$(68)^a$	78
DMPU	$(74)^a$	80

44

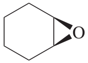
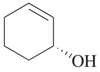
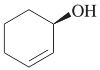
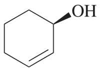
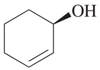
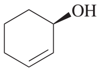
105 (*x* eq), LDA (1.8–1.95 eq), THF



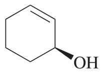
x	Temp (°)	Time (h)		% ee^c
0.2	0	18	$(89)^a$	94
0.1	0	24	$(74)^a$	89
0.05	0	42	$(51)^a$	81
0.2	−5°	24	$(84)^a$	94
0.2	−15°	72	$(73)^a$	93

44

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	**60** (1.5 eq), THF, 0° to rt, 21 h	 (27) 46% ee^{j}	45
	74 (1.5 eq), LiCl (*x* eq) 0° to rt	 *x* Solvent Time (h) % ee^{j} 0 THF 21 (68) 76 0 benzene 21 (42) 75 1.5 THF 46 (55) 55 1.5 benzene 46 (35) 50	45, 46 45 45 45
	74 (0.2 eq), *n*-BuLi (1 eq), hexane/benzene, 5° to rt, 48 h	 (47) 67% ee^{j}	45, 46
	74 (0.2 eq), LDA (1.5 eq), DBU (*x* eq), hexane/THF, 0° to rt	 *x* Time (h) % ee^{j} 0 22 (66) 32 6 43.5 (35) 13	45, 46
	74 (0.2 eq), MeLi (1 eq), 0° to rt	 Solvent Time (h) % ee^{j} THF 20 (54) 60 benzene 68 (56) 67	46

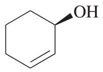
Lithium amide (0.2 eq),
MeLi (1.4 eq),
THF, 0° to rt



Lithium Amide	Time		% ee
65a	21 h	(80)	45
64b	4 d	(71)	56
65b	39 h	(63)	40
65c	46 h	(57)	34
118	63 h	(60)	57
114b	4 d	(29)	10
119b	45 h	(49)	68
122	42 h	(63)	39

46

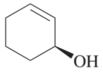
Lithium amide (0.2 eq),
MeLi (1.4 eq),
THF, 0° to rt



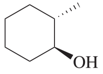
Lithium Amide	Time (h)		% ee
66	23	(80)	59
114a	72	(62)	57
121	40	(67)	16

46

119a (0.2 eq), MeLi (1.4 eq),
THF, 0° to rt, 6 d



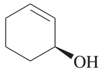
(36) 8% ee +



(11)

46

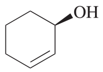
ent-**134** (0.05 eq), LDA (2 eq),
THF/DBU (95:5), 0°, 24 h



(90) 95% ee

107

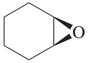
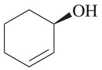
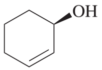
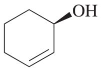
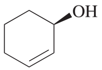
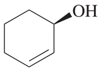
140 (0.05 eq), LDA (2 eq),
THF/DBU (95:5), 0°, 24 h



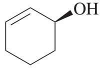
(85) 93% ee

107

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$ 	**134** (0.01 eq), LDA (2 eq), additive (5 eq), THF, 0°, 10 h	 (—) Additive · % Conv · % ee — · 40 · 44 DBU · 92 · 78 DBN · 87 · 67 DABCO · 36 · 41 DMPU · 49 · 44 TMEDA · 67 · 40 HMPA · 80 · 69 pyridine · 30 · 22 DMAP · 33 · 18 1-methylimidazole · <5 · 0 1,3-dioxane · 72 · 41	106
	134 (0.01 eq), LDA (2 eq), DBU (x eq), 0°, 10 h	 (—) x · Solvent · % Conv · % ee 5 · benzene · 58 · 35 5 · Et$_2$O · 63 · 38 10 · 1,4-dioxane · 70 · 65 10 · THF · 85 · 81	106
	134 (0.05 eq), LDA (2 eq), DBU (x eq), THF, 0°, 2 h	 (—) x · % Conv · % ee 1 · 65 · 70 10 · 46 · 97	106
	136 (0.05 eq), LDA (2 eq), DBU (x eq), THF, 0°, 2 h	 (—) x · % Conv · % ee 1 · 22 · 26 10 · 20 · 49	106
	138 (0.05 eq), LDA (2 eq), DBU (x eq), THF, 0°, 2 h	 (—) x · % Conv · % ee 1 · 26 · 24 10 · 20 · 85	106

139 (0.05 eq), LDA (2 eq), DBU (x eq), THF, 0°, 2 h

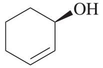


(—)

x	% Conv	% ee
1	38	64
10	31	79

106

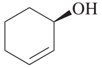
134 (0.02 eq), bulk base (1.5 eq), DBU (x eq), THF, 0°, 4 h



Bulk Base	x		% Conv	% ee
n-BuLi	10	(—)	61	95
n-BuLi	0	(—)	40	11
Et_2NLi	10	(—)	85	94
Et_2NLi	0	(—)	74	29
LDA	10	(—)	70	94
LDA	0	(—)	60	47
i-Bu_2NLi	10	(—)	66	93
i-Bu_2NLi	0	(—)	56	57
sec-Bu_2NLi	10	(—)	48	95
sec-Bu_2NLi	0	(—)	37	44
c-$C_6H_{11}NHLi$	10	(—)	36	68
c-$C_6H_{11}NHLi$	0	(—)	29	34
$(c$-$C_6H_{11})_2NLi$	10	(—)	63	93
$(c$-$C_6H_{11})_2NLi$	0	(—)	36	32
LiTMP	10	(—)	53	94
LiTMP	0	(—)	46	7
Ph_2NLi	10	(—)	5	26
Ph_2NLi	0	(0)	0	—

360

134 (0.05 eq), LDA (1.5 eq), LDA addition time, DBU (x eq), THF, 0°, 16 h

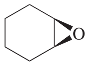
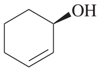
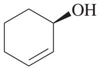
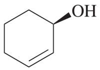
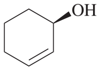
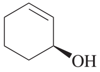


(—)

x	Addition Time	% Conv	% ee
0	5 min	53	70
0	5 h	53	86
10	5 min	98	95
10	5 h	95	98

360

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

<table>
<tr><th>Epoxide</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C$_6$
</td><td>135a (<i>x</i> eq), LDA (<i>y</i> eq), DBU (<i>z</i> eq), THF, 0°, 2 h</td><td> (—)<table><tr><th><i>x</i></th><th><i>y</i></th><th><i>z</i></th><th>% Conv</th><th>% ee</th></tr><tr><td>1.5</td><td>0</td><td>0</td><td>87</td><td>99</td></tr><tr><td>1.5</td><td>0</td><td>10</td><td>80</td><td>99</td></tr><tr><td>0.05</td><td>1.5</td><td>0</td><td>27</td><td>90</td></tr><tr><td>0.05</td><td>1.5</td><td>10</td><td>55</td><td>99</td></tr></table></td><td>105</td></tr>
<tr><td></td><td>137 (<i>x</i> eq), LDA (<i>y</i> eq), DBU (<i>z</i> eq), THF, 0°, 2 h</td><td> (—)<table><tr><th><i>x</i></th><th><i>y</i></th><th><i>z</i></th><th>% Conv</th><th>% ee</th></tr><tr><td>1.5</td><td>0</td><td>0</td><td>16</td><td>86</td></tr><tr><td>1.5</td><td>0</td><td>10</td><td>20</td><td>81</td></tr><tr><td>0.05</td><td>1.5</td><td>0</td><td>7</td><td>20</td></tr><tr><td>0.05</td><td>1.5</td><td>10</td><td>19</td><td>44</td></tr></table></td><td>105</td></tr>
<tr><td></td><td>135b (<i>x</i> eq), LDA (<i>y</i> eq), DBU (<i>z</i> eq), THF, 0°, 2 h</td><td> (—)<table><tr><th><i>x</i></th><th><i>y</i></th><th><i>z</i></th><th>% Conv</th><th>% ee</th></tr><tr><td>1.5</td><td>0</td><td>0</td><td>27</td><td>99</td></tr><tr><td>1.5</td><td>0</td><td>10</td><td>37</td><td>99</td></tr><tr><td>0.05</td><td>1.5</td><td>0</td><td>20</td><td>68</td></tr><tr><td>0.05</td><td>1.5</td><td>10</td><td>29</td><td>94</td></tr></table></td><td>105</td></tr>
<tr><td></td><td>103b (<i>x</i> eq), LDA (<i>y</i> eq), DBU (<i>z</i> eq), THF, 0°, 2 h</td><td> (—)<table><tr><th><i>x</i></th><th><i>y</i></th><th><i>z</i></th><th>% Conv</th><th>% ee</th></tr><tr><td>1.5</td><td>0</td><td>0</td><td>44</td><td>86</td></tr><tr><td>1.5</td><td>0</td><td>10</td><td>77</td><td>91</td></tr><tr><td>0.05</td><td>1.5</td><td>0</td><td>13</td><td>51</td></tr><tr><td>0.05</td><td>1.5</td><td>10</td><td>28</td><td>90</td></tr></table></td><td>105</td></tr>
<tr><td></td><td>100 (0.2 eq), <i>i</i>-Pr$_2$NH (<i>x</i> eq), <i>n</i>-BuLi (2.2 eq), DBU (5 eq), THF, 20°, 7 h</td><td><table><tr><th><i>x</i></th><th></th><th>% ee</th></tr><tr><td>0</td><td>(89)^i</td><td>79</td></tr><tr><td>2</td><td>(81)^i</td><td>74</td></tr></table></td><td>47, 49</td></tr>
</table>

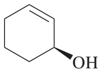
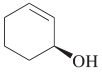
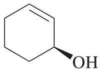
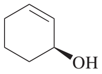
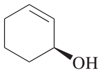
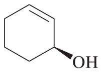
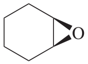
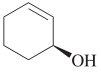
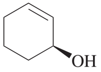
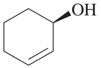
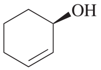
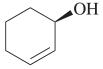
Conditions	Product	*x*	*y*	Base		% ee	Refs.
97 (0.2 eq), *i*-Pr$_2$NH (*x* eq), *n*-BuLi (2.2 eq), DBU (5 eq), THF, 20°, 56–69 h		0			(93)^i	69	47, 49
		2			(82)^i	16	47
97 (1 eq), *n*-BuLi (3 eq), DBU (*x* eq), THF, 20°, 60–240 h		2			(57)^i	89	47, 49
		5			(88)^i	94	
97 (*x* eq), 1-methylimidazole (2 eq), *n*-BuLi (*y* eq), THF, 20°, 28–198 h		0.2	2.2		(96)^i	93	47, 49, 48
		1	3		(96)^i	96	
97 (*x* eq), 1,2-dimethylimidazole (2 eq), *n*-BuLi (*y* eq), THF, 20°, 13–23 h		0.2	2.2		(96)^i	93	47, 49
		1	3		(96)^i	96	
96b (0.2 eq), bulk base (2 eq), THF, 20°, 14–32 h				LDA	(90)^i	22	49, 48
				2-lithiofuran	(91)^i	93	49
95b (*x* eq), bulk base (*y* eq) THF, 20°, 22–69 h		0.2	2	LDA	(86)^i	19	49
		0.2	2	**25**	(58)^i	73	
		0.2	2	**26**	(65)^i	73	
		1	1	**25**	(63)^i	72	
		1	1	**26**	(46)^i	13	

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	**103a** (*x* eq), bulk base (*y* eq) THF, 20°, 1–28 h	 *x* · Bulk Base · *y* · · % ee 0.2 · LDA · 2 · $(63)^i$ · 68 0.2 · **25** · 2 · $(84)^i$ · 76 1 · **25** · 6 · $(81)^i$ · 76 0.2 · **26** · 2 · $(78)^i$ · 80 1 · **25** · 1 · $(82)^i$ · 76 1 · **26** · 1 · $(73)^i$ · 78	49
	107 (*x* eq), bulk base (*y* eq) THF, 20°, 4–12 h	 *x* · Bulk Base · *y* · · % ee 0.2 · LDA · 2 · $(66)^i$ · 59 0.2 · **146** · 2 · $(80)^i$ · 75 1 · **146** · 6 · $(88)^i$ · 75 0.2 · **147** · 2 · $(71)^i$ · 75 1 · **147** · 6 · $(80)^i$ · 74 1 · **146** · 1 · $(86)^i$ · 75 1 · **147** · 1 · $(88)^i$ · 75	49
	131 (*x* eq), LDA (1.25 eq), THF, 0°, 15 h	 *x* · · % ee^d 0.05 · (59) · 80 0.1 · (66) · 81 0.15 · (69) · 83 0.2 · (77) · 95 0.25 · (78) · 89	114, 30
	131 (*x* eq), LDA (1.25 eq), THF, rt, 15 h	 *x* · · % ee^d 0.05 · (62) · 77 0.1 · (68) · 74 0.15 · (73) · 79 0.2 · (82) · 87 0.25 · (79) · 83	114, 30

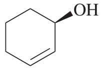
130b (x eq), LDA (1.25 eq),
THF, 0°, 15 h



x		% ee[d]
0.05	(55)	65
0.1	(57)	74
0.15	(66)	76
0.2	(70)	78

114, 30

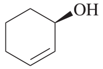
130c (x eq), LDA (1.25 eq),
THF, 0°, 15 h



x		% ee[d]
0.05	(51)	34
0.1	(53)	39
0.15	(58)	46
0.2	(57)	48

114, 30

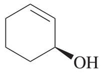
130a (x eq), LDA (1.25 eq),
THF, 0°, 15 h



x		% ee[d]
0.05	(50)	43
0.1	(51)	47
0.15	(55)	51
0.2	(58)	52

114, 30

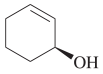
103a (0.5 eq),
bulk base (1.5 eq),
THF, rt, 24 h



Base		% ee[c]
i-PrBnNLi	(86)[a]	64
(c-C_6H_{11})BnNLi	(87)[a]	65

112, 113

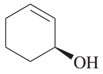
103a (0.5 eq), **177a** (1.5 eq),
THF, rt, 24 h



(84)[a] 73% ee[c]

112, 113

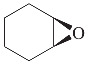
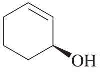
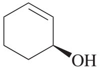
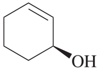
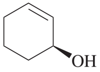
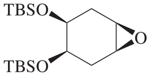
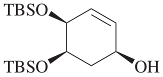
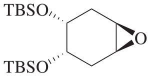
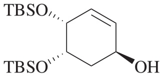
103a (x eq), **177b** (y eq),
THF, rt, 24–96 h



x	y		% ee[c]
0.5	1.5	(89)[a]	73
0.2	1.8	(87)[a]	64
0.1	1.9	(88)[a]	51

112, 113

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6 	**103a** (0.1 eq), **177b** (x eq), DBU (y eq), THF, rt, 24–72 h		x y % ee^c 1.9 2 (82)^a 63 1.9 6 (91)^a 71 1.9 10 (88)^a 71 1.4 6 (71)^a 75	113
	105 (x eq), **177b** (y eq), THF, rt, 12–72 h		x y % ee^c 0.2 1.8 (89)^a 94 0.1 1.9 (91)^a 91 0.05 1.95 (89)^a 89 0.05 1.45 (91)^a 92 0.05 1.3 (76)^a 91	112, 113
	188, THF, 20°, 12 h		(—) 67% conv, 91% ee	357
	191, THF, 20°, 72 h		(—) 12% conv, 70% ee	357
	**95b** (1.3 eq), THF, 0° to rt, 20 h		(38) 92% ee^d	361, 342
	**95b** (x eq), THF, 0° to rt		x Time (h) % ee^d 1.3 5 (93) 76 2 16 (71) 76	361, 342 351, 335, 92

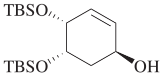
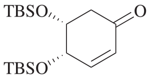
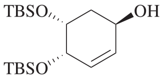
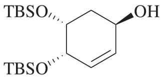
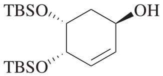
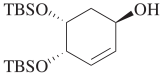
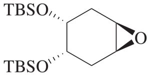
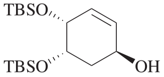
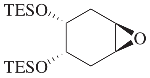
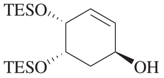
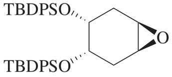
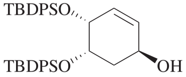
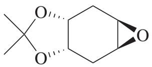
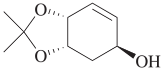
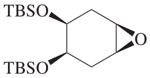
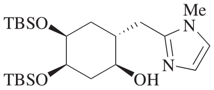
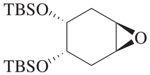
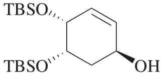
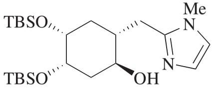
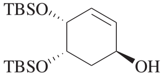
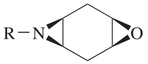
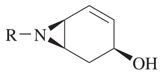
96b (x eq), **146** (y eq), THF, 0° to rt, 18–20 h		x	y		% ee^d	
		2	0	(90–94)	88–95	93, 351, 335, 92, 102
		0.2	1.8	(95)	82	111
		0	2	(43)	0	111
1. *ent*-**96b** (2 eq), THF, 0° to rt, 20 h 2. PCC		(88) 89% ee				93
134 (0.05 eq), LDA (2 eq), DBU (5 eq), THF, 0°, 6 h		(60) 97% ee^d				106
134 (0.2 eq), LDA (1.8 eq), DBU (5 eq), THF, 0° to rt, 20 h		(90) 95% ee^d				92
98 (2 eq), THF, 0° to rt, 20 h		(97) 86% ee^d				335, 92
Lithium amide (2 eq), THF, 0° to rt, 20 h		Lithium Amide			% ee^d	
		103a		(98)	84	92
		2		(65)	20	
		99		(53)	84	
		59		(95)	35	

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	Lithium amide (2 eq), THF, 0° to rt, 20 h	 Lithium Amide / % ee^d **58a** (90) 80 **58b** (93) 84 **95a** (81) 12 **95d** (62) 18	92
	**95b** (2 eq), THF, 0° to rt, 20 h	 (91) 70% ee^d	92
	Lithium amide (2 eq), THF, 0° to rt, 20 h	 Lithium Amide / % ee^d **95b** (76) 68 **96b** (85) 84	92
	Lithium amide (2 eq), THF, 0° to rt, 20 h	 Lithium Amide / % ee^d **95b** (39) 48 **96b** (56) 26	92
	**96b** (0.2 eq), **147** (1.8 eq), THF, 0° to rt, 64 h	 (98) <5% ee^d	111
	**96b** (0.2 eq), **147** (1.8 eq), THF, 0° to rt, 18 h	 (77) 66% ee^d +  (53) ~10% ee	111
	96b (0.2 eq), **148** (1.8 eq), THF, 0° to rt, 18 h	 (86) 73% ee^d	111

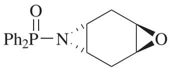


Lithium amide (1.2 eq), THF,
0° to rt, 16 h

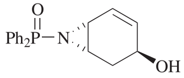


R	Lithium Amide		% ee
$Ph_2(O)P$	**95b**	(53)	45
$Ph_2(O)P$	**96b**	(60)	25
Ts	**95b**	(14)	66
Ts	**96b**	(23)	10

102, 103
102, 103
102
102



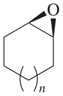
Lithium amide (1.2 eq), THF,
0° to rt, 16 h



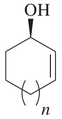
Lithium Amide		% ee[d]
95b	(62)	58
96b	(82)	68

103, 102

C_{6-8}



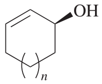
Lithium amide (0.05 eq),
LDA (2 eq),
DBU (5 eq), THF



Lithium Amide	*n*	Temp (°)	Time (h)	% Conv	% ee
141	1	0	2	38	73
141	3	rt	18	43	54
142	1	0	2	46	75
142	3	rt	18	40	37
136	1	0	2	22	46
136	3	rt	18	25	35
138	1	0	2	24	84
138	3	rt	18	22	43
ent-**96b**	1	0	2	3	<5
ent-**96b**	3	rt	18	16	14
ent-**95b**	1	0	2	3	<5
ent-**95b**	3	rt	18	18	9

106

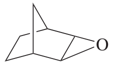
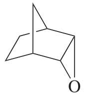
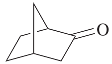
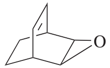
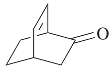
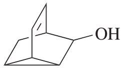
139 (0.05 eq), LDA (2 eq),
DBU (5 eq), THF



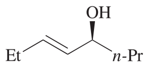
n	Temp (°)	Time (h)	% Conv	% ee
1	0	2	32	79
3	rt	18	24	40

106

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

<table>
<tr><th>Epoxide</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>$C_{6–10}$
</td><td>96b (3 eq), benzene/THF (3:2), 0° to rt, 12 h</td><td>
<table>
<tr><th>R</th><th></th><th>% ee^k</th></tr>
<tr><td>H</td><td>(66)</td><td>>95</td></tr>
<tr><td>Me</td><td>(63)</td><td>99</td></tr>
<tr><td>Bu</td><td>(67)</td><td>96</td></tr>
<tr><td>CH_2OBn</td><td>(76)</td><td>89</td></tr>
</table></td><td>35, 37</td></tr>
<tr><td>C_7
</td><td>Lithium amide (<i>x</i> eq), Et_2O, −78° to rt</td><td>
<table>
<tr><th>Lithium Amide</th><th><i>x</i></th><th></th><th>% ee^k</th></tr>
<tr><td>103a</td><td>1.8</td><td>(22)</td><td>1</td></tr>
<tr><td>96b</td><td>3</td><td>(29)</td><td>8</td></tr>
<tr><td>2</td><td>1.8</td><td>(65)</td><td>47</td></tr>
</table></td><td>299, 300</td></tr>
<tr><td></td><td>2 (1.8 eq), additive, 20 h</td><td>
<table>
<tr><th>Solvent</th><th>Additive</th><th>Temp (°)</th><th></th><th>% ee^k</th></tr>
<tr><td>Et_2O</td><td>—</td><td>0 to rt</td><td>(73)</td><td>49</td></tr>
<tr><td>benzene</td><td>—</td><td>0 to rt</td><td>(76)</td><td>31</td></tr>
<tr><td>pentane</td><td>—</td><td>−78 to rt</td><td>(64)</td><td>25</td></tr>
<tr><td>Et_2O</td><td>LiCl</td><td>−78 to rt</td><td>(68)</td><td>45</td></tr>
<tr><td>Et_2O</td><td>LiBr</td><td>−78 to rt</td><td>(59)</td><td>46</td></tr>
</table></td><td>299, 300</td></tr>
<tr><td></td><td>2 (1.8 eq), Et_2O, 0°</td><td> (40) 32% ee +  (20) 38% ee^k</td><td>299</td></tr>
<tr><td>C_8
</td><td>Lithium amide, Et_2O</td><td> I +  II
<table>
<tr><th>Lithium Amide</th><th>Temp (°)</th><th>Time (h)</th><th>I</th><th>% ee</th><th>II</th><th>% ee^k</th></tr>
<tr><td>2</td><td>0</td><td>16</td><td>(40)</td><td>19</td><td>(30)</td><td>16</td></tr>
<tr><td><i>ent</i>-67</td><td>20</td><td>8</td><td>(50)</td><td>−12</td><td>(15)</td><td>20</td></tr>
</table></td><td>362</td></tr>
</table>

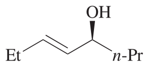
103a (1.5 eq), additive (1.5 eq),
THF, reflux, 1–3 h



Additive		% ee^b
—	(52)	52
pyridine	(63)	56
Et$_3$N	(66)	56
TMEDA	(64)	56
HMPA	(59)	50
DBN	(66)	58
DBU	(64)	60

39

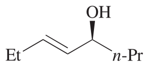
103a (1.5 eq), DBU (1.5 eq),
THF, rt, overnight



(66) 60% ee^b

39

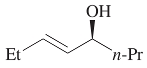
103a (0.2 eq), LDA (1 eq),
DBU (6 eq), THF, rt, 3 d



(54) 60% ee^b

104

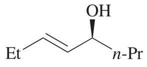
105a (0.2 eq), LDA (1.8 eq),
THF



Temp	Time (h)		% ee
rt	24	(85)	83
0°	48	(84)	86

44

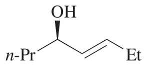
105 (0.1 eq), LDA (1.9 eq),
THF, rt, 24 h



(85) 82% ee

44

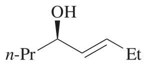
76b (1.5 eq), HMPA (1.65 eq),
THF, rt, overnight



(66) 59% ee^b

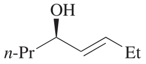
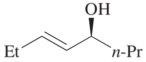
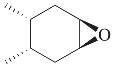
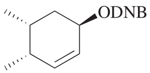
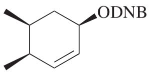
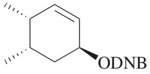
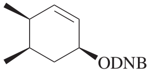
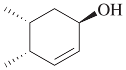
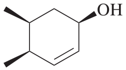
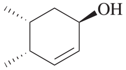
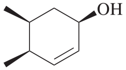
349

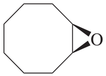
134 (x eq), LDA (2 eq),
DBU (5 eq),
THF, 0°, 24–36 h



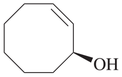
x		% ee^d	
1.2	(88)	67	107, 106
0.05	(82)	66	107

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	**135a** (0.05 eq), LDA (1.5 eq), DBU (5 eq), THF, 0°, 6–24 h	 (80) 91% ee	105
	105 (0.2 eq), **177b** (1.8 eq), THF, rt, 24 h	 $(85)^a$ 83% ee^b	112, 113
 *trans*/*cis* = 9:1	1. *ent*-**103a** (1.2 eq), THF, −78° to rt, 16 h 2. DNBCl, DMAP, py	 +  **I** 69% ee **II** 92% ee **I** + **II** (94), **I**/**II** = 89:11	99
	1. **103a** (1.2 eq), THF, −78° to rt, 16 h 2. DNBCl, DMAP, py	 +  **I** 59% ee **II** 91% ee **I** + **II** (95), **I**/**II** = 89:11	99, 100
	134 (0.05 eq), LDA (1.5 eq), DBU (5 eq), THF, 0°, 6–16 h	 +  (86) 94% ee (10) 97% ee	106, 105
	135a (0.05 eq), LDA (1.5 eq), DBU (5 eq), THF, 0°, 6–24 h	 +  (85) 98% ee (9) 99% ee	105



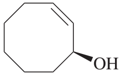
103a (1.5 eq), DBU (1.5 eq), THF



Temp	Time		% ee^{b}
rt	3 d	(45)	58
reflux	7 h	(84)	50

39

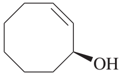
103a (0.2 eq), LDA (1 eq), DBU (6 eq), THF



Temp	Time		% ee^{b}
rt	3 d	(27)	54
reflux	7 h	(86)	45

39

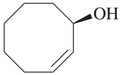
105 (0.2 eq), LDA (1.8 eq), THF, rt, 41 h



(73) 53% ee

44

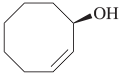
140 (0.05 eq), LDA (2 eq), DBU (5 eq), rt, 18 h



(—) 65% conv, 59% ee

106

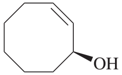
60 (1.5 eq), THF, −80° to rt, 49 h



(23) 4% ee^{j}

45

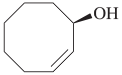
73a (1.5 eq), THF, −80° to rt, 72 h



(59) 21% ee^{j}

45

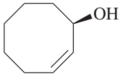
73b (1.5 eq), THF, −80° to rt, 19 h



(77) 32% ee^{j}

45

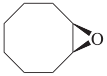
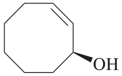
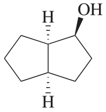
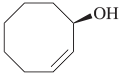
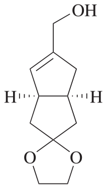
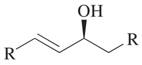
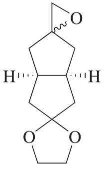
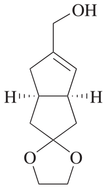
74 (1.5 eq), additive

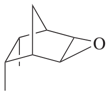
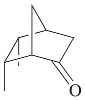
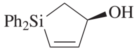
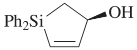
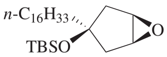
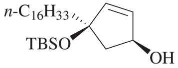
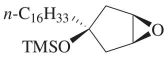
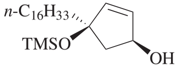


Solvent	Additive	Temp (°)	Time (h)		% ee^{j}
THF	—	−80 to rt	48	(30)	77
THF	*n*-BuLi (1.5 eq)	−80 to rt	48	(56)	76
benzene	—	5 to rt	44	(49)	87
THF	HMPA (6 eq)	−80 to rt	72	(38)	55

45

TABLE 1. TRANSFORMATIONS OF SYMMETRICAL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	**95b**, THF, 0° to rt	 (—) 51% ee	94
	2 (2.5 eq), Et_2O, reflux, 48 h	 +  **I** 10% ee[k] **I** + **II** (74) **I**/**II** = 9:1 **II** —% ee	300
	ent-**3d** (2.4 eq), 0°	 Solvent % ee[l] THF (55) 42 benzene (0) — Et_2O (53) 20	363
C_{8-10}			
	**105** (0.05 eq), **177b** (1.45 eq), THF, rt	 R Time (h) % ee[b] Et 48 (90)[a] 93 *n*-Pr 72 (93)[a] 95	112, 113
C_9			
 *exo*/*endo* ~ 3:2	Lithium amide (2.4 eq), 0°	 Lithium Amide Solvent % ee[l] **103a** THF (58) 21 **103a** benzene (35) 58 *ent*-product **103a** Et_2O (50) 23 **1a** THF (50) 76 **1a** benzene (40) 21 **1a** Et_2O (56) 23	363

C_9			
	**2** (1.85 eq), additive (2 eq), 24 h	 Solvent Additive Temp (°) % ee[k] Et_2O — 0 (58) 35 Et_2O — 40 (87) 18 pentane — 40 (74) 6 THF — 40 (62) 2 THF LiCl 40 (85) 0	362
C_{16}			
	**134** (1.5 eq), DBU, THF, −78 to 0°	 (—) 95% ee	109
	134 (*x* eq), LDA (2 eq), DBU, THF, −78 to 0°	 *x* % ee 0.05 (72) 91 0.1 (78) 93	109
C_{21}			
	**103a** (2 eq), toluene, 0°, 5 h	 (75) 89% ee[d]	278
	**95b** (2 eq), toluene, 0° to rt, 24 h	 (70–83) 94% ee	352, 336

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[a] The yield of isolated product was determined after conversion of the allylic alcohol into the corresponding benzoyl ester.

[b] The enantiomeric excess was determined after acetylation of the allylic alcohol.

[c] The enantiomeric excess was determined after benzoylation of the allylic alcohol.

[d] The enantiomeric excess was determined after conversion of the allylic alcohol into the corresponding Mosher ester.

[e] The enantiomeric excess was determined after conversion of the allylic alcohol to its (*R*)-*O*-acetyl mandelate ester.

[f] The enantiomeric excess was determined after oxidation to the corresponding enone.

[g] The numbers are initial screening results. The sense of asymmetric induction in this instance was not described.

[h] The base (**2**) used in this instance contained 20% of the *meso*-isomer.

[i] The yield was determined by GC using an internal standard.

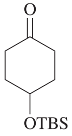
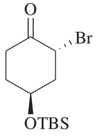
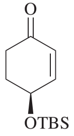
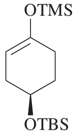
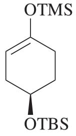
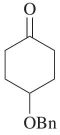
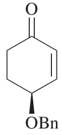
[j] The enantiomeric excess was determined after conversion of the allylic alcohol into a diastereomeric diazaphospholidine or thiophosphonamide.

[k] The enantiomeric excess was determined after conversion of the alcohol into the corresponding 2,4-dinitrobenzoate ester. When necessary, a reduction step was carried out first.

[l] The enantiomeric excess was determined after methylation of the allylic alcohol·

[m] The enantiomeric excess of the product cyclohex-2-en-1-ol is a corrected value based on the maximum optical rotation given in reference 344.

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C$_6$			
	1. **1a** (1.3 eq), TMSCl, THF, −95°, 1.5 h 2. NBS, NaOAc	 (65) 80% ee^a	143
	1. **1a** (1.1 eq), TMSCl, THF, −100°, 3 h 2. Pd(OAc)$_2$, O$_2$	 (72) 77–85% ee	284
	2 (1.5 eq), LiCl (1.5 eq), THF, −78°; then TMSCl	 (91) 70% ee^a	364
	23 (1.5 eq), LiCl (1.5 eq), TMSCl, Et$_3$N (5 eq), THF, 1 h	 Temp (°) — % ee^a −78 (—) 77 −100 (90) 90	364
	1. **3n** (1.1 eq), TMSCl, THF, −78° 2. Pd(OAc)$_2$, *p*-benzoquinone	 (74) 24% ee	365

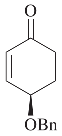
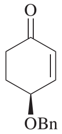
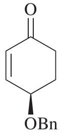
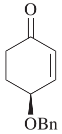
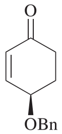
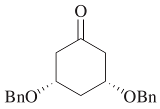
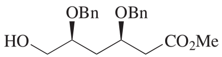
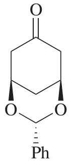
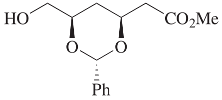
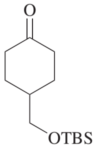
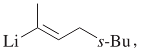
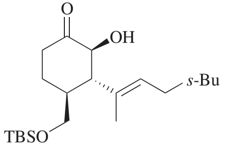
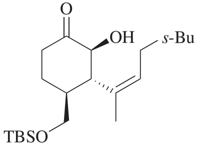
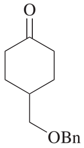
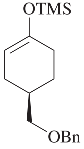
1. *ent*-**3n** (1.1 eq), TMSCl, THF, −78° 2. Pd(OAc)$_2$, *p*-benzoquinone		(77) 26% ee	365
1. **1a** (1.1 eq), TMSCl, THF, 10 min 2. Pd(OAc)$_2$, *p*-benzoquinone		Temp (°) — % ee −78 (85) 80 −95 (64) 82	365
1. **2** (1.1 eq), TMSCl, THF, −78°, 10 min 2. Pd(OAc)$_2$, *p*-benzoquinone		(82) 81% ee	365
1. **22** (1.1 eq), TMSCl, THF, −78° 2. Pd(OAc)$_2$, *p*-benzoquinone		(56) 82% ee	365
1. **23** (1.1 eq), TMSCl, THF, −78° 2. Pd(OAc)$_2$, *p*-benzoquinone		(55) 82% ee	365

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. **2**, TMSCl, THF 2. O_3; then PPh_3 3. $NaBH_4$ 4. MeI, K_2CO_3	 Temp (°) | % ee −78 | (27) | 70 −100 | (—) | 74	366
	1. **2** (3 eq), TMSCl, THF, 10 min 2. O_3; then PPh_3 3. $NaBH_4$ 4. MeI, K_2CO_3	 Temp (°) | % ee −78 | (—) | 95 −100 | (59) | >99.9	123, 141
C_7 	1. **1a** (1.15 eq), TMSCl (4 eq), THF, −95°, 2 h 2. $Pd(OAc)_2$, O_2 3. , $Li(2\text{-}C_4H_3S)CuCN$; then TMSCl 4. *m*CPBA; then TFA	 **I** 85% ee +  **II** **I** + **II** (36), **I/II** = 85:15	284, 285
	*ent*-**3d** (1.3 eq), TMSCl, THF	 Temp (°) | % ee[b] −78 | (83) | 62 −120 | (20) | 70	121

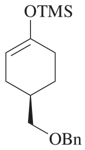
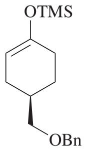
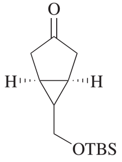
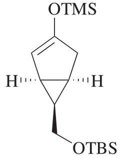
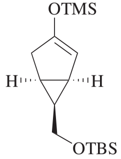
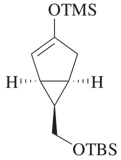
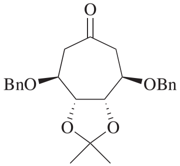
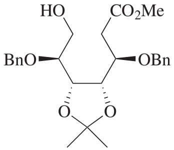
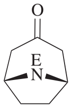
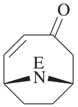
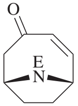
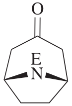
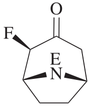
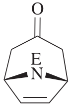
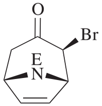
	90a (1.3 eq), HMPA, TMSCl, THF	 Temp (°) / % ee^b −78 (44) 58 −105 (44) 70 −120 (0) —	121
	2 (1.3 eq), TMSCl, THF, −78°, 40 min	 (96) 84% ee^b	121
	**2** (3 eq), LiCl (3 eq), TMSCl, THF, −78°, 20 min	 (52) 86% ee^a	167
	6a (3 eq), LiCl, TMSCl, THF, −78°, 1 h	 (21) 87% ee^a	167
	96b (3 eq), additive, TMSCl, THF, −78°, 2 h	 Additive / % ee^a HMPA (15) 12 LiCl (0) —	167

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. **2** (3 eq), LiCl (3 eq), TMSCl, THF, –78°, 15 min 2. O_3; then PPh_3 3. $NaBH_4$ 4. K_2CO_3, MeI	 (85) 96% ee	125
 $E = CO_2Me$	1. **1a**, TMSCl, THF 2. Et_2Zn, ICH_2Cl 3. $FeCl_3$	 (~60) 15–20% ee	147
	1. **67**, LiCl, TMSCl, THF, –100° 2. Et_2Zn, ICH_2Cl 3. $FeCl_3$	 (60) 78% ee	147
 $E = CO_2Et$	1. *ent*-**67** (1 eq), LiCl (1 eq), TMSCl, THF, –100° to –20° 2. Selectfluor®	 (55) ~60% ee	146
 $E = CO_2Me$	1. **77e** (1.5 eq), TMSCl (3 eq), HMPA (2 eq), THF, –90°, 2 h 2. NBS	 (80) 80% ee	159

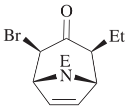
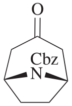
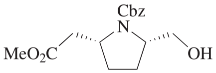
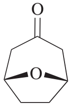
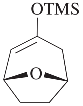
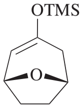
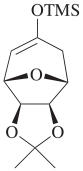
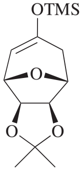
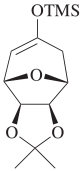
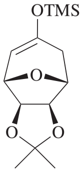
	1. **77e** (1.5 eq), TMSCl (3 eq), HMPA (2 eq), THF, –90°, 2 h 2. TBAT, EtI 3. LDA, TMSCl 4. NBS		(46) 80% ee	159
	1. **90b** (1.5 eq), TMSCl (3 eq), THF, –100°, 2 h 2. O_3, then $NaBH_4$ 3. CH_2N_2		(53) 90% ee	132, 130
	**1a** (1.5 eq), TMSCl, THF, 45 min			
		Temp (°)	% ee^c	
		–78	(78) 82	139
		–95	(79) 88	
	1a (1.5 eq), LiCl (*x* eq), THF, –78°, 15 min; then TMSCl, 30 min			
		x	% ee^c	
		0	(81) 33	139, 58, 59
		0.05	(—) 63	58, 59
		0.1	(75) 84	139, 58, 59
		0.4	(—) 82	58, 59
		0.7	(—) 83	58, 59
		1.5	(—) 84	58, 59

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)						Refs.
			x	*y*	Temp (°)		% ee^c	
C$_7$ 	**1a** (*x* eq), TMSCl (*y* eq), THF, 30 min		1.2	5	−78	(86)	70	367, 139, 58, 59
			1.5	0.3	−78	(10)	75	367
			1.5	5	0	(64)	43	367
			1.5	5	−40	(88)	63	367
			2	5	−78	(86)	70	367
			2	5	−94	(88)	85	367, 139
	1a (1.2 eq), LiCl (0.5 eq), THF, −78°, 15 min; then TMSCl, 30 min	 (—) 58% ee^c						59, 58
	1b (3 eq), *n*-BuLi (1.5 eq), TMSCl, THF, −78°, 30 min	 (98) 72% ee^c						367
	1a (1.5 eq), LiCl (3 eq), TMSCl, THF, −78°, 30 min	 (96) 67% ee^c						367

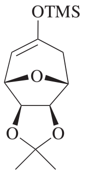
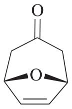
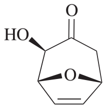
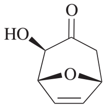
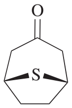
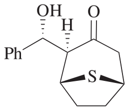
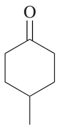
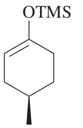
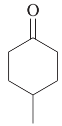
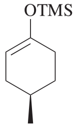
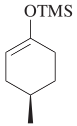
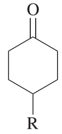
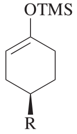
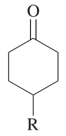
	1a (1.5 eq), THF, −78°, time; then TMSCl		Time (min) (98) % ee^{c} 10 (98) 27 60 (98) 30	367, 139, 58, 59 367
	1. **1a** (1.2 eq), LiCl (0.65 eq), THF, −115°, 3 h; then TESCl (1.4 eq), −78° to rt 2. *m*CPBA; then TFA		(67) 95% ee^{d}	149
	1. **1a** (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then TESCl (1.2 eq), −100°, 30 min 2. *m*CPBA; then TFA		(73) 83% ee^{d}	150
	1. **1a**, TMSCl, THF, −78° 2. $TiCl_4$, PhCHO		(43) 86% ee	63
	**96c** (1 eq), additive(s) (1 eq), THF, −78°, 2–3 h; then TMSCl, 3 min		(—) 73–97% conv Additive(s) % ee **146** 33 **146**, Li-DBU 8	368

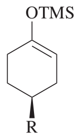
TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	**171** (x eq), THF, rt, time; then Et_3N, TMSCl (4 eq)	 x | Time (min) | | % ee 1.25 | 30 | $(72)^e$ | 28 1.67 | 30 | $(77)^e$ | 31 2.5 | 30 | $(91)^e$ | 33 2.5 | 10 | $(77)^e$ | 33 2.5 | 5 | $(81)^e$ | 36 5 | 30 | $(96)^e$ | 39	369
	171 (2.5 eq), additive, rt, 5 min; then Et_3N, TMSCl (4 eq)	 Solvent | Additive | | % ee THF | LiCl | $(92)^e$ | 36 THF | DMPU | $(78)^e$ | 34 THF | HMPA | $(93)^e$ | 37 Et_2O | LiCl | $(57)^e$ | 33 Et_2O | DMPU | $(76)^e$ | 14 Et_2O | HMPA | $(62)^e$ | 20 toluene | LiCl | $(51)^e$ | 37 toluene | DMPU | $(58)^e$ | 13 toluene | HMPA | $(42)^e$ | 12	369
C_{7-10} 	**96c** (1 eq), THF, −78°, time; then TMSCl, 3 min	 (—) 98% conv R | Time (min) | % ee Me | 180 | 34 *t*-Bu | 70 | 75	368

C$_{7-12}$

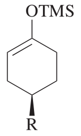


3d (1.2 eq), TMSCl,
THF, −78°



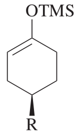
R		% ee	
Me	(69)	74	54, 117
i-Pr	(65)	76	
t-Bu	(88)	76	

90a (1.2 eq), HMPA (1 eq),
TMSCl, THF, −78°



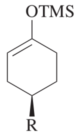
R		% ee	
Me	(68)	46–64	54, 117, 116
i-Pr	(85)	78	54, 117, 116
t-Bu	(87)	77	54, 117, 116
Ph	(93)	75	116

77l (1.2 eq), HMPA (1.2 eq),
TMSCl, THF, −100°



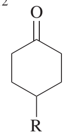
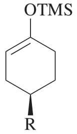
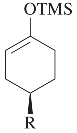
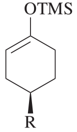
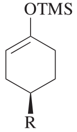
R		% ee	
Me	(76)	94	
i-Pr	(92)	95	67, 68
t-Bu	(88)	93	
Ph	(95)	93	

77h (1.2 eq), HMPA (*x* eq),
TMSCl, THF, −78°

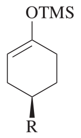


R	*x*		% ee	
Me	0	(86)	84	66
Me	1.2	(77)	92	65
i-Pr	1.2	(91)	89	65
t-Bu	0	(95)	84	66, 65
t-Bu	1.2	(96)	83	65
Ph	1.2	(98)	87	65

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

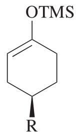
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)					Refs.
C_{7-12} 	**77l** (1.2 eq), HMPA (*x* eq) TMSCl, THF, –78°		R	*x*		% ee	
			Me	0	(88)	84	66
			Me	1.2	(66)	89	65
			i-Pr	1.2	(85)	90	65
			t-Bu	0	(89)	83	66
			t-Bu	1.2	(82)	85	65
			Ph	1.2	(91)	88	65
	86a (1.2 eq), HMPA (*x* eq), TMSCl, THF, –78°		R	*x*		% ee	
			Me	0	(72)	90	66
			Me	1.2	(87)	94	65
			i-Pr	1.2	(91)	93	65
			t-Bu	0	(84)	86	66, 65
			t-Bu	1.2	(87)	85	65
			Ph	1.2	(98)	90	65
	86b (1.2 eq), HMPA (*x* eq), TMSCl, THF, –78°		R	*x*		% ee	
			Me	0	(78)	86	66
			Me	1.2	(90)	89	65
			i-Pr	1.2	(92)	93	65
			t-Bu	0	(89)	85	66
			t-Bu	1.2	(91)	87	65
			Ph	1.2	(96)	91	65
	85a (1.2 eq), HMPA (*x* eq), TMSCl, THF, –78°		R	*x*		% ee	
			Me	0	(74)	86	66
			Me	1.2	(78)	92	65
			i-Pr	1.2	(93)	87	65
			t-Bu	0	(93)	72	66
			t-Bu	1.2	(95)	75	65
			Ph	1.2	(97)	85	65

85b (1.2 eq), HMPA (*x* eq),
TMSCl, THF, –78°



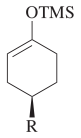
R	*x*		% ee	
Me	0	(87)	84	66
Me	1.2	(69)	92	65
i-Pr	1.2	(82)	88	65
t-Bu	0	(92)	72	66
t-Bu	1.2	(85)	78	65
Ph	1.2	(90)	86	65

83a (1.2 eq), HMPA (*x* eq),
TMSCl, THF, –78°



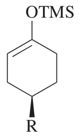
R	*x*		% ee	
Me	0	(76)	86	66
Me	1.2	(84)	86	65
i-Pr	1.2	(95)	80	65
t-Bu	0	(99)	41	66
t-Bu	1.2	(99)	47	65
Ph	1.2	(99)	74	65

83b (1.2 eq), HMPA (*x* eq),
TMSCl, THF, –78°



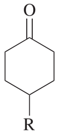
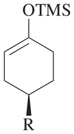
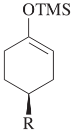
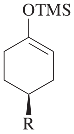
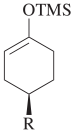
R	*x*		% ee	
Me	0	(85)	82	66
Me	1.2	(68)	91	65
i-Pr	1.2	(77)	80	65
t-Bu	0	(99)	43	66
t-Bu	1.2	(85)	57	65
Ph	1.2	(87)	70	65

84a (1.2 eq), HMPA (*x* eq),
TMSCl, THF, –78°

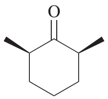


R	*x*		% ee		
Me	0	(57)	49	(*R*)	66
Me	1.2	(67)	66	(*R*)	65
i-Pr	1.2	(85)	33	(*R*)	65
t-Bu	0	(76)	–24	(*S*)	66
t-Bu	1.2	(85)	–16	(*S*)	65
Ph	1.2	(77)	23	(*R*)	65

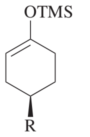
TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)						Refs.
C_{7-12} 	**84b** (1.2 eq), HMPA (*x* eq), TMSCl, THF, −78°		R	*x*		% ee		
			Me	0	(80)	42	(*R*)	66
			Me	1.2	(49)	66	(*R*)	65
			i-Pr	1.2	(56)	43	(*R*)	65
			t-Bu	0	(86)	12	(*S*)	66
			t-Bu	1.2	(54)	0	(*R*) + (*S*)	65
			Ph	1.2	(46)	30	(*R*)	65
	79a (1.2 eq), HMPA (1.2 eq), TMSCl, THF, −78°		R			% ee		65
			Me		(65)	27		
			i-Pr		(78)	17		
			t-Bu		(77)	12		
			Ph		(86)	6		
	79b (1.2 eq), HMPA (1.2 eq), TMSCl, THF, −78°		R			% ee		65
			Me		(79)	70		
			i-Pr		(92)	57		
			t-Bu		(94)	53		
			Ph		(95)	54		
	77l (1.2 eq), HMPA (2.4 eq), THF, −78°; then TMSCl		R			% ee		118, 119
			Me		(82)	78		
			i-Pr		(75)	79		
			t-Bu		(85)	81		
			Ph		(77)	80		

C_8



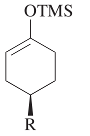
78 (0.3 eq), **162** (2.4 eq), HMPA (2.4 eq), DABCO (1.5 eq), THF, −78°; then TMSCl



R		% ee
Me	(70)	75
i-Pr	(80)	76
t-Bu	(83)	79
Ph	(77)	76

118, 119

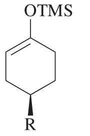
15 (1.2 eq), LiCl (0.6 eq), THF; then TMSCl (1.2 eq)



R	Temp (°)		% ee
Me	−78	(74)	85
i-Pr	−78	(75)	76
t-Bu	−78	(73–82)	83–86
t-Bu	−94	(66)	85
Ph	−78	(86)	90

370

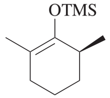
171 (2.5 eq), THF, rt, 5 min; then Et_3N, TMSCl (4 eq)



R		% ee
Me	(94)[e]	41
i-Pr	(91)[e]	34
t-Bu	(93)[e]	31
Ph	(86)[e]	33

369

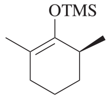
124 (1.2 eq), THF, −78 to −40°, overnight; then TMSCl (3 eq), Et_3N (3 eq), −78°, 1 h



(66) ~70% ee[a,f]

115, 148

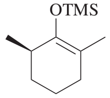
124 (1.2 eq), TMSCl, THF, −78 to −40°, 14 h



(30) 83% ee[a]

115

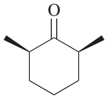
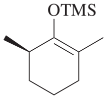
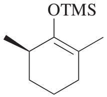
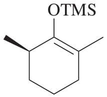
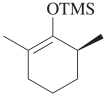
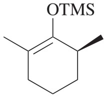
126 (1.2 eq), THF, −78 to −40°, overnight; then TMSCl (1.2–3 eq), Et_3N (3–30 eq), −78°, 1 h



(65) ~70–85% ee[a,d,f]

53, 115, 371

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8				
	**126** (1.2 eq), TMSCl, THF, –78 to –40°, 14 h		(~30) 77% ee[a,f]	115
	1a (1.2 eq), TMSCl, THF, –78 to –40°, 14 h		(~30) 53% ee[a,f]	115
	3d (1.2 eq), TMSCl (*x* eq), THF, –78°, 20 min		*x* % ee[g] 5 (53) 60 10 (63) 65	372
	90a (*x* eq), TMSCl (*y* eq), HMPA (*z* eq), THF, –78°, 20 min		*x* *y* *z* % ee[g] 1.2 10 0 (33) 85 4.4 10 0 (89) 89 1.2 5 1.2 (34) 78	372
	90b (2 eq), TMSCl, HMPA (2 eq), THF, –78°, 20 min		(73) 96% ee[g]	372

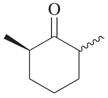
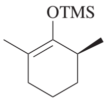
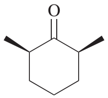
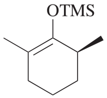
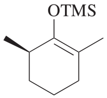
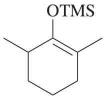
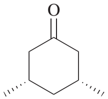
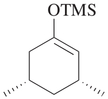
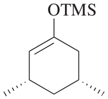
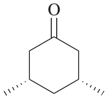
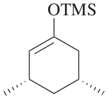
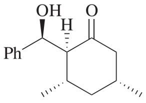
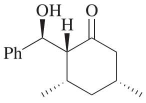
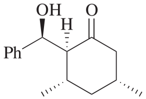
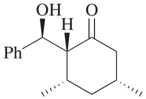
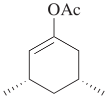
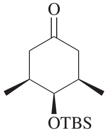
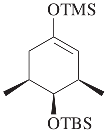
 *cis*/*trans* = 80:20	**171** (2.5 eq), THF, rt, 5 min; then Et_3N, TMSCl (4 eq)		(92)^e 57% ee	369
	Lithium amide (2.5 eq), THF, 5 min; then Et_3N, TMSCl (4 eq)		Lithium Amide — Temp — — % ee **171** rt (92)^e 71 **171** −78° (82)^e 77 **172** rt (82)^e 54 **173** rt (79)^e 62 **174** rt (90)^e 81 **174** rt (94)^e 82	369
	Lithium amide (2.5 eq), THF, rt, 5 min; then Et_3N, TMSCl (4 eq)		Lithium Amide — — % ee **175b** (75)^e 18 **175c** (61)^e 17 **176** (53)^e 15	369
	Lithium amide (2.5 eq), THF, rt, 5 min; then Et_3N, TMSCl (4 eq)		Lithium Amide — — % ee **175a** (68)^e <2 **170** (59)^e <2	369
	**3d** (1.2 eq), TMSCl (10 eq), THF, −78°, 20 min		(54) 76% ee^g	372
	90a (1.2 eq), TMSCl (10 eq), THF, −78°, 20 min		(69) 64% ee^g	372

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	**90b** (2 eq), TMSCl, HMPA, (2 eq), THF, −78°, 20 min	 (88) 90% ee[g]	372
	1. *ent*-**3d** (1.1 eq), TMSCl, THF, −78°, 1 min 2. MeLi; then PhCHO	 +  **I** 61% ee **I** + **II** (51), **I/II** = 1:1 **II** 77% ee	165
	1. *ent*-**3n** (1.1 eq), TMSCl, THF, −78°, 1 min 2. MeLi; then PhCHO	 +  **I** 65% ee **I** + **II** (66), **I/II** = 1:1 **II** 68% ee	165
	1. *ent*-**3n** (1.1 eq), TMSCl, THF 2. MeLi; then Ac_2O	 Temp (°) % ee −78 (—) 74 −100 (13) 79	165
	**1a** (1.5 eq), LiCl (1.5 eq), TMSCl, THF, −110 to −78°	 (54) 97% ee[a]	124

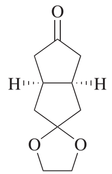
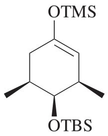
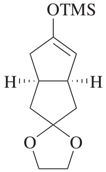
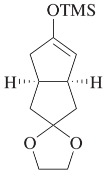
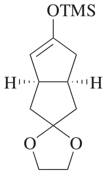
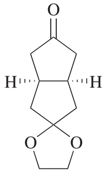
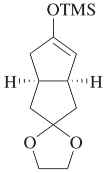
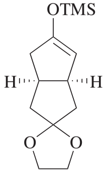
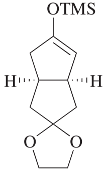
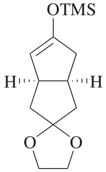
	**1a**, LiCl, THF, –110°, 5 min; then TMSCl, –110 to –78°, 30 min		(80) 94% ee[a]	124
	3d (1.2 eq), TMSCl, –78°, 30 min		Solvent / % ee toluene (20) 2 Et_2O (17) 21 DME (75) 59	152
	3d (*x* eq), TMSCl, HMPA (*y* eq), THF, –78°, 30 min		*x* *y* % ee 1.2 0 (68) 70 2 0 (87) 71 1.2 3.6 (54) 40	152
	ent-**3d** (2.4 eq), TMSCl, THF, –78°, 1 h		(90) 72% ee[h]	373

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	**1a** (2.4 eq), TMSCl, THF, −78°, 1 h	 (90) 48% ee[h]	373
	1a, LiCl, TMSCl, THF, −78°	 (90) 92% ee	190
	Lithium amide (2 eq), TMSCl, THF, −78°, 30 min	 Lithium Amide — % ee **5** (95) 83 **6b** (90) 4 **3e** (84) 30	152
	90a (1.2 eq), TMSCl, HMPA (1.2 eq), THF, −78°, 30 min	 (66) 11% ee	152

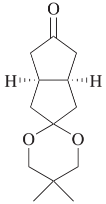
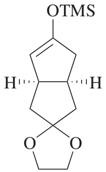
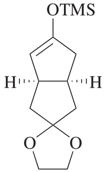
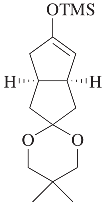
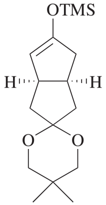
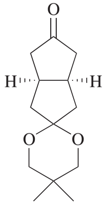
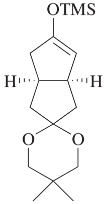
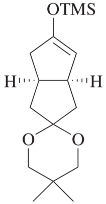
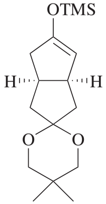
	**90d** (2 eq), TMSCl, HMPA (2 eq), THF, –78°, 30 min		(21) 51% ee	152
	90b (1.9–2 eq), TMSCl (4.8–5 eq), HMPA (*x* eq), THF, –100°, 30 min		*x* — % ee 0 (91) 71 2 (91) 87	152
	5 (2 eq), TMSCl, THF, –78°, 30 min		(93) 84% ee	152
	90b (2 eq), TMSCl (10 eq), HMPA (2 eq), THF, –78°, 30 min		(93) 94% ee	152

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C$_8$ 	*ent*-**90b**, TMSCl, HMPA, THF		(—) 85% ee	155
	1a (2 eq), LiCl (*x* eq), THF, −100°, 15 min; then TMSCl, 1 h		*x* — % ee 0 (30) 62 1.5 (93) 83	155
	1a (2 eq), LiCl (*x* eq), TMSCl, THF, −100°, 30–60 min		*x* — % ee 0 (86) 80 1.5 (92) 88	155

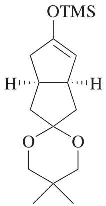
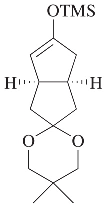
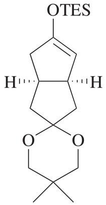
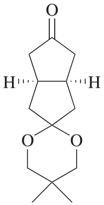
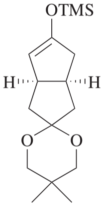
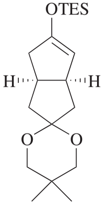
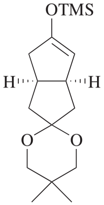
1a (1.6 eq), LiCl (1.6 eq), THF, −100°, 40 min; then TMSCl, 30 min		(80) 90% ee	142, 286, 287, 288
2, TMSCl, THF		(80) 80% ee	374
1a (1.5 eq), LiCl (1.5 eq), THF, −105°, 30 min; then −78°, TESCl (1.3 eq), 15 min		(92) 95% ee	155

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8				
	Lithium amide, LiCl, THF, −100°; then TMSCl		(—) Lithium Amide % ee **127** 22 **103a** 27 **56** 24	155
	159, LiCl, THF, −100°; then −78°, TESCl		(—) 31% ee	155
	31, LiCl, THF, −100°; then TMSCl		(—) 33% ee	155

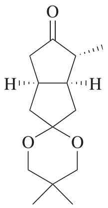
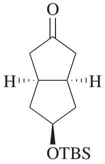
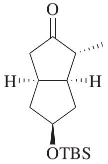
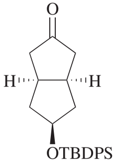
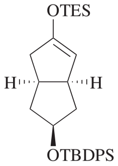
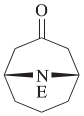
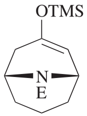
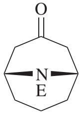
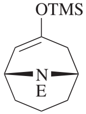
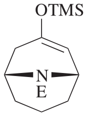
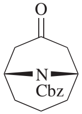
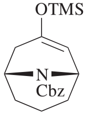
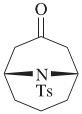
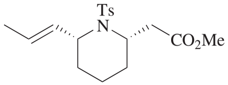
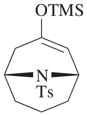
	1. **1a** (1.3 eq), LiCl (1.3 eq), THF, −100°, 1 h; then −78°, TESCl (2 eq), 30 min 2. MeLi; then MeI		(44) 88% ee, dr 93:7	153
	1. **1a** (1.1 eq), LiCl (1.1 eq), THF, −100°, 1 h; then −78°, TESCl (2 eq), 30 min 2. MeLi; then MeI		(21) 90% ee, dr 98:2	153
	**1a** (1.5 eq), LiCl (1.5 eq), THF, −100°; then −78°, TESCl (1.3 eq)		(94) 92% ee	155, 154
 E = CO_2Me	**90b** (1.5 eq), TMSCl (3 eq), HMPA (3 eq), THF, −100°, 2 h		(94) 93% ee	129, 130, 375

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_8$  E = CO$_2$Me	*ent*-**90b**, TMSCl, HMPA, THF, −100°	 (91) ~93% ee	161
	90a, TMSCl, HMPA, THF, −100°	 (—) 70% ee	129
	**90b** (2 eq), TMSCl (3 eq), HMPA (1.1 eq), THF, −100°, 10 min	 (96) 94% ee	174, 375
	1. *ent*-**90b** (5 eq), TMSCl (7 eq), HMPA (7 eq), THF, −100°, 40 min 2. MeCHI$_2$, Et$_2$Zn 3. TBAF 4. PhI(O$_2$CCF$_3$)$_2$, TFOH (cat.), MeOH	 (53) 96% ee	162, 161
	90b (4 eq), TMSCl (6 eq), HMPA (6 eq), THF, −100°	 (63) ~96% ee	162, 161

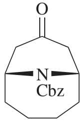
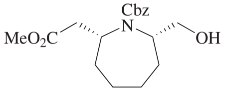
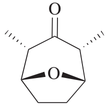
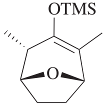
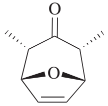
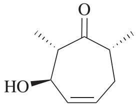
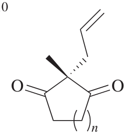
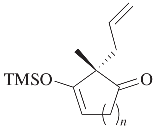
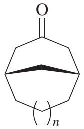
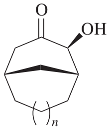
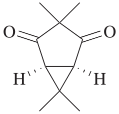
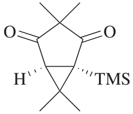
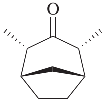
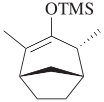
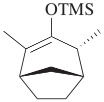
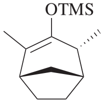
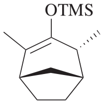
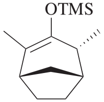
C_9				
	1. **90b** (1.5 eq), TMSCl (3 eq), HMPA (3 eq), THF, −100°, 2 h 2. O_3, then $NaBH_4$ 3. CH_2N_2		(56) 90% ee	130
	**2** (2 eq), LiCl (0.5 eq), THF, −78°, 4 h; then TMSCl (3.5 eq), −78° to rt, 1.5 h		(99) 85% ee[d]	156, 157
	1. **1a**, HMPA, TBSCl, THF, −78°, 24 h 2. DIBAL-H, $LiClO_4$ (5 M in Et_2O)		(63) 75% ee[a]	140
C_{9-10}				
	**1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 1 h		*n* % ee 1 (50) 65 2 (64) 70	198
C_{9-13}				
	1. **90b** (1.2 eq), HMPA (1.1 eq), TMSCl (4 eq), THF, −78° to rt, 35 min 2. DMDO or *m*CPBA		*n* % ee 1 (55) 36 3 (51) 100 5 (10) 95	122

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (10 eq), THF, −78° to rt, 5 h	 (80) >98% ee	376
	**22** (2 eq), TMSCl, THF, −78°, 30 min	 (95) 45% ee [EQ 30% ee]	151
	1a (2 eq), TMSCl, THF, −78°, 30 min	 (96) 23% ee [EQ 15% ee]	151
	3n (2 eq), TMSCl, THF, −78°, 30 min	 (89) 10% ee [EQ 10% ee]	151
	54 (2 eq), TMSCl, THF, −78°, 30 min	 (80) 5% ee	151
	123 (2 eq), TMSCl, THF, −78°, 30 min	 (95) 5% ee [EQ 5% ee]	151

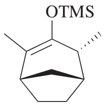
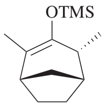
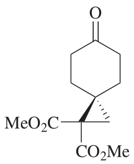
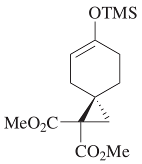
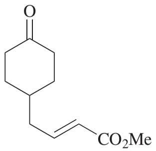
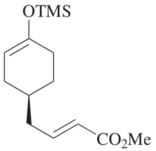
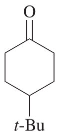
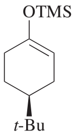
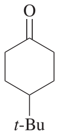
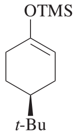
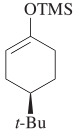
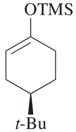
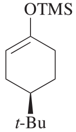
	127 (2 eq), TMSCl, THF, −78°, 30 min	 (75) 76% ee [EQ 46% ee]	151
	90b (2 eq), TMSCl, THF, −78°, 30 min	 (62) 85% ee	151
	**2** (1.3 eq), LiCl (1.3 eq), TMSCl, THF, −95°, 30 min	 (98) 74–82% ee	144
	**48b** (2.4 eq), TMSCl, THF, −100°	 (79) 29% ee^b	163
	**29c** (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min	 (88) 23% ee	54, 116

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	**29b** (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min	 (65) 33% ee	54, 116
	30a (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min	 (91) 36% ee	54, 116
	30b (1.2 eq), TMSCl, HMPA (*x* eq), −78°, 15 min		
		Solvent | *x* | | % ee |	
		THF | 0 | (87) | 6 | (*S*)	54, 117, 116
		DME | 0 | (90) | 25 | (*R*)	116
		Et_2O | 0 | (5) | 12 | (*R*)	116
		toluene | 0 | (31) | 14 | (*R*)	116
		THF | 2.4 | (90) | 43 | (*R*)	54, 117, 377, 116
		DME | 2.4 | (90) | 40 | (*R*)	377, 116
		Et_2O | 2.4 | (88) | 41 | (*R*)	377, 116
		toluene | 2.4 | (27) | 41 | (*R*)	377, 116
	34 (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min	 (35) 46% ee	54, 116

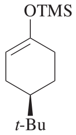
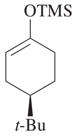
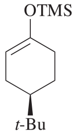
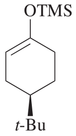
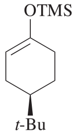
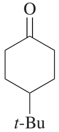
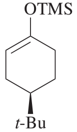
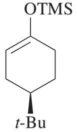
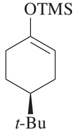
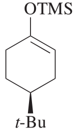
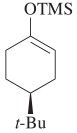
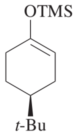
95c (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min		(52) 67% ee	54, 116
77d (1.2 eq), TMSCl, HMPA (*x* eq), THF, −78°, 15 min		*x* % ee 0 (89) 66 2.4 (67) 77	54, 117 54, 117, 116
90a (1.2 eq), TMSCl, HMPA (*x* eq), THF, 15 min		*x* Temp (°) % ee 0 −78 (65) 73 1.2 −78 (87) 77 1.2 −105 (51) 89	54, 117 54, 117, 116 54, 117, 116
27 (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min		(74) 33% ee	54, 116
28 (1.2 eq), TMSCl, HMPA (2.4 eq), THF, −78°, 15 min		(32) 40% ee	54, 116

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10} 	**35**, TMSCl, toluene/HMPA		(—) 84% ee	378
	19, (1.2 eq), TMSCl, HMPA (3.6 eq), THF, –78°, 15 min		(31) 66% ee	54
	3d (1.2 eq), TMSCl, HMPA (*x* eq), THF, 15 min		*x* Temp (°) % ee 0 –78 (82–88) 59–76	54, 117, 56, 115
			0 –90 (81) 66	56, 115
			3.6 –78 (63) 64	54, 117
	3d (1.2 eq), LiCl (*x* eq), THF, –78°; then TMSCl		*x* % ee 0 (72–89) 23 0.5 (72–89) 86	58, 59
	3n (1.2 eq), TMSCl, THF, –78°, 15 min		(71) 51% ee	56, 115

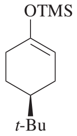
1a (1.2 eq), TMSCl,
THF, 15 min



Temp (°)		% ee
−78	(73)	70
−90	(66)	88
−105 to −78	(96)	89

56, 115
56, 115
168

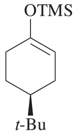
1a (1.2 eq), LiCl (*x* eq),
THF, −78°; then TMSCl



x		% ee
0	(73–85)	23
0.5	(73–85)	83

58, 59

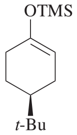
1a (1.2 eq), TMSX,
THF, −78°



X		% ee
Cl	(71)	90
Br	(86)	65
I	(97)	31

60

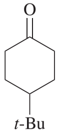
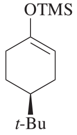
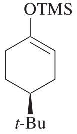
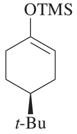
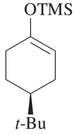
1a (1.2 eq), additive (*x* eq),
THF, −78°; then TMSCl



Additive	*x*		% ee
—	—	(84)	44
LiCl	0.6	(86)	87
LiCl	1.2	(87)	88
LiCl	3.6	(73)	88
LiBr	1.2	(89)	63
LiBr	3.6	(82)	86
LiI	1.2	(85)	44
LiI	3.6	(79)	43

60

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	**1a** (1.2 eq), additive (*x* eq), THF, −114°; then TMSCl	 Additive *x* % ee — — (93) 41 LiCl 0.6 (92) 79 LiCl 1.2 (90) 91 LiCl 3.6 (97) 91 LiBr 1.2 (87) 52 LiBr 3.6 (83) 71 LiI 1.2 (85) 38 LiI 3.6 (79) 37	60
	124 (1.2 eq), TMSCl, THF, −78°, 15 min	 (80) 20% ee	56, 115
	124 (1.2 eq), LiCl (*x* eq), THF, −78°; then TMSCl	 *x* % ee 0 (68–81) 13 0.5 (68–81) 27	58, 59
	126 (1.2 eq), TMSCl, THF, −78°, 15 min	 (75) 27% ee	56, 115

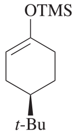
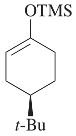
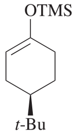
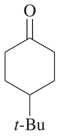
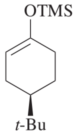
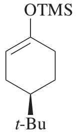
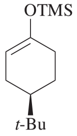
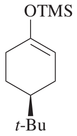
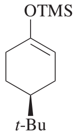
		Solvent	x		% ee	
77h (1.2 eq), TMSCl, HMPA (x eq), −78°, 10–60 min		THF	0	(86–95)	84–86	55, 67, 345, 68
		THF	1.2	(94)	84	67, 65, 68
		THF	2.4	(82)	82	55, 345, 377, 116
		DME	0	(86)	70	55, 345
		DME	2.4	(87)	81	55, 345, 377
		toluene	0	(12)	58	55, 345
		toluene	0.4	(45)	56	345
		toluene	1.2	(72)	76	345
		toluene	2.4	(87)	82	55, 345, 377
		Et_2O	0	(8)	64	55, 345
		Et_2O	2.4	(89)	82	55, 345, 377
		x		% ee		
77h (1.2 eq), TMSCl, HMPA (x eq), THF, −100°		0	(61)	92		68
		1.2	(78)	89		68, 67
77h (1.2 eq), HMPA (2.4 eq), THF, −78°, 1 h; then TMSCl, 15 min		(86) 77% ee				118, 119

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

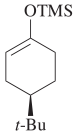
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)				Refs.
C_{10} 	**77h** (1.2 eq), LiBr (x eq), THF, –78°, 10 min; then TMSCl, 30 min		x		% ee	65
			0	(88)	77	
			1.2	(97)	85	
	55 (1.2 eq), TMSCl, HMPA (2.4 eq), –78°, 10 min		Solvent		% ee	377
			THF	(47)	43	
			DME	(41)	38	
			toluene	(44)	51	
			Et_2O	(44)	45	
	111 (1.2 eq), TMSCl, HMPA (2.4 eq), –78°, 10 min		Solvent		% ee	377
			THF	(14)	55	
			DME	(17)	57	
			toluene	(58)	43	
			Et_2O	(38)	61	
	Lithium amide (1.2 eq), TMSCl, THF, –78°, 1 h		Lithium Amide		% ee	
			3b	(55)	41	379, 380
			6b	(94)	32	379, 380
			3h	(61)	43	379, 380
			3i	(66)	59	379, 380
			3j	(92)	83	379, 380
			3k	(92)	18	379, 380
			18	(95)	86	380

6a (1.2 eq), TMSCl,
HMPA (*x* eq), 1h



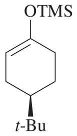
Solvent	Temp (°)	x		% ee		
THF	−78	0	(98)	89	(*S*)	379, 380
THF	−100	0	(86)	92	(*S*)	379, 380
Et_2O	−78	0	(15)	38	(*S*)	380
Et_2O	−78	1.2	(82)	36	(*S*)	380
toluene	−78 to −20	0	(6)	16	(*S*)	380
toluene	−78	1.2	(56)	8	(*R*)	380

ent-**6a** (1.2 eq), TMSCl,
THF, −100°, 1 h



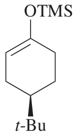
(83) 92% ee 379, 380

36 (1.2 eq), TMSCl,
HMPA (1.2 eq),
THF, −78 to −20°, 1 h



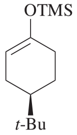
(72) 16% ee 380

77b (1.2 eq), TMSCl,
HMPA (*x* eq),
THF, −78°, 40 min



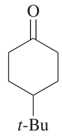
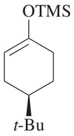
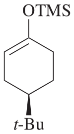
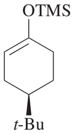
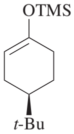
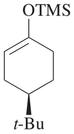
x		% ee	
0	(86)	52	67, 68
1.2	(93)	78	67, 68
2.4	(88)	78	68

77c (1.2 eq), TMSCl,
HMPA (*x* eq),
THF, −78°, 40 min

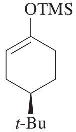


x		% ee	
0	(96)	62	67, 68
1.2	(97)	81	

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

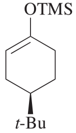
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)					Refs.
C_{10} 	**77f** (1.2 eq), TMSCl, HMPA (*x* eq), THF, −78°, 40 min			*x*		% ee	
				0	(92)	81	68
				1.2	(77)	78	
	77d (1.2 eq), TMSCl, HMPA (*x* eq), THF, −78°, 40 min			*x*		% ee	
				0	(87)	65	67, 68
				1.2	(73)	75	
	77g (1.2 eq), TMSCl, HMPA (*x* eq), THF, −78°, 40 min			*x*		% ee	
				0	(97)	59	68
				1.2	(98)	59	
	77j (1.2 eq), TMSCl, HMPA (*x* eq), THF,−78°, 40 min			*x*		% ee	
				0	(85)	69	67, 68
				1.2	(67)	85	
	77k (1.2 eq), TMSCl, HMPA (*x* eq), THF, 40 min		Temp (°)	*x*		% ee	
			−78	0	(93)	77	67, 68
			−78	1.2	(92)	89	67, 68
			−100	0	(75)	85	68
			−100	1.2	(70)	92	68

77l (1.2 eq), TMSCl,
HMPA (*x* eq),
THF, 40 min



Temp (°)	*x*		% ee	
–78	0	(88)	84	67, 68
–78	1.2	(74)	87	67, 68
–78	2.4	(69)	87	68
–78	4	(53)	82	68
–100	0	(82)	91	68
–100	1.2	(88)	93	67, 68

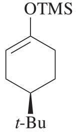
77l (1.2 eq), TMSCl,
HMPA (*x* eq),
–78°, 40 min



Solvent	*x*		% ee
DME	0	(84)	71
DME	1.2	(71)	85
Et_2O	0	(59)	67
Et_2O	1.2	(78)	84

68

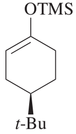
77l (1.2 eq), TMSCl,
HMPA (*x* eq), toluene,
–78 to 0°, 19 h



x		% ee
0	(30)	35
1.2	(71)	87

68

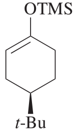
77m (1.2 eq), TMSCl,
HMPA (*x* eq),
THF, 40 min



Temp (°)	*x*		% ee
–78	0	(79)	85
–78	1.2	(77)	87
–100	0	(77)	90
–100	1.2	(84)	92

67, 68

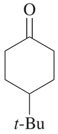
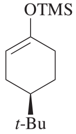
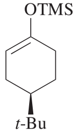
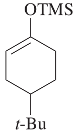
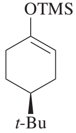
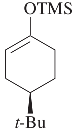
86a (1.2 eq), LiBr (x eq),
THF, –78°, 10 min;
then TMSCl, 30 min



x		% ee
0	(88)	76
1	(94)	87

65

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	**81** (1.2 eq), HMPA (2.4 eq), THF, −78°, 1 h; then TMSCl, 15 min	 (54) 53% ee	118
	96c (1 eq), TMSCl, THF, −78°, 70 min	 (79) 85% ee	368
	167, TMSCl, THF, −70°	 (—) <5% ee	381
	169a, TMSCl, THF, −70°	 (—) 20% ee	381
	169b, TMSCl, THF, −70°	 (—) Temp (°) % ee −70 46 −90 62	381

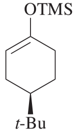
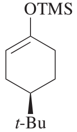
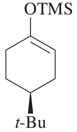
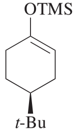
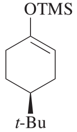
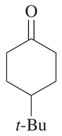
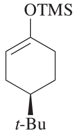
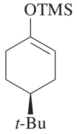
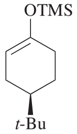
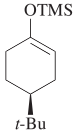
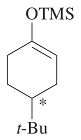
40 (1.5 eq), HMPA (3.1 eq), TMSCl, −70°, 1 h		Solvent % ee[b] toluene (77) 39 THF (70) 50	382
39 (1.5 eq), HMPA (3.1 eq), TMSCl, −70°, 1 h		Solvent % ee[b] toluene (37) 34 THF (51) 34	382
3o, LiBr (2 eq), TMSCl, THF, −100°		(89) 91% ee[b]	383
13 (1.2 eq), LiCl (0.6 eq), THF, −78°, 30 min; then TMSCl (1.2 eq), −78° to rt		(86–93) 57–60% ee	370
14 (1.2 eq), LiCl (1.2 eq), THF, −78°, 30 min; then TMSCl (1.2 eq), −78° to rt		(81) 83% ee	370

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)					Refs.
C_{10}							
	Lithium amide (*x* eq), LiCl (1.2 eq), THF, −78°; then TMSCl		Lithium Amide	*x*		% ee	
			16	1.2	(78)	21	370
			156	1.5	(66)	47	384
			157	1.5	(49)	2	384
	Lithium amide (*x* eq), LiCl (1.2 eq), THF, −78°; then TMSCl		Lithium Amide	*x*		% ee	
			17	1.2	(70)	25	370
			149	1.5	(81)	22	384
			150	1.5	(92)	10	384
			153a	1.5	(41)	24	384
			154a	1.5	(53)	59	384
			158	1.5	(43)	57	384
			153b	1.5	(52)	42	384
			154b	1.5	(64)	31	384
	151 (1.5 eq), TMSCl, THF, 30 min		Temp (°)			% ee	
			−78		(52)	0	384
			−100		(78)	9	
	151 (1.5 eq), HMPA(1.5 eq), THF; then TMSCl		Temp (°)			% ee	
			−78		(82)	54	384
			−100		(98)	38	

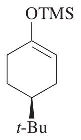
152 (1.5 eq), TMSCl, THF,
30 min



Temp (°)		% ee	
−78	(60)	6	(*R*)
−100	(38)	12	(*S*)

384

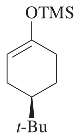
152 (1.5 eq), HMPA (1.5 eq),
THF; then TMSCl



Temp (°)		% ee
−78	(96)	70
−100	(89)	81

384

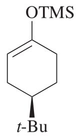
77l (1.2 eq), HMPA (*x* eq),
THF, −78°, 1 h;
then TMSCl, 15 min



x		% ee
0	(83)	79
2.4	(85)	81

118, 119

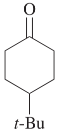
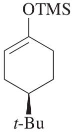
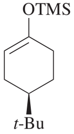
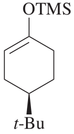
Lithium amide (1.2 eq),
HMPA (2.4 eq),
THF, −78°, 1 h;
then TMSCl, 15 min



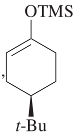
Lithium Amide		% ee
77k	(83)	77
77j	(49)	47
77m	(64)	68

119

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Additive	x	y		% ee	Refs.
C_{10} 	**78** (0.3 eq), **162** (*x* eq), HMPA (*y* eq), THF, −78°, 3 h; then TMSCl, 15 min			3.6	0	(57)	31	118, 119
				3.6	0.9	(74)	61	119
				3.6	1.8	(78)	70	119
				3.6	3.6	(70)	70	119
				3.6	5.4	(69)	55	119
				3.6	7.2	(61)	53	119
				2.4	2.4	(74–75)	70–72	118, 119
				2.0	2.0	(73)	69	119
				1.5	1.5	(59)	47	119
	78 (0.3 eq), **162** (2.4 eq), additive (*x* eq), HMPA (*y* eq), THF, −78°, 1.5 h; then TMSCl, 15 min		LiBr	2.4	2.4	(63)	28	119
			TMEDA	2.4	2.4	(77)	71	119
			DABCO	1.2	2.4	(83)	78	119
			DABCO	1.2	0	(61)	27	119
			DABCO	1.5	2.4	(83)	79	118, 119
	78 (*x* eq), **162** (2.4 eq), additive (1.2 eq), HMPA (2.4 eq), THF, −78°, 1.5 h; then TMSCl, 15 min		bis(2-piperidinoethyl)amine	0.3		(75)	73	119
			DABCO	0.2		(75)	69	

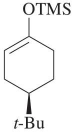
78 (0.3 eq), base (2.4 eq),
DABCO (1.2 eq), HMPA (2.4 eq),
THF, −78°, 1.5 h;
then TMSCl, 15 min



Base		% ee
160a	(8)	5
160b	(30)	27
161	(43)	26
163	(71)	71
164	(78)	76
165	(53)	14
166	(49)	9

119

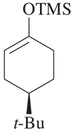
Lithium amide (0.3 eq),
162 (2.4 eq), DABCO (1.5 eq),
HMPA (2.4 eq),
THF, −78°, 1.5 h;
then TMSCl, 15 min



Lithium Amide		% ee
77k	(82)	76
77j	(50)	12
77m	(78)	69

119

96c (1 eq), additive(s) (1 eq),
THF, −78°, 1–1.5 h;
then TMSCl, 3 min

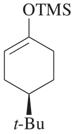


(—)
78–98% conv

Additive(s)	% ee
146	63
1-methylimidazole, **146**	66
DBU, Li-DBU	46
n-BuLi	48

368

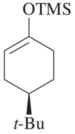
96c (1 eq), **146** (1 eq),
THF, −78°, 3 min;
then TMSCl, 70 min



(—) 98% conv, 63% ee

368

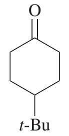
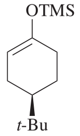
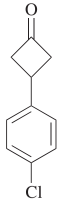
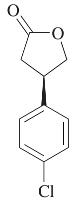
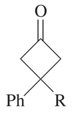
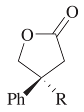
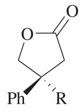
96c (0.2 eq), **146** (1 eq),
THF, −78°, 2 h;
then TMSCl, 3 min



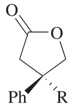
(—) 82% conv, 35% ee

368

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

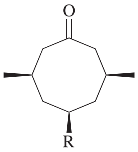
Cyclic Ketone	Conditions		Product(s) and Yield(s) (%)	Refs.
C_{10}				
	**96c** (0.2 eq), 1-methylimidazole (1 eq), **146** (1 eq), THF, –78°, 1 h; then TMSCl, 3 min		(—) 79% conv, 47% ee	368
	1. **2** (1.3 eq), TESCl (1.2 eq), THF, –100°, 15 min 2. O_3; then $NaBH_4$ 3. aq HCl		(49) 97% ee	137
$C_{10–11}$				
	1. **90b**, TESCl, HMPA (*x* eq), THF 2. O_3; then $NaBH_4$ 3. 2 N HCl		R *x* Temp (°) % ee H 1 –78 (58) 45 H 1 –100 (50) 47 Me 0 –78 (50) 51 Me 0 –100 (46) 60 Me 1 –78 (51) 72 Me 1 –100 (49) 78	136
	1. **2**, TESCl, THF 2. O_3; then $NaBH_4$ 3. 2 N HCl		R Temp (°) % ee H –78 (50) 77	136
			H –100 (47) 92	136, 134
			Me –78 (64) 12	136

1. **126**, TESCl, THF, −78°
2. O_3; then $NaBH_4$
3. 2 N HCl

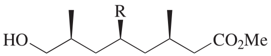


R		% ee
H	(51)	13
Me	(50)	7

136

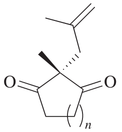


1. **1a** (1.3 eq), LiCl (0–1 eq), TMSCl, THF, −78°
2. O_3; then $NaBH_4$
3. MeOH, TsOH

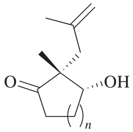


R		% ee
H	(79–81)	96–98
Me	(81)	>98

127
128



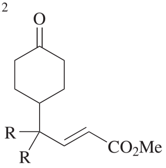
1. **1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°
2. DIBAL-H



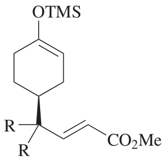
n		% ee
1	(69)	68
2	(71)	81

198

C_{10-12}



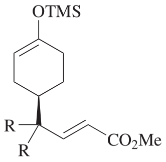
1a (*x* eq), TMSCl, THF, −100°



R	*x*		% ee^b
H	1.3	(0)	—
H	2.4	(80)	65
Me	1.3	(88)	61

163

ent-**5** (*x* eq), TMSCl, THF, −100°



R	*x*		% ee^b
H	2.4	(84)	66
Me	1.3	(85)	79

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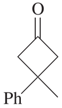
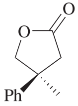
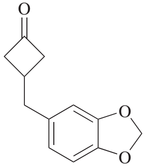
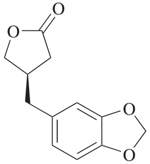
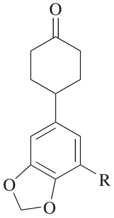
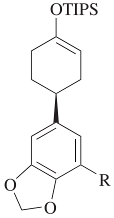
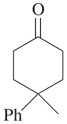
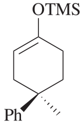
TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	1. **90b**, TESCl, HMPA (1 eq), toluene, −78° 2. O_3; then $NaBH_4$ 3. 2 N HCl	 (50) 73% ee	136
	1. **2** (1.3 eq), THF; then TESCl 2. O_3; then $NaBH_4$ 3. 2 N HCl	 Temp (°) % ee −78 (58) 67 −100 (—) 80	135
C_{12}			
	**1a** (1.5 eq), LiCl (0.5 eq), THF, −78°, 1 h; then TIPSOTf (3–5 eq), −78° to rt, 2 h	 R % ee OMe (95) 85 H (96) >85	 290, 291 292
C_{13}			
	**90b**, TMSCl, THF	 Temp (°) % ee[b] −78 (73) 56 −100 (66) 66	138

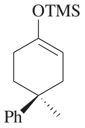
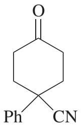
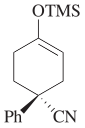
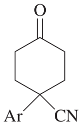
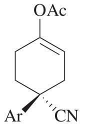
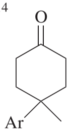
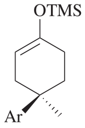
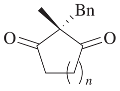
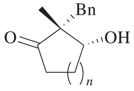
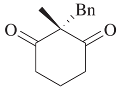
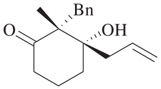
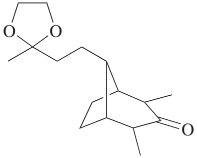
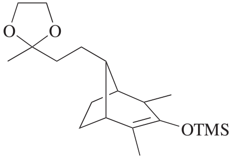
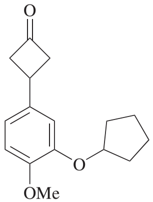
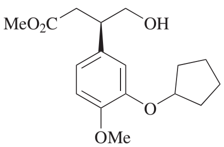
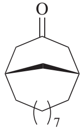
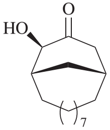
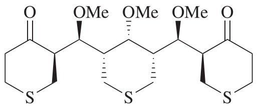
	Lithium amide, TMSCl, THF	 Lithium Amide / Temp (°) / % ee^b **124** / −100 / (21) 19 **126** / −78 / (80) 38 **48a** / rt / (10) 2	138
	**2** (1.4 eq), LiCl (1.4 eq), TMSCl (1 eq), THF, −100°, 1 h	 (64) 64% ee	329
	**2** (1 eq), LiCl (1 eq), THF, −78°, 10 min; then Ac_2O (1.5 eq), −78° to rt, 1 h	 Ar / % ee Ph / (50) 54 3,4-$Cl_2C_6H_3$ / (54) 57	329
C_{13-14}			
	**1a**, TMSCl, THF	 Ar / Temp (°) / % ee^b Ph / −78 / (81) 60 Ph / −100 / (80) 71 4-MeC_6H_4 / −100 / (94) 70	138
	1. **1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 1 h 2. DIBAL-H	 *n* / % ee 1 / (79) 84 2 / (74) 91	198

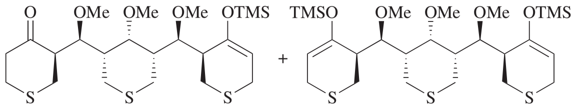
TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	1. **1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 1 h 2. allylMgBr	 (80) 83% ee	198
	Lithium amide (1.7 eq), LiCl (1.7 eq), TMSCl (4 eq), THF, −100°, 1 h	 Lithium Amide — % ee^{i} *ent*-**126** (91) 90–94 **90b** (84) 72–75	126
C_{15}			
	1. **1a**, THF, −100°; then TESCl 2. O_3; then $NaBH_4$ 3. 2 N HCl 4. KOH 5. CH_2N_2	 (29) >95% ee^{a}	133
	1. **90b** (1.2 eq), HMPA (1.1 eq), TMSCl (4 eq), THF, −78° to rt, 35 min 2. DMDO	 (50) 47% ee	122

C$_{17}$



1a (*x* eq), LiCl (*y* eq), TMSCl (10 eq), THF, −100°, 15 min



I + **II**

x	*y*	**I**	% ee **I**	**II**
0.5	0.5	(22)	86	(3)
1	1	(61)	90	(12)
1.4	1.4	(73)	92	(22)
0.5	0	(15)	81	(0)
1.3	0	(61)	94	(8)
1.5	0	(78)	98	(13)
1.7	0	(58)	>98	(34)

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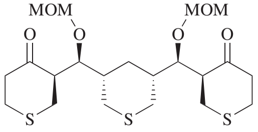
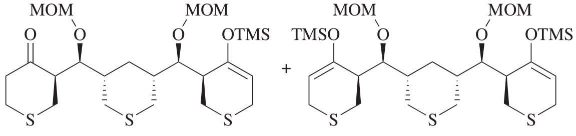
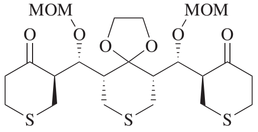


1a (1.2 eq), TMSCl, THF, −100°, 15 min

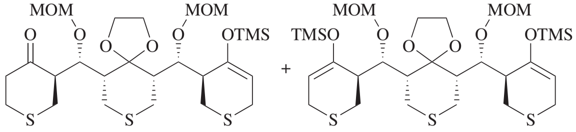


(69) 96% ee + (16)

199



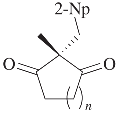
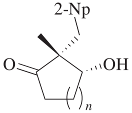
1a (1.4 eq), TMSCl (10 eq), THF, −100°, 15 min



(71) 95% ee + (17)

199

TABLE 2. SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17-18}  	1. **1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 1 h 2. DIBAL-H	 *n* — % ee 1 (71) 73 2 (72) 79	198

[a] The enantiomeric excess was determined after conversion of the product into a suitable Mosher ester derivative.

[b] The enantiomeric excess was determined after Saegusa-Ito oxidation of the silyl enol ether to the corresponding 2-enone.

[c] The enantiomeric excess was determined after conversion of the product into an α-hydroxy ketone by hydroxylation, which was derivatized to the corresponding 2,4-dinitrobenzoate ester.

[d] The enantiomeric excess was determined from an intermediate that occurs at a later stage in the synthesis of a target.

[e] The yield was determined by GC using an internal standard.

[f] The enantiomeric excess was determined after bromination of the product using NBS.

[g] The enantiomeric excess was determined after acetylation.

[h] The enantiomeric excess was determined after oxidation using *m*CPBA to generate an enelactone derivative.

[i] The enantiomeric excess was determined after oxidation of the product using DMDO.

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES

Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*

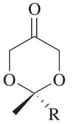
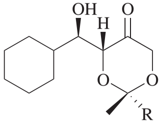
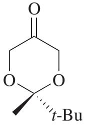
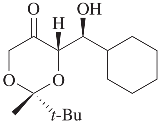
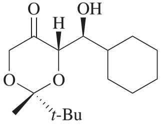
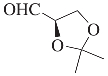
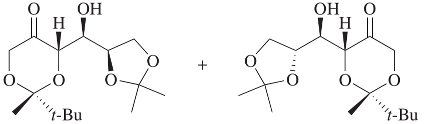
Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)					Refs.
C_3 	Lithium amide (1 eq), LiCl (*x* eq), THF, −78°, 30 min; then *c*-C_6H_{11}CHO (1.1 eq), 5 min						
		R	Lithium Amide	*x*		% ee	
		t-Bu	**4d**	1	(63)	63	187, 185
		t-Bu	*ent*-**3n**	0	(32)	13	187, 186
		t-Bu	*ent*-**3n**	0.5	(56)	39	187, 186
		t-Bu	**4f**	0.5	(51)	20	187
		t-Bu	**8a**	0	(32)	60	186
		t-Bu	**8a**	0.5	(63)	70	186
		t-Bu	**8a**	1	(60)	70–72	185, 187
		Ph	**8a**	1	(68)	53	185
		t-Bu	**8b**	1	(76)	60	187, 185
		t-Bu	*ent*-**6a**	1	(61–86)	87–90	185, 187
		Ph	*ent*-**6a**	1	(64)	54	185
		t-Bu	**3m**	0	(70)	15	187
		t-Bu	**2**	0	(58)	18	187, 186
		t-Bu	**2**	0.5	(51)	60	185, 187, 186
		t-Bu	**2**	1	(49)	59	187
		t-Bu	**4i**	1	(91)	80	187, 185
		t-Bu	**8c**	1	(95)	90	187, 185
		t-Bu	**77h**	0	(28)	23	186
		t-Bu	**77h**	0.5	(51)	20	187, 186

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	Lithium amide, LiCl, THF, –78°; then c-$C_6H_{11}CHO$	 Lithium Amide — % ee **3n** (76) 37 **7a** (77) 50 **7b** (99) 30	185
	Lithium amide (1 eq), LiCl (x eq), THF, –78°, 30 min; then c-$C_6H_{11}CHO$, (1.1 eq), 5 min		
		Lithium Amide — x — % ee	
		3a 0 (43) 10	187, 186
		3a 0.5 (63) 4	187, 186
		3d 0.5 (55) 16	187, 185
		3m 0.5 (53) 32	187
		3m 1 (45) 54	61
		22 0 (41) 50	187, 186
		22 0.5 (41–43) 60	187, 186
	6a (1 eq), LiCl (1 eq), THF, –78°, 30 min; then  (1.1 eq)	 **I** + **II** + uncharacterized product **III** **I** + **II** + **III** (77), **I/II/III** = 82:10:8	187, 185

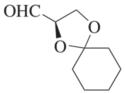
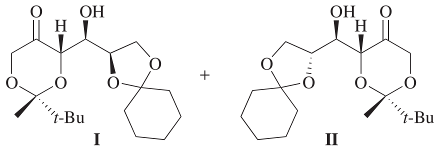
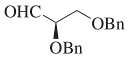
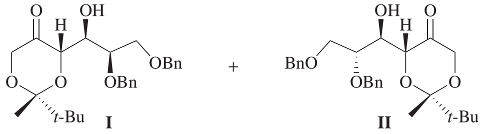
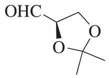
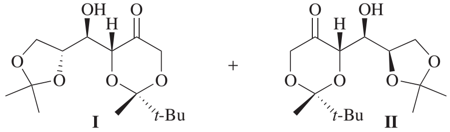
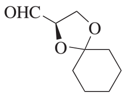
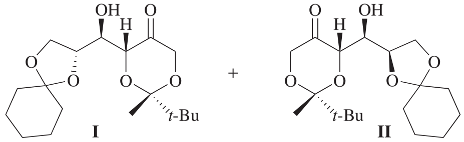
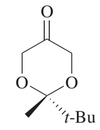
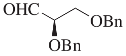
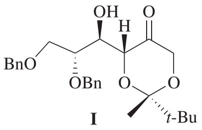
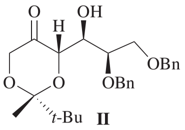
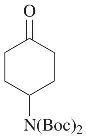
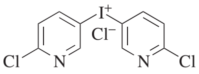
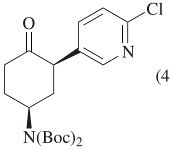
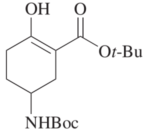
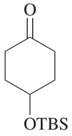
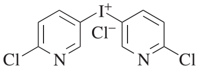
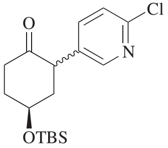
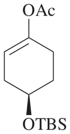
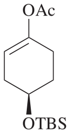
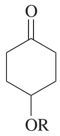
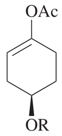
6a (1 eq), LiCl (1 eq), THF, −78°, 30 min; then  (1.1 eq)	 + uncharacterized product **III** **I** + **I** + **III** (96), **I/II/III** = 71:15:14	187
6a (1 eq), LiCl (1 eq), THF, −78°, 30 min; then  (1.1 eq)	 + uncharacterized products **III** + **IV** **I** + **II** + **III** + **IV** (82), **I/II/III/IV** = 60:16:14:10	187
ent-**6a** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then  (1.1 eq)	 **I** + **II** (81), **I/II** = 97:3	187, 185
ent-**6a** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then  (1.1 eq)	 + uncharacterized product **III** **I** + **II** + **III** (97), **I/II/III** = 74:16:10	187

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	*ent*-**6a** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then  (1.1 eq)	 **I** +  **II** + uncharacterized product **III** **I** + **II** + **III** (80), **I/II/III** = 78:16:6	187
C_6 	**1a** (2 eq), LiCl (2 eq), THF, −118°, 2 h; then  (1.1 eq), DMF, −45°, 4 h	 (41) 86% ee +  (14)	195
	**1a** (2 eq), LiCl (2 eq), THF, −118°, 2 h; then  (1.1 eq), DMF, −45°, 4 h	 (70) 90% ee, *cis*/*trans* = 2:1	195
	ent-**3n** (1.2 eq), THF, temp, 2 h; then Ac_2O (2 eq), −78°, 30 min	 Temp (°) % ee[a] −78 (60) 34 −100 (—) 36	164
	ent-**3n** (1.2 eq), HMPA (*x* eq), LiCl (*y* eq), THF, −78°, 2 h; then Ac_2O (2 eq), 30 min	 (—) *x* *y* % ee[a] 1 0 14 0 0.4 45	164

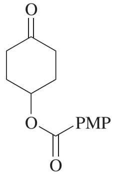


ent-**3n** (1.2 eq),
THF, −78°, 2 h; then
Ac_2O (2 eq), 30 min

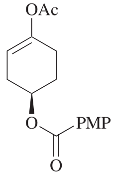


R		% ee[a]
TBDPS	(68)	30
MOM	(92)	20
Me	(66)	18
C(O)*t*-Bu	(69)	30
Bn	(63)	30

164



ent-**3n** (1.2 eq), THF,
temp, 2 h; then
Ac_2O (2 eq), −78°, 30 min



Temp (°)		% ee[a]
−78	(57)	24
−100	(—)	30

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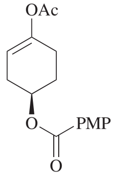
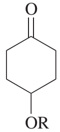
ent-**3n** (1.2 eq), HMPA (*x* eq),
LiCl (*y* eq), THF, −78°, 2 h;
then Ac_2O (2 eq), 30 min



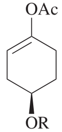
(—)

x	*y*	% ee[a]
1	0	26
0	0.4	47

164



ent-**3d** (1.2 eq), THF,
−78°, 2 h; then
Ac_2O (2 eq), 30 min



R		% ee[a]
TBS	(55)	28
TBDPS	(63)	36
MOM	(64)	16
Me	(60)	22
C(O)*t*-Bu	(76)	30
PMP	(6)	10

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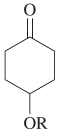
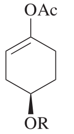
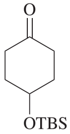
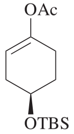
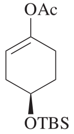
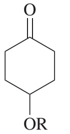
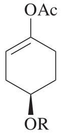
TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

	Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6		**2** (1.2 eq), THF, −78°, 2 h; then Ac_2O (2 eq), 30 min		R | | % ee^a TBS (50) 36 TBDPS (60) 52 MOM (88) 34 Me (75) 42 C(O)*t*-Bu (61) 34 PMP (63) 36 Bn (71) 49	164
		**77d** (1.2 eq), THF, temp, 2 h; then Ac_2O (2 eq), −78°, 30 min		Temp (°) | | % ee^a −78 (74) 52 −100 (—) 50	164
		77d (1.2 eq), HMPA (*x* eq), LiCl (*y* eq), THF, −78°, 2 h; then Ac_2O (2 eq), 30 min	 (—)	*x* *y* % ee^a 1 0 33 0 0.4 27	164
		**77d** (1.2 eq), THF, −78°, 2 h; then Ac_2O (2 eq), 30 min		R | | % ee^a TBDPS (69) 38 MOM (72) 44 Me (69) 34 C(O)*t*-Bu (60) 62 Bn (66) 54	164

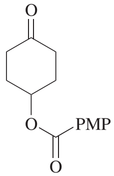
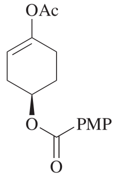
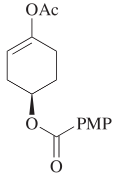
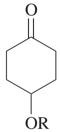
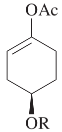
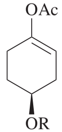
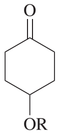
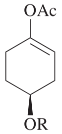
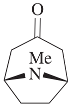
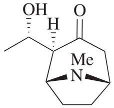
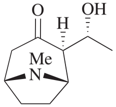
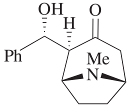
	**77d** (1.2 eq), THF, temp, 2 h; then Ac$_2$O, (2 eq), −78°, 30 min		Temp (°) / % ee^a −78 (78) 48 −100 (—) 58	164
	77d (1.2 eq), HMPA (*x* eq), LiCl (*y* eq), THF, −78°, 2 h; then Ac$_2$O (2 eq), 30 min		(—) *x* *y* % ee^a 1 0 46 0 0.4 48	164
	**90a** (1.2 eq), THF, −78°, 2 h; then Ac$_2$O (2 eq), 30 min		R / % ee^a TBS (39) 26 TBDPS (55) 30 MOM (81) 44 Me (72) 34 C(O)*t*-Bu (73) 56 PMP (75) 31	164
	126 (1.2 eq), THF, −78°, 2 h; then Ac$_2$O (2 eq), 30 min		R / % ee^a TBS (55) 30 TBDPS (71) 22 MOM (87) 22 Me (65) 30 C(O)*t*-Bu (67) 18 PMP (65) 4	164

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	**22** (1.2 eq), THF, −78°, 2 h; then Ac_2O (2 eq), 30 min	 R — % ee[a] TBS (65) 74 TBDPS (90) 50 MOM (77) 66 Me (64) 45 C(O)*t*-Bu (89) 64 PMP (71) 42 Bn (56) 62	164
C_7 	**1a**, LiCl, THF, −78°; then MeCHO	 (65) 99% ee	189
	2, LiCl, THF, −78°; then MeCHO	 (66) 99% ee	189
	1a (1.1 eq), LiCl (*x* eq), THF, −78°, 1 h; then PhCHO	 *x* — % ee 0 (84) 40 1 (80) 90–99	180, 347, 177 177, 61, 189

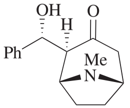
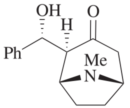
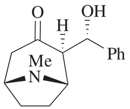
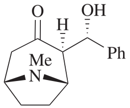
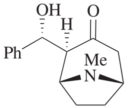
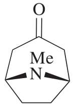
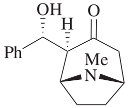
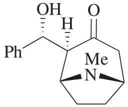
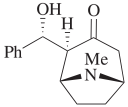
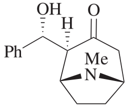
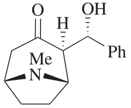
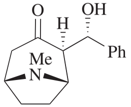
1a (1.5 eq), LiCl (*x* eq), THF, 78°, 1 h; then PhCHO (1.2 eq), 15 min		(~75)	*x* / % ee 0.00 / 24 0.01 / 35 0.03 / 42 0.05 / 59 0.07 / 62 0.09 / 66 0.2 / 79 0.3 / 77 0.5 / 78 0.8 / 80	58, 59 58, 59 58, 59 58, 59 58, 59 58, 59 59 59 58, 59 59
1a, ZnCl$_2$ (~0.5 eq), THF, −78°; then PhCHO		(—) 85% ee		59, 58
2, LiCl, THF, −78°; then PhCHO		(79) 99% ee		189
Lithium amide (1.1 eq), THF, −78°, 1 h; then PhCHO (1 eq), 15 min		Lithium Amide / % ee *ent*-**3d** (88) 34 **90a** (64) 60 **103a** (85) 8		180, 347
3d (1.5 eq), LiCl (*x* eq), THF, −78°, 1 h; then PhCHO (1.2 eq), 15 min		(—)	*x* / % ee 0 / 24 0.5 / 66	59

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7 	**126** (1.1 eq), THF, −78°, 1 h; then PhCHO, 15 min		(75) 40% ee	180, 347
	129 (1.1 eq), THF, −78°, 1 h; then PhCHO, 15 min		(70) 26% ee	180, 347
	133 (1.1 eq), THF, −78°, 1 h; then PhCHO, 15 min		(97) 16% ee	347
	3n (1.5 eq), LiCl (*x* eq), THF, −78°, 1 h; then PhCHO (1.2 eq), 15 min		(—) *x* % ee 0 30 0.5 72	59
	ent-**3n**, LiCl, THF, −78°; then PhCHO		(65) 76% ee	182
	ent-**3n** (1.2 eq), LiCl (1.2 eq), THF, −78°, 3 h; then PhCHO (1.4 eq), 30 min		[M] % ee 0.1 (77) 72 0.08 (67) 73 0.042 (61) 75 0.026 (70) 76	69

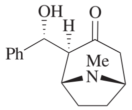
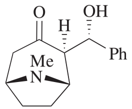
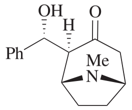
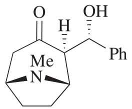
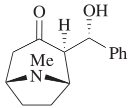
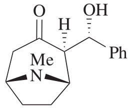
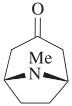
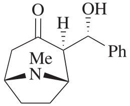
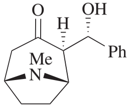
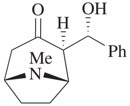
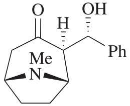
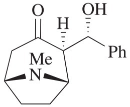
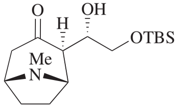
6a (1.2 eq), LiCl (1.2 eq), THF, −78°, 3 h; then PhCHO (1.4 eq), 30 min		[M] % ee 0.1 (76) 80 0.035 (88) 88	69
77h (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then PhCHO (1.3 eq), 15 min		(91) 95% ee	177
38 (1.2 eq), LiCl (1.2 eq), THF, −78°, 3 h; then PhCHO (1.4 eq), 30 min		[M] % ee 0.15 (68) 51 0.1 (74) 57 0.026 (64) 65	69
178a (1.1 eq), LiCl (*x* eq), THF, −78°, overnight; then PhCHO (1.1 eq), 4 h		*x* % ee 0 (38–40) 14–20 1 (45) 24	182, 181
188 (1.1 eq), LiCl (*x* eq), THF, −78°, overnight; then PhCHO (1.1 eq), 4 h		*x* % ee 0 (20–30) 10 1 (26–35) 20	182, 181
192 THF, −78°, overnight; then PhCHO (1 eq)		(71) 12% ee	182

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	**178b** (1.1 eq), LiCl (2 eq), THF, −78°, 3 h; then PhCHO (1.1 eq), 1 h	 (77–83) 75% ee	182, 181
	181 LiCl (2 eq), THF, −78°, overnight; then PhCHO (1 eq)	 (74) 66% ee	182
	179 (1.1 eq), LiCl (2 eq), THF, −78°, 3 h; then PhCHO (1.1 eq), 1 h	 (51) 70% ee	181
	185 (1.1 eq), LiCl (2 eq), THF, −78°, 3 h; then PhCHO (1.1 eq), 1 h	 (35) 26% ee	181
	189 (1.1 eq), LiCl (2 eq), THF, −78°, 3 h; then PhCHO (1.1 eq), 1 h	 (40) 35% ee	181
	2 (1.5 eq), LiCl (1.5 eq), THF, −78°, 3 h; then $TBSOCH_2CHO$ (1.5 eq), 3.5 h	 (72) 90–92% ee, single diast.	188

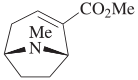
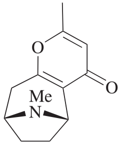
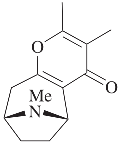
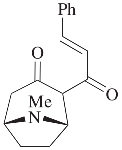
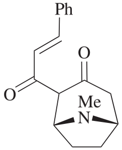
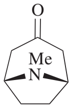
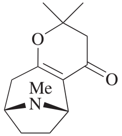
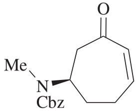
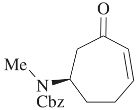
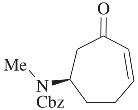
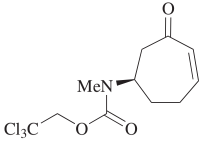
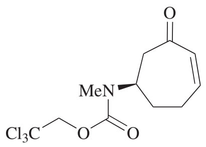
1. **77h** (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then NCCO$_2$Me (1.5 eq), 30 min 2. H$_2$, PtO$_2$ 3. (CF$_3$CO)$_2$O; then K$_2$CO$_3$		(72) 94% ee	177
1. **77h** (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then (*Z*)-MeCH=C(Br)COCN (2.5 eq), 30 min 2. Et$_3$N, reflux		(45) 88–92% ee	192, 177
1. **77h** (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then (*E*)-MeCH=C(Me)COCN 2. Na$_2$CO$_3$, EtOH, reflux 3. CuBr$_2$, EtOAc, reflux 4. Et$_3$N, reflux		(53) 91% ee	192, 177
77h (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then cinnamoyl cyanide (1 eq), 30 min		(75) 90% ee	192, 177
1a (1.2 eq), LiCl (1.2 eq), THF, −78°, 2.5 h; then cinnamoyl cyanide (1 eq), 30 min		(78) 92% ee	177

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1. **77h** (1.2 eq), LiCl (0.5 eq), THF, −78°, 2.5 h; then $Me_2C{=}CHCOCN$ (2.6 eq), 30 min 2. Na_2CO_3, EtOH, reflux	 (90) 92–93% ee	192, 177
	ent-**3d** (1.2 eq), LiCl (*x* eq), THF, −78°; then CbzCl	 (—) *x* % ee 0 45 0.5 63	192
	77h (1.2 eq), LiCl (0.5 eq), THF, −78°; then CbzCl	 (—) 92% ee	192
	2 (1.1 eq), LiCl (1.1 eq), THF, −78°, 3.5 h; then CbzCl (1.2 eq), 30 min	 (85) 95% ee^b	191, 194
	2 (1.1 eq), LiCl (*x* eq), THF, −78°, 3.5 h; then Cl_3CCH_2OCOCl (1.2 eq), 30 min	 *x* % ee 0 (80) 44 0.1 (84) 49 0.25 (92) 85 0.5 (90) 95 1 (92) 96 2 (94) 95	191

2 (1.1 eq), LiBr (*x* eq),
THF, −78°, 3.5 h; then
Cl_3CCH_2OCOCl (1.2 eq),
30 min



x		% ee
0.1	(78)	49
0.25	(82)	54
0.5	(88)	63
1	(93)	73
2	(85)	88

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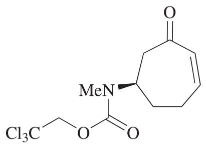
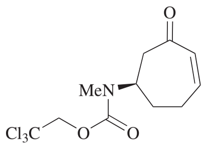
2 (1.1 eq), LiI (2 eq),
THF, −78°, 3.5 h; then
Cl_3CCH_2OCOCl (1.2 eq),
30 min



(78) 41% ee

191

2 (1.1 eq), additive (1 eq),
THF, −78°, 3.5 h; then
Cl_3CCH_2OCOCl (1.2 eq),
30 min



Additive		% ee
LiF	(70)	38
$LiClO_4$	(85)	45
$CeCl_3$	(70)	80
$ZnCl_2$	(40)	87
TMEDA	(45)	40
HMPA	(71)	39
DMPU	(65)	52

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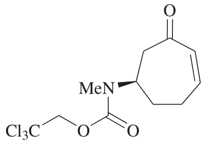
2 (1.1 eq), BuLi (*x* eq),
H_2O (*x* eq), THF, −78°, 3.5 h;
then Cl_3CCH_2OCOCl (1.2 eq),
30 min



x		% ee
0.05	(48)	24
0.2	(13)	5

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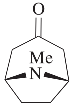
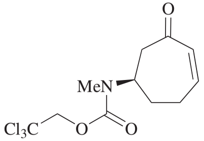
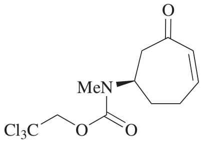
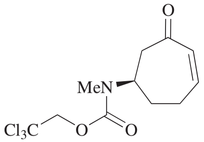
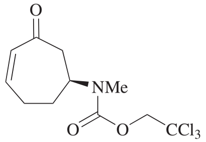
TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	*ent*-**3d** (1.1 eq), THF, −78°; then Cl_3CCH_2OCOCl (1.2 eq)	 (80) 29% ee	191
	Lithium amide (1.1 eq), LiCl (*x* eq), THF, −78°; then Cl_3CCH_2OCOCl (1.2 eq)	 Lithium Amide — *x* — — % ee **8a** — 0 — (86) — 78 **8a** — 1 — (65) — 87 **21** — 0 — (50) — 48 **21** — 1.1 — (89) — 88 **10b** — 0 — (22) — 17 **10b** — 1.1 — (60) — 72 **23** — 1.1 — (71) — 74 **77h** — 0 — (82) — 83 **77h** — 1 — (88) — 95 **90b** — 0 — (80) — 87 **90b** — 1 — (87) — 95	191
	Lithium amide (1.1 eq), LiCl (*x* eq), THF, −78°, overnight; then Cl_3CCH_2OCOCl (1.1 eq), 8 h	 Lithium Amide — *x* — — % ee **178a** — 0 — (13–28) — 2–10 **178a** — 1 — (37) — 59 **183** — 1 — (15) — 36 **184** — 0 — (42) — 3 **184** — 1 — (48) — 6 **188** — 0 — (22) — 2 **188** — 1 — (25) — 22 **186** — 1 — (11) — 9 **187** — 0 — (5) — 3	 182, 181 182, 181 181 182, 181 182, 181 182, 181 182, 181 181 181

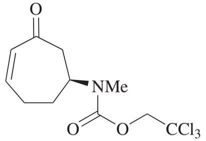
Lithium amide (1.1 eq),
LiCl (x eq),
THF, −78°, overnight; then
Cl_3CCH_2OCOCl (1.1 eq), 8 h



Lithium Amide	x		% ee
183	0	(10)	13
180	0	(7)	6.5
180	1	(10)	13
186	0	(5)	11

181

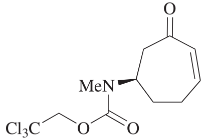
180 (1.1 eq), 2,2,5,5-TMTHF,
−78°; then
Cl_3CCH_2OCOCl (1.1 eq)



(5) 1.5% ee

181

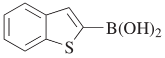
179 (1.1 eq), BuLi (1 eq),
LiCl (1 eq),
THF, −78°, 3 h; then
Cl_3CCH_2OCOCl (1.3 eq), 2 h

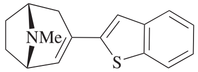


(57) 30% ee

181

1. Lithium amide (1.1 eq),
THF, −70°, 3 h;
then $PhNTf_2$ (1.1 eq),
−70° to rt, overnight
2. $[Pd(PPh_3)_4]$ (cat.),

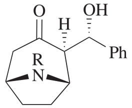




Lithium Amide		% ee
2	(57)	90
1a	(~57)	−90

169

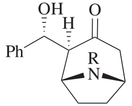
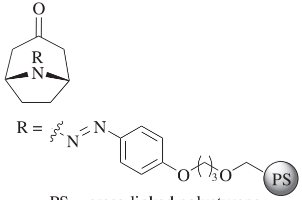
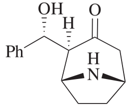
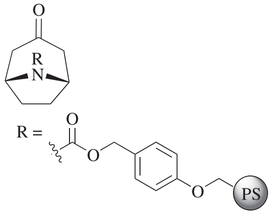
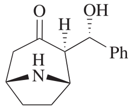
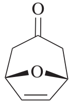
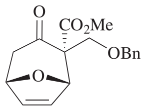
77h, LiCl (x eq),
THF, −78°, 2 h; then
PhCHO, 15 min



R	x		% ee[a]
Bn	0.7	(74)	86
Cbz	0.7	(44)	45
PhN=N	0.7	(82)	63
PhN=N	0	(80)	53

385

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7				
	**1a**, LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO, 15 min		R — % ee[a] Bn (84) 82 Cbz (45) 8 PhN=N (81) 72	385
 PS = cross-linked polystyrene	1. **1a**, LiCl (1.1 eq), THF, −78°, 5 h; then PhCHO, 1.5 h 2. TFA		(55) 48% ee[a]	385
 PS = cross-linked polystyrene	1. **77h**, LiCl (0.7 eq), THF, −78°, 5 h; then PhCHO, 1.5 h 2. TFA		(57) 44% ee[a]	385
	1. **2** (1.2 eq), LiCl (0.6 eq), THF, −94°, 1 h; then $NCCO_2Me$ (5 eq), −94° to rt 2. NaH, $ClCH_2OBn$		(33) 97% ee, single diast.	178

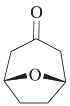
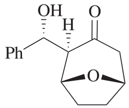
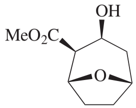
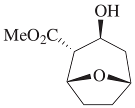
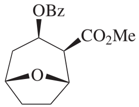
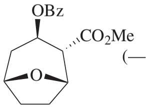
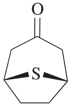
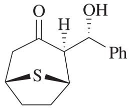
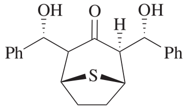
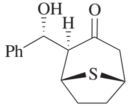
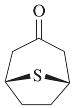
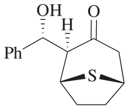
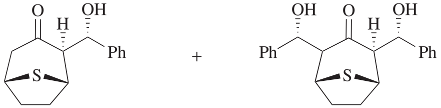
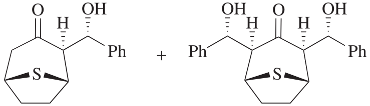
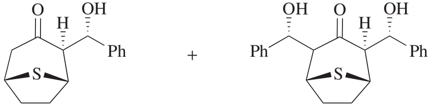
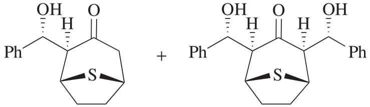
	**1a** (1.5 eq), $ZnCl_2$ (*x* eq), THF, −78°, 15 min; then PhCHO		(—) *x* % ee: 0.0 34; 0.1 74; 0.2 72; 0.4 70; 0.5 74 *x* % ee: 0.6 68; 0.7 62; 0.8 52; 0.9 51; 1.0 47	63
	1. **1a**; then $NCCO_2Me$ 2. Na amalgam		(—) 84% ee +  (—) 88% ee	176, 175
	1. **77h**; then $NCCO_2Me$ 2. Na amalgam 3. BzCl, Et_3N, DMAP		(—) 83% ee +  (—) 84% ee	176, 175
	**2** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO (1.2 eq), 30 min	 **I** 58–70% ee	+  **II** **I** + **II** (80), **I/II** = 75:25	183, 184
	1a, LiCl (*x* eq), THF, −78°; then PhCHO		*x* (yield) % ee: 0 (80) 16; 0.5 (71) 84	63

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	**1a**, $ZnCl_2$ (*x* eq), THF, −78°; then PhCHO	 (—) *x* / % ee: 0.0 / 15; 0.05 / 73; 0.1 / 76; 0.2 / 86; 0.4 / 86; 0.6 / 74; 0.7 / 63; 0.8 / 68; 0.9 / 45; 1.0 / 21	63
	ent-**3n** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO (1.2 eq), 30 min	 **I** 45% ee **I** + **II** (78), **I/II** = 9:1 **II**	183, 184
	ent-**3n**, (1.2 eq), LiCl (1.2 eq), THF, −78°, 3 h; then PhCHO (1.4 eq), 30 min	 **I** **II** (10–15) [M] / **I** / % ee: 0.1 / (72) / 35; 0.035 / (78) / 45	69
	ent-**6a** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO (1.2 eq), 30 min	 **I** 70% ee **I** + **II** (72), **I/II** = 95:5 **II**	183, 184
	6a (1.2 eq), LiCl (1.2 eq), THF, −78°, 3 h; then PhCHO (1.4 eq), 30 min	 **I** **II** (10–15) [M] / **I** / % ee: 0.12 / (55) / 46; 0.1 / (61) / 53; 0.05 / (65) / 64; 0.035 / (72) / 71	69

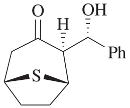
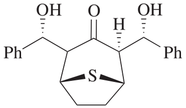
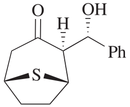
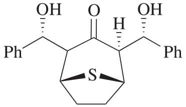
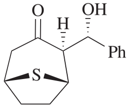
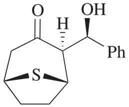
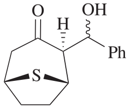
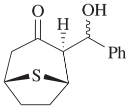
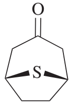
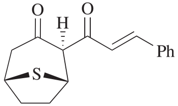
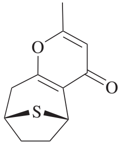
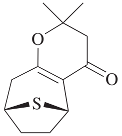
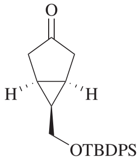
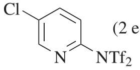
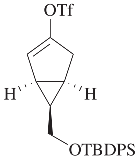
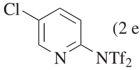
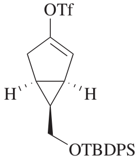
8a (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO (1.2 eq), 30 min	 +  **I** 95% ee **I** + **II** (82), **I/II** = 98:2 **II**	183, 184
90b (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCHO (1.2 eq), 30 min	 +  **I** 74% ee **I** + **II** (75), **I/II** = 9:1 **II**	183, 184
190, THF, −78°, overnight; then PhCHO (1 eq)	 +  **I** % ee n.d. **I** + **II** (63), **I/II** = 95:5 **II** % ee n.d.	182
178b, THF, −78°, overnight; then PhCHO (1 eq)	 (72) 44% ee, dr n.d.	182
181, THF, −78°, overnight; then PhCHO (1 eq)	 (69) 38% ee, dr n.d.	182

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	**8a** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then PhCH=CHCOCN (1.2 eq)	 (61) 87% ee	183, 184
	1. **8a** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then MeCH=CBrCOCN (1.2 eq) 2. Et_3N, reflux	 (48) 87% ee	183, 184
	1. **8a** (1.1 eq), LiCl (1.1 eq), THF, −78°, 2 h; then Me_2C=CHCOCN (1.2 eq) 2. Na_2CO_3	 (78) 92% ee	183, 184
	**2** (3 eq), LiCl, THF, −78°, 1 h; then  (2 eq), 1.5 h	 (32) 75% ee	167
	6a (3 eq), LiCl, THF, −78°, 1 h; then  (2 eq), 1.5 h	 (43) 77% ee	167

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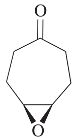
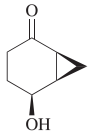
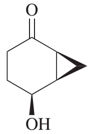
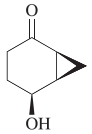
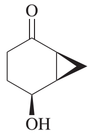
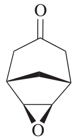
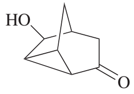
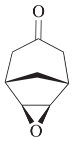
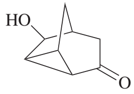
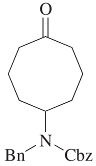
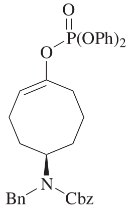
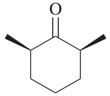
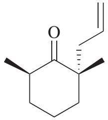
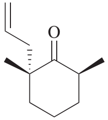
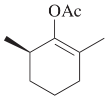
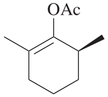
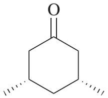
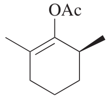
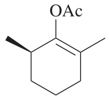
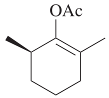
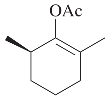
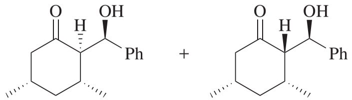
<tr><td></td><td>2, LiCl, THF,
−78° to rt, 2 h</td><td></td><td>(53) 0% ee^c</td><td>197</td></tr>
<tr><td></td><td>Lithium amide, HMPA,
THF, −78° to rt</td><td></td><td><table><tr><th>Lithium Amide</th><th>Time (h)</th><th></th><th>% ee^c</th></tr><tr><td>96b</td><td>6</td><td>(12)</td><td>7</td></tr><tr><td>103a</td><td>4</td><td>(48)</td><td>1</td></tr></table></td><td>197</td></tr>
<tr><td></td><td>Lithium amide,
HMPA, THF,
−78° to rt, 4 h</td><td></td><td><table><tr><th>Lithium Amide</th><th></th><th>% ee</th></tr><tr><td>101a</td><td>(61)</td><td>3</td></tr><tr><td>108</td><td>(47)</td><td>6</td></tr></table></td><td>197</td></tr>
<tr><td></td><td>120, THF, −78° to rt, 21 h</td><td></td><td>(34) 8% ee^c</td><td>197</td></tr>
<tr><td>C$_8$
</td><td>2, THF, −78°, 1 h</td><td></td><td><table><tr><th>Additive</th><th></th><th>% ee^d</th></tr><tr><td>—</td><td>(66)</td><td>22</td></tr><tr><td>LiCl</td><td>(71)</td><td>88</td></tr></table></td><td>197</td></tr>
</table>

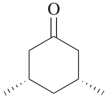
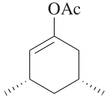
TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	**96b**, HMPA, THF, −78°, 1 h	 (67) 14% ee[d]	197
	**1a**, LiCl, THF, −100°; then $(PhO)_2POCl$	 (89) 89% ee	171
	Lithium amide (1.1 eq), THF, −78°, 3 h; then allyl bromide (6 eq), −78 to 0°, 4–6 h	 Lithium Amide — % ee **3n** (50–65) 25 **126** (—) 68	53, 115 115
	Lithium amide (1.1 eq), THF, −78°, 3 h; then allyl bromide (6 eq), −78 to 0°, 4–6 h	 (—) Lithium Amide — % ee *ent*-**3n** 25 **124** 64	53, 115 115
	Lithium amide (1.2 eq), THF, −78 to −40°, overnight; then Ac_2O (8 eq), 40 min	 Lithium Amide — % ee **1a** (71) 43 **3n** (75) 29 **3d** (71) 32 **126** (68) 74	53, 115
	124 (1.2 eq), THF, −78 to −40°, overnight; then Ac_2O (8 eq), 40 min	 (65) 65% ee	53, 115

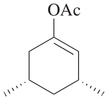
	*ent*-**3n** (1.2 eq), LiCl (1.2 eq), THF, −78°; then Ac$_2$O (1.4 eq)		[M] / / % ee 0.15 (58) 47 0.10 (62) 53 0.035 (64) 55	69
	128 (1.2 eq), THF, −78 to −40°, overnight; then Ac$_2$O (8 eq), 40 min		(76) 5% ee	53, 115
	132 (1.2 eq), THF, −78 to −40°, overnight; then Ac$_2$O (8 eq), 40 min		(70) 14% ee	53, 115
	57 (1.2 eq), THF, −78 to −40°, overnight; then Ac$_2$O (8 eq), 40 min		(28) 8% ee	115
	Lithium amide (1.1 eq), THF, −78°, 2 h; then PhCHO (1 eq), 2 min	 **I** + **II**		165

Lithium Amide	**I** + **II**	**I**/**II**	% ee **I**	% ee **II**
126	(76)	63:37	3	11
6b	(59)	66:34	24	21
5	(50)	63:37	34	32
1a	(55)	64:36	42	52
3d	(52)	63:37	43	54

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

<table>
<tr><th>Cyclic Ketone</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_8
</td><td>Lithium amide (1.1 eq), THF, −78°, 2 h; then PhCHO (1 eq), 2 min</td><td>
I + II
<table>
<tr><th>Lithium Amide</th><th>I + II</th><th>I/II</th><th>% ee I</th><th>% ee II</th></tr>
<tr><td>10a</td><td>(56)</td><td>61:39</td><td>25</td><td>43</td></tr>
<tr><td>4f</td><td>(61)</td><td>66:34</td><td>30</td><td>51</td></tr>
<tr><td><i>ent</i>-3d</td><td>(42)</td><td>63:37</td><td>41</td><td>52</td></tr>
<tr><td><i>ent</i>-3n</td><td>(51)</td><td>60:40</td><td>51</td><td>57</td></tr>
</table></td><td>165</td></tr>
<tr><td></td><td><i>ent</i>-3n (1.1 eq), THF, −78°, 2–3 min; then PhCHO (1 eq), 2 min</td><td>
I 57% ee I + II (45), I/II = 50:50 II 74% ee</td><td>165</td></tr>
<tr><td></td><td><i>ent</i>-3n (1.1 eq), LiBr (3 eq), THF, −78°, 2 h; then PhCHO (1 eq), 2 min</td><td>
I 57% ee I + II (42), I/II = 49:51 II 61% ee</td><td>165</td></tr>
<tr><td></td><td><i>ent</i>-3d (1.1 eq), THF, −78°, 2 h; then PhCHO (1 eq), 30 min</td><td>
I 39% ee I + II (61), I/II = 66:34 II 53% ee</td><td>165</td></tr>
<tr><td></td><td>10a (1.1 eq), THF, −78°, 2 h; then Ac₂O (3 eq), 30 min</td><td> (52) 29% ee</td><td>165</td></tr>
</table>

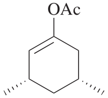
1a (1.1 eq), THF,
−78°, 2 h; then
Ac_2O (3 eq), 30 min



(77) 34% ee

165

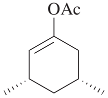
ent-**3n** (*x* eq),
−78°, 2 h; then
Ac_2O (3 eq), 30 min



Solvent	*x*		% ee
THF	1.1	(38)	62
hexane	1.1	(20)	39
hexane, THF (4 eq)	1.1	(26)	40
THF	2	(37)	70

165

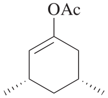
ent-**3d** (*x* eq), THF,
−78°, 2 h; then
Ac_2O (3 eq), 30 min



x		% ee
0.5	(52)	51
1	(79)	53
2	(67)	45

165

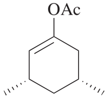
ent-**3d** (1.1 eq), additive (*x* eq),
−78°, 2 h; then
Ac_2O (3 eq), 30 min



Solvent	Additive	*x*		% ee
Et_2O	—	—	(62)	47
hexane	—	—	(44)	30
hexane	THF	4	(58)	48
toluene	—		(29)	30
toluene	THF	4	(40)	41
THF	HMPA	4	(42)	35
THF	HMPA	0.5	(76)	41
THF	TMEDA	4	(33)	44

165

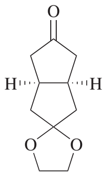
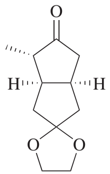
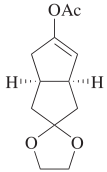
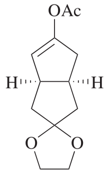
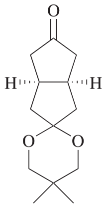
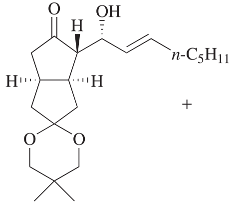
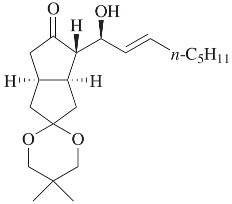
ent-**3d** (1.1 eq), LiBr (1 eq),
THF (6 eq), toluene,
−78°, 2 h; then
Ac_2O (3 eq), 30 min

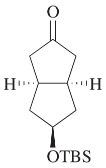


(67) 64% ee

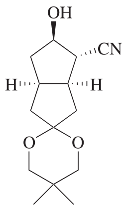
165

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	**53**, THF; then MeI	 (—) 20% ee	158
	1a (2 eq), THF, −78°, 30 min; then Ac_2O, 30 min	 (74) 35% ee	373
	ent-**3d** (2 eq), THF, −78°, 30 min; then Ac_2O, 30 min	 (60) 35% ee	373
	**1a** (1.3 eq), LiCl (1.3 eq), THF, −105°, 30 min; then (*E*)-oct-2-enal (1.5 eq), −78°, 3 h	 +  **I** % ee n.d. **I** + **II** (95), **I/II** = 2:1 **II** % ee n.d.	155

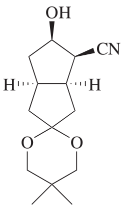


1. **1a** (1.3 eq), LiCl (1.3 eq),
THF, −105°, 1 h; then
2. TsCN (2 eq),
−105 to −78°, 100 min;
3. EtOH, $NaBH_4$ (6 eq), –40°, 4 h



I 92% ee

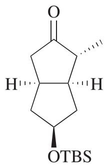
+



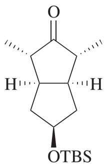
I + **II** (95), **I**/**II** = 3.6:1 **II** % ee n.d.

154

1a (1.5 eq), LiCl (1.5 eq),
THF, −100°, 23 h;
then MeI (2 eq), −50 to 0°, 6 h



(30) 60% ee, dr 99:1 +



(12)

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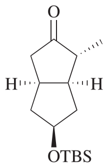
1a (1.1 eq), LiCl (1.1 eq),
THF, −100°, 1 h; then
MeI (2 eq), temp, 23 h



Temp (°)		% ee	dr
−10	(71)	82	99:1
−20	(40)	84	99:1
−30	(64)	86	98.5:1.5
−40	(68)	92	98:2

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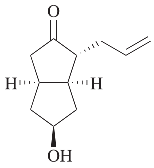
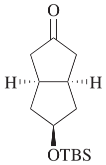
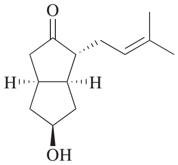
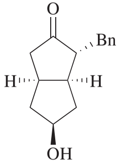
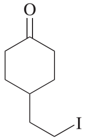
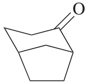
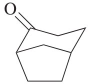
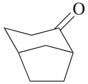
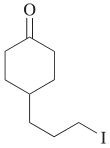
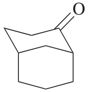
1. **1a** (1.1 eq), LiCl (1.1 eq),
THF, −100°, 1 h; then
allyl iodide (2 eq), –40°, 23 h
2. TBAF



(72) 94% ee, dr 84:16

153

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	1. **1a** (1.2 eq), LiCl (1.2 eq), THF, −100°, 1 h; then prenyl bromide (2 eq), −45°, 23 h 2. TBAF	 (31) 88% ee, dr 86:14	153
	1. **1a** (1.2 eq), LiCl (1.2 eq), THF, −100°, 1 h; then BnBr (2 eq), −45°, 23 h 2. TBAF	 (8) 82% ee, dr 81:19	153
	**2** (*x* eq), LiCl (*y* eq), THF, 18 h	 *x* | *y* | Temp (°) | | % ee 1.5 | 2.5 | −60 to −20 | (53) | 58 1.05 | 2.05 | −80 to −40 | (58) | 80	196
	6a (*x* eq), LiCl (1 eq), THF, 18 h	 *x* | Temp (°) | | % ee 1.5 | −60 to −20 | (61) | 70 1.05 | −80 to −40 | (45) | 78 1.5 | −80 to −40 | (70) | 80	196
	67 (*x* eq), LiCl (1 eq), THF, 18 h	 *x* | Temp (°) | | % ee 1.1 | −60 to −20 | (57) | 36 1.05 | −80 to −40 | (79) | 46	196
C_9 	**2** (1.3 eq), LiCl (1.3 eq), HMPA (*x* eq), THF, 18 h	 *x* | Temp (°) | | % ee 2.4 | −40 to rt | (58) | 18 2.5 | −50 to −10 | (29) | 64 0 | −50 to −10 | (44) | 74	196

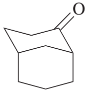
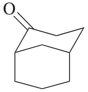
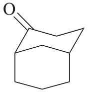
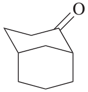
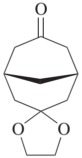
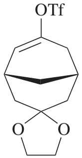
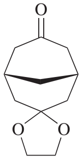
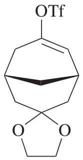
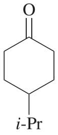
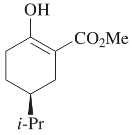
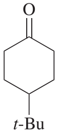
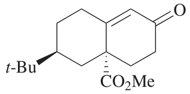
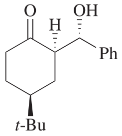
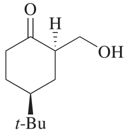
	2 (1.5 eq), LiCl (2.5 eq), THF, −60 to −20°, 18 h		(62) 74% ee	196
	6a (1.5 eq), LiCl (*x* eq), THF, −60 to −20°, 18 h		*x* % ee 2 (38) 46 1 (39) 56	196
	6a (1.5 eq), LiBr (1 eq), THF, −60 to −20°, 18 h		(42) 60% ee	196
	67 (*x* eq), LiCl (*y* eq), THF, −60 to −20°, 18 h		*x* *y* % ee 1.5 2 (61) 52 1.1 1 (60) 52	196
	**1a** (1.2 eq), LiCl (0.2 eq), THF, −78°, 15 min; then $PhNTf_2$ (1.5 eq), −78° to rt, 16 h		(64) 81% ee	166

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	**2** (1.2 eq), LiCl (0.2 eq), THF, −78°, 15 min; then PhNTf$_2$ (1.5 eq), −78° to rt, 16 h	 (79) 79% ee	166
	**1a** (2 eq), LiCl (2.4 eq), THF, −100°, 4 h; then NCCO$_2$Me (2 eq), 30 min	 (82) 94% ee	173
C_{10} 	1. **3o**, LiBr (2 eq), THF, −100°; then NCCO$_2$Me, TMEDA (2 eq), 2 h 2. *i*-Pr$_2$NEt, MVK, −78° 3. *p*-TsOH, benzene, 80°	 (48) 89% ee	383
	3o, LiBr (2 eq), THF, −100°; then PhCHO	 (58) 89% ee	383
	3o, LiBr (2 eq), THF, −100°; then CH$_2$O	 (~50) 89% ee	383

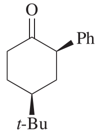
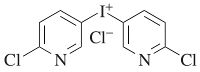
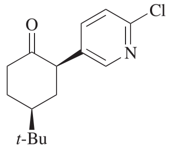
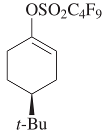
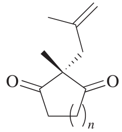
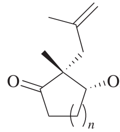
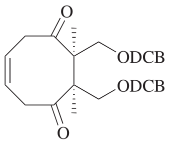
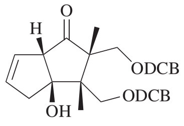
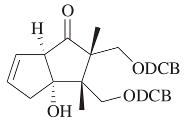
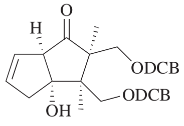
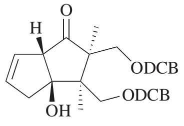
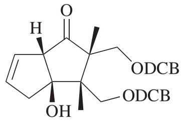
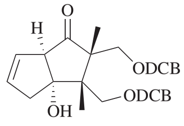
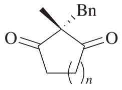
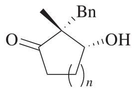
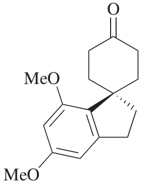
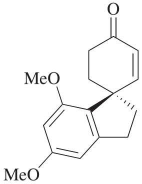
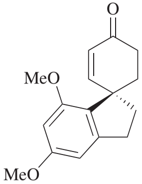
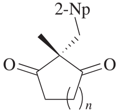
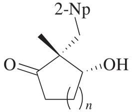
	1a (2 eq), LiCl (2 eq), THF, −118°, 2 h; then $Ph_2I^+(OTf)^-$ (1 eq), DMF, −45°, 3.5 h	 (84) 90% ee, dr >20:1	195
	1a (2 eq), LiCl (2 eq), THF, −118°, 2 h; then  DMF, −45°, 4 h	 (51) 90% ee	195
	1a, LiCl, THF, −105°; then $C_4F_9SO_2F$ (1.3 eq), −105° to rt	 (77) ~89% ee	168
$C_{10–11}$ 	**1a** (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then DIBAL-H (3.3 eq), 4 h	 *n* — % ee — % de 1 (69) 77 31 2 (69) 99 99	198

TABLE 3. NON-SILYLATIVE TRANSFORMATIONS OF PROCHIRAL CYCLIC KETONES (*Continued*)

Cyclic Ketone	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	Lithium amide (10 eq), LiCl (10 eq), THF, −78°, 10 min	 **I** +  **II** Lithium Amide / **I + II** / **I/II** / % ee **I** **4h** / (87) / 19:1 / 41 **4e** / (73) / 15:1 / 13 **4i** / (100) / 6:1 / 0	293
	Lithium amide (10 eq), LiCl (10 eq), THF, −78°, 10 min	 **I** +  **II** Lithium Amide / **I + II** / **I/II** / % ee **I** **2** / (88) / 7:1 / 31 *ent*-**6a** / (94) / 8.1:1 / 38 **125** / (94) / 3:1 / 46 **144** / (90) / 6:1 / 65	293
	145 (3.6 eq), LiCl (3.6 eq), THF, −78°, 10 min	 (79) 57% ee +  (17)	293
C_{13-14} 	**1a** (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then DIBAL-H (3.3 eq), 4 h	 *n* / / % ee / % de 1 / (71) / 74 / 58 2 / (77) / 99 / 95	198

C_{14}		1. **1a** (2 eq), LiCl (2 eq), THF, temp, 3 h; then 2. PhSeBr (1.2 eq), 0°; 3. H_2O, AcOH, H_2O_2 (6 eq), 0° to rt, 4 h		Temp (°) — % ee^e −78 (43) 45 −110 (35) 54	172
		1. **96b** (2 eq), LiCl (2 eq), THF, −110°, 3 h; then 2. PhSeBr (1.2 eq), 0°; 3. H_2O, AcOH, H_2O_2 (6 eq), 0° to rt, 4 h		(33) 84% ee^e	172
C_{17-18}		**1a** (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then DIBAL-H (3.3 eq), 4 h		*n* — % ee — % de 1 (81) 67 35 2 (70) 88 98	198

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[a] The absolute configuration of the product was not provided and is assumed based on the known behavior of the chiral lithium amide.

[b] The enantiomeric excess was determined at a later stage in the synthesis of a target.

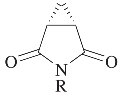
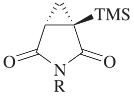
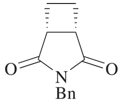
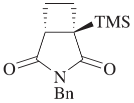
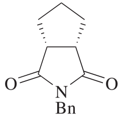
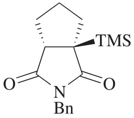
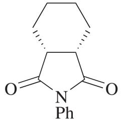
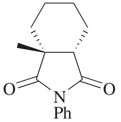
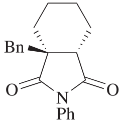
[c] The enantiomeric excess of the product was determined after benzoylation.

[d] The enantiomeric excess was determined after conversion of the product into the corresponding Mosher ester.

[e] The enantiomeric excess was determined by forming a pair of diastereomeric acetals using (*R*,*R*)-2,3-butanediol.

TABLE 4. DEPROTONATIONS OF CYCLIC IMIDES

*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

	Imide	Conditions	Product(s) and Yield(s) (%)				Refs.
C$_5$		**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (10 eq), THF, −100° to rt, 4 h		R		% ee	
				Ph	(80)	91–95	203, 204
				Bn	(67)	91	204
				OBn	(66)	89	204
C$_6$		**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (10 eq), THF, −100° to rt, 4 h		(37) 93–94% ee			203, 204
C$_7$		**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (10 eq), THF, −100° to rt, 4 h		(72) 91% ee			203, 204
C$_8$		**68** (1.1 eq), THF, −78°, 1 h; then MeI (5 eq), 3 h		(62) >98% ee			200
		68 (1.1 eq), THF, −78°, 1 h; then BnBr (5 eq), 3 h		(68) % ee n.d.			200

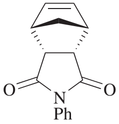
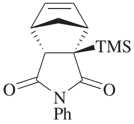
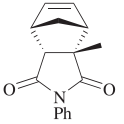
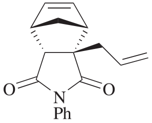
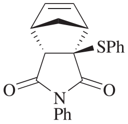
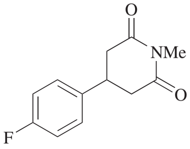
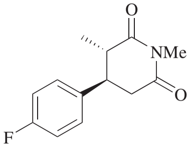
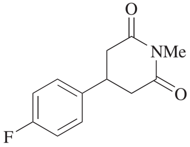
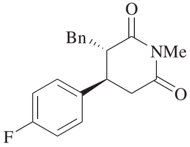
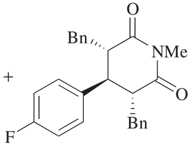
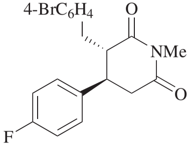
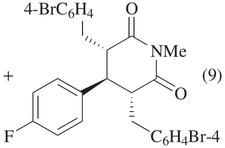
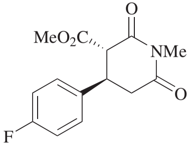
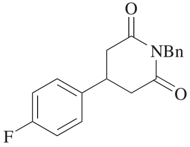
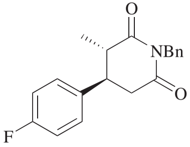
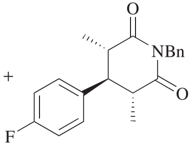
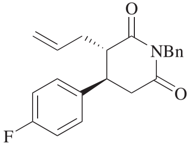
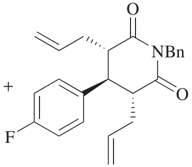
C_9		**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (10 eq), THF, −100° to rt, 4 h		(76) 98% ee	203, 204
		1a (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then MeI (40 eq), −78° to rt, overnight		(36) % ee n.d.	204
		1a (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then allyl bromide (28 eq), −78° to rt, overnight		(33) % ee n.d.	204
		1a (1.2 eq), LiCl (1.2 eq), THF, −78°, 1 h; then PhSSPh (5 eq), −78° to rt, overnight		(50) 97% ee	204
C_{11}		**67** (1.2 eq), THF, −78°, 45 min; then MeI (10 eq), −40°, 4 h		(73) 86% ee	201, 200

TABLE 4. DEPROTONATIONS OF CYCLIC IMIDES (*Continued*)

	Imide	Conditions	Product(s) and Yield(s) (%)				Refs.
C_{11}		**67** (1.2 eq), THF, –78°, 45 min; then BnBr (10 eq), –40°, 4 h		(58) 74% ee	+	 (7)	201, 200
		67 (1.2 eq), THF, –78°, 45 min; then 4-$BrC_6H_4CH_2Br$ (10 eq), –40°, 4 h		(63) 77% ee	+	 (9)	201, 200
		67 (1.2 eq), THF, –78°, 45 min; then MeO_2CCN (1.5 eq), –40°, 30 min		(87) 75% ee			201, 200
		**67** (1.2 eq), THF, –78°, 45 min; then MeI (10 eq), –40°, 4 h		(65) 97% ee	+	 (14)	201, 200
		67 (1.2 eq), THF, –78°, 45 min; then allyl bromide (34 eq), –40°, 4 h		(52) 90% ee	+	 (7)	201, 200

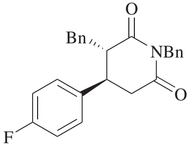
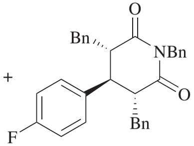
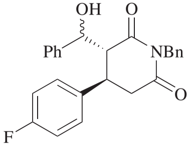
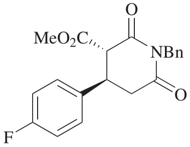
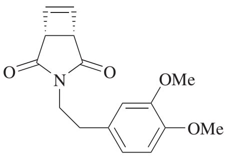
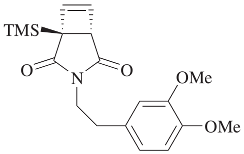
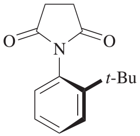
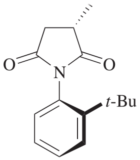
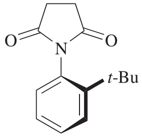
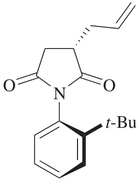
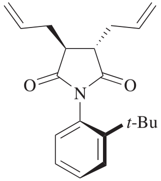
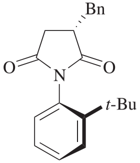
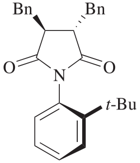
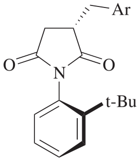
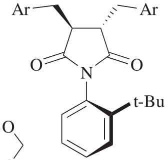
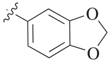
	67 (1.2 eq), THF, –78°, 45 min; then BnBr (25 eq), –40°, 4 h	 (61) 97% ee +  (22)	201, 200
	67 (1.2 eq), THF, –78°, 45 min; then PhCHO (2 eq), –40°, 4 h	 (75) 97% ee, dr 1:1	201, 200
	67 (1.2 eq), THF, –78°, 45 min; then MeO_2CCN (1.5 eq), –40°, 30 min	 (71) 97% ee	201, 200
C_{14} 	**67** (2.1 eq), TMSCl (10 eq), THF, –100°, 4 h	 (88) >99% ee	206
	**68** (1.4 eq), THF, –78°, 1 h; then DMPU (1.4 eq), MeI (10 eq), 2 h	 (56) 85% ee	205

TABLE 4. DEPROTONATIONS OF CYCLIC IMIDES (*Continued*)

Imide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	**68** (1.4 eq), THF, –78°, 1 h; then DMPU (1.4 eq), allyl bromide (10 eq), 2 h	 (55) 94% ee +  (7)	205
	68 (1.4 eq), THF, –78°, 1 h; then DMPU (1.4 eq), BnBr (10 eq), 2 h	 (50) 92% ee +  (6)	205
	68 (1.4 eq), THF, –78°, 1 h; then DMPU (1.4 eq), piperonyl bromide (10 eq), 2 h	 (40) 95% ee +  (7) Ar = 	205

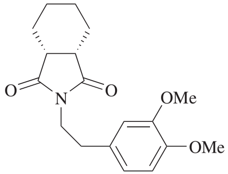
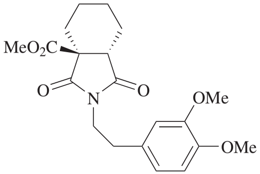
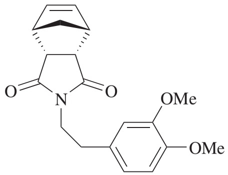
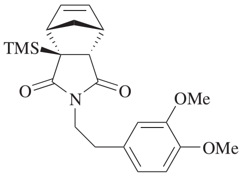
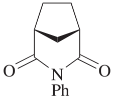
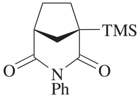
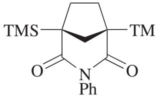
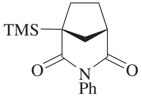
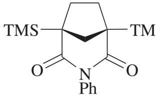
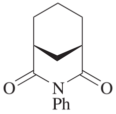
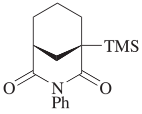
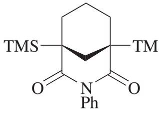
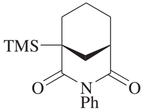
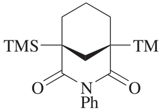
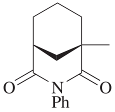
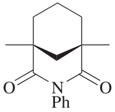
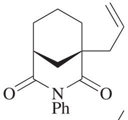
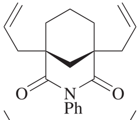
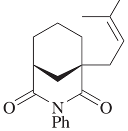
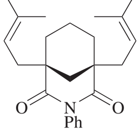
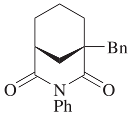
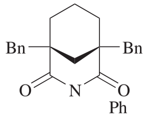
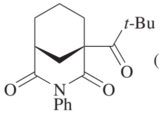
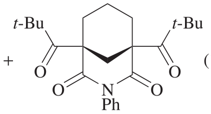
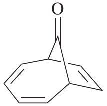
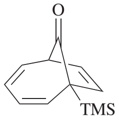
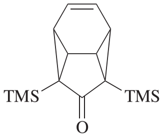
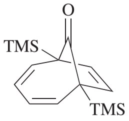
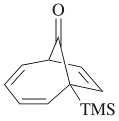
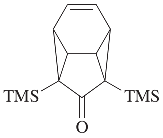
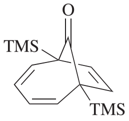
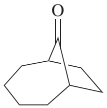
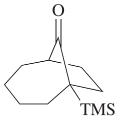
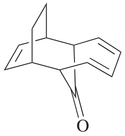
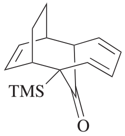
C_{16} 	**68** (1.1 eq), THF, −78°, 1 h; then MeO_2CCN (2 eq), 1 h		(85) 95–98% ee	200, 209, 202
C_{17} 	**67** (1.2 eq), TMSCl (10 eq), THF, −100°, 3 h; then −100° to rt, overnight		(82) 92–94% ee	207, 208, 206

TABLE 5. DEPROTONATIONS AT BRIDGEHEAD CARBONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C_7 	**1a** (1.1 eq), LiCl (1.1 eq), TMSCl (3 eq), THF, −105° to rt, 3 h	 (63) 70% ee +  (18)	211, 210
	67, TMSCl, THF, −105° to rt	 (47) 94% ee +  (24)	211, 210
C_8 	**1a** (1.2 eq), LiCl (1.2 eq), TMSCl (3 eq), THF, −105° to rt, 3 h	 (74) 98% ee +  (12)	211, 210
	2 (1.2 eq), LiCl (1.2 eq), TMSCl (3 eq), THF, −105° to rt, 3 h	 (56) 98% ee +  (15)	211, 210
	1a (1.2 eq), LiCl (1.2 eq), MeI (3 eq), THF, −105° to rt, 3 h	 (57) 97% ee +  (11)	211, 210
	1a (1.2 eq), LiCl (1.2 eq), allyl bromide (3 eq), THF, −105° to rt, 3 h	 (42) 95% ee +  (7)	211, 210
	1a (1.2 eq), LiCl (1.2 eq), prenyl bromide (3 eq), THF, −105° to rt, 3 h	 (50) 98% ee +  (12)	211, 210

	1a (1.2 eq), LiCl (1.2 eq), BnBr (3 eq), THF, −105° to rt, 3 h	 (52) 95% ee +  (3)	211, 210
	1a (1.2 eq), LiCl (1.2 eq), *t*-BuCOCl (3 eq), THF, −105° to rt, 3 h	 (56) 98% ee +  (17)	211, 210
C_9 	**1a** (1 eq), LiCl (1 eq), TMSCl (3 eq), THF, −78° to rt, 3 h	 +  +  (46) 92% ee **I** **I** + **II** (12) **II**	212, 210
	1a (1 eq), LiCl (1 eq), TMSCl (3 eq), THF, −105° to rt, 3 h	 +  +  (76) 98% ee **I** **I** + **II** (23) **II**	212, 210
	**1a** (1 eq), LiCl (1 eq), TMSCl (3 eq), THF, −105° to rt	 (53–78) 92% ee	212, 210
C_{13} 	Lithium amide (1.1 eq), TMSCl, THF, −105°	 Lithium Amide % ee **1a** (—) ~20 **67** (30) ~70	210[a]

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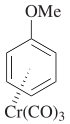
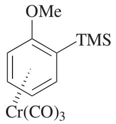
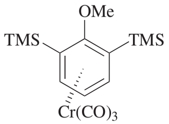
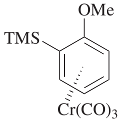
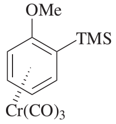
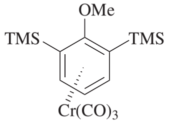
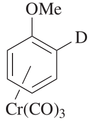
[a] The sense of asymmetric induction has not been assigned for this reaction.

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C_6			
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 (83–90) 84–90% ee +  (~4)	76, 75, 214, 77
	2 (1.1 eq), TMSCl (6 eq), THF, −100°, 5 min	 (87–95) 87–91% ee	215, 78, 79
	1a, THF, −78°, time; then TMSCl, 30 min	 **I** (~84) +  (~4) Time (min) % ee **I** 0.5 73 10 70 20 67 40 59 60 52 100 39 140 33 180 25	75
	1a(1.1 eq), LiCl (*x* eq), THF, −78°, time; then D_2O (12 eq), −78° to rt	 (100) *x* Time (min) % D 0 5 28 0 30 55 0 60 72 0 120 93 0 180 97 0.5 2 100	75

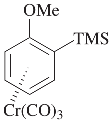
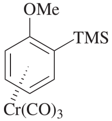
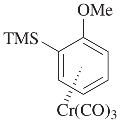
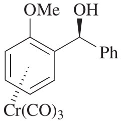
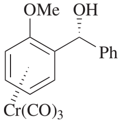
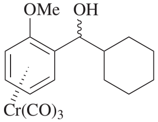
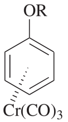
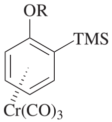
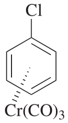
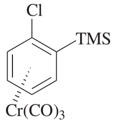
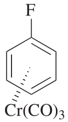
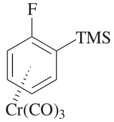
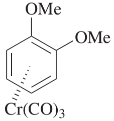
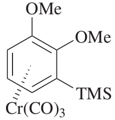
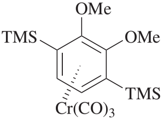
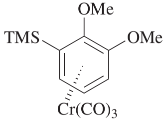
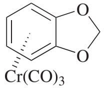
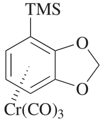
	Lithium amide (1.1 eq) TMSCl (3 eq), THF, −78°, 30 min		Lithium Amide — % ee **3n** (67–93) 48–59 **3d** (65) 59 **3l** (73) 54 **124** (59) 25	75, 77 75 75 75
	Lithium amide (1.1 eq), TMSCl (3 eq), THF, −78°		Lithium Amide — % ee **49** (69) 0 **25** (67) 9 **155** (43) 14 **6a** (81) 13	77
	Lithium amide (1.1 eq), TMSCl (3 eq), THF, −78°		Lithium Amide — % ee **50a** (72) 73 **24** (40) 22	77
	1a (3.3 eq), LiCl (1.5 eq), THF, −78°, 5 min; then PhCHO (10 eq), −78°, 30 min		(67) 65% ee +  (7)	75, 80
	1a (3.3 eq), LiCl (1.5 eq), THF, −78°, 5 min; then c-C_6H_{11}CHO, −78°, 30 min		(83) 73% ee, dr 1: 1	75, 80
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min		R — % ee Et (82) 81 *i*-Pr (65) 90 *t*-Bu (0) — MOM (76) 80	75

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 (27) 51% ee	75
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 (57) 16% ee	75
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 (~70) 92–95% ee +  (10–12)	75
	2 (1.1 eq), TMSCl (4 eq), THF, −78°, 30 min	 (92) 97% ee	215
	**2** (1.1 eq), TMSCl (4 eq), THF, −78°, 30 min	 (72) <10% ee	215

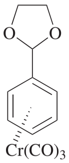
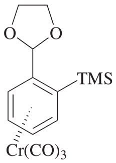
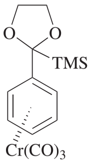
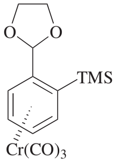
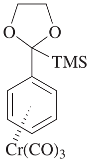
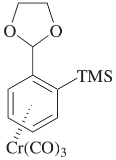
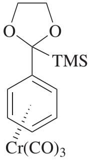
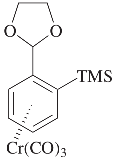
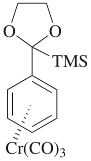
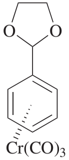
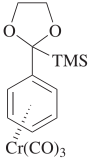
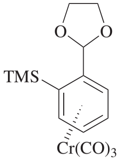
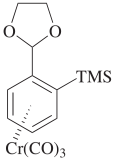
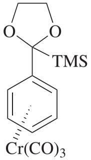
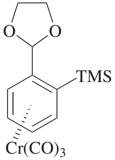
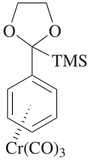
C_7 	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 (36–40) 81–84% ee +  (34–53)	75, 216, 77
	1a (1.1 eq), THF, −78°, 1.5 h; then TMSCl (1.2 eq)	 **I** 77% ee +  **II** **I** + **II** (67), **I/II** = 26:74	216
	124 (1.1 eq), TMSCl (1.2 eq), THF, −78°	 **I** 76% ee +  **II** **I** + **II** (85), **I/II** = 65:35	216, 77
	124 (1.1 eq), THF, −78°, 1.5 h; then TMSCl (1.2 eq)	 **I** 70% ee +  **II** **I** + **II** (87), **I/II** = 53:47	216

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	**49** (1.1 eq), TMSCl (3 eq), THF, −78°	 (46)	77
	50a (1.1 eq), TMSCl (3 eq), THF, −78°	 (—) 51% ee	77
	25 (1.1 eq), TMSCl (3 eq), THF, −78°	 **I** 5% ee +  **II** **I** + **II** (—), **I/II** = 30:70	77
	26 (1.1 eq), TMSCl (3 eq), THF, −78°	 **I** 4% ee +  **II** **I** + **II** (—), **I/II** = 57:43	77

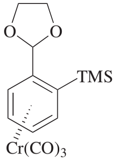
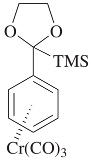
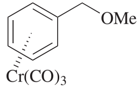
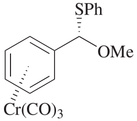
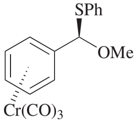
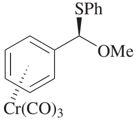
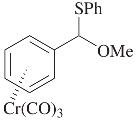
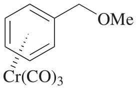
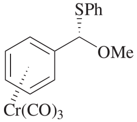
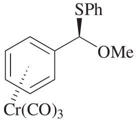
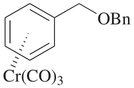
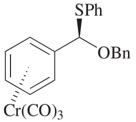
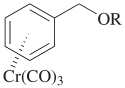
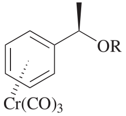
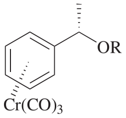
	155 (1.1 eq), TMSCl (3 eq), THF, −78°	 **I** 11% ee +  **II**	**I** + **II** (—), **I/II** = 57:43	77
	**1a** (1.1 eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min		(52) 22% ee	85, 89
	67 (1.1 eq), LiCl (1 eq), THF; then PhSSPh (2 eq), 30 min		Temp (°) — % ee −78 (86–95) 97–98 −23 (87) 93	85, 89 89
	69 (*x* eq), *n*-BuLi (*y* eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min		*x* *y* — % ee 1.1 1.1 (96) 95 1.1 0.55 (60) 92 1.1 0.275 (21) 96 0.55 1.1 (88) 96 0.275 1.1 (64) 73	89
	3d (1.1 eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min		(87) 0% ee	89

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	Lithium amide (1.1 eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min	 Lithium Amide — % ee **124** (99) 29 **12** (83) 49 **95e** (55) 27 **60** (88) 5	89
	Lithium amide (1.1 eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min	 Lithium Amide — % ee **11** (58) 10 **62** (93) 32 **70** (80) 40	89
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 30 min; then PhSSPh (2 eq), 30 min	 (95) 99% ee	85, 89
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 1 h; then MeI, 1 h	 R — % ee Me (96) 97 Bn (89) 99 *i*-Pr (98) 33	85, 222, 89, 86 85, 86 86
	ent-**67** (1.1 eq), LiCl (1 eq), THF, −78°; 1 h; then MeI, 1 h	 R — % ee Me (90) 96 Bn (88) 99	222

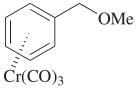
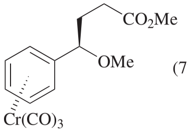
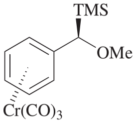
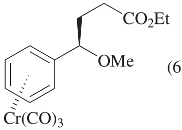
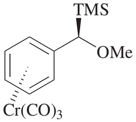
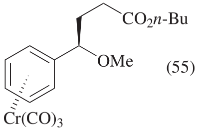
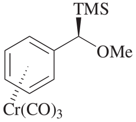
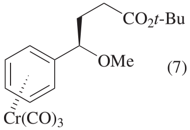
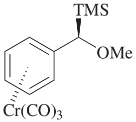
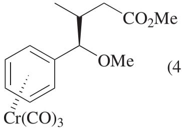
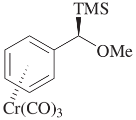
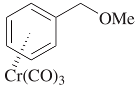
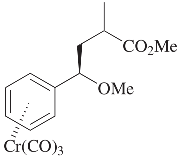
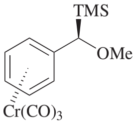
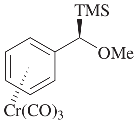
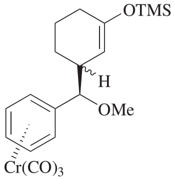
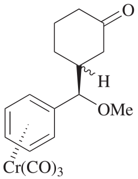
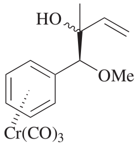
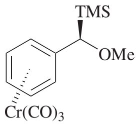
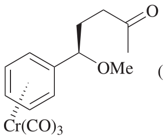
	**67** (1 eq), LiCl (1 eq), THF, −78°, 1 h; then methyl acrylate (3 eq), TMSCl (1.5 eq), 10 min	 (77) 96% ee +  (<5)	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then ethyl acrylate (3 eq), TMSCl (1.5 eq), 10 min	 (69) % ee n.d. +  (<5)	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then *n*-butyl acrylate (3 eq), TMSCl (1.5 eq), 10 min	 (55) % ee n.d. +  (10)	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then *t*-butyl acrylate (3 eq), TMSCl (1.5 eq), 10 min	 (7) % ee n.d. +  (21)	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then methyl (*E*)-2-butenoate (3 eq), TMSCl (1.5 eq), 10 min	 (45) % ee n.d. +  (14)	219

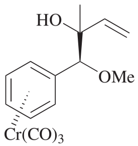
TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	**67** (1 eq), LiCl (1 eq), THF, –78°, 1 h; then methyl methacrylate (3 eq), TMSCl (1.5 eq), 10 min	 (7) ee n.d. +  (20)	219
	67 (1 eq), LiCl (1 eq), THF, –78°, 1 h; then *t*-butyl methacrylate (3 eq), TMSCl (1.5 eq), 10 min	 (17)	219
	67 (1 eq), LiCl (1 eq), THF, –78°, 1 h; then 2-cyclohexenone (3 eq), TMSCl (1.5 eq), 10 min	 (67) % ee n.d. dr 2.5:1 +  (4) dr 2.5:1	219
	67 (1 eq), LiCl (1 eq), THF, –78°, 1 h; then MVK (3 eq), TMSCl (1.5 eq), 10 min	 (75) % ee n.d. dr 2:1 +  (5)	219

67 (1 eq), THF/HMPA (3:1), −78°, 1 h; then MVK (3 eq), TMSCl (1.5 eq), 5 h



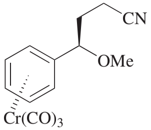
(57) % ee n.d. +



(6) dr 2:1

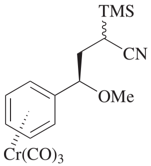
219

67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then acrylonitrile (3 eq), TMSCl (1.5 eq), 10 min



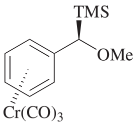
(39) % ee n.d.

+



(22) dr 1: 1

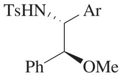
+



(18)

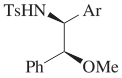
219

1. **67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then ArCH=NTs, 2 h
2. *h*ν, air



I

+

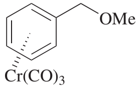
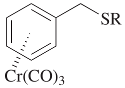
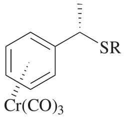
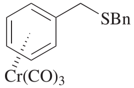
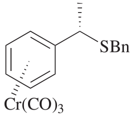
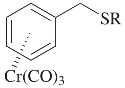
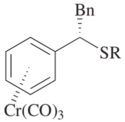
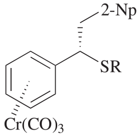


II

221

Ar	**I + II**	**I/II**	% ee **I**	% ee **II**
Ph	(83)	51:49	95	96
4-ClC_6H_4	(57)	44:56	96	94
2-ClC_6H_4	(62)	47:53	90	93
4-MeC_6H_4	(69)	57:43	92	93
2-$CF_3C_6H_4$	(75)	51:49	93	94
2-$MeOC_6H_4$	(81)	55:45	91	94

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. *ent*-**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then ArCH=NTs, 2 h 2. *h*ν, air	 Ar / **I** + **II** / **I**/**II** / % ee **I** / % ee **II** Ph (80) 51:49 91 90 2-ClC$_6$H$_4$ (60) 46:54 96 91 4-MeC$_6$H$_4$ (70) 55:45 93 94	221
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 6 h; then MeI (3 eq), 2 h	 R / % ee Ph (94) 63 *i*-Pr (94) 18	88
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 1 h; then MeI (3 eq), 1 h	 (84) 91% ee	88
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 1 h; then BnBr (3 eq), 1 h	 R / % ee Me (91) 88 Et (75) 78	88
	67 (1.1 eq), LiCl (1 eq), THF, −78°, 1 h; then 2-(bromomethyl)naphthalene (3 eq), 1 h	 R / % ee Me (93) 88 Et (88) 80 Bn (83) 91	88

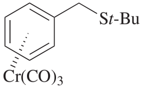
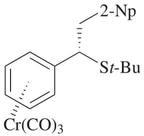
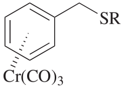
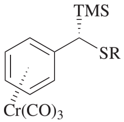
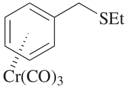
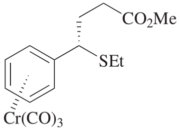
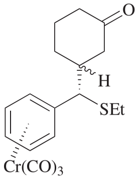
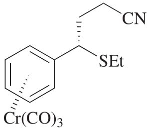
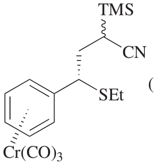
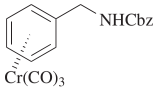
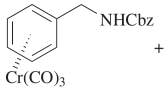
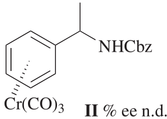
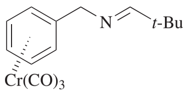
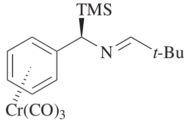
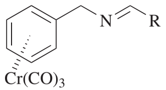
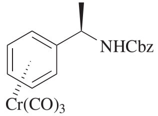
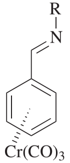
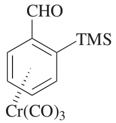
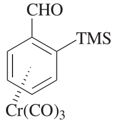
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 6 h; then 2-(bromomethyl)naphthalene (3 eq), 2 h		(45) 20% ee	88
	**67** (1.1 eq), LiCl (1 eq), THF, −78°, 1 h; then TMSCl (3 eq), 1 h		R (%) % ee Me (62) 89 Et (72) 82	88
	**67** (1 eq), LiCl (1 eq), THF, −78°, 1 h; then methyl acrylate (3 eq), TMSCl (1.5 eq), 10 min		(72) 74% ee	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then 2-cyclohexenone (3 eq), TMSCl (1.5 eq), 10 min		(50) % ee n.d., dr 1.6:1	219
	67 (1 eq), LiCl (1 eq), THF, −78°, 1 h; then acrylonitrile (3 eq), TMSCl (1.5 eq), 10 min	 (45) % ee n.d. + 	(15) % ee n.d. dr 1:1	219

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	*n*-BuLi (0.95 eq), THF, –78°; then **67** (1.1 eq), LiCl, –40°, 2.5 h; MeI (4 eq), 1 h	 **I** +  **II** % ee n.d. **I** + **II** (69), **I/II** = 62:38	225
	**67** (1.1 eq), LiCl (1 eq), TMSCl (2.5 eq), –78°, 30 min	 (89) 87% ee	225
	1. **67** (1.1 eq), LiCl, –78°, 2 h; then MeI (10 eq), 1 h 2. MeOH, aq HCl 3. K_2CO_3, CbzCl	 R / (yield) / % ee: *t*-Bu (69) 81 Ph (69) 55 4-$Me_2NC_6H_4$ (61) 80	225
	1. **1a** (1.1 eq), TMSCl (3 eq), THF, –78° 2. aq HCl	 R / (yield) / % ee: *c*-C_6H_{11} (84) 84 Ph (76) 88	77
	1. **1a** (1.1 eq), THF, –78°, 2 h; then TMSCl (3 eq), 1 h 2. aq HCl	 R / (yield) / % ee: *c*-C_6H_{11} (82) 78 Ph (67) 92	77

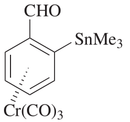
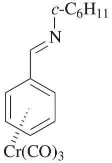
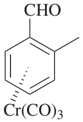
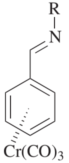
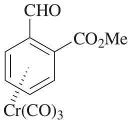
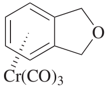
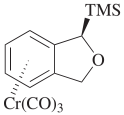
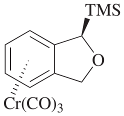
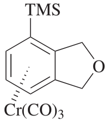
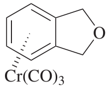
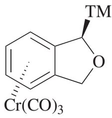
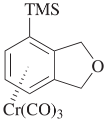
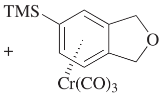
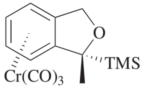
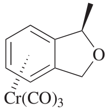
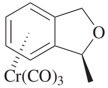
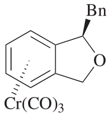
	1. **1a** (1.1 eq), THF, −78°, 2 h; then Me_3SnCl (3 eq), 1 h 2. aq HCl	 R — c-C_6H_{11} (67) 78 % ee; Ph (65) 89 % ee	77
	1. **1a** (1.1 eq), THF, −78°, 2 h; then MeI (3 eq), 1 h 2. aq HCl	 (62) 72% ee	77
	1. **1a** (1.1 eq), THF, −78°, 2 h; then $ClCO_2Me$ (3 eq), 1h 2. aq HCl	 R — c-C_6H_{11} (66) 74 % ee; Ph (68) 90 % ee	77
C_8 	**1a** (1.1 eq), TMSCl (3 eq), THF, 30 min	 Temp (°) — −78 (82) 71 % ee; −100 (82) 76 % ee	386, 75
	3n (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 **I** 42% ee +  **II** **I** + **II** (74), **I/II** = 9:1	386, 75

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	**3d** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min	 **I** 42% ee +  **II** +  **III** **I** + **II** + **III** (39), **I/II/III** = 67:30:3	386, 75
	1. **67** (1.1 eq), TMSCl (1 eq), THF, −100 to −85°, 45 min 2. *t*-BuLi (2.3 eq), −78°, 1 h; then MeI (5 eq), 1 h	 (75) >99% ee	387
	1a (1.2 eq), LiCl (1.2 eq), THF, −100°, 5 min; then MeI (10 eq), 30 min	 (75) 79% ee	386, 75
	67 (1.1 eq), LiCl (1.1 eq), THF, −78°, 10 min; then MeI (10 eq), 4 h	 (60) ee n.d.	226
	1a (1.2 eq), LiCl (1.2 eq), THF, −100°, 5 min; then BnBr (3 eq), 30 min	 (85) 79% ee	386, 75

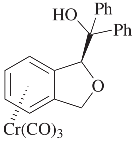
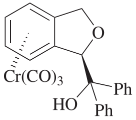
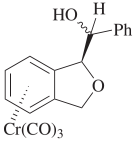
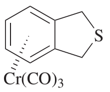
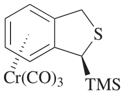
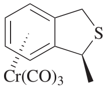
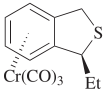
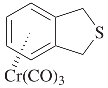
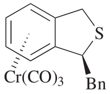
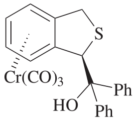
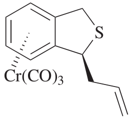
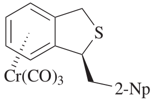
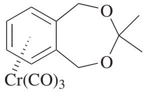
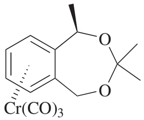
	1a (1.2 eq), LiCl (1.2 eq), THF, −100°, 5 min; then Ph_2CO (3 eq), 30 min		(72) 75% ee	386, 75
	67 (1 eq), LiCl (1 eq), THF, −100°, 5 min; then Ph_2CO (3 eq), 30 min		(70) 99% ee	75
	1a (1.2 eq), LiCl (1.2 eq), THF, −100°, 5 min; then PhCHO (2 eq), 30 min		(70) 80% ee, dr 1: 1	386, 75
	**67** (1.2 eq), TMSCl (5 eq), THF, −100°, 1 h		(95) 89% ee	224, 82
	67 (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then MeI (5 eq), 1 h		(95) 94% ee	224, 82
	67 (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then EtI (5 eq), 1 h		(91) 87% ee	224, 82

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	**67** (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then BnBr (5 eq), 1 h	 (70) % ee n.d.	224, 82
	67 (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then Ph_2CO (5 eq), 1 h	 (88) 95% ee	224, 82
	67 (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then allyl bromide (5 eq), 1 h	 (75) % ee n.d.	224, 82
	67 (1.1 eq), LiCl (0.5 eq), THF, −100°, 1 h; then 2-(bromomethyl)naphthalene (5 eq), 1 h	 (89) 95% ee	224, 82
	*ent*-**67** (1.1 eq), LiCl (1.1 eq), THF, –40°, 45 min; then MeI (10 eq), 1.5 h	 (86) % ee n.d.	226

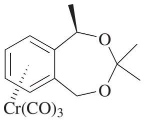
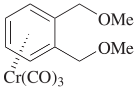
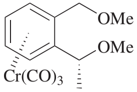
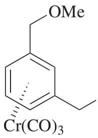
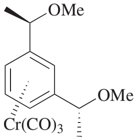
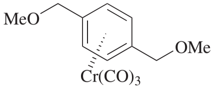
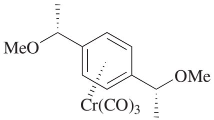
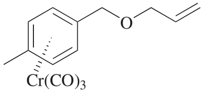
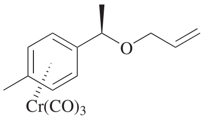
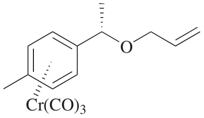
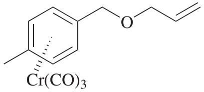
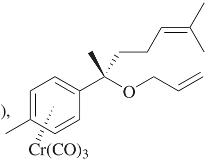
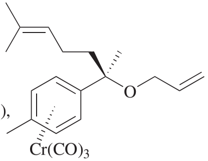
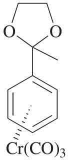
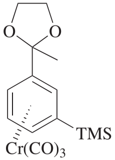
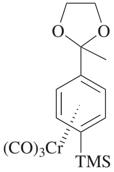
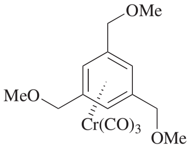
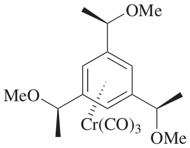
	ent-**67** (1.1 eq), LiCl (1.1 eq), THF, −20°, 45 min; then MeI (10 eq), 2 h		(60) % ee n.d.	226
	**67** (1 eq), THF, −78°; then MeI		(99) 99% ee	218
	**67** (1 eq), THF, −78°; then MeI		(71) 99% ee	218
	**67** (1.5 eq), THF, −78°; then MeI		(98) 99% ee	218
	**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then MeI (3 eq), 30 min		(84) 98% ee	223
	ent-**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then MeI (3 eq), 30 min		(87) 98% ee	223

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

	Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8		1. **67** (1.1 eq), LiCl (1.1 eq), MeI (1 eq), THF, −78°, 45 min 2. *t*-BuLi (2.3 eq), 50 min 3. 5-iodo-2-methylpent-2-ene (3 eq), 2.5 h	 (60) ~98% ee	223
		1. *ent*-**67** (1.1 eq), LiCl (1.1 eq), MeI (1 eq), THF, −78°, 45 min 2. *t*-BuLi (2.3 eq), 50 min 3. 5-iodo-2-methylpent-2-ene (3 eq), 2.5 h	 (60) ~98% ee	223
		**1a** (1.2 eq), THF, −78°, 1.5 h; then TMSCl (1.2 eq)	 **I** 6% ee +  **II** **I** + **II** (55), **I**/**II** = 1:1	216
C_9		**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then MeI (6 eq), 1 h	 (85) 95% ee	218, 217

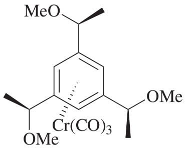
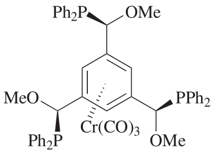
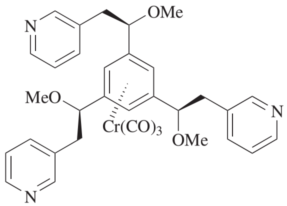
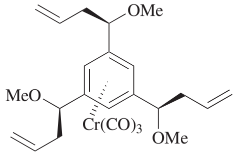
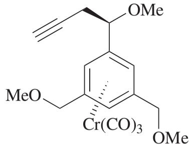
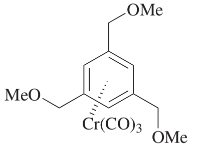
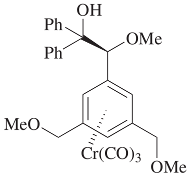
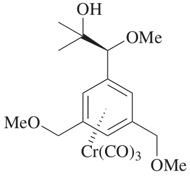
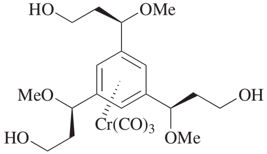
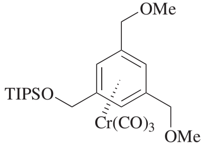
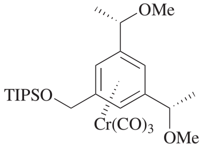
ent-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then MeI (6 eq), 1 h		(—) 95% ee	217
67 (3.1 eq), LiCl (3.1 eq), THF, −78°, 1 h; then Ph_2PCl (9 eq), −78 to −40°, 3 h		(47) 95% ee	218, 217
67 (3 eq), LiCl (3 eq), THF, −78°, 1 h; then 3-(bromomethyl)pyridine, 2 h		(84) 95% ee	218, 217
67 (3 eq), LiCl (3 eq), THF, −78°, 1 h; then allyl bromide (9 eq), 1.5 h		(77) 98% ee	217
67 (3 eq), LiCl (3 eq), THF, −78°, 1 h; then propargyl bromide (9 eq), 1 h		(92) 75% ee	217

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	**67** (3 eq), LiCl (3 eq), THF, –78°, 1 h; then Ph_2CO (9 eq), BF_3•OEt_2 (6 eq), 1 h	 (97) 76% ee	217
	67 (3 eq), LiCl (3 eq), THF, –78°, 1 h; then acetone (9 eq), BF_3•OEt_2 (6 eq), 1 h	 (88) 78% ee	217
	67 (3 eq), LiCl (3 eq), THF, –78°, 1 h; then ethylene oxide (50 eq), BF_3•OEt_2(6 eq), 1.5 h	 (72) 93% ee	217
	*ent*-**67** (1.5 eq), LiCl (1.5 eq), THF, –78°, 1 h; then MeI (6 eq)	 (77) 90% ee	388

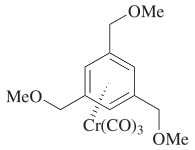
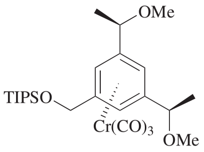
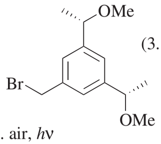
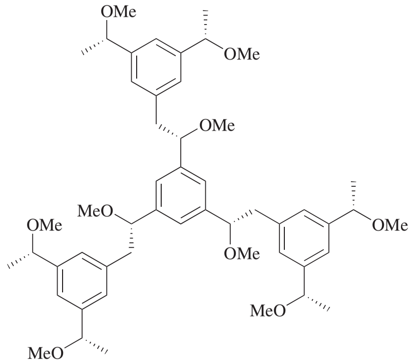
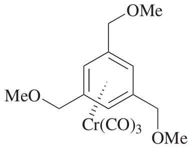
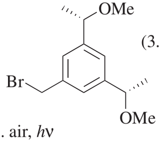
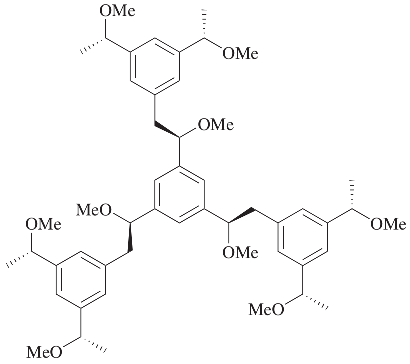
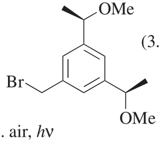
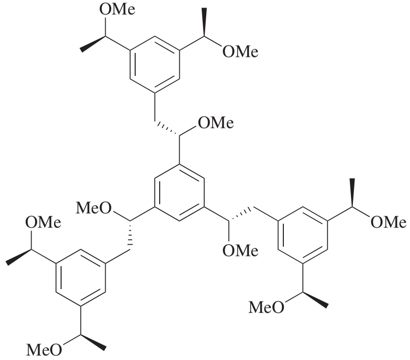
	**67** (1.5 eq), LiCl (1.5 eq), THF, −78°, 1 h; then MeI (6 eq)		(68) 90% ee	388
	1. *ent*-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (3.8 eq), 5 h 2. air, *h*ν		(75)	388, 389

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. **67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (3.8 eq), 5 h 2. air, *hν*	 (86)	388, 389
	1. *ent*-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (3.8 eq), 5 h 2. air, *hν*	 (32)	388, 389

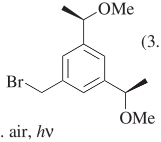
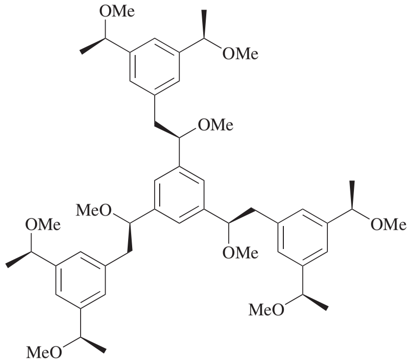
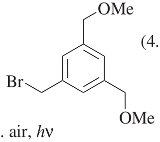
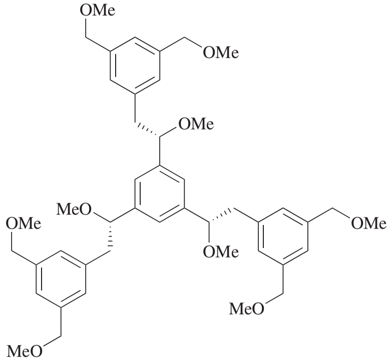
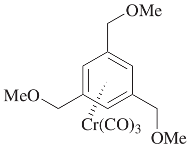
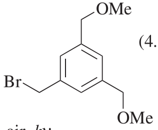
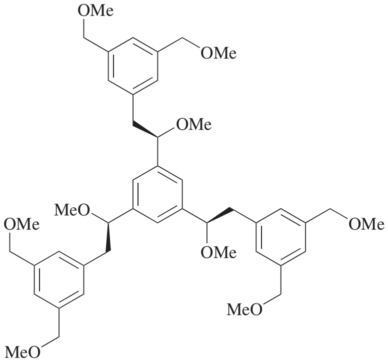
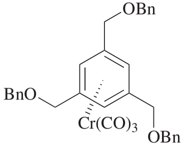
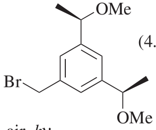
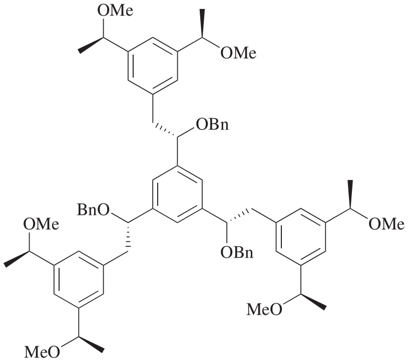
1. **67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (3.8 eq), 5 h 2. air, *h*ν		(55)	388, 389
1. *ent*-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (4.6 eq), 2.5 h 2. air, *h*ν		(30)	389

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. **67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (4.6 eq), 2.5 h 2. air, *h*ν	 (45)	389
	1. *ent*-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (4.2 eq), 4 h 2. air, *h*ν	 (45)	389

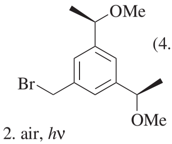
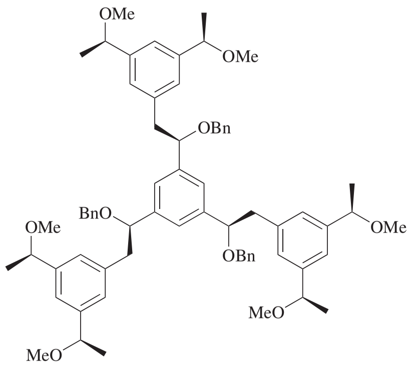
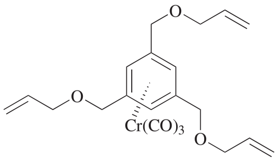
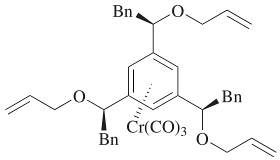
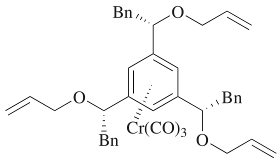
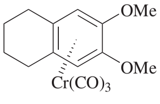
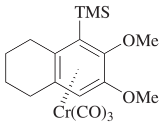
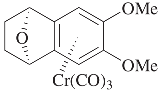
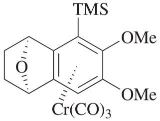
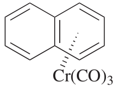
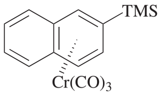
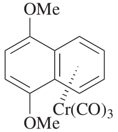
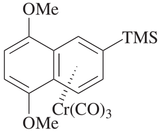
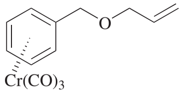
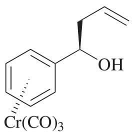
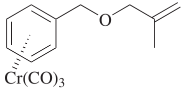
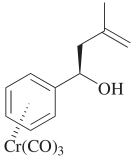
	1. **67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then  (4.2 eq), 4 h 2. air, *h*ν	 (52)	389
	**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then BnBr (9 eq), 15 min	 (78) >99% ee	86
	ent-**67** (3 eq), LiCl (3 eq), THF, −78°, 1 h; then BnBr (9 eq), 15 min	 (91) >99% ee	86
C_{10}			
	**2** (1.1 eq), TMSCl (4 eq), THF, −78°, 30 min	 (78) 76% ee	215

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}				
	**2** (1.1 eq), TMSCl (4 eq), THF, −78°, 30 min		(50) 68% ee	215
	**124**, THF, −78°; then TMSCl		(56) 8% ee[a]	216
	**124**, THF, −78°; then TMSCl		(68) 20% ee[a]	216
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h		(80) 96% ee	390
C_{11}				
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h		(33) 91% ee	390

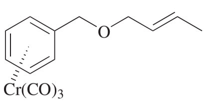
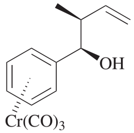
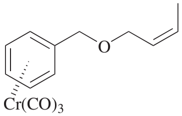
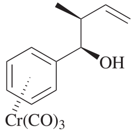
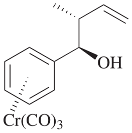
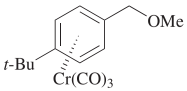
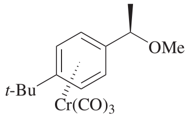
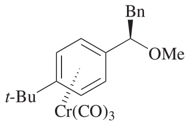
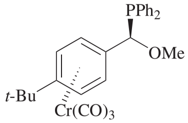
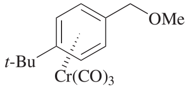
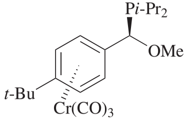
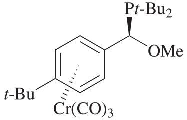
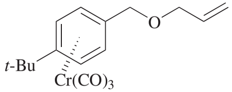
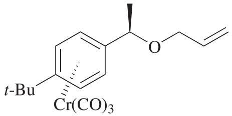
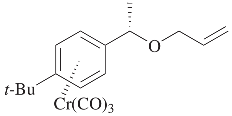
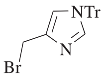
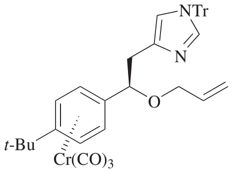
C$_{11}$				
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h		(82) 96% ee, dr 95: 5	390
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h	 **I** 90% ee +  **II** 90% ee	**I** + **II** (24), **I/II** = 1:1	390
	**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then MeI (3 eq), 40 min		(94) 96% ee	391, 87
	67 (1.1 eq), LiCl (1.1 eq), THF, −78°, 30 min; then BnBr (3 eq), 50 min		(92) 97% ee	391, 87
	67 (1.1 eq), LiCl (1.1 eq), THF, −78°, 30 min; then Ph$_2$PCl (3 eq), 50 min		(90) 97% ee	87

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then *i*-Pr_2PCl (2 eq), 2 h	 (81) 97% ee	87
	67 (1 eq), LiCl (1 eq), THF, −78°, 30 min; then *t*-Bu_2PCl (2 eq), 6 h	 (79) 86% ee	87
	**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then MeI (3.2 eq), 30 min	 (97) 98% ee	86
	ent-**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min; then MeI (3.2 eq), 30 min	 (97) 99% ee	86
	67 (1.1 eq), LiCl (1.1 eq), THF, −78°, 45 min; then  , 2 h	 (73) 99% ee	86

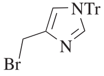
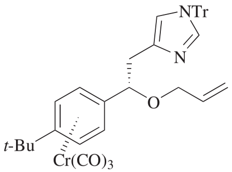
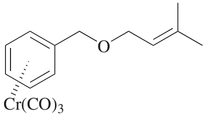
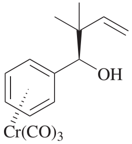
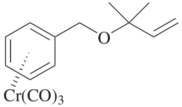
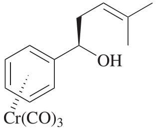
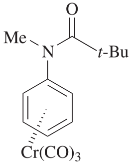
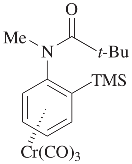
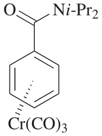
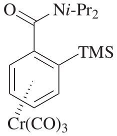
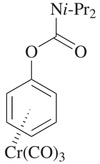
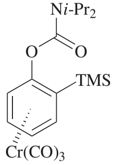
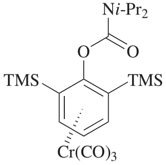
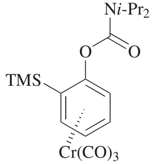
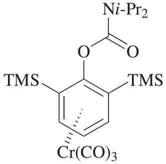
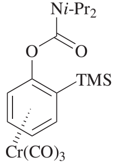
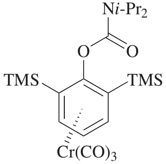
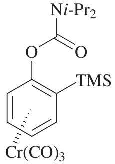
	ent-**67** (1.1 eq), LiCl (1.1 eq), THF, −78°, 45 min; then  , 2 h		(69) 99% ee	86
C_{12}				
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h		(82) 84% ee	390
	**67** (1.1 eq), LiCl (1 eq), THF, −78 to −50°, 7 h		(25) 94% ee	390
	**1a** (1.1 eq), TMSCl (10 eq), THF, −78°, 30 min		(65) 44% ee	75
C_{13}				
	**1a** (1.1 eq), TMSCl (3 eq), THF, −78°, 30 min		(87) 48% ee	76

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	**1a** (*x* eq), THF, −78°, 2.5 h; then TMSCl (3 eq)	 **I** +  **II** *x* — **I + II** — **I/II** — % ee **I** 1.15 — (83) — 100:0 — 2 1.53 — (88) — 62:38 — 66 1.73 — (90) — 50:50 — 67	216, 83
	1a (1.2 eq), TMSCl (3 eq), THF, −78°, 1 h	 **I** 39% ee +  **II** **I + II** (60), **I/II** = 92:8	216, 83
	124 (1.2 eq), TMSCl (3 eq), THF, −78°, 1 h	 **I** 64% ee +  **II** **I + II** (80–85), **I/II** = 92:8	216, 83
	124 (1.2 eq), LiCl (*x* eq), THF, −78°, 2.5 h; then TMSCl (3 eq)	 *x* — — % ee 0 — (83–86) — 67 1 — (90) — 31	216, 83

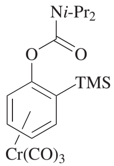
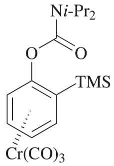
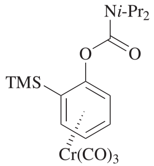
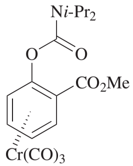
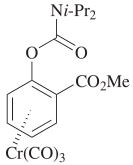
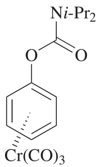
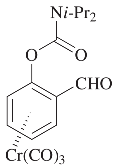
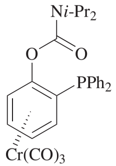
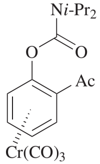
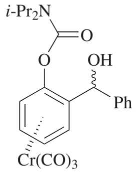
Lithium amide (1.1 eq), TMSCl (3 eq) , THF, −78°		0% ee Lithium Amide **49** (51) **6a** (88)	77
Lithium amide (1.1 eq) TMSCl (3 eq), THF, −78°		Lithium Amide % ee **50b** (97) 27 **25** (65) 29 **155** (48) 62 **3n** (49) 13	77
24 (1.1 eq), TMSCl (3 eq), THF, −78°		(72) 24% ee	77
124 (1.15 eq), THF, −78°, 2.5 h; then $ClCO_2Me$ (3 eq), 15 min		(71) 73% ee	216, 83
124 (1.15 eq), THF, −78°, 2.5 h; then Me_2NCOCl (3 eq)		(85) 68% ee	216, 83

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	**124** (1.2 eq), THF, −78°, 2.5 h; then DMF (3 eq); H_2O	 (93) 69% ee	216, 83
	124 (1.2 eq), THF, −78°, 2.5 h; then Ph_2PCl (3 eq)	 (81) 74% ee	83
	124 (1.2 eq), THF, −78°, 2.5 h; then CuI•SMe_2 (1.2 eq), −20°, 1 h; AcCl (3 eq), rt	 (70) 67% ee	83
	124 (1.2 eq), THF, −100°, 2.5 h; then PhCHO (3 eq)	 (85) 78% ee, dr 3: 1	83

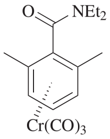
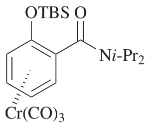
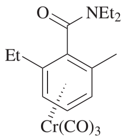
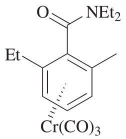
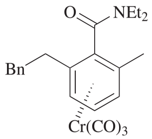
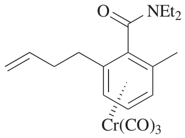
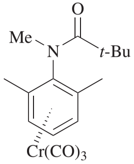
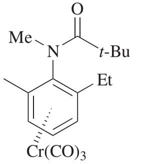
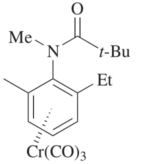
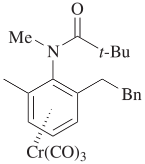
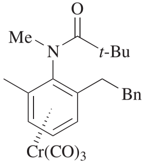
	**124** (1.1 eq), THF, −78 to −20°, 15 h; then TBSOTf (1.5 eq), −78 to −20°, 5 h	 (42) 54% ee	83
	Lithium amide (1.2 eq), THF, −78 to −30°, 1 h; then MeI (2 eq), −78 to −30°	 Lithium Amide — % ee **1a** (85) 86 **3d** (82) 51 **124** (15) 21 **77h** (41) 6 **103a** (18) 27	74
	82 (1.2 eq), THF, −78 to −30°, 1 h; then MeI (2 eq), −78 to −30°	 (10) 44% ee	74
	1a (1.2 eq), THF, −78 to −30°, 1 h; then BnBr (2 eq), −78 to −30°	 (41) 83% ee	74
	1a (1.2 eq), THF, −78 to −30°, 1 h; then allyl bromide,−78 to −30°	 (52) 83% ee	74

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	Lithium amide (1.2 eq), THF, –78 to –30°, 1 h; then MeI (2 eq), –78 to –30°	 Lithium Amide — % ee **1a** (50) 44 **3d** (51) 72 **124** (86) 42 **77h** (80) 79 **103a** (44) 78	73, 74
	77d (1.2 eq), THF, –78 to –30°, 1 h; then MeI (2 eq), –78 to –30°	 (60) 65% ee	73, 74
	77h (1.2 eq), THF, –78 to –30°, 1 h; then BnBr (2 eq), –78 to –30°	 (78) 80% ee	73, 74
	82 (1.2 eq), THF, –78 to –30°, 1 h; then BnBr (2 eq), –78 to –30°	 (48) 89% ee	73, 74

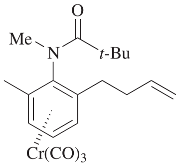
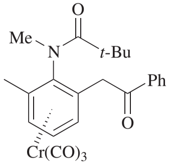
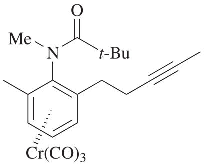
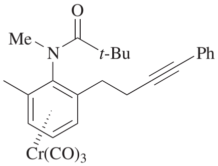
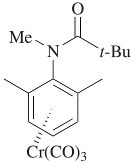
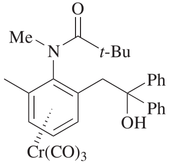
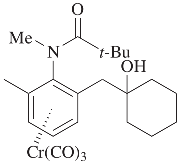
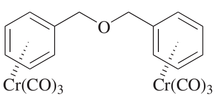
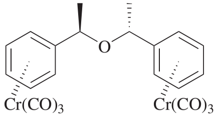
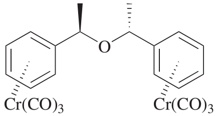
90b (1.2 eq), THF, −78 to −30°, 1 h; then allyl bromide (2 eq), −78 to −30°		(81) 92% ee	73, 74
90b (1.2 eq), THF, −78 to −30°, 1 h; then PhCOCl (2 eq), −78 to −30°		(31) 97% ee	73, 74
90b (1.2 eq), THF, −78 to −30°, 1 h; then 1-bromo-2-butyne (2 eq), −78 to −30°		(86) 96% ee	73, 74
90b (1.2 eq), THF, −78 to −30°, 1 h; then PhC≡CCH$_2$Br (2 eq), −78 to −30°		(84) 96% ee	73, 74

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	**90b** (1.2 eq), THF, −78 to −30°, 1 h; then Ph_2CO (2 eq), −78 to −30°	 (73) 96% ee	73, 74
	90b (1.2 eq), THF, −78 to −30°, 1 h; then cyclohexanone (2 eq) , −78 to −30°	 (58) 96% ee	73, 74
	**67** (2 eq), THF, −78°; then MeI	 (99) 99% ee, dr 93:7	220
	1. **67** (0.7 eq), LiCl (0.7 eq), THF, −78°, 40 min 2. MeI (1 eq), 15 min 3. **67** (1 eq), LiCl (1 eq), THF, −78°, 30 min 4. MeI (3 eq), 1 h	 (86) 99% ee, 99% de	220

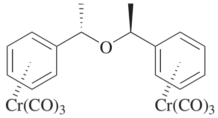
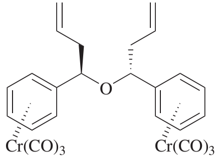
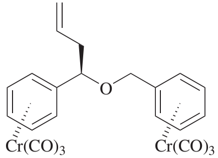
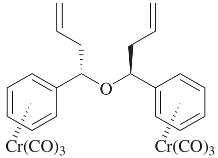
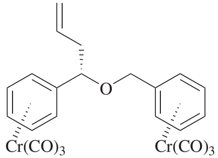
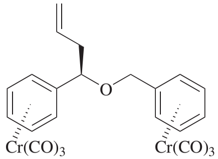
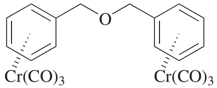
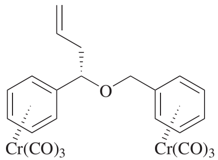
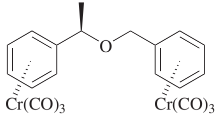
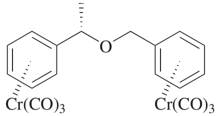
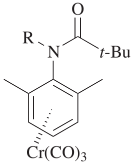
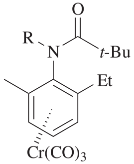
1. *ent*-**67** (0.7 eq), LiCl (0.7 eq), THF, −78°, 40 min 2. MeI (1 eq), 15 min 3. *ent*-**67** (1 eq), LiCl (1 eq), THF, −78°, 30 min 4. MeI (3 eq), 1 h	 (82) 99% ee, 99% de	220
67 (2 eq), LiCl (2 eq), THF, −78°, 1 h; then allyl bromide (6 eq), 2 h	 (17) 99% ee +  (35) 97% ee	220
ent-**67** (2 eq), LiCl (2 eq), THF, −78°, 1 h; then allyl bromide (6 eq), 2 h	 (19) 99% ee +  (35) 97% ee	220
67 (1.1 eq), LiCl (1.1 eq), THF, −78°, 40 min; then allyl bromide (3 eq), 20 min	 (89) 99% ee	220

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	*ent*-**67** (1.1 eq), LiCl (1.1 eq), THF, −78°, 40 min; then allyl bromide (3 eq), 20 min	 (86) 99% ee	220
	67 (0.7 eq), LiCl (0.7 eq), THF, −78°, 40 min; then MeI (1 eq), 30 min	 (59) 99% ee	220
	ent-**67** (0.7 eq), LiCl (0.7 eq), THF, −78°, 40 min; then MeI (1 eq), 30 min	 (66) 99% ee	220
$C_{14–15}$			
	**90b** (1.2 eq), THF, −78 to −30°, 1 h; then MeI (2 eq), −78 to −30°	 R / % ee Me (90) 95 Et (83) 98 CH_2OMe (73) 96	73, 74

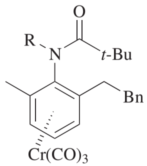
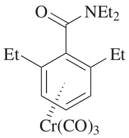
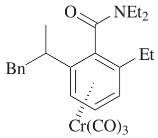
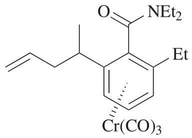
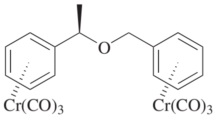
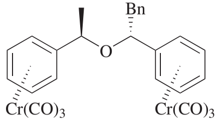
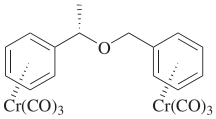
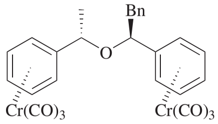
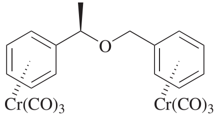
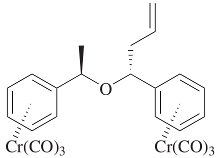
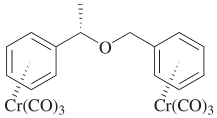
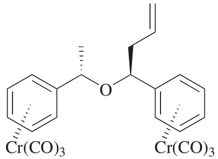
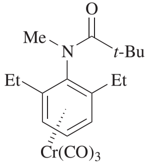
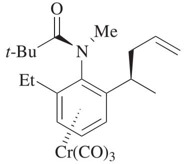
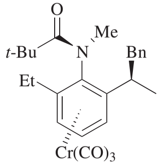
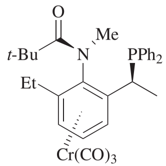
	90b (1.2 eq), THF, −78 to −30°, 1 h; then BnBr (2 eq), −78 to −30°		R — % ee Me (90) 97 Et (71) 99 CH_2OMe (78) 94	73, 74
C_{15} 	**1a**, THF, −78 to −30°; then BnBr, −78°		(13) 66% ee single diast.	74
	1a, THF, −78 to −30°; then allyl bromide, −78°		(19) 74% ee single diast.	74
	**67** (1 eq), LiCl (1 eq), THF, −78°, 40 min; then BnBr (3 eq), 1 h		(63) 99% ee, 99% de	220
	*ent*-**67** (1 eq), LiCl (1 eq), THF, −78°, 40 min; then BnBr (3 eq), 1 h		(70) 99% ee, 99% de	220

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	**67** (1 eq), LiCl (1 eq), THF, −78°, 40 min; then allyl bromide (3 eq), 45 min	 (72) 99% ee, 99% de	220
	*ent*-**67** (1 eq), LiCl (1 eq), THF, −78°, 40 min; then allyl bromide (3 eq), 45 min	 (72) 99% ee, 99% de	220
C_{16}			
	**90b** (1.2 eq), THF, −78 to −30°, 1 h; then allyl bromide (2 eq) , −78 to −30°	 (92) 86% ee	74
	90b (1.2 eq), THF, −78 to −30°, 1 h; then BnBr (2 eq), −78 to −30°	 (91) 86% ee	74

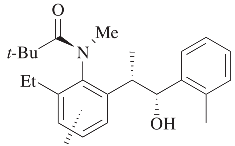
90b (1.2 eq),
THF, −78 to −30°, 1 h; then
Ph$_2$PCl (2 eq), −78 to −30°



(82) 86% ee

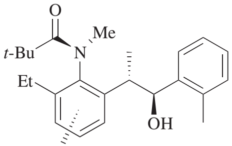
74

90b (1.2 eq),
THF, −78 to −30°, 1 h; then
o-tolualdehyde (2 eq),
−78 to −30°



(62) % ee n.d.

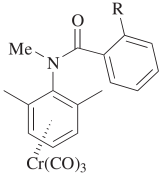
+



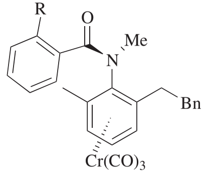
(34)

74

C$_{16-17}$



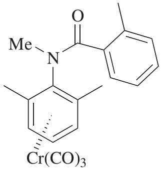
Lithium amide (2 eq),
THF, −78 to −30°,
30 min; then BnBr (2 eq),
−78 to −30°, 30 min



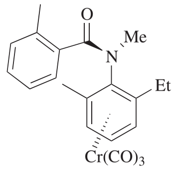
R	Lithium Amide		% ee
H	**1a**	(26)	35
H	**3d**	(63)	67
H	**90b**	(25)	36
H	**103a**	(41)	22
Me	**1a**	(58)	94
Me	**3d**	(62)	81
Me	**90b**	(48)	8
Me	**103a**	(76)	61

72

C$_{17}$



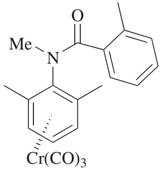
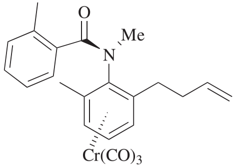
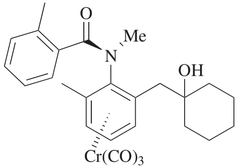
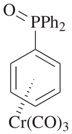
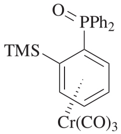
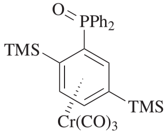
1a (2 eq), THF, −78 to −30°,
30 min; then MeI (2 eq),
−78 to −30°, 30 min

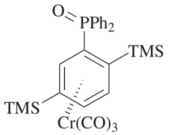
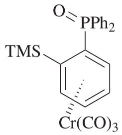
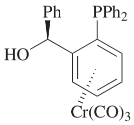
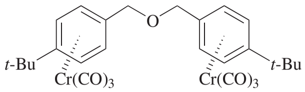
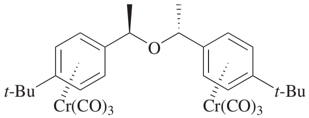
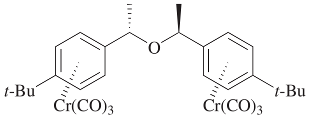


(48) 99% ee

72

TABLE 6. METALATIONS–SUBSTITUTIONS OF TRICARBONYL(η^6-ARENE)CHROMIUM(0) COMPLEXES (*Continued*)

Chromium(0) Arene Complex	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17}			
	**1a** (2 eq), THF, −78 to −30°, 30 min; then allyl bromide (2 eq) , −78 to −30°, 30 min	 (52) 94% ee	72
	1a (2 eq), THF, −78 to −30°, 30 min; then cyclohexanone (2 eq) , −78 to −30°, 30 min	 (67) 91% ee	72
C_{18}			
	**1a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 30 min	 (90) 73% ee	82, 81
	1a (2 eq), LiCl (2 eq), TMSCl (11 eq), THF, −78°, 30 min	 (82) 79% ee	82, 81

	67 (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 30 min	 (59) 82% ee +  (7) % ee n.d.	82
	1. **1a** (1.2 eq), LiCl (1.2 eq), Bu$_3$SnCl (4 eq), THF, −100°, 30 min 2. PMHS, Ti(O*i*-Pr)$_4$ 3. *n*-BuLi; then PhCHO	 (76) 81% ee, single diast.	82, 81
C$_{22}$			
	**67** (2 eq), LiCl (2 eq), THF, −78°, 1 h; then MeI (6 eq), 1 h	 (98) 99% ee, 98% de	220
	ent-**67** (2 eq), LiCl (2 eq), THF, −78°, 1 h; then MeI (6 eq), 1 h	 (98) 99% ee, 96% de	220

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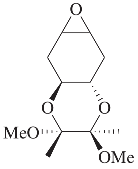
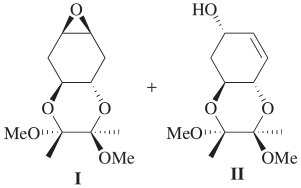
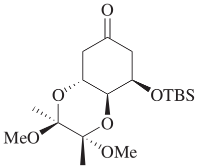
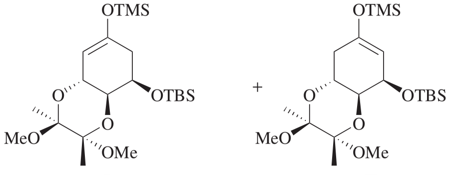
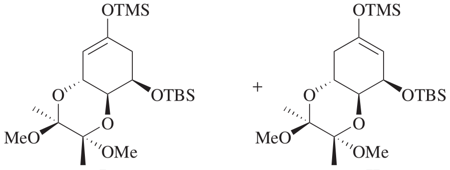
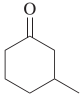
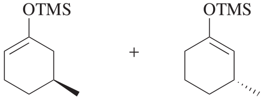
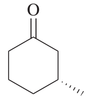
[a] The absolute configuration of the product is unknown and could be opposite to the shown structure.

TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C_6			
	**96b** (*x* eq), THF, 0°, 2 h	 *x* · **I** · % ee **I** · **II** · % ee **II** 0.7 · (51) · 44 · (32) · 63 0.5 · (—) · — · (26) · 64	232
	*ent*-**6a** (1.2 eq), LiCl (1.2 eq), THF, −78°, 30 min; then TMSCl	 **I** + **II** (41), **I/II** = 9:1	229
	ent-**6a** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°	 **I** + **II** (—), **I/II** = 87:13	229
C_7			
	**1a** (1.5 eq), TMSCl, THF, −70°, 15 min	 **I** ~23% ee · **II** ~67% **I** + **II** (62), **I/II** = 64:36	240



Lithium amide (1.5 eq), TMSCl, THF, –90°

I **I + II** (—) **II**

Lithium Amide	**I/II**
1a	64:36
2	93:7
124	90:10

240

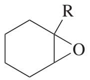
90a (1.5 eq), TMSCl, THF, –90°

I **II**

I + II (—), **I/II** = 95:5

240

$C_{7–10}$



134 (0.1 eq), LDA (2 eq), DBU (5 eq), THF, 0°

I **II**

R	% Conv	**I**	% ee **I**	**II**	% ee **II**
Me	43	(45)	78	(30)	96
Me	52	(38)	87	(40)	94
Et	40	(53)	30	(31)	90
Et	63	(32)	70	(47)	90
i-Pr	46	(48)	73	(41)	n.d.
i-Pr	52	(41)	92	(45)	n.d.
t-Bu	44	(51)	64	(36)	99
t-Bu	58	(36)	99	(40)	99

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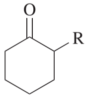
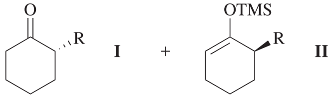
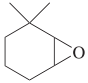
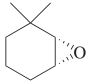
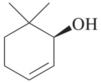
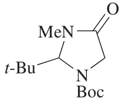
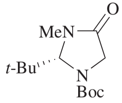
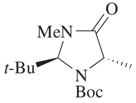
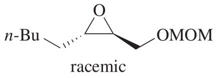
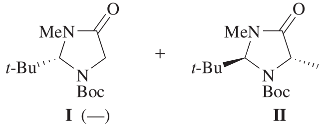
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

<table>
<tr><th>Substrate</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td colspan="4">C_{7-12}</td></tr>
<tr><td> </td><td>90b (<i>x</i> eq), TMSCl, HMPA, THF, 1 h</td><td>
<table>
<tr><th>R</th><th><i>x</i></th><th>Temp (°)</th><th>I</th><th>% ee I</th><th>II</th><th>% ee II[a]</th></tr>
<tr><td>Me</td><td>0.7</td><td>−105</td><td>(—)</td><td>38</td><td>(—)</td><td>90</td></tr>
<tr><td><i>i</i>-Pr</td><td>0.8</td><td>−105</td><td>(—)</td><td>18</td><td>(—)</td><td>94</td></tr>
<tr><td><i>t</i>-Bu</td><td>1</td><td>−78</td><td>(54)</td><td>61</td><td>(40)</td><td>94</td></tr>
<tr><td><i>t</i>-Bu</td><td>1</td><td>−105</td><td>(45)</td><td>90</td><td>(51)</td><td>94</td></tr>
<tr><td>Ph</td><td>0.8</td><td>−105</td><td>(66)</td><td>30</td><td>(33)</td><td>98</td></tr>
<tr><td>Ph</td><td>1.3</td><td>−105</td><td>(24)</td><td>94</td><td>(72)</td><td>48</td></tr>
</table></td><td>14</td></tr>
<tr><td colspan="4">C_8</td></tr>
<tr><td> </td><td>134 (0.1 eq), LDA (2 eq), DBU (5 eq), THF, 0°</td><td> I (47) 99% ee +  II (43) 94% ee
52% conv</td><td>234</td></tr>
<tr><td> </td><td>1a (0.6 eq), THF, −55°, 2 h; then MeI (3 eq), 1 h</td><td> I (—) +  II
<table>
<tr><th>% Conv</th><th>% ee I</th></tr>
<tr><td>46</td><td>14</td></tr>
<tr><td>48</td><td>20</td></tr>
<tr><td>57</td><td>29</td></tr>
<tr><td>69</td><td>40</td></tr>
<tr><td>88</td><td>61</td></tr>
</table></td><td>238</td></tr>
</table>



1a (0.6 eq), THF, −78°, 2 h;
then MeI (3 eq), 1 h



% Conv	% ee **I**
14	9
25	28
44	45
56	53
76	80

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103a (0.5 eq),
additive (0.5 eq), 12 h

Solvent	Additive	Temp (°)	**I** + **II**	**I**/**II**	% ee **I**	% ee **II**
THF	KO*t*-Bu	−70	(20)	5:95	14	4
THF	DBU	25	(28)	46:54	10	18
benzene	DBU	25	(45)	45:55	29	30
benzene	—	25	(15)	54:46	20	25

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Lithium amide (1 eq)

Lithium Amide	Solvent	Temp (°)	Time (h)	**I** + **II**	**I**/**I**	% ee **I**	% ee **II**
51	benzene	0	12	(41)	31:69	30	21
52	benzene	0	3	(41)	32:68	20	20
52	pentane	rt	2	(24)	39:61	20	14

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Lithium amide (0.5–1 eq),
THF, rt, 12 h

Lithium Amide	**I** + **II**	**I**/**II**	% ee **I**	% ee **II**
44a	(30)	65:35	5	16
1a	(25)	56:44	2	34
124	(11)	60:40	4	10

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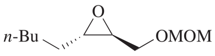
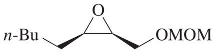
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

<table>
<tr><th>Substrate</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_8</td><td></td><td></td><td></td></tr>
<tr><td>
racemic</td><td>44a (1 eq), benzene, rt, 5 h</td><td>
I 40% ee II 2% ee
I + II (39), I/II = 73:27</td><td>236</td></tr>
<tr><td></td><td>1a (0.5 eq), rt, 12 h</td><td>
I II
<table><tr><th>Solvent</th><th>I + II</th><th>I/II</th><th>% ee I</th><th>% ee II</th></tr><tr><td>pentane</td><td>(25)</td><td>32:68</td><td>16</td><td>33</td></tr><tr><td>benzene</td><td>(20)</td><td>23:77</td><td>8</td><td>28</td></tr></table></td><td>236</td></tr>
<tr><td></td><td>124 (0.5 eq), benzene, rt, 12 h</td><td>
I 14% ee II 14% ee
I + II (15), I/II = 20:80</td><td>236</td></tr>
<tr><td></td><td>124 (0.5 eq), DBU (0.5 eq), THF, rt, 12 h</td><td>
I 16% ee II 22% ee
I + II (28), I/II = 47:53</td><td>236</td></tr>
<tr><td>
racemic</td><td>103a (0.5 eq), DBU (0.5 eq), benzene, rt, 20 h</td><td>
I 43% ee I + II (25), I/II = 98:2 II</td><td>236</td></tr>
</table>

Lithium amide (*x* eq)

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Lithium Amide	*x*	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	% ee **I**
51	1	pentane	−50	18	(50)	98:2	36
53	0.5	benzene	0	20	(39)	98:2	28
1a	0.5	benzene	rt	20	(26)	98:2	32
1a	0.25	pentane	−50	20	(16)	98:2	42
1a	0.75	pentane	−50	20	(55)	98:2	20
1a	1.0	pentane	−50	20	(49)	98:2	36

Lithium amide (1 eq)

236

Lithium Amide	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	% ee **I**
51	pentane	0	18	(45)	98:2	32
52	pentane	−50	16	(34)	98:2	10
52	benzene	0	20	(47)	98:2	12

44a (1 eq), benzene, rt, 20 h

I 33% ee **I + II** (10), **I/II** = 9:1 **II**

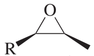
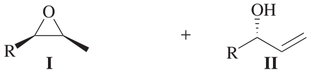
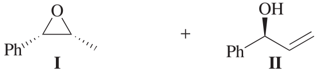
236

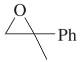
1a (0.5 eq), THF, rt, 20 h

I 22% ee **I + II** (10), **I/II** = 95:5 **II** 7% ee

236

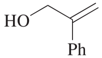
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

<table>
<tr><th>Substrate</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_9</td><td></td><td></td><td></td></tr>
<tr><td>
racemic</td><td>103a (<i>x</i> eq), DBU, THF, 0°</td><td>
<table>
<tr><th>R</th><th><i>x</i></th><th>I</th><th>% ee I</th><th>II</th><th>% ee II[b]</th></tr>
<tr><td>Ph</td><td>0.75</td><td>(31)</td><td>>95</td><td>(60)</td><td>35</td></tr>
<tr><td>Ph</td><td>0.66</td><td>(37)</td><td>89</td><td>(56)</td><td>62</td></tr>
<tr><td>Ph</td><td>0.5</td><td>(52)</td><td>62</td><td>(38)</td><td>70</td></tr>
<tr><td>Ph</td><td>0.33</td><td>(67)</td><td>30</td><td>(21)</td><td>72</td></tr>
<tr><td><i>n</i>-C_6H_{13}</td><td>0.75</td><td>(29)</td><td>>95</td><td>(63)</td><td>55</td></tr>
<tr><td><i>n</i>-C_6H_{13}</td><td>0.33</td><td>(66)</td><td>25</td><td>(22)</td><td>77</td></tr>
</table></td><td>233</td></tr>
<tr><td></td><td>134 (0.05 eq), LDA (2 eq),
DBU (5 eq), THF, 0°</td><td>
<table>
<tr><th>% Conv</th><th>I</th><th>% ee I</th><th>II</th><th>% ee II</th></tr>
<tr><td>48</td><td>(87)</td><td>77</td><td>(73)</td><td>88</td></tr>
<tr><td>55</td><td>(89)</td><td>94</td><td>(85)</td><td>84</td></tr>
</table></td><td>106</td></tr>
<tr><td>
racemic</td><td>103a (<i>x</i> eq), DBU, THF, 0°</td><td>
<table>
<tr><th><i>x</i></th><th>I</th><th>% ee I</th><th>II</th><th>% ee II[b]</th></tr>
<tr><td>0.75</td><td>(27)</td><td>45</td><td>(63)</td><td>15</td></tr>
<tr><td>0.33</td><td>(67)</td><td>11</td><td>(20)</td><td>34</td></tr>
</table></td><td>233</td></tr>
</table>



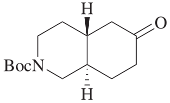
103a (0.75 eq), DBU, THF, 0°

(11) 39% ee +

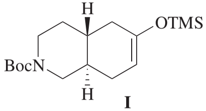


(69)

233

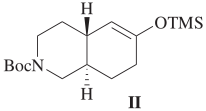


Lithium amide (1.5 eq),
TMSCl, THF, 15 min



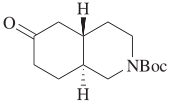
I

+

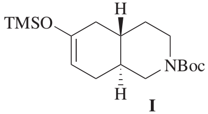


II

Lithium Amide	Temp (°)	I + II	I/II	
1a	−73	(—)	90:10	240
1a	−90	(97)	94:6	241, 240
90a	−70	(—)	74:26	240
124	−70	(—)	87:13	240

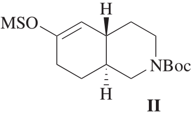


Lithium amide (1.5 eq),
TMSCl, THF, 15 min



I

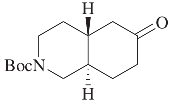
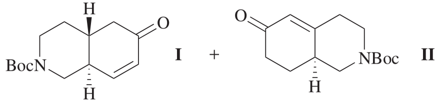
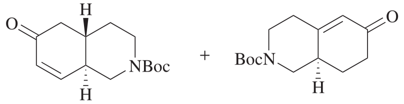
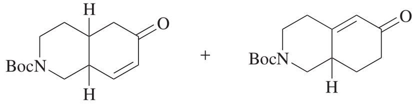
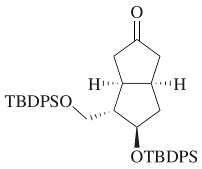
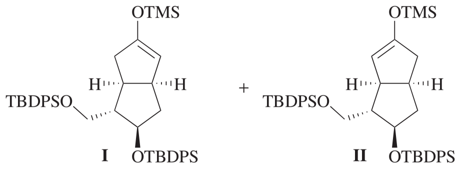
+

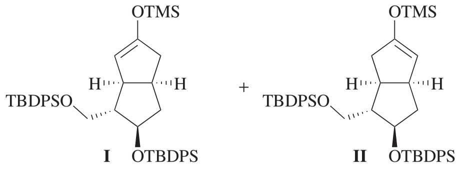
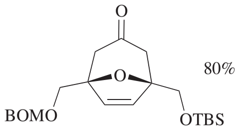
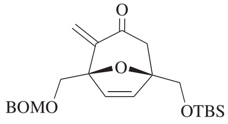
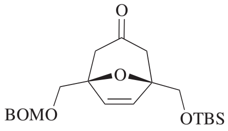
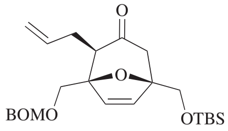
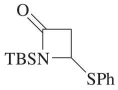
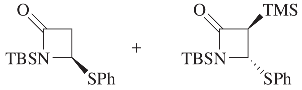


II

Lithium Amide	Temp (°)	I + II	I/II	
1a	−73	(—)	32:68	240
1a	−90	(97)	21:79	241, 240
2	−90	(—)	94:6	240
90a	−70	(—)	97:3	240
124	−70	(—)	87:13	240

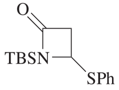
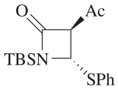
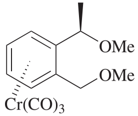
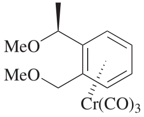
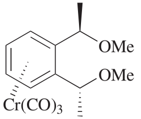
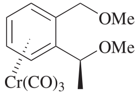
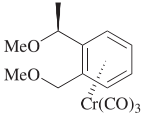
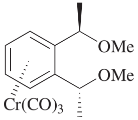
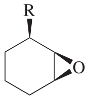
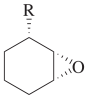
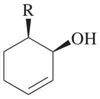
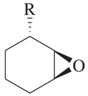
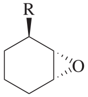
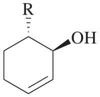
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

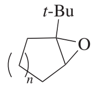
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
 racemic	1. **1a** (1.5 eq), TMSCl, THF, 20 min 2. PhSeCl 3. DMDO	 **I** + **II** Temp (°) | **I** | % ee **I** | **II** | % ee **II** –70 | (31) | 46 | (15) | 78 –96 | (33) | 60 | (17) | 83	241, 240
	1. **90a** (1.5 eq), TMSCl, THF, –70°, 20 min 2. PhSeCl 3. DMDO	 **I** 12% ee **II** 66% ee **I**+ **II** (—), **I/II** = 86:14	240
	1. **124** (1.5 eq), TMSCl, THF, –70°, 20 min 2. PhSeCl 3. DMDO	 **I** 4% ee **II** 3% ee **I** + **II** (—), **I/II** = 86:14	240
	**1a** (2 eq), THF, –95°; then TMSCl, –90°, 30 min	 **I** **II** **I**+ **II** (87), **I/II** = 95:5	155

	2 (2 eq), THF, –95°; then TMSCl, –90°, 30 min	 **I** + **II** **I** + **II** (85), **I/II** = 86:14	155
 80% ee	1. **1a** (1.5 eq), LiCl (1.5 eq), THF, –78°, 1 h; then $Me_2\overset{+}{N}{=}CH_2I^-$, 1 h 2. MeI; then $NaHCO_3$	 (70) 97% ee	145
	1. **1a** (1.5 eq), LiCl (1.5 eq), THF, –78°, 1 h; then TMSCl, 30 min 2. NIS 3. allyltributyltin, AIBN	 (75) ~97% ee, dr 7: 1	145
	**1a**, THF, –90°, 40 min; then TMSCl	 **I** (—) + **II** (—)	239

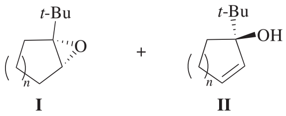
% Conv	% ee **I**	% ee **II**
19	16	72
36	36	64
45	51	61
52	68	55
57	70	50
59	69	45
70	88	31
88	n.d.	22

TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. **1a**, THF, –90°, 35 min; then MeCHO, 30 min 2. Dess-Martin periodinane	 (16) 70% ee	239
 racemic	**68** (0.5 eq), LiCl (0.5 eq), THF, –78°, 45 min; then MeI (5 eq), 1 h	 (73) 35% ee +  (27) 85% ee	226
 35% ee	**68** (0.5 eq), LiCl (0.5 eq), THF, –78°, 45 min; then MeI (5 eq), 1 h	 (65) 96% ee +  (25) 95% ee	226
C_{9-10}			
 racemic	**135a** (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°	 +  **I** (—) **II** (—) R % Conv % ee **I** % ee **II** *i*-Pr 60 99 90 *n*-Bu 80 99 64	235
 racemic	**135a** (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°	 +  **I** (—) **II** (—) R % Conv % ee **I** % ee **II** *i*-Pr 65 21 20 *n*-Bu 30 5 16 *t*-Bu 32 n.d. 94	235



134 (0.1 eq), LDA (2 eq), DBU (5 eq), THF, 0°



n	% Conv	**I**	% ee **I**	**II**	% ee **II**
1	42	(50)	n.d.	(34)	79
1	63	(32)	n.d.	(52)	60
2	44	(51)	64	(36)	99
2	58	(36)	99	(40)	99
3	41	(51)	n.d.	(34)	94
3	47	(48)	n.d.	(40)	90

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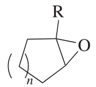
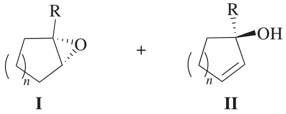


135a (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°



n	R	% Conv	% ee **I**	% ee **II**
3	Et	49	51	95
2	*n*-Bu	41	42	94
1	*t*-Bu	32	n.d.	96
2	*t*-Bu	46	72	99
3	*t*-Bu	34	n.d.	96

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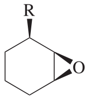
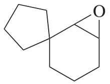
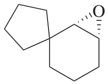
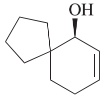
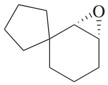
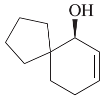
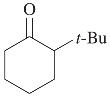
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-12}			
 racemic	**103a** (*x* eq), DBU (*y* eq), THF, rt, 16 h	 I + II	392

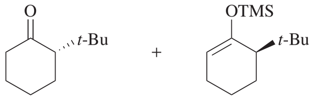
R	*x*	*y*	**I**	% ee **I**	**II**	% ee **II**
t-Bu	0.5	0.55	(61)	24	(25)	68
t-Bu	0.75	0.82	(49)	49	(44)	58
t-Bu	1	1.1	(39)	63	(55)	52
t-Bu	1.2	1.32	(21)	92	(73)	29
i-Pr	0.6	0.66	(71)	26	(28)	66
i-Pr	0.75	0.82	(62)	35	(37)	61
i-Pr	1.1	1.21	(27)	95	(72)	35
i-Pr	1.2	1.32	(15)	>98	(84)	21
n-C_6H_{13}	0.75	0.82	(57)	40	(42)	60
n-C_6H_{13}	1.10	1.21	(30)	84	(65)	42

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	**134** (0.1 eq), LDA (2 eq), DBU (5 eq), THF, 0°	 (40) 93% ee +  (45) 90% ee 56% conv	234
	135a (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°	 (—) 96% ee +  (—) 85% ee 56% conv	235

C_{10}



Lithium amide (*x* eq),
TMSCl, HMPA,
THF, −78°, 1 h



I + **II**

Lithium Amide	*x*	**I**	% ee **I**	**II**	% ee **II**[a]
30b	0.77	(45)	2	(46)	3
34	0.77	(67)	4	(22)	15
90a	0.77	(53)	27	(40)	37
90e	1	(39)	77	(54)	65
92	1	(35)	96	(60)	63

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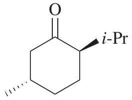
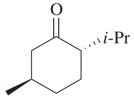
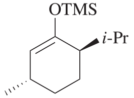


racemic

90b (0.68 eq),
TMSCl, HMPA,
THF, − 105°, 1 h

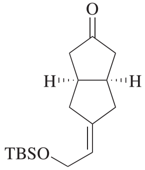


(42) 94% ee +



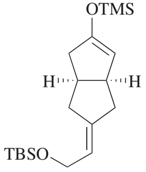
(54) 76% ee[c]

14



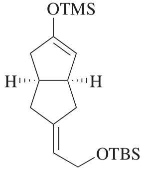
racemic

1a (2 eq), LiCl (1.5 eq),
THF, −100°, 15 min; then
TMSCl, 1 h



I 88% ee

+



II 88% ee

I + **II**(89),**I/II** = 49:51

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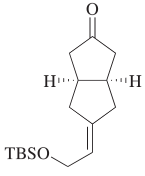
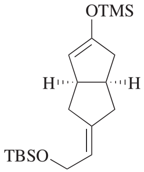
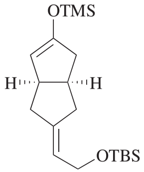
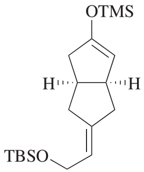
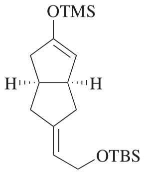
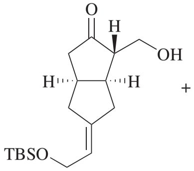
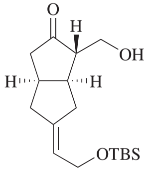
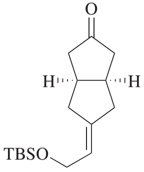
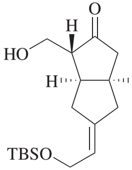
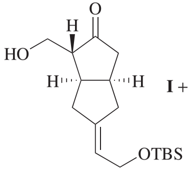
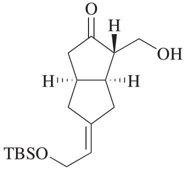
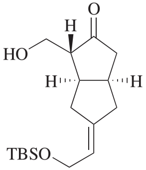
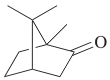
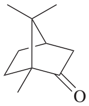
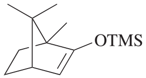
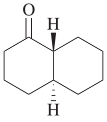
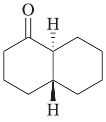
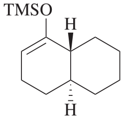
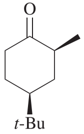
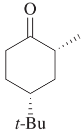
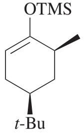
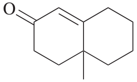
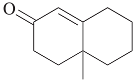
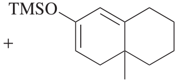
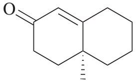
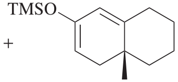
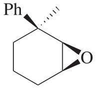
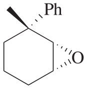
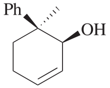
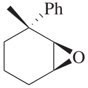
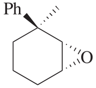
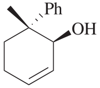
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}				
 racemic	**2** (1.2 eq), LiCl (0.5 eq), THF, −100°, 15 min; then TMSCl, 1 h	 **I** 80% ee +  **II** 88% ee	**I** + **II** (90), **I/II** = 51:49	190
	2, LiBr, THF, −100°, 15 min; then TMSCl, 1 h	 **I** 18% ee +  **II** 33% ee	**I** + **II** (—), **I/II** = 49:51	190
	1a (2 eq), LiCl (1.5 eq), THF, −100°, 2.5 h; then CH_2O	 **I** 80% ee +  **II**	**I** + **II** (64), **I/II** = 1:1	190

 91% ee	**2** (1.5 eq), LiCl (1.7 eq), THF, −100°, 2.5 h; then CH$_2$O	 **I** 80% ee +  **II** 80% ee **I** + **II** (54), **I/II** = 1:1	190
	1a (1.7 eq), LiCl (1.7 eq), THF, −100°, 2.5 h; then CH$_2$O	 **I** +  **II** 14% ee **I** + **II** (—), **I/II** = 79:21	190
 racemic	**90b** (0.85 eq), TMSCl, HMPA, THF, −100°	 (37) 72% ee +  (62) 44% ee	237
 racemic	Lithium amide (0.85 eq), TMSCl, HMPA, THF, −100°	 **I** +  **II**	237

Lithium Amide	**I**	% ee **I**	**II**	% ee **II**
90b	(79)	8	(15)	52
93	(43)	78	(55)	59

TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
 racemic	**93** (0.8 eq), TMSCl, HMPA, THF, –105°	 (48) 93% ee +  (52) 90% ee[a]	14
	**90a** (0.85 eq), TMSCl, HMPA, THF, –100°	 (73) 1% ee +  (26) 2% ee	237
	90b (0.85 eq), TMSCl, HMPA, THF, –100°	 (74) 11% ee +  (25) 35% ee	237
C_{13}			
 racemic	**135a** (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°	 (—) 99% ee + 62% conv  (—) 55% ee	235
 racemic	**135a** (0.05 eq), LDA (1.2 eq), DBU (5 eq), THF, 0°	 (—) 99% ee + 70% conv  (—) 40% ee	235

C$_{14}$

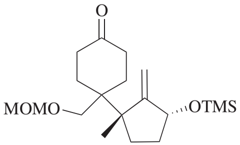
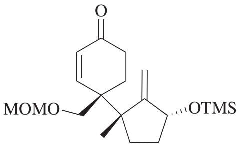
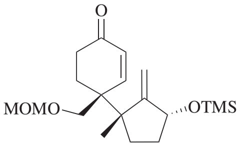
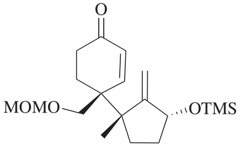
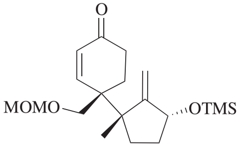
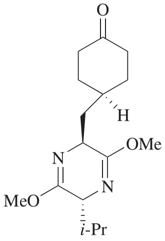
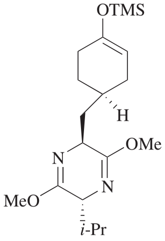
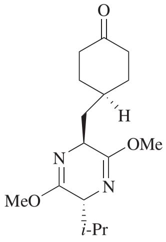
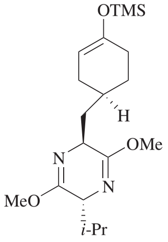
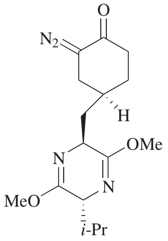
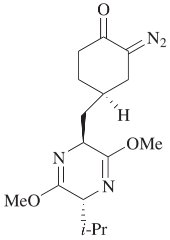
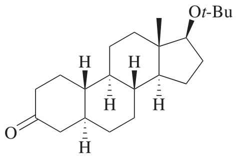
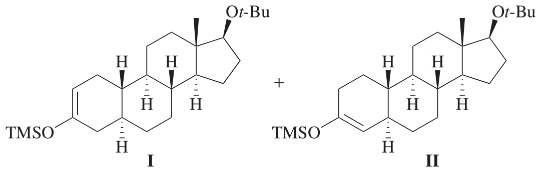
	1. **2** (2.5 eq), TMSCl (20 eq), THF, −78°, 30 min 2. Pd(OAc)$_2$	 **I** +  **II** **I** + **II** (88), **I/II** = 2:1	230
	1. **1a** (2.5 eq), TMSCl (20 eq), THF, −78°, 30 min 2. Pd(OAc)$_2$	 **I** +  **II** **I** + **II** (—), **I/II** = 4:1	230
	**1a**, TMSCl, THF, −78°	 (76) 59% de	231

TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{14} 	**2**, TMSCl, THF, −78°		(71) 60% de	231, 179
	1. **2** (2.5 eq), LiCl (1.3 eq), THF, −78°, 45 min; then $CF_3CO_2CH_2CF_3$ (3 eq) 2. TsN_3, Et_3N		(48) 80% de	179
	1. **1a** (2.5 eq), LiCl (1.3 eq), THF, −78°, 45 min; then $CF_3CO_2CH_2CF_3$ (3 eq) 2. TsN_3, Et_3N		(32) 80% de	179



Lithium amide (2 eq), TMSCl, HMPA (2 eq), toluene, –78°, 20 min



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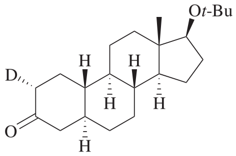
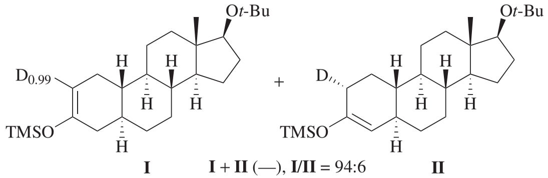
Lithium Amide	**I + II**	**I/II**
90b	(97)	95:5
92	(96)	91:9
ent-**90b**	(98)	24:76
91	(92)	24:76



90b (2 eq), TMSCl, HMPA (2 eq) , toluene, –78°, 20 min



I + II (—), **I/II** = 94:6

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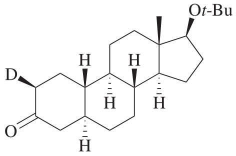
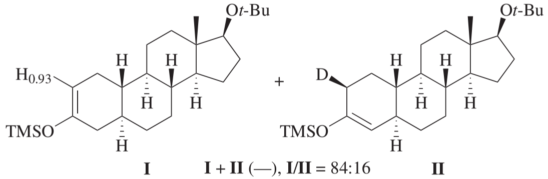


90b (2 eq), TMSCl, HMPA (2 eq) , toluene, –78°, 20 min



I + II (—), **I/II** = 84:16

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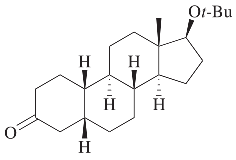
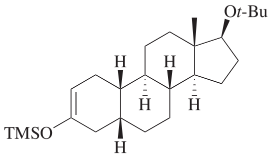
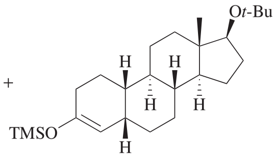
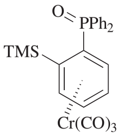
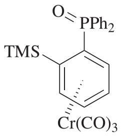
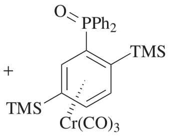
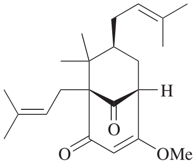
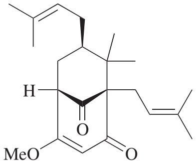
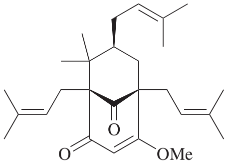
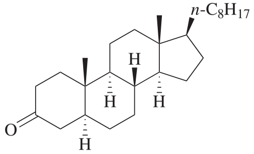
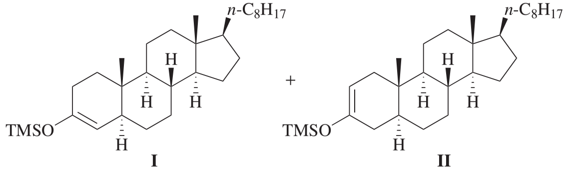
TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}			
	Lithium amide (2 eq), TMSCl, HMPA (2 eq), toluene, −78°, 20 min	 **I** +  **II** Lithium Amide / **I + II** / **I/II** **90b** (92) 89:11 **92** (99) 95:5 *ent*-**90b** (95) <2:98 **91** (97) <2:98	227
 racemic	**67** (1.2 eq), LiCl (1.2 eq), TMSCl, THF, −78°, 30 min	 (36) 73% ee +  (46) 64% ee	82
C_{21}			
 racemic	**67** (2 eq), THF, −40°; then prenyl bromide (6 eq), 2 h	 (24–27) >98% ee +  (65) ~50% ee 60–70% conv	213

C_{27}



Lithium amide (2 eq),
TMSCl, HMPA (2 eq),
toluene, −78°, 20 min



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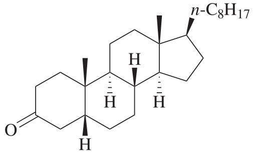
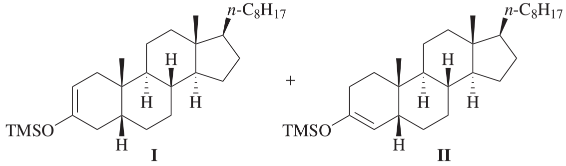
Lithium Amide	**I + II**	**I/II**
90b	(86)	61:39
92	(98)	70:30
88	(94)	98:2
ent-**90b**	(83)	2:98
91	(98)	2:98
89	(97)	<2:98



Lithium amide (2 eq),
TMSCl, HMPA (2 eq),
toluene, −78°, 20 min



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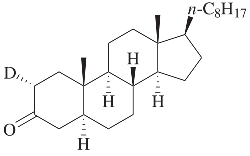
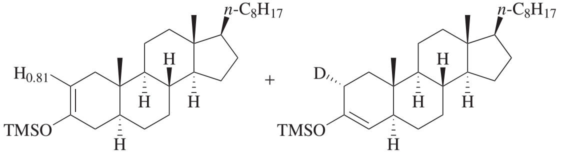
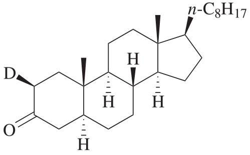
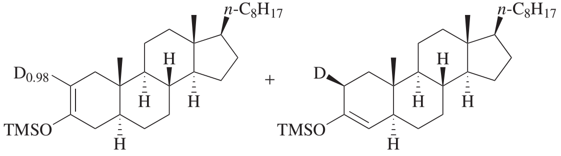
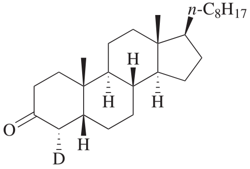
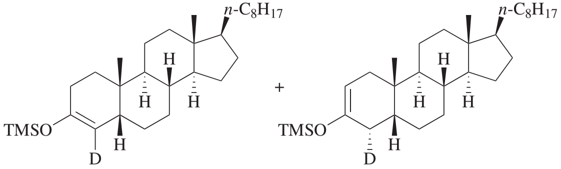
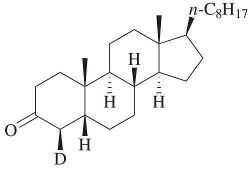
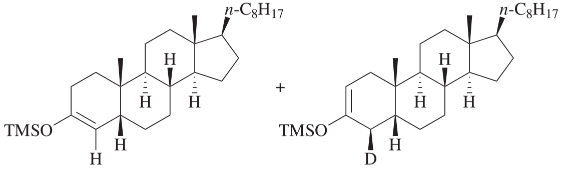
Lithium Amide	**I + II**	**I/II**
90b	(92)	84:16
92	(99)	97:3
88	(98)	96:4
ent-**90b**	(78)	<2:98
91	(99)	<2:98
89	(90)	<2:98

TABLE 7. SITE–SELECTIVE ENOLIZATIONS AND KINETIC RESOLUTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27}			
	*ent*-**90b** (2 eq), TMSCl, HMPA (2 eq), toluene, −78°, 20 min	 **I** + **II** (—), **I/II** = 90:10	228
	*ent*-**90b** (2 eq), TMSCl, HMPA (2 eq), toluene, −78°, 20 min	 **I** + **II** (—), **I/II** = 97:3	228
	*ent*-**90b** (2 eq), TMSCl, HMPA (2 eq), toluene, −78°, 20 min	 **I** + **II** (—), **I/II** = 99:1	228

	*ent*-**90b** (2 eq), TMSCl, HMPA (2 eq), toluene, −78°, 20 min	 **I** **I** + **II** (—), **I**/**II** = 98:2 **II**	228

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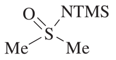
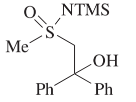
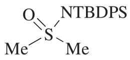
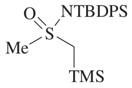
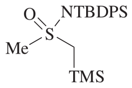
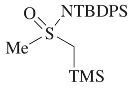
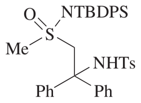
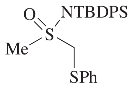
[a] The enantiomeric excess of the silyl enol ether product was determined after conversion into the corresponding enol acetate.

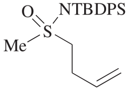
[b] The enantiomeric excess of the allylic alcohol product was determined after catalytic hydrogenation of the alkene group.

[c] The enantiomeric excess of the silyl enol ether product was determined after conversion back into the parent ketone.

TABLE 8. DEPROTONATIONS ADJACENT TO SULFUR

*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

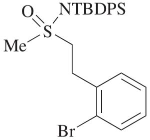
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_2$			
	Lithium amide (1.5 eq), LiCl (1.5 eq), THF, 1 h; then Ph$_2$CO (1.7 eq), 30 min	 Lithium Amide / Temp (°) / % ee *ent*-**3d** / −105 / (41) 38 **1a** / −78 / (70) 42 **2** / −105 / (86) 70	250
	**2** (1.5 eq), LiCl (1.5 eq), THF, 1 h; then TMSCl (1.3 eq), 30 min	 Temp (°) / % ee −78 / (72) 36 −105 / (58) 61	250
	1a (1.5 eq), LiCl (1.5 eq), THF, –94°, 1 h; then TMSCl (1.3 eq), 30 min	 (27) 54% ee	250
	63 (1.5 eq), LiCl (3 eq), THF, −105°, 1 h; then TMSCl (1.3 eq), 30 min	 (53) 0% ee	250
	2 (1.5 eq), LiCl (1.5 eq), THF, −105°, 1 h; then Ph$_2$C=NTs (1.2 eq), 30 min	 (30) 28% ee	250
	2 (1.5 eq), LiCl (1.5 eq), THF, −105°, 1 h; then PhSSPh (1.3 eq), 30 min	 (6) 62% ee	250



2 (1.5 eq), LiCl (1.5 eq), THF, −105°, 1 h; then allyl iodide (2.2 eq), 30 min

(34) % ee n.d.

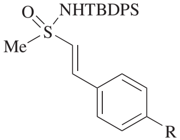
250



2 (1.5 eq), LiCl (1.5 eq), THF, time; then 2-$BrC_6H_4CH_2Br$ (2.3 eq), 30 min

Temp (°)	Time (min)		% ee
−105	60	(70)	57
−105	10	(28)	57
−105 to −78	60	(48)	57

250

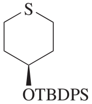


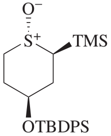
2 (1.5 eq), LiCl (1.5 eq), THF, −105°, 1 h; then $ClPO(OEt)_2$ (1.3 eq), 5 min; *t*-BuOK, 10 min; 4-RC_6H_4CHO (*x* eq), −105 to 0°, 1 h

R	*x*		% ee
Cl	1.7	(52)	55
Ph	1.3	(46)	50

250

C_5

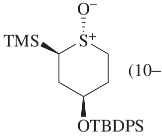




Lithium amide (1.5 eq), THF, −78°, 1 h; then TMSCl (8 eq), 15 min

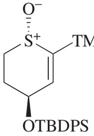
Lithium Amide		% ee
124	(91)	~60
1a	(—)	0

244, 245



1a (1.5 eq), TMSCl (8 eq), THF, −78°

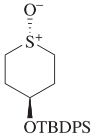
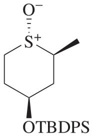
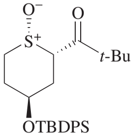
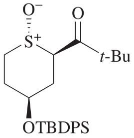
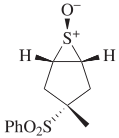
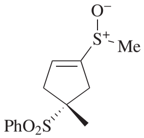
(10–20) 65–69% ee +



(40–50)

244, 245

TABLE 8. DEPROTONATIONS ADJACENT TO SULFUR (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	**124** (1.5 eq), THF, −78°, 1 h; then MeI (3 eq), 15 min	 (85) 55–60% ee[a]	244, 245
	124 (1.5 eq), THF, −78°, 1.5 h; then *t*-BuCO$_2$Et (2 eq), 20 min	 (72) 55% ee	245
	124, THF, −78°; then *t*-BuCOCl	 (38) % ee n.d.	245
C_6			
	**1a** (1.2 eq), THF, −78°; then MeI (10 eq)	 (79) ~10% ee	244, 248

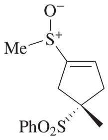
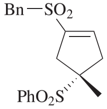
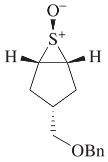
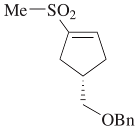
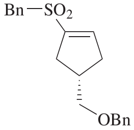
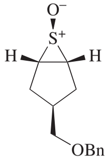
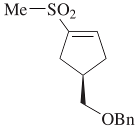
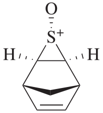
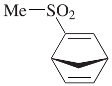
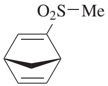
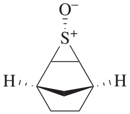
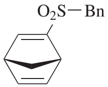
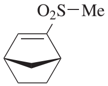
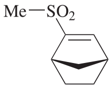
	67 (1.2 eq), MeI (10 eq), THF, −78°, 1 h	 (85) 82% ee, dr ~2:1	249, 248
	1. **67** (1.2 eq), BnBr, THF, −78°, 1 h 2. Oxone®	 (72) 85% ee	249, 248
	1. **67** (1.2 eq), MeI (10 eq), THF, −78°, 1 h 2. Oxone®	 (72) 85% ee	249, 248
	1. **67** (1.2 eq), BnBr, THF, −78°, 1 h 2. Oxone®	 (53) 88% ee	249, 248
	1. **67** (1.2 eq), MeI (10 eq), THF, −78°, 1 h 2. Oxone®	 (31) 85% ee	249, 248

TABLE 8. DEPROTONATIONS ADJACENT TO SULFUR (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1. **1a** (1.2 eq), LiCl (1.2 eq), THF, −78°; then MeI (10 eq) 2. Oxone®	 (52) 43% ee	248
	1. **67** (1.2 eq), MeI (10 eq), THF, −78°, 1 h 2. Oxone®	 (46–53) 62–73% ee	249, 248
	1. **67** (1.2 eq), BnBr, THF, −78°, 1 h 2. Oxone®	 (43) 66% ee	248
	1. **67** (1.2 eq), MeI (10 eq), LiCl (*x* eq), THF, −78°, 1 h 2. Oxone®	 *x* — % ee 0 (57) <5 0.8 (58) 27	248
	1. **1a** (1.2 eq), LiCl (1.2 eq), THF, −78°; then MeI (10 eq) 2. Oxone®	 (81) 76% ee	248

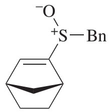
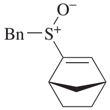
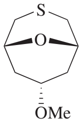
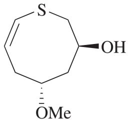
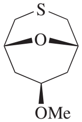
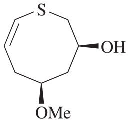
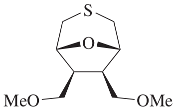
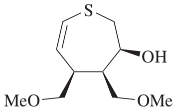
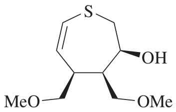
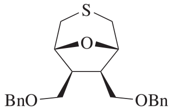
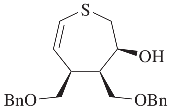
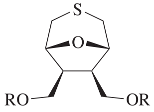
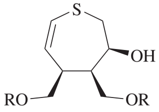
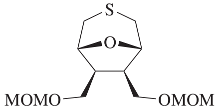
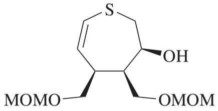
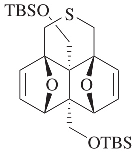
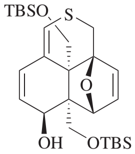
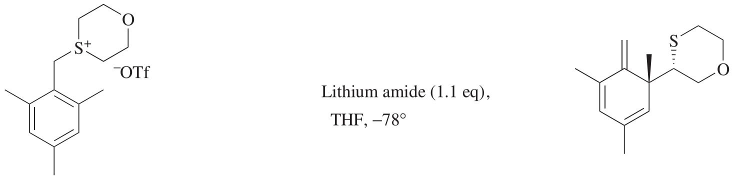
	67 (1.2 eq), BnBr, LiCl (*x* eq) THF, −78°, 1 h	 x — — % ee 0 (50) <5 0.8 (46) 17	248
	1a (1.2 eq), LiCl (1.2 eq), THF, −78°; then BnBr	 (82) 70% ee	248
	**2** (3 eq), LiCl (3 eq), benzene, rt, 40 h	 (37) 97% ee^b	246
	**2** (3 eq), LiCl (3 eq), benzene, rt, 48 h	 (60) 43% ee^b	246
C$_8$ 	**2** (3 eq), LiCl (3 eq)	 Solvent — Temp (°) — Time (h) — — % ee^b THF — rt — 24 — (26) — 8 benzene — 5 — 1 — (91) — 89 toluene — −50 — 24 — (79) — 95	246
	2 (*x* eq), LiCl (*y* eq), benzene, 5°	 x — y — — % ee^b 6 — 0 — (96) — 71 5 — 1 — (97) — 91 4 — 2 — (93) — 90 3 — 3 — (91) — 89	246

TABLE 8. DEPROTONATIONS ADJACENT TO SULFUR (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	**2** (3 eq), LiCl (3 eq), benzene, 8°, 10 h	 (81) 76% ee[b]	246
	**2** (3 eq), LiCl (*x* eq), benzene, rt, 24 h	 R — *x* — — % ee[b] *t*-Bu — 0 — (76) — 43 *t*-Bu — 3 — (0) — — TBS — 3 — (0) — —	246
	**2** (3 eq), LiCl (3 eq), benzene, 9°, 10 h	 (86) 86% ee[b]	246
C_{14}			
	**2** (3 eq), LiCl (3 eq), THF, −78°, 5 h; then −78 to −30°	 (73) >95% ee	247



Lithium amide (1.1 eq),
THF, −78°

Lithium Amide		% ee[c,d]	
1a	(76)	0	251
67	(84)	50	
103a	(33)	0	
63	(41)	12	
61	(84)	6	
72	(79)	0	
71	(78)	16	

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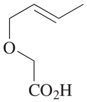
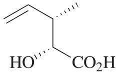
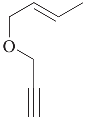
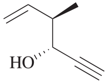
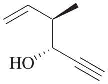
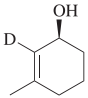
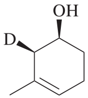
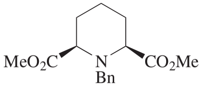
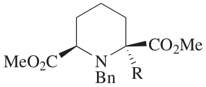
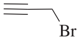
[a] The enantiomeric excess was determined after desilylation and reduction of the cyclic sulfoxide to a known thiapyran.

[b] The enantiomeric excess was determined by conversion of the alcohol into the corresponding Mosher ester.

[c] The enantiomeric excess was determined upon Diels-Alder adduct formation using 4-phenyl-[1,2,4]-triazoline-3,5-dione

[d] The absolute configuration of the rearrangement product was not determined.

TABLE 9. MISCELLANEOUS TRANSFORMATIONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C_6 	**2**, THF, −78 to −50°, 4 h	 (85) 0% ee, dr 9:1	267
C_7 	**2**, Et_2O, −78 to −15°, 4 h	 (68) 0% ee^a, dr 95:5	267
	2, −78 to −20°	 dr = 98:2 Solvent — Time (h) — % ee^a THF — 4 — (50) — <5 pentane/THF (9:1) — 10 — (70) — 0	267
	**103a** (0.7 eq), *n*-BuLi (0.5 eq), 2,5-DMTHF, 30°, 240 h	 (47)	43, 42
	**67** (1.2 eq), THF, −78°, 1 h; then RX (*x* eq), −78° to rt, overnight	 RX — *x* — % ee	
		BnBr — 25 — (78) — 98	252
		4-$BrC_6H_4CH_2Br$ — — — (73) — n.d.	252
		MeI — — — (75) — 98	252
		allylBr — — — (77) — 90	253, 252, 254
		$PhCH{=}CHCH_2Cl$ — — — (67) — 98	252
		 — — — (64) — n.d.	252

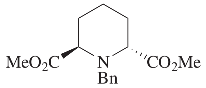
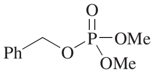
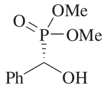
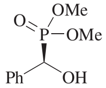
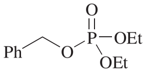
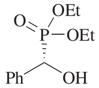
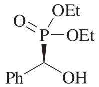
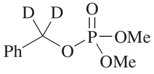
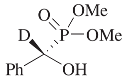
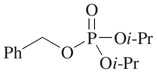
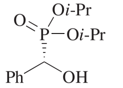
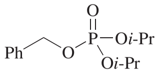
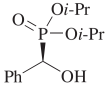
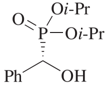
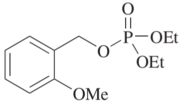
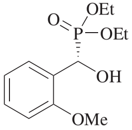
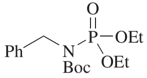
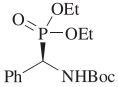
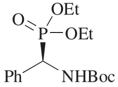
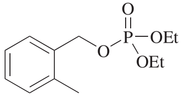
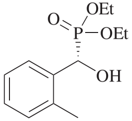
	67 (1.2 eq), THF, −78°, 1 h; then MeOH, −78° to rt, overnight		(30) 89% ee	252
	*ent*-**3d** (1.5 eq), −78°, 1 h		Solvent — % ee Et_2O (26) 13 THF (35) 28	298
	1a (1.5 eq), THF, −78°, 1 h		(30) 52% ee	298
	*ent*-**3d** (*x* eq), 1 h		Solvent — *x* — Temp (°) — % ee Et_2O 1.5 −78 (47) 27 THF 1.5 −78 (63) 23 Et_2O 4 −78 (58) 36 Et_2O 4 −100 (46) 25 toluene 2 −78 (10) 10	298
	1a (*x* eq), THF, −78°		*x* — Time (min) — % ee 1.5 60 (60) 37 4 60 (22) 47 1.5 5 (64) 41	298
	Lithium amide (1.5 eq), −78°, 1 h		Lithium Amide — Solvent — % ee **2** THF (68) 44 *ent*-**3d** Et_2O (43) 13	298
	*ent*-**3d** (*x* eq), Et_2O, 1 h		*x* — Temp (°) — % ee 4 −78 (76) 49 4 −100 (80) 49 1.5 −78 (67) 31	298

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	**1a** (1.5 eq), THF, –78°, 1 h	 (63) 24% ee	298
	2 (1.5 eq), THF, –78°, 1 h	 (52) 28% ee	298
	**2** (1.5 eq), THF, –78°, 1 h	 (48) 63% ee	298
	**3d** (1.5 eq), Et_2O, –78°, 30 min	 (65) 13% ee	301
	1a (1.5 eq), Et_2O, –78°, 30 min	 (55) 26% ee	301
C_8			
	**2** (1.5 eq), THF, –78°, 1 h	 (57) 24% ee	298

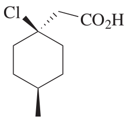
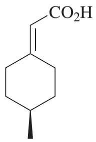
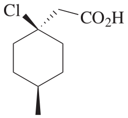
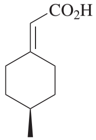
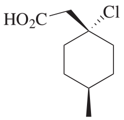
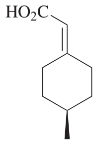
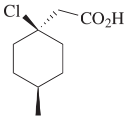
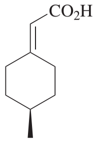
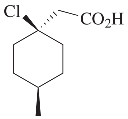
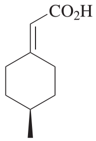
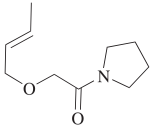
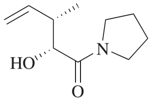
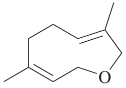
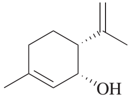
C$_9$			
	**6b** (2.5 eq), THF, −72°, 18 h	 (73) 52% ee	263
 *cis/trans* = 83:17	**6b** (2.5 eq), THF, −72°, 18 h	 (64) 30% ee	263
 *cis/trans* = 46:54	**6b** (2.5 eq), THF, −72°, 18 h	 (64) 14% ee	263
	**6c** (2.5 eq), THF, −72°, 18 h	 (75) 80% ee	263
 *cis/trans* = 55:45	**6c** (2.5 eq), THF, −72°, 18 h	 (70) 10% ee	263

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

<table>
<tr><th>Substrate</th><th>Conditions</th><th colspan="2">Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_{10}
</td><td>2, THF,–78°, 5 h</td><td></td><td>(85) 0% ee, dr 95:5</td><td>267</td></tr>
<tr><td></td><td>2 (2 eq), THF, HMPA (<i>x</i> eq)</td><td></td><td>
<table>
<tr><th><i>x</i></th><th>Temp (°)</th><th>Time (h)</th><th></th><th>% ee[a]</th></tr>
<tr><td>0</td><td>0</td><td>24</td><td>(40)</td><td>25</td></tr>
<tr><td>0</td><td>25</td><td>36</td><td>(52)</td><td>25</td></tr>
<tr><td>2</td><td>0</td><td>24</td><td>(45)</td><td>25</td></tr>
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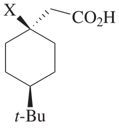
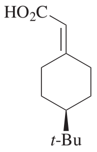
</td><td>268</td></tr>
<tr><td>C_{12}
</td><td>Lithium amide (2.5 eq),
THF, –72°, 18 h</td><td></td><td>
<table>
<tr><th>X</th><th>Lithium Amide</th><th></th><th>% ee</th></tr>
<tr><td>Br</td><td>3a</td><td>(78)</td><td>16</td></tr>
<tr><td>Cl</td><td>3b</td><td>(93)</td><td>23</td></tr>
<tr><td>Br</td><td>3b</td><td>(95)</td><td>35</td></tr>
<tr><td>Br</td><td>3c</td><td>(71)</td><td>32</td></tr>
<tr><td>Cl</td><td>3d</td><td>(85)</td><td>58</td></tr>
<tr><td>Br</td><td>3d</td><td>(78)</td><td>62</td></tr>
<tr><td>Br</td><td>3n</td><td>(80)</td><td>29</td></tr>
<tr><td>Br</td><td>3f</td><td>(80)</td><td>8</td></tr>
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</td><td>265</td></tr>
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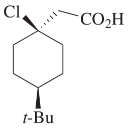
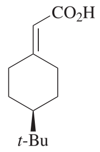
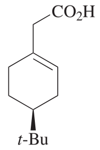


Lithium amide (2.5 eq),
THF, −72°, 18 h

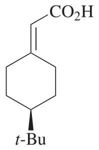


X	Lithium Amide		% ee	
Cl	**6b**	(88)	54	263
Br	**6b**	(72)	51	263, 265
Cl	**6c**	(84)	82	263
Br	**6c**	(60)	70	263, 265
Br	**3g**	(91)	18	265
Cl	**2**	(96)	74	265
Br	**2**	(74)	70	265
Cl	**9b**	(87)	52	265
Cl	**9a**	(70)	36	265
Cl	**143**	(73)	<1	265

6c (5 eq), THF, −72°, 18 h

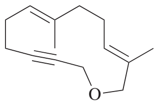


(55) 52% ee +

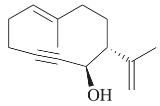


(45) 263

C_{14}



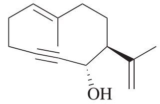
1a (3 eq), THF



Temp (°)	Time (min)		% ee
−35 to −25	60	(78)	73
−20	40	(75)	62

269, 267

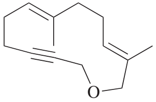
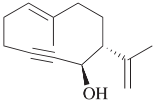
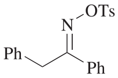
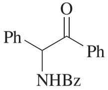
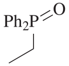
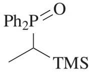
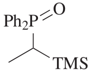
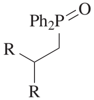
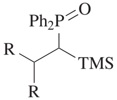
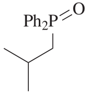
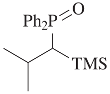
2 (3 eq)



269, 267

Solvent	Temp (°)	Time (min)		% ee	
THF	−70 to −15	45	(82)	71	
Et_2O	−25 to −15	30	(70)	9	"rearranged"
pentane/THF (9:1)	−25 to 0	90	(68)	45	

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	*ent*-**3d** (3 eq), THF, −20°, 60 min	 (82) 2% ee	269, 267
	1. Lithium amide (1.1 eq), THF, −78° to rt; then MeOH (5 eq), 0° to rt 2. BzCl, py 3. 6 N HCl	 Lithium Amide % ee **103a** (27) 5 **1a** (42) 3	302
	**124**, TMSCl, THF, −78°	 (11) 6% ee	297
	44a, THF, −78°; then TMSCl	 (44) <5% ee	297
C_{14-16}			
	**1a**, TMSCl, THF, −78°	 R % ee H (26) 6 Me (46) 10	297
C_{16}			
	**1a**, THF, −78°; then TMSCl	 (25) 7% ee	297

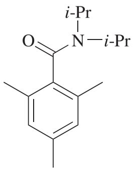
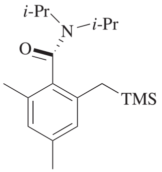
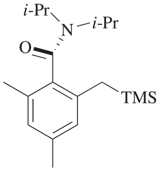
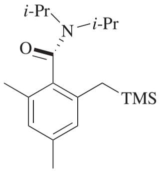
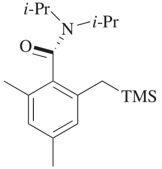
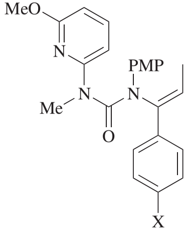
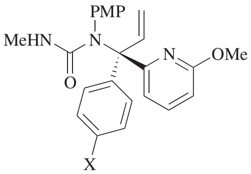
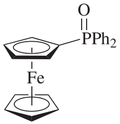
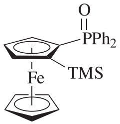
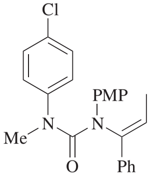
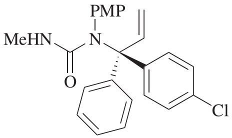
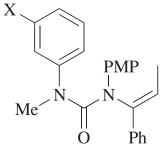
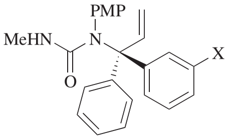
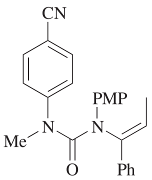
	**2** (1.3 eq), THF, −78°, 30 min; then TMSCl (2 eq)		Additive % ee — (54) 78 LiCl (33) 75	258
	Lithium amide (1.3 eq), TMSCl, THF, −78°, 30 min		Lithium Amide % ee **2** (55) 89 *ent*-**3d** (64) 62	258
	ent-**3n** (1.3 eq), THF, −78°, 30 min; then TMSCl (2 eq)		(25) 59% ee	258
	ent-**3n** (1.3 eq), TMSCl, THF, −78°, 30 min		(45) 79% ee	258

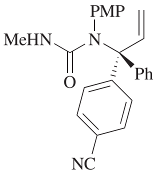
TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	**3d** (2 eq), LiCl (2 eq), THF, −78°, 20 min	 X — % ee H (87) 76 Cl (88) 68	272
C_{17} 	**1a**, TMSCl, THF, −78°	 (95) 54% ee	257
	**3d** (2 eq), LiCl (2 eq), THF, 20 min	 Temp (°) — % ee −60 (—) 74 −78 (78) 84	272
	**3d** (2 eq), LiCl (2 eq), THF, −78°, 20 min	 X — % ee F (86) 84 OMe (63) 72	272

C_{18}



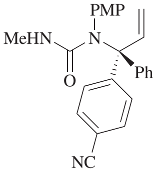
ent-**3d** (2 eq), LiCl (2 eq),
THF, 10 min; then
DMPU, 3 h



Temp (°)		% ee
−60	(—)	78
−78	(72)	84
−90	(63)	84

272

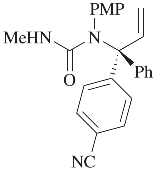
Lithium amide (2 eq),
LiCl (2 eq), THF, −78°, 10 min;
then DMPU, 3 h



Lithium Amide		% ee
4f	(71)	80
19	(66)	56
20	(58)	84

272

Lithium amide (2 eq),
THF, −78°, 10 min;
then DMPU, 3 h

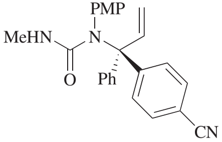


(—)[c]

Lithium Amide	% ee
ent-**3n**	58
4b	28

272

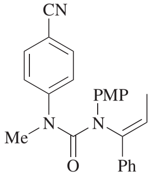
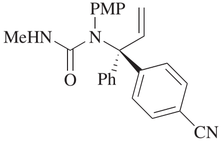
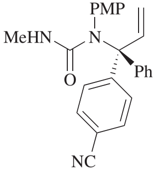
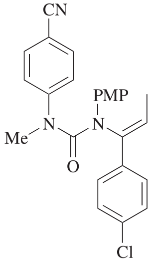
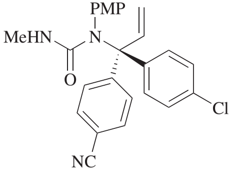
Lithium amide (2 eq), LiCl (2 eq),
THF, −78°, 10 min;
then DMPU, 3 h



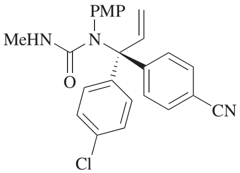
Lithium Amide		% ee
1a	(72)	66
22	(—)[c]	30

272

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

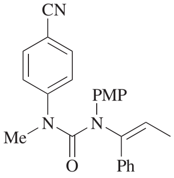
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18} 	**49** (2 eq), THF, −78°, 10 min; then DMPU, 3 h	 (—)^{c} 44% ee	272
	ent-**3d** (2 eq), LiCl (2 eq), −78°, 20 min	 Solvent % ee THF (91) 88 Et_2O (—) 42 cumene (0) — toluene (—) 16	272
	*ent*-**3d** (2 eq), LiCl (2 eq), THF, −78°, 20 min	 (79) 82% ee	272

3d (2 eq), THF, –78°, 20 min



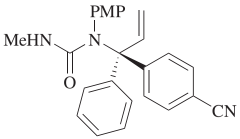
(54) 76% ee

272



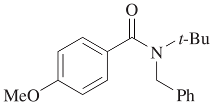
(*E*)/(*Z*) = 4:1

3d (2 eq), LiCl (2 eq), THF, –78°

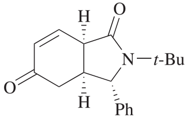


Time (min)		% ee
30	(21)	46
60	(41)	28

272



1. Lithium amide, LiCl, THF, temp, 1.5 h
2. aq HCl



Lithium Amide	Temp (°)		% ee
1a	–78 to rt	(73)	80
1a	–78 to –60	(65)	50
3d	–78 to rt	(72)	80
3a	–78 to rt	(72)	17

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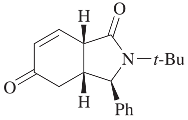
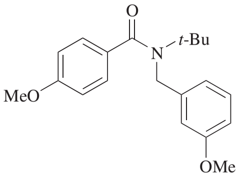
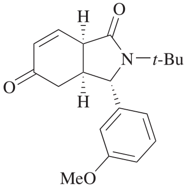
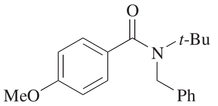
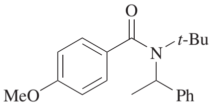
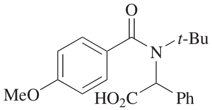
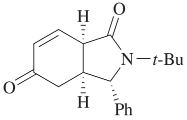
1. *ent*-**67**, LiCl, THF, –78° to rt, 1.5 h
2. aq HCl



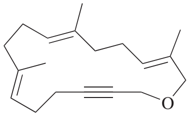
(38) 75% ee

259

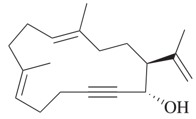
TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}			
	1. **1a**, LiCl, THF, temp, 1.5 h 2. aq HCl	 Temp (°) — % ee −78 to rt (59) 73 −50 to rt (67) 60	259
	**3d**, LiCl, THF, −78 to −40°, 1 h; then MeI (or MeOTf)	 (50) 0% ee	259
	3d, LiCl, THF, −78 to −40°, 1 h; then CO_2	 (50) 44% ee	259
	1. **3d** (*x* eq), THF, 0–20°, 2 h 2. Dry air 3. MsCl, Et_3N	 *x* — % ee 1 (55) 70 2 (—) 50	261

C$_{19}$



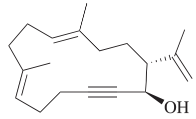
2 (4.2 eq), solvent



Solvent	Temp (°)	Time (h)		% ee^a	dr
THF	−55 to −10	1.5	(56)	<5	7:3
pentane/THF (9:1)	−35 to 10	2	(78)	29	7:3
Et$_2$O	−35 to −20	1.5	(73)	10	7:3

267

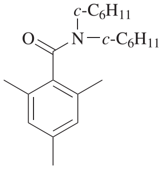
Lithium amide (4.2 eq), solvent



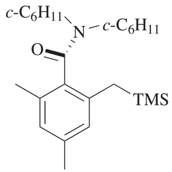
Lithium Amide	Solvent	Temp (°)	Time (h)		% ee^a	dr
2	pentane	−10 to 20	10	(23)	33	6:4
1a	pentane/THF (9:1)	−40 to −5	2	(73)	23	7:3

267

C$_{22}$



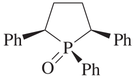
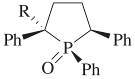
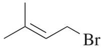
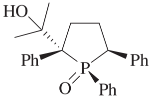
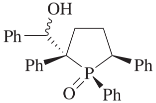
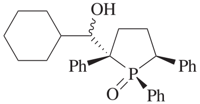
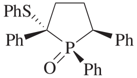
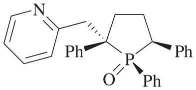
2 (1.3 eq), THF, −78°,
30 min; then TMSCl (2 eq)



(57) 85% ee

258

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{22} 	**1a** (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then RX (10 eq), time		RX — Time (min) — % ee MeI — — — (87) 85 EtI — — — (89) 90 BnBr — — — (62) n.d. allylBr — 2 — (72) 87  — — — (93) 88	255, 256
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then acetone (10 eq)		(85) 87% ee	255, 256
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then PhCHO (10 eq)		(82) 92% ee, dr 7:1	255, 256
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then $C_6H_{11}CHO$ (10 eq)		(74) 82% ee, dr 1:1	255, 256
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then $PhSSO_2Ph$ (10 eq)		(60) 82% ee	255, 256
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then 2-picolyl chloride (10 eq)		(61) 84% ee	256

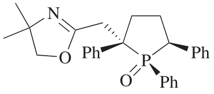
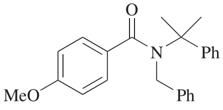
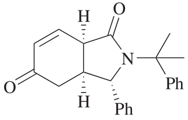
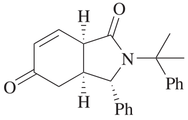
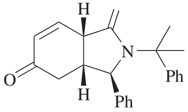
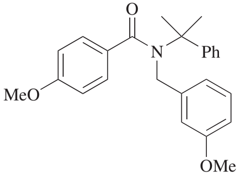
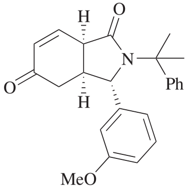
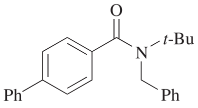
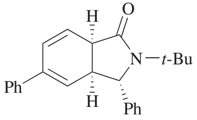
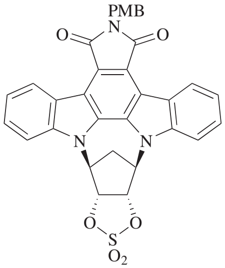
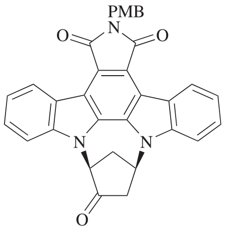
	1a (1.1 eq), LiCl (1.1 eq), THF, −100°, 30 min; then 2-chloromethyl-4,4-dimethyl- oxazoline (10 eq)		(74) 82% ee	256
C_{23}				
	1. **1a** (1.3 eq), LiCl (1.3 eq), THF, −78° to rt, 1.5 h 2. aq HCl		(64–66) 73–75% ee	259, 262
	1. **3d** (1.3 eq), LiCl (1.3 eq), THF, −78° to rt, 1.5 h 2. aq HCl		(62–88) 81–86% ee	259, 262, 260
	1. *ent*-**67**, LiCl, THF, −78° to rt, 1.5 h 2. aq HCl		(23) 30% ee	259
	1. **3d**, LiCl, THF, −78° to rt, 1.5 h 2. aq HCl		(87) 84% ee	259, 262

TABLE 9. MISCELLANEOUS TRANSFORMATIONS (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{24}		1. **3d**, LiCl, THF, −78° to rt, 1.5 h 2. aq HCl	 (70) 60% ee	259
C_{25}		**1a** (4 eq), LiCl (4 eq), THF, −78°, 4 h	 (39) 87% ee	271, 270

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[a] The enantiomeric excess of the product was determined after conversion into the corresponding *O*-methyl mandelate ester.

[b] The enantiomeric excess of the product was determined after conversion to the corresponding Mosher ester.

[c] The product was not isolated, but complete conversion to the product was indicated by NMR spectroscopy.

REFERENCES

[1] Simpkins, N. S. *Pure Appl. Chem.* **1996**, *68*, 691.

[2] Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1991**, *2*, 1.

[3] Magnus, A.; Bertilsson, S. K.; Andersson, P. G. *Chem. Soc. Rev.* **2002**, *31*, 223.

[4] O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1439.

[5] Koga, K.; Shindo, M. *J. Synth. Org. Chem., Jpn* **1995**, *53*, 1021.

[6] Koga, K. *Pure Appl. Chem.* **1994**, *66*, 1487.

[7] Gibson, S. E.; Reddington, E. G. *Chem. Commun.* **2000**, 989.

[8] Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361.

[9] Simpkins, N. S.; Weller, M. D. In *Topics in Stereochemistry*; Gawley, R. E., Ed.; Wiley-VCH: 2010; Vol. 26, pp 1–52.

[10] Honda, T. *J. Synth. Org. Chem., Jpn* **2002**, *60*, 1104.

[11] Simpkins, N. S. In *Advanced Asymmetric Synthesis*; Stephenson, G. R., Ed.; Blackie Academic and Professional: London, 1996, pp 111–125.

[12] Koga, K.; Odashima, K. *Yakugaku Zasshi* **1997**, *117*, 800.

[13] Gais, H. J. In *Stereoselective Synthesis (Houben-Weyl)*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Georg Thieme Verlag: Stuttgart, 1996; Vol. 1, pp 589–644.

[14] Kim, H. D.; Kawasaki, H.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 6537.

[15] Stivala, C. E.; Zakarian, A. *Org. Lett.* **2009**, *11*, 839.

[16] Qin, Y. C.; Stivala, C. E.; Zakarian, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7466.

[17] Gu, Z. H.; Herrmann, A. T.; Stivala, C. E.; Zakarian, A. *Synlett* **2010**, 1717.

[18] Stivala, C. E.; Zakarian, A. *J. Am. Chem. Soc.* **2008**, *130*, 3774.

[19] Stivala, C. E.; Zakarian, A. *Tetrahedron Lett.* **2007**, *48*, 6845.

[20] Rutherford, J. L.; Collum, D. B. *J. Am. Chem. Soc.* **2001**, *123*, 199.

[21] Crandall, J. K.; Apparu, M. *Org. React.* **1983**, *29*, 345.

[22] Satoh, T. *Chem. Rev.* **1996**, *96*, 3303.

[23] Eames, J. *Eur. J. Org. Chem.* **2002**, 393.

[24] Morgan, K. M.; Gajewski, J. J. *J. Org. Chem.* **1996**, *61*, 820.

[25] Thummel, R. P.; Rickborn, B. *J. Am. Chem. Soc.* **1970**, *92*, 2064.

[26] Dinér, P.; Pettersen, D.; Lill, S. O. N.; Ahlberg, P. *Tetrahedron: Asymmetry* **2005**, *16*, 2665.

[27] Yoshida, T.; Sakakibara, K.; Asami, M. *Chem. Lett.* **2003**, *32*, 150.

[28] Lill, S. O. N.; Arvidsson, P. I.; Ahlberg, P. *Tetrahedron: Asymmetry* **1999**, *10*, 265.

[29] Hoshino, H.; Asami, M.; Sakakibara, K.; Lii, J. H.; Allinger, N. L. *Tetrahedron* **2008**, *64*, 575.

[30] Xiao, Y.; Jung, D.; Gund, T.; Malhotra, S. V. *J. Mol. Model.* **2006**, *12*, 681.

[31] Mordini, A.; Rayana, E. B.; Margot, C.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2401.

[32] Margot, C.; Rizzolio, M.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2411.

[33] Milne, D.; Murphy, P. J. *J. Chem. Soc., Chem. Commun.* **1993**, 884.

[34] Brookes, P. C.; Milne, D. J.; Murphy, P. J.; Spolaore, B. *Tetrahedron* **2002**, *58*, 4675.

[35] Hodgson, D. M.; Gibbs, A. R. *Tetrahedron: Asymmetry* **1996**, *7*, 407.

[36] Hodgson, D. M.; Witherington, J.; Moloney, B. A. *Tetrahedron: Asymmetry* **1994**, *5*, 337.

[37] Hodgson, D. M.; Gibbs, A. R.; Drew, M. G. B. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3579.

[38] Hodgson, D. M.; Gibbs, A. R. *Tetrahedron Lett.* **1997**, *38*, 8907.

[39] Asami, M. *Bull. Chem. Soc. Jpn* **1990**, *63*, 721.

[40] Asami, M. *Chem. Lett.* **1984**, 829.

[41] Khan, A. Z. Q.; Arvidsson, P. I.; Ahlberg, P. *Tetrahedron: Asymmetry* **1996**, *7*, 399.

[42] Arvidsson, P. I.; Hansson, M.; Khan, A. Z. Q.; Ahlberg, P. *Can. J. Chem.* **1998**, *76*, 795.

[43] Hansson, M.; Arvidsson, P. I.; Lill, S. O. N.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 2* **2002**, 763.

[44] Asami, M.; Suga, T.; Honda, K.; Inoue, S. *Tetrahedron Lett.* **1997**, *38*, 6425.

[45] Tierney, J. P.; Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1019.

[46] Equey, O.; Alexakis, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1069.

[47] Pettersen, D.; Amedjkouh, M.; Lill, S. O. N.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1397.

[48] Amedjkouh, M.; Pettersen, D.; Lill, S. O. N.; Davidsson, Ö.; Ahlberg, P. *Chem.—Eur. J.* **2001**, *7*, 4368.

[49] Pettersen, D.; Amedjkouh, M.; Ahlberg, P. *Tetrahedron* **2002**, *58*, 4669.

[50] Pettersen, D.; Amedjkouh, M.; Lill, S. O. N.; Dahlén, K.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1654.

[51] Olsson, R. I.; Ahlberg, P. *Tetrahedron: Asymmetry* **1999**, *10*, 3991.

[52] Pettersen, D.; Dinér, P.; Amedjkouh, M.; Ahlberg, P. *Tetrahedron: Asymmetry* **2004**, *15*, 1607.

[53] Simpkins, N. S. *J. Chem. Soc., Chem. Commun.* **1986**, 88.

[54] Shirai, R.; Tanaka, M.; Koga, K. *J. Am. Chem. Soc.* **1986**, *108*, 543.

[55] Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1992**, *114*, 761.

[56] Cousins, R. P. C.; Simpkins, N. S. *Tetrahedron Lett.* **1989**, *30*, 7241.

[57] Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

[58] Bunn, B. J.; Simpkins, N. S. *J. Org. Chem.* **1993**, *58*, 533.

[59] Bunn, B. J.; Simpkins, N. S.; Spavold, Z.; Crimmin, M. J. *J. Chem. Soc., Perkin Trans. 1* **1993**, 3113.

[60] Sugasawa, K.; Shindo, M.; Noguchi, H.; Koga, K. *Tetrahedron Lett.* **1996**, *37*, 7377.

[61] Majewski, M.; Lazny, R.; Nowak, P. *Tetrahedron Lett.* **1995**, *36*, 5465.

[62] Lipshutz, B. H.; Wood, M. R.; Lindsley, C. W. *Tetrahedron Lett.* **1995**, *36*, 4385.

[63] Coggins, P.; Gaur, S.; Simpkins, N. S. *Tetrahedron Lett.* **1995**, *36*, 1545.

[64] Edwards, A. J.; Hockey, S.; Mair, F. S.; Raithby, P. R.; Snaith, R.; Simpkins, N. S. *J. Org. Chem.* **1993**, *58*, 6942.

[65] Toriyama, M.; Sugasawa, K.; Motohashi, S.; Tokutake, N.; Koga, K. *Chem. Pharm. Bull.* **2001**, *49*, 468.

[66] Toriyama, M.; Sugasawa, K.; Shindo, M.; Tokutake, N.; Koga, K. *Tetrahedron Lett.* **1997**, *38*, 567.

[67] Aoki, K.; Noguchi, H.; Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1993**, *34*, 5105.

[68] Aoki, K.; Tomioka, K.; Noguchi, H.; Koga, K. *Tetrahedron* **1997**, *53*, 13641.

[69] Majewski, M.; Wang, F. *Tetrahedron* **2002**, *58*, 4567.

[70] Rosillo, M.; Dominguez, G.; Pérez-Castells, J. *Chem. Soc. Rev.* **2007**, *36*, 1589.

[71] Gibson, S. E.; Ibrahim, H. *Chem. Commun.* **2002**, 2465.

[72] Hata, T.; Koide, H.; Uemura, M. *Synlett* **2000**, 1145.

[73] Hata, T.; Koide, H.; Taniguchi, N.; Uemura, M. *Org. Lett.* **2000**, *2*, 1907.

[74] Koide, H.; Hata, T.; Yoshihara, K.; Kamikawa, K.; Uemura, M. *Tetrahedron* **2004**, *60*, 4527.

[75] Ewin, R. A.; MacLeod, A. M.; Price, D. A.; Simpkins, N. S.; Watt, A. P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 401.

[76] Price, D. A.; Simpkins, N. S.; MacLeod, A. M.; Watt, A. P. *J. Org. Chem.* **1994**, *59*, 1961.

[77] Pache, S.; Botuha, C.; Franz, R.; Kündig, E. P.; Einhorn, J. *Helv. Chim. Acta* **2000**, *83*, 2436.

[78] Schmalz, H. G.; Schellhaas, K. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2146.

[79] Schellhaas, K.; Schmalz, H. G.; Bats, J. W. *Chem.—Eur. J.* **1998**, *4*, 57.

[80] Price, D. A.; Simpkins, N. S.; MacLeod, A. M.; Watt, A. P. *Tetrahedron Lett.* **1994**, *35*, 6159.

[81] Ariffin, A.; Blake, A. J.; Li, W. S.; Simpkins, N. S. *Synlett* **1997**, 1453.

[82] Ariffin, A.; Blake, A. J.; Ewin, R. A.; Li, W. S.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3177.

[83] Quattropani, A.; Bernardinelli, G.; Kündig, E. P. *Helv. Chim. Acta* **1999**, *82*, 90.

[84] Merlic, C. A.; Hietbrink, B. N.; Houk, K. N. *J. Org. Chem.* **2001**, *66*, 6738.

[85] Cowton, E. L. M.; Gibson, S. E.; Schneider, M. J.; Smith, M. H. *Chem. Commun.* **1996**, 839.

[86] Abecassis, K.; Gibson, S. E.; Martin-Fontecha, M. *Eur. J. Org. Chem.* **2009**, 1606.

[87] Gibson, S. E.; Ibrahim, H.; Pasquier, C.; Steed, J. W. *Tetrahedron* **2002**, *58*, 4617.

[88] Gibson, S. E.; Ham, P.; Jefferson, G. R.; Smith, M. H. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2161.

[89] Gibson, S. E.; O'Brien, P.; Rahimian, E.; Smith, M. H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 909.

[90] Whitesell, J. K.; Felman, S. W. *J. Org. Chem.* **1980**, *45*, 755.

[91] Varie, D. L.; Beck, C.; Borders, S. K.; Brady, M. D.; Cronin, J. S.; Ditsworth, T. K.; Hay, D. A.; Hoard, D. W.; Hoying, R. C.; Linder, R. J.; Miller, R. D.; Moher, E. D.; Remacle, J. R.; Rieck, J. A. *Org. Proc. Res. Dev.* **2007**, *11*, 546.

[92] de Sousa, S. E.; O'Brien, P.; Pilgram, C. D. *Tetrahedron* **2002**, *58*, 4643.

[93] de Sousa, S. E.; O'Brien, P.; Pilgram, C. D. *Tetrahedron Lett.* **2001**, *42*, 8081.

[94] Bhuniya, D.; DattaGupta, A.; Singh, V. K. *J. Org. Chem.* **1996**, *61*, 6108.

[95] Bhuniya, D.; DattaGupta, A.; Singh, V. K. *Tetrahedron Lett.* **1995**, *36*, 2847.

[96] Asami, M.; Ogawa, M.; Inoue, S. *Tetrahedron Lett.* **1999**, *40*, 1563.

[97] Barrett, S.; O'Brien, P.; Steffens, H. C.; Towers, T. D.; Voith, M. *Tetrahedron* **2000**, *56*, 9633.

[98] O'Brien, P.; Towers, T. D.; Voith, M. *Tetrahedron Lett.* **1998**, *39*, 8175.

[99] Kasai, T.; Wantanabe, H.; Mori, K. *Bioorg. Med. Chem.* **1993**, *1*, 67.

[100] Mori, K.; Murata, N. *Liebigs Ann. Chem.* **1995**, 2089.

[101] O'Brien, P.; Tournayre, J. J. *Tetrahedron* **1997**, *53*, 17527.

[102] O'Brien, P.; Pilgram, C. D. *Org. Biomol. Chem.* **2003**, *1*, 523.

[103] O'Brien, P.; Pilgram, C. D. *Tetrahedron Lett.* **1999**, *40*, 8427.

[104] Asami, M.; Ishizaki, T.; Inoue, S. *Tetrahedron: Asymmetry* **1994**, *5*, 793.

[105] Bertilsson, S. K.; Södergren, M. J.; Andersson, P. G. *J. Org. Chem.* **2002**, *67*, 1567.

[106] Södergren, M. J.; Bertilsson, S. K.; Andersson, P. G. *J. Am. Chem. Soc.* **2000**, *122*, 6610.

[107] Södergren, M. J.; Andersson, P. G. *J. Am. Chem. Soc.* **1998**, *120*, 10760.

[108] Dinér, P. *Tetrahedron: Asymmetry* **2010**, *21*, 2733.

[109] Liu, D.; Kozmin, S. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4757.

[110] Lill, S. O. N.; Pettersen, D.; Amedjkouh, M.; Ahlberg, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3054.

[111] Oxenford, S. J.; Wright, J. M.; O'Brien, P.; Panday, N.; Shipton, M. R. *Tetrahedron Lett.* **2005**, *46*, 8315.

[112] Asami, M.; Seki, A. *Chem. Lett.* **2002**, 160.

[113] Seki, A.; Asami, M. *Tetrahedron* **2002**, *58*, 4655.

[114] Malhotra, S. V. *Tetrahedron: Asymmetry* **2003**, *14*, 645.

[115] Cain, C. M.; Cousins, R. P. C.; Coumbarides, G.; Simpkins, N. S. *Tetrahedron* **1990**, *46*, 523.

[116] Shirai, R.; Sato, D.; Aoki, K.; Tanaka, M.; Kawasaki, H.; Koga, K. *Tetrahedron* **1997**, *53*, 5963.

[117] Aoki, K.; Nakajima, M.; Tomioka, K.; Koga, K. *Chem. Pharm. Bull.* **1993**, *41*, 994.

[118] Yamashita, T.; Sato, D.; Kiyoto, T.; Kumar, A.; Koga, K. *Tetrahedron Lett.* **1996**, *37*, 8195.

[119] Yamashita, T.; Sato, D.; Kiyoto, T.; Kumar, A.; Koga, K. *Tetrahedron* **1997**, *53*, 16987.

[120] Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.

[121] Smith, A. B.; Nolen, E. G.; Shirai, R.; Blase, F. R.; Ohta, M.; Chida, N.; Hartz, R. A.; Fitch, D. M.; Clark, W. M.; Sprengeler, P. A. *J. Org. Chem.* **1995**, *60*, 7837.

[122] Underiner, T. L.; Paquette, L. A. *J. Org. Chem.* **1992**, *57*, 5438.

[123] Honda, T.; Endo, K.; Ono, S. *Chem. Pharm. Bull.* **2000**, *48*, 1545.

[124] Poupon, J. C.; Demont, E.; Prunet, J.; Férézou, J. P. *J. Org. Chem.* **2003**, *68*, 4700.

[125] Honda, T.; Kimura, N. *Org. Lett.* **2002**, *4*, 4567.

[126] MaGee, D. I.; Shannon, D. E. *Can. J. Chem.* **2004**, *82*, 333.

[127] Berkowitz, W. F.; Wu, Y. *J. Org. Chem.* **1997**, *62*, 1536.

[128] Gambacorta, A.; Tofani, D.; Lupattelli, P.; Tafi, A. *Tetrahedron Lett.* **2002**, *43*, 2195.

[129] Momose, T.; Toyooka, N.; Hirai, Y. *Chem. Lett.* **1990**, 1319.

[130] Momose, T.; Toshima, M.; Toyooka, N.; Hirai, Y.; Eugster, C. H. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1307.

[131] Hirai, Y.; Momose, T. *J. Synth. Org. Chem., Jpn* **1993**, *51*, 25.

[132] Momose, T.; Toyooka, N.; Seki, S.; Hirai, Y. *Chem. Pharm. Bull.* **1990**, *38*, 2072.

[133] Honda, T.; Ishikawa, F.; Kanai, K.; Sato, S.; Kato, D.; Tominaga, H. *Heterocycles* **1996**, *42*, 109.

[134] Honda, T.; Kimura, N. *J. Chem. Soc. Chem. Commun.* **1994**, 77.

[135] Honda, T.; Kimura, N.; Sato, S.; Kato, D.; Tominaga, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1043.

[136] Honda, T.; Kimura, N.; Tsubuki, M. *Tetrahedron: Asymmetry* **1993**, *4*, 1475.

[137] Resende, P.; Almeida, W. P.; Coelho, F. *Tetrahedron: Asymmetry* **1999**, *10*, 2113.

[138] Honda, T.; Kimura, N.; Tsubuki, M. *Tetrahedron: Asymmetry* **1993**, *4*, 21.
[139] Bunn, B. J.; Cox, P. J.; Simpkins, N. S. *Tetrahedron* **1993**, *49*, 207.
[140] Hunt, K. W.; Grieco, P. A. *Org. Lett.* **2002**, *4*, 245.
[141] Honda, T.; Endo, K. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2915.
[142] van Bergen, M.; Gais, H. J. *J. Am. Chem. Soc.* **2002**, *124*, 4321.
[143] Parker, K. A.; Dermatakis, A. *J. Org. Chem.* **1997**, *62*, 6692.
[144] Carson, C. A.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 777.
[145] Lee, K.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 5590.
[146] Armstrong, A.; Ahmed, G.; Dominguez-Fernandez, B.; Hayter, B. R.; Wailes, J. S. *J. Org. Chem.* **2002**, *67*, 8610.
[147] Newcombe, N. J.; Simpkins, N. S. *J. Chem. Soc., Chem. Commun.* **1995**, 831.
[148] Cain, C. M.; Simpkins, N. S. *Tetrahedron Lett.* **1987**, *28*, 3723.
[149] Kim, H.; Hoffmann, H. M. R. *Eur. J. Org. Chem.* **2000**, 2195.
[150] Hoffmann, H. M. R.; Dunkel, R.; Mentzel, M.; Reuter, H.; Stark, C. B. W. *Chem.—Eur. J.* **2001**, *7*, 4771.
[151] Magee, D. I.; Setiadji, S.; Martin, R. A. *Tetrahedron: Asymmetry* **1995**, *6*, 639.
[152] Izawa, H.; Shirai, R.; Kawasaki, H.; Kim, H.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 7221.
[153] Lutz, V.; Baro, A.; Fischer, P.; Laschat, S. *Eur. J. Org. Chem.* **2010**, 1149.
[154] Lerm, M.; Gais, H. J.; Cheng, K.; Vermeeren, C. *J. Am. Chem. Soc.* **2003**, *125*, 9653.
[155] Vaulont, I.; Gais, H. J.; Reuter, N.; Schmitz, E.; Ossenkamp, R. K. L. *Eur. J. Org. Chem.* **1998**, 805.
[156] Montaña, Á. M.; Fernández, D. *Tetrahedron Lett.* **1999**, *40*, 6499.
[157] Montaña, Á. M.; Fernández, D.; Pagès, R.; Filippou, A. C.; Kociok-Köhn, G. *Tetrahedron* **2000**, *56*, 425.
[158] Leonard, J.; Ouali, D.; Rahman, S. K. *Tetrahedron Lett.* **1990**, *31*, 739.
[159] Hodgson, D. M.; Galano, J. M. *Org. Lett.* **2005**, *7*, 2221.
[160] Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073.
[161] Kirihara, M.; Nishio, T.; Yokoyama, S.; Kakuda, H.; Momose, T. *Tetrahedron* **1999**, *55*, 2911.
[162] Momose, T.; Nishio, T.; Kirihara, M. *Tetrahedron Lett.* **1996**, *37*, 4987.
[163] Takasu, K.; Misawa, K.; Ihara, M. *Tetrahedron Lett.* **2001**, *42*, 8489.
[164] Majewski, M.; MacKinnon, J. *Can. J. Chem.* **1994**, *72*, 1699.
[165] Majewski, M.; Gleave, D. M. *J. Org. Chem.* **1992**, *57*, 3599.
[166] Camps, P.; Contreras, J.; Font-Bardia, M.; Morral, J.; Muñoz-Torrero, D.; Solans, X. *Tetrahedron: Asymmetry* **1998**, *9*, 835.
[167] Abe, H.; Tsujino, T.; Araki, K.; Takeuchi, Y.; Harayama, T. *Tetrahedron: Asymmetry* **2002**, *13*, 1519.
[168] Lyapkalo, I. M.; Webel, M.; Reissig, H. U. *Synlett* **2001**, 1293.
[169] Peters, D.; Olesen, D. F.; Dam, E. U.S. Patent 0030208 A1 (2009).
[170] Iguchi, M.; Tomioka, K. *Org. Lett.* **2002**, *4*, 4329.
[171] Aggarwal, V. K.; Humphries, P. S.; Fenwick, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 1985.
[172] Braun, M.; Meyer, B.; de Lacroix, B. F. *Eur. J. Org. Chem.* **2002**, 1424.
[173] Lachia, M.; Dénès, F.; Beaufils, F.; Renaud, P. *Org. Lett.* **2005**, *7*, 4103.
[174] Muraoka, O.; Okumura, K.; Maeda, T.; Tanabe, G.; Momose, T. *Tetrahedron: Asymmetry* **1994**, *5*, 317.
[175] Kozikowski, A. P.; Simoni, D.; Roberti, M.; Rondanin, R.; Wang, S.; Du, P.; Johnson, K. M. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1831.
[176] Simoni, D.; Roberti, M.; Rondanin, R.; Kozikowski, A. P. *Tetrahedron Lett.* **1999**, *40*, 4425.
[177] Majewski, M.; Lazny, R. *J. Org. Chem.* **1995**, *60*, 5825.
[178] Nowakowski, M.; Hoffmann, H. M. R. *Tetrahedron Lett.* **1997**, *38*, 1001.
[179] Wild, H. *J. Org. Chem.* **1994**, *59*, 2748.
[180] Majewski, M.; Zheng, G. Z. *Synlett* **1991**, 173.
[181] Majewski, M.; Ulaczyk-Lesanko, A.; Wang, F. *Can. J. Chem.* **2006**, *84*, 257.
[182] Majewski, M.; Ulaczyk, A.; Wang, F. *Tetrahedron Lett.* **1999**, *40*, 8755.
[183] Majewski, M.; DeCaire, M.; Nowak, P.; Wang, F. *Synlett* **2000**, 1321.

[184] Majewski, M.; DeCaire, M.; Nowak, P.; Wang, F. *Can. J. Chem.* **2001**, *79*, 1792.
[185] Majewski, M.; Nowak, P. *Synlett* **1999**, 1447.
[186] Majewski, M.; Gleave, D. M.; Nowak, P. *Can. J. Chem.* **1995**, *73*, 1616.
[187] Majewski, M.; Nowak, P. *J. Org. Chem.* **2000**, *65*, 5152.
[188] Lee, J. C.; Lee, K.; Cha, J. K. *J. Org. Chem.* **2000**, *65*, 4773.
[189] Sienkiewicz, M.; Wilkaniec, U.; Lazny, R. *Tetrahedron Lett.* **2009**, *50*, 7196.
[190] Ossenkamp, R. K. L.; Gais, H. J. *Liebigs Ann. Chem.* **1997**, 2433.
[191] Majewski, M.; Lazny, R.; Ulaczyk, A. *Can. J. Chem.* **1997**, *75*, 754.
[192] Majewski, M.; Lazny, R. *Tetrahedron Lett.* **1994**, *35*, 3653.
[193] Simpkins, N. S. *Chem. Soc. Rev.* **1990**, *19*, 335.
[194] Majewski, M.; Lazny, R. *Synlett* **1996**, 785.
[195] Aggarwal, V. K.; Olofsson, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 5516.
[196] Kropf, J. E.; Weinreb, S. M. *Chem. Commun.* **1998**, 2357.
[197] Abe, H.; Tsujino, T.; Tsuchida, D.; Kashino, S.; Takeuchi, Y.; Harayama, T. *Heterocycles* **2002**, *56*, 503.
[198] Butler, B.; Schultz, T.; Simpkins, N. S. *Chem. Commun.* **2006**, 3634.
[199] Ward, D. E.; Gillis, H. M.; Akinnusi, O. T.; Rasheed, M. A.; Saravanan, K.; Sasmal, P. K. *Org. Lett.* **2006**, *8*, 2631.
[200] Gill, C. D.; Greenhalgh, D. A.; Simpkins, N. S. *Tetrahedron* **2003**, *59*, 9213.
[201] Greenhalgh, D. A.; Simpkins, N. S. *Synlett* **2002**, 2074.
[202] Rodeschini, V.; Simpkins, N. S.; Zhang, F. *Org. Synth.* **2007**, *84*, 306.
[203] Adams, D. J.; Simpkins, N. S.; Smith, T. J. N. *Chem. Commun.* **1998**, 1605.
[204] Adams, D. J.; Blake, A. J.; Cooke, P. A.; Gill, C. D.; Simpkins, N. S. *Tetrahedron* **2002**, *58*, 4603.
[205] Bennett, D. J.; Pickering, P. L.; Simpkins, N. S. *Chem. Commun.* **2004**, 1392.
[206] Zhang, F.; Simpkins, N. S.; Blake, A. J. *Org. Biomol. Chem.* **2009**, *7*, 1963.
[207] Blake, A. J.; Gill, C.; Greenhalgh, D. A.; Simpkins, N. S.; Zhang, F. *Synthesis* **2005**, 3287.
[208] Gill, C.; Greenhalgh, D. A.; Simpkins, N. S. *Tetrahedron Lett.* **2003**, *44*, 7803.
[209] Simpkins, N. S.; Gill, C. D. *Org. Lett.* **2003**, *5*, 535.
[210] Hayes, C. J.; Simpkins, N. S.; Kirk, D. T.; Mitchell, L.; Baudoux, J.; Blake, A. J.; Wilson, C. *J. Am. Chem. Soc.* **2009**, *131*, 8196.
[211] Giblin, G. M. P.; Kirk, D. T.; Mitchell, L.; Simpkins, N. S. *Org. Lett.* **2003**, *5*, 1673.
[212] Blake, A. J.; Giblin, G. M. P.; Kirk, D. T.; Simpkins, N. S.; Wilson, C. *Chem. Commun.* **2001**, 2668.
[213] Rodeschini, V.; Simpkins, N. S.; Wilson, C. *J. Org. Chem.* **2007**, *72*, 4265.
[214] Quattropani, A.; Anderson, G.; Bernardinelli, G.; Kündig, E. P. *J. Am. Chem. Soc.* **1997**, *119*, 4773.
[215] Schmalz, H. G.; Schellhaas, K. *Tetrahedron Lett.* **1995**, *36*, 5515.
[216] Kündig, E. P.; Quattropani, A. *Tetrahedron Lett.* **1994**, *35*, 3497.
[217] Castaldi, M. P.; Gibson, S. E.; Rudd, M.; White, A. J. P. *Chem.—Eur. J.* **2006**, *12*, 138.
[218] Castaldi, M. P.; Gibson, S. E.; Rudd, M.; White, A. J. P. *Angew. Chem., Int. Ed.* **2005**, *44*, 3432.
[219] Beckwith, R. E. J.; Heron, N.; Simpkins, N. S. *J. Organomet. Chem.* **2002**, *658*, 21.
[220] Felstead, R.; Gibson, S. E.; Rooney, A.; Tse, E. S. Y. *Eur. J. Org. Chem.* **2008**, 4963.
[221] Zhao, C. H.; Liu, L.; Chen, Y. J.; Wang, D. *J. Chem. Res.* **2004**, 589.
[222] Gibson, S. E.; Potter, P. C. V.; Smith, M. H. *Chem. Commun.* **1996**, 2757.
[223] Abecassis, K.; Gibson, S. E. *Eur. J. Org. Chem.* **2010**, 2938.
[224] Ariffin, A.; Blake, A. J.; Ewin, R. A.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1998**, *9*, 2563.
[225] Gibson, S. E.; Smith, M. H. *Org. Biomol. Chem.* **2003**, *1*, 676.
[226] Castaldi, M. P.; Gibson, S. E.; White, A. J. P. *Eur. J. Org. Chem.* **2006**, 1867.
[227] Sobukawa, M.; Nakajima, M.; Koga, K. *Tetrahedron: Asymmetry* **1990**, *1*, 295.
[228] Sobukawa, M.; Koga, K. *Tetrahedron Lett.* **1993**, *34*, 5101.
[229] Murray, L. M.; O'Brien, P.; Taylor, R. J. K.; Wünnemann, S. *Tetrahedron Lett.* **2004**, *45*, 2597.
[230] Miyata, J.; Nemoto, H.; Ihara, M. *J. Org. Chem.* **2000**, *65*, 504.
[231] Wild, H.; Born, L. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1685.

[232] Kee, A.; O'Brien, P.; Pilgram, C. D.; Watson, S. T. *Chem. Commun.* **2000**, 1521.

[233] Asami, M.; Kanemaki, N. *Tetrahedron Lett.* **1989**, *30*, 2125.

[234] Gayet, A.; Bertilsson, S.; Andersson, P. G. *Org. Lett.* **2002**, *4*, 3777.

[235] Gayet, A.; Andersson, P. G. *Tetrahedron Lett.* **2005**, *46*, 4805.

[236] Bigi, A.; Mordini, A.; Thurner, A.; Faigl, F.; Poli, G.; Tõke, L. *Tetrahedron: Asymmetry* **1998**, *9*, 2293.

[237] Kim, H. D. *Arch. Pharm. Res.* **1995**, *18*, 369.

[238] Coggins, P.; Simpkins, N. S. *Synlett* **1991**, 515.

[239] Coggins, P.; Simpkins, N. S. *Synlett* **1992**, 313.

[240] Bambridge, K.; Clark, B. P.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2535.

[241] Bambridge, K.; Simpkins, N. S.; Clark, B. P. *Tetrahedron Lett.* **1992**, *33*, 8141.

[242] Armer, R.; Begley, M. J.; Cox, P. J.; Persad, A.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 3105.

[243] Cox, P. J.; Persad, A.; Simpkins, N. S. *Synlett* **1992**, 197.

[244] Cox, P. J.; Persad, A.; Simpkins, N. S. *Synlett* **1992**, 194.

[245] Armer, R.; Begley, M. J.; Cox, P. J.; Persad, A.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 3099.

[246] Lautens, M.; Fillion, E.; Sampat, M. *J. Org. Chem.* **1997**, *62*, 7080.

[247] Lautens, M.; Fillion, E. *J. Org. Chem.* **1998**, *63*, 647.

[248] Blake, A. J.; Cooke, P. A.; Kendall, J. D.; Simpkins, N. S.; Westaway, S. M. *J. Chem. Soc. Perkin Trans. 1* **2000**, 153.

[249] Blake, A. J.; Westaway, S. M.; Simpkins, N. S. *Synlett* **1997**, 919.

[250] McGrath, M. J.; Bolm, C. *Beilstein J. Org. Chem.* **2007**, *3*, 33.

[251] McComas, C. C.; Van Vranken, D. L. *Tetrahedron Lett.* **2003**, *44*, 8203.

[252] Goldspink, N. J.; Simpkins, N. S.; Beckmann, M. *Synlett* **1999**, 1292.

[253] Huxford, T.; Simpkins, N. S. *Synlett* **2004**, 2295.

[254] Clive, D. L. J.; Wang, J.; Yu, M. *Tetrahedron Lett.* **2005**, *46*, 2853.

[255] Hume, S. C.; Simpkins, R. S. *J. Org. Chem.* **1998**, *63*, 912.

[256] Blake, A. J.; Hume, S. C.; Li, W. S.; Simpkins, N. S. *Tetrahedron* **2002**, *58*, 4589.

[257] Price, D.; Simpkins, N. S. *Tetrahedron Lett.* **1995**, *36*, 6135.

[258] Clayden, J.; Johnson, P.; Pink, J. H. *J. Chem. Soc., Perkin Trans. 1* **2001**, 371.

[259] Clayden, J.; Menet, C. J.; Mansfield, D. J. *Chem. Commun.* **2002**, 38.

[260] Clayden, J.; Knowles, F. E.; Baldwin, I. R. *J. Am. Chem. Soc.* **2005**, *127*, 2412.

[261] Clayden, J.; Menet, C. J. *Tetrahedron Lett.* **2003**, *44*, 3059.

[262] Clayden, J.; Menet, C. J.; Tchabanenko, K. *Tetrahedron* **2002**, *58*, 4727.

[263] Duhamel, L.; Ravard, A.; Plaquevent, J. C. *Tetrahedron: Asymmetry* **1990**, *1*, 347.

[264] Duhamel, L.; Ravard, A.; Plaquevent, J. C.; Davoust, G. P. D. *Bull. Soc. Chim. Fr.* **1990**, 787.

[265] Duhamel, L.; Ravard, A.; Plaquevent, J. C.; Davoust, D. *Tetrahedron Lett.* **1987**, *28*, 5517.

[266] Plaquevent, J. C.; Perrard, T.; Cahard, D. *Chem.—Eur. J.* **2002**, *8*, 3300.

[267] Marshall, J. A.; Lebreton, J. *J. Am. Chem. Soc.* **1988**, *110*, 2925.

[268] Marshall, J. A.; Lebreton, J. *J. Org. Chem.* **1988**, *53*, 4108.

[269] Marshall, J. A.; Lebreton, J. *Tetrahedron Lett.* **1987**, *28*, 3323.

[270] Moffat, D.; Nichols, C. J.; Riley, D. A.; Simpkins, N. S. *Org. Biomol. Chem.* **2005**, *3*, 2953.

[271] Nichols, C. J.; Simpkins, N. S. *Tetrahedron Lett.* **2004**, *45*, 7469.

[272] Tetlow, D. J.; Hennecke, U.; Raftery, J.; Waring, M. J.; Clarke, D. S.; Clayden, J. *Org. Lett.* **2010**, *12*, 5442.

[273] Asami, M. *Bull. Chem. Soc. Jpn* **1990**, *63*, 1402.

[274] Asami, M. *Tetrahedron Lett.* **1985**, *26*, 5803.

[275] Asami, M.; Inoue, S. *Tetrahedron* **1995**, *51*, 11725.

[276] Sabol, J. S.; Cregge, R. J. *Tetrahedron Lett.* **1989**, *30*, 3377.

[277] Hayes, R.; Wallace, T. W. *Tetrahedron Lett.* **1990**, *31*, 3355.

[278] Asami, M.; Ishizaki, T.; Inoue, S. *Tetrahedron Lett.* **1995**, *36*, 1893.

[279] Asami, M.; Takahashi, J.; Inoue, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1649.

[280] Hodgson, D. M.; Witherington, J.; Moloney, B. A. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3373.

[281] Oxenford, S. J.; O'Brien, P.; Shipton, M. R. *Tetrahedron Lett.* **2004**, *45*, 9053.
[282] Hodgson, D. M.; Gibbs, A. R. *Synlett* **1997**, 657.
[283] Greene, A. E.; Serra, A. A.; Barreiro, E. J.; Costa, P. R. R. *J. Org. Chem.* **1987**, *52*, 1169.
[284] Rodeschini, V.; Van de Weghe, P.; Salomon, E.; Tarnus, C.; Eustache, J. *J. Org. Chem.* **2005**, *70*, 2409.
[285] Eustache, J.; Van de Weghe, P.; Rodeschini, V.; Tarnus, C. U.S. Patent 7,396,953 B2 (2008).
[286] Kramp, G. J.; Kim, M.; Gais, H. J.; Vermeeren, C. *J. Am. Chem. Soc.* **2005**, *127*, 17910.
[287] Kim, M.; Gais, H. J. *J. Org. Chem.* **2006**, *71*, 4642.
[288] van de Sande, M.; Gais, H. J. *Chem.—Eur. J.* **2007**, *13*, 1784.
[289] Magnus, P.; Lacour, J.; Evans, P. A.; Roe, M. B.; Hulme, C. *J. Am. Chem. Soc.* **1996**, *118*, 3406.
[290] Magnus, P.; Sebhat, I. K. *J. Am. Chem. Soc.* **1998**, *120*, 5341.
[291] Magnus, P.; Sebhat, I. K. *Tetrahedron* **1998**, *54*, 15509.
[292] Magnus, P.; Bailey, J. M.; Porter, M. J. *Tetrahedron* **1999**, *55*, 13927.
[293] Inoue, M.; Lee, N.; Kasuya, S.; Sato, T.; Hirama, M.; Moriyama, M.; Fukuyama, Y. *J. Org. Chem.* **2007**, *72*, 3065.
[294] Siwek, M. J.; Green, J. R. *Chem. Commun.* **1996**, 2359.
[295] Maercker, A.; Schuhmacher, R.; Buchmeier, W.; Lutz, H. D. *Chem. Ber.* **1991**, *124*, 2489.
[296] Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2283.
[297] O'Brien, P.; Warren, S. *Synlett* **1996**, 579.
[298] Hammerschmidt, F.; Hanninger, A. *Chem. Ber.* **1995**, *128*, 823.
[299] Hodgson, D. M.; Wisedale, R. *Tetrahedron: Asymmetry* **1996**, *7*, 1275.
[300] Hodgson, D. M.; Lee, G. P.; Marriott, R. E.; Thompson, A. J.; Wisedale, R.; Witherington, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2151.
[301] Hammerschmidt, F.; Hanbauer, M. *J. Org. Chem.* **2000**, *65*, 6121.
[302] Ooi, T.; Takahashi, M.; Doda, K.; Maruoka, K. *J. Am. Chem. Soc.* **2002**, *124*, 7640.
[303] Uemura, M.; Hayashi, Y.; Hayashi, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 1427.
[304] Metallinos, C.; Snieckus, V. *Org. Lett.* **2002**, *4*, 1935.
[305] Tsukazaki, M.; Tinkl, M.; Roglans, A.; Chapell, B. J.; Taylor, N. J.; Snieckus, V. *J. Am. Chem. Soc.* **1996**, *118*, 685.
[306] Graf, C. D.; Malan, C.; Harms, K.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 5581.
[307] Graf, C. D.; Malan, C.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 3014.
[308] Bassindale, M. J.; Crawford, J. J.; Henderson, K. W.; Kerr, W. J. *Tetrahedron Lett.* **2004**, *45*, 4175.
[309] Carswell, E. L.; Hayes, D.; Henderson, K. W.; Kerr, W. J.; Russell, C. J. *Synlett* **2003**, 1017.
[310] Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Tetrahedron* **2002**, *58*, 4573.
[311] Anderson, J. D.; Garcia, P. G.; Hayes, D.; Henderson, K. W.; Kerr, W. J.; Moir, J. H.; Fondekar, K. P. *Tetrahedron Lett.* **2001**, *42*, 7111.
[312] Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Synlett* **2001**, 1253.
[313] Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Chem. Commun.* **2001**, 1722.
[314] Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Chem. Commun.* **2000**, 479.
[315] Ward, D. E.; Lu, W. L. *J. Am. Chem. Soc.* **1998**, *120*, 1098.
[316] Naruse, Y.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 6021.
[317] Naruse, Y.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 1363.
[318] Pakulski, Z.; Koprowski, M.; Pietrusiewicz, K. M. *Tetrahedron* **2003**, *59*, 8219.
[319] Pietrusiewicz, K. M.; Koprowski, M.; Pakulski, Z. *Tetrahedron: Asymmetry* **2002**, *13*, 1017.
[320] Valero, G.; Companyó, X.; Bravo, N.; Alba, A. N. R.; Moyano, A.; Rios, R. *Synlett* **2010**, 1883.
[321] Chen, X. H.; Yu, J.; Gong, L. Z. *Chem. Commun.* **2010**, *46*, 6437.
[322] Zhang, L.; Cui, L. Y.; Li, X.; Li, J. Y.; Luo, S. Z.; Cheng, J. P. *Eur. J. Org. Chem.* **2010**, 4876.
[323] Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921.
[324] García-Urdiales, E.; Alfonso, I.; Gotor, V. *Chem. Rev.* **2005**, *105*, 313.
[325] Carnell, A. J. *J. Mol. Cat. B: Enzymatic* **2002**, *19*, 83.
[326] Murai, M.; Uenishi, J.; Uemura, M. *Org. Lett.* **2010**, *12*, 4788.
[327] Ogasawara, M.; Watanabe, S. *Synthesis* **2009**, 1761.
[328] Ogasawara, M.; Watanabe, S. *Synthesis* **2009**, 3177.

[329] Allan, G.; Carnell, A. J.; Hernandez, M. L. E.; Pettman, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3382.

[330] Carnell, A. J.; Barkley, J.; Singh, A. *Tetrahedron Lett.* **1997**, *38*, 7781.

[331] Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753.

[332] Toriyama, M.; Tokutake, N.; Koga, K. *Chem. Pharm. Bull.* **2001**, *49*, 330.

[333] Shirai, R.; Aoki, K.; Sato, D.; Kim, H. D.; Murakata, M.; Yasukata, T.; Koga, K. *Chem. Pharm. Bull.* **1994**, *42*, 690.

[334] Curthbertson, E.; O'Brien, P.; Towers, T. D. *Synthesis* **2001**, 693.

[335] Colman, B.; de Sousa, S. E.; O'Brien, P.; Towers, T. D.; Watson, W. *Tetrahedron: Asymmetry* **1999**, *10*, 4175.

[336] Saravanan, P.; Bisai, A.; Baktharaman, S.; Chandrasekhar, M.; Singh, V. K. *Tetrahedron* **2002**, *58*, 4693.

[337] Overberger, C.; Marullo, N. P.; Hiskey, R. G. *J. Am. Chem. Soc.* **1961**, *83*, 1374.

[338] Alexakis, A.; Gille, S.; Prian, F.; Rosset, S.; Ditrich, K. *Tetrahedron Lett.* **2004**, *45*, 1449.

[339] Mejía, R. G.; Reyes-Rangel, G.; Juaristi, E. *Nat. Protoc.* **2007**, *2*, 2759.

[340] Eleveld, M. B.; Hogeveen, H.; Schudde, E. P. *J. Org. Chem.* **1986**, *51*, 3635.

[341] Bambridge, K.; Begley, M. J.; Simpkins, N. S. *Tetrahedron Lett.* **1994**, *35*, 3391.

[342] O'Brien, P.; Poumellec, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2435.

[343] Brown, H. C.; Bhat, K. S.; Jadhav, P. K. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2633.

[344] Fukazawa, T.; Hashimoto, T. *Tetrahedron: Asymmetry* **1993**, *4*, 2323.

[345] Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. *Tetrahedron* **1997**, *53*, 7191.

[346] Stork, G. *Pure Appl. Chem.* **1989**, *61*, 439.

[347] Majewski, M.; Zheng, G. Z. *Can. J. Chem.* **1992**, *70*, 2618.

[348] Hirai, Y.; Terada, T.; Yamazaki, T.; Momose, T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 517.

[349] Asami, M.; Kirihara, H. *Chem. Lett.* **1987**, 389.

[350] Asami, M. *J. Synth. Org. Chem., Jpn* **1996**, *54*, 188.

[351] de Sousa, S. E.; O'Brien, P.; Steffens, H. C. *Tetrahedron Lett.* **1999**, *40*, 8423.

[352] Saravanan, P.; Singh, V. K. *Tetrahedron Lett.* **1998**, *39*, 167.

[353] Bhuniya, D.; Singh, V. K. *Synth. Commun.* **1994**, *24*, 375.

[354] Khan, A. Z. Q.; de Groot, R. W.; Arvidsson, P. I.; Davidsson, Ö. *Tetrahedron: Asymmetry* **1998**, *9*, 1223.

[355] Bhuniya, D.; Singh, V. K. *Synth. Commun.* **1994**, *24*, 1475.

[356] Shin, S. H.; Kang, S. K.; Cho, B. T. *Bull. Korean Chem. Soc.* **2003**, *24*, 1695.

[357] Johansson, A.; Abrahamsson, P.; Davidsson, Ö. *Tetrahedron: Asymmetry* **2003**, *14*, 1261.

[358] Johansson, A.; Davidsson, Ö. *Chem.—Eur. J.* **2001**, *7*, 3461.

[359] Sott, R.; Granander, J.; Williamson, C.; Hilmersson, G. *Chem.—Eur. J.* **2005**, *11*, 4785.

[360] Bertilsson, S. K.; Andersson, P. G. *Tetrahedron* **2002**, *58*, 4665.

[361] O'Brien, P.; Poumellec, P. *Tetrahedron Lett.* **1996**, *37*, 8057.

[362] Hodgson, D. M.; Marriott, R. E. *Tetrahedron: Asymmetry* **1997**, *8*, 519.

[363] Leonard, J.; Hewitt, J. D.; Ouali, D.; Simpson, S. J.; Newton, R. F. *Tetrahedron Lett.* **1990**, *31*, 6703.

[364] Majewski, M.; Irvine, N. M.; Mackinnon, J. *Tetrahedron: Asymmetry* **1995**, *6*, 1837.

[365] Suzuki, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **2001**, *66*, 1494.

[366] Honda, T.; Ono, S.; Mizutani, H.; Hallinan, K. O. *Tetrahedron: Asymmetry* **1997**, *8*, 181.

[367] Cox, P. J.; Simpkins, N. S. *Synlett* **1991**, 321.

[368] Amedjkouh, M. *Tetrahedron: Asymmetry* **2004**, *15*, 577.

[369] Ma, L.; Williard, P. G. *Tetrahedron: Asymmetry* **2006**, *17*, 3021.

[370] Matsubara, H.; Maeda, L.; Sugiyama, H.; Ryu, I. *Synthesis* **2007**, 2901.

[371] Almeida, W. P.; Correia, C. R. D. *J. Braz. Chem. Soc.* **1999**, *10*, 401.

[372] Kim, H. D.; Shirai, R.; Kawasaki, H.; Nakajima, M.; Koga, K. *Heterocycles* **1990**, *30*, 307.

[373] Leonard, J.; Hewitt, J. D.; Ouali, D.; Rahman, S. K.; Simpson, S. J.; Newton, R. F. *Tetrahedron: Asymmetry* **1990**, *1*, 699.

[374] Hemmerle, H.; Gais, H. J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 349.

[375] Muraoka, O.; Zheng, B. Z.; Okumura, K.; Tanabe, G.; Momose, T.; Eugster, C. H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1567.

[376] Krief, A.; Kremer, A. *Synlett* **2007**, 607.

[377] Chatani, H.; Nakajima, M.; Kawasaki, K.; Koga, K. *Heterocycles* **1997**, *46*, 53.

[378] Barr, D.; Berrisford, D. J.; Jones, R. V. H.; Slawin, A. M. Z.; Snaith, R.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1044.

[379] Aoki, K.; Koga, K. *Tetrahedron Lett.* **1997**, *38*, 2505.

[380] Aoki, K.; Koga, K. *Chem. Pharm. Bull.* **2000**, *48*, 571.

[381] Schwink, L.; Knochel, P. *Tetrahedron Lett.* **1997**, *38*, 3711.

[382] Tobe, Y.; Iketani, H.; Tsuchiya, Y.; Konishi, M.; Naemura, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3735.

[383] Busch-Petersen, J.; Corey, E. J. *Tetrahedron Lett.* **2000**, *41*, 6941.

[384] Aggarwal, V. K.; Humphries, P. S.; Fenwick, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2883.

[385] Lazny, R.; Nodzewska, A.; Sienkiewicz, M. *Lett. Org. Chem.* **2010**, *7*, 21.

[386] Ewin, R. A.; Simpkins, N. S. *Synlett* **1996**, 317.

[387] Zemolka, S.; Lex, J.; Schmalz, H. G. *Angew. Chem., Int. Ed.* **2002**, *41*, 2525.

[388] Brewer, A. R. E.; Drake, A. F.; Gibson, S. E.; Rendell, J. T. *Org. Lett.* **2007**, *9*, 3487.

[389] Brewer, A. R. E.; Drake, A. F.; Gibson, S. E.; Rendell, J. T. *Tetrahedron* **2008**, *64*, 6615.

[390] Gibson, S. E.; Ham, P.; Jefferson, G. R. *Chem. Commun.* **1998**, 123.

[391] Gibson, S. E.; Ibrahim, H. *Chem. Commun.* **2001**, 1070.

[392] Asami, M.; Sato, S.; Honda, K.; Inoue, S. *Heterocycles* **2000**, *52*, 1029.