CHAPTER 1

RING-EXPANDING CARBONYLATION OF EPOXIDES

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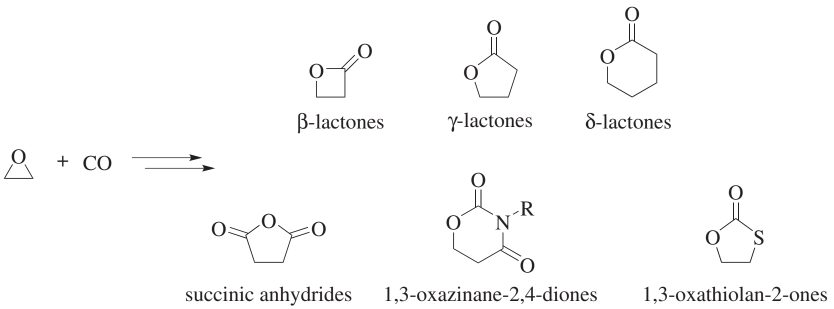
Organic Reactions, Vol. 86, Edited by Scott E. Denmark et al.

INTRODUCTION

Epoxide carbonylation represents a powerful synthetic method for the production of ring-expanded heterocycles in an atom-economical manner. Reactions involving the incorporation of carbon monoxide, particularly in the formation of new carbonyl-containing compounds, are among the most important industrial and synthetic transformations.[1–4] The carbonylation of epoxides has received much interest in recent years and has been reviewed.[5–10]

Epoxides are particularly attractive substrates, as there are many commercially available epoxides and a variety of practical methods for their synthesis.[11] Furthermore, a number of excellent methods for producing enantiopure epoxides exist,[12–16] and this enantiopurity is retained in the carbonylation products.

This chapter focuses on the ring-expanding carbonylation of epoxides, defined as reactions in which both an epoxide and CO are incorporated into a larger heterocyclic ring. The ring-expanding carbonylation of epoxides has received the most attention for its application to the synthesis of strained β-lactones.[17–41] However, a number of five- and six-membered heterocycles are also accessible through epoxide carbonylation, including γ-lactones,[28,42–45] δ-lactones,[24,40,46–53] succinic anhydrides,[21,54] 1,3-oxazinane-2,4-diones,[22,25] and 1,3-oxathiolan-2-ones[55,56] (Scheme 1). In this chapter, each of these product classes will be discussed separately, focusing primarily on the scope and limitations of the carbonylations, but also on the reaction mechanism and non-carbonylative routes to similar products.



Scheme 1

Although these reactions are thermodynamically favored, they are kinetically inaccessible, requiring the addition of catalytic or stoichiometric amounts of reagents to sequester and insert CO into the epoxide ring. Thus, the development of transition-metal catalysts for epoxide carbonylation has enabled much of the research in this field and has led to the discovery of new epoxide carbonylation reactions.

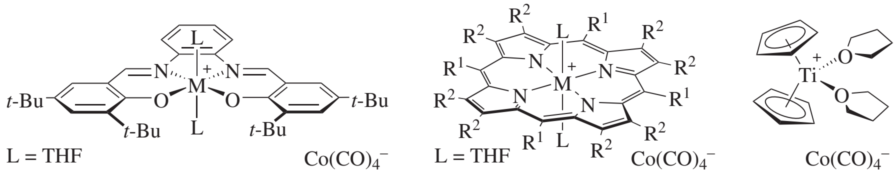
Epoxide carbonylation has also been employed for the production of ring-opened β-hydroxy esters,[57–59] amides,[60] and aldehydes,[61] as well as the direct copolymerization of epoxides and CO to produce poly(β-hydroxyalkanoates);[31,62,63] these topics are outside the scope of this chapter, but have been previously reviewed.[5,6,8] Likewise, other heterocycles including aziridines,[64,65] azetidines,[66] β-lactones,[54] oxetanes,[54,67] tetrahydrofuran,[68] and oxazolines[69,70] have been carbonylated. These reactions were recently reviewed[5,7–10] and are not discussed within this chapter.

EPOXIDE CARBONYLATION TO β-LACTONES

β-Lactones have found numerous applications both as synthetic intermediates[71,72] and as monomers for the ring-opening polymerization to produce poly(β-hydroxyalkanoates),[73] a class of biodegradable and biocompatible polyesters.[74,75] Furthermore, these strained heterocycles are common in a number of biologically active natural products,[76] in which the β-lactone moiety is necessary for bioactivity. One of these important natural product classes includes tetrahydrolipstatin and valilactone which, along with other related natural products, have shown potent activity as lipase inhibitors.[77]

Despite the well-established significance of β-lactones in synthetic chemistry, only a few methods for their synthesis have been developed.[72,76,78,79] Traditional methods are still used, but recently the ring-expanding carbonylation of epoxides to β-lactones has received a good deal of attention.[5] Within epoxide carbonylation, two distinct classes of reactions exist, which are treated separately in this section. The first utilizes bimetallic catalysts comprised of a Lewis acid and a metal carbonyl anion, typically $[\mathrm{Co(CO)_4}]^-$. These catalyst systems can either be formed in situ[31–33,36,37] or prepared as discrete complexes.[21,26–30,34,35] In particular, the well-defined, bimetallic complexes shown in Fig. 1 are highly active and selective catalysts for the carbonylation of a broad range of epoxides to β-lactones. However, these catalysts are ineffective for carbonylation of alkenyl epoxides.

The second class of epoxide carbonylations, which are specific for alkenyl-substituted epoxides, relies on neutral metal complexes of palladium and iron and operates through a different mechanism than the Lewis acid derived catalysts. Thus



salphAl; M = Al
salphCr; M = Cr

TPPAl; M = Al, $R^1 = 4\text{-ClC}_6\text{H}_4$, $R^2 = \text{H}$
TPPCr; M = Cr, $R^1 = \text{Ph}$, $R^2 = \text{H}$
OEPCr; M = Cr, $R^1 = \text{H}$, $R^2 = \text{Et}$

Cp$_2$Ti

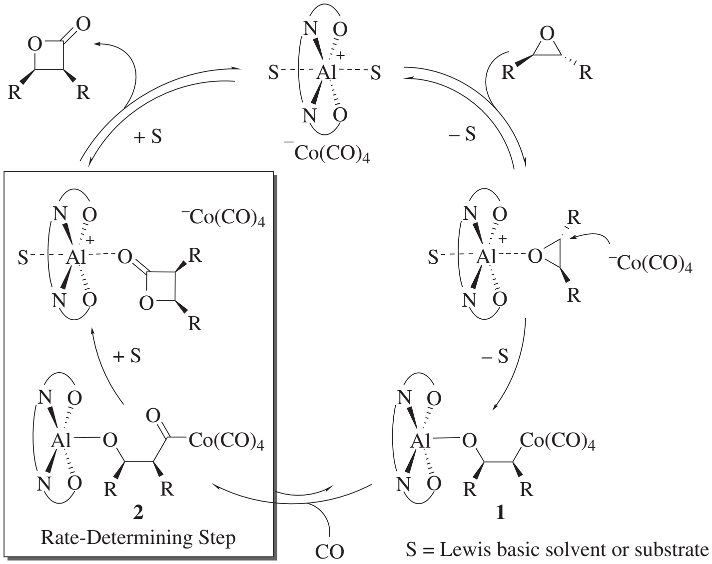
Figure 1. Well-defined, [Lewis acid]$^+$$[\mathrm{Co(CO)_4}]^-$ Catalysts that are highly active for epoxide carbonylation to form β-lactones.

two complementary sets of substrates and metal reagents are available for epoxide carbonylation to β-lactones.

MECHANISM AND STEREOCHEMISTRY

[Lewis Acid]$^+$[Co(CO)$_4$]$^-$ Catalysts

The mechanism of epoxide ring-expanding carbonylation to β-lactones has been the subject of a number of studies employing a variety of methods and catalytic systems.[21,25,32,33,80] Though each [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalyst system has its nuances, the general mechanism remains the same (Scheme 2). First, the Lewis acid coordinates an epoxide, activating it for ring-opening nucleophilic attack by [Co(CO)$_4$]$^-$ at the less hindered carbon of the epoxide. This attack occurs in an S_N2 fashion, with complete inversion of the stereocenter. The resulting cobalt alkyl species **1** undergoes migratory insertion into a bound CO, followed by coordination of another CO to the cobalt to give intermediate **2**. Nucleophilic attack of the metal alkoxide onto the cobalt acyl group of intermediate **2** closes the β-lactone ring and releases catalyst to complete the cycle.



Scheme 2

Detailed experimental investigations have been carried out on three specific catalysts, which all feature a cationic aluminum atom as the Lewis acid.[21,25,33] In the presence of an epoxide and CO, these catalysts react rapidly to form intermediate **2**, the resting state of the catalytic cycle. Ring closing of intermediate **2** is the rate-determining step for production of the β-lactone (Scheme 2). Formation of this resting state complex and its subsequent reactivity are crucial in determining both catalyst activity[21,25] and product selectivity.[21,22] The Lewis acidity of the catalyst component determines the relative lability of the metal alkoxide bond, and thereby the ease of ring closing; thus, selection of the Lewis acid component is crucial for efficient catalysis. In addition, the Lewis acidity may be modulated by solvent coordination that weakens the metal alkoxide bond and stabilizes the Lewis acidic cation, thus accelerating the rate of ring closing. The importance of solvent coordination has been demonstrated by kinetic experiments which show that for salphAl and TPPAl (Fig. 1), the reaction displays a first-order dependence on the concentration of a donor solvent such as THF: rate $= \mathrm{k[epoxide]^0[CO]^0[catalyst]^1[THF]^1}$. The practical implication of these studies is that using THF as the reaction solvent greatly accelerates the carbonylation of epoxides to β-lactones using salphAl[25] and TPPAl.[21,81]

The general mechanism in Scheme 2 is believed to hold for all $[\text{Lewis acid}]^+[\mathrm{Co(CO)_4}]^-$ catalysts; however, some catalysts display slightly different reactivity. In particular, the rate of carbonylation with salphCr slows in THF solvent. In this case, THF may be too strongly donating, coordinating to the chromium center in competition with the epoxide.[19]

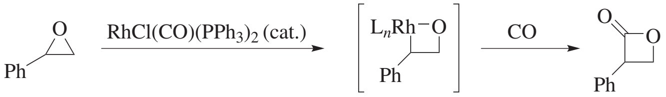
The $\mathrm{S_N2}$-type ring opening of an epoxide by $[\mathrm{Co(CO)_4}]^-$ results in complete inversion of the stereocenter adjacent to the inserted carbonyl. Thus, *trans*-disubstituted epoxides are carbonylated to form *cis*-lactones (Scheme 2), and *cis*-disubstituted epoxides are carbonylated to form *trans*-lactones (Scheme 3).[26,28–30,34,36] Ring opening of monosubstituted epoxides occurs with excellent site selectivity, with attack occurring at the unsubstituted carbon. Because the more hindered stereocenter retains its configuration, monosubstituted epoxides are carbonylated to the corresponding β-lactones with excellent conservation of enantiomeric purity (Scheme 4).[18,34,35]

Scheme 3

Scheme 4

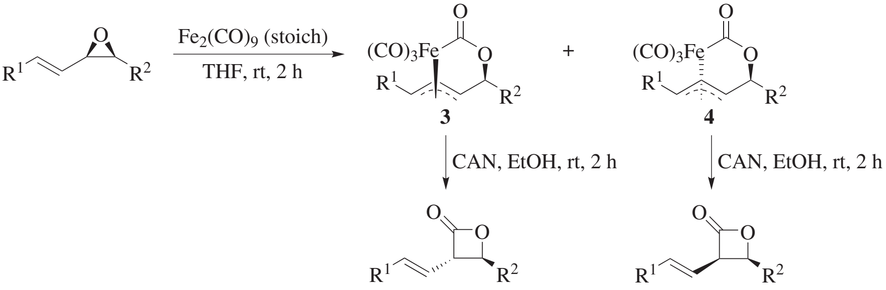
Rhodium, Iron, and Palladium Catalysts

A few examples of ring-expanding carbonylation of epoxides to β-lactones are mediated by rhodium,[41] iron,[39,40,51] and palladium.[38] These reactions likely proceed by an alternative mechanism, as only epoxides with adjacent alkenyl or aryl groups are reactive. In the case of rhodium-catalyzed carbonylation, styrene oxide is the only substrate that forms significant amounts of the β-lactone, and CO is inserted adjacent to the aromatic ring (Scheme 5). Possible pathways have been proposed, but the mechanism of this catalytic transformation remains unknown.[41]



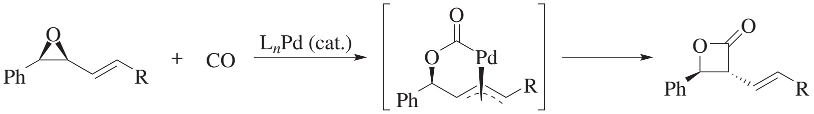
Scheme 5

The mechanism of the stoichiometric, iron-mediated carbonylation of alkenyl epoxides has been established for the formation of δ-lactones,[40,51] and an analogous mechanism is presumed for β-lactones. First, $Fe(CO)_4$, which is formed in situ from either $Fe(CO)_5$ or $Fe_2(CO)_9$, reacts with an alkenyl epoxide to form an isolable π-allyltricarbonyliron lactone complex as a 4:1 mixture of *exo*-isomer **3** and *endo*-isomer **4** (Scheme 6).[39] In both isomers the iron has site selectively inserted into the carbon–oxygen bond of the epoxide adjacent to the alkene, thus forming an allyl complex. Separation of the *exo*-isomer **3** followed by oxidation gives the β-lactone in moderate yield as a single *trans*-diastereomer (Scheme 6), which represents a net inversion of configuration from the *cis*-epoxide. Oxidation of the *endo* π-allyltricarbonyliron complex **4** affords the *cis*-lactone.[39,40,51]



Scheme 6

The palladium-catalyzed ring-expanding carbonylation of epoxides is proposed to occur via a mechanism similar to that of reactions that employ a stoichiometric amount of iron. Epoxides bearing both aryl and alkenyl substituents are opened with inversion of configuration at the carbon adjacent to the alkene, thus forming an allyl–Pd complex that undergoes insertion of CO. The intermediate metallolactone is not isolated and undergoes reductive elimination to form the β-lactone and regenerate the catalyst (Scheme 7). However, it remains unexplained why only phenyl-substituted epoxides are effective substrates for β-lactone formation, and why palladium and rhodium exhibit different site selectivities.[38]

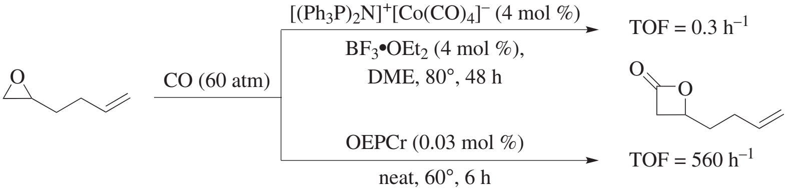


Scheme 7

SCOPE AND LIMITATIONS

[Lewis Acid]$^+$[Co(CO)$_4$]$^-$ Catalysis

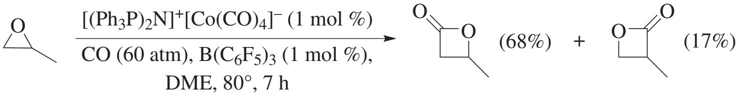
Catalysts. Active catalysts for the carbonylation of epoxides to β-lactones contain both a Lewis acidic component and a nucleophilic metal carbonyl. To date, all of these catalyst systems have utilized $[\mathrm{Co(CO)_4}]^-$ as the metal carbonyl either as a discrete complex or generated in situ.[5] On the other hand, a diverse family of Lewis acids have been employed that have shown similar scope but significantly different reaction rates. These Lewis acids can be either neutral or cationic. In general, in situ generated catalysts using Lewis acids, such as $\mathrm{BF_3{\bullet}OEt_2}$,[36] $\mathrm{B(C_6F_5)_3}$,[36] or $\mathrm{AlMe_3}$[32,33] in combination with cobalt tetracarbonyl salts, show relatively low activity (Scheme 8). The activity of these catalyst systems is in contrast to the well-defined [Lewis acid]$^+[\mathrm{Co(CO)_4}]^-$ complexes, which display high turnover numbers (TON) and turnover frequencies (TOF).[21,26–30,35] As previously shown in Fig. 1, these well-defined catalysts consist of aluminum[21,27,30,35] or chromium[26,28,29] cations ligated by salen-type[26,27,30,35] or porphyrin[21,28,29] ligands, with one example of a titanocene cation.[34] In each case, the counter anion is $[\mathrm{Co(CO)_4}]^-$. Among these well-defined catalysts, the porphyrin-based catalysts[21,28] are generally the most active for epoxide carbonylation (Scheme 8). The trade-off for well-defined catalysts is that although they exhibit higher activity and selectivity, they typically require a few steps to synthesize.



Scheme 8

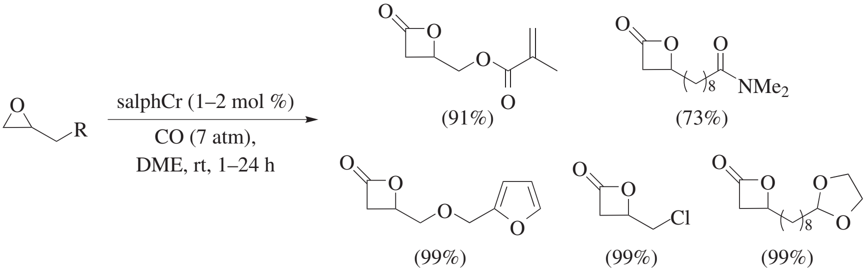
A Lewis acid is necessary to activate the epoxide for carbonylation.[35] In the cases when $[\mathrm{Co(CO)_4}]^-$ salts with non-Lewis acidic cations, such as $\mathrm{PPh_4}^+$, $(n\text{-Bu})_4\mathrm{N}^+$, or the coordinatively saturated $\mathrm{Cp_2Co}^+$, are used, no carbonylation activity is observed. Simple metal carbonyl catalysts such as $\mathrm{Co_2(CO)_8}$ produce small amounts of β-lactone;[36] however, this activity is proposed to result from the dissociation of $\mathrm{Co_2(CO)_8}$ in the presence of a Lewis base to form $[\mathrm{L_2Co(CO)_3}]^+[\mathrm{Co(CO)_4}]^-$.[82] This hypothesis is further supported by the observation that $\mathrm{Co_2(CO)_8}$ catalyzed epoxide carbonylations are more efficient in Lewis basic solvents such as THF than in the non-coordinating solvent benzene.[36]

Although a Lewis acid is required for activity, the use of strong Lewis acids can reduce site selectivity in β-lactone formation. In one particular reaction,[36] use of the highly Lewis acidic $\mathrm{B(C_6F_5)_3}$ in place of $\mathrm{BF_3{\bullet}OEt_2}$ for the carbonylation of propylene oxide gives a 4:1 mixture of the expected β-substituted lactone and the constitutionally isomeric α-substituted lactone (Scheme 9). Although trace amounts of α-substituted lactones are produced using the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, this generally accounts for <1% of the total conversion.



Scheme 9

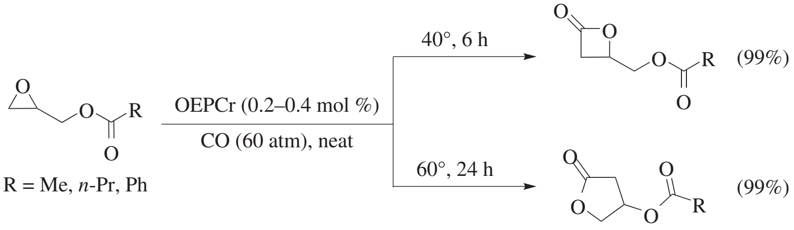
Functional Group Tolerance. The carbonylation of epoxides catalyzed by [Lewis acid]$^+$[Co(CO)$_4$]$^-$ complexes has a very broad functional group tolerance, and in general all of the different catalysts are tolerant of the same types of functional groups. Catalysts that are formed in situ with either boron- or aluminum-based Lewis acids and cobaltate sources have demonstrated success for many alkyl-, alkenyl-, and ether-substituted epoxides.[32,33,36] The well-defined [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, which display higher activities under milder conditions than their in situ generated analogs, have been successful for the carbonylation of a broader range of epoxides that includes esters, amides, aromatics, nitriles, halides, acetals, and unprotected alcohols (Scheme 10).[17–21,23,26,28,29,34,35]



Scheme 10

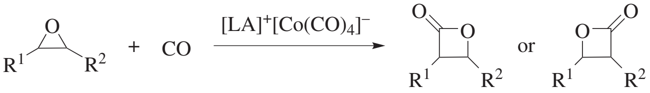
Some functional groups are not tolerated by Lewis acid derived catalysts. One such functionality is the vinyl group, which in certain cases causes the catalysts to be inactive. Substrates containing alkenes separated from the epoxide by at least one carbon are active, but the attempted carbonylation of 3,4-epoxy-1-butene results in a number of unidentified products.[83] Amines are also not tolerated, as it is thought that such strong Lewis bases likely bind irreversibly to the Lewis acid, precluding epoxide coordination. Although they have not been examined, it is presumed that epoxides tethered with other strong Lewis bases such as phosphines would likely exhibit a similar lack of reactivity.

Glycidol and other epoxides with β-hydroxy groups are carbonylated exclusively to γ-lactones instead of β-lactones (see the γ-lactone section). Glycidyl esters require particularly mild reaction conditions to produce β-lactones. At room temperature or 40°, the β-lactone is produced efficiently and in good yield (Scheme 11).[18,26,28] However, at reaction temperatures of 60° or higher, the β-lactone that is produced is not stable in the presence of the Lewis acid and undergoes a catalytic rearrangement to the ring-expanded γ-lactone (Scheme 11).[28] This rearrangement is discussed further in the γ-lactone section of this chapter.



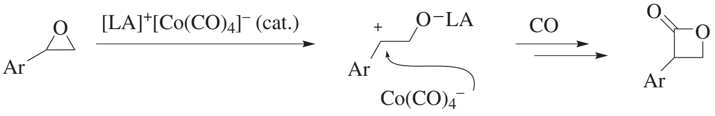
Scheme 11

Epoxide Substitution. The number and configuration of epoxide substituents are important factors for both conversion and product distribution. Because the ring opening can occur at either of the two epoxide carbon–oxygen bonds, two constitutionally isomeric products are always possible (Scheme 12). The ability to control the epoxide ring opening is thus important for obtaining the desired β-lactone product. Because nearly all of the known bioactive β-lactones are single constitutional isomers of *trans*-1,2-disubstituted β-lactones,[77] site control in epoxide carbonylation is of particular importance.



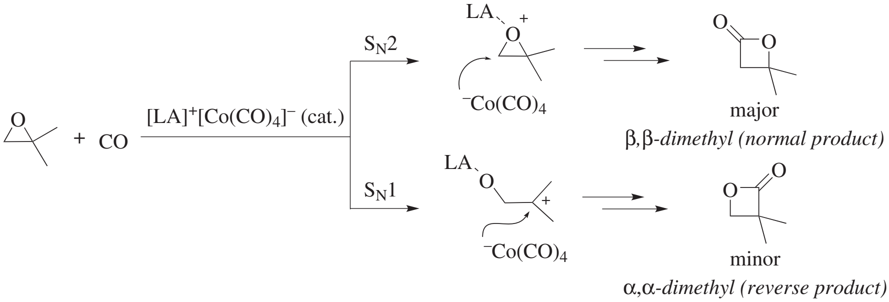
Scheme 12

Monosubstituted epoxides are carbonylated with >100:1 selectivity for CO insertion at the less-substituted carbon. An exception to this trend are aryl-substituted epoxides such as styrene oxide, which insert CO into the more substituted C–O bond to produce α-substituted β-lactones. It is believed that this opposite site selectivity results from an S_N1-like mechanism in which epoxide ring opening occurs to form a stable benzylic carbocation that is then trapped by $[Co(CO)_4]^-$ (Scheme 13).[21]



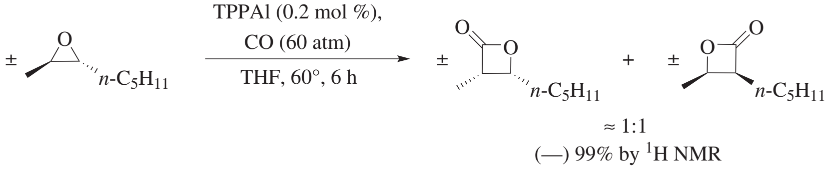
Scheme 13

The carbonylation of 1,1-disubstitued epoxides is complicated by the production of constitutional isomers. Although the unsubstituted site is more sterically accessible to an S_N2-type ring opening, the disubstituted carbon is able to effectively sustain a partial positive charge upon activation by the Lewis acid (Scheme 14). Thus, ring opening occurs at both sites and a mixture of constitutionally isomeric β-lactones is formed. To date, attempts to produce either α,α- or β,β-dimethyl β-propiolactone cleanly from 2-methyl-1,2-epoxypropane have proven unsuccessful. Attempts to carbonylate trisubstituted and tetrasubstituted epoxides using Lewis acid based catalysts have resulted in mixtures of unidentified products, possibly resulting from an analogous S_N1-type ring opening at the geminally disubstituted carbon.



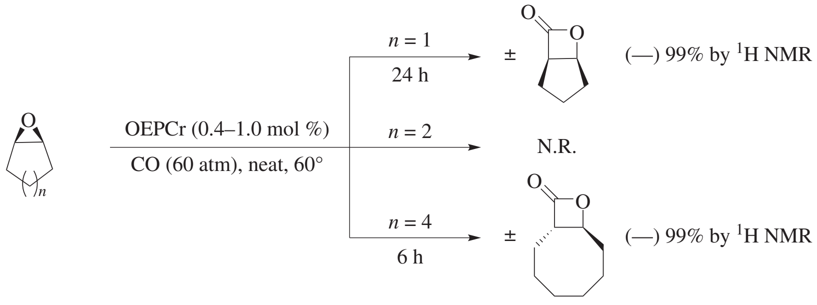
Scheme 14

Lewis acid derived catalysts are effective for the carbonylation of 1,2-disubstituted epoxides. The reaction occurs with inversion of configuration at the carbon adjacent to the inserted CO. *cis*-1,2-Disubstituted epoxides are typically carbonylated faster than their *trans*-analogs, a result of a faster ring closing due to less steric repulsion while forming the *trans*-β-lactone ring. 1,2-Disubstituted epoxides are not carbonylated with site selectivity. Thus, in the carbonylation of unsymmetrically substituted epoxides, the two isomers are formed in an approximately 1:1 ratio as shown by the carbonylation of *trans*-2,3-epoxyoctane (Scheme 15).[21]



Scheme 15

Alicyclic epoxides present a special case of 1,2-disubstituted epoxides. For epoxides fused to rings with at least eight atoms, the carbonylation proceeds in the usual manner, in that *cis*-epoxides are converted into *trans*-lactones.[26,28,29] Epoxides fused to smaller rings, however, do not produce the expected β-lactones. Cyclohexene oxide does not produce any carbonylated product; the expected *trans*-[4.2.0] bicyclic β-lactone is not stable because of high ring strain.[28] The carbonylation of cyclopentene oxide with OEPCr does produce a β-lactone, though it is not the expected *trans*-product. Instead, only the more stable *cis*-β-lactone is observed, and it is proposed that the mechanism involves a carbocation intermediate (Scheme 16).[28]

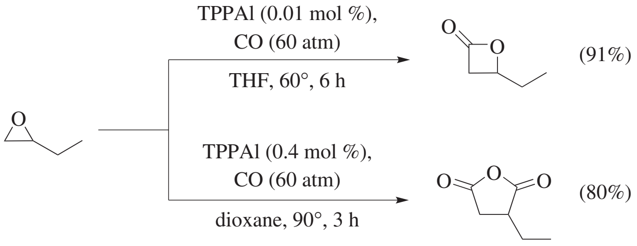


Scheme 16

Reaction Conditions *Reaction Solvent.* In all of the epoxide carbonylation systems, the solvent is a significant factor for both reaction rate and product ratios. Some of the carbonylation systems have been studied in great detail, and the mechanistic role of solvent is well-understood;[21,25] in other systems the solvent effects are simply empirical. Several catalysts have been demonstrated to work efficiently in the absence of solvent,[28,29,35] which permits relatively simple isolation of the neat β-lactones from catalyst residue. Solvent-free reactions are, however, more prone to produce poly(β-lactone)s, common side products observed at high temperatures when reactions are run to complete conversion. The use of solvent generally eliminates this oligomerization.[21]

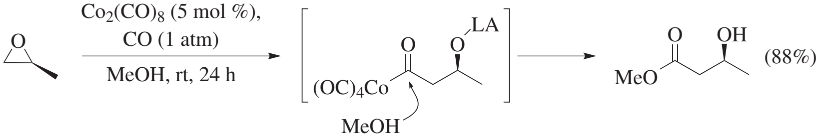
Solvents significantly affect the rate of reaction. This effect has been most thoroughly studied with the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts. For most of these catalysts, ethers are optimal solvents, with more strongly donating ethers generally increasing the rate of carbonylation.[25] For example, the carbonylation of 1,2-epoxybutane to β-valerolactone is nearly twice as fast in THF as the analogous reaction in any other ethereal solvent. This effect has been attributed to donicity rather than polarity, as the hindered solvents 2-methyl-THF and 2,5-dimethyl-THF[84] do not facilitate the carbonylation as well as THF,[25] despite their similar polarities. This solvent trend is reversed for one catalyst, salphCr, as THF actually diminishes the carbonylation rate significantly.[19] For this particular catalyst, more weakly donating ethers such as DME, dioxane, or 2,5-dimethyl-THF are optimal solvents. The rate of carbonylation of 1,2-disubstituted epoxides by any of the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts is also retarded by the use of donating solvents such as THF. In both of these cases, it is believed that THF binding to the Lewis acid inhibits epoxide coordination and activation, thus reducing the rate of carbonylation.

Solvent also affects the rate of formation of side products. Succinic anhydrides can be formed with most [Lewis Acid]$^+$[Co(CO)$_4$]$^-$ catalysts as a result of subsequent carbonylation of the β-lactone product (see below). The formation of anhydride is negligible with donor solvents such as THF, but in less polar solvents such as dioxane, the β-lactone product is rapidly converted into an anhydride. For example, using TPPAl and the proper reaction solvent, either β-lactone or succinic anhydride can be formed with >100:1 selectivity (Scheme 17).[21]



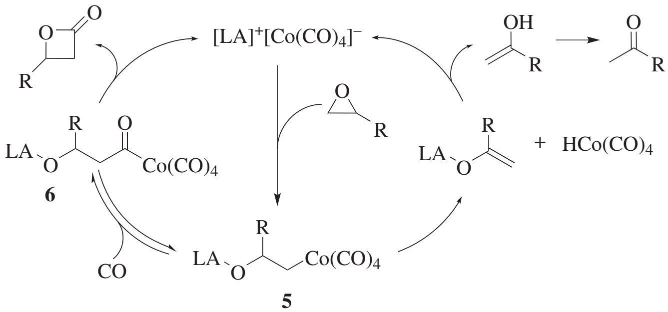
Scheme 17

Some solvents are not practical for epoxide carbonylation using Lewis acid derived catalysts. Noncoordinating and nonpolar solvents such as hexanes do not lead to β-lactone formation. The poor activity in hexanes has, however, been exploited for the development of a carbonylative multicomponent coupling reaction involving epoxides that is discussed later in this chapter.[22] Alcohol solvents are also not practical as the alcohol can react with the ring-opened cobalt acyl to form a β-hydroxy ester (Scheme 18).[57] Other solvents, including CH_2Cl_2 and MeCN, inhibit carbonylation and are thought to react with either the cobaltate anion or the Lewis acid.



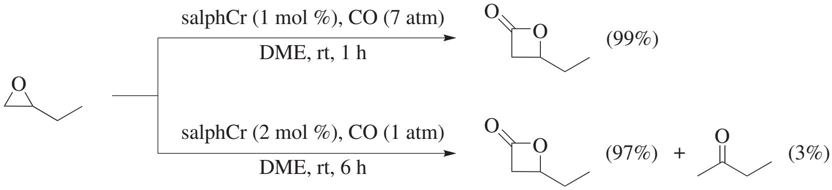
Scheme 18

CO Pressure. Lewis acid derived epoxide carbonylation catalysts generally require at least 14 atm of CO for efficient carbonylation, and most examples use 50–60 atm. Although the reaction is zero-order in CO, at lower CO pressures it is proposed that diffusion of CO into solution may become rate limiting. Furthermore, low concentrations of CO in solution coupled with higher temperatures result in the non-carbonylative rearrangement of epoxides to ketones (Scheme 19). It is believed that ketones are produced through a β-hydride elimination from intermediate **5** followed by protonation of the metal alkoxide to form an enol; tautomerization forms the ketone and the catalyst is regenerated.[26,35] Because intermediate **5** is in equilibrium with the CO-inserted species **6** and higher pressures of CO shift the equilibrium towards intermediate **6**,[85] CO pressures greater than 14 atm are often used to produce β-lactones cleanly without ketone contamination.



Scheme 19

Epoxide carbonylation can be performed under pressures of CO as low as 1 atm. However, to avoid rearrangement to ketones, a sufficient concentration of CO must be maintained in solution. This is accomplished by running the reactions at lower temperatures and with solvent, thus decreasing the rate of CO consumption. High selectivity at low CO pressure was first demonstrated with SalphCr.[26] At 7 atm of CO, several functionally diverse epoxides are carbonylated to β-lactones with complete conversion and 99% selectivity (1 mol % of salphCr, TOF = 33–100 h^{-1}) (Scheme 20). When the pressure is dropped further to 1 atm, the carbonylation takes 6 hours to complete (2 mol % of salphCr, TOF = 8 h^{-1}) and small quantities of a ketone (generally <5%) are produced.[26] Under these reaction conditions, carbonylation of epoxides can be performed in standard glassware, in contrast to the stainless steel reactors required for carbonylation reactions performed at high pressure.



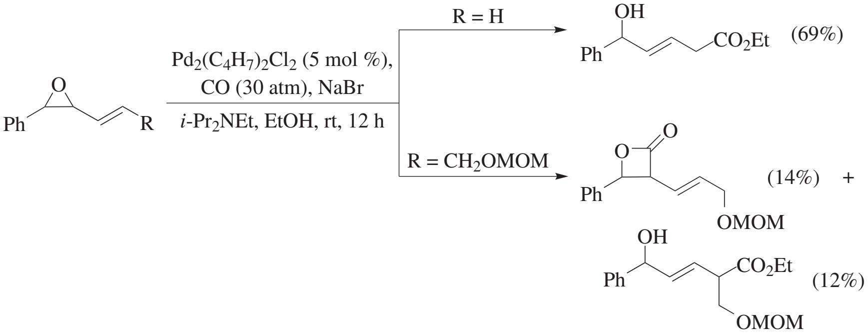
Scheme 20

Catalytic Reactions Using Rh and Pd, and Stoichiometric Reactions Using Fe Complexes

Relatively simple, commercially available transition-metal complexes of rhodium, palladium, and iron have demonstrated activity for the carbonylation of aryl and vinyl epoxides to form β-lactones. For example, the carbonylation of vinyl epoxides to β-lactones proceeds using catalytic amounts of $Pd_2(C_4H_7)_2Cl_2$[38] or stoichiometric amounts of $Fe(CO)_5$[40,51] and $Fe_2(CO)_9$.[39] These metal complexes are only viable with vinyl epoxides because, as has been discussed previously, the mechanism of carbonylation requires alkene coordination followed by ring opening to produce a π-allyl complex. Furthermore, yields of β-lactone are generally low due to formation of side products including ring-expanded δ-lactones,[40,51] β- and δ-hydroxy esters,[38] and 1,3-dienes which result from decarboxylation of the β-lactone product.[38] The carbonylation of styrene oxide and propylene oxide to the respective β-lactones has been reported using $RhCl(CO)(PPh_3)_2$.[41]

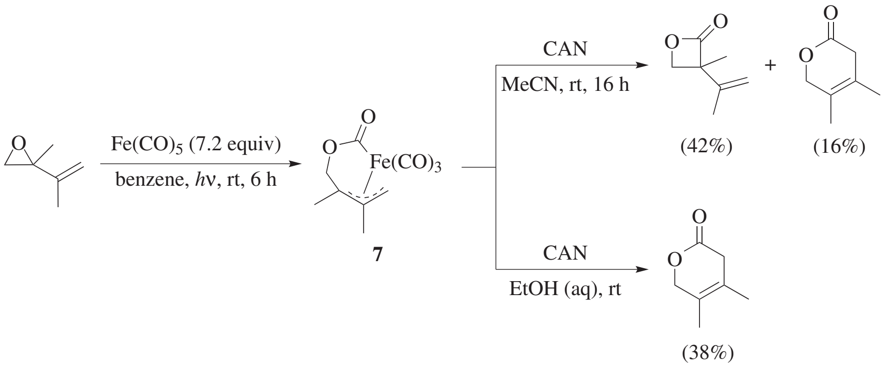
Functional Group and Substitution Tolerance. Few studies have examined the functional group tolerance of vinyl epoxide carbonylations. Iron-mediated carbonylations have been performed primarily with alkyl-substituted vinyl epoxides,[40,51] with one isolated reaction of a hydroxyl-substituted epoxide, albeit in low yield.[39] To test whether the hydroxyl group was the cause of the low yield, the alcohol was protected as an acetate and the yield improved nearly two-fold. Palladium-catalyzed carbonylations of vinyl epoxides have an equally narrow functionality tolerance, as only alkyl- and ether-substituted epoxides are viable substrates.[38]

The carbonylation of vinyl epoxides by iron or palladium is compatible with highly substituted epoxides and, unlike the case of Lewis acid catalyzed carbonylation, vinyl epoxide carbonylation is perfectly site selective for CO insertion at the allylic carbon. Therefore, mono-, di-, and trisubstituted epoxides are all suitable substrates and produce a single β-lactone product. Iron-mediated carbonylations are equally compatible with terminal and internal alkenes.[40] The substitution on the alkene is important for Pd-catalyzed carbonylations, in that terminal vinyl epoxides react with the solvent to produce δ-hydroxy esters, whereas epoxides with internal alkenes produce some β-lactone (Scheme 21).[38]



Scheme 21

Reaction Conditions. The choice of reaction solvent has a dramatic effect on the product distribution. For example, the $Fe(CO)_5$ mediated carbonylation of vinyl epoxides can form both β- and δ-lactones from the same intermediate. The tricarbonyliron lactone intermediate complex **7** is oxidized with ceric ammonium nitrate (CAN) to induce lactonization (Scheme 22). When this oxidation is performed in acetonitrile, the β-lactone is formed as the major product. However, when the reaction solvent is aqueous ethanol, no β-lactone is formed and the δ-lactone is the only product observed.[40]



Scheme 22

The CO pressure required for the carbonylation of vinyl epoxides varies greatly depending on the particular catalyst system. The stoichiometric carbonylation of vinyl epoxides mediated by iron carbonyl compounds, either $Fe_2(CO)_9$ or $Fe(CO)_5$, does not require CO.[39,40] In these reactions, the CO that is incorporated into the β-lactone comes from the iron reagent. On the other hand, palladium-catalyzed carbonylations of vinyl epoxides do require CO. Thirty atm of CO is the optimal pressure when $Pd_2(C_4H_7)_2Cl_2$ is used as a catalyst, although even under these conditions, 1,3-dienes are the major products formed due to decarboxylation.[38]

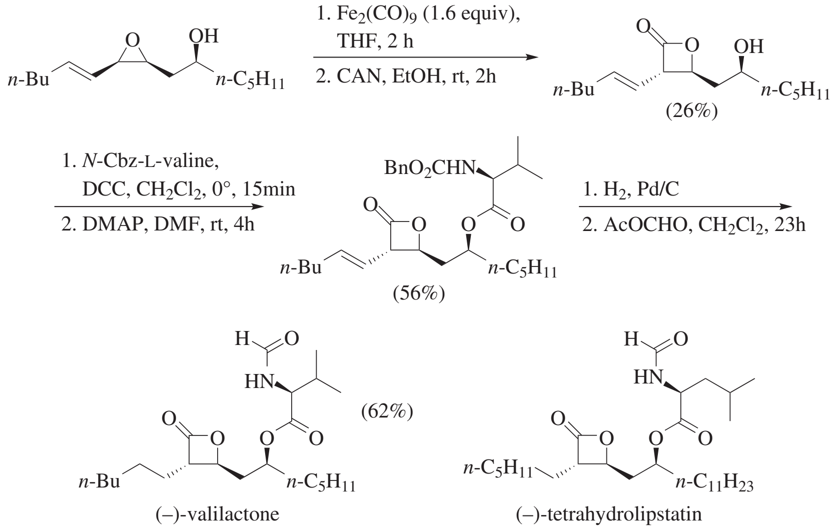
APPLICATIONS TO SYNTHESIS

(−)-Valilactone

Valilactone is a β-lactone-containing natural product belonging to the family of biologically active natural products that includes tetrahydrolipstatin (THL) (Scheme 23).[86] Both compounds are potent lipase inhibitors. In fact, THL is the active compound in the pharmaceutical Xenical, which is marketed for the treatment of obesity.[87] Because both of these natural products contain a β-lactone, they are attractive targets for demonstrating the effectiveness of epoxide carbonylation as a route to produce β-lactones. (−)-Valilactone has been synthesized using epoxide carbonylation to install the β-lactone functionality. Although the 26% yield for the carbonylation step is disappointing, (−)-valilactone is prepared in 9% overall yield from the vinyl epoxide through two further straightforward steps (Scheme 23).[39] This method would likely be useful for the synthesis of other members of this natural product family, including THL.

COMPARISON WITH OTHER METHODS

Although the first synthesis of β-lactones was reported in 1881,[88,89] for many years there were relatively few methods for the synthesis of these strained heterocycles.[72] Recently, however, renewed interest in synthetic methods for β-lactones has stemmed

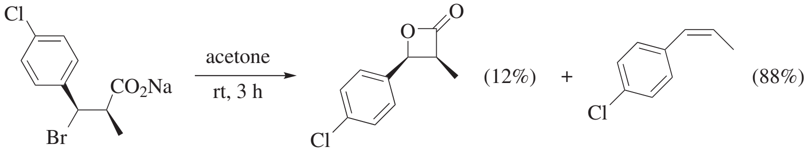


Scheme 23

from the fact that this moiety is present in a number of biologically active natural products.[76] Moreover, the ring-opening polymerization of β-lactones produces biodegradable polyesters with potentially important biomedical applications.[75] Other than epoxide carbonylation, the two most common methods for the synthesis of β-lactones are the ring closing of carboxylic acid derivatives and the [2+2] cycloaddition of ketenes and carbonyl compounds.[72]

Ring Closing of β-Halo Carboxylic Acids

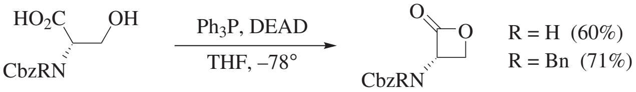
Base-catalyzed ring closing of β-halo carboxylic acids produce β-lactones with inversion of configuration at the carbon bearing the halogen.[90] This was the first known method for β-lactone preparation,[88] and it is generally performed in aqueous media, though examples in organic solvents exist. Although some substrates are efficient ring-closing precursors, this method is limited by the deleterious elimination of HX and CO_2 to form alkenes (Scheme 24).[91] Because more efficient ring-closing methods have been developed, and particularly ring closing of β-hydroxy carboxylic acids, lactonization from β-halo carboxylic acids is rarely used.



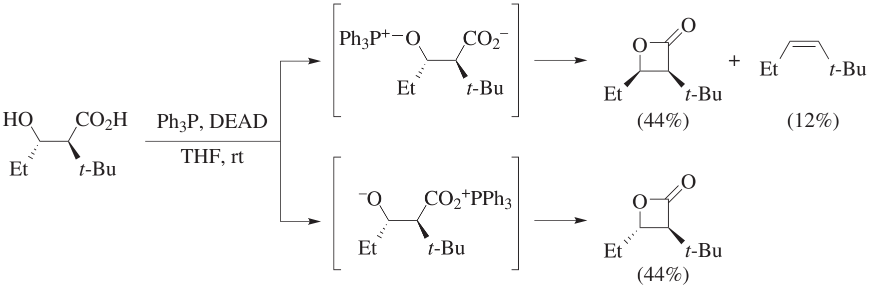
Scheme 24

Ring Closing of β-Hydroxy Carboxylic Acids

The synthesis of β-lactones by ring closing of hydroxy acids requires activation of either the hydroxy functionality or the carboxylic acid. By the use of standard Mitsunobu conditions,[92] the hydroxy group can be activated by Ph_3P for attack by the carboxylate, producing β-lactones with inversion of configuration at the hydroxyl-substituted carbon (Scheme 25).[93,94] Unfortunately, 2,3-disubstituted hydroxy acids are not suitable for Mitsunobu cyclization because they are prone to undergo elimination to form alkenes (Scheme 26),[95] as is the case with β-halo carboxylic acids. Furthermore, for certain substrates, Mitsunobu activation of the hydroxyl group is competitive with activation of the carboxylic acid by Ph_3P. Because carboxylic acid activation results in a β-lactone with retention of configuration, whereas hydroxyl activation results in inversion, this mixture of intermediates produces both diastereomers of the β-lactone product (Scheme 26).[96]

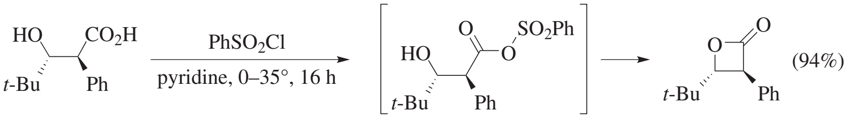


Scheme 25



Scheme 26

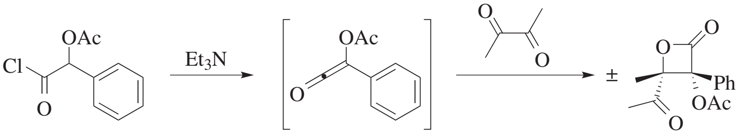
To avoid these problems, selective activation of the carboxylic acid portion of the hydroxy acid is commonly employed, most often using an arenesulfonyl chloride.[97] The latter produces β-lactones in good yields with retention of configuration at the hydroxyl-bearing carbon (Scheme 27).[98] Furthermore, this ring-closing method is compatible with diversely substituted hydroxy acids.



Scheme 27

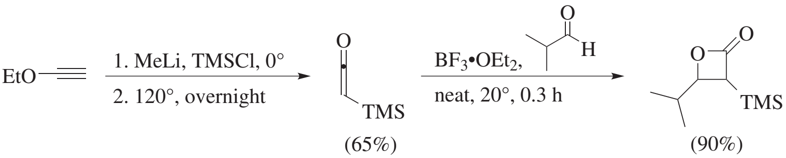
[2+2] Cycloaddition of Ketenes and Carbonyl Compounds

Ketenes have been shown to react with a wide range of carbonyl compounds, which makes this cycloaddition a versatile synthetic method.[99,100] One of the most challenging aspects of the [2+2] cycloaddition method for the synthesis of β-lactones is the generation of ketenes. Only a few ketenes are stable, and most are known to dimerize and react readily with water;[101] therefore, most ketenes are generated in situ (Scheme 28).[102−104] Ketenes are most commonly generated through the dehydrohalogenation of acid chlorides,[105,106] though other methods have also been successful.[107,108]



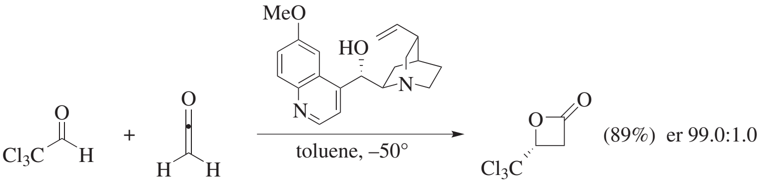
Scheme 28

Although many [2+2] cycloaddition reactions occur spontaneously due to the high reactivity of ketenes, some require a catalyst to efficiently produce β-lactones. Relatively stable ketenes, such as trimethylsilyl-substituted ketenes, often undergo Lewis acid catalyzed cycloaddition with aldehydes (Scheme 29),[109] as the Lewis acid effectively activates the aldehyde toward attack.[110] Alternatively, Lewis bases have been used to activate the ketene for attack of the aldehyde; tertiary amines are common catalysts for this purpose.[111]

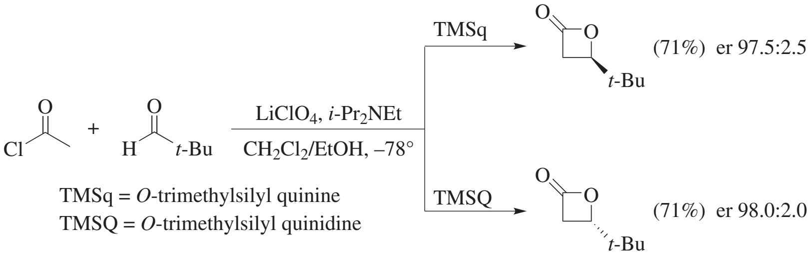


Scheme 29

A large body of work describes the enantioselective synthesis of β-lactones by [2+2] cycloaddition.[102,111−118] Both chiral Lewis acids and Lewis bases have been shown to successfully catalyze the enantioselective addition, and each has its advantages and disadvantages. The reaction of ketene with chloral is catalyzed by the *cinchona* alkaloid quinidine, a naturally occurring chiral Lewis base (Scheme 30).[112] Unfortunately, this method is successful only for the highly activated aldehyde chloral, but this innovation inspired further exploration into asymmetric β-lactone synthesis through Lewis base catalyzed [2+2] cycloaddition.[111,113,114] An example is a tandem *cinchona* alkaloid–Lewis acid catalyzed reaction that is both highly enantioselective and active for non-activated aldehydes (Scheme 31).[102] Enantiomeric ratios range from 92.0:8.0 to 99.5:0.5, and both enantiomers of the β-lactones can be obtained through the proper choice of the *cinchona* alkaloid catalyst.

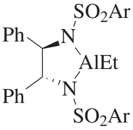


Scheme 30



Scheme 31

Chiral Lewis acids have been explored for enantioselective [2+2] cycloaddition of non-activated aldehydes, but they have not shown the high selectivities associated with the base-catalyzed reactions discussed above. Examples include bis(sulfonamide) aluminum catalysts **8** (Fig. 2)[115,116] and TADDOL titanium complexes **9** (Fig. 2),[117] but the enantiomeric purity of the β-lactone products is only moderate. Lewis acid catalyzed reactions do not, however, suffer from reduced activity when non-activated aldehydes are used, so more diverse β-lactones can be prepared.[81,118]



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Ar = 3,5-$(CF_3)_2C_6H_3$

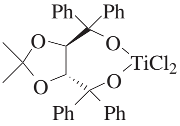

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Figure 2. Chiral Lewis acids employed in the enantioselective [2+2] cycloaddition of ketenes and aldehydes.

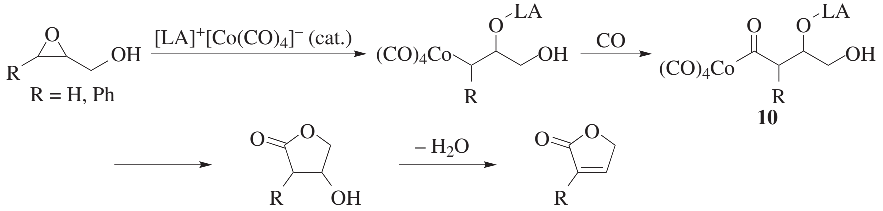
EPOXIDE CARBONYLATION TO γ-LACTONES

The γ-lactone core commonly appears in natural products,[119] many of which exhibit bioactivity attributed to this functionality.[120] Butenolides, a class of unsaturated γ-lactones, have been the focus of much research, and their synthesis and reactivity have been reviewed.[121–123] γ-Lactones are arguably the most easily synthesized type of lactones due to their low ring strain. As such, there are a multitude of possible synthetic methods,[124,125] and even within epoxide carbonylation, a number of diverse routes to γ-lactones are known.[28,42–45]

MECHANISM AND STEREOCHEMISTRY

Carbonylation of Glycidols

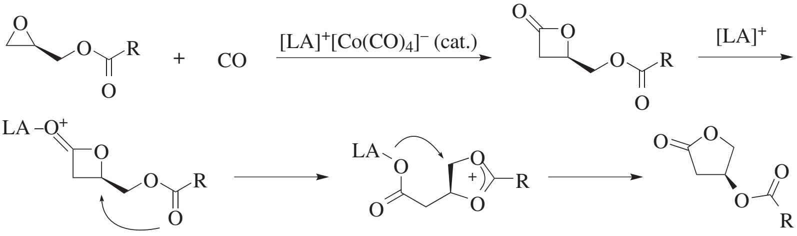
The mechanism of glycidol carbonylation has not been studied in detail, as the active catalytic species are not well-defined for most systems.[42,43] One common feature is that all catalysts contain a cobalt carbonyl compound. Most systems are believed to react via similar pathways, and a general mechanism is presented which illustrates the important steps in the reaction (Scheme 32). First, the epoxide ring is opened by cobalt at either the less-substituted (R = H) or benzylic carbon (R = Ph). Insertion of CO forms intermediate **10**, and then nucleophilic attack of an alcohol or alkoxide on this acyl ligand forms the lactone. Selectivity for γ-lactone is dictated by the presence of a nucleophilic oxygen in the γ-position. Closing from this alcohol to form a five-membered ring is highly favored over closing from the epoxide oxygen to form a strained β-lactone. Post-carbonylation dehydration of the product yields α,β-unsaturated-γ-lactones (Scheme 32).[42,43] In one system, further carbonylation of the γ-lactone is possible; however, the mechanism of this transformation is unclear.[43]



Scheme 32

Carbonylation of Glycidyl Esters

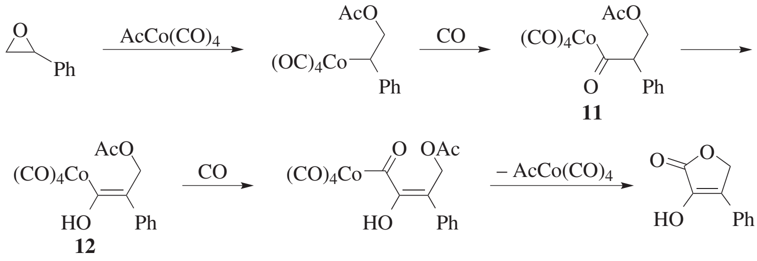
If the alcohol of glycidol is protected, then epoxide carbonylation proceeds with [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts to form the expected β-lactones (Scheme 33). However, in the specific case of glycidyl esters, the product β-lactone can undergo an in situ Lewis acid catalyzed rearrangement to a γ-lactone (Scheme 33). The proposed mechanism involves coordination of the β-lactone to the Lewis acid catalyst, activating it for ring-opening attack by the ester carbonyl, which proceeds with inversion of configuration to form an intermediate 1,3-dioxolanyl cation. Ring closing of the carboxylate reforms the ester and the expanded lactone.[28]



Scheme 33

Double Carbonylation of Styrene Oxides

In epoxide carbonylation reactions, aryl epoxides typically ring open such that the cobalt is bound to the benzylic carbon. Double carbonylation of styrene oxides is unique in that two molecules of CO are inserted adjacent to one another in the ring. Although migratory insertion of CO into a cobalt alkyl bond is facile, a second insertion of CO into cobalt acyl **11** is not observed.[126] However, the aryl group helps to stabilize tautomerization to enol **12**, which is more electron-donating and thus allows insertion of CO.[127] Once the second CO is inserted, ring closing can occur, forming a γ-lactone (Scheme 34).[44]

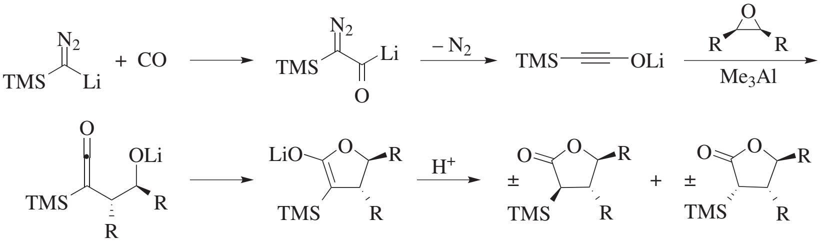


Scheme 34

Carbonylation of Epoxides with Ynolates

Unlike most epoxide carbonylations, this method does not employ a catalytic amount of cobalt to sequester CO. Instead, CO is trapped by a stoichiometric amount of an organolithium compound and is converted into a reactive ynolate, which then undergoes a ring-expanding reaction with an epoxide. A relatively straightforward mechanism has been proposed (Scheme 35). First, trimethylsilyldiazomethane is deprotonated with BuLi and is exposed to CO, forming a highly reactive acyllithium reagent that rapidly loses nitrogen to form a silylethynolate. In the presence of a

Lewis acid, this ynolate ring opens an epoxide, unmasking a ketene, which readily closes to a five-membered ring. Protic workup provides the γ-lactone product.[45]



Scheme 35

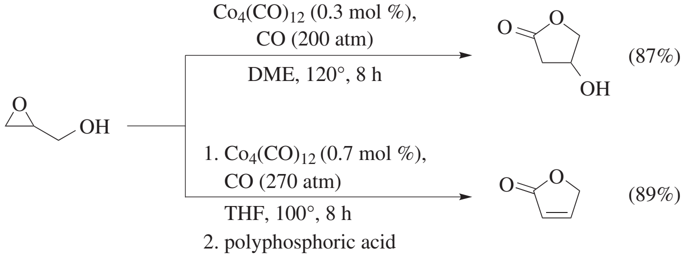
Nucleophilic attack of the epoxide always occurs at the carbon of the ynolate and opens the epoxide with inversion of configuration at this site. Thus, *cis*-epoxides are carbonylated to *trans*-lactones (Scheme 35) and *trans*-epoxides to *cis*-lactones. This reaction is highly site selective and stereospecific with regard to ring opening of the epoxide; however, the orientation of the silyl group is less controlled and is determined by the protonation step (Scheme 35). One diastereomer typically predominates, and its yield can be increased through the use of a bulky proton source, but the configuration at this center has not been definitively established.[45]

SCOPE AND LIMITATIONS

Although a number of routes to γ-lactones via ring-expanding carbonylation of epoxides exist, the scope of these methods has remained largely unexplored. For each method just a handful of examples are known. Extending these reactions to more general syntheses of γ-lactones remains to be explored.

Carbonylation of Glycidols

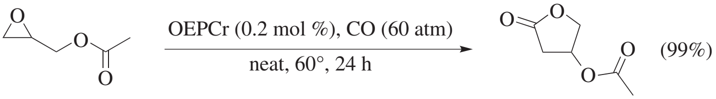
The parent glycidol is readily carbonylated to afford good yields of 3-hydroxy-γ-lactone using cobalt carbonyl catalysts, with or without a well-defined Lewis acid (Scheme 36).[5,42] Substituted glycidols also give the desired products, although the yields are generally lower and often poor in the case of aryl-substituted epoxides.[43] Although only alkyl and aryl substituents have been reported, it is expected this reaction may also be tolerant of a range of functional groups similar to that seen for epoxide carbonylation to β-lactones. Further research is required to examine the broader applicability of this method to the synthesis of substituted 3-hydroxy-γ-lactones. Alternative products may also be formed by in situ dehydration of the hydroxy lactone to give the α,β-unsaturated-γ-lactone (Scheme 36).[42]



Scheme 36

Carbonylation of Glycidyl Esters

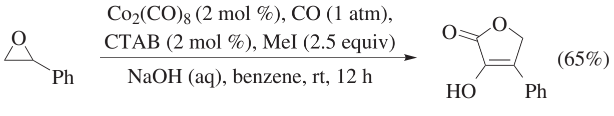
Glycidyl esters are a distinctive class of protected glycidols that form β-lactones upon carbonylation but, due to a pendant ester group, readily rearrange to form γ-lactones. The Lewis acid promoted rearrangement of glycidyl esters is observed with all [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts at elevated temperatures. Functional group tolerance is essentially the same as for carbonylation to β-lactone (see above), but a β-alkanoate substituent is required. The reaction is both stereospecific and nearly quantitative. Lower reaction temperature (40°) results in formation of β-lactone without rearrangement (Scheme 11), but higher temperatures and longer times cause complete rearrangement to the γ-lactone product (Scheme 37).[28]



Scheme 37

Double Carbonylation of Styrene Oxides

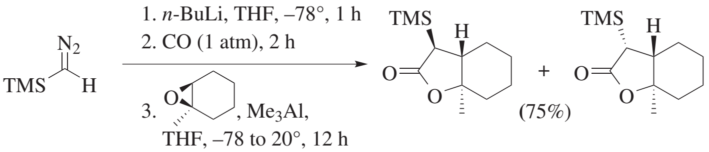
Only two examples of this transformation are known; thus, the scope of the reaction has not been explored. The primary substrate requirement is that epoxides must be able to form the relatively stable enolate intermediate **12** (Scheme 34) that is required for the insertion of a second molecule of CO.[127] Styrene oxide gives a moderate yield of γ-lactone (Scheme 38), but only a 34% yield is obtained with β-methylstyrene oxide.[44]



Scheme 38

Carbonylation of Epoxides with Ynolates

This reaction is a unique method for the incorporation of CO into an epoxide, as CO is sequestered by an organolithium reagent rather than a transition metal. This method has the advantage of being able to produce fused ring systems in a stereo- and regiospecific manner. Thus far, the substrate scope only includes di- and trisubstituted epoxides with alkyl and alkenyl substituents which form the product in good yield, but as a mixture of two diastereomers that were not separated (Scheme 39).[45] To increase the general utility of this reaction, further studies are required to extend this method to monosubstituted and more functionally diverse substrates.[45] Although the reaction has only been demonstrated to form 2-trimethylsilyl γ-lactones, the silyl group can be used as a reactive functional group for further synthetic transformations.[128–131]

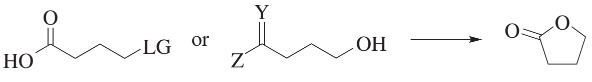


Scheme 39

COMPARISON WITH OTHER METHODS

Unlike for strained β-lactones, there are a multitude of methods for the synthesis of γ-lactones, and this topic has recently been reviewed.[124] A comprehensive discussion of the many other methods is beyond the scope of this work; thus, only very general methods and those that form the same products as ring-expanding epoxide carbonylation are covered.

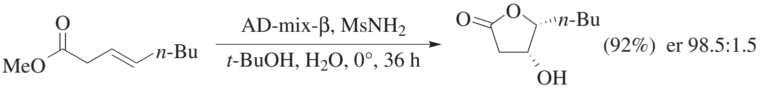
The simplest method of forming a γ-lactone is the intramolecular condensation of a γ-hydroxy acid. This type of reaction is not limited to hydroxy acids, and may be extended to a very general ring closing involving any molecule containing an acid and a leaving group in the γ-position, or containing a γ-alcohol and a carboxyl equivalent (Scheme 40). There are numerous examples,[124] and some common variations of these ring closings include Mitsunobu lactonization,[92] halo lactonization,[132] as well as addition of activating agents such as trifluoroacetic acid[133] or *N,N′*-dicyclohexylcarbodiimide[134] to γ-hydroxy acids. Alternative syntheses include the ring-expanding Baeyer-Villiger oxidation of cyclobutanes,[135] reduction of succinic anhydrides,[136] and oxidative coupling with furans.[137,138]



Y/Z = carboxyl equivalent

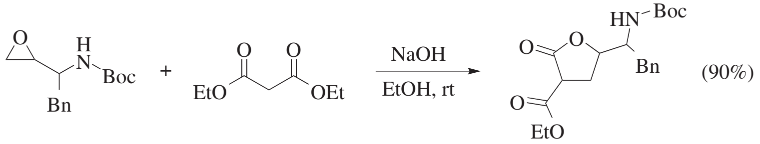
Scheme 40

Of particular relevance to glycidol carbonylation is the synthesis of 3-hydroxy γ-lactones via asymmetric dihydroxylation[139] of a β,γ-unsaturated ester, followed by spontaneous lactonization (Scheme 41).[140] This versatile method produces γ-lactones with good yields and enantioselectivities, and the starting material is readily available through a modified Knoevenagel condensation.[141]



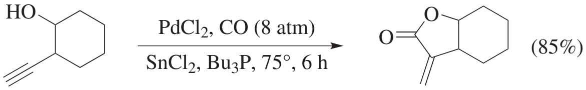
Scheme 41

γ-Lactones can also be made through non-carbonylative ring expansion of epoxides by incorporating C_2 fragments in a method comparable to epoxide coupling with ynolates. For example, the sodium salt of diethyl malonate opens an epoxide to give an intermediate that then closes to form a γ-lactone (Scheme 42).[142]



Scheme 42

Palladium-catalyzed carbonylations of alkenols[143] and alkynols[144] also produce γ-lactones (Scheme 43). Although this method provides an alternative carbonylation route, yields are variable depending on the substrate substitution pattern. Ring-expanding carbonylation of oxetanes, the four-membered analogs of epoxides, with a [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalyst yields nearly quantitative conversion to γ-lactones.[54,67] However, the utility of this route is diminished as methods for the synthesis of substituted oxetanes are limited.



Scheme 43

Ring-expanding carbonylation of epoxides is a viable method for the synthesis of γ-lactones, and it has the advantage of employing readily accessible starting materials that can be made with high enantiomeric purity. However, this method has not yet demonstrated applicability to a broad range of substrates or to the synthesis of larger, more structurally and functionally complex molecules, for which numerous other synthetic pathways exist. Because of the mechanism of lactone formation, the scope is limited to a handful of specific product substitution patterns (2-silyl, 3-hydroxy, 3-alkanoxy, 2-hydroxy, 3-aryl, and α,β-unsaturated γ-lactones). For these particular product classes, epoxide carbonylation is an efficient and effective synthetic method and more research in this area is warranted.

EPOXIDE CARBONYLATION TO δ-LACTONES

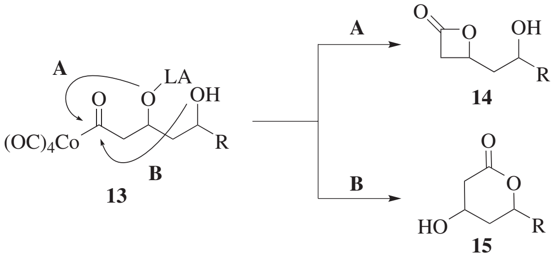
The δ-lactone functionality is also ubiquitous in synthetic chemistry as both a vital intermediate as well as an important synthetic target.[145] The two classes of δ-lactones that are accessible through epoxide carbonylation include 3-hydroxy δ-lactones and α,β-unsaturated δ-lactones. These products are particularly important because of their dense functionality as well as their prevalence in biologically relevant natural products. 3-Hydroxy δ-lactones are most prominent in the class of HMG-CoA reductase inhibitors known as statins, which are among the most potent cholesterol-lowering drugs available.[146,147] The α,β-unsaturated δ-lactone motif, on the other hand, is one of the most commonly occurring lactone frameworks in natural products.[119] These lactone scaffolds occur in bioactive natural products including antiproliferative agents, immunosuppressants, and enzyme inhibitors.[148] Epoxide carbonylation offers a versatile route to a diverse set of important δ-lactones that are difficult to access through other straightforward means.

MECHANISM AND STEREOCHEMISTRY

The mechanism for the carbonylation of epoxides to δ-lactones varies according to the particular epoxide substrate and catalyst system. All of these carbonylation reactions can be divided into two main categories, consisting of reactions employing homoglycidol substrates and carbonylations of vinyl and alkynyl epoxides. Because the catalyst systems and mechanisms for these two substrate classes are significantly different, each is discussed in turn, and vinyl and alkynyl epoxides are treated separately due to their mechanistic differences.

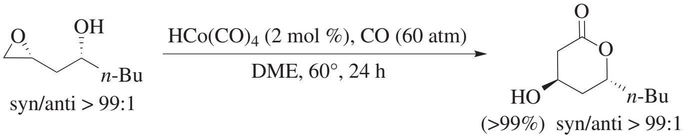
Carbonylation of Homoglycidols

Homoglycidols are effectively carbonylated to form 3-hydroxy δ-lactones using $[Co(CO)_4]^-$ based catalysts.[24] The key to efficient catalysis is the selectivity for the formation of δ-lactone over β-lactone, as both potential products are formed from a common intermediate (Scheme 44). The initial step of the reaction involves coordination of the epoxide by the Lewis acid followed by ring opening by $[Co(CO)_4]^-$. Insertion of CO into the cobalt alkyl forms cobalt acyl intermediate **13**, which can ring close to form the two different lactone products. As seen in β-lactone synthesis, pathway **A** produces the hydroxy-substituted β-lactones **14**. However, in pathway **B** the cobalt acyl is attacked by the alcohol substituent to form the 6-membered δ-lactones **15**. Hydroxy-substituted β-lactones are also known to undergo rearrangement to δ-lactones;[149] however, under conditions optimized for δ-lactone synthesis, this pathway has been discounted because β-lactones cannot be observed by infrared spectroscopy during the reaction, and independently synthesized β-lactones do not produce δ-lactones when subjected to these reaction conditions.[24] The choice of catalyst has a significant impact on product ratios, as is discussed in the Scope and Limitations section, and judicious selection of catalyst and reaction conditions provides complete and selective conversion to δ-lactones.



Scheme 44

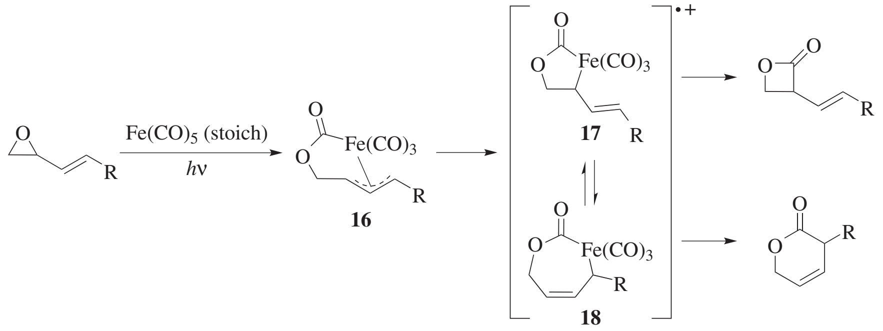
The configuration of the δ-lactone products is predictable based on that of the homoglycidol substrates. Although a stereoselective method for the carbonylation of racemic homoglycidols is not known, when enantiopure substrates are employed, δ-lactones are produced with complete retention of configuration at the hydroxyl-bearing carbons (Scheme 45).[24]



Scheme 45

Carbonylation of Vinyl Epoxides

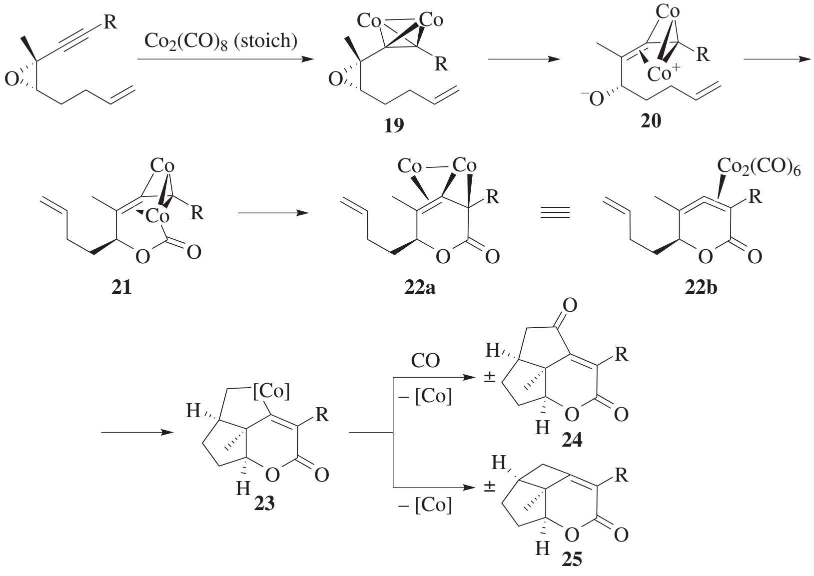
The carbonylation of vinyl epoxides to δ-lactones takes place through a different mechanism than that of homoglycidol carbonylation (Scheme 46). The metal carbonyl reagent typically used for this substrate class is $Fe(CO)_5$, which coordinates to the vinyl group upon loss of CO. Oxidative addition and insertion of CO forms the π-allyltricarbonyliron acyl intermediate **16**, which is isolable and has been characterized.[40] Reductive elimination of intermediate **16** is initiated by either oxidation with reagents such as cerium ammonium nitrate,[40] or by thermolysis under an argon atmosphere[51] or high pressures of CO.[52] As with homoglycidol carbonylation, the carbonylation of vinyl epoxides to δ-lactones is complicated by the formation of β-lactones. An equilibrating mixture of radical cation intermediates **17** and **18** is proposed to form after oxidation, followed by reductive elimination to form vinyl-substituted β-lactones and β,γ-unsaturated δ-lactones, respectively (Scheme 46).[40] Product ratios are determined by reaction conditions and the epoxide substrates used.



Scheme 46

Carbonylation of Alkynyl Epoxides

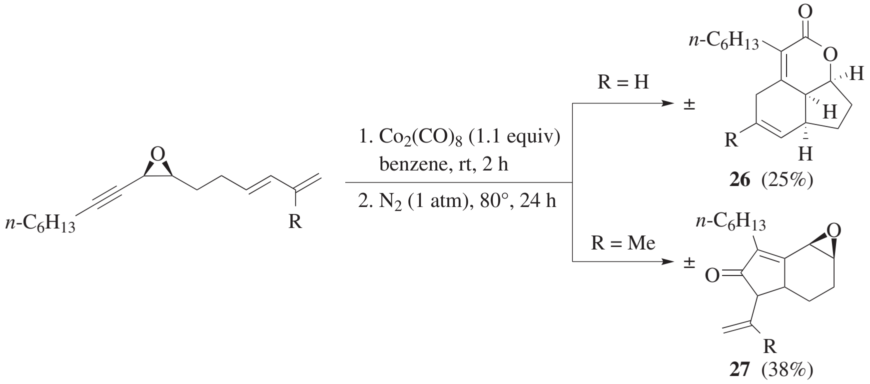
The mechanism of the carbonylation of alkynyl epoxides is comparable to that of the Pauson–Khand reaction[150] with $Co_2(CO)_8$ as the catalyst (Scheme 47; CO ligands are omitted from [Co] in the scheme). The reaction is formally a [5 + 1]/[2 + 2 + 1] cycloaddition in which, depending on the reaction conditions, one or two molecules of CO are incorporated to produce a tricyclic product. The initial step involves coordination of both cobalt centers to the alkyne with concomitant loss of two CO molecules to produce complex **19**[47] (Scheme 47), which has been observed in the Pauson–Khand reaction.[151] The epoxide is then ring opened by nucleophilic attack of the $Co_2(CO)_6$ fragment to give the zwitterion **20**. The alkoxide of intermediate **20** can attack one of the bound CO molecules to give intermediate **21**, which undergoes a reductive elimination to produce the core δ-lactone structure in complex **22a**. This allene-containing δ-lactone



Scheme 47

(as depicted in structure **22b**) is well-suited for cyclization with the tethered alkene to produce the tricyclic metallocyclopentane **23**. This metallocycle is the common intermediate for two different products, depending on the reaction conditions. When the cyclization is run under relatively high pressures of CO (3.5 atm), product **24** is formed via CO insertion followed by reductive elimination. However, under 1 atm CO or N_2, significant quantities of cyclobutane product **25** are formed from the direct reductive elimination of the metallocyclopentane. The relative configuration of the epoxide is very important for successful reaction. The alkyne and alkene substituents of the epoxides must be in a *cis* orientation; the *trans*-epoxides do not produce any cyclic products and only epoxide starting material is recovered (see footnote a in Table 3B).[46]

An alternative reaction pathway that is operative for dienynes involves a [5+1]/[4+2] cyclization to form δ-lactone **26** or a competing [2+2+1] cyclization to form the traditional Pauson–Khand ketone product **27**. Subtle changes in alkene substitution can result in exclusive formation of product **26** or product **27**, or mixtures of the two (Scheme 48).[46]

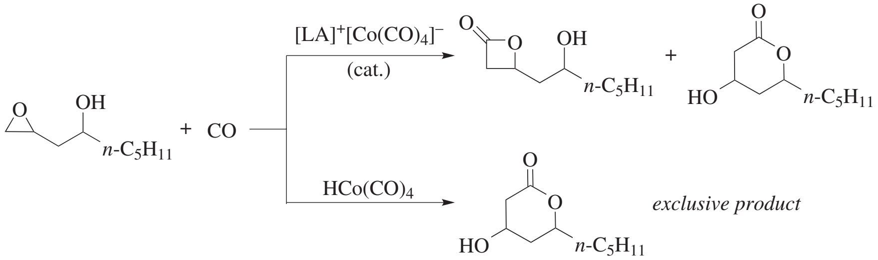


Scheme 48

SCOPE AND LIMITATIONS

Carbonylation of Homoglycidols

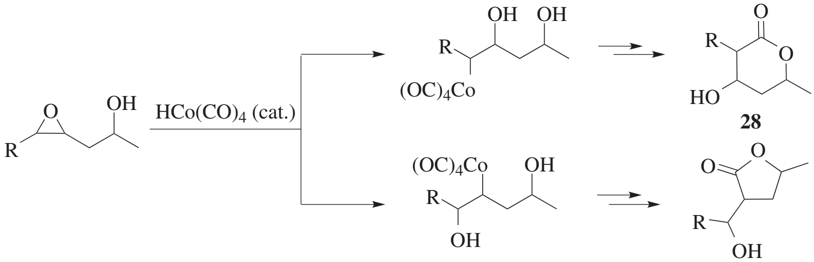
The choice of catalyst is vital for the efficient carbonylation of homoglycidols to δ-lactones. Although a number of Lewis acid based catalysts successfully produce 3-hydroxy δ-lactones, these reactions are always complicated by β-lactone formation. The δ- to β-lactone ratios range from about 4:1 to 1:4, but neither product is cleanly produced in any of these examples. The only catalyst that has been demonstrated to cleanly convert homoglycidols to 3-hydroxy δ-lactones is $HCo(CO)_4$ (Scheme 49).[24] This catalyst is ineffective for the carbonylation of epoxides to β-lactones,[59] and it is speculated that a β-hydroxy cobalt acyl species is formed but does not ring close. Such a species is analogous to structure **13** (Scheme 44, LA = H) such that only pathway B is kinetically accessible, resulting in a δ-lactone as the exclusive product (Scheme 49).



Scheme 49

When $HCo(CO)_4$ is employed under the optimized reaction conditions, a functionally diverse set of 3-hydroxy δ-lactones can be prepared (see Table 3A). A number of sterically diverse alkyl-substituted homoglycidols are efficient substrates. Despite $HCo(CO)_4$ being a common catalyst for olefin hydroformylation,[152] homoglycidols with pendant olefins are selectively carbonylated at the epoxide without reaction of the olefin. Ethers and halogenated side chains are also compatible.

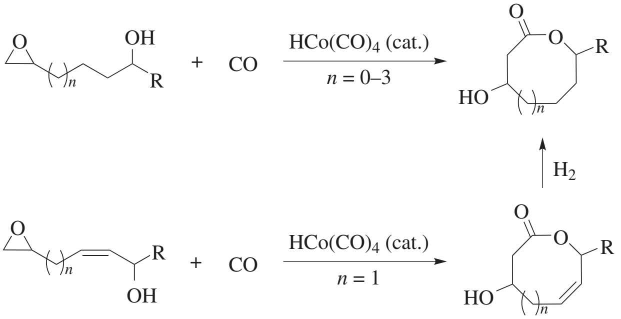
One limitation to this procedure is that it is only selective with monosubstituted homoglycidols. Epoxide ring opening by $[Co(CO)_4]^-$ is highly dependent on epoxide substitution.[25] Therefore, ring opening of monosubstituted epoxides occurs exclusively at the unsubstituted position to produce an intermediate that is well-suited for ring closing to form δ-lactones. Although ring opening of 1,1-disubstituted epoxides has not been attempted, 1,2-disubstituted epoxides ring open at both positions without site selectivity, producing two different intermediates that ring close to produce both δ- and γ-lactones (Scheme 50). Therefore, δ-lactones with substituents at the 2-position (product **28**, R ≠ H) are not selectively produced through homoglycidol carbonylation.



28

Scheme 50

An extension of alcohol-substituted epoxide carbonylation that has not yet been attempted is the synthesis of larger lactone rings (Scheme 51). Although ring closing to form lactones with ring sizes of seven, eight, nine, and ten has been shown to be several orders of magnitude slower than the analogous four-, five-, and six-membered ring closing,[153] one strategy that improves ring closing is the incorporation of *cis* double bonds into the tether.[154,155] Because alkenes are tolerated under epoxide carbonylation conditions,[24] this strategy may also be applicable to the carbonylation of hydroxy-substituted epoxides (Scheme 51). Thus, extending the range of lactones accessible through epoxide carbonylation could have applications in the synthesis of macrolactone-containing natural products.[156]

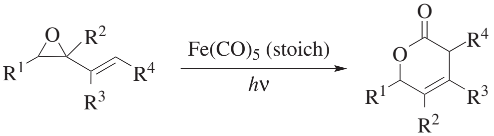


Scheme 51

Carbonylation of Vinyl Epoxides

The carbonylation of vinyl epoxides is generally catalyzed by iron carbonyl species. Both $Fe_2(CO)_9$[50] and $Fe(CO)_5$[52] have been used. Iron pentacarbonyl requires irradiation to form the reactive $Fe(CO)_4$ species, and the same catalytic species can be formed through the thermolysis of $Fe_2(CO)_9$.[157] Other transition metal catalysts containing palladium, rhodium, and cobalt have been used with varying degrees of success.[52,53]

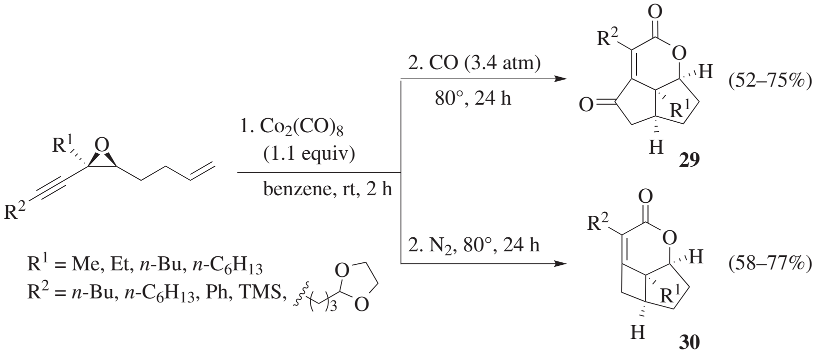
Highly substituted vinyl epoxides are viable substrates for the iron-mediated carbonylation to form δ-lactones. 1,1-Disubstituted, 1,2-disubstituted, and trisubstituted epoxides all are reactive, and although the ratios of δ- to β-lactones are variable, overall yields are not diminished with highly substituted epoxides. Furthermore, substituted alkenes (both 1,1- and 1,2-disubstituted) are effective substrates. The high tolerance for substituted epoxides allows access to substitution at every carbon of the δ-lactone product (Scheme 52). Unfortunately, the functional group tolerance has not been well studied, as alkyl groups are the only substituents that have been reported for this carbonylation.



Scheme 52

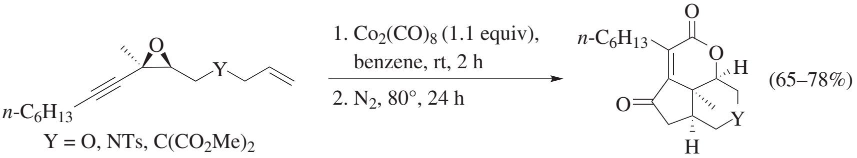
Carbonylation of Alkynyl Epoxides

As mentioned above, the cobalt-mediated carbonylation of alkynyl epoxides has the potential to form two different tricyclic δ-lactone products via [5+1]/[2+2+1] and [5+1]/[2+2] cycloadditions. The product ratios are highly dependent on both the reaction conditions and the epoxide substrates. When the reaction is run under a pressure of CO, the [5+1]/[2+2+1] mechanism generally dominates to form product **29** exclusively (Scheme 53, see footnote a in Table 3B).[46] However, under a nitrogen atmosphere, the intermediate cobalt metallocycle **23** (Scheme 47) undergoes a reductive elimination without CO insertion to form product **30** predominantly.[46] Reductive elimination prior to CO insertion is not observed with some substrates: disubstituted epoxides and epoxides with an ether linkage in the alkene side chain do not form cyclobutane-containing products, even when the reaction is performed without CO. In these cases, two molecules of CO are provided by $Co_2(CO)_8$ to give the [5+1]/[2+2+1] products. Similar reactivity with heteroatom-containing substrates has been documented for the Pauson–Khand reaction.[151,158]

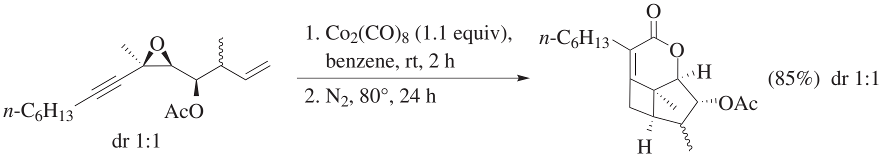


Scheme 53

The cyclocarbonylation of alkynyl epoxides is tolerant of a number of functional groups and substitution patterns. Trimethylsilyl- and 1,3-dioxolane-substituted alkynes afford tricyclic products that are well-suited for further functionalization (Scheme 53).[46] Alkenes with propylene tether lengths result in 6-membered rings fused to the δ-lactones, and the inclusion of heteroatoms such as an oxygen or tosylamide in the tether facilitates the cycloaddition (Scheme 54, see footnote a in Table 3B).[46] Functional groups on the alkene tether are well-tolerated, as epoxides with methyl, methoxy, and acetoxy substitution form δ-lactone products under standard conditions (Scheme 55, see footnote a in Table 3B).[46] Finally, further substitution on the fused ring can be achieved with a 1,2-disubstituted alkene and an α,α-dimethyl alkene, though harsher conditions are required for reaction of these substrates.[46]



Scheme 54

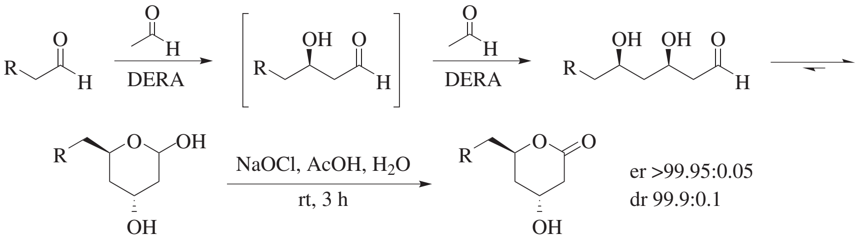


Scheme 55

COMPARISON WITH OTHER METHODS

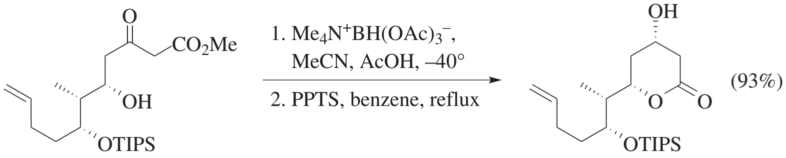
δ-Lactones are commonly prepared through the acid-induced ring closing of δ-hydroxy acids and esters.[124] Although this ring closing is relatively efficient, it is not as facile as the analogous procedure for producing γ-lactones and can sometimes be complicated by polymer formation.[124] There are, however, many methods for producing δ-lactones, and this section focuses on alternative syntheses specific to 3-hydroxy δ-lactones and α,β-unsaturated δ-lactones, which are the primary products from epoxide carbonylation.

Substituted 3-hydroxy δ-lactones constitute the biologically relevant portion of HMG-CoA reductase inhibitors, commonly known as statin drugs.[159] Because of their importance in pharmaceutical development, a large body of work has focused on their efficient synthesis. Biocatalytic routes have shown a good deal of promise, as δ-lactones can be prepared with excellent enantioselectivity from prochiral starting materials.[160] The most established of these methods involves the DERA-catalyzed (DERA = 2-deoxyribose-5-phosphate aldolase) tandem aldol reaction to form an enantiopure lactol that can be oxidized to the lactone (Scheme 56).[159,161] This is an excellent method for the few specific substrates that are important pharmaceutical intermediates, but poor substrate generality and the necessity for enzyme optimization limit the broad applicability of this reaction for the synthesis of diversely substituted δ-lactones.

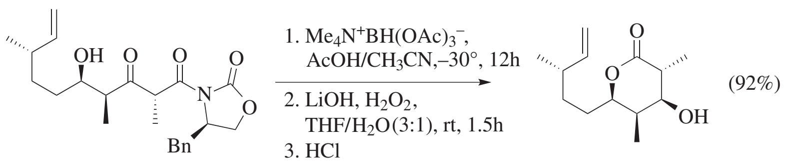


Scheme 56

In the chemical synthesis of 3-hydroxy δ-lactones, a common step prior to ring closing is the reduction of a β-keto ester, which can be performed stereoselectively using a directing group. As shown in Scheme 57, a hydroxy group with defined configuration can be used for that purpose.[162] Another strategy employs a chiral auxiliary to direct consecutive aldol additions. Then, directed reduction of the β-keto amide followed by acid-promoted ring closing forms the diastereomerically pure 3-hydroxy δ-lactone (Scheme 58).[163]

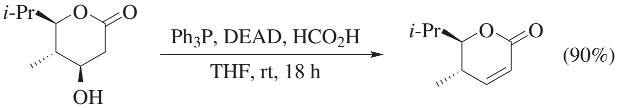


Scheme 57

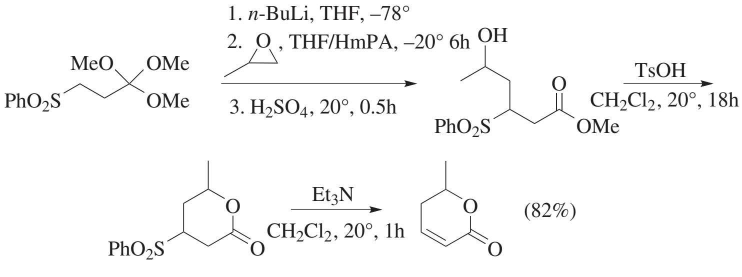


Scheme 58

Unsaturated δ-lactones are commonly produced by the elimination of a suitable leaving group in the 3-position of the lactone. For example, 3-hydroxy δ-lactones, which can be prepared by homoglycidol carbonylation as well as the methods discussed above, can be dehydrated to form α,β-unsaturated δ-lactones under typical Mitsunobu conditions (Scheme 59).[164] Another method employs epoxide ring opening by trimethyl 3-(phenylsulfonyl)orthopropanoate, a practical homoenolate equivalent, which forms an intermediate that undergoes lactonization upon acidic workup (Scheme 60).[165,166] Elimination of the sulfonyl group under basic conditions produces the corresponding α,β-unsaturated δ-lactones in good yields when monosubstituted epoxides are used.



Scheme 59



Scheme 60

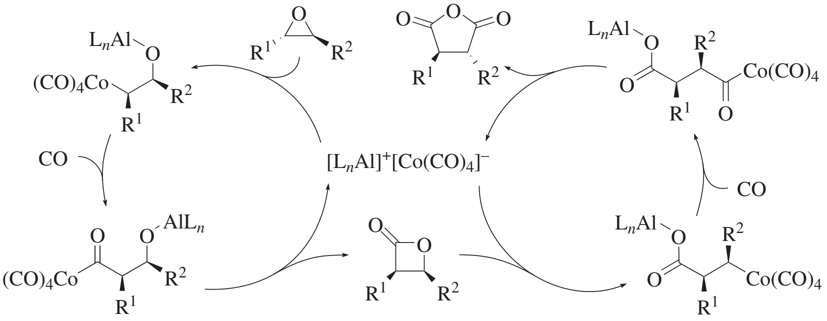
These elimination methods are useful for the preparation of α,β-unsaturated lactones, but lactones with unsaturation elsewhere are not accessible. One the other hand, the carbonylation of vinyl epoxides has the potential advantage of producing both α,β- and β,γ-unsaturated δ-lactones (Table 3B).

EPOXIDE CARBONYLATION TO SUCCINIC ANHYDRIDES

Succinic anhydrides may be formed by the catalytic insertion of two molecules of CO, one into each carbon–oxygen bond of the epoxide. β-Lactones formed from the single carbonylation of epoxides may undergo a second ring-expanding carbonylation to afford the five-membered succinic anhydrides. Under favorable reaction conditions this double carbonylation may be performed in one pot. The product succinic anhydrides are useful as synthetic intermediates[167–169] and as monomers for polymerization.[170,171]

MECHANISM AND STEREOCHEMISTRY

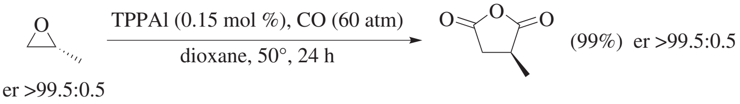
The mechanism of epoxide double carbonylation has been the subject of a detailed study.[21] In every case, the reaction first effects carbonylation of the epoxide to a β-lactone, followed by a second catalytic carbonylation to yield the anhydride (Scheme 61). Both epoxide and lactone carbonylation cycles proceed through the same elementary steps: (1) coordination to the Lewis acidic cation, which activates the substrate for ring-opening S_N2-type attack by $[Co(CO)_4]^-$; (2) migratory insertion of CO; and (3) nucleophilic attack of the alkoxide or carboxylate on the cobalt acyl, resulting in ring closing and formation of the product. Ring closing is the rate determining step for the first cycle and ring opening is the rate determining step for the second.[21]



Scheme 61

An interesting and practical consequence of the different rate-determining steps in each of these parallel cycles is that the first carbonylation of the epoxide to the β-lactone proceeds to completion before any of the β-lactone intermediate is consumed to form the anhydride in the second carbonylation step. Furthermore, the donicity and polarity of the reaction solvent drastically affect the rate of each carbonylation, such that the choice of solvent determines whether single or double carbonylation will occur (Scheme 17). Kinetic studies indicate that epoxide carbonylation is accelerated by coordinating solvents such as THF, whereas lactone carbonylation is inhibited by THF and accelerated by nonpolar solvents such as toluene. Thus, to obtain good activity for both of these catalytic cycles, the reaction is performed in 1,4-dioxane, which has the appropriate combination of moderate donating ability and low polarity.[21]

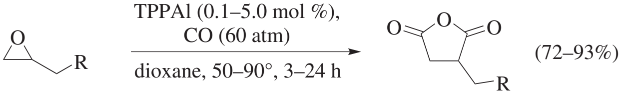
A significant outcome of the S_N2-type mechanism as opposed to an oxidative addition/reductive elimination mechanism is that the stereocenter adjacent to each inserted carbonyl is inverted with each ring-opening step, resulting in a net double inversion. Thus, *cis*-epoxides are carbonylated to *cis*-anhydrides via *trans*-lactones, and *trans*-epoxides are carbonylated to *trans*-anhydrides via *cis*-lactones (Scheme 61). Because each carbonylation occurs with complete inversion of configuration, anhydrides with high diastereomeric and enantiomeric purity are produced. For example, (*R*)-propylene oxide is converted into (*S*)-methylsuccinic anhydride with excellent preservation of enantiopurity (Scheme 62).[21] Given the many excellent methods for the highly stereoselective synthesis of epoxides,[12–16] this method can be used to produce diastereomerically and enantiomerically pure anhydrides. One limitation is that under typical reaction conditions, the catalyst epimerizes the product after it is formed. However, epimerization can easily be avoided by carrying out the carbonylation at lower temperatures (Scheme 62).[21,54]



Scheme 62

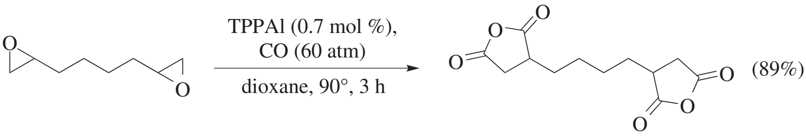
SCOPE AND LIMITATIONS

Epoxide double carbonylation is effective for the majority of substrates that can be carbonylated to β-lactones, and it is compatible with a range of functional groups including alkanes, alkenes, aromatics, ethers, esters, ketones, acetals, alcohols, nitriles, and amides (Scheme 63), as well as substrates with multiple epoxides (Scheme 64).[21] Tolerance of the alcohol functional group is particularly interesting, as epoxides are known to react with alcohols under carbonylation conditions, resulting in ring-opening alkoxycarbonylation. Furthermore, alcohols may react with the product anhydride; however, the use of solvent reduces intermolecular reactions, and steric or geometric constraints may prevent intramolecular reactions (Scheme 65).[21]

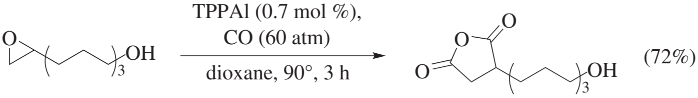


R = alkane, alkene, aromatic, ether, ester, ketone, acetal, alcohol, nitrile, amide

Scheme 63



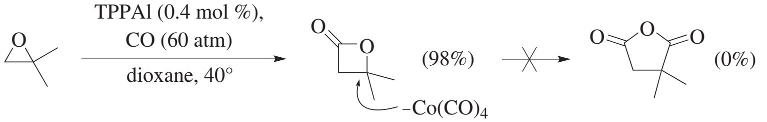
Scheme 64



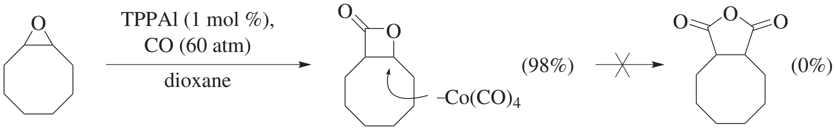
Scheme 65

Epoxides containing strongly Lewis basic groups such as primary amines are typically unreactive for anhydride formation, presumably due to competitive coordination of these groups to the Lewis acidic catalyst. Anhydrides are generally not formed in good yield from glycidyl esters, as the β-lactone intermediates preferentially rearrange to form γ-lactones (see above), and epoxides with multiple sites for nucleophilic attack, such as epichlorohydrin and 1,2-epoxy-3-butene, do not form anhydrides cleanly.[21]

Anhydrides are readily obtained from both monosubstituted and vicinally disubstituted epoxides. Products with *trans*-substituents generally require lower catalyst loading and are formed with higher selectivity than the corresponding *cis*-substituted products, which have more steric hindrance. Geminally disubstituted epoxides are unreactive. For example, 1,2-epoxy-2-methylpropane is carbonylated to the β-lactone, but further carbonylation would require an S_N2 attack on the tertiary center of the lactone, which is not observed (Scheme 66).[21] Disubstituted epoxides as part of fused rings have, thus far, also been unreactive for anhydride formation (Scheme 67).[83]



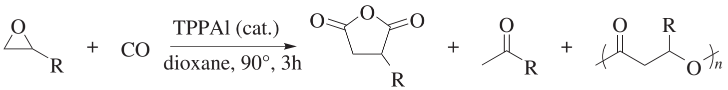
Scheme 66



Scheme 67

The selectivity for anhydride formation is typically very high, but it can be significantly affected by reaction conditions. The most common side products are ketones

(Scheme 68), which result from the catalytic isomerization of the epoxides under low CO pressures and high temperatures (see above). Thus, to avoid ketone formation at the higher temperatures (90°) used for accelerating the reaction, high CO pressure (14–60 atm) must be used. However, it is possible to maintain good selectivity and moderate activity at lower CO pressure (4–7 atm) if the reaction mixture is not heated until after the starting epoxide has been converted into the β-lactone. Polyesters are the other potential side products (Scheme 68), which are formed by the ring-opening polymerization of β-lactone intermediates. However, substrate concentrations of 1.0–2.0 M are typically dilute enough to avoid this polymerization and maintain high selectivity (>98%) for the anhydrides.[21]

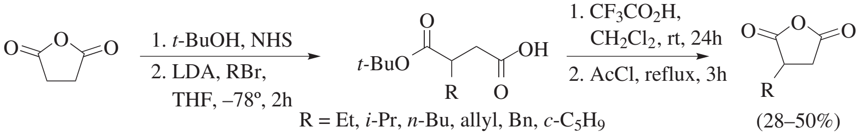


Scheme 68

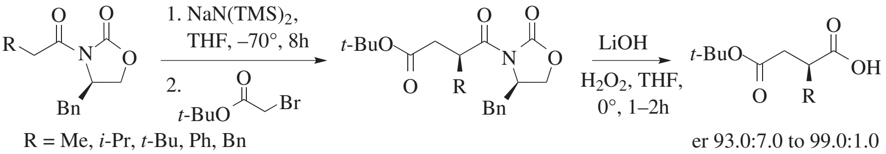
Ring-expanding carbonylation of epoxides to succinic anhydrides is only possible in the presence of a catalyst, and the majority of catalysts that are efficient for carbonylation of epoxides to β-lactones will also carbonylate β-lactones to succinic anhydrides. However, higher temperatures and longer reaction times, as well as the appropriate solvent, are typically required for efficient conversion. The double carbonylation can be run in a number of solvents, but it is uniquely rapid in 1,4-dioxane, which facilitates both the first and second carbonylation steps. The most active catalysts for carbonylation to anhydrides are based on the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ motif, and contain porphyrin metal cations. Catalysts with chromium porphyrin cations tend to produce more poly(lactone) side products. Thus the preferred catalysts, which demonstrate the highest activity and selectivity, are based on porphyrin aluminum cations, such as the commercially available TPPAl (Fig. 1). As with all [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, TPPAl is air-sensitive, and must be handled under nitrogen. Thus, solvents and substrates are typically dried and degassed prior to carbonylation.[21]

COMPARISON WITH OTHER METHODS

Substituted succinic anhydrides have previously been synthesized by a number of methods.[172] Ring-closing condensation of 1,4-diacids or their derivatives is a straightforward transformation, and there are many reagents known to facilitate anhydride formation.[173] There are many methods for the synthesis of succinate esters, which can be cyclized to the corresponding anhydride (Scheme 69).[172,174] The most widely used approach to enantiomerically enriched succinates employs chiral enolates (Scheme 70).[175–177] Although this method is more versatile for the synthesis of highly substituted anhydrides, the diastereoselectivity of vicinally substituted succinates synthesized via chiral enolates[178] is lower than in succinates made by epoxide carbonylation.

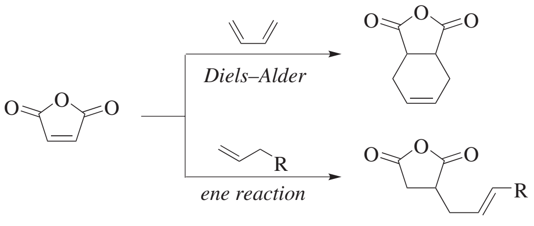


Scheme 69



Scheme 70

Derivatization of maleic anhydride via the Diels–Alder or ene reactions is another common method for the synthesis of succinic anhydrides (Scheme 71). Maleic anhydride is an excellent dienophile,[179] readily forming fused rings which are inaccessible via epoxide carbonylation. The ene reaction, a mono-alkene variation of the Diels–Alder reaction,[180–182] is used industrially for the synthesis of alkenyl succinic anhydrides. Substrates other than epoxides, such as alkenes,[183,184] alkynes,[185] and alkenoic acids,[186] can also be carbonylated to succinic anhydrides; however, these carbonylations are less synthetically useful due to low yields, formation of significant amounts of side products, or lack of demonstrated substrate generality.



Scheme 71

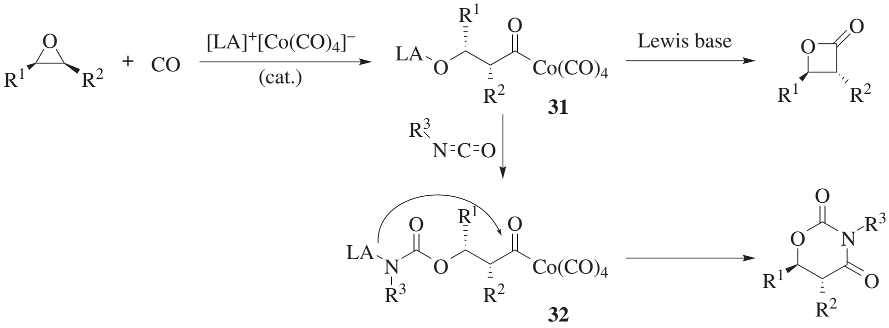
In general, the advantage of the epoxide double carbonylation is its efficiency as a catalytic method for the synthesis of anhydrides in a single step from readily available epoxides and catalysts. The products can be mono- or disubstituted and contain a range of functional groups, and high levels of stereochemical purity are retained through the carbonylation. The reaction is limited by the requirements for high-pressure and air-free reaction conditions and by the scope of substrates containing strong electrophiles and nucleophiles or steric and conformational restrictions.

EPOXIDE CARBONYLATION TO 1,3-OXAZINANE-2,4-DIONES

The carbonylation of epoxides has been expanded to include multicomponent coupling reactions. The addition of isocyanate to an epoxide carbonylation reaction results in formation of a 1,3-oxazinane-2,4-dione.[22] This class of heterocycles has received interest as synthetic intermediates[187−190] and has been investigated as potential therapeutic agents.[191−194]

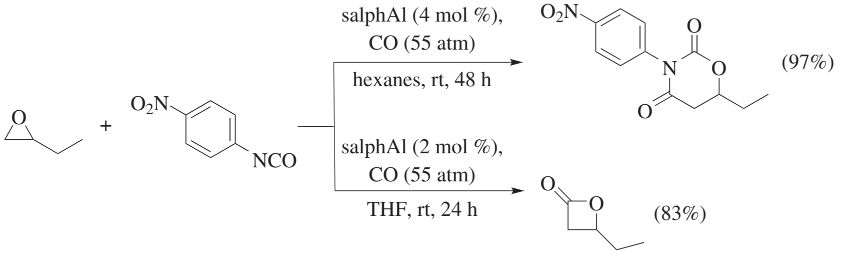
MECHANISM AND STEREOCHEMISTRY

The discovery of epoxide carbonylation to oxazinanediones resulted from mechanistic studies of epoxide carbonylation to β-lactones.[22,25] The initial steps of β-lactone and oxazinanedione formation are identical (Scheme 2 and Scheme 72). The mechanisms diverge when the catalytic resting state **31** is intercepted by an isocyanate, resulting in the formation of an aluminum carbamate **32**. Nucleophilic attack on the cobalt acyl by this carbamate closes the ring, regenerates catalyst, and forms the product oxazinanedione. Conditions that slow the formation of a β-lactone will increase the relative lifetime of the catalyst resting state, thus improving the probability that it will react with an isocyanate to form the oxazinanedione.[22,25]



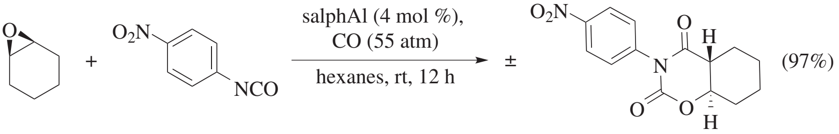
Scheme 72

As with other epoxide carbonylations employing [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, the solvent dramatically influences product selectivity (Scheme 73).[22] Coordinating Lewis basic solvents such as THF accelerate the formation of β-lactones, whereas nonpolar and noncoordinating solvents such as hexanes slow the ring-closing step, increasing the lifetime of the catalyst resting state **31**. Thus hexane, which is a poor solvent for β-lactone formation, facilitates the reaction of the ring-opened epoxide with an isocyanate prior to ring closing, improving the selectivity for oxazinanedione.[22]

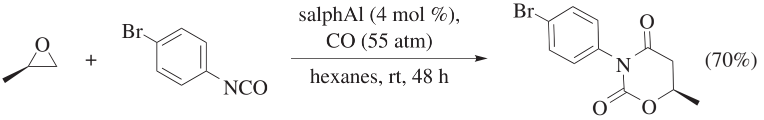


Scheme 73

As in most other epoxide carbonylations, initial nucleophilic attack by $[Co(CO)_4]^-$ occurs with excellent site selectivity at the least-substituted carbon of the epoxide. This attack results in inversion of the stereocenter, while the configuration of the other stereocenter is retained. For example, cyclohexene oxide is carbonylated to the *trans*-oxazinanedione (Scheme 74),[22] whereas (*R*)-propylene oxide gives the (*R*)-oxazinanedione (Scheme 75).[22]



Scheme 74

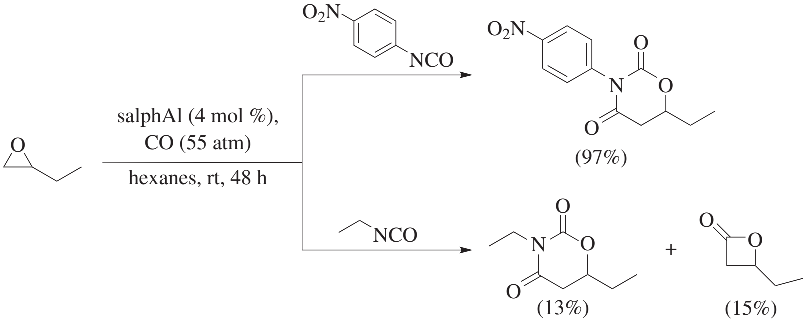


Scheme 75

SCOPE AND LIMITATIONS

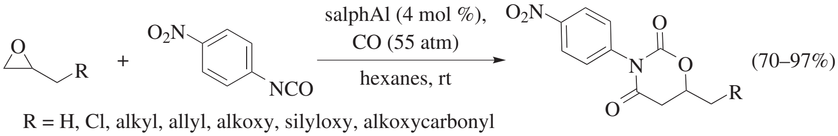
The multicomponent coupling of epoxides, isocyanates, and CO is typically run in hexanes at room temperature and 50 atm of CO with 1.0 equivalent of an isocyanate and 0.04 equivalent of salphAl. The primary concern in optimizing reaction conditions is improving the selectivity for oxazinanediones over β-lactones. For this reason, salphAl is the preferred catalyst because it is one of the slowest well-defined catalysts for β-lactone ring closing. The addition of an excess of isocyanate decreases selectivity for oxazinanedione, as it can accelerate the ring closing to β-lactone. Higher temperature and lower catalyst loading also result in decreased selectivity. Finally, the high pressure of CO is used to avoid the catalytic isomerization of epoxide to ketone that has been observed in other carbonylation systems at low CO pressures (Scheme 19).[22]

Selectivity for oxazinanedione also depends critically on the electrophilicity of the isocyanate. Electron-rich alkyl isocyanates react slowly with the aluminum alkoxide **31**, which permits the competitive, intramolecular ring closing to form β-lactones. More electron-deficient aryl isocyanates react faster with alkoxide **31**, diverting the ring-opened epoxide intermediate away from β-lactone formation and improving selectivity for the oxazinanedione. Thus, whereas most isocyanates react to form some oxazinanedione, the multicomponent coupling is most efficient using highly electrophilic aryl isocyanates with electron-withdrawing substituents (Scheme 76).[22]



Scheme 76

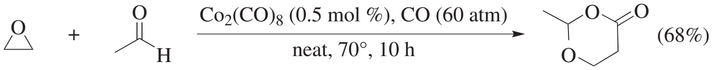
The epoxide component may include a much broader scope of starting materials than the isocyanate, and a number of pendant functional groups are tolerated (Scheme 77). Depending on the specific substrate, selectivity for oxazinanedione versus β-lactone varies, but is generally >10:1, and when using 4-nitrophenyl isocyanate, oxazinanedione is generally the only product observed. Epoxides with bulky substituents, such as 1,2-epoxy-3,3-dimethylbutane, give low conversion and poor selectivity for oxazinanedione and styrene oxide is inactive.[22] However, most of the epoxides that are active for carbonylation with Lewis acid cobaltate catalysts (see β-lactone section) are also expected to be active for the formation of oxazinanediones.



Scheme 77

Bicyclic and *cis*-disubstituted epoxides readily undergo carbonylation and trapping with isocyanates to afford the corresponding *trans*-oxazinanediones (Scheme 74). However, *trans*-disubstituted epoxides exhibit much lower activity, which may be due to the increased steric hindrance in forming the *cis*-product. Cyclohexene oxide does not carbonylate to form a β-lactone, due to the ring strain of *trans*-[4.2.0] bicyclic rings (Scheme 16), but it readily forms the much less strained *trans*-oxazinanedione (Scheme 74).[22]

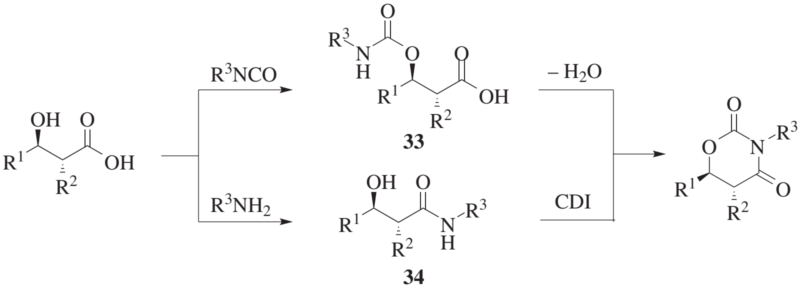
Although isocyanates are the only reagents that have been successfully employed, it is possible that other amphoteric electrophiles may be used to intercept the ring-opened intermediate **31** (Scheme 72) in epoxide carbonylation. These other electrophiles would result in new multicomponent coupling products via epoxide carbonylation. For example, a report in the patent literature describes the coupling of epoxide, CO, and aldehyde using a cobalt carbonyl catalyst (Scheme 78).[195]



Scheme 78

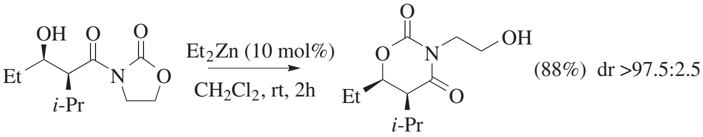
COMPARISON WITH OTHER METHODS

Oxazinanediones have been synthesized by a few methods, most often via a β-hydroxy acid derivative, commonly by reaction with a cyanate or an isocyanate to form intermediate **33** followed by cyclization (Scheme 79, top).[190,196−199] Formation of β-hydroxy amide **34**, followed by ring closing using a carbonyl equivalent such as carbonyl diimidazole (CDI) or diphosgene, also gives good yields of the products (Scheme 79, bottom).[191,200,201] Although these methods require two steps and necessarily generate byproducts, they have the advantage of being applicable to a broader range of substrates than epoxide carbonylation.



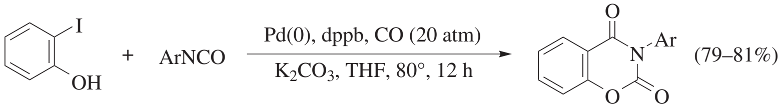
Scheme 79

The rearrangement of β-hydroxy-*N*-acyl-2-oxazolidinones is another route to oxazinanediones (Scheme 80).[202] This method is stereoselective and can produce highly stereo-enriched products. Additionally, the aldol reaction is a convenient method to access a large number of possible starting materials. This rearrangement is specific for the formation of *N*-(β-hydroxyalkyl)-substituted oxazinanediones, a class of products that is inaccessible via epoxide carbonylation.



Scheme 80

Carbonylation of iodophenols in the presence of isocyanates is a complementary method for oxazinanedione synthesis in that it forms benzo-fused products which are inaccessible via epoxide carbonylation (Scheme 81).[203] This method proceeds in good yields and is one of the few transition-metal-catalyzed multicomponent coupling reactions that involve incorporation of CO.[22] Benzo-1,3-oxazinane-2,4-diones have received attention as biologically active compounds.[191−194]



Scheme 81

The main advantages of epoxide carbonylation as a route to oxazinanediones are the availability of epoxides, the conservation of stereochemical purity, and its efficiency as a one-pot, atom-economical, multicomponent coupling reaction.

EPOXIDE CARBONYLATION TO 1,3-OXATHIOLAN-2-ONES

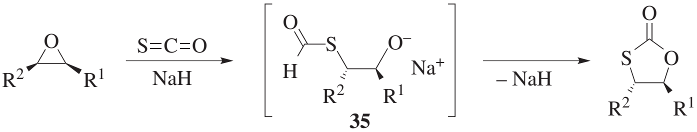
In most ring-expanding carbonylations of epoxides, CO is activated and introduced to the ring via coordination to a transition metal. In the case of epoxide carbonylation to 1,3-oxathiolan-2-ones, insertion of CO is mediated by sulfur, which is also incorporated into the expanded heterocycle.[55,56] Oxathiolanones have demonstrated some utility as synthetic intermediates.[204,205]

MECHANISM AND STEREOCHEMISTRY

The ring-expanding conversion of epoxides into oxathiolanones occurs by first reacting CO with elemental sulfur to generate carbonyl sulfide, which subsequently reacts with an epoxide to form the product. The mechanism of this transformation has not been fully elucidated, but a reaction pathway has been proposed.[55] Carbonyl sulfide is formed catalytically in the presence of base, and this reaction is facilitated by selenium (Scheme 82).[206] The authors propose that nucleophilic ring opening of the epoxide by thioformate results in inversion of the stereocenter bearing the inserted sulfur. Ring closing of the proposed alkoxide intermediate **35** forms the oxathiolane and regenerates the catalyst (Scheme 83).[55] A more plausible mechanism to this and related transformations involves the catalytic action of trace amounts of NaOH in the NaH.

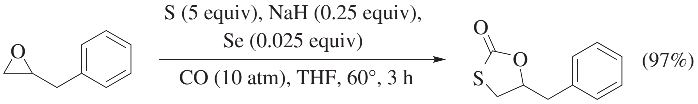
$$\mathrm{CO} \quad + \quad \mathrm{Se} \longrightarrow \mathrm{Se{=}C{=}O} \xrightarrow[-\,\mathrm{Se}]{\mathrm{S}} \mathrm{S{=}C{=}O}$$

Scheme 82



Scheme 83

Ring-opening inversion of the epoxide converts *cis*-epoxides into *trans*-oxathiolanones (Scheme 83), and *trans*-epoxides into *cis*-oxathiolanones. Nucleophilic attack occurs at the least hindered carbon of the epoxide, resulting in good site selectivity for product 1,3-oxathiolan-2-ones in which the 5-position is the most heavily substituted (Scheme 84).[55]

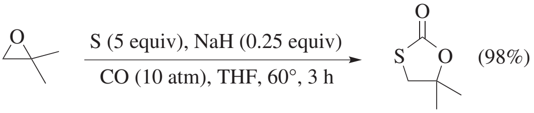


Scheme 84

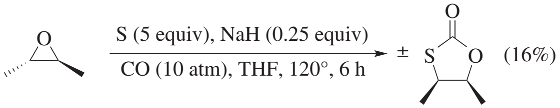
SCOPE AND LIMITATIONS

The carbonylation of epoxides in the presence of sulfur is catalyzed by a number of metal hydrides, as well as amines, such as 1,8-diazabicyclo[5.4.0]undec-7-ene. However, the choice of base is crucial for activity, and NaH gives the highest yields of oxathiolanones (the likely role of NaOH in these reactions, see above). Optimal conditions for this reaction include 5 equivalents of sulfur, 10 atm of CO, and a temperature of 60°. Decreasing the reaction temperature or equivalents of reagents results in lower yields. Using THF as the solvent provides the highest yield, whereas no product is formed in toluene or hexane. Though the cause remains unclear, addition of selenium sometimes catalyzes the reaction, increasing yields for substrates with aryl and benzyl groups but decreasing yields for all other substrates.[55]

Thus far, with the exception of phenyl glycidyl ether, only hydrocarbon-substituted epoxides have demonstrated reasonable activity for this carbonylation; other functional groups remain either unexamined or result in poor yields. The epoxide substitution pattern dramatically affects the yield. Monosubstituted and geminally disubstituted epoxides give high yields of products (Scheme 85),[55] but vicinally disubstituted epoxides are carbonylated in reduced yield. In particular, trisubstituted and *trans*-disubstituted epoxides give very poor yields (Scheme 86).[55]



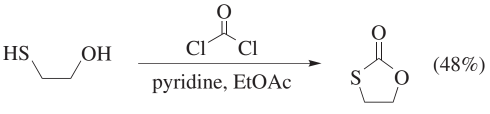
Scheme 85



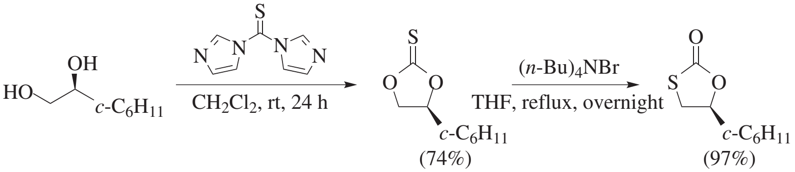
Scheme 86

COMPARISON WITH OTHER METHODS

A straightforward method for the formation of oxathiolanones is the condensation of a β-hydroxythiol with a carbonyl equivalent such as phosgene;[205] however, this pathway is undesirable because it requires the synthesis and handling of malodorous thiols as well as hazardous phosgene (Scheme 87). Other less hazardous carbonyl equivalents, such as ethylene carbonate[207] or ethyl chloroformate,[208,209] have been used in a few examples. A more practical method may be the condensation of a diol with a thiocarbonyl equivalent such as thiophosgene[210] or thiocarbonyldiimidazole,[204,211] followed by a catalyzed rearrangement (Scheme 88).[211] Diols are an attractive starting material, as they are less noxious and excellent methods for their stereoselective synthesis are available.[139]

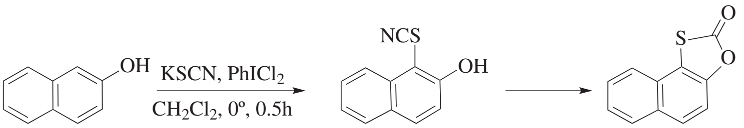


Scheme 87



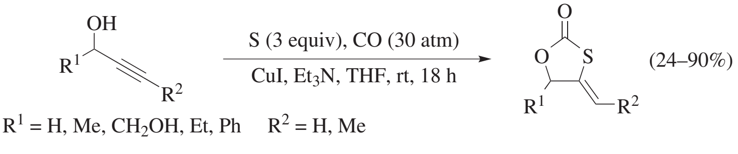
Scheme 88

Benzo-fused oxathiolanones, which cannot be synthesized directly from epoxides, can be formed by the methods discussed above, as well as by a few reactions that are specific to aromatic substrates.[212,213] For example, benzo-oxathiolanones can be synthesized from phenols and potassium thiocyanate (Scheme 89).[214]



Scheme 89

A major advantage of the epoxide carbonylation method is that elemental sulfur is easy to handle and carbonyl sulfide is formed in situ. In a similar reaction, alkynols can be used in place of epoxides to yield analogous products (Scheme 90).[215,216]



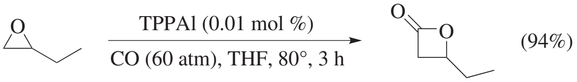
Scheme 90

EXPERIMENTAL CONDITIONS

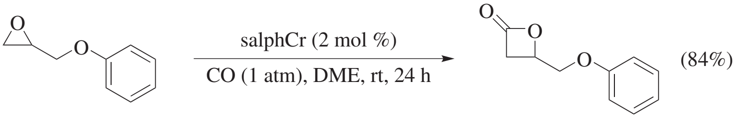
As discussed throughout this chapter, the optimal conditions for epoxide carbonylation reactions are quite diverse. However, one consistent feature to all reactions is that the various catalysts are sensitive to water and O_2. To avoid catalyst decomposition and the occurrence of side reactions, carbonylations are performed in dry reactors using solvents and reagents that have been thoroughly dried and degassed. This restriction likely necessitates the use of a drybox for preparing the reactions, though standard Schlenk techniques can be employed as well.

The reagents required for the carbonylation of epoxides can be hazardous if handled improperly. Epoxides, and particularly the low boiling ones, are highly toxic and as such should only be used in fume hood. Carbon monoxide is a highly toxic gas that is both invisible and odorless. All manipulations involving CO must be performed in a well-ventilated fume hood equipped with a working CO detector. Finally, there is an inherent risk involving any reaction run under elevated pressures. The proper equipment should always be employed (see manufacturer's specifications for pressure ratings), and reactors under pressure should be equipped with a pressure-release device and shielded at all times.

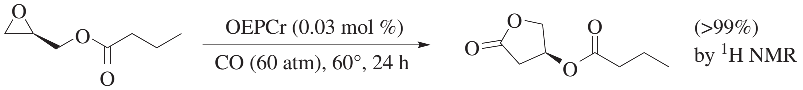
EXPERIMENTAL PROCEDURES



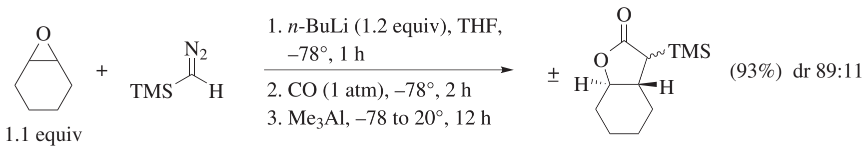
β-Valerolactone [Epoxide Carbonylation to a β-Lactone at High CO Pressure].[81] In a nitrogen-filled drybox, a 300 mL stainless steel Parr reactor was charged with TPPAl (38 mg, 35 μmol), 1,2-epoxybutane (30-mL, 0.35 mol), and THF (30 mL). The reactor was removed from the drybox and pressured with CO (60 atm), followed by rapid stirring and slow heating to 80°. After 3 h, the reactor was cooled on dry ice and carefully vented. The reaction mixture was rinsed out of the reactor and solvent was removed by rotary evaporation. Vacuum distillation gave the product as a clear colorless oil (33 g, 94%): IR 1825 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.44 (dddd, $^3J = 4.3, 5.8, 5.9, 7.0$ Hz, 1H), 3.47 (dd, $^3J = 5.8$ Hz, $^2J = 16.3$ Hz, 1H), 3.03 (dd, $^3J = 4.3$ Hz, $^2J = 16.3$ Hz, 1H), 1.81 (m, 2H), 0.99 (t, $^3J = 7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.53, 72.38, 42.39, 27.75, 8.93.



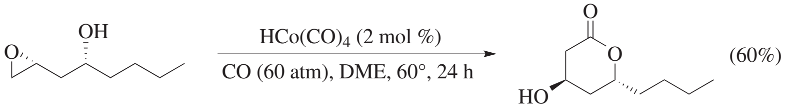
4-Phenoxymethyl-2-propiolactone [Epoxide Carbonylation to a β-Lactone at Low CO Pressure].[18] In a drybox, salphCr (182 mg, 0.200 mmol) was weighed into a 500-mL, oven-dried, three-neck round-bottomed flask with a magnetic stir bar. A dry, 50-mL addition funnel was attached, along with a stopper and a rubber septum. DME (9.0 mL) was drawn into a Gastight syringe while phenyl glycidyl ether (1.50 g, 10.0 mmol) was drawn into a separate syringe with 1.0 mL DME. The flask was removed to a fume hood where the flask was sparged with CO for 10 min before a double balloon of CO was attached to the flask using a needle to puncture the septum. The flask was then placed into an ice bath, the DME was added to the catalyst, and the mixture was stirred for 10 min. The epoxide solution was added dropwise at 0° via the addition funnel over the course of 30 min while stirring. After epoxide addition was complete, the ice bath was removed and the flask was allowed to warm to rt and the mixture was stirred for 24 h. The flask was vented in a fume hood and the reaction mixture was concentrated under vacuum to an oil. The crude oil was purified by chromatography through silica gel with CH_2Cl_2, and then was recrystallized from CH_2Cl_2/hexanes to afford 4-phenoxymethyl-2-propiolactone (1.5 g, 84%): mp 75–77°; IR (neat, NaCl) 1818 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.31 (t, $^3J = 7.9$ Hz, 2H), 7.00 (t, $^3J = 7.3$ Hz, 1H), 6.92 (d, $^3J = 8.2$ Hz, 2H), 4.83 (dddd, $^3J = 3.0, 4.4, 5.1, 9.5$ Hz, 1H), 4.32 (dd, $^2J = 11.1$ Hz, $^3J = 3.0$ Hz, 1H), 4.19 (dd, $^2J = 11.1$ Hz, $^3J = 4.2$ Hz, 1H), 3.55 (d, $^3J = 5.1$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 158.1, 129.8, 121.8, 114.8, 68.5, 67.3, 40.0; HRMS (EI) *m*/*z*: calcd for $C_{10}H_{10}O_3$, 178.0630; found, 178.0630.



(*S*)-β-Butyroxy-γ-butyrolactone [Epoxide Carbonylation to a γ-Lactone].[28] In a nitrogen-filled drybox at rt, a 4-mL glass vial equipped with a stir bar was charged with OEPCr (9.0 mg, 12 μmol) and (*R*)-glycidyl butyrate (515 mg, 3.57 mmol). The vial was transferred to a stainless steel high-pressure reactor. The reactor was pressured with CO (60 atm) and heated to 60° with stirring. The temperature was held constant for 6 h, at which point the reactor was placed in dry ice for 15 min. After careful venting of excess CO, the glass vial was removed and the mixture was analyzed by ^1H NMR (>99% product). Separation of product from catalyst was accomplished by filtering through a short column of silica gel with $CHCl_3$: IR (neat, KCl) 1789 (C=O), 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.40 (dd, $^3J = 5, 7$ Hz, 1H), 4.48 (dd, $^3J = 5$ Hz, $^2J = 11$ Hz, 1H), 4.31 (d, $^2J = 11$ Hz, 1H), 2.84 (dd, $^3J = 7$ Hz, $^2J = 18$ Hz, 1H), 2.55 (d, $^2J = 18$ Hz, 1H), 2.28 (t, $^3J = 7$ Hz, 2H), 1.61 (sext, $^3J = 7$ Hz, 2H), 0.91 (t, $^3J = 7$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.9, 173.2, 73.4, 69.8, 36.0, 34.8, 18.4, 13.8; HRMS (EI) *m*/*z*: calcd for $[C_8H_{12}O_4 + H]^+$, 173.0814; found, 173.0812.

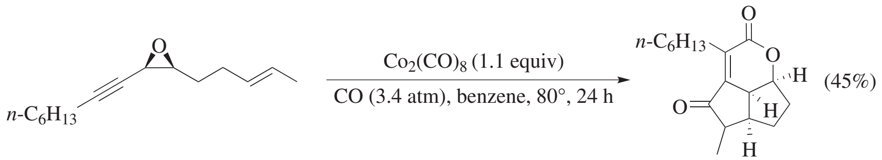


3-(Trimethylsilyl)hexahydrobenzofuran-2(3*H*)-one [Epoxide Carbonylation to a γ-Lactone Using an Ynolate].[45] A 30-mL, round-bottomed flask equipped with a magnetic stir bar, three-way stopcock, and a nitrogen line was flame dried under a stream of nitrogen. In the reaction flask were placed anhydrous THF (10 mL) and a 2 M hexane solution of trimethylsilyldiazomethane (1 mL, 2 mmol), and the solution was cooled to −78°. A 1.5 M hexane solution of BuLi (1.6 mL, 2.4 mmol) was added dropwise to the solution, which was stirred for 1 h. The three-way stopcock was then connected to a vacuum line and to a balloon of CO through a glass column packed with soda lime and anhydrous calcium sulfate. After two cycles of evacuation and refilling with CO, the reaction mixture was stirred under an atmosphere of CO for 2 h at −78°. A hexane solution of Me_3Al (1.1 mL) was added to the solution of ynolate, which was then warmed to 0° and stirred for 1 h. The solution was cooled to −78° for addition of cyclohexene oxide (215 mg, 2.2 mmol), then gradually warmed to 20° and stirred for 12 h. The resulting mixture was quenched with saturated aqueous NH_4Cl (2.0 mL) at −78°. The solution was filtered through Celite 545, and the residue was washed with Et_2O (2 × 20 mL). The filtrate was washed with saturated aqueous NH_4Cl (20 mL), and the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined ether solutions were dried over anhydrous K_2CO_3, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 15:1, R_f = 0.09, 0.06) to give a mixture of diastereomers (89:11) as a white solid (93%), mp 39–42°. The isomers were separated by HPLC. Major isomer (R_f = 0.09): IR (KBr) 1759 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.65 (td, ^3J = 10.8, 3.5 Hz, 1H), 2.25–1.20 (m, 10H), 0.15 (s, 9H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 178.65, 85.52, 46.88, 36.71, 30.05, 29.24, 25.59, 24.10, −2.33. Minor isomer (R_f = 0.06): IR (KBr) 1744 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.82 (td, ^3J = 10.5, 3.8 Hz, 1H), 2.40–2.15 (m, 3H), 2.00–1.20 (m, 7H), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 178.71, 83.25, 47.73, 38.49, 30.84, 28.45, 25.73, 23.99, −0.63. Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.33; H, 9.71.

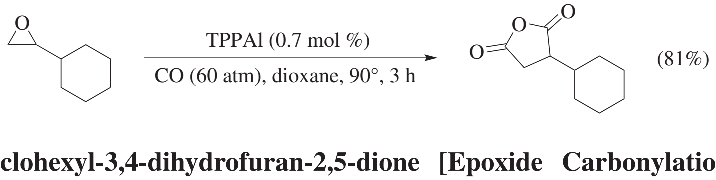


(4*R*,6*R*)-6-Butyl-4-hydroxytetrahydro-2-pyranone [Epoxide Carbonylation to a δ-Lactone].[24] In a drybox, $Ph_3SiCo(CO)_4$[69] (52 mg, 0.12 mmol) and 4-toluenesulfonic acid (21 mg, 0.12 mmol) were weighed into separate flame-dried vials. DME (6.0 mL) was divided evenly into the vials to completely dissolve the catalyst components, then the two solutions were combined to form a colorless solution of $HCo(CO)_4$ (6 mL, 0.02 M in DME). In a drybox an 8-mL vial was charged with (2*R*,4*R*)-4-hydroxy-1,2-epoxyoctane (140 mg, 1.0 mmol) and a magnetic stir bar. A portion of the freshly prepared $HCo(CO)_4$ solution (1.0 mL, 0.02 M in DME) was transferred to the vial via syringe. The vial was transferred to a stainless-steel reactor and pressured with CO (60 atm) and heated at 60° with stirring. After 24 h, the reactor was cooled in dry ice for 10 min then vented in a well-ventilated fume hood. The mixture was concentrated to an oil under vacuum, and the crude product was passed through silica gel, first using hexanes/EtOAc

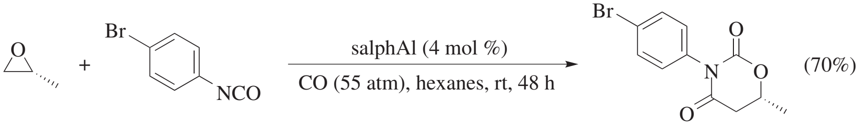
(70:30) to remove catalyst residue, then with EtOAc/hexanes (70:30) to elute (4*R*,6*R*)-6-butyl-4-hydroxy-δ-lactone (103 mg, 60%): $[\alpha]^{23}_{D}$ + 32.6 (*c* 1.0, $CHCl_3$); IR (neat, NaCl) 3423 (OH), 1719 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.67 (dddd, ^3J = 3.1, 5.1, 7.5, 11.1 Hz, 1H), 4.37–4.30 (m, 1H), 2.97 (d, ^3J = 3.3 Hz, 1H), 2.68 (dd, ^3J = 4.8 Hz, ^2J = 17.7 Hz, 1H), 2.58 (ddd, ^4J = 1.6 Hz, ^3J = 3.6 Hz, ^2J = 17.7 Hz, 1H), 1.95 (dddd, ^4J = 1.6 Hz, ^3J = 4.8 Hz, 3.3 Hz, ^2J = 14.4 Hz, 1H), 1.76–1.24 (m, 7H), 0.89 (t, ^3J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.45, 76.34, 62.65, 38.74, 35.94, 35.33, 27.11, 22.61, 14.09; HRMS (EI) *m*/*z*: calcd for $C_9H_{16}O_3$, 172.1100; found, 172.1102.



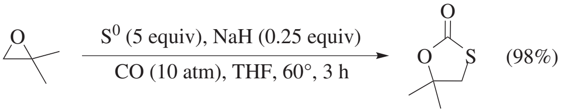
***rel*-(5a*S*, 7a*R*, 7b*R*)-3-Hexyl-5-methyl-2,4,5,5a,6,7,7a,7b-octahydropentaleno[1,6,*bc*]pyran-2,4-dione [Epoxide Carbonylation to a Fused δ-Lactone].**[46] To a benzene solution (5 mL) of the epoxy enyne (100 mg, 0.45 mmol; see footnote a in Table 3B) was added $Co_2(CO)_8$ (170 mg, 0.50 mmol) under nitrogen, and the mixture was stirred for 2 h at rt. The solution was transferred to a high-pressure reactor and heated to 80° under CO (3.4 atm) for 24 h. The solution was filtered through a short silica pad; the filtrate was concentrated and purified using preparative TLC (silica gel, Et_2O/hexane, 1:1) to afford the title product (56 mg, 45%): IR (neat) 1722, 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.08 (q, ^3J = 8.0 Hz, 1H), 3.36 (t, ^3J = 6.8 Hz, 1H), 2.91–2.81 (m, 1H), 2.64–2.57 (m, 1H), 2.97–2.03 (m, 1H), 2.35–2.20 (m, 2H), 2.02–1.85 (m, 2H), 1.49–1.12 (m, 8H), 1.14 (d, ^3J = 7.6 Hz, 3H), 1.18–0.98 (m, 1H), 0.83 (t, ^3J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.0, 163.7, 141.8, 136.0, 81.3, 50.8, 43.1, 40.4, 31.4, 30.6, 29.6, 29.3, 29.2, 25.8, 22.5, 17.3, 14.0; HRMS *m*/*z*: calcd for $C_{17}H_{24}O_3$, 276.1725; found, 276.1722.



3-Cyclohexyl-3,4-dihydrofuran-2,5-dione [Epoxide Carbonylation to a Succinic Anhydride].[21] A 100-mL, stainless-steel Parr reactor was dried overnight at 120° under vacuum. In a nitrogen drybox, the reactor was charged with TPPAl (262 mg, 0.240 mmol) and 1,4-dioxane (20 mL), then closed and removed from the drybox. The reactor was pressured with CO (14 atm), and the contents were stirred for 10 min to dissolve CO into solution, then the reactor was vented down to 1.5 atm without stirring. 2-Cyclohexyloxirane (4.88 mL, 36.0 mmol) was injected via syringe into the CO-filled reactor at rt, and the reactor was immediately pressured to 60 atm of CO, followed by rapid stirring and heating to 90°. After 3 h, the reactor was placed on dry ice, cooled to below 0°, and slowly vented. Volatiles were removed under vacuum, and the resulting oil was vacuum distilled to afford a clear oil that solidified on standing. Recrystallization from Et_2O/hexanes yielded the crystalline product (5.32 g, 81%): mp 36°; IR (melt, NaCl) 1861 (C=O), 1785 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.00 (m, 2H), 2.74 (m, 1H), 1.90 (m, 1H), 1.78 (m, 3H), 1.69 (m, 1H), 1.58 (m, 1H) 1.36–0.95 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.14, 170.70, 46.50, 39.12, 31.36, 30.34, 28.47, 26.07, 25.88; HRMS (EI) *m/z*: calcd for $C_{10}H_{14}O_3$, 182.0943; found, 182.0945.



(*R*)-3-(4-Bromophenyl)-6-methyl-1,3-oxazinane-2,4-dione [Epoxide Carbonylation to a 1,3-Oxazinane-2,4-dione].[22] A 60-mL, stainless steel, high-pressure Parr reactor was dried at 120° under vacuum for 16 h, refilled with N_2, and brought into a nitrogen drybox. In the drybox, salphAl (43.7 mg, 0.050 mmol) was weighed into an oven-dried glass insert, and a stir bar was added. Dry hexanes (5.0 mL), (*R*)-propylene oxide (88.0 μL, 1.26 mmol), and 4-bromophenyl isocyanate (248 mg, 1.5 mmol) were added. The reactor was sealed, removed from the drybox, and pressured with CO (55 atm). After stirring the mixture at rt for 48 h, the reactor was vented slowly. Volatiles were removed by rotary evaporation, and the resulting solid was washed through silica gel with EtOAc to remove catalyst residue. The filtrate was concentrated under reduced pressure, then redissolved in CH_2Cl_2, and layered with hexanes to afford the crystalline product (0.250 g, 70%): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.59 (pseudo-d, 2H), 7.07 (pseudo-d, 2H), 4.81 (m, 1H), 2.94 (dd, $^2J = 17.1$ Hz, $^3J = 6.3$ Hz, 1H), 2.81 (dd, $^2J = 17.1$ Hz, $^3J = 11.1$ Hz, 1H), 1.56 (d, $^3J = 6.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.9, 151.2, 133.7, 132.8, 130.2, 123.3, 71.3, 38.6, 20.4; HRMS (EI) *m/z*: calcd for $C_{11}H_{10}NO_3{}^{79}Br$, 282.9831; found, 282.9834; calcd for $C_{11}H_{10}NO_3{}^{81}Br$, 284.9824; found, 284.9825.



5,5-Dimethyl-1,3-oxathiolan-2-one [Epoxide Carbonylation to a 1,3-Oxathiolan-2-one].[55] In a 50-mL stainless steel autoclave were placed powdered sulfur (0.321 g, 10 mmol), THF (2 mL), isobutylene oxide (144 mg, 2 mmol), and NaH (24 mg in mineral oil, 0.5 mmol). The apparatus was flushed several times with CO and then was charged with 10 atm of CO. The mixture was heated with stirring at 60° for 3 h. The reaction was quenched with water and the resulting mixture was extracted with diisopropyl ether (15 × 3 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (hexane/EtOAc, 3:1) gave the title product as a yellow oil (282 mg, 98%): IR (neat) 2981, 2937, 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.38 (s, 2H), 1.58 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.66, 85.38, 42.43, 26.45; MS *m/z*: M^+ 132. Anal. Calcd for $C_5H_8O_2S$: C, 45.43; H, 6.10; S, 24.26. Found: C, 45.27; H, 6.21; S, 24.35.

TABULAR SURVEY

To remain consistent with the organization of this chapter, the following tabular survey of ring expanding carbonylation reactions is organized according to the heterocyclic products formed. However, several of the tables are further divided by substrates or reaction conditions in the cases where significantly dissimilar conditions are utilized to produce the same class of products. Within each table the entries are organized by increasing carbon count for the epoxide substrate, but the following groups are not included in the carbon count: typical protecting groups, simple alkyl ethers, the OR group of esters, the NR_2 group of amides, and carbon-bound silyl groups. In situations where many procedures have been employed to produce the same products, the catalyst (including catalyst loading) is highlighted to emphasize the different selectivity and activity obtained using each procedure. The tabular survey includes reactions reported up through 2008. References appearing after 2008 are listed at the end of the bibliography, organized by table.

The following abbreviations (excluding those listed in "*The Journal of Organic Chemistry* Standard Abbreviations and Acronyms") are used within the Tabular Survey:

CDI	1,1′-carbonyldiimidazole
CF_3TPPAl	[(tetrakis(4-trifluoromethylphenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
Cp_2Ti	$[Cp_2Ti(THF)_2]^+[Co(CO)_4]^-$
CTAB	cetyltrimethylammonium bromide
1,2-DFB	1,2-difluorobenzene
2,5-DMTHF	2,5-dimethyltetrahydrofuran (*cis/trans* mixture)
FTPPAl	[(tetrakis(4-fluorophenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
HTPPAl	[(tetrakis(phenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
MeTPPAl	[(tetrakis(4-methylphenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
OEP	octaethylporphyrin
OEPCr	[(OEP)Cr$(THF)_2]^+[Co(CO)_4]^-$
PPN	bis(triphenylphosphine)iminium
salph	*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-phenylenediamine
salphAl	[(salph)Al$(THF)_2]^+[Co(CO)_4]^-$
salphCr	[(salph)Cr$(THF)_2]^+[Co(CO)_4]^-$
TDA-1	tris(poly-oxaheptyl)amine
TMTU	*N,N′*-tetramethylthiourea
TPP	tetraphenylporphyrin
TPPAl	[(tetrakis(4-chlorophenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
TPPCr	[(TPP)Cr$(THF)_2]^+[Co(CO)_4]^-$

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES

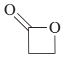
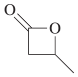
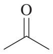
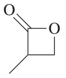
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_2				
	$[PPN]^+[Co(CO)_4]^-$ (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), DME, 80°, 24 h	 (—), 44	36
C_3				
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96) +  **II** (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 63	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	$Co(acac)_3$ (0.6 mol %), $AlEt_3$ (0.6 mol %)	CO (90 atm), 105°, 48 h	**I** (25)	33
	$[PPN]^+[Co(CO)_4]^-$ (0.6 mol %), BF_3•OEt_2 (0.6 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (79)	32
	$[PPN]^+[Co(CO)_4]^-$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (60)	32
	$NaCo(CO)_4$ (1.2 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (10)	32
	$NaCo(CO)_4$ (1.2 mol %), Et_2AlCl (1.2 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (64)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (92)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 95°, 1.5 h	**I** (92)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 105°, 0.5 h	**I** (91)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (1.2 mol %)	CO (60 atm), diglyme, 75°, 5 h	**I** (96)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (92)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 75°, 5 h	**I** (93)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 95°, 2 h	**I** (92)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 95°, 4 h	**I** (92)	32
	$Co_2(CO)_8$ (0.3 mol %), $AlMe_3$ (1.3 mol %)	CO (60 atm), diglyme, 75°, 10 h	**I** (92)	33
	$Co_2(CO)_8$ (0.2 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 95°, 7 h	**I** (94)	33
	$Co_2(CO)_8$ (0.08 mol %), $AlMe_3$ (0.3 mol %)	CO (60 atm), diglyme, 95°, 16 h	**I** (72)	32, 33
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	**I** (95)	35
	$NaCo(CO)_4$ (2 mol %)	CO (70 atm), triglyme, 80°, 16 h	**I** (6)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (95)	34
	$RhClCO(PPh_3)_2$ (1 mol %)	CO (30 atm), MeOH, 20°, 170 h	**I** (5)	41
	$RhClCO(PPh_3)_2$ (0.5 mol %)	CO (30 atm), MeOH, 110°, 14 h	**I** (4)	41
	$[PPN]^+[Co(CO)_4]^-$ (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (64)	36
	$[PPN]^+[Co(CO)_4]^-$ (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (77)	36
	$[PPN]^+[Co(CO)_4]^-$ (1 mol %), $B(C_6F_5)_3$ (1 mol %)	CO (60 atm), DME, 80°, 7 h	**I** (68) +  (17)	36
	$Co_2(CO)_8$ (5 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (7)	36
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (x mol %)	CO (60 atm), DME, 80°, 24 h	**I** *x* 1 (13) 2 (11)	36

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

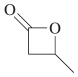
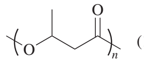
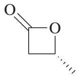
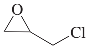
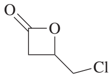
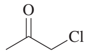
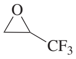
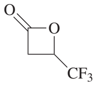
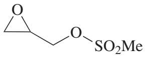
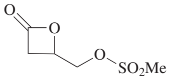
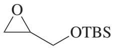
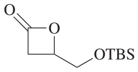
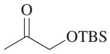
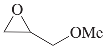
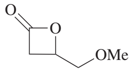
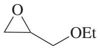
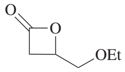
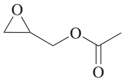
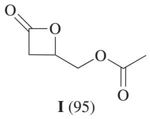
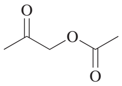
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_3				
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), THF, 80°, 24 h	 **I** (35)	36
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), dioxane, 80°, 24 h	**I** (11)	36
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), benzene, 80°, 24 h	**I** (<5)	36
	$Co_2(CO)_8$ (1 mol %), PPNCl (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (76)	36
	$Co_2(CO)_8$ (1 mol %), CTAB (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (23) +  (15)	36
 er 99.5:0.5	salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	 **I** (95) er 99.5:0.5	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (95) er 99.5:0.5	34
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	 **I** (98)	26
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (31) +  (4)	26
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 9.5 h	**I** (73)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 5 h	**I** (60)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (83)	36
	salphCr (2 mol %)	CO (7 atm), DME, rt	 Time (h) 8 (26) 48 (87)	19 23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (37)	23
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 +  **I** (96) **II** (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (98)	26
	OEPCr (0.06 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (30)	29
	OEPCr (0.13 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
	TPPAl (0.1 mol %)	CO (60 atm), THF, 50°, 2 h	 (99)	83
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 +  **I** (95) (5)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 82	18
	OEPCr (0.3 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (99)	28

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

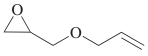
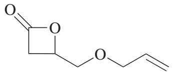
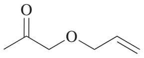
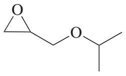
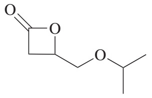
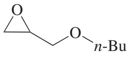
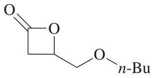
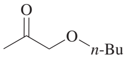
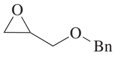
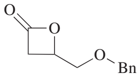
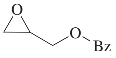
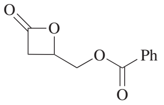
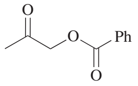
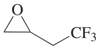
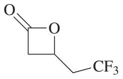
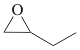
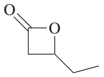
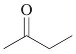
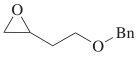
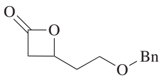
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_3				
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (91), 75 +  **II** (9)	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	18
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (93) + **II** (7)	18
	OEPCr (0.4 mol %)	CO (60 atm), toluene, 60°, 6 h	**I** (88)	28
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $BF_3{\bullet}OEt_2$ (4 mol %)	CO (60 atm), DME, 80°, 48 h	 (—), 86	36
	salphCr (2 mol %)	CO (7 atm), DME, 80°, 0.01 h	 **I** (99), 98	81
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (99), 88	26
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (89) +  (11)	26
	OEPCr (0.04 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 99	18
	OEPCr (0.1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (85) +  (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (98)	26
	OEPCr (0.4 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (97)	28
C_4				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99)	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (97) +  (3)	26
	TPPAl (0.01 mol %)	CO (60 atm), THF, 80°, 2 h	**I** (99)	21
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (98)	26
	salphAl (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (46)	26
	TPPCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (66)	26
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (60)	29
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 2.5 h	**I** (99)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (99)	34
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1.5 h	 (99)	23

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

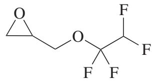
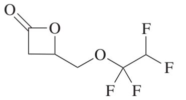
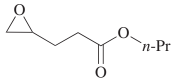
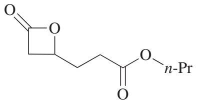
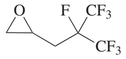
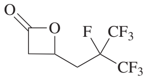
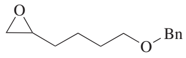
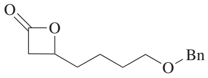
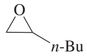
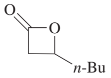
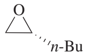
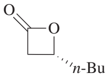
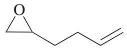
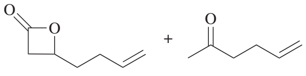
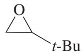
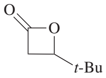
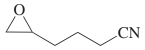
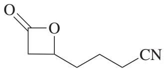
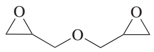
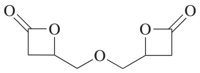
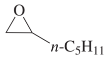
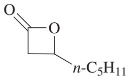
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_5				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 79	19
	OEPCr (0.07 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
C_6				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (—)	19
	salphCr (2 mol %)	CO (7 atm), DME, rt, 20 h	 (99)	23
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 93	18
	OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	$[PPN]^+[Co(CO)_4]^-$ (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (—), 66	36
 er 99.5:0.5	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 92 er 99.5:0.5	18
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (95) (5)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 94	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (90)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (—), 63	36
	OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (99)	28
	TPPCr (0.1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	TPPAl (0.2 mol %)	CO (60 atm), THF, 60°, 6 h	 (—)	21
	salphCr (2 mol %)	CO (7 atm), DME, rt, 3 h	 (—)	23
C_7				
	OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (40)	29

TABLE 1A. β–LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

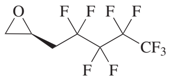
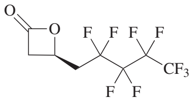
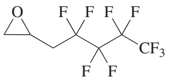
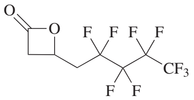
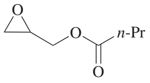
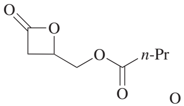
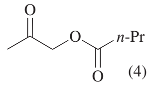
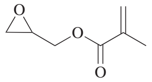
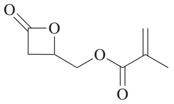
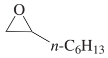
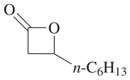
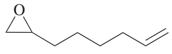
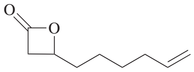
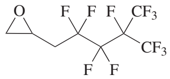
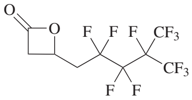
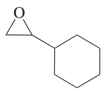
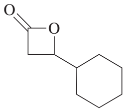
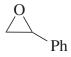
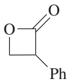
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_7				
 er 99.5:0.5	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 88, er 99.5:0.5	19
	salphCr (2 mol %)	CO (55 atm), DME, rt, 6 h	 **I** (99)	19
	salphCr (2 mol %)	CO (30 atm), DME, rt, 6 h	**I** (99)	19
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 85	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (44)	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (36)	19
	salphCr (1 mol %)	CO (7 atm), toluene, rt, 3 h	**I** (18)	19
	salphCr (1 mol %)	CO (7 atm), 1,2-DFB, rt, 3 h	**I** (46)	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (9)	19
	salphCr (1 mol %)	CO (7 atm), 2,5-DMTHF, rt, 3 h	**I** (47)	19
	salphCr (1 mol %)	CO (7 atm), dioxane, rt, 3 h	**I** (43)	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96), 70 +  (4)	18
	OEPCr (0.2 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (99)	28
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1 h	 (91)	23
C_8				
	$[PPN]^+[Co(CO)_4]^-$ (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), DME, 80°, 24 h	 (—), 77	36
	TPPAl (0.1 mol %)	CO (60 atm), THF, 60°, 6 h	 **I** (—)	21
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (—), 87	36
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 91	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 92	18
	TPPAl (0.5 mol %)	CO (60 atm), THF, 50°, 50 h	 **I** (—)	21
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (25 atm), MeOH, 110°, 20 h	**I** (—), 67	41
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (95 atm), MeOH, 110°, 20 h	**I** (3)	41
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (95 atm), MeOH, 110°, 2 h	**I** (3)	41

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

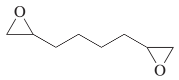
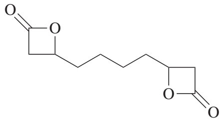
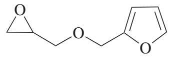
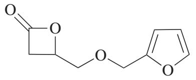
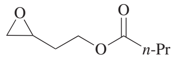
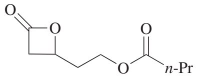
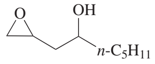
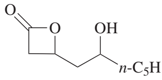
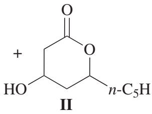
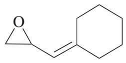
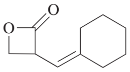
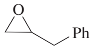
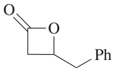
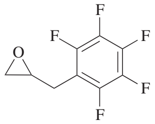
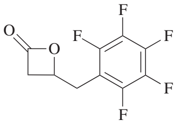
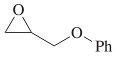
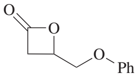
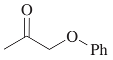
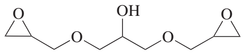
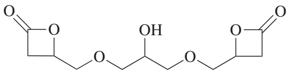
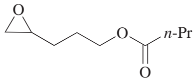
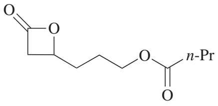
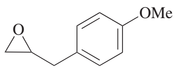
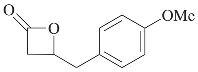
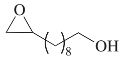
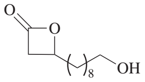
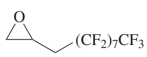
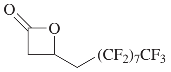
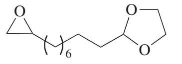
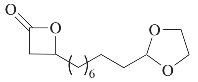
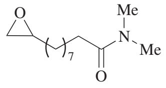
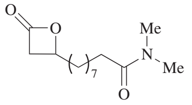
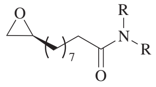
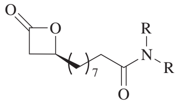
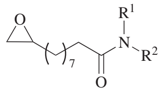
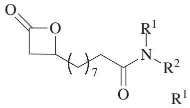
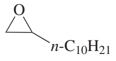
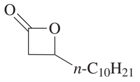
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C$_8$				
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 86	18
	salphCr (2 mol %)	CO (7 atm), DME, rt, 2 h	**I** (99)	23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 23 h	 **I** (99)	23
	OEPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
C$_9$				
	Catalyst (2 mol %)	CO (55 atm), DME, 60°, 24 h	 **I** +  **II** **I + II** (—) Catalyst **I/II** HCo(CO)$_4$ 1:99 Cp$_2$Ti 17:83 salphAl 27:73 Co$_2$(CO)$_8$ 33:67 HTPPAl 42:58 TPPCr 67:33 salphCr 84:16	24
	—	1. Fe(CO)$_5$, *hν*, benzene, rt, 6 h 2. CAN, MeCN, –78°	 (—)^a	40
	TPPAl (0.1 mol %)	CO (60 atm), THF, 60°, 18 h	 (99)	81
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 82	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96), 86 +  (4)	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 96	18
	TPPAl (0.03 mol %)	CO (60 atm), THF, 75°, 15 h	 (95)	81
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1.5 h	 (99)	23
C$_{11}$				
	TPPAl (0.5 mol %)	CO (60 atm), THF, 90°, 3 h	 (—)	83
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 71	19

Table 1A. β-Lactones from Monosubstituted Epoxides (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_{11}				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 2.5 h	 (99)	23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 3 h	 **I** (73)	23
	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	salphCr (2 mol %)	CO (60 atm), DME, 60°, 6 h	 R Me (99) *i*-Pr (99)	24
	salphCr (2 mol %)	CO (7 atm), DME, rt, 24 h	 R^1 R^2 H *c*-C_6H_{11} (71) *i*-Pr *i*-Pr (85)	23
C_{12}				
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (99), 93	18, 26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	OEPCr (0.01 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (10)	29

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[a] The β-lactone product was not stable enough to be characterized, so it was reduced to the diol with $LiAlH_4$ for characterization.

Table 1B. β-Lactones from Disubstituted Epoxides

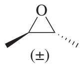
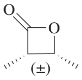
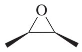
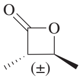
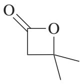
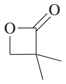
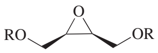
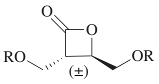
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 8 h	 **I** (98)	26
	OEPCr (0.2 mol %)	CO (60 atm), toluene, 60°, 6 h	**I** (88)	28
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 20 h	**I** (99)	30
	TPPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (56)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 10 h	**I** (99)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $B(C_6F_5)_3$ (4 mol %)	CO (60 atm), DME, 110°, 48 h	**I** (—), 20	36
	salphAl (1 mol %)	CO (60 atm), neat, 75°, 7.5 h	 **I** (40)	30
	TPPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (56)	29
	salphAl (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (20)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 10 h	**I** (75)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $B(C_6F_5)_3$ (4 mol %)	CO (60 atm), DME, 110°, 48 h	**I** (24)	36
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	 **I** (83) +  **II** (7)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 50°, 3 h	**I** (72) + **II** (18)	34
	TPPAl (1 mol %)	CO (60 atm), THF, 2 h	 R Temp (°) TBS 60 (95), 63 Bn 60 (95) Bz 30 (90), 48	20 81 20

TABLE 1B. β-LACTONES FROM DISUBSTITUTED EPOXIDES (*Continued*)

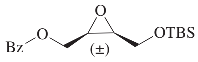
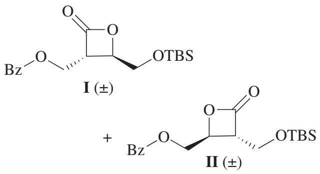
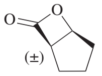
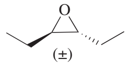
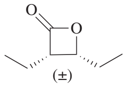
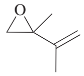
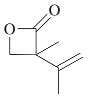
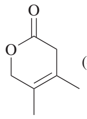
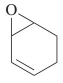
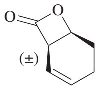
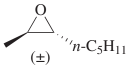
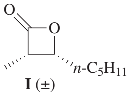
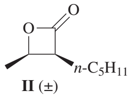
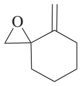
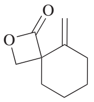
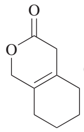
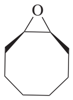
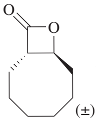
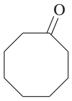
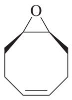
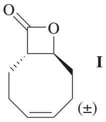
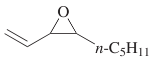
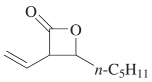
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4 	TPPAl (2 mol %)	CO (50 atm), THF, 40°, 24 h	 **I** + **II** (95), **I**/**II** = 1:1	81
C_5 	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 24 h	 (99)	28
C_6 	TPPAl (1 mol %)	CO (60 atm), THF, 50°, 24 h	 (—)	21
	—	1. $Fe(CO)_5$, *hν*, benzene, rt, 6 h 2. CAN, MeCN, rt, 16 h	 (—), 42 +  (—), 16	40
	—	1. $Fe(CO)_5$, *hν*, benzene, rt, 6 h 2. CAN, EtOH, –5°	 (—), 28	40
C_8 	TPPAl (0.5 mol %)	CO (60 atm), THF, 50°, 24 h	 +  **I** + **II** (99), **I**/**II** = 50:50	83
	—	1. $Fe(CO)_5$, *hν*, benzene, rt, 6 h 2. CAN, MeCN, –5°, 16 h	 (—), 15 +  (—), 55	40
	salphCr (1 mol %)	CO (7 atm), DME, 60°, 24 h	 **I** (94) +  (3)	26
	OEPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (10)	29
	salphCr (2 mol %)	CO (7 atm), DME, rt, 24 h	 **I** (20)	23
	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.6 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (20)	29
C_9  (±) cis/trans	—	1. $Fe(CO)_5$, *hν*, benzene, rt, 6 h 2. CAN, MeCN, –30°	 (—), 68 (±) cis/trans	40

TABLE 1B. β-LACTONES FROM DISUBSTITUTED EPOXIDES (*Continued*)

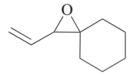
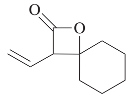
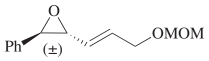
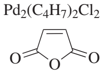
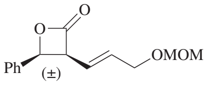
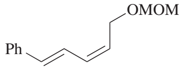
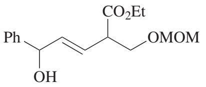
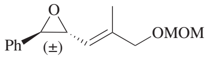
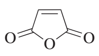
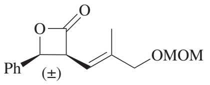
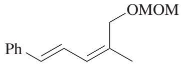
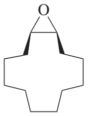
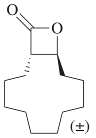
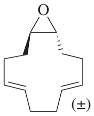
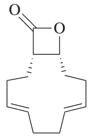
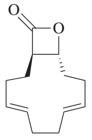
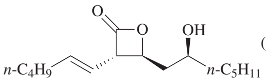
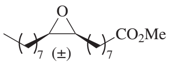
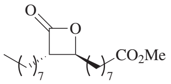
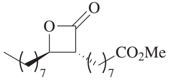
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_9 	—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –5°	 (—), 52	40
C_{11} 	$Pd_2(C_4H_7)_2Cl_2$ (5 mol %),  (10 mol %)	CO (30 atm), NaBr, (i-Pr)$_2$NEt, EtOH, rt, 12 h	 (—), 14 +  (—), 44 +  (—), 12	38
C_{12} 	$Pd_2(C_4H_7)_2Cl_2$ (5 mol %),  (10 mol %)	CO (30 atm), NaBr, (i-Pr)$_2$NEt, EtOH, rt, 12 h	 (—), 9 +  (—), 55	38
 66% *cis*	OEPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (66) 99% *trans*	28
	TPPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (66) 97% *trans*	29
 96% *trans*	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (±) +  **II** (±) **I** + **II** (57), **I/II** = 93:7	28
87% *trans*	TPPCr (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** + **II** (35), **I/II** = 66:34	29
C_{15} 	—	1. $Fe_2(CO)_9$, THF, 2h 2. CAN, EtOH, 2h	 (—), 26	39
C_{18} 	TPPAl (0.5 mol %)	CO (60 atm), THF, 60°, 6 h	 **I** (±) +  **II** (±) **I** + **II** (99), 83, **I/II** = 50:50	81

TABLE 2A. γ-LACTONES FROM EPOXIDES

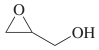
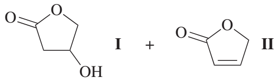
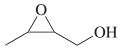
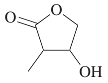
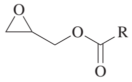
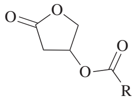
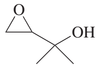
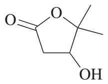
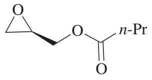
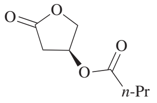
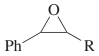
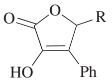
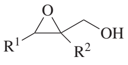
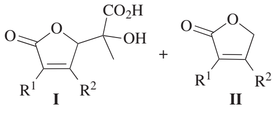
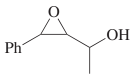
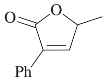
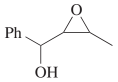
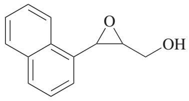
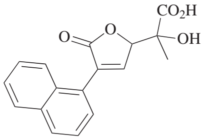
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	CO (270 atm), $Co_4(CO)_{12}$, THF, 100°, 8 h	 **I** + **II** (93), **I**/**II** = 80:20	42
	CO (60 atm), $[PPN]^+[Co(CO)_4]^-$, $BF_3•OEt_2$, DME, 80°, 24 h	**I** (—)	5
	CO (200 atm), H_2 (4 atm), $Co_2(CO)_8$, THF, 100°, 2 h	**I** + **II** (89), **I**/**II** = 93:7	42
	CO (200 atm), H_2 (4 atm), $Co_2(CO)_8$, THF, 100°, 4 h	**I** + **II** (97), **I**/**II** = 70:30	42
	CO (200 atm), $Co_2(CO)_8$, THF, 100°, 2 h	**I** + **II** (86), **I**/**II** = 94:6	42
	CO (200 atm), $Co_4(CO)_{12}$, DME, 120°, 8 h	**I** (87)	42
	1. CO (270 atm), $Co_4(CO)_{12}$, THF, 100°, 8 h 2. Polyphosphoric acid	**II** (89)	42
	CO (200 atm), $Ni(acac)_2$, THF, 100°, 8 h	**I** + **II** (80), **I**/**II** = 60:40	42
C_4			
	CO (240 atm), $Co_4(CO)_{12}$, THF, 120°, 8 h	 (60)	42
C_{4-7}			
	CO (60 atm), OEPCr, neat, 60°, 24 h	 R Me (99) *n*-Pr (99) Ph (99)	28
C_5			
	CO (240 atm), $Co_4(CO)_{12}$, THF, 120°, 8 h	 (76)	42
C_7			
 er 99.5:0.5	CO (60 atm), OEPCr, neat, 60°, 24 h	 (99) er 99.5:0.5	28
C_{8-9}			
	CO (1 atm), $Co_2(CO)_8$, CTAB, MeI, NaOH (aq), benzene, rt, 12 h	 R H (65) Me (34)	44
C_{9-10}			
	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h	 R^1 / R^2 / **I** / **II** Ph / H / (42) / (10) Ph / Me / (33) / (36) 4-MeC_6H_4 / H / (50) / (0)	43
C_{10}			
	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h	 (—) +  (—)	43
C_{13}			
	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h	 (46)	43

TABLE 2B. γ-LACTONES FROM EPOXIDES VIA A SILYL YNOLATE

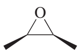
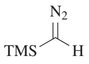
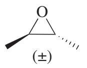
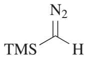
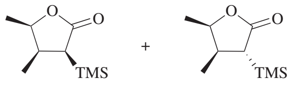
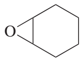
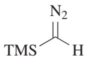
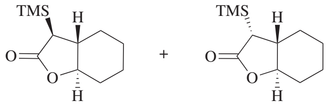
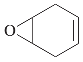
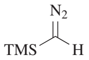
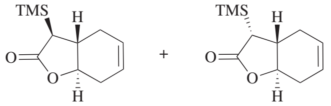
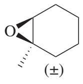
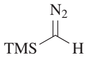
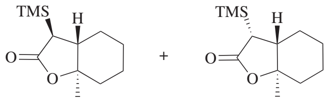
Epoxide	Reagent	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 I (±) + II (±) **I** + **II** (72)	45
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 I (±) + II (±) **I** + **II** (71)	45
C_6				
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 I (±) + II (±) **I** + **II** (93)	45
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 I (±) + II (±) **I** + **II** (72)	45
C_7				
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 I (±) + II (±) **I** + **II** (75)	45

TABLE 3A. δ-LACTONES FROM HOMOGLYCIDOLS

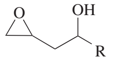
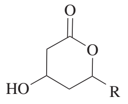
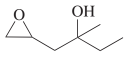
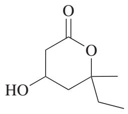
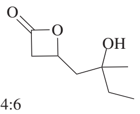
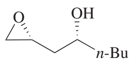
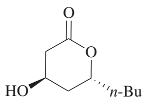
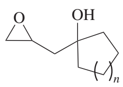
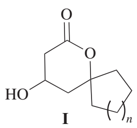
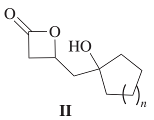
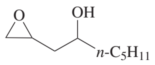
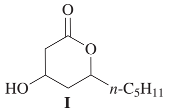
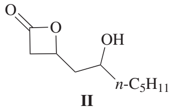
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-10}			
	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 R Me (73) $ClCH_2$ (81) $TBSOCH_2$ (52) CH_2=$CHCH_2$ (76) *n*-Bu (60) Ph (81)	24
C_7			
	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 **I** (58) +  **II** (—) **I/II** = 94:6	24
C_8			
 er >99.5:0.5	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 (—) er >99.5:0.5	24
C_{8-15}			
	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 +  **I** **II** *n* **I** **II** **I/II** 1 (67) (—) 96:4 8 (75) (—) 96:4	24

TABLE 3A. δ-LACTONES FROM HOMOGLYCIDOLS (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	CO (55 atm), catalyst, DME, 60°, 24 h	 **I** +  **II**	24

Catalyst	**I + II**	**I/II**
$HCo(CO)_4$	(—)	99:1
Cp_2Ti	(—)	83:17
salphAl	(—)	73:27
$Co_2(CO)_8$	(—)	67:33
HTPPAl	(—)	58:42
TPPCr	(—)	33:67
salphCr	(—)	16:84

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES

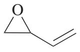
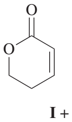
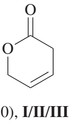
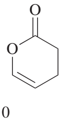
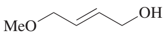
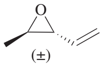
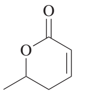
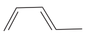
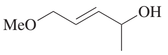
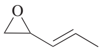
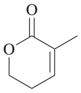
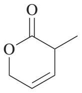
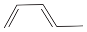
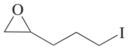
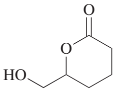
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	 **I** +  **II** +  **III** **I + II + III** (80), **I/II/III** = 58:32:10	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I + II** (40), **I/II** = 23:77 +  (45)	52
C_5			
	1. $Fe_2(CO)_9$, THF 2. CO (60 atm), benzene, 195°, 4 h	 **I** (23)	50
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	**I** (65) +  (5)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** (15) +  (50)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	 **I** +  **II** +  (5) **I + II** (67), **I/II** = 7:93	52
	1. $Na^+[CpMo(CO)_3]^-$, THF 2. PPh_3, MeCN 3. $SnCl_4$ (5 eq), CH_2Cl_2, 0°, 0.5 h 4. $NaBH_4$, MeOH 5. Pyridine *N*-oxide, CH_2Cl_2, rt, 4 h	 (18)	49

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

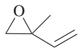
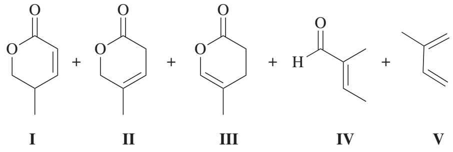
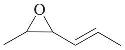
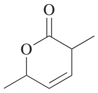
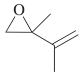
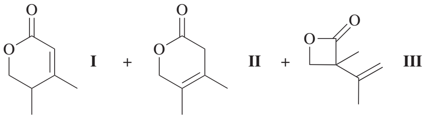
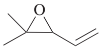
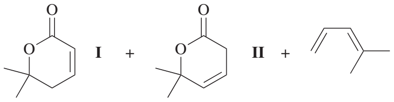
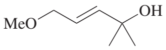
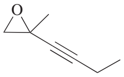
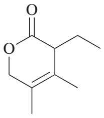
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 			
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	**I** (37) + **II** (48) + **III** (15)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** (17) + **II** (66)	52
	CO (150 atm), $(CODRhCl)_2$, CCl_4, 70°, 50 h	**I** (75)	53
	CO (200 atm), Na_2PdCl_4, THF, 75°, 17 h	**II** (6) + **IV** (57)	52
	CO (200 atm), Na_2PdCl_4, LiBr, THF, 75°, 17 h	**II** (86) + **IV** (1) + **V** (1)	52
	CO (200 atm), $Pd(acac)_2$, THF, 75°, 17 h	**II** (1) + **IV** (71)	52
	CO (200 atm), $Pd(acac)_2$, PPh_3, THF, 75°, 17 h	**II** (40) + **IV** (1)	52
	CO (200 atm), $Co_2(CO)_8$, benzene, 85°, 20 h	**II** (37) + **IV** (13) + **V** (19)	52
C_6 	1. $Fe_2(CO)_9$, ultrasound, 1 h 2. CO (300 atm), 90°, 24 h	 **I** (49) dr 1:1	50
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	**I** (75)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), solvent, 16 h	 **I** + **II** + **III** Solvent | I | II | III benzene | (45) | (45) | (—) MeOH | (24) | (56) | (—)	52
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, rt, solvent, 16 h	**II** + **III** Solvent | II | III $EtOH/H_2O$ | (38) | (0) MeCN | (16) | (42)	40
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	 **I** + **II** + (10) **I** + **II** (75), **I**/**II** = 66:33	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** + **II** (65), **I**/**II** = 20:80 +  (20)	52
C_7 	1. CO (1 atm), $Pd(PPh_3)_4$, MeOH, rt, 18 h 2. Me_2CuLi, Et_2O, –78 to –40°	 (41)	48

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

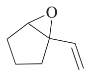
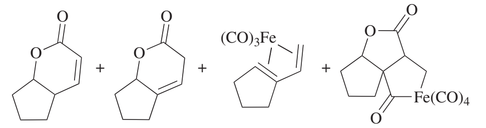
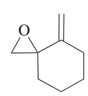
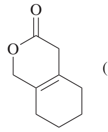
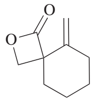
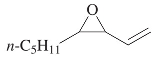
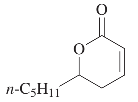
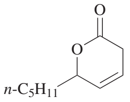
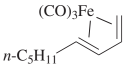
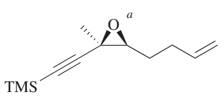
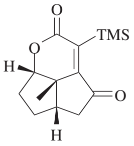
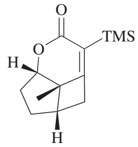
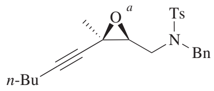
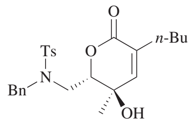
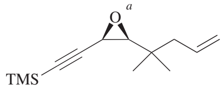
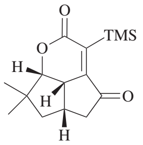
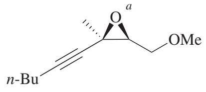
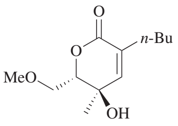
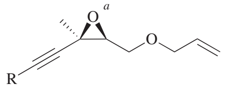
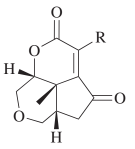
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. Benzene, 70°, 12 h	 **I** (50) **II** (9) **III** (7) **IV** (5)	51
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. THF, 70°, 2.5 h	**I** (40) + **II** (16) + **III** (30)	51
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, rt, 16 h	**I** + **II** (80)	40
C_8			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –5°, 16 h	 (55) +  (15)	40
C_9			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. THF, 70°, 3 h	 (8) +  (6) +  (40)	51
 [a]	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 **I** (65)	46, 47
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	**I** (2) +  (75)	46, 47
C_{10}			
 [a]	1. $Co_2(CO)_8$ 2. H_2O/THF, rt, 8 h 3. CO (1 atm), 75°, 6 h	 **I** (25)	46, 47
	1. $Co_2(CO)_8$ 2. Pyridine *N*-oxide, 80°, 8 h 3. CO (1 atm), 75°, 6 h	**I** (35)	46, 47
 [a]	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (73)	46
 [a]	1. $Co_2(CO)_8$ 2. H_2O/THF, rt, 8 h 3. CO (1 atm), 75°, 6 h	 (28)	46, 47
$C_{10–12}$			
 [a]	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 R *n*-Bu (75) *n*-C_6H_{13} (78)	46, 47

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

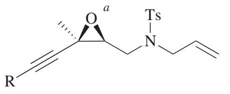
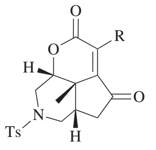
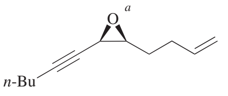
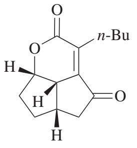
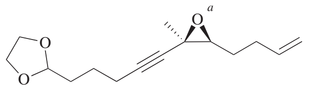
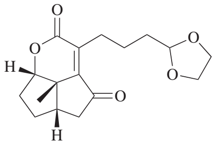
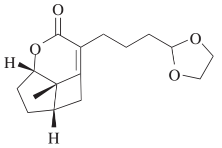
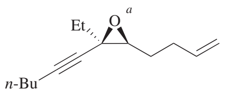
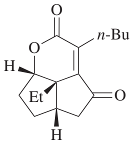
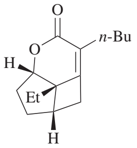
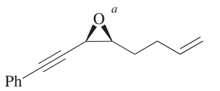
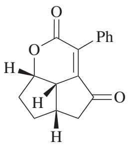
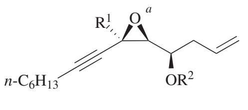
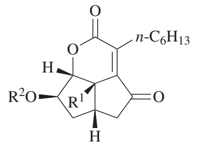
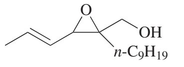
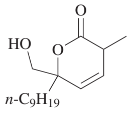
Epoxide	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10-12}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (1 atm), benzene, 80°, 24 h		R *n*-Bu (66) *n*-C_6H_{13} (68)	46, 47
C_{12}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h		*x* 0 (82) 3.4 (7)	46
C_{13}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h		(66)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h		(52)	46
C_{14}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h		(71)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h		(68)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h		(82)	46
C_{14-15}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h		R^1 R^2 *x* H Ac 0 (83) Me Me 1 (74) Me Ac 1 (77)	46, 47
C_{15}				
	1. $Fe_2(CO)_9$, THF 2. CO (300 atm), 90°, 24 h		(53)	50

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

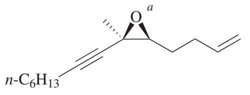
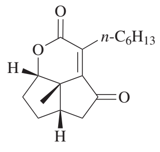
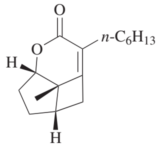
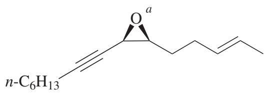
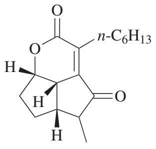
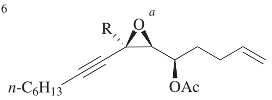
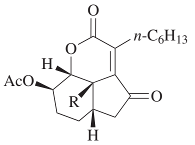
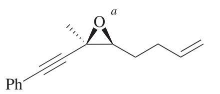
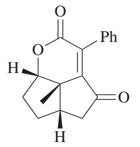
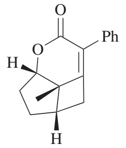
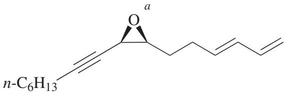
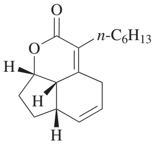
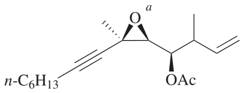
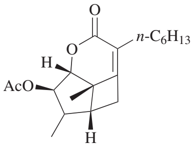
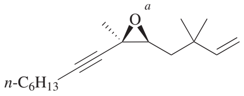
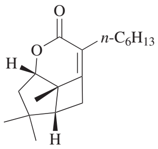
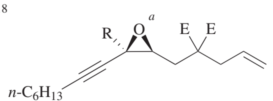
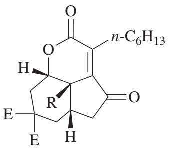
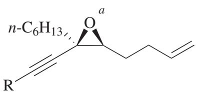
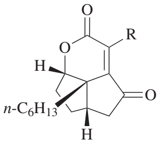
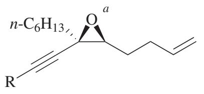
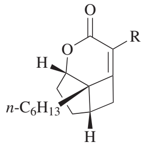
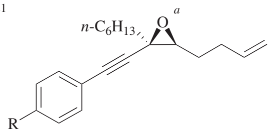
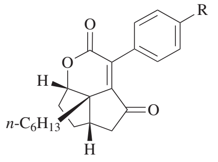
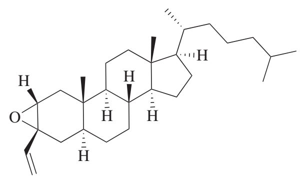
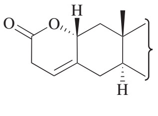
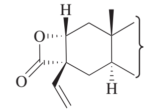
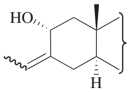
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 **I** +  **II** *x* **I** **II** 0 (3) (72) 1 (34) (39) 3.4 (77) (0)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (45)	46
C_{15-16} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 R H (70) Me (65)	46
C_{15} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 **I** +  **II** *x* **I** **II** 0 (3) (75) 1 (38) (32) 3.4 (74) (0)	46
C_{16} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (25)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (85)	46, 47
C_{17} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (89)	46, 47
C_{17-18}  E = CO_2Me	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 R *x* H 0 (71) Me 1 (71)	46, 47
C_{20} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 R *n*-C_6H_{13} (59) Ph (58)	46

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 R n-C_6H_{13} (63) Ph (61)	46
$C_{20–21}$ 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 R F (59) MeO (63)	46
C_{29} 	1. $Fe(CO)_5$, $h\nu$, benzene, rt, 6 h 2. CAN, MeCN/benzene (1:1), rt, 16 h	 **I** (26) +  (6)	40
	1. $Fe(CO)_5$, $h\nu$, benzene, rt, 6 h 2. THF, 70°, 2.5 h	**I** (31) +  (36)	51

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[a] The epoxide configuration as shown is opposite that depicted in the original disclosure, which used racemic epoxides. Based on the current mechanistic understanding, the enantiomer of epoxide shown should produce the enantiomer of product shown.

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES

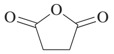
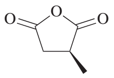
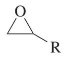
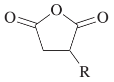
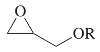
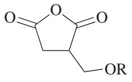
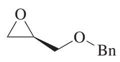
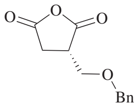
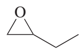
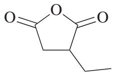
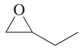
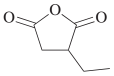
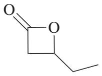
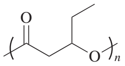
Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_2 	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (98), 93	21
C_3  er >99.5:0.5	CO (60 atm), TPPAl, dioxane	 Temp (°) Time (h) er 90 3 (97) 98.5:1.5 50 24 (99) >99.5:0.5	21
$C_{3–9}$ 	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 R Me (99), 89 n-Bu (97), 88 $NC(CH_2)_3$ (99), 77 CH_2=$CH(CH_2)_4$ (99), 85 c-C_6H_{11} (97), 81 Bn (99), 78	21
C_3 	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 R TBS (98), 83 n-Bu (99), 80 Bn (96), 87	21
 er >99.5:0.5	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 (96), 87 er >99.5:0.5	21
C_4 	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (99), 80	21

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4			
	CO (60 atm), catalyst, solvent, 60°, 6 h	 **I** +  **II** +  **III**	21

Catalyst	Solvent	**I**	**II**	**III**
salphAl	none	(0)	(99)	(0)
salphAl	toluene	(0)	(58)	(0)
OEPCr	none	(7)	(0)	(93)
OEPCr	toluene	(33)	(0)	(67)
TPPAl	none	(22)	(0)	(78)
TPPAl	toluene	(99)	(0)	(0)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
	CO (60 atm), catalyst, dioxane, 90°, 2 h	**I** + **II** + **III**	21

Catalyst	**I**	**II**	**III**
Cp_2Ti	(0)	(6)	(0)
salphAl	(2)	(85)	(0)
salphCr	(32)	(64)	(0)
TPPCr	(47)	(38)	(12)
OEPCr	(76)	(4)	(19)
OEPAl	(68)	(31)	(0)
HTPPAl	(80)	(19)	(0)
MeTPPAl	(79)	(19)	(0)
FTPPAl	(84)	(14)	(0)
TPPAl	(83)	(16)	(0)
CF_3TPPAl	(81)	(16)	(0)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
	CO (60 atm), TPPAl, solvent, 90°, 2 h	**I** + **II** + **III**	21

Solvent	**I**	**II**	**III**
hexane	(16)	(9)	(66)
toluene	(45)	(37)	(4)
Et_2O	(38)	(42)	(11)
DME	(43)	(55)	(0)
dioxane	(80)	(19)	(0)
THF	(18)	(82)	(0)
EtOAc	(42)	(51)	(6)
acetone	(17)	(52)	(30)
1,2-difluorobenzene	(12)	(83)	(0)
MeCN	(0)	(93)	(4)

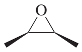
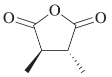
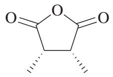
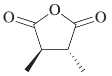
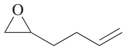
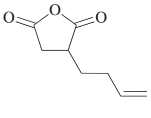
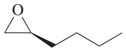
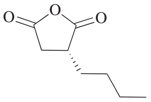
Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 **I** +  **II** **I** + **II** (95), **I/II** = 1:20	21
	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 **I** (99)	21
	CO (60 atm), salphAl, neat, 50°, 24 h	**I** (—)	54
C_6			
	CO (60 atm), TPPAl, dioxane, 50°, 3 h	 (90), 82	21
 er >99.5:0.5	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 (99) er >99.5:0.5	21

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES (*Continued*)

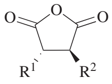
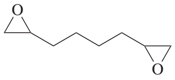
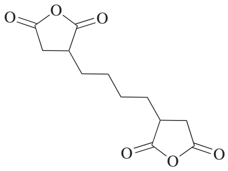
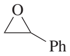
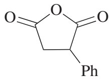
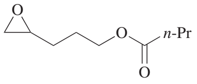
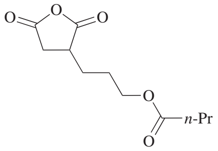
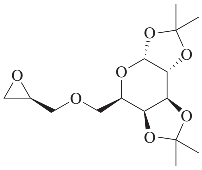
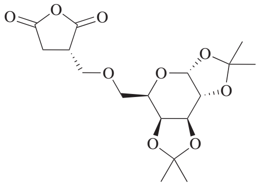
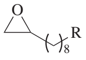
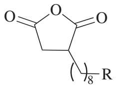
Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_{6-8}			
	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 R^1 R^2 Et Et (99) Me n-C_5H_{11} (99)	21
C_8			
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (98), 89	21
	CO (60 atm), TPPAl, dioxane, 50°, 12 h	 (93), 72	21
C_9			
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (99), 89	21
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (95)	81
C_{11-12}			
	CO (60 atm), TPPAl, dioxane, 90°	 R Time (h) Me_2NCO 24 (98), 79 $HOCH_2$ 3 (93), 72 Et 3 (99), 93	21

TABLE 5. 1,3-OXAZINANE-2,4-DIONES FROM EPOXIDES AND ISOCYANATES

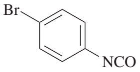
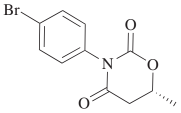
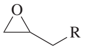
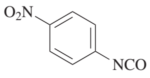
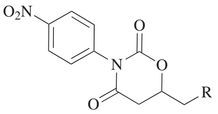
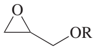
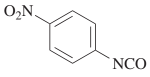
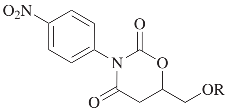
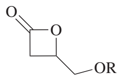
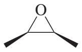
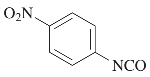
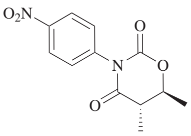
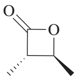
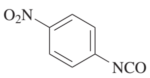
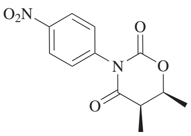
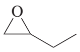
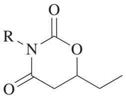
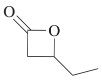
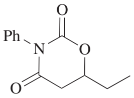
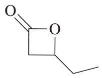
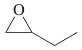
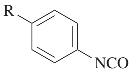
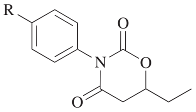
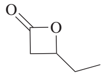
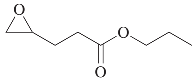
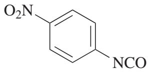
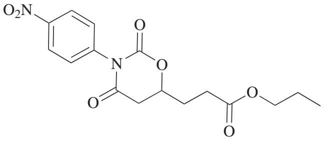
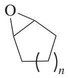
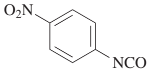
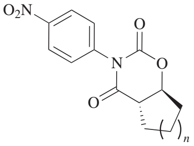
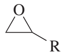
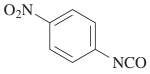
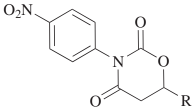
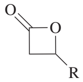
Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_3				
		CO (55 atm), salphAl, hexanes, rt, 48 h	 (97), 70[a]	22
C_{3-6}				
		CO (55 atm), salphAl, hexanes, rt, 12 h	 R H (97) Cl (70) Me (97) *n*-Pr (97) CH_2=$CHCH_2$ (97)	22
C_3				
		CO (55 atm), salphAl, hexanes, rt, 12 h	 **I** +  **II** R **I** **II** TBS (97) (3) CH_2=$CHCH_2$ (94) (6) *n*-Bu (97) (2) Bn (80) (8)	22
C_4				
		CO (55 atm), salphAl, hexanes, rt, 12 h	 (89) +  (11)	22
		CO (55 atm), salphAl, hexanes, rt, 24 h	 (19)	22
	RNCO	CO (55 atm), salphAl, hexanes, rt, 48 h	 **I** +  **II** R **I** **II** Et (13) (15) Bn (39) (19)	22
	PhNCO	CO (55 atm), salphAl, hexanes, rt, 48 h	 **I** (97), 71[a] +  **II** (0)	22
	PhNCO	CO (55 atm), salphAl, solvent, rt, 24 h	Solvent[b] **I** **II** hexanes (40) (8) pentane (24) (5) toluene (10) (20) Et_2O (17) (36) 1,2-difluorobenzene (14) (36) *t*-BuOMe (13) (34) tetrahyropyran (4) (74) MeCN (3) (77) dioxane (0) (97) DME (0) (91) THF (0) (83)	22

TABLE 5. 1,3-OXAZINANE-2,4-DIONES FROM EPOXIDES AND ISOCYANATES (*Continued*)

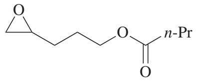
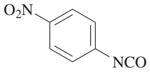
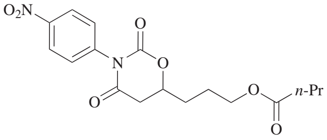
	Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_4			CO (*x* atm), salphAl, solvent, rt	 **I** +  **II**	

R	*x*	Solvent	Time (h)	**I**	**II**	Refs.
F	55	hexanes	48	(97)	(0)	22
F	20	DME	5	(7)	(93)	25
Br	55	hexanes	48	(97)	(0)	22
MeO	55	hexanes	48	(60)	(20)	22
Me	55	hexanes	48	(42)	(14)	22
Me	20	DME	5	(17)	(83)	25

	Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_5			CO (55 atm), salphAl, hexanes, rt, 12 h	 (97)	22
C_{5-6}			CO (55 atm), salphAl, hexanes, rt, 12 h	 *n* 1 (97) 2 (97)	22

	Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_{6-8}			CO (55 atm), salphAl, hexanes, rt, 12 h	 **I** +  **II**	22

R	**I**	**II**
t-Bu	(10)	(9)
c-C_6H_{11}	(94)	(3)

	Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_9			CO (55 atm), salphAl, hexanes, rt, 12 h	 (97)	22

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[a] The value is the yield of isolated product (%).

[b] The epoxide concentration was 0.5 M in the solvent.

TABLE 6. 1,3-OXATHIOLAN-2-ONES FROM EPOXIDES

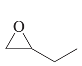
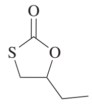
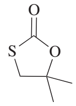
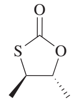
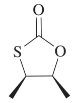
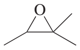
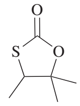
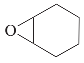
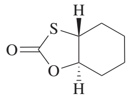
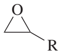
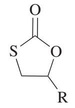
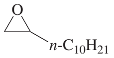
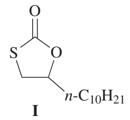
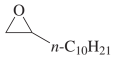
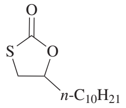
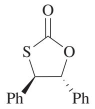
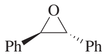
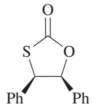
Epoxide	Conditions	Product(s) and GC Yield(s) (%)				Refs.
C_4						
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 60°, 3 h		(87)			56
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 60°, 3 h		(98)			56
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h		*x*			
			0	(87)		55
			0.025	(31)		
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h		*x*			
			0	(16)		55
			0.025	(7)		
C_5						
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 150°, 8 h		*x*			
			0	(4)		56
			0.025	(4)		55
C_6						
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 60°, 3 h		*x*			
			0	(61)		55
			0.025	(16)		
C_{8-9}						
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 60°, 3 h		R	*x*		
			Ph	0	(39)	56
			Ph	0.025	(79)	56
			4-BrC_6H_4	0	4	55
			4-BrC_6H_4	0.025	(22)	55
			4-MeC_6H_4	0	(53)	55
			4-MeC_6H_4	0.025	(50)	55
			Bn	0	(53)	56
			Bn	0.025	(97)	56
			$PhOCH_2$	0	(24)	56
			$PhOCH_2$	0.025	(66)	56
C_{12}						
	S (5 eq), CO (*x* atm), NaH (1 eq), THF, 3 h	 **I**	*x*	Temp (°)		
			10	60	(95), 92^a	55
			10	50	(72)	
			10	40	(29)	
			5	60	(37)	
			1	60	(0)	
	S (*x* eq), CO (10 atm), NaH (1 eq), THF, 60°, 3 h	**I**	*x*			
			1	(28)		55
			2	(67)		
			3	(76)		
			4	(85)		
			5	(96)		
	S (5 eq), CO (10 atm), NaH (1 eq), solvent, 60°, 3 h	**I**	Solvent			
			dioxane	(22)		55
			DMSO	(56)		
			DMF	(82)		
			MeCN	(60)		
			toluene	(0)		
			hexane	(0)		

TABLE 6. 1,3-OXATHIOLAN-2-ONES FROM EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and GC Yield(s) (%)	Refs.
C_{12}			
	S (5 eq), CO (10 atm), base (0.25 eq), THF, 60°, 3 h	 Base **I** LiH (0) KH (28) KH (82)[b] NaH (95) $NaBH_4$ (7) CaH_2 (61) DBU (56) DBN (23) NMP (0) Et_3N (0) pyridine (0) NaOH (0)	55
C_{14}			
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h	 *x* 0 (35) 0.025 (10)	55
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 120°, 6 h	 (0)	55

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[a] The value is the yield of isolated product (%).

[b] Dibenzo-18-crown-6 (25 mol %) was added to the reaction mixture.

REFERENCES

[1] Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987.

[2] Heck, R. F. In *Organic Synthesis via Metal Carbonyls*; Wender, I., Pino, P., Eds.; Interscience: New York, 1968.

[3] Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, 1991.

[4] Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Sausalito, CA, 1994.

[5] Church, T. L.; Getzler, Y.; Byrne, C. M.; Coates, G. W. *Chem. Commun.* **2007**, 657.

[6] Nakano, K.; Nozaki, K. *Top. Organomet. Chem.* **2006**, *18*, 223.

[7] Vasapollo, G.; Mele, G. *Curr. Org. Chem.* **2006**, *10*, 1397.

[8] Liu, J.; Chen, J. *Huaxue Jinzhan* **2004**, *16*, 989.

[9] Vasapollo, G.; Mele, G. *Targets in Heterocycl. Systems* **2002**, *6*, 197.

[10] Khumtaveeporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414.

[11] *Aziridines and Epoxides in Organic Synthesis*; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, 2006.

[12] Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603.

[13] Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488.

[14] Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.

[15] Tokunga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936.

[16] Katsuki, T.; Martin, V. S. *Org. React.* **1995**, *48*, 1.

[17] Dekker, F. J.; Balamurugan, R.; Wetzel, S.; Koch, M. A.; Kramer, J. W.; Coates, G. W.; Odermatt, A.; Waldmann, H. Manuscript in preparation.

[18] Kramer, J. W.; Treitler, D. S.; Coates, G. W. *Org. Synth.* **2009**, *86*, 287.

[19] Kramer, J. W.; Coates, G. W. *Tetrahedron* **2008**, *64*, 6973.

[20] Liang, Y.; Hnatiuk, N. E.; Rowley, J. M.; Whiting, B. T.; Coates, G. W.; Rablen, P. R.; Morton, M.; Howell, A. R. *J. Org. Chem.* **2011**, *76*, 9962.

[21] Rowley, J. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 4948.

[22] Church, T. L.; Byrne, C. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 8156.

[23] Coates, G. W.; Kramer, J. W. Intl. Patent WO **2007**/106329 (*2007*).

[24] Kramer, J. W.; Joh, D. Y.; Coates, G. W. *Org. Lett.* **2007**, *9*, 5581.

[25] Church, T. L.; Getzler, Y. D. Y. L.; Coates, G. W. *J. Am. Chem. Soc.* **2006**, *128*, 10125.

[26] Kramer, J. W.; Lobkovsky, E. B.; Coates, G. W. *Org. Lett.* **2006**, *8*, 3709.

[27] Getzler, Y. D. Y. L.; Schmidt, J. A. R.; Coates, G. W. *J. Chem. Educ.* **2005**, *82*, 621.

[28] Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426.

[29] Schmidt, J. A. R.; Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Org. Lett.* **2004**, *6*, 373.

[30] Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *Pure Appl. Chem.* **2004**, *76*, 557.

[31] Allmendinger, M.; Zintl, M.; Eberhardt, R.; Luinstra, G. A.; Molnar, F.; Rieger, B. *J. Organomet. Chem.* **2004**, *689*, 971.

[32] Molnar, F.; Luinstra, G. A.; Allmendinger, M.; Rieger, B. *Chem.—Eur. J.* **2003**, *9*, 1273.

[33] Allmendinger, M.; Eberhardt, R.; Luinstra, G. A.; Molnar, F.; Rieger, B. Z. *Anorg. Allg. Chem.* **2003**, *629*, 1347.

[34] Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2781.

[35] Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174.

[36] Lee, J. T.; Thomas, P. J.; Alper, H. *J. Org. Chem.* **2001**, *66*, 5424.

[37] Drent, E.; Kragtwijk, E. European Patent 577206 (1994).

[38] Shimizu, I.; Maruyama, T.; Makuta, T.; Yamamoto, A. *Tetrahedron Lett.* **1993**, *34*, 2135.

[39] Bates, R. W.; Fernandez-Moro, R.; Ley, S. V. *Tetrahedron* **1991**, *47*, 9929.

[40] Annis, G. D.; Ley, S. V.; Self, C. R.; Sivaramakrishnan, R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 270.

[41] Kamiya, Y.; Kawato, K.; Ohta, H. *Chem. Lett.* **1980**, 1549.

[42] Brima, T. S. U.S. Patent 4968817 (1990).

[43] Alper, H.; Eisenstat, A.; Satyanarayana, N. *J. Am. Chem. Soc.* **1990**, *112*, 7060.

[44] Alper, H.; Arzoumanian, H.; Petrignani, J. F.; Saldana-Maldonado, M. *J. Chem. Soc., Chem. Commun.* **1985**, 340.

[45] Kai, H.; Iwamoto, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 7634.

[46] Odedra, A.; Lush, S.-F.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 567.

47 Odedra, A.; Wu, C.-J.; Madhushaw, R. J.; Wang, S.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125*, 9610.
48 Knight, J. G.; Ainge, S. W.; Baxter, C. A.; Eastman, T. P.; Harwood, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3188.
49 Marson, C. M.; Randall, L.; Winter, M. J. *Tetrahedron Lett.* **1994**, *35*, 6717.
50 Horton, A. M.; Ley, S. V. *J. Organomet. Chem.* **1985**, *285*, C17.
51 Annis, G. D.; Ley, S. V.; Self, C. R.; Sivaramakrishnan, R.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1355.
52 Aumann, R.; Ring, H.; Kruger, C.; Goddard, R. *Chem. Ber.* **1979**, *112*, 3644.
53 Aumann, V. R.; Ring, H. *Angew. Chem.* **1977**, *89*, 47.
54 Getzler, Y. D. Y. L.; Kundnani, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2004**, *126*, 6842.
55 Nishiyama, Y.; Katahira, C.; Sonoda, N. *Tetrahedron* **2006**, *62*, 5803.
56 Nishiyama, Y.; Katahira, C.; Sonoda, N. *Tetrahedron Lett.* **2004**, *45*, 8539.
57 Denmark, S. E.; Ahmad, M. *J. Org. Chem.* **2007**, *72*, 9630.
58 Hinterding, K.; Jacobsen, E. N. *J. Org. Chem.* **1999**, *64*, 2164.
59 Heck, R. F. *J. Am. Chem. Soc.* **1963**, *85*, 1460.
60 Goodman, S. N.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 4703.
61 Nakano, K.; Katayama, M.; Ishihara, S.; Hiyama, T.; Nozaki, K. *Synlett* **2004**, 1367.
62 Lee, J. T.; Alper, H. *Macromolecules* **2004**, *37*, 2417.
63 Allmendinger, M.; Eberhardt, R.; Luinstra, G.; Rieger, B. *J. Am. Chem. Soc.* **2002**, *124*, 5646.
64 Davoli, P.; Moretti, I.; Prati, F.; Alper, H. *J. Org. Chem.* **1999**, *64*, 518.
65 Piotti, M. E.; Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 111.
66 Roberto, D.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 7539.
67 Wang, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20.
68 Jenner, G.; Kheradmand, H.; Kiennemann, A. *J. Organomet. Chem.* **1984**, *277*, 427.
69 Byrne, C. M.; Church, T. L.; Kramer, J. W.; Coates, G. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 3979.
70 Xu, H. Y.; Jia, L. *Org. Lett.* **2003**, *5*, 1575.
71 Wang, Y.; Tennyson, R. L.; Romo, D. *Heterocycles* **2004**, *64*, 605.
72 Pommier, A.; Pons, J.-M. *Synthesis* **1993**, 441.
73 Rieth, L. R.; Moore, D. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 15239.
74 Lenz, R. W.; Marchessault, R. H. *Biomacromolecules* **2005**, *6*, 1.
75 Müller, H.-M.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 477.
76 Pommier, A.; Pons, J.-M. *Synthesis* **1995**, 729.
77 Wu, Y.; Sun, Y.-P. *J. Org. Chem.* **2006**, *71*, 5748.
78 Schneider, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 744.
79 Yang, H. W.; Romo, D. *Tetrahedron* **1999**, *55*, 6403.
80 Stirling, A.; Iannuzzi, M.; Parrinello, M.; Molnar, F.; Bernhart, V.; Luinstra, G. A. *Organometallics* **2005**, *24*, 2533.
81 Rowley, J. M. Ph. D. Dissertation, Cornell University, 2008.
82 Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987; pp 266–267.
83 Coates, et al., Cornell University, Ithaca, NY, unpublished results.
84 Wax, M. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 7028.
85 Roe, D. C. *Organometallics* **1987**, *6*, 942.
86 Wedler, C.; Costisella, B.; Schick, H. *J. Org. Chem.* **1999**, *64*, 5301.
87 Sjostrom, L.; Rissanen, A.; Anderson, T.; Boldrin, M.; Golay, A.; Koppeschaar, H. P. F.; Krempf, M. *The Lancet* **1998**, *352*, 167.
88 Einhorn, A. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2208.
89 Zaugg, H. E. *Org. React.* **1954**, *8*, 305.
90 Bartlett, P. D.; Rylander, P. N. *J. Am. Chem. Soc.* **1951**, *73*, 4275.
91 Noyce, D. S.; Banitt, E. H. *J. Am. Chem. Soc.* **1966**, *31*, 4043.
92 Hughes, D. L. *Org. React.* **1992**, *42*, 335.
93 Arnold, L. D.; Drover, J. C. G.; Vederas, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4649.
94 Arnold, L. D.; Kalantar, T. H.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 7105.
95 Pansare, S. V.; Vederas, J. C. *J. Org. Chem.* **1989**, *54*, 2311.
96 Mulzer, J.; Bruentrup, G.; Chucholowski, A. *Angew. Chem.* **1979**, *91*, 654.
97 Adam, W.; Baeza, J.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2000.
98 Black, T. H.; Hall, J. A.; Sheu, R. G. *J. Org. Chem.* **1988**, *53*, 2371.
99 Staudinger, H.; Bereza, S. *Liebigs Ann. Chem.* **1911**, *380*, 243.
100 Orr, R. K.; Calter, M. A. *Tetrahedron* **2003**, *59*, 3545.

[101] Tidwell, T. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5778.

[102] Zhu, C.; Shen, X.; Nelson, S. G. *J. Am. Chem. Soc.* **2004**, *126*, 5352.

[103] Masters, A. P.; Sorensen, T. S. *Tetrahedron Lett.* **1989**, *30*, 5869.

[104] Dominguez, D.; Cava, M. P. *Tetrahedron Lett.* **1982**, *23*, 5513.

[105] Taggi, A. E.; Hafez, A. M.; Wack, H.; Young, B.; Ferraris, D.; Lectka, T. *J. Am. Chem. Soc.* **2002**, *124*, 6626.

[106] Lynch, J. E.; Riseman, S. M.; Laswell, W. L.; Tschaen, D. M.; Volante, R. P.; Smith, G. B.; Shinkai, I. *J. Org. Chem.* **1989**, *54*, 3792.

[107] Brady, W. T.; Smith, L. *J. Org. Chem.* **1971**, *36*, 1637.

[108] Kagan, H. B.; Jacques, J. *Bull. Soc. Chim. Fr.* **1958**, 1600.

[109] Brady, W. T.; Saidi, K. *J. Org. Chem.* **1979**, *44*, 733.

[110] Pons, J.-M.; Oblin, M.; Pommier, A.; Rajzmann, M.; Liotard, D. *J. Am. Chem. Soc.* **1997**, *119*, 3333.

[111] Cortez, G. C.; Tennyson, R. L.; Romo, D. *J. Am. Chem. Soc.* **2001**, *123*, 7945.

[112] Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166.

[113] France, S.; Guerin, D. J.; Miller, S. J.; Lectka, T. *Chem. Rev.* **2003**, *103*, 2985.

[114] Cortez, G. C.; Oh, S. H.; Romo, D. *Synthesis* **2001**, 1731.

[115] Dymock, B. W.; Kocienski, P. J.; Pons, J.-M. *Synthesis* **1998**, 1655.

[116] Dymock, B. W.; Kocienski, P. J.; Pons, J.-M. *Chem. Commun.* **1996**, 1053.

[117] Yang, H. W.; Romo, D. *Tetrahedron Lett.* **1998**, *39*, 2877.

[118] Tamai, Y.; Yoshiwara, H.; Someya, M.; Fukumoto, J.; Miyano, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2281.

[119] Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; Waldmann, H. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 17272.

[120] Chen, M. J.; Lo, C. Y.; Chin, C. C.; Liu, R. S. *J. Org. Chem.* **2000**, *65*, 6362.

[121] Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679.

[122] Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287.

[123] Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625.

[124] Gil, S.; Parra, M.; Rodriguez, P.; Segura, J. *Mini-Rev. Org. Chem.* **2009**, *6*, 345.

[125] Laduwahetty, T. *Contemp. Org. Synth.* **1995**, *2*, 133.

[126] des Abbayes, H.; Salaün, J.-Y. *Dalton Trans.* **2003**, 1041.

[127] Cassar, L. *Ann. N. Y. Acad. Sci.* **1980**, *333*, 208.

[128] Tan, Z.; Negishi, E. *Org. Lett.* **2006**, *8*, 2783.

[129] Larson, G. L.; Deperez, R. M. B. *J. Org. Chem.* **1985**, *50*, 5257.

[130] Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer: Berlin, 1983.

[131] Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981.

[132] Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819.

[133] D'Aniello, F.; Mann, A.; Mattii, D.; Taddei, M. *J. Org. Chem.* **1994**, *59*, 3762.

[134] Nicolaou, K. C.; Pfefferkorn, J. A.; Kim, S.; Wei, H. X. *J. Am. Chem. Soc.* **1999**, *121*, 4724.

[135] Belluš, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797.

[136] Bailey, D. M.; Johnson, R. E. *J. Org. Chem.* **1970**, *35*, 3574.

[137] Ma, S. M.; Lu, L. H.; Lu, P. *J. Org. Chem.* **2005**, *70*, 1063.

[138] Bur, S. K.; Martin, S. F. *Tetrahedron* **2001**, *57*, 3221.

[139] Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

[140] Harcken, C.; Brückner, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 2750.

[141] Ragoussis, N.; Ragoussis, V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3529.

[142] Chun, J.; Yin, Y. I.; Yang, G. L.; Tarassishin, L.; Li, Y. M. *J. Org. Chem.* **2004**, *69*, 7344.

[143] Alper, H.; Leonard, D. *Tetrahedron Lett.* **1985**, *26*, 5639.

[144] Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520.

[145] Oguma, T. *J. Chromatogr. B: Biomed. Sci. Appl.* **2001**, *764*, 46.

[146] de Lorenzo, F.; Feher, M.; Martin, J.; Collot-Teixeira, S.; Dotsenko, O.; McGregor, J. L. *Curr. Med. Chem.* **2006**, *13*, 3385.

[147] Tolbert, J. A. *Nat. Rev. Drug Discovery* **2003**, *2*, 517.

[148] Leßmann, T.; Leuenberger, M. G.; Menninger, S.; Lopez-Canet, M.; Müller, O.; Hümmer, S.; Bormann, J.; Korn, K.; Fava, E.; Zerial, M.; Mayer, T. U.; Waldmann, H. *Chem. Biol.* **2007**, *14*, 443.

[149] Fournier, L.; Gaudel-Siri, A.; Kocienski, P. J.; Pons, J.-M. *Synlett* **2003**, 107.

[150] Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635.

[151] Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199.

[152] Heck, R. F.; Breslow, D. S. *J. Am. Chem. Soc.* **1961**, *83*, 4023.

[153] Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591.

[154] Buszek, K. R.; Sato, N.; Jeong, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5511.

[155] Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.

[156] Dai, W.-M.; Guan, Y.; Jin, J. *Curr. Med. Chem.* **2005**, *12*, 1947.

[157] Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987; pp 750–751.

[158] Krafft, M. E.; Scott, I. L.; Romero, R. H. *Tetrahedron Lett.* **1992**, *33*, 3829.

[159] Greenberg, W. A.; Varvak, A.; Hanson, S. R.; Wong, K.; Huang, H.; Chen, P.; Burk, M. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5788.

[160] Thayer, A. M. *Chem. Eng. News* **2006**, *84* (33), 26.

[161] Gijsen, H. J.; Wong, C.-H. *J. Am. Chem. Soc.* **1995**, *117*, 7585.

[162] Evans, D. A.; Black, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 4497–4513.

[163] Mulzer, J.; Pichlmair, S.; Green, M. P.; Marques, M. M. B.; Martin, H. *J. Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11980–11985.

[164] Csaky, A. G.; Mba, M.; Plumet, J. *Synlett* **2003**, 2092.

[165] Carretero, J. C.; Ghosez, L. *Tetrahedron Lett.* **1988**, *29*, 2059.

[166] De Lombaert, S.; Nemery, I.; Roekens, B.; Carretero, J. C.; Kimmel, T.; Ghosez, L. *Tetrahedron Lett.* **1986**, *27*, 5099.

[167] Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 247.

[168] Chen, Y. G.; McDaid, P.; Deng, L. *Chem. Rev.* **2003**, *103*, 2965.

[169] Stoncius, A.; Nahrwold, M.; Sewald, N. *Synthesis* **2005**, 1829.

[170] Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 11330.

[171] Ranucci, E.; Liu, Y.; Lindblad, M. S.; Albertsson, A. C. *Macromol. Rapid Commun.* **2000**, *21*, 680.

[172] Arason, K. M.; Bergmeier, S. C. *Org. Prep. Proced. Int.* **2002**, *34*, 337.

[173] Sustmann, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, **1991**; Vol. *6*, pp 309–316.

[174] Bergmeier, S. C.; Ismail, K. A. *Synthesis* **2000**, 1369.

[175] Evans, D. A.; Wu, L. D.; Wiener, J. J. M.; Johnson, J. S.; Ripin, D. H. B.; Tedrow, J. S. *J. Org. Chem.* **1999**, *64*, 6411.

[176] Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 77.

[177] Fadel, A.; Salaün, J. *Tetrahedron Lett.* **1988**, *29*, 6257.

[178] Beckett, R. P.; Crimmin, M. J.; Davis, M. H.; Spavold, Z. *Synlett* **1993**, 137.

[179] Kloetzel, M. C. *Org. React.* **1948**, *4*, 1.

[180] Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.

[181] Benn, F. R.; Dwyer, J.; Chappell, I. *J. Chem. Soc., Perkin Trans. 2* **1977**, 533.

[182] Rondestvedt, C. S.; Filbey, A. H. *J. Org. Chem.* **1954**, *19*, 548.

[183] Heck, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 2712.

[184] Stille, J. K.; Divakaruni, R. *J. Org. Chem.* **1979**, *44*, 3474.

[185] Chiusoli, G. P.; Costa, M.; Cucchia, L.; Gabriele, B.; Salerno, G.; Veltri, L. *J. Mol. Catal. A: Chem.* **2003**, *204*, 133.

[186] Osakada, K.; Doh, M. K.; Ozawa, F.; Yamamoto, A. *Organometallics* **1990**, *9*, 2197.

[187] Feuillet, F. J. P.; Cheeseman, M.; Mahon, M. F.; Bull, S. D. *Org. Biomol. Chem.* **2005**, *3*, 2976.

[188] Kamino, T.; Murata, Y.; Kawai, N.; Hosokawa, S.; Kobayashi, S. *Tetrahedron Lett.* **2001**, *42*, 5249.

[189] Kende, A. S.; Kawamura, K.; Devita, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4070.

[190] Katagiri, N.; Hirose, M.; Sato, M.; Kaneko, C. *Chem. Pharm. Bull.* **1989**, *37*, 933.

[191] Kurz, T. *Tetrahedron* **2005**, *61*, 3091.

[192] Chollet, A. M.; Le Diguarher, T.; Kucharczyk, N.; Loynel, A.; Bertrand, M.; Tucker, G.; Guilbaud, N.; Burbridge, M.; Pastoureau, P.; Fradin, A.; Sabatini, M.; Fauchere, J. L.; Casara, P. *Bioorg. Med. Chem.* **2002**, *10*, 531.

[193] Heinisch, L.; Wittmann, S.; Stoiber, T.; Berg, A.; Ankel-Fuchs, D.; Mollmann, U. *J. Med. Chem.* **2002**, *45*, 3032.

[194] Mu, F. R.; Lee, D. J.; Pryor, D. E.; Hamel, E.; Cushman, M. *J. Med. Chem.* **2002**, *45*, 4774.

[195] Yamashita, M.; Nishida, H. Japanese Patent 09087275 (1997).

[196] Shibuya, I.; Goto, M.; Shimizu, M.; Yanagisawa, M.; Gama, Y. *Heterocycles* **1999**, *51*, 2667.

[197] Boontheung, P.; Perlmutter, P. *Tetrahedron Lett.* **1998**, *39*, 2629.

[198] Lapkin, I. I.; Semenov, V. I.; Saitkulova, F. G. *Zh. Org. Khim.* **1982**, *18*, 2468.

[199] Testa, E.; Fontanella, L.; Cristiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1928.

[200] Kolasa, T.; Miller, M. J. *Tetrahedron* **1989**, *45*, 3071.

[201] Shapiro, S. L.; Rose, I. M.; Freedman, L. *J. Am. Chem. Soc.* **1957**, *79*, 2811.

[202] Feuillet, F. J. P.; Niyadurupola, D. G.; Green, R.; Cheeseman, M.; Bull, S. D. *Synlett* **2005**, 1090.

[203] Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9194.
[204] Roush, W. R.; Gustin, D. *Tetrahedron Lett.* **1994**, *35*, 4931.
[205] Reynolds, D. D. *J. Am. Chem. Soc.* **1957**, *79*, 4951.
[206] Sonoda, N.; Mizuno, T.; Murakami, S.; Kondo, K.; Ogawa, A.; Ryu, I.; Kambe, N. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 452.
[207] Hata, S.; Goto, H.; Tanaka, S.; Oku, A. *J. Appl. Polym. Sci.* **2003**, *90*, 2959.
[208] Reynolds, D. D.; Johnson, D. L.; Fields, D. L. *J. Org. Chem.* **1961**, *26*, 5119.
[209] Reynolds, D. D.; Johnson, D. L.; Fields, D. L. *J. Org. Chem.* **1961**, *26*, 5122.
[210] Ko, S. Y. *J. Org. Chem.* **1995**, *60*, 6250.
[211] Hauptman, E.; Fagan, P. J.; Marshall, W. *Organometallics* **1999**, *18*, 2061.
[212] Traxler, J. T. *J. Org. Chem.* **1979**, *44*, 4971.
[213] Shimizu, M.; Kikumoto, H.; Konakahara, T.; Gama, Y.; Shibuya, I. *Heterocycles* **1999**, *51*, 3005.
[214] Prakash, O.; Kaur, H.; Pundeer, R.; Dhillon, R. S.; Singh, S. P. *Synth. Commun.* **2003**, *33*, 4037.
[215] Dorofeev, A.; Mal'kina, A. G.; Trofimov, B. A. *Chem. of Heterocycl. Comp.* **2001**, *37*, 903.
[216] Mizuno, T.; Nakamura, F.; Ishino, Y.; Nishiguchi, I.; Hirashima, T.; Ogawa, A.; Kambe, N.; Sonoda, N. *Synthesis* **1989**, 770.

TABLE 1A

Kramer, J. W.; Treitler, D. S.; Coates, G. W. *Org. Synth.* **2009**, *86*, 287.
Woelfle, H.; Kopacka, H.; Wurst, K.; Preishuber-Pfluegl, P.; Bildstein, B. *J. Organomet. Chem.* **2009**, *694*, 2493.
Dunn, E. W.; Coates, G. W. *J. Am. Chem. Soc.* **2010**, *132*, 11412.

TABLE 1B

Ganji, P.; Doyle, D. J.; Ibrahim, H. *Org. Lett.* **2011**, *13*, 3142.
Liang, Y.; Hnatiuk, N.; Rowley, J. M.; Whiting, B. T.; Coates, G. W.; Rablen, P. R.; Morton, M.; Howell, A. R. *J. Org. Chem.* **2011**, *76*, 9962.
Chen, Q.; Mulzer, M.; Shi, P.; Beuning, P. J.; Coates, G. W.; O'Doherty, G. A. *Org. Lett.* **2011**, *13*, 6592.
Ganji, P.; Ibrahim, H. *Chem. Commun.* **2012**, *48*, 10138.
Mulzer, M.; Whiting, B. T.; Coates, G. W. *J. Am. Chem. Soc.* **2013**, *135*, 10930.
Mulzer, M.; Ellis, W. C.; Lobkovsky, E. B.; Coates, G. W. *Chem. Sci.* **2014**, *5*, 1928.

CHAPTER 2

THE TISHCHENKO REACTION

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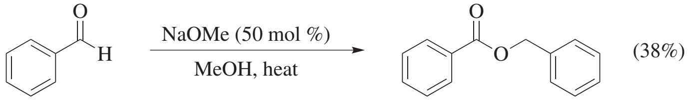
Organic Reactions, Vol. 86, Edited by Scott E. Denmark et al.

INTRODUCTION

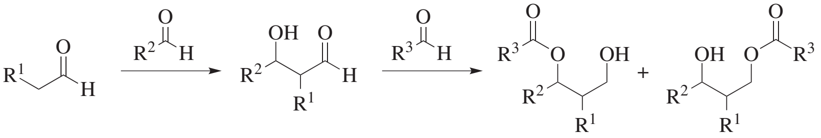
The dimerization of an aldehyde in the presence of a metal alkoxide to form a symmetrical ester is a well-known reaction, first observed by Claisen in the formation of benzyl benzoate by treating benzaldehyde with sodium alkoxides (Scheme 1).[1] The reaction has since been named after the Russian chemist V. E. Tishchenko, whose seminal research on the subject established the general reaction for ester formation through metal (Al or Mg) alkoxide catalyzed aldehyde dimerization.[2−5]



Scheme 1

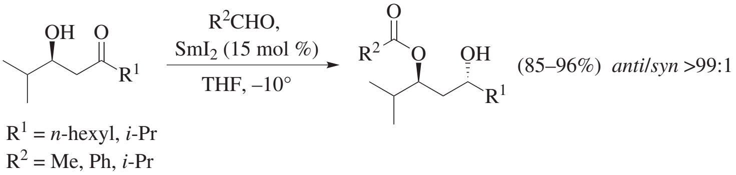
The Tishchenko (also Tischtschenko, Tischenko) reaction is mechanistically related to the Cannizzaro reaction,[6,7] the Meerwein–Ponndorf–Verley reduction,[8−13] and the Oppenauer oxidation.[14,15] The latter two processes are also catalyzed by metal alkoxides. The mechanisms of these reactions all include a hydride transfer step from one carbonyl group to another, assisted by substrate coordination to a Lewis acidic catalyst. The Tishchenko reaction can be promoted by either homogeneous or heterogeneous catalysts. The classic homogeneous reaction is catalyzed by aluminum alkoxides,[2−5,16−38] which is still a feasible approach. Several different catalyst systems have been developed for the Tishchenko reaction with regard to both the coordinating metal and the surrounding ligands. Metal-based catalysts include complexes with alkali metals,[1,39−45] alkaline earth metals (including Grignard-type compounds),[4,46−51] transition metals,[52−68] and lanthanoids.[69−74] Research on heterogeneous catalysts has focused mostly on alkaline earth metal oxides[75−81] and different modifications of alumina.[82−89] In addition to synthesizing symmetrical esters, reactions between two different aldehydes via the Tishchenko method have also been explored.[90]

Interest in the Tishchenko reaction was rekindled in the late 20th century with the realization of the potential stereoselectivity of its variant, the tandem aldol–Tishchenko reaction.[91−93] This variant is a two-step reaction, the first step being an aldol reaction between two aldehydes, and the second a subsequent coordination of another aldehyde followed by a Tishchenko-type hydride transfer (Scheme 2). The trimeric end product is a secondary 1,3-diol monoester, which often equilibrates to the thermodynamically more stable primary ester, thus giving a mixture of products.[94] This trimerization of aldehydes to 1,3-diol monoesters was first observed and studied a century ago.[95−99] With ketones as the enol equivalent, the aldol–Tishchenko reaction produces a 1,3-*anti*-diol with high diastereoselectivity.[100] Hence, during the last decade, research on the aldol–Tishchenko reaction has been directed toward creating multiple adjacent stereocenters in relatively few steps, with increasingly improved diastereomeric and enantiomeric control.[101−107]



Scheme 2

The aldol–Tishchenko reaction was further modified by Evans using samarium diiodide as the catalyst to reduce β-hydroxy ketones to 1,3-*anti*-diol monoesters, and a sacrificial aldehyde as the hydride donor (Scheme 3).[108] Since then the reduction of β-hydroxy ketones with an aldehyde hydride donor has generally been called the Evans–Tishchenko reaction or reduction. The Evans–Tishchenko variation has been used as a mild and efficient stereoselective method to create 1,3-*anti*-diol structures in the total synthesis of several natural products.[109–124]



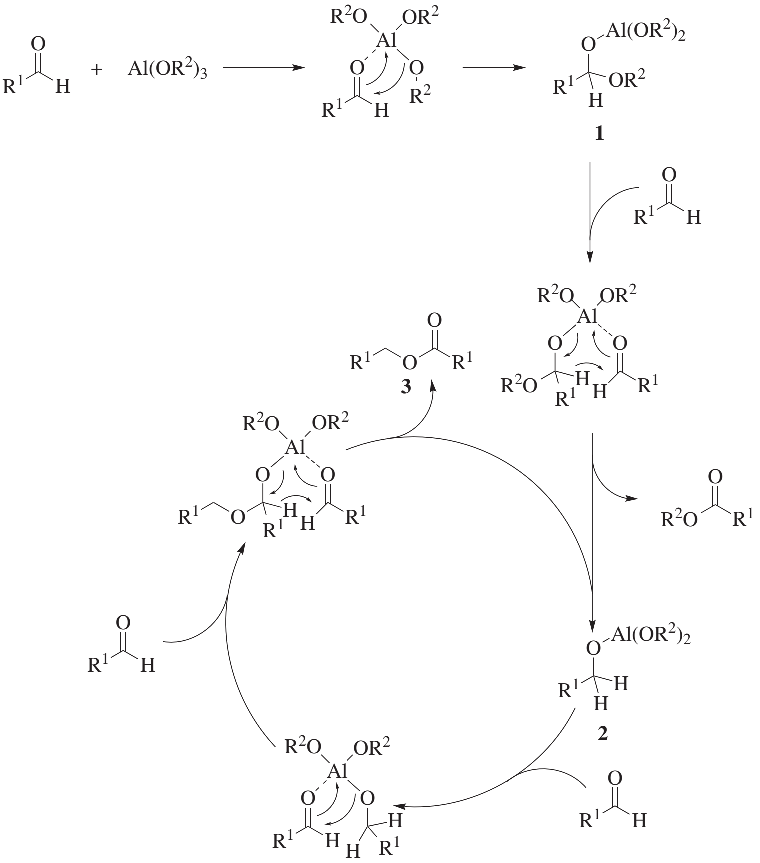
Scheme 3

The first in-depth reviews of the Tishchenko reaction and the aldol–Tishchenko reactions have only been published in this century.[125–131] The aim of this chapter is to provide a comprehensive review of the scope and limitations of the Tishchenko reaction and its variants, including the associated catalyst systems. For this purpose, the appropriate literature from the late 19th century until April 2014 is reviewed.

MECHANISM AND STEREOCHEMISTRY

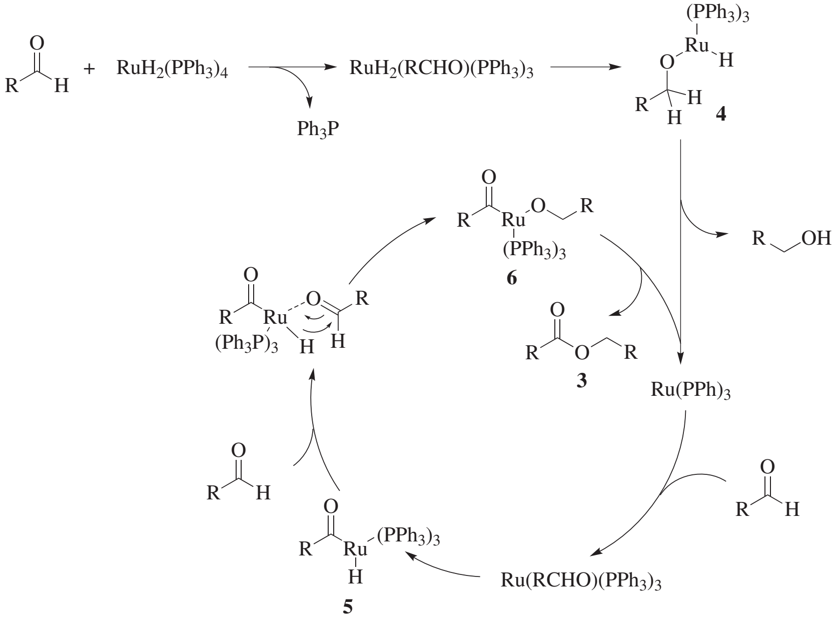
The Classical Tishchenko Reaction

The exact mechanism of the classical Tishchenko reaction has not been fully elucidated, although several plausible pathways have been suggested. Some evidence suggests that the mechanism is dependent on the type of catalyst. The generally accepted mechanism[30] for the classical Tishchenko reaction involves initial coordination of the aldehyde to the Lewis acidic aluminum alkoxide catalyst (Scheme 4). An alkoxide group is then transferred to the aldehyde, forming the coordinated hemiacetal **1**. Another molecule of aldehyde then coordinates to the central aluminum. A hydride transfer from the hemiacetal to the new aldehyde takes place, a mixed ester is released, and the reduced aldehyde now becomes a new alkoxide ligand for the aluminum. The cycle is repeated with a third molecule of aldehyde coordinating to the new aluminum complex **2**, and the previously formed alkoxide group is now transferred to the aldehyde. At completion of the cycle, symmetrical ester **3** is cleaved off, and the catalyst is able to initiate another cycle. Simple metal alkoxides are generally considered to follow this mechanism.



Scheme 4

The mechanism of the transition metal catalyzed Tishchenko reaction is believed to be somewhat different from the aluminum-catalyzed reaction (Scheme 5). The following mechanism has been suggested for $RuH_2(PPh_3)_4$, which is the first transition-metal complex discovered to catalyze the Tishchenko reaction.[57] The reaction is again initiated through coordination of an aldehyde to the catalyst metal. The carbonyl group of the aldehyde is then inserted into a Ru–H bond, giving complex **4**. An active $Ru(PPh_3)_3$ species is created via reductive elimination of the corresponding alcohol. A second aldehyde molecule then coordinates to the catalyst, followed by oxidative addition to the metal. A third aldehyde coordinates to the hydrido acyl intermediate **5** and is similarly inserted into the Ru–H bond. The acyl–alkoxo complex **6** undergoes reductive elimination, releasing the symmetrical ester **3** and regenerating the catalytically active $Ru(PPh_3)_3$ species. The experimental proof for this mechanism is limited, and the reaction could in fact proceed through the same mechanism as the metal alkoxide catalyzed reaction. The exact mechanism remains to be elucidated.

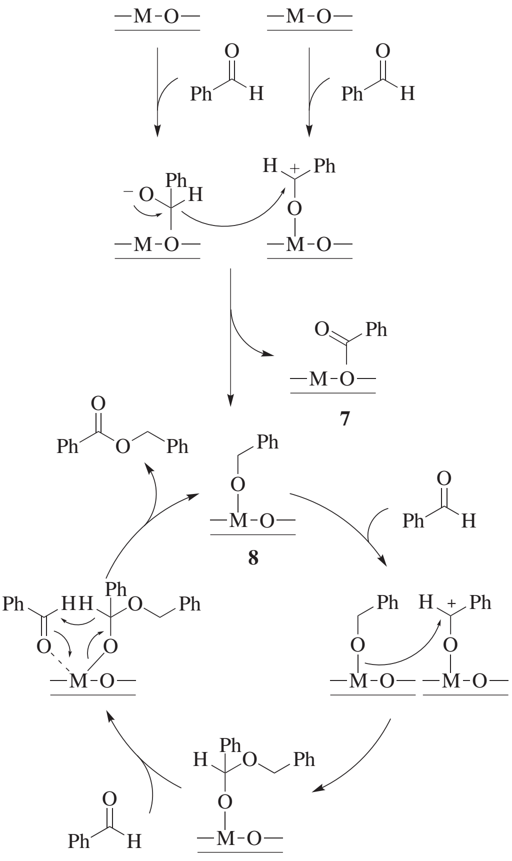


Scheme 5

Several heterogeneous base catalysts are effective in the Tishchenko reaction. It has been proposed that with alkaline earth metal oxides, both basic and acidic sites on the catalyst surface participate in the reaction (Scheme 6).[76] It is believed that the aldehyde initially coordinates to the catalyst surface and undergoes a Cannizzaro-type oxidation–reduction step, forming acyl and alkoxide complexes **7** and **8**. From here on the mechanism is similar to that of the classic Tishchenko reaction. Another molecule of aldehyde coordinates to the catalyst followed by alkoxide transfer from **8** to the carbonyl group, forming the hemiacetal intermediate **9**. A third molecule of aldehyde coordinates to the catalyst and is reduced to an alkoxide via hydride transfer from **9**. The latter is subsequently cleaved off as a symmetrical ester and the intermediate **8** is regenerated.

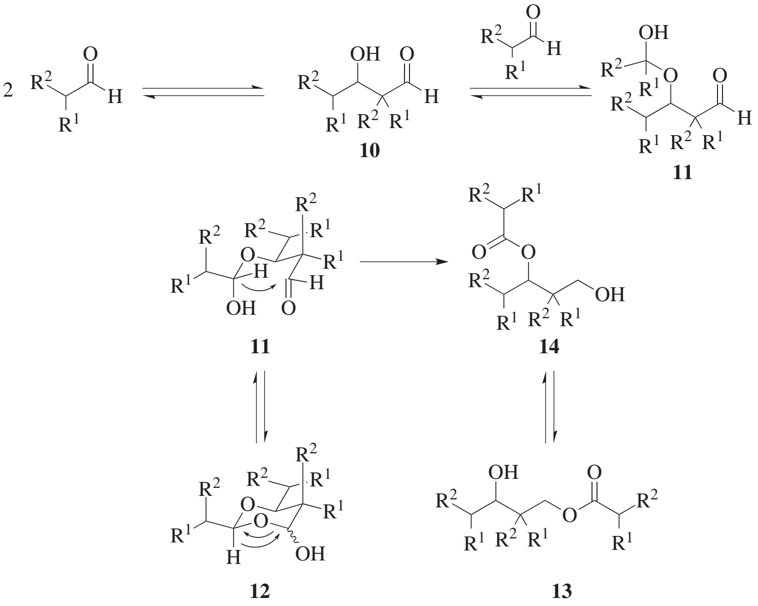
The Aldol–Tishchenko Reaction

The classical aldol–Tishchenko reaction leads to the trimerization of an enolizable aldehyde (Scheme 7). A basic catalyst first transforms the aldehyde into an enolate species, and an aldol addition occurs. The aldol **10** can then form an intermediate hemiacetal **11** with another aldehyde molecule. Current evidence suggests that this hemiacetal is in equilibrium with a 1,3-dioxan-4-ol structure **12**, which can also be isolated. The Tishchenko step takes place when a metal catalyst coordinates

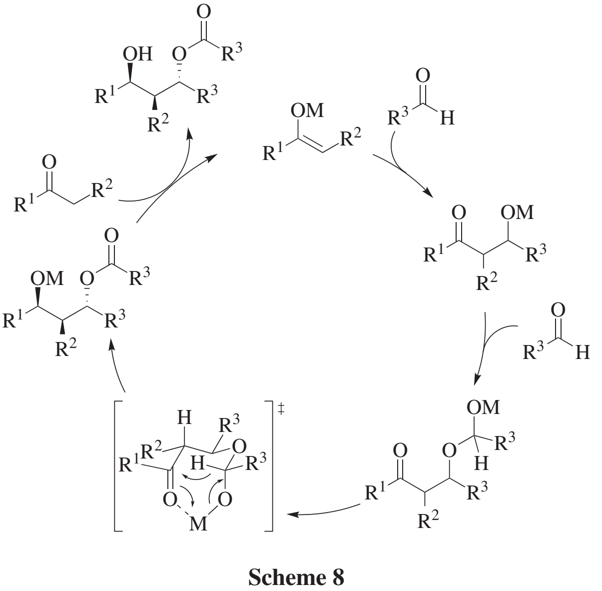


Scheme 6

to intermediate **11**, promoting a hydride transfer to the carbonyl group of the original aldol **10**. A six-membered transition state has been proposed for this reaction (see also Scheme 8),[100,108] and kinetic studies reveal the hydride transfer to be the rate-determining step.[132] Placing the sterically demanding substituents in equatorial positions of the intermediate **11** leads to a product that contains a 1,3-*anti*-diol structure, usually with excellent diastereoselectivity. Depending on the catalyst and reaction conditions, ester migration from the 3-hydroxyl to the 1-hydroxyl may occur, and both primary and secondary esters are produced.[133] Thermodynamic equilibrium usually favors the primary ester **13** over the secondary **14** in these cases.[94] The aldol–Tishchenko reaction has also been applied to reactions between ketone-derived enolates and aldehydes (Scheme 8). The mechanism is very similar to the one presented in Scheme 7. The metal enolate undergoes aldol addition to an aldehyde, and the alkoxo–aldol product forms a hemiacetal with another aldehyde. Intramolecular coordination of the aldehyde oxygen to the metal ion promotes the six-membered transition state, and the intramolecular hydride transfer takes place. The metal catalyst can then form a new enolate from the starting material, thus liberating the 1,3-*anti*-diol monoester.



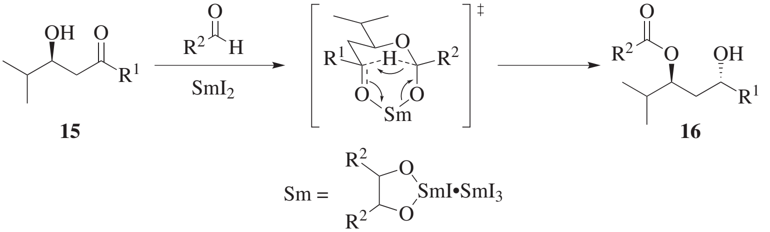
Scheme 7



Scheme 8

The Evans–Tishchenko Reaction

The mechanism for the Evans–Tishchenko reaction is similar to the aldol–Tishchenko reaction of two different aldehydes. The hydride-donor aldehyde forms a hemiacetal with the β-hydroxy ketone **15**. The subsequent Tishchenko step proceeds through the metal-coordinated bicyclic transition structure, leading to the 1,3-*anti*-diol structure **16** with excellent stereoselectivity (Scheme 9).[108] The enantiopurity of the starting material **15** is retained in the product. It has been proposed that the actual catalytic species is a complex of samarium triiodide and a pinacol species derived from the aldehyde via a radical coupling (Scheme 9).[109]



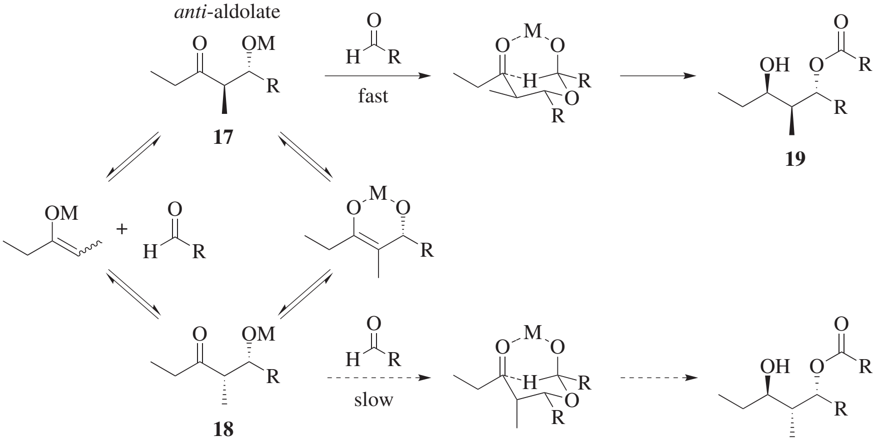
15

16

Scheme 9

β-Hydroxy ketones with alkyl substituents at the 2-position readily undergo a rapid retro-aldol equilibration with Lewis acidic catalysts. This has been proven through an Evans–Tishchenko reaction of a 1:1 mixture of deuterated *anti*- and *syn*-aldol adducts.[134] The complete absence of deuterium in the final product is proof positive of a retro-aldol reaction via dissociation and subsequent recombination. The aldol adducts thus equilibrate between *anti*-configuration **17** and *syn*-configuration **18** (Scheme 10). The *anti*-aldolate **17** reacts more rapidly via an Evans–Tishchenko

anti-aldolate



17

19

18

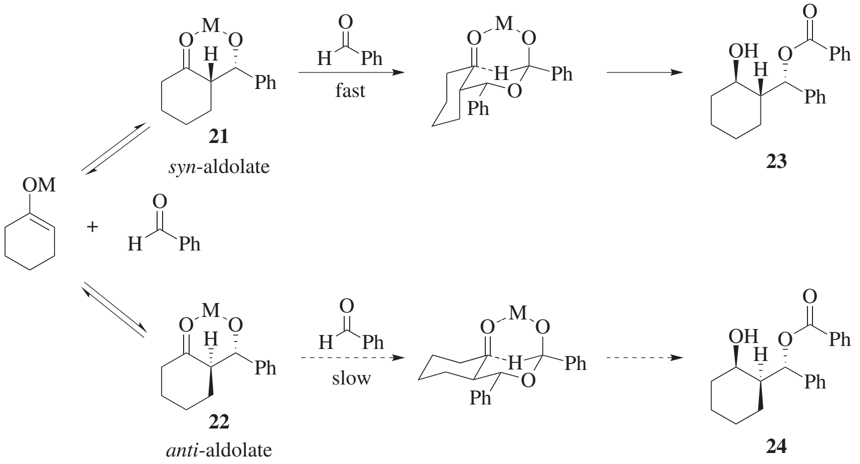
20

syn-aldolate

Scheme 10

reaction due to the equatorial position of the 2-substituent. For the *syn*-aldolate **18,** the retro-aldol reaction proceeds at a greater rate than the Evans–Tishchenko reaction. Thus the reaction mixture contains mostly the 1,2-*anti*-1,3-*anti* product **19**, with 1,2-*syn*-1,3-*anti* products **20** rarely present.

It is worth noting that cyclic ketones act in an opposite manner, thus giving 1,2-*syn*-1,3-*anti* products like **23** instead of 1,2-*anti*-1,3-*anti* structures like **24** (Scheme 11).[134] Both *syn*- and *anti*-aldolates **21** and **22** are formed in the initial aldol reaction, and a retro-aldol equilibration between the two configurations takes place. In this case the *syn*-aldolate **21** gives a more favorable transition state in which the ring is in a *cis* conformation. This orientation leads to a better axial attack of the hydride on the carbonyl group, as opposed to an equatorial attack in the case of *anti*-aldolates.

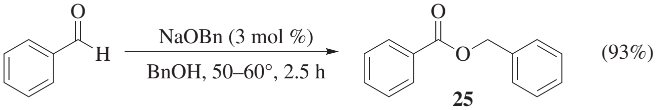


Scheme 11

SCOPE AND LIMITATIONS

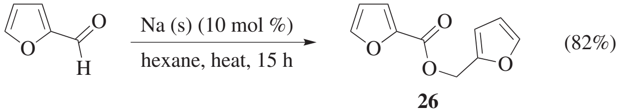
The Classical Tishchenko Reaction

Alkali Metal and Alkaline Earth Metal Catalysts. Alkali metal alkoxides are applicable as catalysts in the Tishchenko reaction. Thus, benzaldehyde is converted into benzyl benzoate (**25**) in fair to good yields with sodium methoxide[1] and sodium benzyloxide prepared in situ (Scheme 12).[1,39] Magnesium methoxide also catalyzes the dimerization of formaldehyde into methyl formate as effectively as aluminum methoxide.[2,4]



Scheme 12

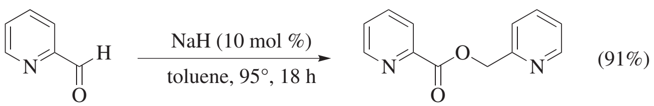
Furfuryl furoate (**26**) is prepared on a large scale from furfuraldehyde via the Tishchenko reaction in good yield.[135] A catalyst solution is prepared by dissolving metallic sodium in furfuryl alcohol analogous to the synthesis of benzyl benzoate mentioned above.[39] Furfuryl furoate is obtained in 78% yield in this manner. Other Tishchenko-type syntheses of **26** include catalysis by sodium phenoxide in phenol,[42] or by metallic sodium in hexane.[43] In the latter case, **26** is obtained in 82% yield (Scheme 13).[43]



26

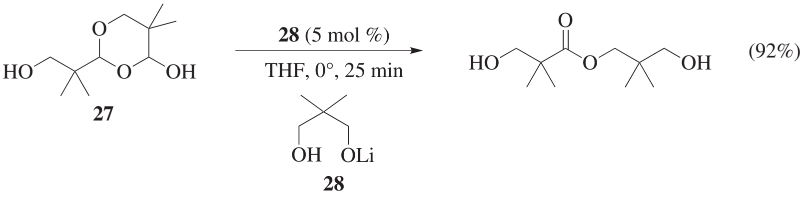
Scheme 13

Sodium hydride has been reported to dimerize benzaldehyde in refluxing benzene.[136] The reaction is thought to proceed through initial formation of a catalytic amount of sodium benzyloxide, which then initiates the Tishchenko reaction. The reduction of aromatic aldehydes to the corresponding alkoxides by sodium or potassium hydride has been reported, although alkoxide formation through a Cannizzaro reaction due to corresponding metal oxide contaminants has not been conclusively excluded.[137,138] Heteroaromatic aldehydes can be converted into dimeric esters in good yields in the presence of sodium hydride (Scheme 14).[139] The basicity of sodium hydride prevents its use in the Tishchenko reaction of aliphatic aldehydes. Potassium hydride, potassium *tert*-butoxide, and alkali metal bis(trimethylsilyl)amides function similarly as catalyst precursors by forming an active metal alkoxide species from the reactant aldehyde.[140]

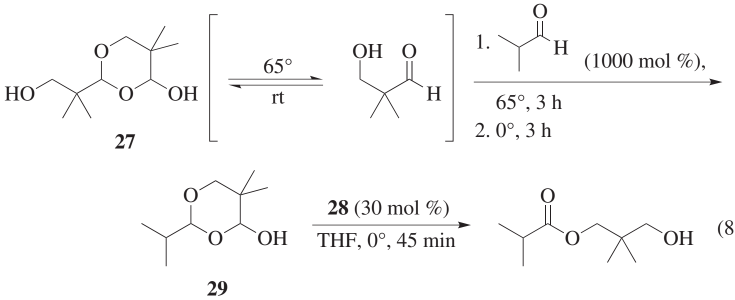


Scheme 14

The lithium monoalkoxide of 2,2-dimethyl-1,3-propanediol (**28**) is used to catalyze the Tishchenko reaction of 5,5-dimethyl-2-(1′,1′-dimethyl-2′-hydroxyethyl)-4-hydroxy-1,3-dioxane (**27**) (dimeric hydroxypivalaldehyde) (Scheme 15).[141] The catalyst is extremely efficient, and the reaction goes to completion in less than 30 minutes. This catalyst system has also been applied in a mixed aldol–Tishchenko reaction where **27** is first monomerized and converted into a "mixed" 1,3-dioxan-4-ol **29** in the presence of an excess of another aldehyde. The hydride-transfer/esterification step can then be achieved in the presence of **28** (Scheme 16).[142]

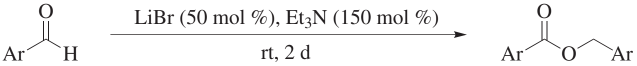


Scheme 15



Scheme 16

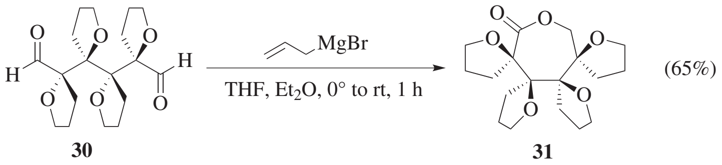
Lithium bromide with Et_3N comprises a catalyst system that is able to convert aromatic aldehydes into the corresponding Tishchenko esters under solvent-free conditions (Scheme 17).[45] Electron-withdrawing substituents at the 4-position of the benzene ring lead to slightly lower yields. Heterocyclic aldehydes, such as nicotinaldehyde and 2-thiophenecarboxaldehyde, also react to give the corresponding esters in moderate to good yields. The catalyst system can also catalyze Cannizzaro and Meerwein–Ponndorf–Verley reactions, depending on the choice of substrates and work-up method.



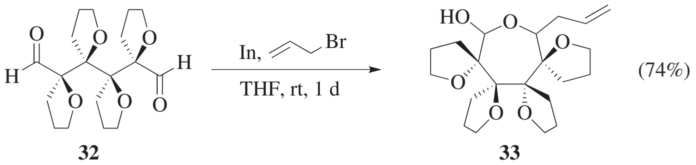
Ar	Yield (%)
Ph	96
4-ClC_6H_4	85

Scheme 17

Grignard reagents can be used to catalyze the Tishchenko reaction. According to an early example, benzaldehyde is converted into benzyl benzoate by EtMgBr in anhydrous diethyl ether, albeit in only 17% yield.[46] EtMgBr has also been used with (−)-sparteine as a chiral ligand in an enantioselective Tishchenko reaction[49] and in polymerization reactions,[47,48] which are both discussed below. Allylmagnesium bromide promotes the Tishchenko-type lactonization of a tetrakis (tetrahydrofuranyl) dialdehyde **30** instead of an expected addition and acetalization.[143] The 7-membered tetrahydrofuranyl-substituted lactone **31** is obtained in 65% yield in this case (Scheme 18).[143] In an interesting comparison, indium-promoted allylation of the isomeric dialdehyde **32** having all the tetrahydrofuranyl oxygens in *syn* configurations gives the allylated 7-membered lactol **33** as the main product (Scheme 19).[143]

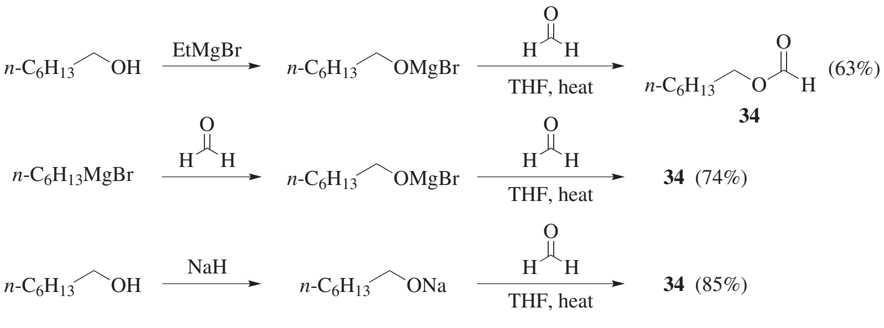


Scheme 18



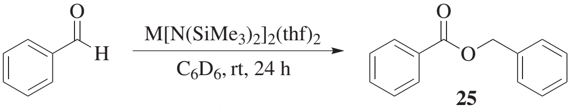
Scheme 19

Sodium and magnesium alkoxides are used to generate formate esters of several alcohols in reactions with formaldehyde.[44] For example in the synthesis of *n*-heptyl formate (**34**), the alkoxide can be generated either by deprotonation of the corresponding alcohol with EtMgBr, by addition of the corresponding alkyl Grignard reagent directly to formaldehyde, or by deprotonation of the alcohol with NaH (Scheme 20).[44] A wide structural variety of formate esters can be generated with this method from primary, secondary, and tertiary alkoxides. The reaction differs from the classical Tishchenko reaction in that a stoichiometric amount of Grignard reagent or sodium methoxide is involved.



Scheme 20

Heavy alkaline earth metal bis(trimethylsilyl)amide complexes have recently been introduced as active Tishchenko reaction catalysts for aromatic and α-substituted aliphatic aldehydes.[51] The complexes $M[N(SiMe_3)_2]_2(thf)_2$ show greatest activity when M = calcium, giving benzyl benzoate in 97% yield (based on ^1H NMR measurements) (Scheme 21).[51] Strontium and barium catalysts both give slightly lower yields, although barium clearly has a lower turnover rate. Electron-donating substituents at the 4-position of the aromatic ring decrease reactivity, but otherwise aromatic substitution is well-tolerated by the catalyst system.



25

M	TOF (h^{-1})	Yield* (%)
Ca	52	97
Sr	41	78
Ba	1.6	86

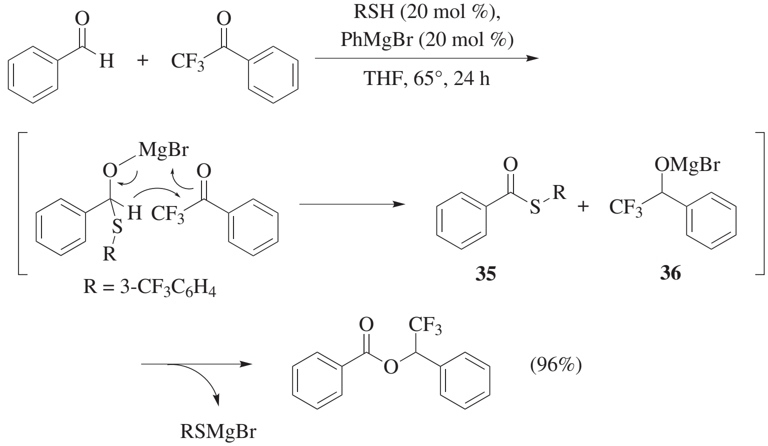
* by NMR

Scheme 21

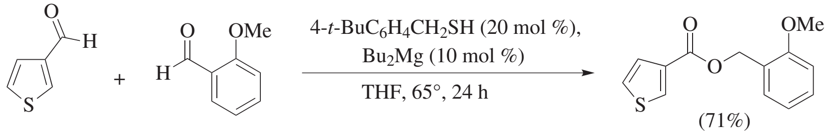
Selective Crossed Tishchenko Reactions with Alkaline Earth Metal Catalysts. Crossed Tishchenko reactions between two different aldehydes are usually difficult to control. All four possible esters are usually formed and product distribution depends on the relative reactivities of the participating aldehydes. An example of a controlled intermolecular crossed Tishchenko reaction includes a combination of a Grignard reagent and a thiol as the catalyst system.[144,145]

Trifluoroacetophenone and analogous aromatic non-enolizable ketones are used as coupling partners with aromatic aldehydes to give mixed esters in good yields (Scheme 22).[144] The reaction proceeds via addition of a thiolate to the aldehyde, and subsequent formation of thioester **35** with hydride transfer to the ketone. The newly formed alkoxide species **36** then attacks the thioester, thus forming the product ester and liberating the magnesium thiolate back into the catalytic cycle. A combination of diaryl selenide and dialkyl magnesium catalyzes the same reaction at room temperature, and tolerates substituted aromatic aldehydes and heteroaromatic aldehydes well.[146] A selective, crossed Tishchenko reaction between two aromatic aldehydes can be achieved with magnesium thiolate catalysis by placing a substituent capable of chelation at the 2-position of the aromatic ring.[147] Chelation of the catalyst enhances the steric bulk around the aldehyde, which makes it more selective towards hydride transfer than thiolate addition (Scheme 23).[147]

Aluminum Catalysts. Aluminum alkoxides are the original and most common catalysts for the Tishchenko reaction, and have been widely studied.[2–5,16–22] Kinetic studies indicate an induction period in the reaction, during which an alkoxide

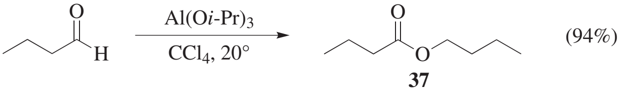


Scheme 22



Scheme 23

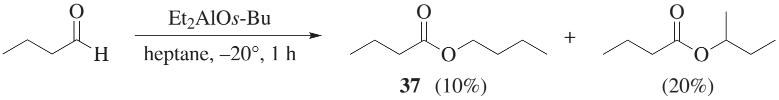
ligand of the metal catalyst is replaced with a new alkoxide derived from the reactant aldehyde.[27,30] As discussed in connection with the mechanistic aspects, the alkoxide transfer leads to the formation of a mixed ester side product. To shorten the induction period and to avoid such side products, it may be beneficial to use an alkoxide ligand corresponding to the aldehyde, e.g. $Al(OBn)_3$ with benzaldehyde. However, this is not necessary for an efficient reaction: for example, *n*-butyraldehyde can be converted into *n*-butyl *n*-butyrate (**37**) in 94% yield with $Al(Oi\text{-}Pr)_3$ in CCl_4 if the reaction temperature is kept at or below 20° (Scheme 24).[90]



37

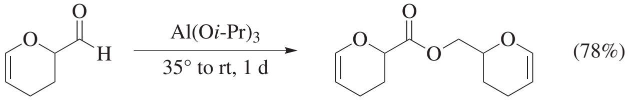
Scheme 24

The effects of concentration, solvent, and different additives such as acids, alcohols, and metal salts have been widely studied.[16,17,27,30,31] The presence of water and simple aliphatic alcohols is observed to be mostly inhibitory to the reaction. Lewis acidic metal chlorides such as $AlCl_3$, $HgCl_2$, $ZnCl_2$, $CaCl_2$, and $FeCl_3$ act as promoters, significantly increasing the reaction rates and yields.[17] These promoters may be used together with a small amount of an alcohol, which increases the solubility of the complexes formed by the metal chloride and the catalyst.[16,17] Surprisingly, benzoic acid, acetic acid, and their respective anhydrides are also efficient promoters for the reaction.[31] The corresponding sodium salts have no promoting effect. Mildly polar or non-polar aprotic solvents are usually applicable to the aluminum alkoxide catalyzed Tishchenko reaction.[17] Choosing the correct amount of aluminum alkoxide catalyst is also of importance. For optimal yields, approximately 3–5 mol % of catalyst is used. Stoichiometric amounts of aluminum alkoxides can lead to suppression of the actual Tishchenko catalytic cycle, and to formation of a mixed ester, a result of alkoxide transfer from the catalyst to the aldehyde. In the reaction of *n*-butyraldehyde with an equimolar amount of diethylaluminum *sec*-butoxide, the mixed ester *s*-butyl *n*-butyrate is formed together with the Tishchenko product **37** (Scheme 25).[148] The Meerwein–Ponndorf–Verley reaction and alkoxide transfer Tishchenko esterification are dominant pathways at temperatures from −65° to 20°, and aldol addition becomes the major competing pathway at temperatures above 20°.

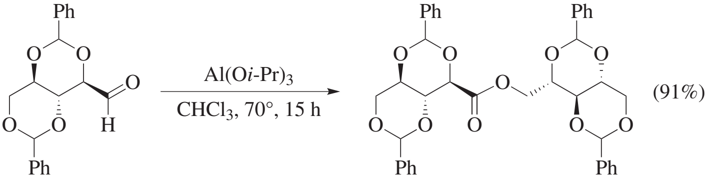


Scheme 25

Simple aliphatic and aromatic aldehydes are usually the best substrates for the Tishchenko reaction, but aldehydes containing heterocyclic or sterically bulky substituents can also be converted into their respective esters with aluminum isopropoxide (Schemes 26 and 27).[149–151]

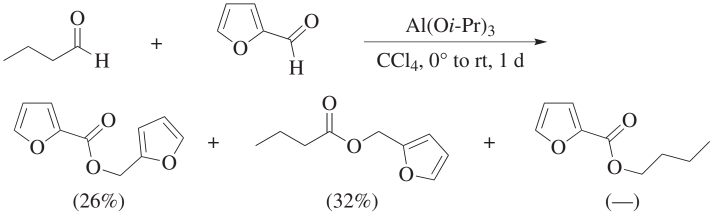


Scheme 26



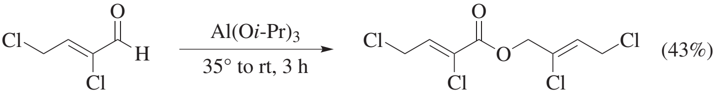
Scheme 27

Furfuraldehyde, whose efficient esterification has been achieved with other catalysts, is usually a problematic substrate for classic Tishchenko catalyst systems. It has been reported to form furfuryl *n*-butyrate in a crossed Tishchenko reaction whereas only minor amounts of *n*-butyl furoate are detected (Scheme 28).[90]

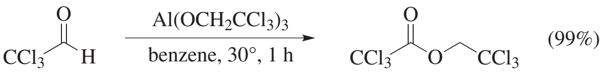


Scheme 28

Chlorinated aldehydes can be relatively unreactive substrates in the Tishchenko reaction with aluminum isopropoxide. Chloroacetaldehyde gives 13% of 2-chloroethyl 2-chloroacetate, and 2,4-dichlorocrotonaldehyde gives the corresponding ester in a fair yield (Scheme 29).[26] Chloral reacts sluggishly with traditional aluminum alkoxides.[90,152] The combined inductive effect of three electronegative substituents makes trihalogenated aldehydes very unsuitable as hydride donors and, conversely, good acceptors. In a crossed reaction with *n*-butyraldehyde, chloral only forms trichloroethyl esters or is reduced to 2,2,2-trichloroethanol.[90] However, aluminum catalysts bearing chlorinated alkoxide groups, and alkylaluminum compounds such as $AlEt_3$ and $AlEt_2Cl$, are rather effective catalysts for chloral. $Al(OCH_2CCl_3)_3$ catalyzes the formation of 2,2,2-trichloroethyl 2,2,2-trichloroacetate (**38**) in nearly quantitative yield from chloral (Scheme 30).[28] Similarly, $Al(OCH_2CBr_3)_3$ is not only an effective catalyst for bromal, but is also an excellent catalyst for *n*-butyraldehyde. In this case the exact effect of halogenation on the catalyst activity cannot be completely quantified because the bromoalkoxide groups are gradually exchanged with *n*-butoxide groups during the course of the reaction.[28]



Scheme 29

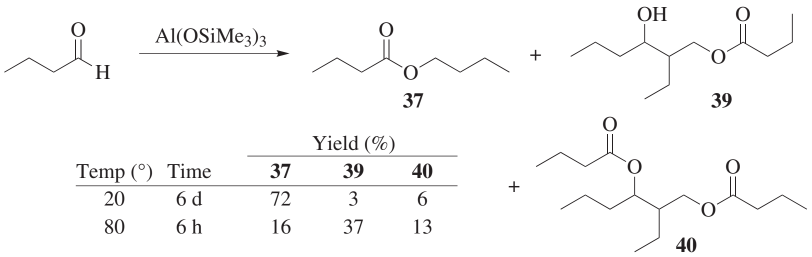


38

Scheme 30

Conjugated unsaturated aldehydes are usually problematic in the aluminum-catalyzed Tishchenko reaction. For instance, acrolein has been reported to form polymers.[153]

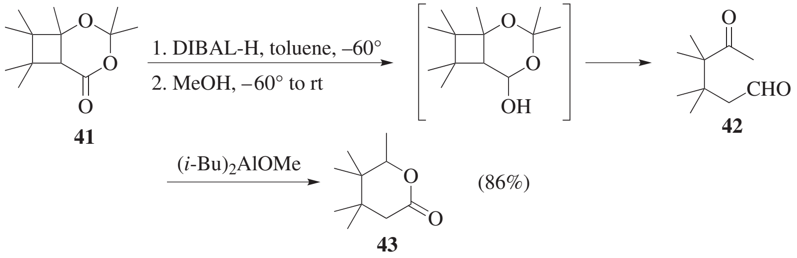
Tris(trimethylsilyloxy)aluminum has been used to catalyze the Tishchenko reaction of *n*-butyraldehyde, benzaldehyde, and chloral.[32,154] *n*-Butyl *n*-butyrate is formed with good selectivity at ambient temperature, but at higher temperatures the aldol–Tishchenko product **39** becomes the major product, and the corresponding diester **40** is also formed (Scheme 31).[154] By comparison, $Al(Ot\text{-}Bu)_3$ is more selective for the classical Tishchenko reaction at both temperatures. $Al(OSiMe_3)_3$ does not catalyze the Tishchenko reaction of benzaldehyde, but it does convert chloral into **38** in 70% yield, although in an excessively long reaction time of 13 days.[32]



Temp (°)	Time	Yield (%) 37	39	40
20	6 d	72	3	6
80	6 h	16	37	13

Scheme 31

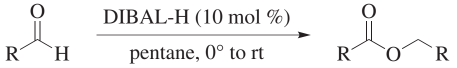
DIBAL-H reduction of the fused lactone **41** yields another lactone product **43**, which is thought to arise from an intramolecular Tishchenko reaction of the intermediate δ-keto aldehyde **42** (Scheme 32).[155] The quenching of excess DIBAL-H with MeOH forms diisobutylaluminum methoxide, which then functions as the Tishchenko catalyst.



Scheme 32

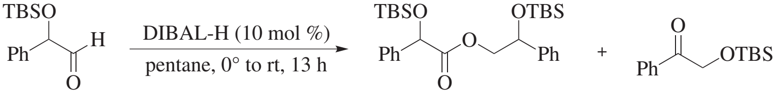
DIBAL-H itself is an active catalyst precursor for the Tishchenko reaction.[156,157] Slow addition of DIBAL-H to a solution of an aldehyde in anhydrous pentane at 0° followed by warming to ambient temperature usually yields the ester in fair to excellent yields. A wide structural variety of aldehydes containing different functionalities such as alkynes, ethers, esters, ketones, and halogens can be dimerized to esters using this method (Scheme 33).[157] α-Substitution imposes some limits on this method. For example, the α-silyloxy-β-arylaldehyde **44** reacts with DIBAL-H via both the Tishchenko route and a competing 1,4-silyl migration/Oppenauer oxidation route, giving a mixture of products **45** and **46**, respectively

(Scheme 34).[157] This method has also been used in the synthesis of macrocyclic lactones such as **47** in a three-step sequence of Tishchenko reaction/olefin metathesis/catalytic hydrogenation starting from aldehydes containing terminal double bonds (Scheme 35).[157]



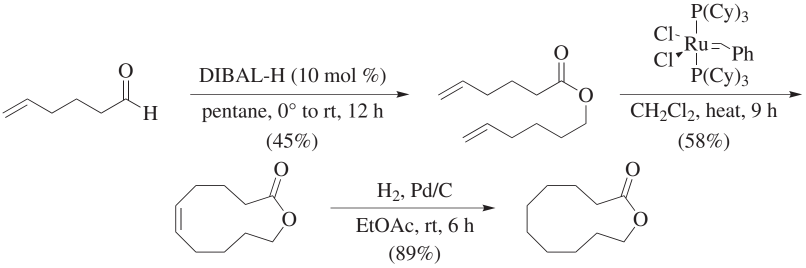
R	Time (h)	Yield (%)
t-Bu	5	95
$Br(CH_2)_5$	5	70
$HC{\equiv}C(CH_2)_6$	14	62
$MeO_2C(CH_2)_6$	12	61

Scheme 33



44 **45** (37%) **46** (26%)

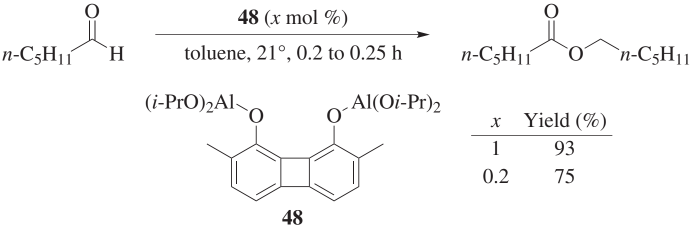
Scheme 34



47

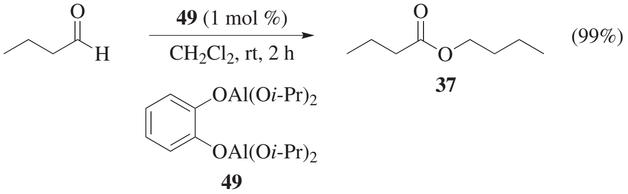
Scheme 35

Bidentate Lewis acids are powerful catalysts for activating carbonyl compounds. (2,7-Dimethyl-l,8-biphenylenedioxy)bis(diisopropoxyaluminum) (**48**) is a highly efficient catalytic system[158] that is also applicable to Meerwein–Ponndorf–Verley and Oppenauer reactions.[159] Reactions of aliphatic aldehydes catalyzed by **48** are usually complete in less than one hour, and catalyst loading can be as low as 0.2 mol % (Scheme 36).[158] Aromatic aldehydes usually react more sluggishly, reactions taking several hours to reach completion, but the intramolecular lactonization of phthalaldehyde is completed as rapidly as the reactions of aliphatic aldehydes. Catechol- and gallol-based multidentate catalysts such as **49** are also active in the Tishchenko reaction, although longer reaction times are needed for full conversion to products than with the biphenylene system (Scheme 37).[160] The biphenyl-based sulfonamide catalyst **50** is somewhat more active than the catechol- and gallol-based catalysts, with most reactions going to completion in one hour (Scheme 38).[161] All these compounds can also catalyze the Tishchenko reaction of enolizable aldehydes with little or no aldol–Tishchenko side products.

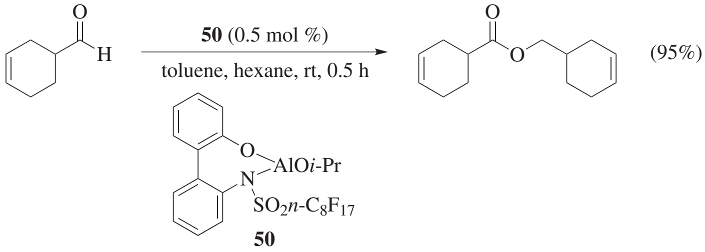


x	Yield (%)
1	93
0.2	75

Scheme 36

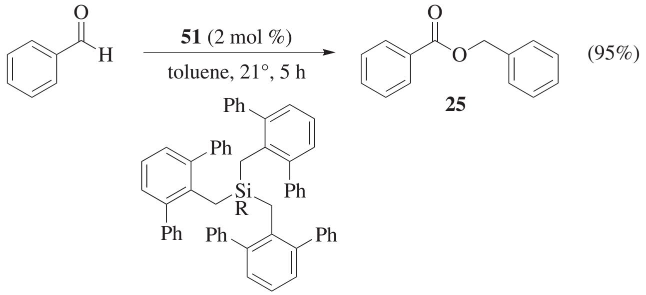


Scheme 37



Scheme 38

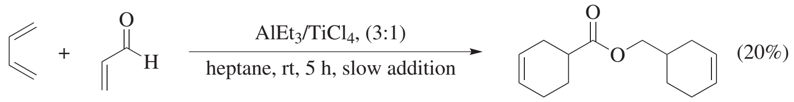
The effectiveness of bidentate Lewis acid catalysts is partially based on allowing the substrate aldehydes to adopt a close spatial arrangement that promotes the rate-determining alkoxide transfer step and the subsequent hydride transfer step. A similar effect is achieved with the bowl-shaped aluminum catalyst [tris(2,6-diphenylbenzyl)siloxy]dimethylaluminum **51**.[162] Thus, using 2 mol % of **51** affords benzyl benzoate from benzaldehyde in 95% yield (Scheme 39),[162] whereas similar siloxyaluminum species such as t-$BuPh_2SiOAlMe_2$, $Ph_3SiOAlMe_2$, or $Bn_3SiOAlMe_2$ give poor yields or are completely unreactive.



51 R= OAlMe$_2$

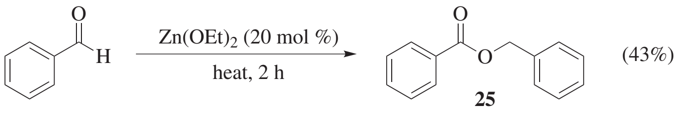
Scheme 39

The coupling of Tishchenko and Diels–Alder reactions is achieved with the Ziegler-type catalyst $AlEt_3/TiCl_4$ (3:1).[163] Thus, an α,β-unsaturated aldehyde dienophile and an alkyl-substituted butadiene undergo the Diels–Alder reaction, which gives cyclohex-3-enecarboxaldehyde derivatives. The aldehyde immediately reacts via a Tishchenko reaction to give the corresponding ester (Scheme 40).[163] A catalytic aluminum alkoxide species is likely formed via C-ethylation of the aldehyde and subsequent complexation with aluminum.

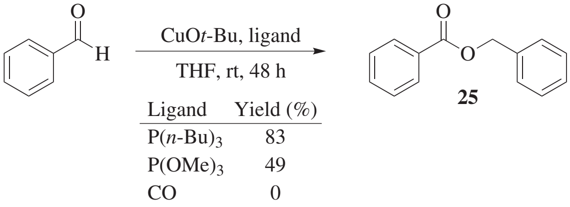


Scheme 40

Transition-Metal Catalysts. Transition-metal salts and complexes are widely used as catalysts in the Tishchenko reaction. The most common catalysts usually contain Ph_3P or other phosphine ligands, but some simple transition-metal alkoxides have also been examined. Zinc diethoxide and diisopropoxide are mildly active in the dimerization of benzaldehyde (Scheme 41).[164] Different complexes of CuO*t*-Bu give mixed results for the Tishchenko reaction of benzaldehyde (Scheme 42).[53] The activity varies greatly depending on the additional ligand used with CuO*t*-Bu. The iron dibenzyloxide bipyridyl complex is likewise able to catalyze the formation of benzyl benzoate (Scheme 43).[56] Titanium ethoxide is reported to be mildly active in the dimerization of acetaldehyde.[17]

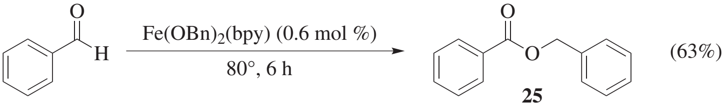


Scheme 41



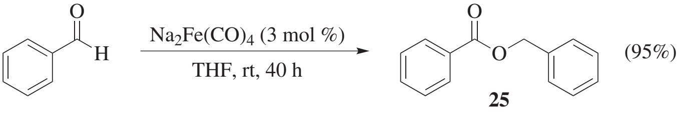
Ligand	Yield (%)
P(n-Bu)$_3$	83
P(OMe)$_3$	49
CO	0

Scheme 42

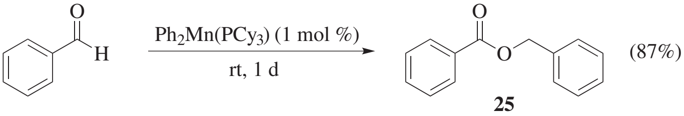


Scheme 43

The Tishchenko reaction can be catalyzed by tetracarbonyl ferrate complexes such as $Na_2Fe(CO)_4$[54] or $K_2Fe(CO)_4$.[62] Aromatic aldehydes are effectively converted into the corresponding esters by these complexes (Scheme 44).[54] Owing to the high basicity of the tetracarbonyl ferrate complex, aliphatic aldehydes react exclusively through an aldol addition pathway. The manganese complex Ph_2MnPCy_3 reacts with anhydrous benzaldehyde to form benzyl benzoate in 87% yield (Scheme 45).[55] Reaction of this complex with aliphatic aldehydes gives secondary alcohols arising from addition of a phenyl group from the catalyst to the aldehyde, among other products.

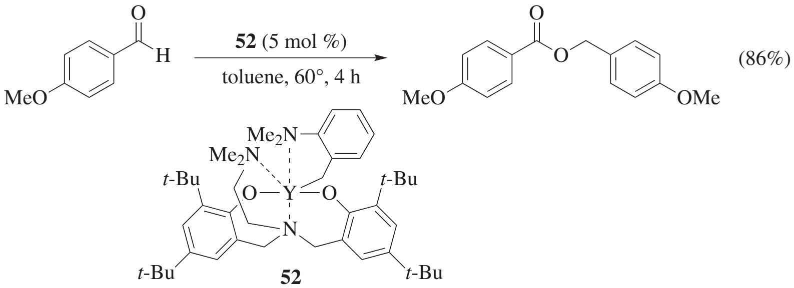


Scheme 44



Scheme 45

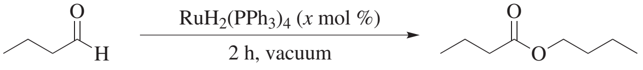
The yttrium complex **52** is an active catalyst in the Tishchenko reaction of aromatic aldehydes.[165] Benzyl benzoate is obtained in moderate to very good yields under relatively mild conditions. Electron-withdrawing substituents at the 4-position of the aromatic ring generally enhance reactivity with **52**. The reaction is also successful with an electron-donating methoxy group in the 4-position when the amount of catalyst is raised from 1 to 5 mol %, giving 4-methoxybenzyl-4-methoxybenzoate in 86% yield (Scheme 46).[165]



52

Scheme 46

A wide variety of ruthenium complexes have been studied as catalysts in the Tishchenko reaction.[52,57,59,60,63,67,166,167] $RuH_2(PPh_3)_4$ is a highly efficient catalyst over a wide range of conditions for aliphatic aldehydes and benzaldehyde (Scheme 47).[57] The reactions may be run under vacuum, in an inert atmosphere, or under a hydrogen atmosphere, and catalyst loading can be as low as 0.05 mol %. The use of a solvent is not necessary, although possible. When the reaction is run in hexane, toluene, or THF, butyraldehyde is dimerized in over 90% yield, but pyridine and *n*-butanol both greatly inhibit the reaction. Ruthenium catalysts retain their activity to a certain degree when bearing carbonyl, chloride, ethenyl, or methacrylate ester ligands, although $RuCl_2(PPh_3)_3$ and $Ru(CO)_3(PPh_3)_2$ are completely inactive as Tishchenko catalysts. Analogous iron, cobalt, molybdenum, palladium, and platinum complexes are likewise inactive.[57]

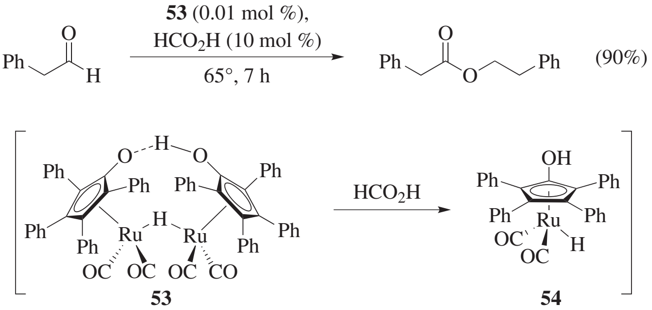


37

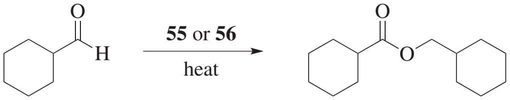
x	Temp (°)	Yield (GC, %)
0.8	100	90
0.9	20	98
0.25	0	99
0.05	0	89
0.25	–20	61

Scheme 47

Ruthenium carbonyl complex **53** is a highly effective catalyst precursor in the Tishchenko reaction (Scheme 48).[59] It reacts with formic acid to form the mononuclear hydride complex **54,** which acts as the catalytic species. Aliphatic and aromatic aldehydes alike are dimerized to the corresponding esters in good conversion, with turnover numbers reaching almost 20,000. However, an isoelectronic osmium complex is actually an inactive catalyst in the Tishchenko reaction.[168] Catalysis by osmium complexes has, however, been achieved, for instance with the hexahydrido osmium species **55**, which similarly functions as a catalyst precursor. The compound $OsH_2(CO)_2[P(i\text{-}Pr)_3]_2$ (**56**) is slightly less active (Scheme 49).[66]



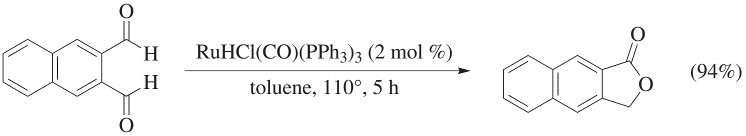
Scheme 48



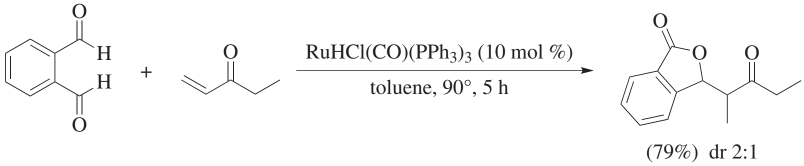
Complex	Time (h)	Yield (%)
55 $OsH_6[P(i\text{-}Pr)_3]_2$	0.5	98
56 $OsH_2(CO)_2[P(i\text{-}Pr_3)]_2$	22	92

Scheme 49

Complex $RuHCl(CO)(PPh_3)_3$ efficiently catalyzes the intramolecular Tishchenko reaction of aromatic dialdehydes and keto aldehydes (Scheme 50).[167] Aliphatic dialdehydes react more sluggishly, and with keto aldehydes the intermolecular Tishchenko reaction may be preferred. The complex can also be used in a cascade reaction between an α,β-unsaturated ketone and a dialdehyde to give a substituted lactone (Scheme 51).[167] Although formally a Tishchenko-type product, the reaction likely proceeds through a reductive aldol/oxidative lactonization pathway.

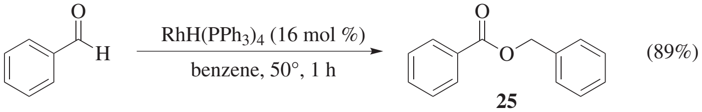


Scheme 50



Scheme 51

Rhodium complexes such as $RhH(PPh_3)_4$ are functional catalysts in the Tishchenko reaction of aromatic aldehydes (Scheme 52).[58] The active catalyst species is thought to be $RhH(PPh_3)_3$, which is formed via a dissociative process under the reaction conditions. $Rh(PPh_3)_3$ is likewise a functional catalyst, albeit less active than the hydridorhodium species. Electron-donating substituents at the 4-position of the aromatic ring lower the initial reaction rate, and electron-withdrawing substituents at the 3- and 4-positions raise it by an order of magnitude, although 4-nitrobenzaldehyde is completely unreactive with the $RhH(PPh_3)_4$ complex.[58]



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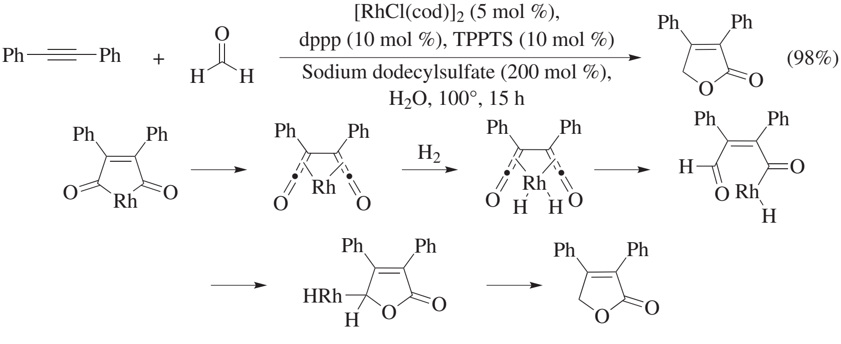
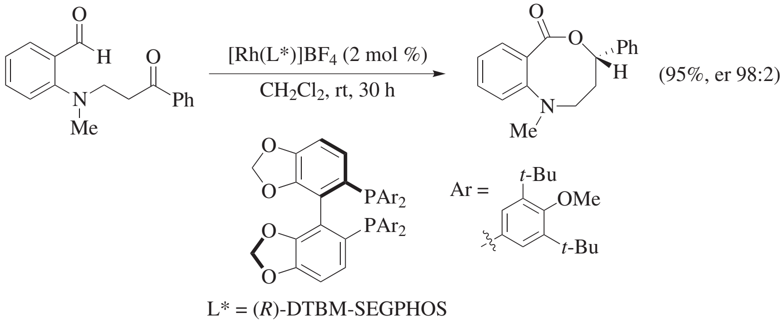
Scheme 52

The rhodium-catalyzed hydrocarbonylation of internal alkynes by using an excess of formaldehyde results in the formation of α,β-butenolides, arising from the Tishchenko lactonization of an intermediate dicarbonylrhodium complex (Scheme 53).[169] Rhodium complexes can also be used to catalyze the intramolecular hydroacylation of ketones.[170–172] For example, 8-membered nitrogen-containing lactones may be synthesized in excellent yield and enantioselectivity when a chiral rhodium catalyst is used (Scheme 54).[173] Tishchenko-type side reactions have also been reported in connection with other rhodium- or ruthenium-catalyzed hydroformylation and hydroacylation reactions.[174,175]

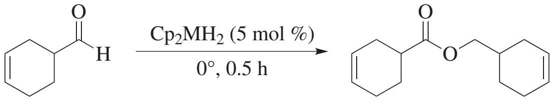


Scheme 53



Scheme 54

The zirconocene and hafnocene complexes Cp_2MH_2 and Cp_2MHCl (M = Zr, Hf) are efficient catalysts for the Tishchenko reaction of aliphatic aldehydes (Scheme 55).[61] Similar titanocene complexes are inactive, as are the corresponding Cp_2MCl_2 complexes, unless they are treated with *n*-BuLi to form a putative low-valent complex Cp_2M. Aromatic aldehydes are rather unreactive in the presence of these catalysts, e.g. benzyl benzoate is formed in only 13% yield. In a crossed reaction between benzaldehyde and butyraldehyde, butyl butyrate and benzyl butyrate are formed. The intrinsic hydride-acceptor nature of benzaldehyde, partly caused by the electron-withdrawing nature of the aromatic ring, is thus emphasized.

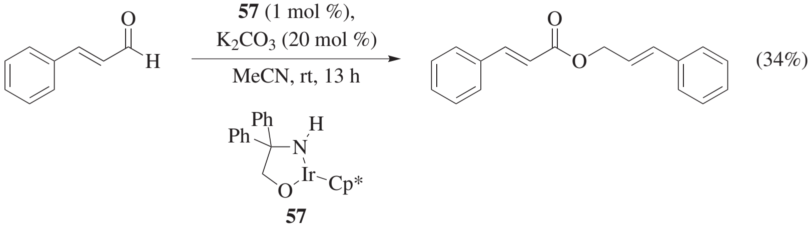


M	Yield (%)
Zr	90
Hf	87

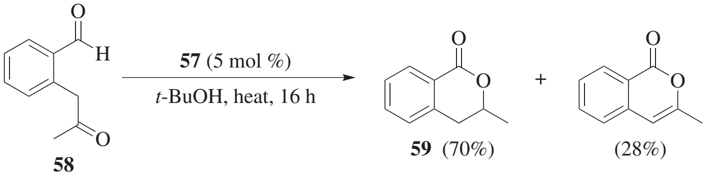
Scheme 55

Iridium complex **57** catalyzes the Tishchenko reaction under mild conditions.[68] Aromatic and aliphatic aldehydes are dimerized to esters in good yields. Cinnamaldehyde, usually a problematic substrate in the Tishchenko reaction along with other conjugated unsaturated aldehydes, is successfully converted into the ester in 34% yield (Scheme 56).[68] The catalyst system has also been used in an intramolecular Tishchenko reaction of the δ-keto aldehyde **58** in the synthesis of 3,4-dihydroisocoumarin **59** and its analogs (Scheme 57).[176]

The nickel complex **60** (Scheme 58)[177] is one of the most versatile catalysts for the classical Tishchenko reaction. It is equally powerful for primary, secondary, and tertiary aliphatic and aromatic aldehydes alike. Aromatic substitution is well tolerated, and variation of catalyst loading and the reaction temperature allows the conversion of even sterically congested aldehydes to symmetrical esters in excellent yields. Complex **61** with a slightly different NHC ligand enables the synthesis of

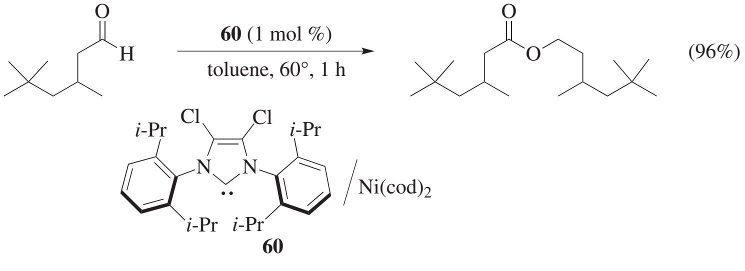


Scheme 56

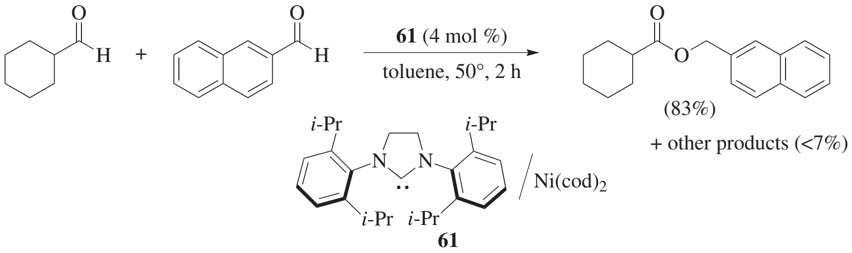


Scheme 57

crossed Tishchenko esters from a 1:1 mixture of an aliphatic and an aromatic aldehyde with excellent selectivity, wherein the aromatic aldehydes act as the hydride acceptor (Scheme 59).[178] It is noteworthy that very small amounts (<5%) of symmetric aliphatic esters are formed in the crossed reaction, unless the aromatic partner is highly hindered and unreactive. However, poor or no selectivity is observed when two different aliphatic or aromatic aldehydes are used.[178]

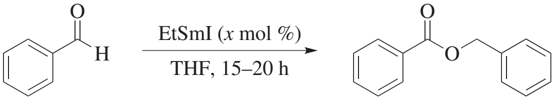


Scheme 58



Scheme 59

Lanthanoid Catalysts. Ethyllanthanoid iodides are among the first discovered lanthanoid catalysts for the Tishchenko reaction. Reaction of benzaldehyde with a stoichiometric amount of EtLnI (Ln = Pr, Nd, Sm) gives benzyl benzoate in fair yields (Scheme 60).[69] Common ring substituents are also tolerated by the catalyst system, although anisaldehyde is clearly a less reactive substrate. The reaction can also be run with substoichiometric amounts of ethyllanthanoid iodide complexes.



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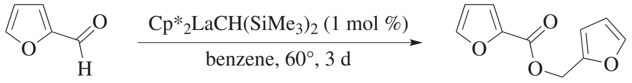
x	Temp (°)	Yield (%)
100	65	32
10	rt	58

Scheme 60

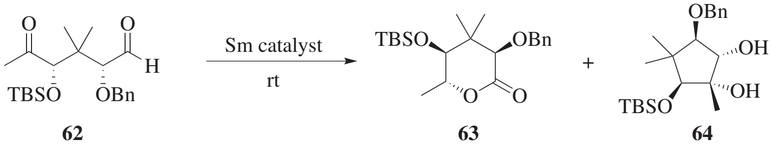
Metallocene complexes $Cp^*_2LnCH(SiMe_3)_2$ with a lanthanum or neodymium core are versatile catalysts for the Tishchenko reaction of aromatic aldehydes and non-enolizable aliphatic aldehydes, although long reaction times are usually required.[70,71] The dimerization of furfuraldehyde is often difficult to achieve, but catalysis by lanthanocenes affords furfuryl furoate in 77% yield (Scheme 61).[71] $Cp^*_2LaCH(SiMe_3)_2$ is also one of the best reported catalysts for electron-rich aldehydes; for instance, it catalyzes the dimerization of anisaldehyde in 95% yield. Additionally, lanthanocene complexes are applicable to intramolecular lactonization of phthalaldehyde, oligomerization of isophthalaldehyde, and polymerization of terephthalaldehyde.[71]



(77%)

Scheme 61

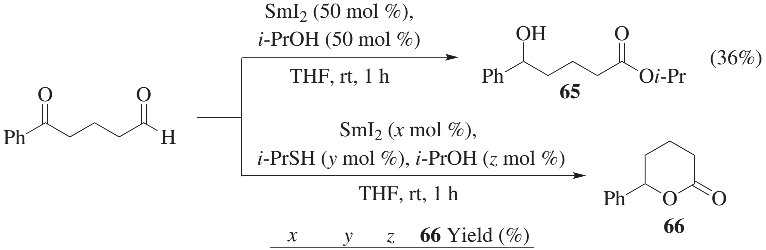
Samarium-based catalysts bear a special importance for the Evans–Tishchenko variant, which is discussed in more detail below. Samarium diiodide catalyzes both the classic Tishchenko and aldol–Tishchenko reactions.[179] Efficient intramolecular and stereoselective lactonizations of δ-keto aldehydes is also achieved with samarium iodide complexes.[180–182] α-Silylated δ-keto aldehydes such as **62** are lactonized with good stereoselectivity with $SmI_2Ot\text{-}Bu$ (Scheme 62).[180] The product ratio is very sensitive to the exact catalyst system. One equivalent of SmI_2 in THF affords the pinacol product **64** exclusively, and $SmI_2Ot\text{-}Bu$ in THF gives lactone **63**. Using SmI_2 in a 1:1 mixture of THF/hexane, and premixing the catalyst in MeOH (1:99), leads to a mixture of the two products with a 65:18 preference for the lactone.



Catalyst	Solvent	Yield (%) **63**	Yield (%) **64**
SmI_2	THF	0	80
SmI_2	THF/hexane (1:1)	65	18
SmI_2Ot-Bu	THF	89	0

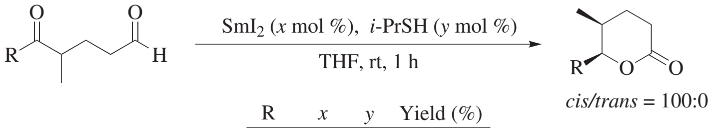
Scheme 62

Another route to the stereoselective lactonization of δ-keto aldehydes involves the use of a thiol co-catalyst.[181,182] The thiol is a crucial element in the catalytic system, since SmI_2 with *i*-PrOH does not result in the desired reaction, but rather affords the open-chain δ-hydroxy ester **65** (Scheme 63).[182] The simultaneous presence of both *i*-PrOH and *i*-PrSH affords the desired lactone **66** in poorer yields than *i*-PrSH alone with SmI_2. The thioester analog of **65** is formed in the presence of *i*-PrSH, and it is more active in the lactonization step, hence the reaction is halted at the open-chain ester stage in the presence of *i*-PrOH. Reactions of substituted δ-keto aldehydes proceed with good to excellent diastereocontrol (Scheme 64),[182] and the use of chiral thiols affords lactonization with fair to good enantioselectivity (Scheme 65).[182] It is of interest that no asymmetric induction is found when other chiral ligands, such as (−)-sparteine or salen complexes are used. Samarium iodide also promotes the lactonization of δ-silyl keto aldehydes in the presence of methanol.[183]



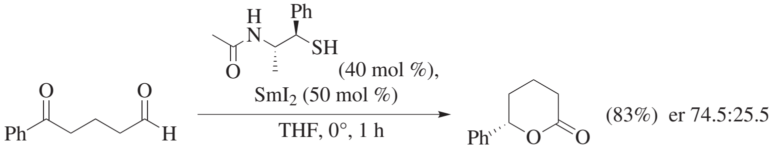
x	*y*	*z*	**66** Yield (%)
50	50	50	53
40	50	0	99

Scheme 63



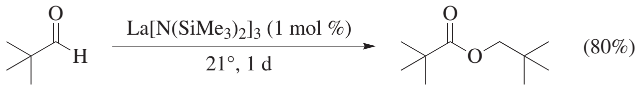
R	*x*	*y*	Yield (%)
Et	40	35	91
Ph	80	50	94

Scheme 64

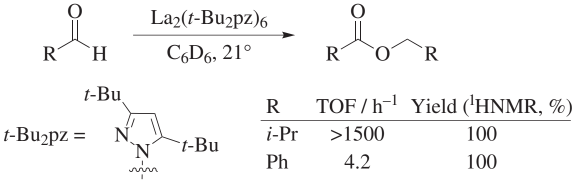


Scheme 65

Homoleptic lanthanoid amides such as La[N(SiMe$_3$)$_2$]$_3$ are highly active catalysts for the Tishchenko reaction of aromatic and α-substituted and non-enolizable aliphatic aldehydes with turnover frequencies reaching over 1500 h^{-1} and giving products in good to excellent yields (Scheme 66).[72,74] Linear aliphatic aldehydes react through both Tishchenko and aldol–Tishchenko routes; for example *n*-butyraldehyde gives *n*-butyl *n*-butyrate in 45% yield and fair amounts of a trimeric 1,3-diol monoester. Aromatic ring substituents usually have a retarding effect on turnover frequency. As an exception, electron-withdrawing 4-Br- and 4-NC-substitutents have an accelerating effect. The Lewis basic and electron-donating 4-dimethylamino group reduces the yield of the ester to 35%. This outcome has been attributed to competitive Lewis acid/base complex formation between the amino group and the carbonyl group. The pyrazolate complex La$_2$(*t*-Bu$_2$pz)$_6$ (*t*-Bu$_2$pz = 3,5-di-*tert*-butyl pyrazolate) is likewise highly active in the Tishchenko reaction of both aliphatic and aromatic aldehydes (Scheme 67).[73]



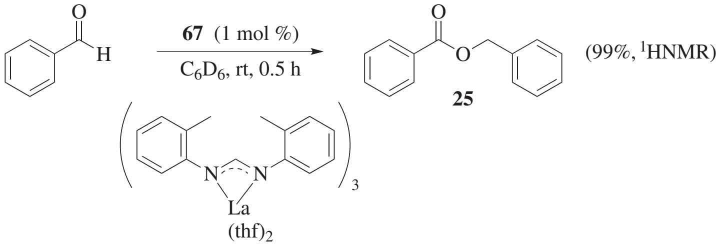
Scheme 66



R	TOF / h^{-1}	Yield (^{1}HNMR, %)
i-Pr	>1500	100
Ph	4.2	100

Scheme 67

A further advance in enhancing catalyst activity is the introduction of tris(formamidinato)lanthanoid complexes.[184] Lanthanum complexes with *N*,*N*′-bis(*o*-tolyl)formamidinate, *N*,*N*′-bis(2,6-dimethylphenyl)formamidinate, and *N*,*N*′-bis(2,6-diethylphenyl)formamidinate ligands surpass the activity of previously established homoleptic lanthanoid amide catalysts.[72,74] Aromatic aldehydes and non-enolizable and α-substituted aliphatic aldehydes react rapidly in the presence of catalyst **67**, in most cases leading to quantitative yields of products and high turnover frequencies (Scheme 68).[184] Although heteroaromatic aldehydes such as furfuraldehyde and thiophene-2-carboxaldehyde react more sluggishly, they form esters in good yields (Scheme 69).[184] As is observed with other homoleptic lanthanoid catalysts, easily enolizable aliphatic aldehydes react preferentially via the aldol–Tishchenko pathway.



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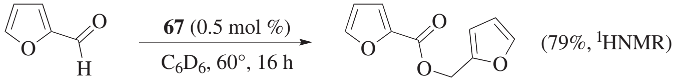
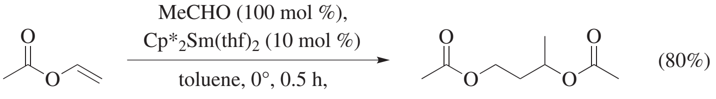
67

Scheme 68



Scheme 69

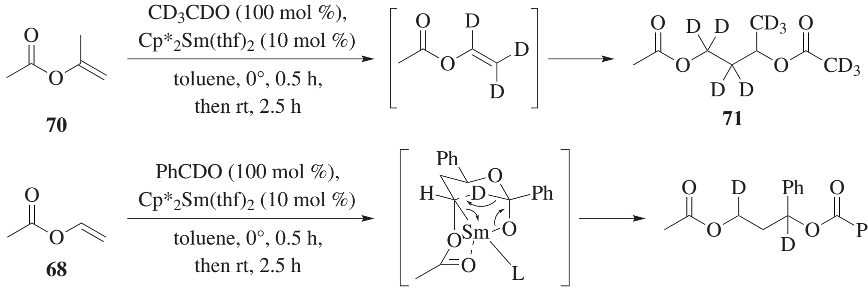
An interesting variant of the Tishchenko reaction involves $Cp^*_2Sm(thf)_2$ complexes. Vinyl esters **68** are coupled with an aldehyde, and the coupling product reacts seemingly through a Tishchenko reaction, forming the saturated diester **69** (Scheme 70).[185] Labelling studies with fully deuterated acetaldehyde show that isopropenyl esters such as **70** undergo transesterification with deuterated vinyl alcohol derived from acetaldehyde to form an intermediate deuterated vinyl ester, which subsequently reacts with the aldehyde to give **71** (Scheme 71).[185] Similarly, the reaction between vinyl acetate and PhCDO affords a coupling product that has two deuterium atoms incorporated into the alcohol moiety of the original ester, with the hydride transfer step taking place through the proposed intermediate shown in Scheme 71.[185]



68

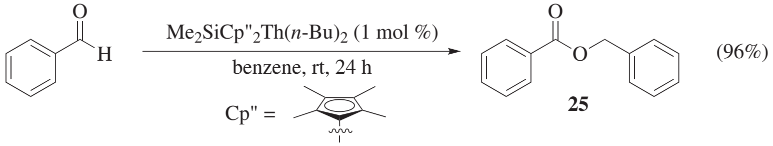
69

Scheme 70



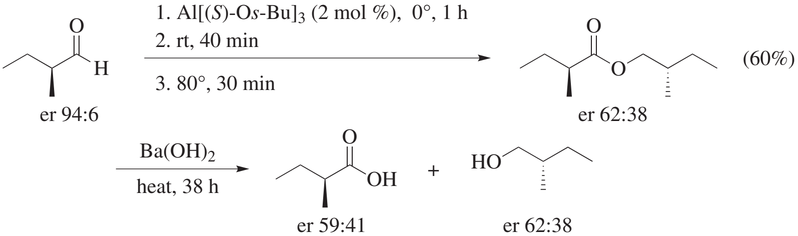
Scheme 71

Actinoid Catalysts.[186] The classic and crossed Tishchenko reactions of aromatic aldehydes may be carried out with organothorium complexes $Cp^*{}_2ThMe_2$, $Th(NEtMe)_4$, and $SiMe_2Cp''_2Th(n\text{-}Bu)_2$ ($Cp'' = C_5Me_4$) in moderate to good yields (Scheme 72).[187,188] A Tishchenko-type catalytic cycle involving dynamic participation of metal alkoxide bonds has previously been considered to be unlikely for actinoid compounds, owing to their highly oxophilic nature.



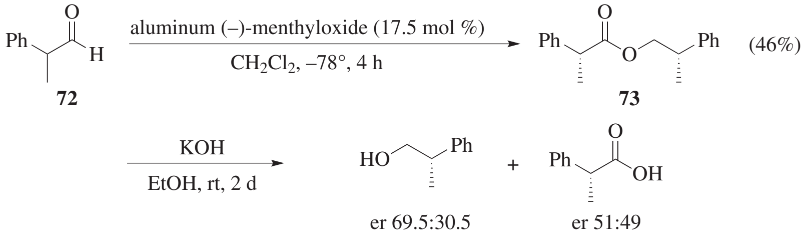
Scheme 72

Stereoselectivity in the Classical Tishchenko Reaction. Only a few attempts at effecting an asymmetric intermolecular classical Tishchenko reaction have been reported. An example is shown in Scheme 73.[20] Heating the ester product with the catalyst does not cause the observed racemization. Formation of an enol intermediate has been proposed as an explanation for the loss of enantiopurity. Alkoxide transfer from the catalyst to the ester may account for the higher enantiomeric purity of the alcohol component.



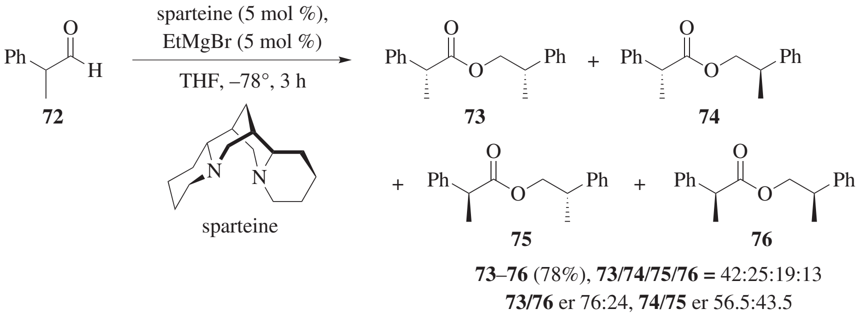
Scheme 73

Other chiral aluminum alkoxides have been used as a source for asymmetric induction in the Tishchenko reaction. Reaction of racemic 2-phenylpropanal (**72**) with aluminum (−)-menthyloxide, (−)-2-methylbutoxide, (−)-2-butoxide, or (−)-2-bornanyl oxide results in a simple chiral ester (*S*)-2-phenylpropyl (*R*)-2-phenylpropanoate (**73**) and mixed esters arising from alkoxide transfer and oxidation of alkoxide groups to the corresponding aldehydes (Scheme 74).[36] Hydrolysis of the ester affords enantiomerically enriched alcohol and acid components with maximum enantiomeric ratios of 69.5:30.5 and 51:49 respectively. The catalyst undergoes an alkoxide exchange during the course of the reaction, which causes the enantioselectivity to deteriorate over time. Recycling the catalyst in another experiment results in a nearly racemic product.



Scheme 74

Performing the Tishchenko reaction of 2-phenylpropanal with the ethylmagnesium bromide/(−)-sparteine complex produces all possible stereoisomers **73–76** with a clear preference for (*S*)-2-phenylpropyl (*R*)-2-phenylpropanoate (**73**) (Scheme 75).[49] Optimization of reaction conditions results in a maximum enantiomeric ratio of 77.5:22.5 for the (*R*,*S*)/(*S*,*R*) (note: first letter indicates acid portion) pair and 17% for the (*R*,*R*)/(*S*,*S*) pair. An observation of the time course of the reaction reveals that the enantiomeric ratio reaches its peak (83.5:16.5) at low conversion values and decreases over time. Kinetic studies show that a 2-phenylpropoxymagnesium bromide/(−)-sparteine complex, which is formed from (*S*)-**72**, reacts preferentially with (*R*)-**72**. The complex formed from (*R*)-**72** behaves similarly but with lower selectivity.

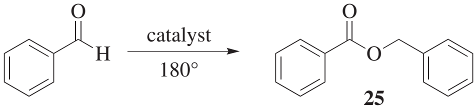


Scheme 75

The reaction conditions do not cause significant racemization. Reaction of (*R*)-2-phenylpropanal gives the (*R*,*R*)-ester with nearly complete selectivity. Less than 2% of (*R*,*S*)/(*S*,*R*) enantiomeric pairs are present in the product. The Grignard reagent/(−)-sparteine complex has likewise been used in an asymmetric polymerization of dihydrocinnamaldehyde and in the polymerization of terephthalaldehyde and isophthalaldehyde.[47,48]

Heterogeneous Catalysis. Heterogeneous catalysts and solid base catalysts[189] that have been applied to the Tishchenko reaction include alkaline earth metal oxides, alkali metals, different modifications of alumina, and transition-metal oxides. Aromatic aldehydes and formaldehyde readily undergo classic Tishchenko reactions and dimerize to the corresponding esters with solid base catalysts. Enolizable aldehydes may react through the aldol–Tishchenko reaction if the catalyst is sufficiently basic for the aldol formation to take place.[190] However, the few studies on enolizable aldehydes show a preference for aldol addition and condensation reactions instead of classic Tishchenko or aldol–Tishchenko reactions. Aromatic aldehydes have also been reported to afford Tishchenko products in good yields with a catalytic amount of metallic sodium in a non-polar solvent.[43]

Studies of the Tishchenko reaction of benzaldehyde on alkaline earth metal oxides reveal a trend of increasing catalytic activity in the order MgO < CaO < SrO < BaO (Scheme 76).[76] The catalysts are usually prepared by calcining the corresponding metal hydroxide at high temperatures. The catalytic activity has a clear positive linear correlation with the surface basicity of the oxide. For CaO the surface basicity and hence the catalytic activity are both strongly dependent on the pre-treatment temperature of the catalyst. Kinetic studies establish that the reaction has an induction period that can be shortened by the addition of benzyl alcohol.[76] This observation indicates that the formation of the benzyloxide via an initial Cannizzaro-type reaction is crucial for the catalytic cycle. The reaction of α-deuterated benzaldehyde has a longer induction period, but the rate of the reaction is equal to that of benzaldehyde.[76] According to a later computational study on the same system, the oxygen electronic polarizability and oxygen Madelung potential also correlate with catalyst activity.[191] The softer and more polarizable the surface ions, the more active the catalyst. Studies with ^{18}O-enriched MgO also reveal that the catalyst surface participates dynamically in the reaction, yielding ^{18}O-enriched products as revealed by electron ionization mass spectrometric analysis (Scheme 77).[81,192]



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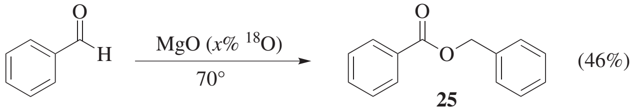
Catalyst	Time (min)	Yield (%)
MgO	180	~40
CaO	150	90
SrO	40	100
BaO	20	100

Scheme 76

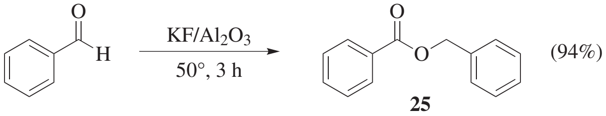


			Mass Peak Intensity (%)		
x	Time (min)	Conversion (%)	M	M + 2	M + 4
98	6	46	100	12.4	0.4
0.2*	3	32	100	1.7	0.1

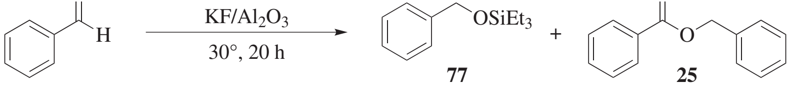
*natural abundance of ^{18}O

Scheme 77

Unmodified Al_2O_3 is usually in itself an ineffective catalyst for the Tishchenko reaction[76,79,84] but in intramolecular reactions of aromatic dialdehydes it is active.[80] The dimerization of benzaldehyde is achieved in 90–94% yields with Al_2O_3 doped with metallic sodium or *n*-BuLi.[83] Loading Al_2O_3 with KF, KNH_2, or K_2CO_3 results in efficient catalysts for non-enolizable aldehydes (Scheme 78).[84,85] Fluoride ions function as strongly basic sites that can initiate the Tishchenko reaction. Best results can usually be attained when about 5.0 mmol/g of KF are used and the catalyst is heated to 500°. KF-loaded Al_2O_3 also functions as a catalyst in the hydrosilylation of benzaldehyde by Et_3SiH.[86] Use of polar solvents such as DMF affords the hydrosilylation product **77**, but lowering the solvent polarity (e.g. THF, hexane) or eliminating the solvent results nearly exclusively in Tishchenko products (Scheme 79).[86]



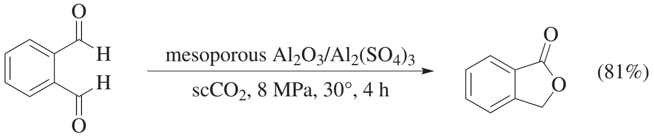
Scheme 78



	Yield (%)	
Solvent	**77**	**25**
DMF	100	0
hexane	1	98

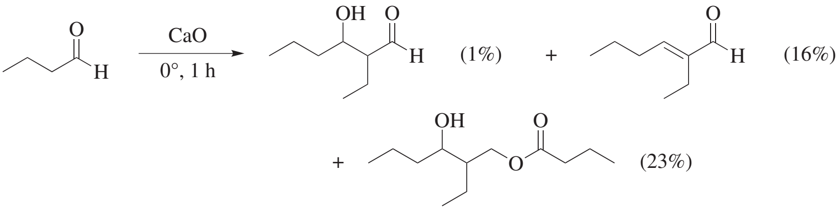
Scheme 79

Supercritical carbon dioxide may be used as a reaction medium with heterogeneous catalysts in the Tishchenko reaction.[87–89] The intramolecular reaction of *o*-phthalaldehyde is nearly completely suppressed on traditional catalysts such as CaO and unmodified Al_2O_3, but mesoporous Al_2O_3 with sulfate ions incorporated into the catalyst framework is an efficient catalyst (Scheme 80).[87] The conditions required to turn carbon dioxide into a supercritical fluid are relatively mild: temperatures are usually kept at 40°, although a pressure of 8.0 MPa is required. Using benzene or THF as a cosolvent also increases the reaction rate noticeably.



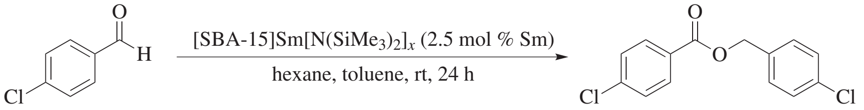
Scheme 80

Research on metal oxide catalyzed Tishchenko reactions of aliphatic aldehydes has been quite limited. The behavior of *n*-butyraldehyde with solid base catalysts has been well-characterized; reaction of *n*-butyraldehyde with unmodified alkaline earth metal oxides or alumina yields a mixture of aldol condensation, aldol addition, and aldol–Tishchenko products (Scheme 81).[190] Only CaO shows a slight preference for the aldol–Tishchenko pathway. Various modifications of alumina mostly result in a preference for aldol products over aldol–Tishchenko products, and the symmetrical Tishchenko product is present only in trace amounts. The amount and ratio of acidic and basic sites on the catalyst surface has been determined to play a critical role in catalyst selectivity.[190] Catalysts having a sufficient number of both basic and acidic surface sites are more selective toward the aldol–Tishchenko reaction whereas an excess of basic sites clearly favors the formation of aldol products.[190]



Scheme 81

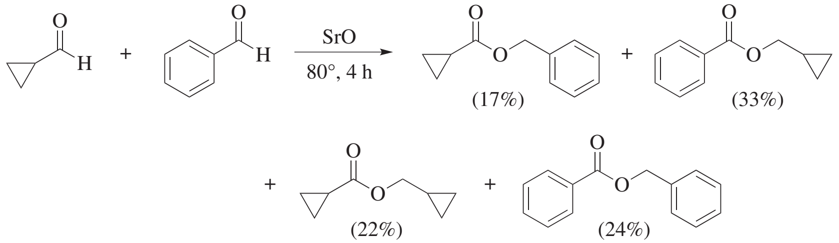
Grafting a catalyst molecule onto a heterogeneous carrier is a well-known method for creating recyclable and easily isolable solid catalysts. For instance, lanthanoid amides[72,74] have been grafted onto silica surfaces.[193,194] As an example, $Sm[N(SiMe_3)_2]_3$ grafted onto mesoporous silicate SBA-15 retains its activity, is easily recovered from the reaction mixture, and can be re-used in subsequent runs with no loss of activity (Scheme 82).[194] In accordance with the homogeneous reaction, aliphatic aldehydes give mostly aldol–Tishchenko products when this type of catalyst is employed.



Run	Yield (%)
1	82
2	80
3	81

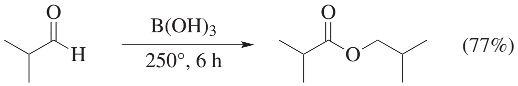
Scheme 82

Crossed Tishchenko reactions with heterogeneous catalysts usually give results similar to those of homogeneous catalysts, producing a mixture of all four possible esters in a ratio determined by steric and electronic factors (Scheme 83).[79] The alkaline earth metal oxides MgO, CaO, and SrO are generally efficient catalysts. In this connection neither regular Al_2O_3 nor that loaded with KF or KOH shows activity toward the Tishchenko reaction.



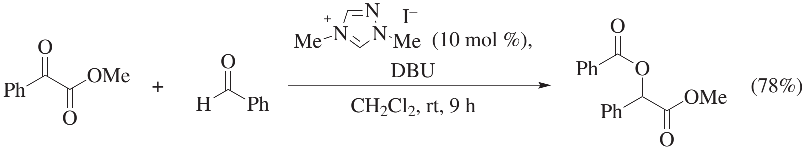
Scheme 83

Non-Metal-Catalyzed Tishchenko Reactions and Other Catalyst Systems. Boric acid can be used to catalyze the Tishchenko reaction of formaldehyde, benzaldehyde, and some simple aliphatic saturated aldehydes (Scheme 84).[195] The reaction requires rather high temperatures, and there are also some issues of selectivity. Enolizable aldehydes may undergo an aldol reaction under the conditions used; reaction with *n*-butyraldehyde gives a conversion of 82%, but the ester *n*-butyl *n*-butyrate is isolated in only 17% yield.

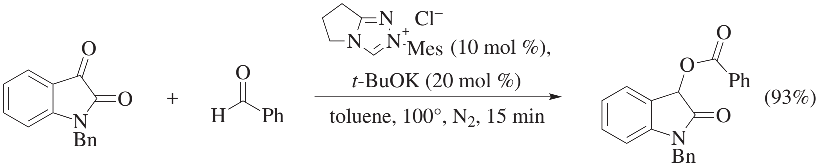


Scheme 84

Some recent examples of ketone hydroacylations may be considered to be the first organocatalytic Tishchenko reactions.[196–198] Thus, treatment of methyl benzoylformate with a triazolium salt in the presence of an aromatic aldehyde and DBU gives the hydroacylated product in good yield (Scheme 85).[196] If the reaction is run in a protic solvent, only the reduced ketone is produced. In similar fashion, the reaction between *N*-benzylisatin and an aldehyde catalyzed by a triazolium salt provides the hydroacylation product (Scheme 86).[197] In both examples, nucleophilic catalysis is the key feature. As in benzoin and Stetter reactions, the catalyst reacts with the aldehyde to form an adduct, which acts as a hydride donor by collapsing to an acyl triazolium species. The catalyst is then released by *O*-acylation of the reduced ketone. Cyanide ions react similarly, catalyzing the intramolecular hydroacylation of aromatic keto aldehydes.[198]

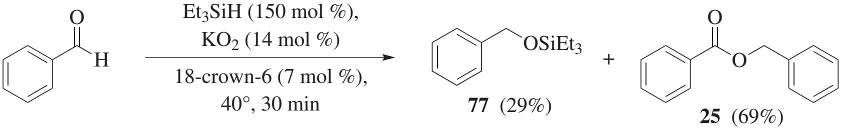


Scheme 85



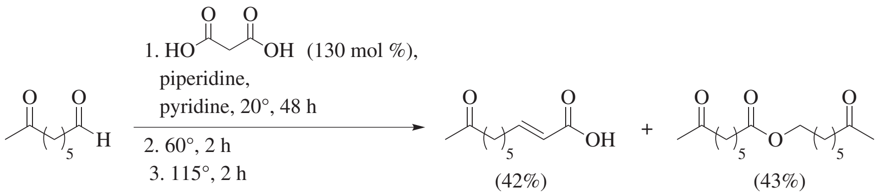
Scheme 86

The Tishchenko reaction occurs as a side reaction with several widely varied catalyst systems. A study of the reactivity of potassium superoxide with aromatic aldehydes shows a tendency for a Tishchenko side reaction.[199] The reaction of an aldehyde with Et_3SiH and a KO_2/18-crown-6 catalyst system yields a mixture of hydrosilation (structure **77**) and Tishchenko products (Scheme 87).[199] Doebner condensation of 7-oxooctanal with malonic acid produces 7-oxooctyl 7-oxooctanoate as a side product (Scheme 88).[200] A condensation reaction of aromatic aldehydes with dimethyl sulfone in the presence of $NaNH_2$ is used to produce 2,6-diphenyl-1,4-oxathiane-4,4-dioxide derivatives. Under these reaction conditions, 4-nitrobenzaldehyde gives the Tishchenko product 4-nitrobenzyl 4-nitrobenzoate in 55% yield (Scheme 89).[201]

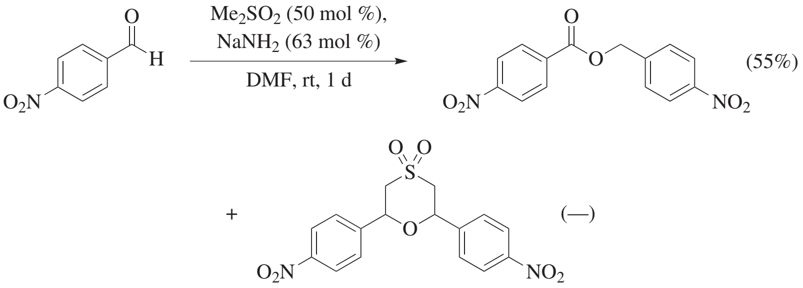


77 (29%) **25** (69%)

Scheme 87

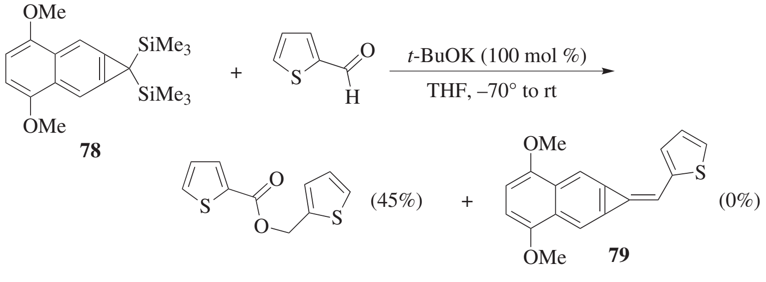


Scheme 88

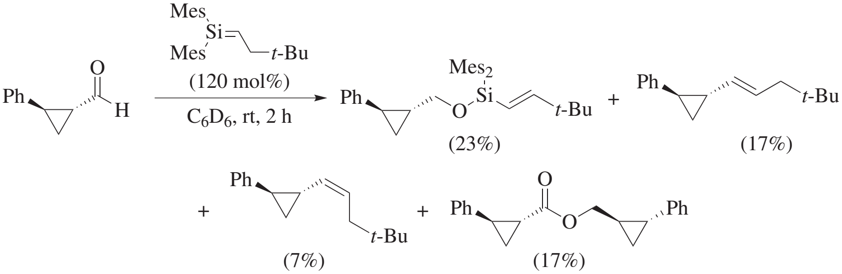


Scheme 89

The reaction of cyclopropanaphthalene disilane **78** with KO*t*-Bu in the presence of 2-thiophenecarboxaldehyde or 4-trifluoromethylbenzaldehyde yields the Tishchenko products of both aldehydes instead of the expected Peterson olefination product **79** (Scheme 90).[202] It has been suggested that the base removes a silane group to form an α-silyl anion that attacks the aldehyde. An intermolecular hydride transfer reduces another molecule of aldehyde to an alkoxide anion that in turn attacks the acylsilane carbonyl. The ester is eliminated from the complex and the α-silyl anion is regenerated. A silene compound has also been reported to catalyze the Tishchenko reaction. The silene is assumed to function as a Lewis acid in a reaction with *trans*-2-phenylcyclopropanecarboxaldehyde and convert it into the corresponding ester via a Tishchenko mechanism (Scheme 91).[203]



Scheme 90



Scheme 91

Substrate Limitations in the Classical Tishchenko Reaction. In general, only a few catalyst systems promote the Tishchenko reaction of both aliphatic and aromatic aldehydes equally effectively. The enolization of aliphatic aldehydes sets strict limits on the catalyst basicity, which is evident in several catalyst systems that give only aldol–Tishchenko products for aliphatic aldehydes but are otherwise good catalysts for the Tishchenko reaction of aromatic aldehydes. Since the coordination of oxygen to a Lewis acidic metal complex is a required factor in the reaction, free hydroxy, amino, or thiol groups are obviously not well-tolerated in substrate structures, and such examples are practically absent in the literature. Even the presence of alkylated Lewis basic heteroatoms has been reported to decrease reaction rates and yields.[74] For the same reason, some heteroaromatic aldehydes are usually difficult substrates. For instance, heteroaromatic aldehydes such as 2-furfuraldehyde may chelate the catalyst to form a five-membered metallacycle species, which ostensibly terminates the catalytic cycle. The presence of double bonds is not a hindering factor in general, but conjugated aldehydes are usually somewhat unreactive substrates.[160] This limitation may be accounted for by the extra demand in energy needed to break the conjugation to form the intermediate alcoholate species. For aromatic aldehydes in general, any substitution usually leads to lower yields from the reaction, although electronic and steric factors may either increase or decrease the reaction rate.

The original aluminum alkoxides and especially their derivatives (such as **48–50** in Fig. 1)[158,160,161] are still some of the most efficient catalysts for aliphatic aldehydes. Reactions with aromatic aldehydes tend to be slower, although reaction times are still within reasonable limits. On the other hand, catalyst **67**[184] and $La[N(SiMe_3)_2]_3$[74] are among the most active catalysts for aromatic aldehydes and, to some extent, for aliphatic aldehydes. The recently reported nickel complexes **60** and **61**[177,178] deserve mention since their substrate scope qualifies them as perhaps the most versatile catalysts for the classical Tishchenko reaction. In addition, they are currently the best catalysts for the crossed Tishchenko reaction between aliphatic and aromatic aldehydes, providing excellent selectivity. Furthermore, a selective crossed Tishchenko reaction between two aromatic aldehydes may be achieved with an effective combination of substrate design and catalyst selection.[144–147] Simple aluminum alkoxides are applicable to the industrial synthesis of aliphatic esters (see “Applications to Synthesis”). For the large-scale synthesis of aromatic esters, the method described in

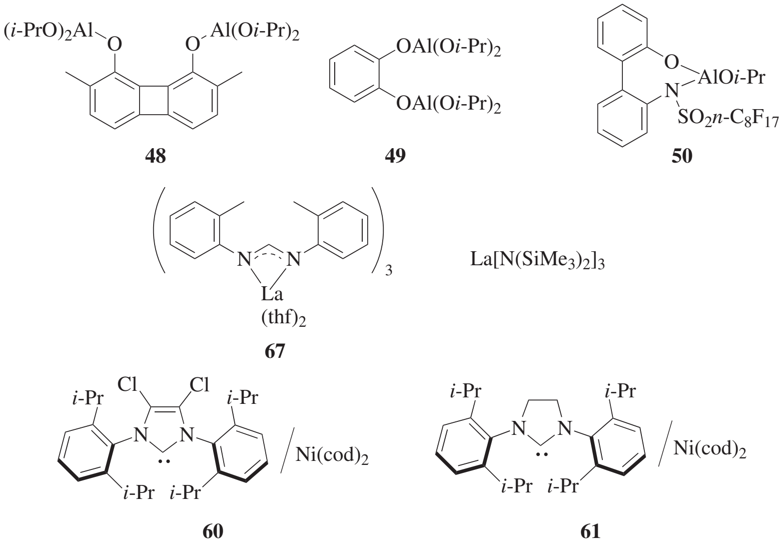
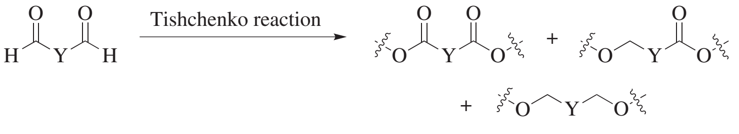


Figure 1. Choice catalysts for the classical Tishchenko reaction.

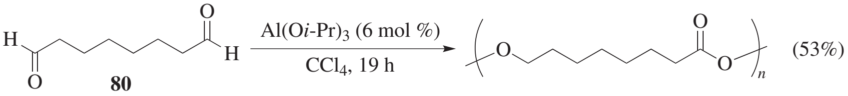
“Experimental Procedures” for benzyl benzoate[39] is recommended for its simplicity and economy (see also Ref. 135 for the same method for furfuryl furoate).

The Tishchenko Reaction in Polymer Chemistry. The synthesis of polyesters has been carried out via the Tishchenko reaction using aromatic or aliphatic dialdehydes as starting materials. Tishchenko-type polymerization usually yields a polyester with a 1:2:1 distribution of the three structural subunits: the diacyl, acyl alcohol, and diol moieties (Scheme 92). In the following examples only the acyl alcohol subunits are presented for clarity.

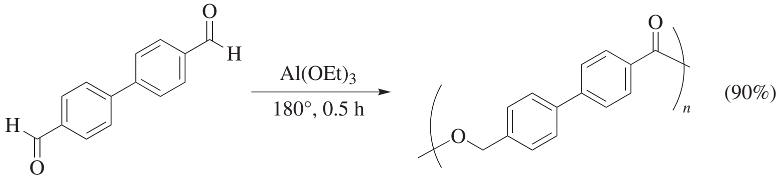


Scheme 92

The classic catalyst $Al(Oi\text{-}Pr)_3$ can show substrate selectivity. It is reported to be unreactive with aromatic dialdehydes under anhydrous conditions,[204,205] but it is able to catalyze the polymerization of the linear aliphatic 1,8-octanedial (**80**) (Scheme 93).[23] However, another report states the successful polymerization of terephthalaldehyde with $Al(Oi\text{-}Pr)_3$ when the reaction is run in dichloromethane.[48] Terephthalaldehyde has likewise been successfully polymerized by $AlEt_3$, $Al(i\text{-}Bu)_3$, $Al(i\text{-}Pr)_3$, and $AlEt_2Br$.[205] $Al(OEt)_3$ is an effective catalyst in the polymerization of several aromatic dialdehydes, such as terephthalaldehyde, isophthalaldehyde, 2,5-dimethylterephthalaldehyde, and diphenyl-4,4′-dicarboxaldehyde (Scheme 94).[204]

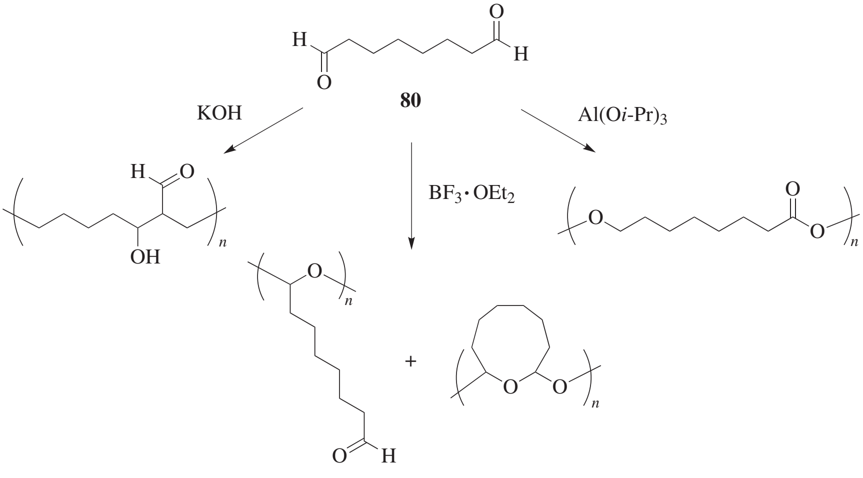


Scheme 93

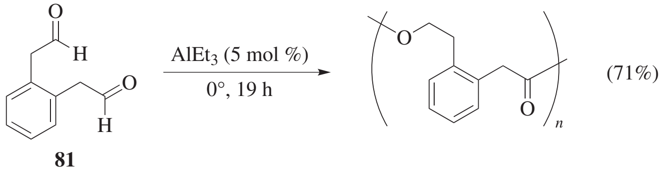


Scheme 94

Three structurally different polymers are available from dialdehyde **80** depending on the choice of polymerization catalyst (Scheme 95).[23] Whereas Al(O*i*-Pr)$_3$ yields the polyester, potassium hydroxide yields an aldol addition polymer, and BF$_3$•OEt$_2$ affords a polyacetal with alternating structural subunits. Polymerization of 2,2′-(1,2-phenylene)diacetaldehyde (**81**) with BF$_3$•OEt$_2$ similarly gives the polyacetal with either open-chain acetal or cyclic acetal groups depending on the participation of individual aldehyde groups.[206] The use of AlEt$_3$ as catalyst with **81** yields a polyester structure via the Tishchenko reaction (Scheme 96). Mechanistic similarities between aluminum alkoxide promoted polymerization, Tishchenko, Meerwein–Ponndorf–Verley, and Oppenauer reactions have been suggested.[207] It is plausible that the polyacetal chain elongation proceeds via an analogous alkoxide transfer sequence as in the Tishchenko reaction.

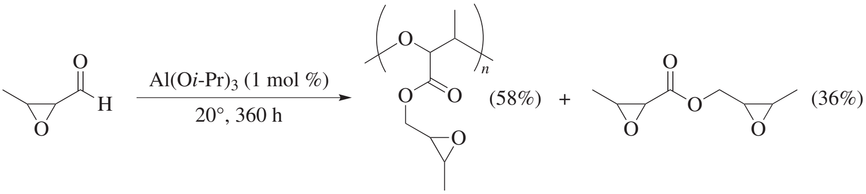


Scheme 95



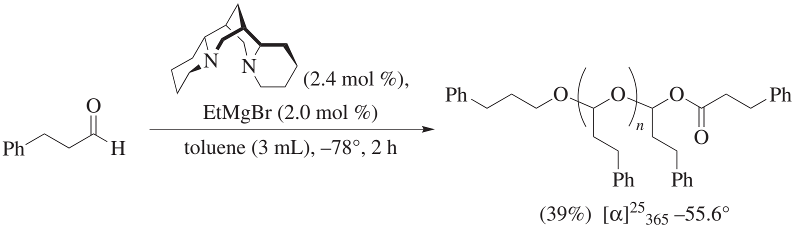
Scheme 96

The Tishchenko reaction is an intermediate stage in the polymerization of glycidaldehyde and its mono- and dimethyl derivatives.[208,209] In the presence of $Al(Oi\text{-}Pr)_3$ the aldehyde first forms a dimeric ester through a Tishchenko reaction, which is followed by an epoxide ring-opening polymerization (Scheme 97).[208] The polymer backbone has a polyether structure with epoxy ester side chains. The α-methylated epoxide also undergoes ring-opening rearrangement and forms β-propiolactone derivatives.[210] Increasing the catalyst concentration diminishes the amount of Tishchenko product and increases the β-propiolactone yields.



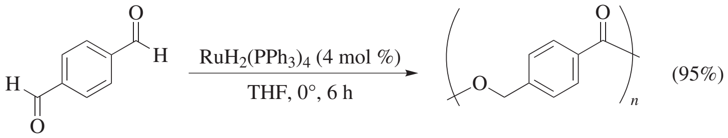
Scheme 97

Polyacetal-type polymers are common products from the polymerization of aldehydes. By using a Tishchenko-type catalyst, the polymer chain can be terminated or “end-capped” with an ester functionality. Ethyl- and *n*-octylmagnesium bromide have been used together with (−)-sparteine as a catalyst to polymerize dihydrocinnamaldehyde, ending the polyacetal chain in a dihydrocinnamate ester via Tishchenko reaction (Scheme 98).[47] The chiral catalyst also effects asymmetric induction, and the resulting polymer is optically active with specific rotation values between −33° and −56°. EtMgBr/(−)-sparteine is also active in the Tishchenko polymerization of terephthalaldehyde and isophthalaldehyde.[48]



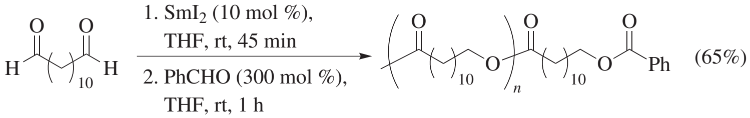
Scheme 98

The ruthenium complex $RuH_2(PPh_3)_4$ is an effective catalyst in the polymerization of terephthalaldehyde and 1,12-dodecanedial.[65] Polymerization reactions are carried out in THF/catalyst solution at 0° for 2–6 hours, with 80 to 95% yields. Isophthalaldehyde is less active in the polymerization, giving a 49% yield. The spatial arrangement of the aldehyde groups also gives isophthalaldehyde a tendency to form macrocyclic oligomers.[71] The reaction is quite sensitive to changes in both temperature and the amount of catalyst. Using 1 mol % of catalyst results in no reaction, whereas 4 mol % gives a 95% yield (Scheme 99).[65] Both raising and lowering the temperature results in diminished yields. Copolymerization between two aldehydes is also possible with this catalyst. The composition of the mixed polyester can be influenced by the ratio of starting monomers and amount of catalyst.



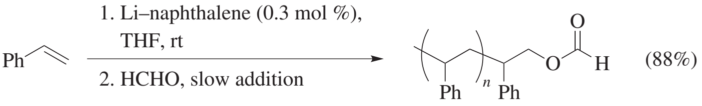
Scheme 99

Samarium iodide is also an efficient catalyst for both terephthalaldehyde and 1,12-dodecanedial, and their copolymerization (Scheme 100).[65,211] End-capping of the polymer chain may likewise be done with benzaldehyde, which forms a benzyl ester group. An aluminum-(*R*)-BINOL complex is also effective in the polymerization of terephthalaldehyde.[48]

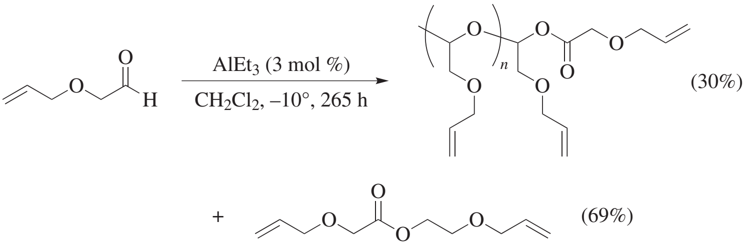


Scheme 100

The Tishchenko reaction is a frequent side reaction in polymerizations where metal catalysts are used. In an attempt to prepare a polystyrene-polyformaldehyde block copolymer with lithium–naphthalene as the catalyst, polystyrene chains terminating in a formate ester are formed (Scheme 101).[212] The polymerization of thioether-containing aldehydes with $AlEt_3$ yields not only the expected polyacetal, but also simple ester products from a Tishchenko side reaction.[213] The polymerization of allyloxyacetaldehyde with $AlEt_3$ is highly temperature-dependent.[214] At room temperature only the Tishchenko ester is formed, but at slightly lower temperatures the reaction yields a mixture of the dimeric ester and a methanol-soluble oligomer of low molecular weight (Scheme 102).[214] The polymerization reaction is predominant at temperatures below −20°. The resulting polyacetal also contains an ester group as a chain terminating element.



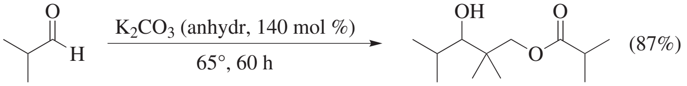
Scheme 101



Scheme 102

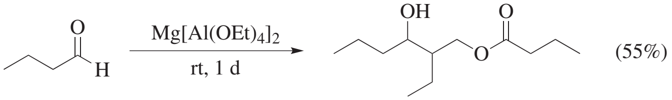
The Aldol–Tishchenko Reaction

Trimerization of Enolizable Aldehydes. Enolizable aldehydes are trimerized to 1,3-diol monoesters through a base-mediated aldol reaction, subsequent acetalization, and a Tishchenko-type intramolecular hydride transfer (see Scheme 7). In the earliest examples, this process is achieved with bases such as NaOAc,[95] K_2CO_3 (Scheme 103),[98] or alcoholic KOH.[99] Using protic basic media can lead to subsequent hydrolysis of the 1,3-diol monoester and thus give the dimeric glycol and monomeric acid as products.



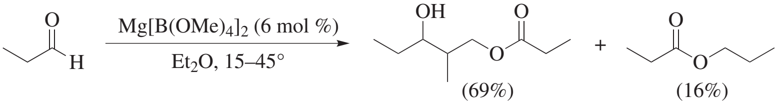
Scheme 103

Traditional aluminum alkoxides are so selective for the classic Tishchenko reaction that enolizable aldehydes mostly react to form symmetrical esters. This results from the Lewis acidity of the catalysts. Increasing the basicity of the catalyst, for instance by forming magnesium–aluminum alkoxide complexes, allows the aldol–Tishchenko reaction to become the dominant pathway.[91–93] Linear aliphatic aldehydes give 1,3-diol monoesters with modest selectivity, whereas α-alkyl-substituted aldehydes predominantly form symmetrical Tishchenko esters with magnesium–aluminum alkoxide catalysts (Scheme 104).[91] The simple bases mentioned above function in a reverse fashion, producing glycol monoesters from α-alkyl-substituted aldehydes.

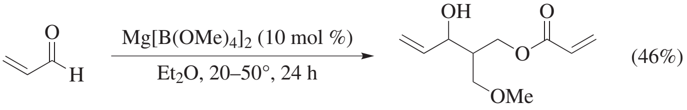


Scheme 104

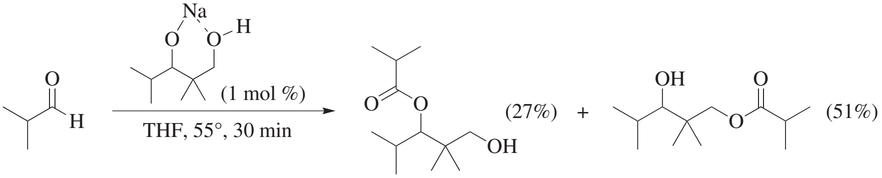
Alkaline earth metal alkoxides[93] and alkali metal alkoxides[215] are also sufficiently basic to catalyze the aldol–Tishchenko reaction, although the latter catalysts usually lead to aldol condensation products from aldehydes lacking α-alkyl substituents. Magnesium– and calcium–boron methoxide complexes catalyze the reaction of simple aliphatic aldehydes to form aldol–Tishchenko products with fair selectivity, affording simple esters as minor products (Scheme 105).[216] Magnesium tetramethylborate gives an atypical aldol–Tishchenko product with acrolein. A methoxy group from the catalyst first undergoes conjugate addition to acrolein, forming a magnesium enolate. The subsequent Tishchenko step with acrolein gives 3-hydroxy-2-methoxypent-4-enyl acrylate (Scheme 106).[216] Alkali metal monoalkoxides of 2,2-dimethyl-1,3-propanediol are also effective catalysts in the trimerization of isobutyraldehyde (Scheme 107).[217]



Scheme 105

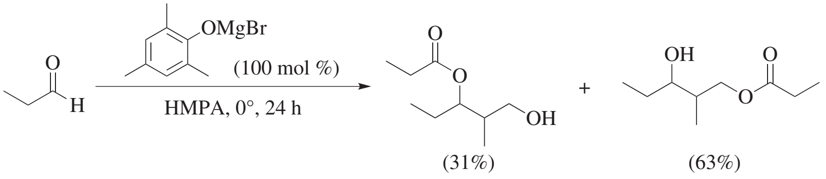


Scheme 106



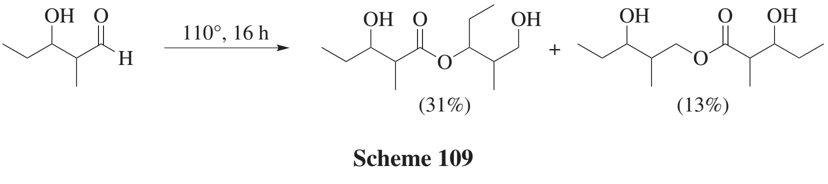
Scheme 107

Aromatic magnesium alkoxides, such as 2,4,6-trimethylphenoxymagnesium bromide and its derivatives, selectively catalyze aldol addition reactions or aldol–Tishchenko reactions depending on the solvent system used.[218−220] In benzene, α,β-unsaturated aldehydes are obtained selectively with 90% to 96% yields. When HMPA is used, the selectivity is reversed toward aldol–Tishchenko products with similar conversions (Scheme 108).[218−220] Both primary and secondary 1,3-diol monoesters are present in the product mixture. When the reaction is run in benzene and the catalyst/substrate ratio is varied, mixtures with different ratios of α,β-unsaturated aldehydes and 1,3-diol monoesters are produced. Changing the metal counterion of the phenol salt from Mg to Li or Na affects the composition of the product mixture, and also leads to other reaction pathways such as Cannizzaro reactions.[220]



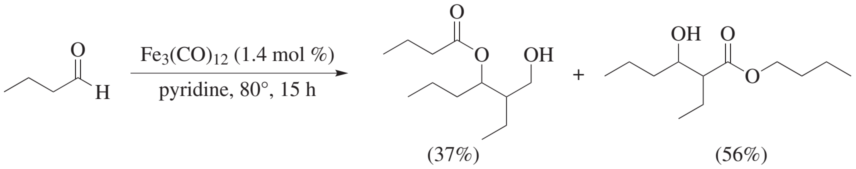
Scheme 108

Isolated aldol products can react in a non-catalyzed thermal reaction to form dimeric esters,[94,221] affording essentially tetrameric products of the parent aldehyde in the case of aldehyde self-addition (Scheme 109).[94] The 3-hydroxy aldehyde first dimerizes to a hemiacetal, which undergoes a subsequent intramolecular hemiacetalization to form 1,3-dioxan-4-ol type structures (also called aldoxanes, see structure **12** in Scheme 7).[222,223] Whether the hydride transfer step takes place in the open chain hemiacetal or the cyclic aldoxane form has been discussed.[94] Coordination of a metal ion to the oxygen atoms incorporated in the ring may promote opening of the ring and the hydride transfer step.[141,142]



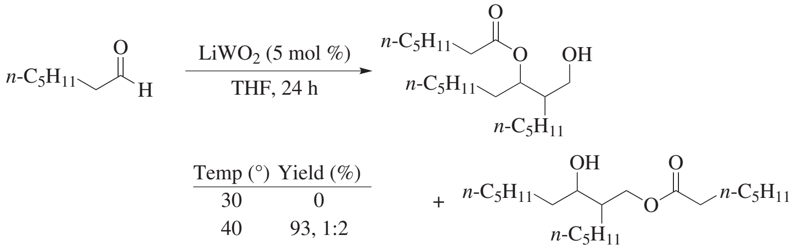
Scheme 109

Polynuclear carbonylferrates induce aldol–Tishchenko reactions of simple aliphatic aldehydes with pyridine or pyridine *N*-oxide in benzene as the solvent (Scheme 110).[224] α-Substituted aldehydes generally react more slowly than unsubstituted aldehydes. For example α-ethylbutyraldehyde does not react with $[Fe_2(CO)_8]^{2-}$ prepared in situ.



Scheme 110

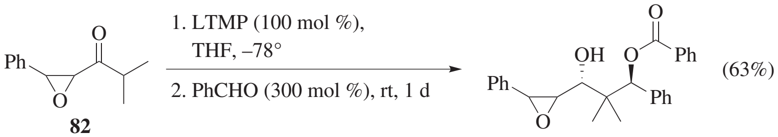
The bimetallic compound $LiWO_2$ catalyzes both classical Tishchenko and aldol–Tishchenko reactions.[225] Aromatic aldehydes are converted into symmetrical esters in good yields. Near-stoichiometric amounts of the catalyst give poorer yields, and benzil and benzyl alcohol are formed as side products. A catalytic amount of $LiWO_2$ (5 mol %) gives the corresponding esters with good selectivity. Aliphatic aldehydes react exclusively through the aldol–Tishchenko reaction and give 1,3-diesters as side products (Scheme 111).[225] The amount of $LiWO_2$ now has the opposite effect: more catalyst is needed to achieve better yields. In both cases the best results are obtained at high temperatures. Anhydrous THF is used as solvent and the temperatures range from 30–75°.



Temp (°)	Yield (%)
30	0
40	93, 1:2

Scheme 111

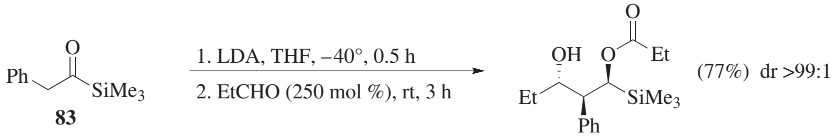
The Lithium Enolate Mediated Aldol–Tishchenko Reaction. Ketone enolates react with an excess of aldehyde to form 1,3-*anti*-diol monoesters in the aldol–Tishchenko reaction (see Scheme 8). Strong lithium bases such as LDA, LiHMDS, or LTMP may be used for the enolization step.[132,226,227] The enolate is usually generated under traditional conditions at −78° in THF, and subsequently can be directed toward the Tishchenko pathway by warming the reaction mixture to ambient temperature and extending the reaction time, as opposed to the standard aldol reaction conditions. High diastereoselectivity is usually observed. As an example, LTMP is used for the enolization of the α-epoxy ketone **82** (Scheme 112).[226] Subsequent addition of an excess of benzaldehyde and stirring at room temperature affords the epoxy-1,3-diol monoester in good yield. The isolated aldol adduct from the first step can also react with an equimolar amount of base (*n*-BuLi, LDA, LTMP) and excess benzaldehyde to give the same product.



82

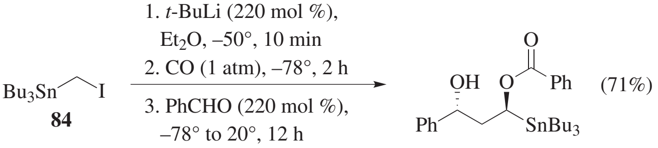
Scheme 112

Acylsilanes react through an aldol–Tishchenko pathway when treated with LDA and an excess of aldehyde.[228] The presence of different silyl groups is tolerated in this process. Benzyl trimethylsilyl ketone (**83**) affords products with three adjacent stereocenters of 1,2-*anti*-1,3-*anti* configuration with excellent diastereoselectivity (Scheme 113).[228] Several aliphatic and aromatic aldehydes can be used as aldol acceptors. Tributylstannylmethyl iodide (**84**) may be used as a precursor to synthesize 1,3-*anti*-diol 1-tributylstannanes (Scheme 114).[229] In the reaction cascade, iodide **84** undergoes a halogen-lithium exchange and carbonylation to give an intermediate acyllithium species, which is then transformed into an acyltin species via a rare 1,2-anionic stannyl rearrangement, eventually affording the lithium enolate **85** (Scheme 115).[229] Treating enolate **85** with an excess of aldehyde then affords the aldol–Tishchenko product **86**.



83

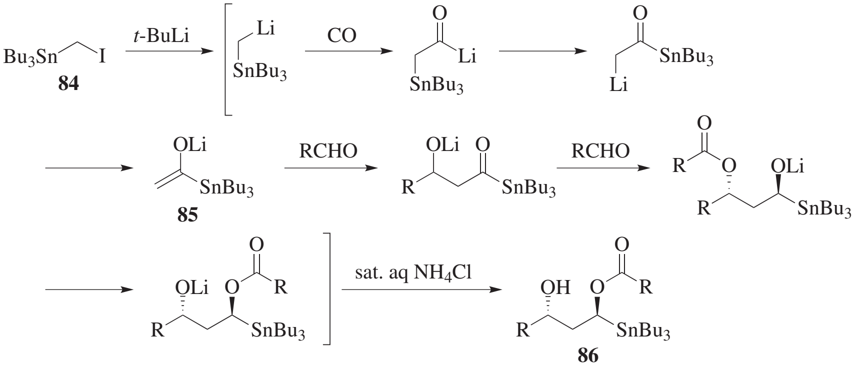
Scheme 113



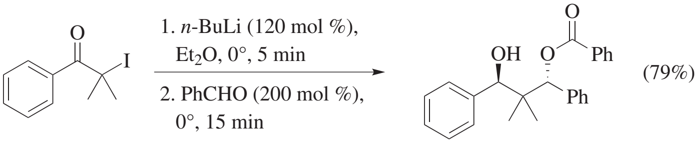
84

Scheme 114

α-Halogenated carbonyl compounds can react via Reformatsky-type aldol reactions when treated with an appropriate organometallic reagent. Thus, when treated with *n*-BuLi, α-iodoisobutyrophenone undergoes halogen–metal exchange to generate the lithium enolate, but subsequent reaction with benzaldehyde gives the aldol–Tishchenko product instead of an aldol addition product (Scheme 116).[230] Using EtMgBr, $AlMe_3$, or BEt_3 leads to the normal Reformatsky product, whereas Et_2Zn gives a mixture of both aldol–Tishchenko and Reformatsky products.

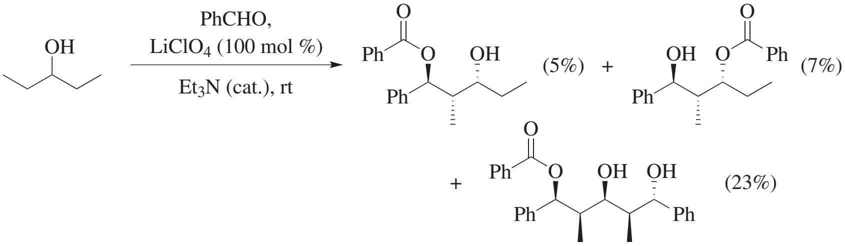


Scheme 115



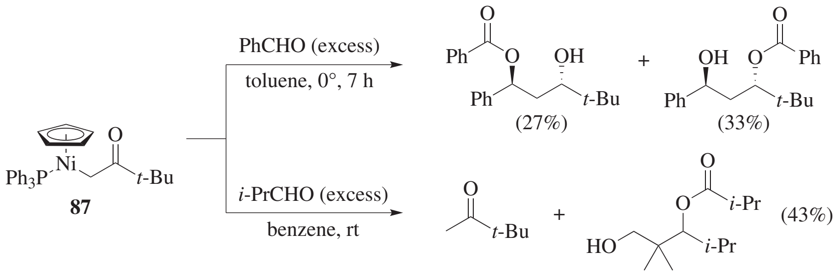
Scheme 116

The combination of $LiClO_4$ and Et_3N has been used to mediate a direct aldol reaction of alcohols and aldehydes.[231] The alcohol is first oxidized to the ketone via a Meerwein–Ponndorf–Verley and Oppenauer type process, thus becoming the aldol donor for the latter stages of the reaction. Secondary alcohols with longer side chains, such as 3-pentanol, surprisingly react also through an aldol–Tishchenko pathway, giving products with both classical aldol–Tishchenko and non-classical 1,2-*syn*-1,3-*syn* configurations (Scheme 117).[231] Primary alcohols are also able to react through the aldol–Tishchenko pathway but to a slightly lesser extent. When applied to enolizable aldehydes alone, the same catalyst system produces trimeric aldol–Tishchenko products.



Scheme 117

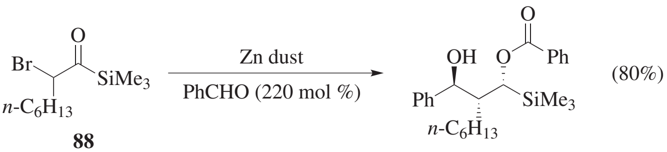
The Transition Metal Enolate Mediated Aldol–Tishchenko Reaction. The use of nickel enolate complexes produces 1,3-*anti*-diols via the aldol–Tishchenko reaction.[100] In the reaction between the C-bound enolate complex **87** and excess benzaldehyde in toluene at 0°, benzaldehyde first acts as the aldol acceptor, after which the Tishchenko step takes place (Scheme 118).[100] Both constitutionally isomeric esters are again formed in the reaction as a result of acyl migration. An enolizable aldehyde, such as isobutyraldehyde, first donates a proton to the enolate complex **87**, liberating pinacolone and thus forming a new nickel enolate complex. Subsequent aldol–Tishchenko reaction occurs, giving the trimeric ester of isobutyraldehyde. Enolates with α-methyl substituents give both aldol addition and aldol–Tishchenko products, whereas ester-derived enolates give only the aldol products. Analogous palladium-based enolates are less reactive, requiring longer reaction times and giving more complex mixtures consisting of aldol addition, aldol condensation, and aldol–Tishchenko products.



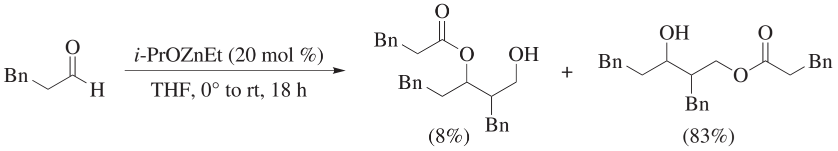
Yields based on **87**

Scheme 118

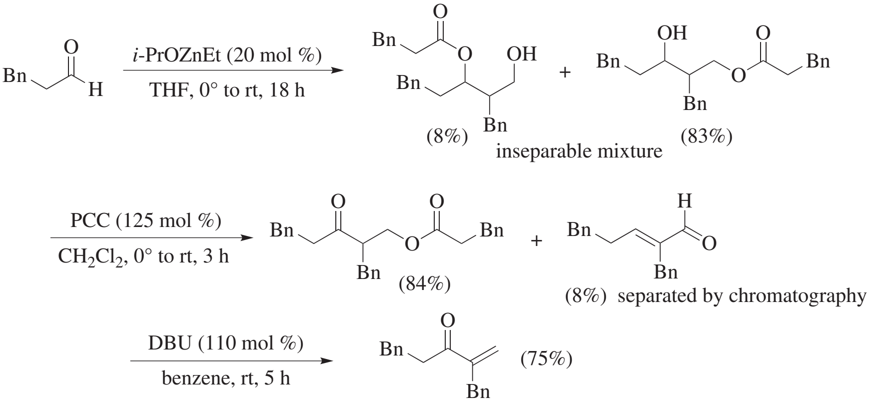
The Reformatsky reaction of α-haloacylsilane **88** and its analogs with zinc dust in the presence of benzaldehyde affords the aldol–Tishchenko product in 80% yield (Scheme 119).[232] Diethylzinc and $GaMe_3$ also react in a similar manner, generating the same product as a single diastereomer in 87% and 95% yields, respectively. The zinc alkoxide *i*-PrOZnEt is an efficient catalyst for the aldol–Tishchenko reaction of a broad range of enolizable aldehydes (Scheme 120).[233] When combined with subsequent oxidation and elimination reactions, the aldol–Tishchenko reaction is a feasible route for the synthesis of α-methylene ketones (Scheme 121).[233]



Scheme 119

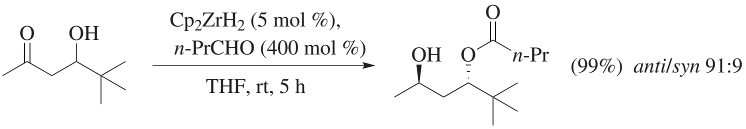


Scheme 120

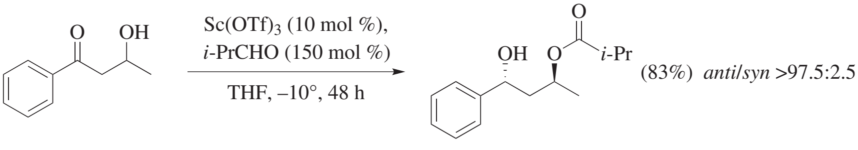


Scheme 121

Reductive methods similar to the samarium-catalyzed Evans–Tishchenko reaction are achieved with transition-metal catalysts. Zirconocene and hafnocene complexes, which catalyze the classical Tishchenko reaction of aliphatic aldehydes, can also catalyze the 1,3-*anti*-selective reduction of β-hydroxy ketones (Scheme 122).[234] β-Hydroxy ketones bearing primary hydroxy groups react in the same manner. Simple aliphatic aldehydes are the best hydride donors in this reaction, and aromatic and α,β-unsaturated aldehydes are unreactive. $Sc(OTf)_3$ is also applicable to the same kind of reaction, and it has the advantage of being less sensitive to air and moisture than the other catalyst systems used in aldol–Tishchenko reactions (Scheme 123).[235]

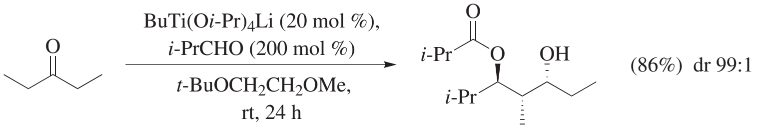


Scheme 122



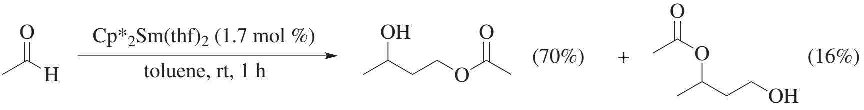
Scheme 123

The titanium ate complex $BuTi(OPr\text{-}i)_4Li$ catalyzes the direct aldol–Tishchenko reaction between diethyl ketone and different aldehydes in good yields (Scheme 124).[236] When the complex is employed in the reaction of the *syn*-aldol adduct of benzaldehyde and diethyl ketone, an equilibration is established and the thermodynamically more stable 1,2-*anti*-1,3-*anti*-product is produced. Acyl migration likewise takes place in the presence of the titanium ate complex. It has been suggested that the actual catalytic species is in situ formed LiO*i*-Pr; activity similar to that of $BuTi(O\text{-}i\text{-}Pr)_4Li$ has been reported for LiO*i*-Pr in an aldol–Tishchenko reaction between isobutyraldehyde and benzaldehyde.[237]



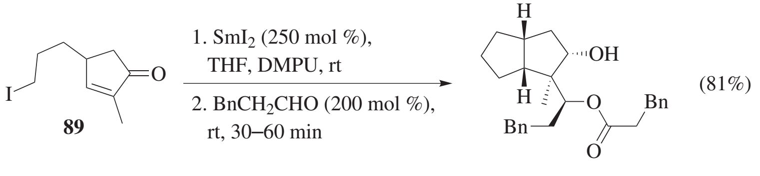
Scheme 124

The Lanthanoid Enolate Mediated Aldol–Tishchenko Reaction. The trimerization of simple aliphatic aldehydes via an aldol–Tishchenko reaction is achieved with $Cp^*{}_2Sm(thf)_2$ and $Cp^*{}_2Yb(thf)_2$ complexes, $Sm(O\text{-}i\text{-}Pr)_3$, or SmI_2 (Scheme 125).[238] The reaction is complete in one hour at room temperature, affording the trimeric 1- and 3-monoesters in good yields.



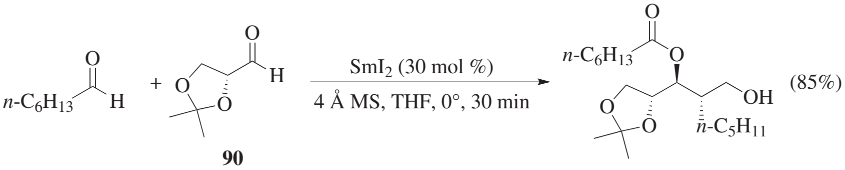
Scheme 125

Samarium iodide is commonly used in intermolecular and intramolecular Barbier reactions. Application of SmI_2 to an intramolecular Barbier reaction of 4-(3-iodopropyl)cyclopent-2-en-1-one derivatives and subsequent quenching with 4-(*tert*-butyldimethylsiloxy)butyraldehyde leads to aldol addition and aldol condensation products.[239] However, when the same reaction is carried out with the 2-methyl-substituted enone **89** in the presence of excess dihydrocinnamaldehyde, aldol–Tishchenko products are isolated almost exclusively (Scheme 126).[239] A rapid Tishchenko step follows the initial aldol addition reaction, and the original unsaturated ketone is fully reduced to a saturated alcohol.



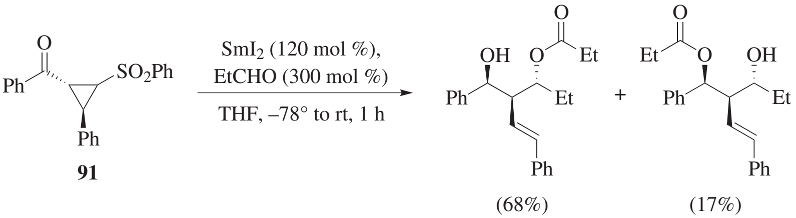
Scheme 126

Samarium iodide accomplishes crossed aldol–Tishchenko reactions between a wide range of ketones and aldehydes.[134] Both acyclic and cyclic ketones can be used as aldol donors, but as discussed in the "Mechanism and Stereochemistry" section, the configuration of the aldol adduct is determined by the structure of the ketone. For acyclic ketones, 1,2-*anti*-1,3-*anti* products are thermodynamically most preferred. For cyclic ketones the situation is reversed, with 1,2-*syn*-1,3-*anti* products being predominant. Using enantiomerically pure starting materials, such as (*R*)-glyceraldehyde acetonide (**90**), allows the possibility of creating multiple adjacent stereocenters with excellent stereocontrol (Scheme 127).[134]



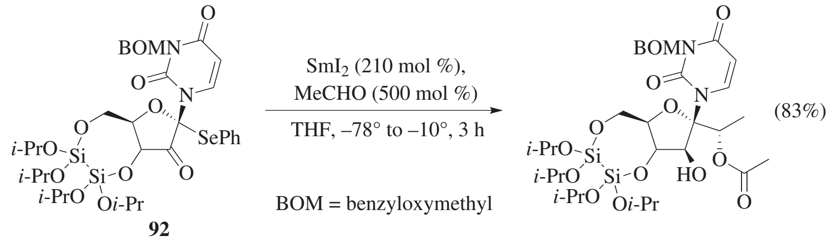
Scheme 127

Samarium iodide has been used to form a samarium dienolate from phenylsulfonyl-activated cyclopropyl ketone **91** through site-selective cleavage and reduction (Scheme 128).[240] The dienolate reacts with an aldol acceptor through the α-carbon to give the *anti*-aldol adduct. The subsequent Tishchenko step gives 1,3-*anti*-diol monoesters with three adjacent stereocenters. The reaction gives fair to good yields depending on the aldehyde acceptor. Aromatic aldehydes are in general slightly less reactive than aliphatic aldehydes. Samarium iodide is also used in an aldol–Tishchenko reaction of the 1′-phenylseleno-2′-keto nucleoside **92** to afford 1′-branched "arabino"-type nucleosides (Scheme 129).[241]



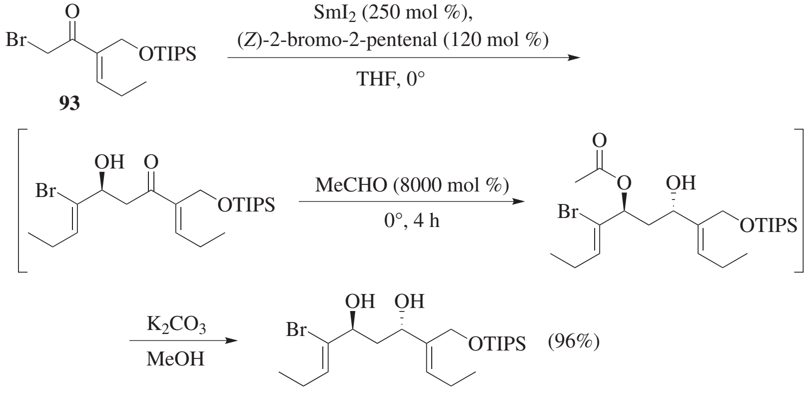
Scheme 128

Lanthanoid-catalyzed Reformatsky-type aldol–Tishchenko reactions of α-halogenated compounds have been reported for neodymium[242] and samarium catalysts.[243,244] In a total synthesis of luminacin D, this type of aldol Evans–Tishchenko is used. Addition of SmI_2 to the unsaturated α-bromo ketone **93** generates the samarium enolate that is then treated with (*Z*)-2-bromo-2-pentenal.

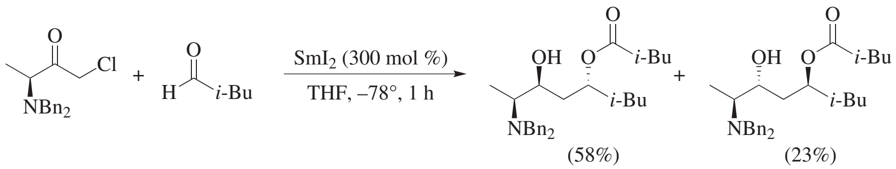


Scheme 129

After the first aldol reaction has taken place, acetaldehyde is added to the system in great excess to effect the subsequent Evans–Tishchenko reduction (Scheme 130).[243] Enantiopure α-amino-α′-halo ketones react with an excess of SmI_2 and an aldehyde to give 4-amino-1,3-diol monoester products (Scheme 131).[244] The initial aldol step prefers the 1,4-*anti* product in mediocre diastereoselectivity, but the 1,3-*anti*-diol is formed with high stereocontrol. Thus, only two diastereoisomers are usually isolated from the reaction mixture.

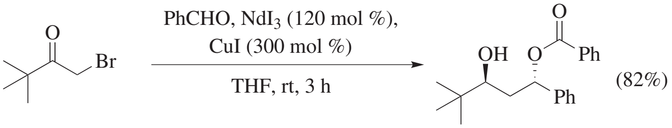


Scheme 130



Scheme 131

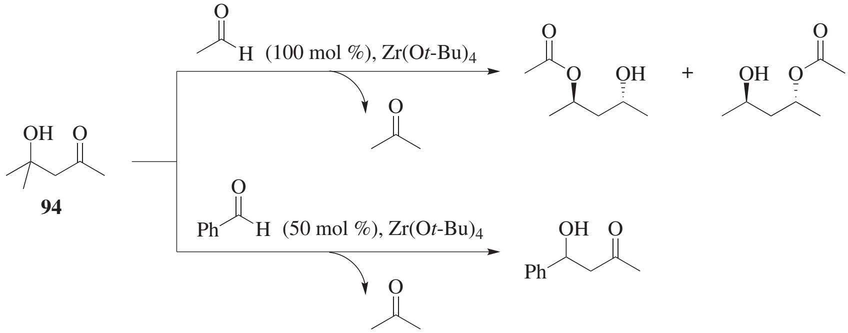
Neodynium triiodide catalyzes the Reformatsky reaction of α-brominated carbonyl compounds at room temperature in CH_2Cl_2. The use of additives such as CuI, SbI_3, or $Sc(OTf)_3$ in the reaction of α-bromopinacolone and benzaldehyde surprisingly affords aldol–Tishchenko products nearly exclusively (Scheme 132).[242] The combination of $NdBr_3$ and NaI also gives aldol–Tishchenko products from α-bromopinacolone and α-bromoacetophenone, although slightly longer reaction times and higher temperatures are needed to achieve similar results.



Scheme 132

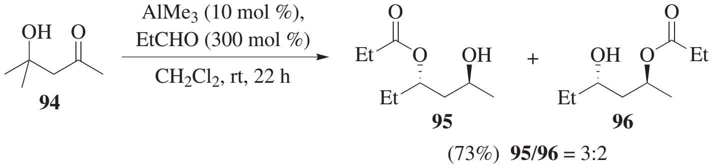
Lanthanoid catalysts are further discussed in connection with enantioselective aldol–Tishchenko and Evans–Tishchenko reactions, in which they find frequent use.

Tandem Retro-Aldol–Tishchenko Reactions. Ketone aldol self-adducts are excellent precursors for the aldol–Tishchenko reaction.[245,246] The self-adduct of acetone (**94**) reacts rapidly via a retro-aldol reaction in the presence of aluminum compounds[245,247] or Zr(O*t*-Bu)$_4$,[246,248,249] forming a ketone enolate that reacts with an aldehyde either through an aldol or an aldol–Tishchenko pathway depending on the exact conditions (Scheme 133). Complexing the zirconium catalyst with a TADDOL ligand creates an enantioselective aldol–Tishchenko catalyst system, which is discussed below in connection with other enantioselective methods.

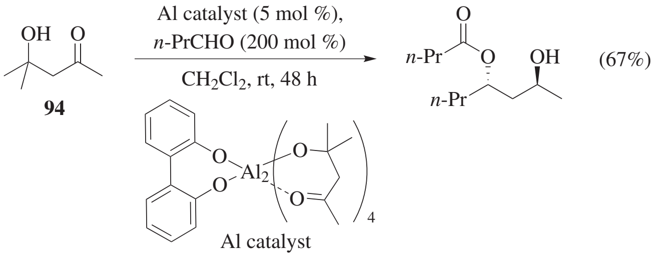


Scheme 133

The aldol-transfer Tishchenko reaction of **94** with aliphatic aldehydes can be catalyzed with $AlMe_3$ to give aldol–Tishchenko products **95** and **96** in moderate to good yields (Scheme 134).[245] Aluminum–biphenol and aluminum–catechol complexes are also able to catalyze the reaction (Scheme 135).[247] Aldol self-adducts of isopropyl methyl and diethyl ketones also function as sources of enolates. The catalyst complex can also be created in situ from the source aldols by treating them with $AlMe_3$.

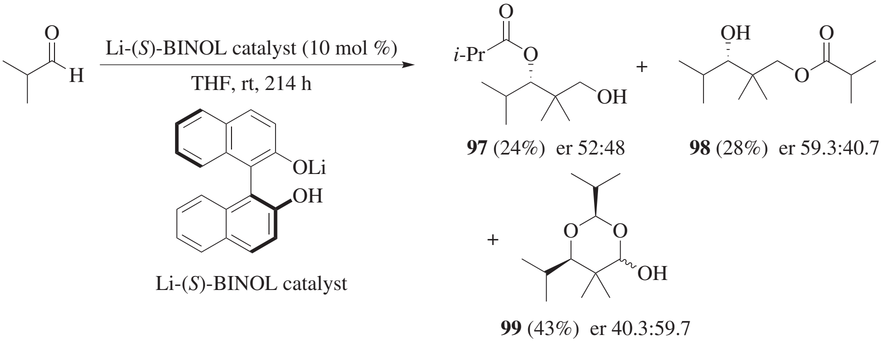


Scheme 134



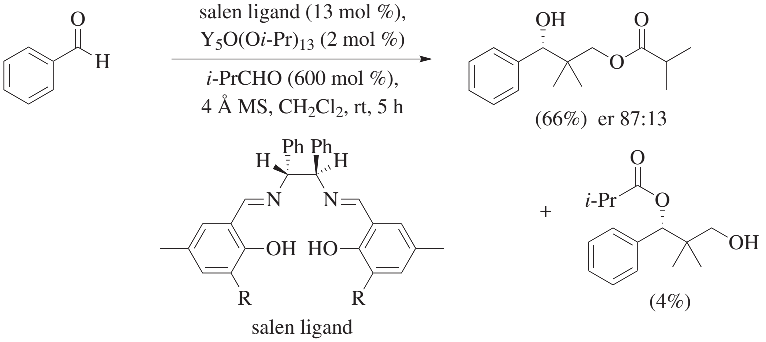
Scheme 135

Enantioselectivity in the Aldol–Tishchenko Reaction. A chiral, monolithium *S*-BINOL catalyst has been used in the aldol–Tishchenko reaction of isobutyraldehyde (Scheme 136).[101] Monitoring the composition of the reaction mixture reveals that the aldol reaction step initially produces a small excess of the (*R*)-isomer, but as the reaction proceeds further, an excess of (*S*)-isomers of the aldol–Tishchenko products **97** and **98** is observed. The (*R*)-isomer of aldoxane **99** is also produced in the reaction in slight enantiomeric excess. In the presence of the same catalyst, the racemic aldol–Tishchenko products of isobutyraldehyde undergo acyl migration with a slight preference for the (*S*)-enantiomer.[250]



Scheme 136

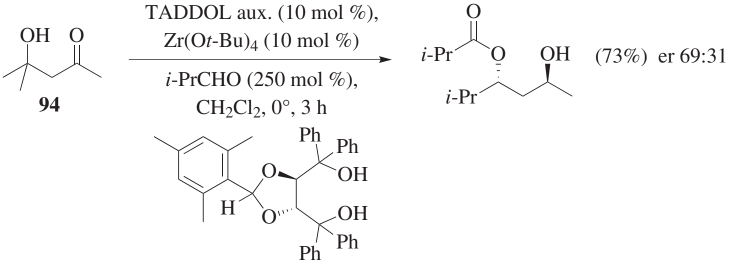
Salen complexes are the first highly enantioselective catalysts for the aldol–Tishchenko reaction.[103] The reaction between benzaldehyde and isobutyraldehyde affords moderate yields and enantioselectivities when catalyzed by complexes prepared from $Y_5O(Oi\text{-}Pr)_{13}$ and different salens (Scheme 137).[103] Among substituted benzaldehydes, electron-donating groups in the 4-position give poorer yields but enantioselectivity is maintained. Reactions are usually run in CH_2Cl_2 in the presence of molecular sieves, with 2 mol % of the yttrium complex and 13 mol % of salen ligand.



salen ligand
R = 1-adamantyl

Scheme 137

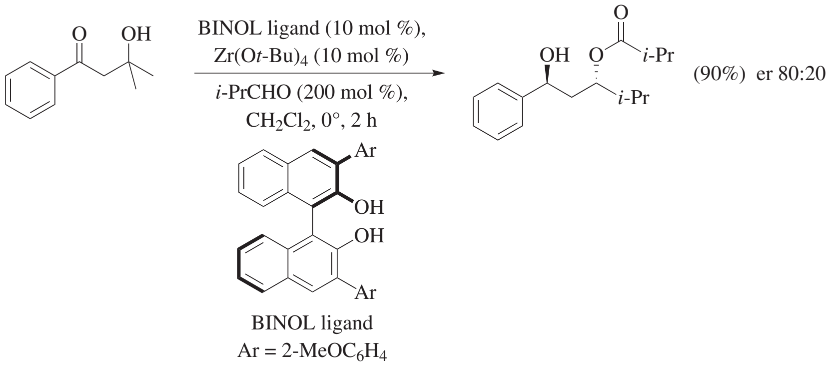
Chiral zirconium-TADDOL[248] and –BINOL[107] complexes show asymmetric induction in the retro-aldol–Tishchenko reaction of ketone aldol adducts. Both systems catalyze the reaction in good yields, although at best with only moderate enantioselectivities in the range of 75:25 to 80:20 (Schemes 138 and 139).[107,248] Zirconium *tert*-butoxide-TADDOL complexes produce the monoester products with diminished acyl migration, and are applicable to a wide structural range of ketone-based enol equivalents and aldehydes.[249] Zirconium *tert*-butoxide alone does not have a racemizing effect in the reaction. Enantiomerically enriched β-hydroxy ketones are reduced via an Evans–Tishchenko-type mechanism with no loss of enantiomeric purity (Scheme 140).[248] The $Zr(Ot\text{-}Bu)_4$-catalyzed reduction of β-hydroxy ketones has a broad substrate scope and can be considered an alternative to the samarium-catalyzed Evans–Tishchenko reaction.[251]



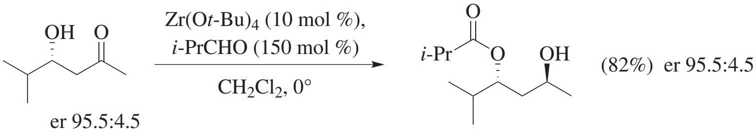
94

TADDOL auxiliary

Scheme 138

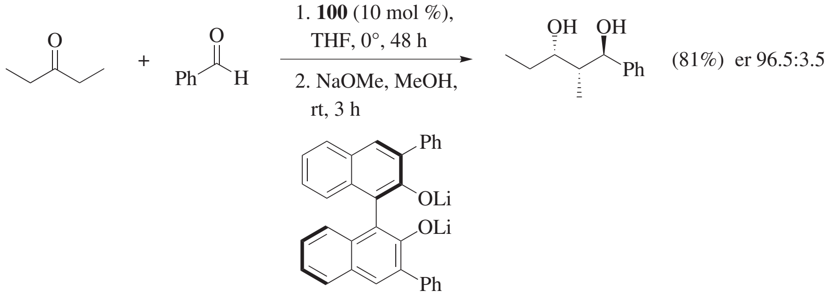


Scheme 139



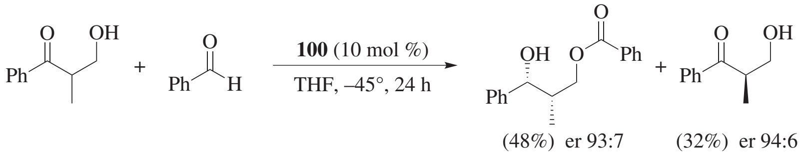
Scheme 140

A highly enantioselective direct catalytic aldol–Tishchenko reaction of ketones is achieved with the dilithium salt of 3,3′-diphenylbinaphthol (**100**) (Scheme 141).[252,253] This catalyst can also be used to enantioselectively reduce α-disubstituted β-hydroxy ketones to the corresponding diol monoesters, but monosubstitution at the α-position leads to kinetic resolution of the β-hydroxy ketone (Scheme 142).[254] α-Unsubstituted β-hydroxy ketones behave in a similar manner as other aliphatic ketones, and undergo a traditional aldol–Tishchenko reaction. α-Disubstituted trimethoxysilyl enol ethers can also be used as the aldol donors to synthesize 1,3-*anti*-diols with quaternary carbons at the 2-position (Scheme 143).[255]

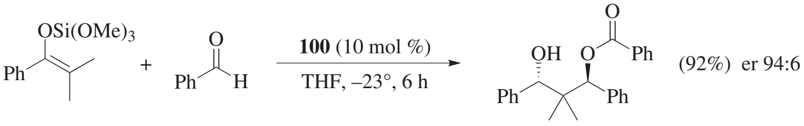


100

Scheme 141

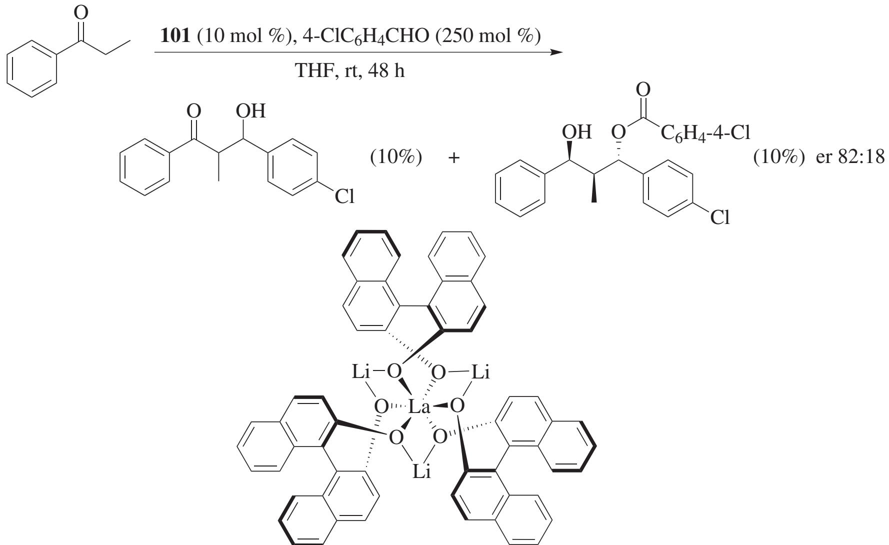


Scheme 142



Scheme 143

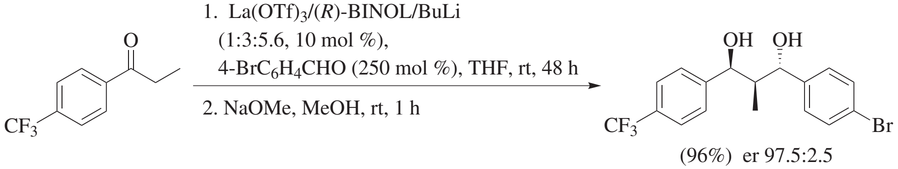
Originally developed for direct asymmetric aldol reactions, heterobimetallic asymmetric lanthanum–lithium–BINOL complexes such as **101** have been applied successfully to enantioselective aldol–Tishchenko reactions.[104,256] The $LaLi_3(BINOL)_3$ (LLB, **101**) complex itself is mildly active but unselective in the reaction of propiophenone with 4-chlorobenzaldehyde, giving a 1:1 mixture of aldol adduct and aldol–Tishchenko product in 20% yield and er = 82:18 (Scheme 144).[104] Addition of lithium salts improves the yields but not the product selectivity, still giving a 1:1 product mixture. The addition of LiOTf is postulated to lead to a dynamic reassembly of the catalyst structure, forming a binuclear $La_2Li_4(BINOL)_5$ complex.



101

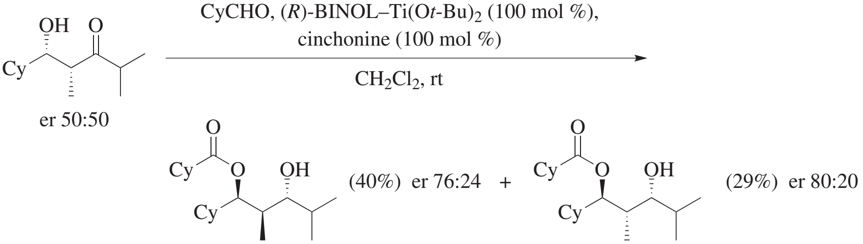
Scheme 144

In optimized conditions the catalyst system is generated in situ from a 1:3:5.6 mixture of $La(OTf)_3$, (*R*)-BINOL, and *n*-BuLi. However, the applicability of this catalyst system seems to be restricted to activated aldol donors only. For instance, 1-[(4-trifluoromethyl)phenyl]propan-1-one gives aldol–Tishchenko products in excellent yield and enantioselectivity under these conditions (Scheme 145).[256]



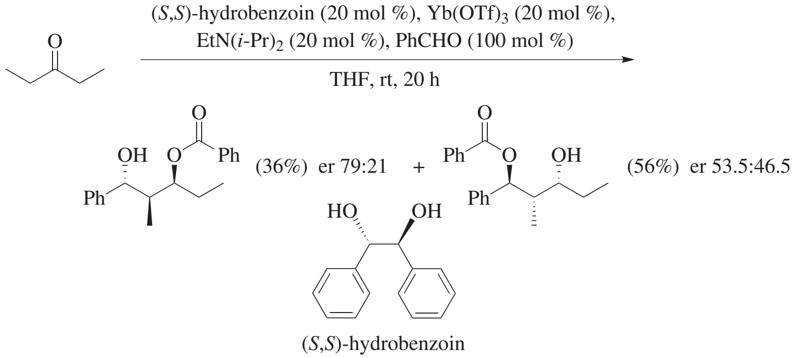
Scheme 145

The combination of *cinchona* alkaloids and BINOL–Ti(O*t*-Bu)$_2$ may be used as a catalyst system to obtain enantioenriched aldol–Tishchenko products from racemic propionate aldol adducts.[257] The substrate undergoes retro-aldol equilibration under the reaction conditions, and both 1,2-*syn*-1,3-*anti*, and 1,2-*anti*-1,3-*anti* products are isolated in varying degrees of enantioselectivity (Scheme 146).[257] When propyl phenyl or isobutyl phenyl ketone-derived aldol adducts are used, the retro-aldol equilibration leads to 1,2-*anti*-1,3-*anti* products exclusively. However, stoichiometric amounts of both the BINOL–Ti(IV) complex and the *cinchona* alkaloid are needed for the reaction.

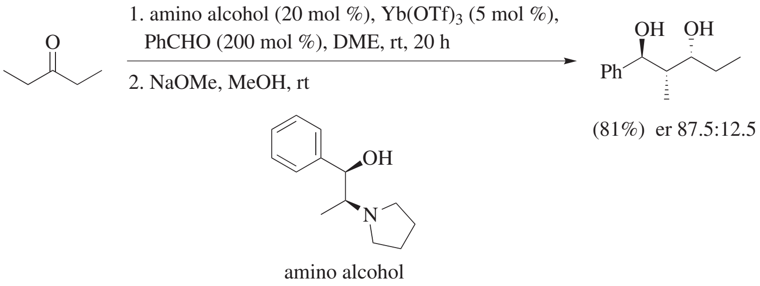


Scheme 146

In addition to TADDOL-, BINOL- and salen-derived catalysts, other chiral diol and amino alcohol derivatives complexed with $Yb(OTf)_3$ catalyze the direct aldol–Tishchenko reaction of aromatic aldehydes and aliphatic ketones with moderate to good enantioselectivities.[105,258,259] For example, reaction of diethyl ketone and benzaldehyde catalyzed by the (*S*,*S*)-hydrobenzoin–$Yb(OTf)_3$ complex yields two constitutionally isomeric esters, but with different yields, enantioselectivities, and opposite absolute configurations, indicating different paths of formation for each constitutional isomer (Scheme 147).[258] Yield and enantioselectivity are also affected by substitution of the aromatic aldehyde. The $Yb(OTf)_3$–(1*R*,2*S*)-1-phenyl-2-(1-pyrrolidynyl)-1-propanol (1:4) complex catalyzes the direct aldol–Tishchenko reaction of diethyl ketones, dipropyl ketones, and propiophenone derivatives with good yields and enantioselectivities (Scheme 148).[105,259] C_2-Symmetric amino esters, bisamido complexes, and simple amino acid derived esters are also effective catalysts, giving aldol–Tishchenko products in high yields, albeit with poorer enantioselectivities.[260–262]

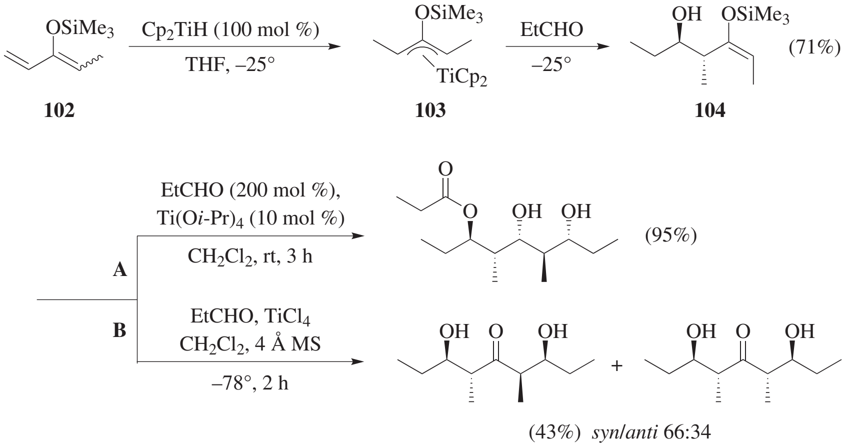


Scheme 147

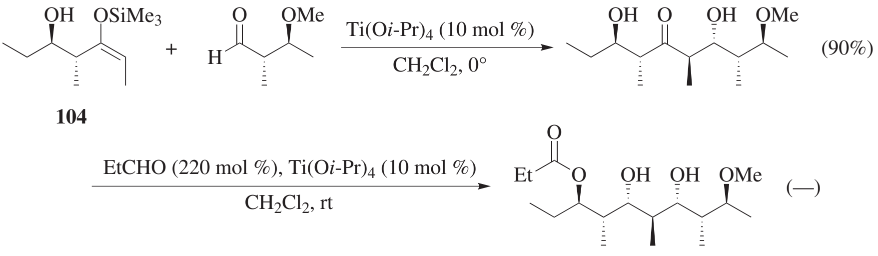


Scheme 148

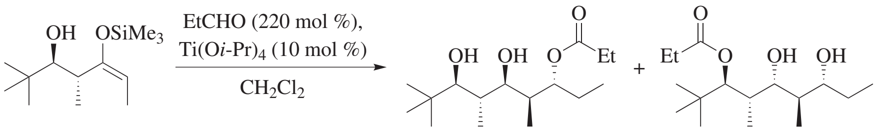
Synthesis of Multiple Adjacent Stereocenters via Aldol–Tishchenko Reactions. The aldol–Tishchenko reaction is a powerful tool for creating multiple adjacent stereocenters with excellent selectivity in relatively few or even one step. The combination of an allyltitanation and the Ti(O*i*-Pr)$_4$-mediated aldol–Tishchenko reaction is used as a method to create stereopentads and stereohexads (Scheme 149).[102,263–265] The allyltitanation of a silyloxy-substituted diene **102** forms the intermediate **103**, which undergoes subsequent aldol reaction, forming the silyl enol equivalent **104**. Mukaiyama-type aldol reaction of the enolsilane (step **B**) is also a valid route for stereopentad systems, but it requires an additional reduction step of the aldol product to yield the triol (Scheme 149).[266] The aldol–Tishchenko reaction (step **A**) turns out to be advantageous, since the reduction of the resulting ketone is a part of the reaction mechanism, although the remaining ester moiety must be hydrolyzed to yield the desired triol. Using chiral α-substituted aldehydes can easily yield up to seven contiguous stereocenters in sequential aldol addition/Evans–Tishchenko reactions (Scheme 150).[102] The free hydroxy group β to the enol ether is essential for the aldol–Tishchenko step in this method. Protection of the alcohol with a carbamate group eliminates reactivity.[265] The allyltitanation step can be used to control the configuration of the enolsilane. The standard procedure with THF as solvent leads to *anti*-aldol products. Replacing THF with 3:1 HMPA/THF conversely affords the *syn* product, which is attributed to the formation of an open transition state instead of the Zimmerman–Traxler cyclic transition structure, which normally operates in the reaction.[267] The stereoselectivity of the final reduction step is also determined by steric factors involving the surrounding 1- and 5-hydroxy groups. The less hindered group is more likely to coordinate with the aldehyde and thus promote the *anti*-selective hydride transfer step (Scheme 151).[264] A retro-aldol reaction also takes place under the reaction conditions, but can be suppressed by lowering the temperature to 0°.



Scheme 149



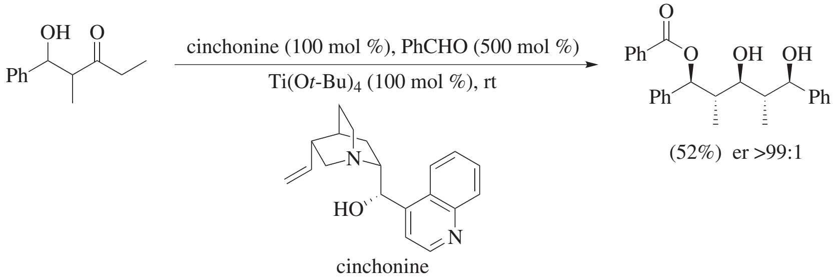
Scheme 150



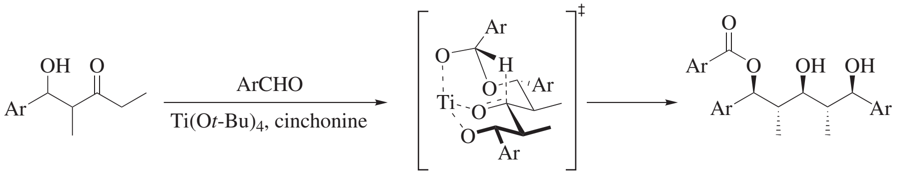
Temp	Yield (%)	dr
rt	95	70:30
0°	95	>95:5

Scheme 151

Stereopentad systems have also been obtained by carrying out an aldol–Tishchenko reaction with $Ti(Ot\text{-}Bu)_4$ as the catalyst and *cinchona* alkaloids as the ligands (Scheme 152).[106] Surprisingly, the products contain a 1,3,5-*syn-syn* triol structure instead of the *anti*-diol usually associated with aldol- and Evans–Tishchenko reactions. A tentative explanation points to a possible tricyclic transition state **105** that directs the hydride transfer step to yield a *syn-syn* reduction product (Scheme 153, corrected from ref. 106).[106] The configuration of the starting material does not affect the diastereomeric ratio of the product, since a retro-aldol cleavage takes place in the beginning of the reaction cascade.



Scheme 152



105

Ti = $Ti(OBu\text{-}t)_4$ / cinchonine

Scheme 153

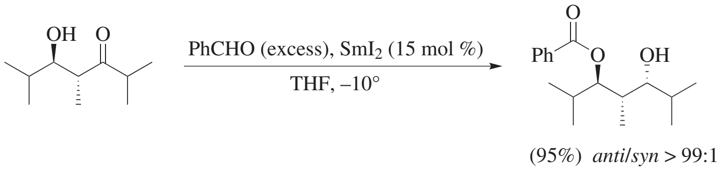
Substrate Limitations in the Aldol–Tishchenko Reaction. The examples shown above in this section have been chosen to give an overview on general substrate applicability to the aldol–Tishchenko reaction. In the trimerization of enolizable aldehydes, facility of enolization is an obvious requirement. However, the literature contains mostly examples of unfunctionalized aliphatic aldehydes. The studies with *i*-PrOZnEt[233] indicate that the presence of, for example, isolated double bonds, esters, acetals, and halogens is tolerated, although adding complexity to the substrate clearly decreases the yields. The zinc alkoxide, therefore, has the widest proven substrate scope in the trimerization of aliphatic aldehydes. However, the samarium complex $Cp^*{}_2Sm(thf)_2$ is one of the catalysts that render the fastest reaction rates.[238]

Successful enolization is required for the crossed aldol–Tishchenko reaction between ketones and aldehydes, as is the protection of sensitive functionalities. Care must be taken in choosing correct conditions for substrates that are apt to undergo retro-aldol equilibration, unless the equilibration to a thermodynamically more stable configuration is a desired aspect in the reaction. Target-oriented examples with highly functionalized aldol donors remain few, but SmI_2 and SmI_3 have been shown to be applicable to a wide variety of substrates in a direct catalytic aldol–Tishchenko process.[134] The Mukaiyama-type aldol–Tishchenko cascade with catalytic amounts of $Ti(O\textit{i}\text{-}Pr)_4$ and excess aldehyde is also quite promising for the stereocontrolled synthesis of polyketide-type structures.[102,263–265] For alkyl phenyl ketones, activating aromatic substitution generally increases reactivity. Sterically bulky alkyl chains generally hinder the reaction.

Simple aliphatic and aromatic aldehydes such as benzaldehyde generally perform well as the aldol acceptor/hydride donor partners in the aldol–Tishchenko reaction. Electron-rich aldehydes give slightly lower yields in direct asymmetric aldol–Tishchenko reactions.[104,105,261] As is the case for aldol reactions in general, even highly functionalized aldehydes should be tolerated in the aldol step, as long as care is taken with an adequate protecting group strategy. Examples in the following sections on “The Evans–Tishchenko Reaction” and “Applications to Synthesis” show that complex aldehydes may also be used in the hydride transfer/esterification step.

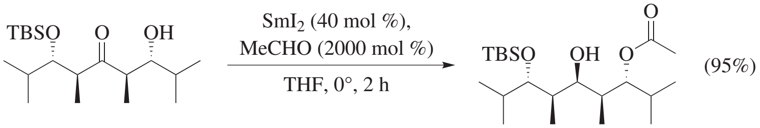
The Evans–Tishchenko Reaction

β-Hydroxy ketones are readily reduced to 1,3-*anti*-diols through the Evans–Tishchenko reaction.[108] Wide variation of substrate structure is possible as shown by the many applications of the Evans–Tishchenko reaction in total syntheses of natural products. The presence of aliphatic substituents poses no significant restrictions on the reaction (Scheme 154).[108] If the substrate structure bears additional β-hydroxy groups relative to the ketone, these groups should be protected to prevent them from competing with the actual directing hydroxy group (Scheme 155).[268]



(95%) *anti*/*syn* > 99:1

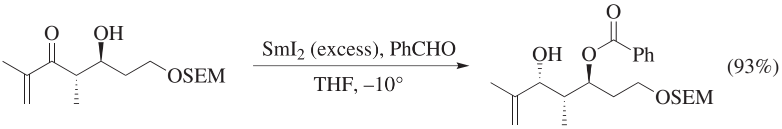
Scheme 154



(95%)

Scheme 155

β-Hydroxy enones can also be used as substrates in the Evans–Tishchenko reaction. The conjugated double bond is not reduced in the reaction nor does it hinder the reduction of the ketone, as illustrated for a key step in the total synthesis of ansatrienine A (Scheme 156).[114]

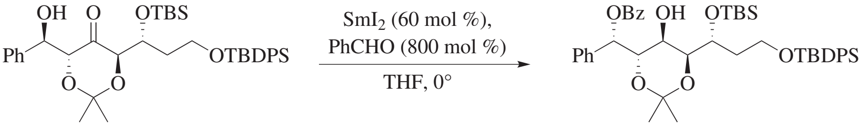


(93%)

SEM = 2-trimethylsilylethoxymethoxy

Scheme 156

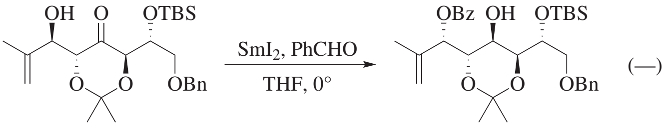
The rapid retro-aldol equilibration discussed above may occur in some Evans–Tishchenko reactions. For instance, the cyclic *anti*-aldol adduct **106** is used as a substrate in synthetic approaches to the styryllactone family of natural products. However, the product unexpectedly contains the 1,2-*syn*-1,3-*anti* structure instead of retaining its original 1,2-*anti* configuration (Scheme 157).[117] As further proof, model substrate **107** undergoes retro-aldol cleavage under the same conditions (Scheme 158).[117] The original methacrylaldehyde unit is replaced by benzaldehyde.



106

(95%)

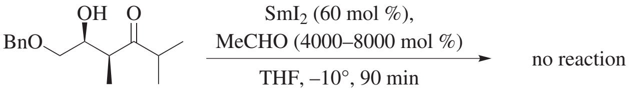
Scheme 157



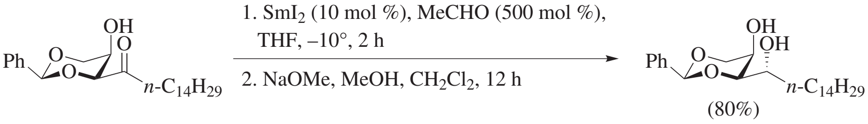
107

Scheme 158

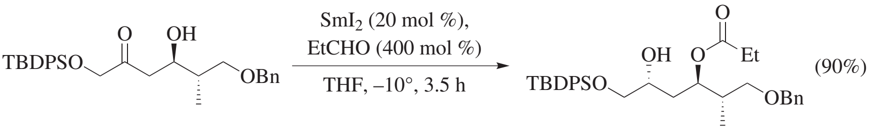
In a rare example where an Evans–Tishchenko reaction is unsuccessful, the substrate β-hydroxy ketone includes a benzyloxy group vicinal to the hydroxy group (Scheme 159).[108] When the hydroxy and benzyloxy groups are in a 3,5-relationship to each other, the reaction proceeds in a normal fashion. The reason behind this failure is unclear, since the presence of a conformationally locked, protected vicinal hydroxy group in itself is not inhibitory to the reaction, as can be seen from an example of an Evans–Tishchenko reaction used in the synthesis of sphingosine and phytosphingosine (Scheme 160).[269] A silyl-protected hydroxy group vicinal to the ketone moiety likewise does not hinder the reaction (Scheme 161).[124] Further instances of the Evans–Tishchenko reaction performing less than satisfactorily are observed in the syntheses of amphidinolide T3[270] and clavulactone.[271]



Scheme 159

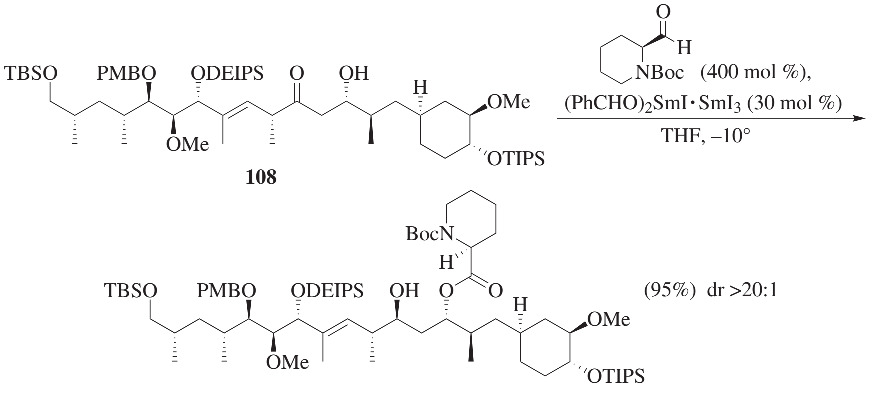


Scheme 160

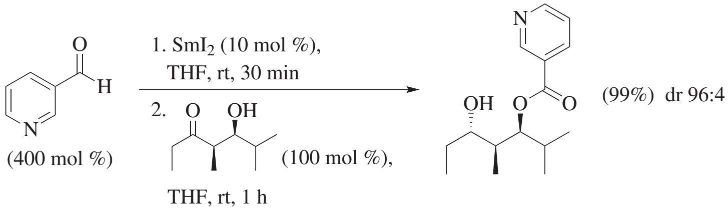


Scheme 161

The mild conditions usually required for the Evans–Tishchenko reaction allow it to be used with highly complex and sensitive substrates such as **108** in a total synthesis of (−)-rapamycin (Scheme 162).[109] This example is also noteworthy for its use of a heterocyclic aldehyde, which is later incorporated into the (−)-rapamycin skeleton. Similar coupling of heteroaromatic aldehydes can be used as a possible route to access natural products that contain heteroaryl ester moieties (Scheme 163).[272] Further examples of the Evans–Tishchenko reaction in the synthesis of natural products are discussed in the section "Applications to Synthesis".



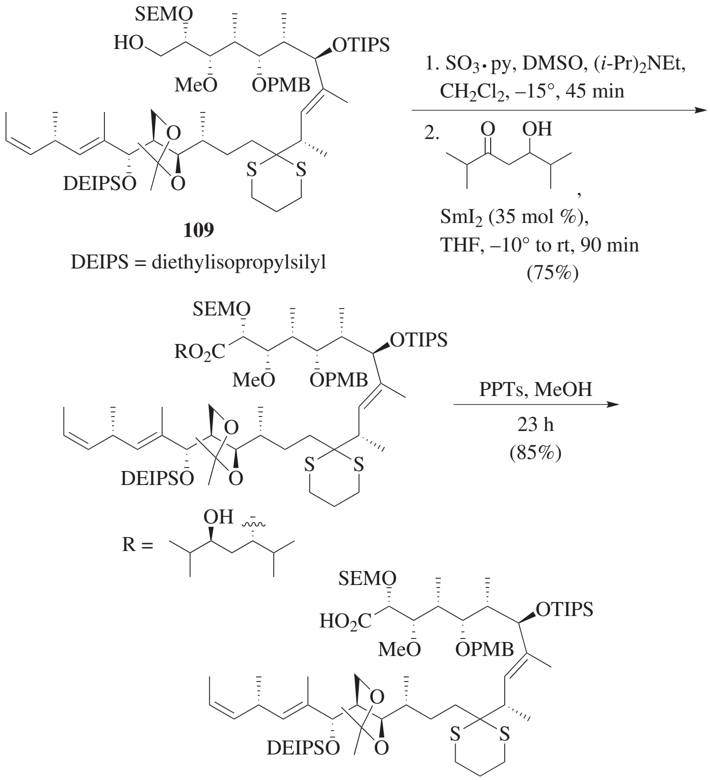
Scheme 162



Scheme 163

The Evans–Tishchenko reaction has also been used in an inventive inverse fashion to oxidize an aldehyde moiety to a carboxylic acid under mild conditions. This is highlighted in a total synthesis of (+)-13-deoxytedanolide, where a readily available racemic β-hydroxy ketone is used as a sacrificial oxidant (Scheme 164).[120] The aldehyde is prepared by Parikh–Doering oxidation of the corresponding alcohol **109**, isolated, and subjected to an Evans–Tishchenko reaction. The acid is obtained via hydrolysis of the 1,3-diol monoacyl moiety.

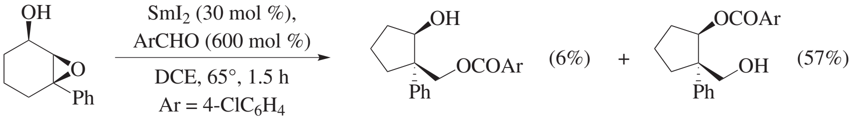
The Evans–Tishchenko reaction can be coupled with a semipinacol reaction.[273,274] The samarium-catalyzed reaction of the tertiary α-hydroxy epoxide **110** with an aldehyde leads to 1,3-*anti*-diol monoesters with a quaternary carbon at the 2-position (Scheme 165).[274] Using an epoxide with the hydroxy group attached to a six-membered ring leads to a rearrangement that gives a five-membered ring. Electron-donating substituents in the aromatic aldehydes are generally unfavorable for this reaction. The use of aliphatic aldehydes has not been extensively screened but the results indicate their equal applicability. It is noteworthy that the reaction of a mixture of stereoisomers may yield a single product with three well-defined contiguous stereocenters in a single step (Scheme 166).[273]



109

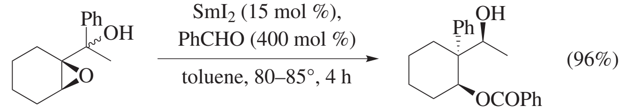
DEIPS = diethylisopropylsilyl

Scheme 164



110

Scheme 165



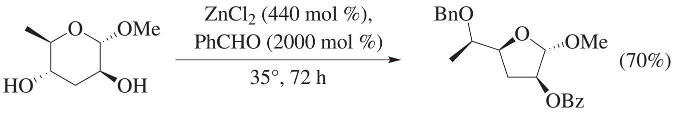
syn/*anti* = 70:30

Scheme 166

APPLICATIONS TO SYNTHESIS

The Tishchenko reaction has been established in industry since the early 20th century. The production of simple esters, such as the industrial-scale production of ethyl acetate,[275,276] is a classic example with several patents covering this area. The reaction is industrially attractive for its complete atom economy, and it is widely used in countries where ethanol is not a feasible starting material for the production of ethyl acetate, for instance due to high taxation. Preparation of industrial aluminum alkoxide catalysts used in the production of reagents such as ethyl acetate differs somewhat from that of laboratory-scale catalysts.[37] For example, it has been noted that it is advantageous to have minor amounts of water present in the catalyst preparation process, and $ZnCl_2$ or $FeCl_3$ are frequently used as co-catalysts.

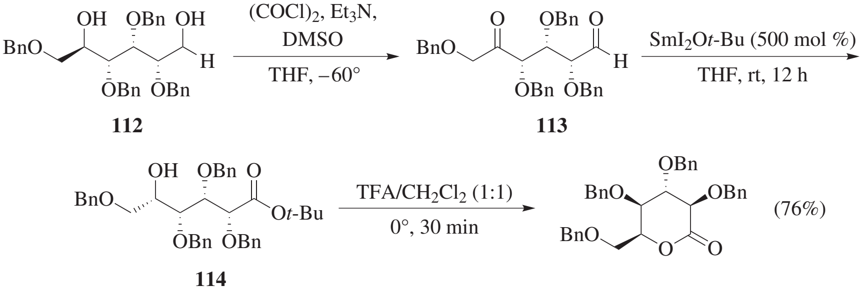
The Tishchenko reaction has been applied to carbohydrate chemistry with some success. The rearrangement of methyl 3,6-dideoxy-α-arabinohexopyranoside to the corresponding furanoside is achieved in the presence of benzaldehyde and a Lewis-acid catalyst (Scheme 167).[277–279] Zinc chloride, $TiCl_4$, and $AlCl_3$ are all active catalysts and usually give the rearranged methyl 2-*O*-benzoyl-5-*O*-benzyl-3,6-dideoxy-α-hexofuranoside **111** in good yields. The reaction is also applicable to 6-acetamido derivatives and can be considered as a route to the synthesis of aminoglycoside antibiotics.



111

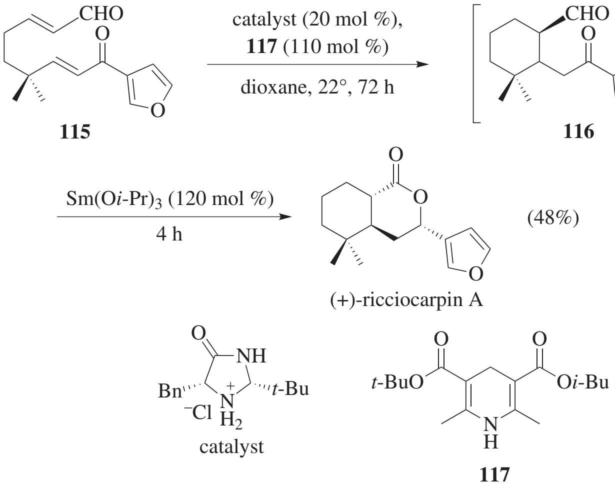
Scheme 167

SmI_2Ot-Bu is used in the synthesis of L-idose and L-altrose.[280] The diol precursor **112** is oxidized to the δ-keto aldehyde **113**, which is then treated with the samarium catalyst in THF, yielding δ-hydroxy ester **114** in an intramolecular Tishchenko-type reaction (Scheme 168).[280] The δ-carbon of **114** undergoes complete inversion, but when D-galactitol is used as starting material, a 5:1 mixture of epimers is obtained.



Scheme 168

The Tishchenko reaction has been coupled to an organocatalytic reductive Michael-addition in a synthesis of ricciocarpin A and its analogs.[281] In a one-pot procedure, enal-enone **115** is first treated with an imidazolidinone catalyst and a stoichiometric amount of Hantzsch ester **117** to give the cyclized δ-keto aldehyde **116** (Scheme 169).[281] Addition of Sm(O*i*-Pr)$_3$ then effects epimerization and an intramolecular Tishchenko reaction to give (+)-ricciocarpin A.



Scheme 169

The aldol–Tishchenko reaction is used as a method for producing 1,3-diol monoesters on an industrial scale.[282] The monoesters may be used as coalescing agents, as solvents for paints, or as lubricants.[283] The corresponding glycols (neopentyl glycol, 2,2,4-trimethyl-1,3-pentanediol) are commonly used in polyester resins and surface coatings. The Tishchenko reaction is also used in the production of 3-hydroxy-2,2-dimethylpropyl 3-hydroxypivalate, which is likewise used in polyester resins and surface coatings.[284]

In addition to the aforementioned syntheses of (−)-rapamycin and (+)-13-deoxytedanolide, numerous reports illustrate the use of the Evans–Tishchenko reaction in the total syntheses of natural products. The convergent synthesis of (+)-concanamycin F, a macrolide compound containing 14 stereocenters, invokes the reaction at an early stage of the synthesis (Scheme 170).[285,286] The Evans–Tishchenko reaction is used to control the configuration of a hydroxy group at C_{19} in the synthesis of the C_{14}–C_{22} subunit.

In several syntheses of the important natural product (+)-discodermolide (Fig. 2),[287] the Evans–Tishchenko reaction is used to control the configuration of various hydroxy groups (Schemes 171[116,288,289] and 172[121,290]).

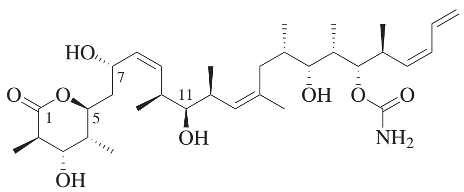
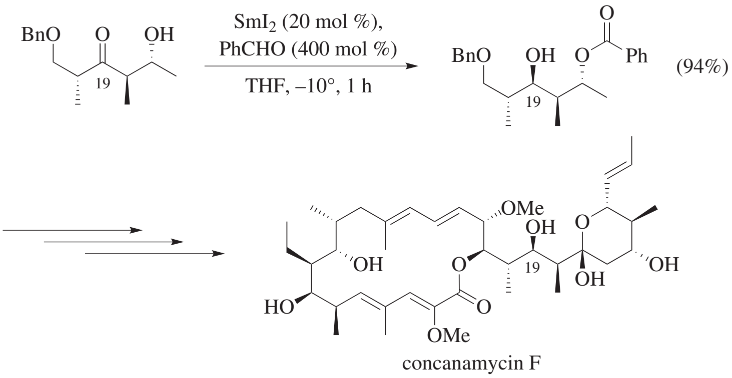
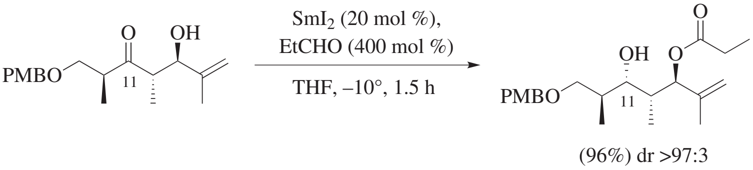


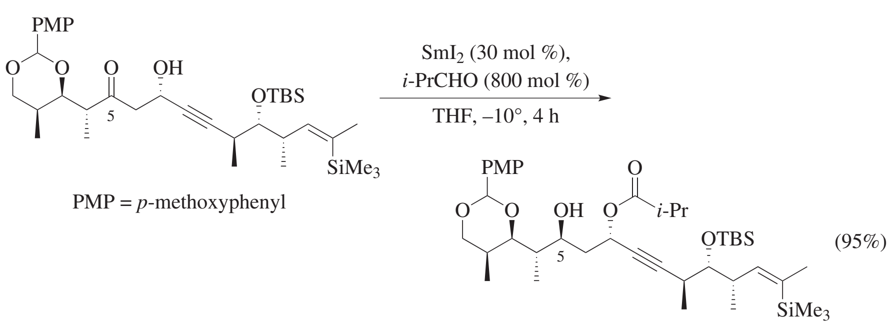
Figure 2. The structure of (+)-discodermolide 1.



Scheme 170



Scheme 171



Scheme 172

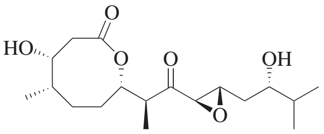
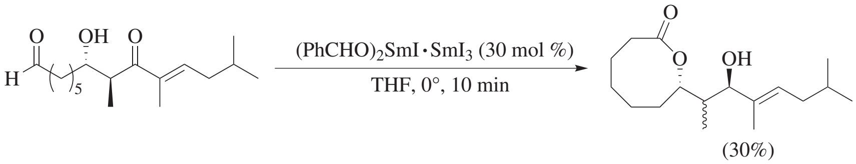
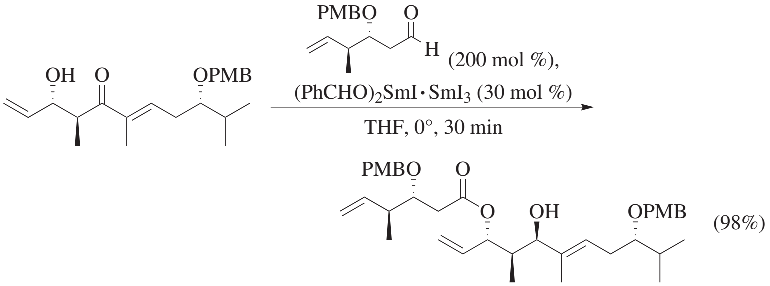


Figure 3. The structure of octalactin A.

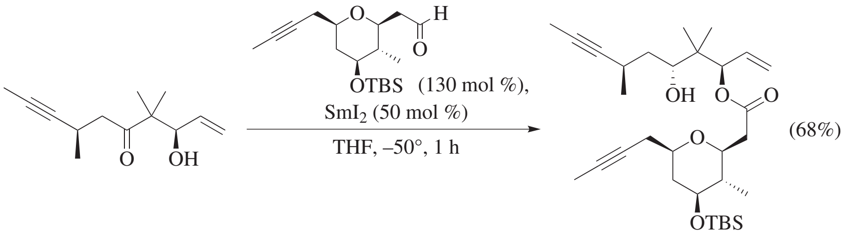
In a total synthesis of octalactin A (Fig. 3), a rapid retro-aldol reaction causes the epimerization of the stereocenter α to the ketone during an attempted intramolecular Evans–Tishchenko lactonization (Scheme 173).[111] This problem is solved in an inventive fashion by using a properly functionalized aldehyde as the hydride donor in the Evans–Tishchenko reaction of a different precursor (Scheme 174).[123] Terminal double bonds are included both in the β-hydroxy ketone substrate and the hydride donor aldehyde. The synthesis of the 8-membered lactone is then completed with a ring-closing olefin metathesis reaction. The Evans–Tishchenko reaction is also used to couple complex fragments together in a total synthesis of (−)-polycarvenoside A (Scheme 175).[291]



Scheme 173



Scheme 174



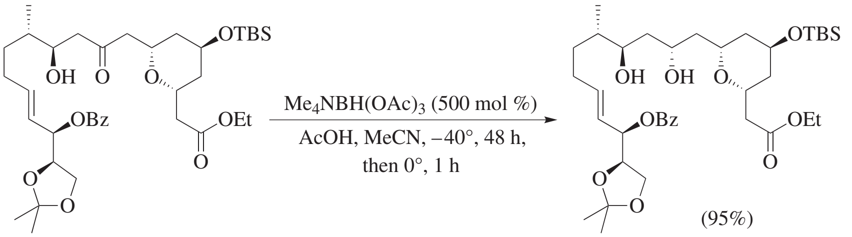
Scheme 175

The above-discussed syntheses of (+)-13-deoxytedanolide and (−)-rapamycin are classic examples of the use of the Evans–Tishchenko reaction with highly complex substrates in the late stages of a synthesis. Other natural compounds in whose syntheses Evans–Tishchenko reactions are used include rhizoxin D,[292−294] bryostatin 2,[112,113] dermostatin A,[295,296] and callipeltoside and its aglycon,[115,297] to name a few.

COMPARISON WITH OTHER METHODS

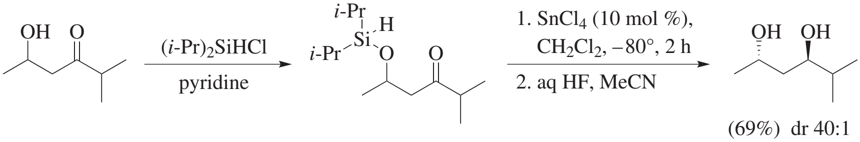
The Tishchenko reaction is an excellent method for producing simple esters, and has advantages over several other methods due to its excellent atom economy. It is suitable for both laboratory and industrial scales. However, in the synthesis of unsymmetrical esters and ester functionalities in complex molecules, other methods are usually more efficient. With the exception of a few recent examples,[144−147,178] the Tishchenko reaction between two different aldehydes usually gives a product mixture whose exact composition is dependent on the relative reactivities and steric and electronic properties of the aldehydes. Selective synthesis of unsymmetrical esters can more easily be achieved with classic methods such as Fischer esterification, alcoholysis of acid chlorides or anhydrides, or the Mitsunobu reaction.[298,299]

The aldol–Tishchenko and Evans–Tishchenko reactions are efficient ways to create 1,3-*anti*-diol structures. The latter reaction is especially useful since there is no need for exotic catalyst systems, and the reaction conditions are usually mild enough not to cause undesired side reactions. Another versatile method for reducing β-hydroxy ketones is the widely used Evans modification[300] of the Saksena reduction[301] which utilizes $Me_4NBH(OAc)_3$ as the reducing agent. A comparison between the two is highlighted in the total synthesis of leucascandrolide A.[302] In this synthesis the Evans–Tishchenko reaction is effective in the reduction of an undesired epimeric model compound, but leads mostly to retro-aldol products and recovery of unchanged starting material when the correct stereoisomer is used. Reduction of the correct substrate with $Me_4NBH(OAc)_3$ gives the desired 1,3-*anti*-diol structure (Scheme 176),[302] whereas there is no reaction using the Evans–Tishchenko protocol. On the other hand, the Saksena–Evans and Evans–Tishchenko methods are equally effective with respect to yield and stereochemistry in the synthesis of (+)-discodermolide.[116] The Saksena-Evans method has an advantage in that it does not require subsequent hydrolysis of the 1,3-diol monoester.



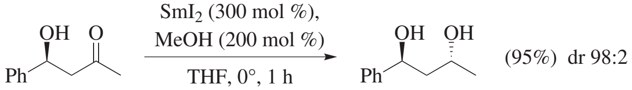
Scheme 176

The complete reaction arsenal for creating 1,3-*syn*- and *anti*-diols is too broad to discuss in great detail, and different methods for stereoselective syntheses have been recently reviewed.[303] The Evans–Tishchenko method has proven to be quite generally applicable, with only a few reported cases where it does not work. On the basis of similar premises, an intramolecular hydrosilylation can be used to reduce β-hydroxy ketones to 1,3-*anti*-diols.[304] An advantage of this type of reaction is that several different kinds of catalysts can be used to achieve the *anti*-selective reduction step. Overall, $SnCl_4$ is a good catalyst with selectivities in the range of 30:1 to 120:1, with $BF_3{\bullet}OEt_2$ rendering the best selectivity. With some β-silyloxy ketone–catalyst combinations, reverse selectivity towards *syn*-diols is observed. The reaction requires much lower temperatures (−80°) than the Evans–Tishchenko reaction, and the overall yields are around 60–70% (Scheme 177).[304]



Scheme 177

Samarium diiodide is a one-electron reducing agent for β-hydroxy ketones in combination with excess water or methanol as the proton source.[305] Unhindered β-hydroxy ketones are readily reduced in this manner to 1,3-*anti*-diols at 0° (Scheme 178).[305] Some β-alkoxy ketones can also be reduced to monoprotected 1,3-*anti*-diols in the same manner when THF is used as a solvent, but β-silyloxy ketones are completely unreactive.[306] The stereoselectivity of the method is greatly influenced by both the solvent system used and the substrate structure.[307,308] Hence, the Evans–Tishchenko and Saksena–Evans methods are more generally applicable to these reductions.



Scheme 178

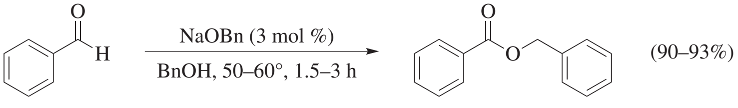
Classic methods for the synthesis of polyesters are similar to those for normal esterification. Polyesters can be synthesized by, among other methods, polycondensation of dicarboxylic acids and diols,[309] or by transesterification of diacid esters and diols. Ring-opening polymerization of lactones is another classic method, for which several new catalyst systems such as (tetraphenylporphinato)aluminum complexes[310] have been created. In comparison to the Tishchenko polymerization of 1,12-dodecanedial, the 13-membered lactone 12-dodecanolide has been polymerized to the same polyester by lipase enzymes.[311] Ring-opening polymerization is similar to the Tishchenko polymerization with respect to its excellent atom economy, whereas traditional polycondensation and transesterification methods produce stoichiometric amounts of cleavage products. However, the number of industrial applications of the Tishchenko reaction in polyester synthesis remains small.

EXPERIMENTAL CONDITIONS

The traditional Tishchenko reaction is usually carried out under an inert atmosphere with complete exclusion of moisture, since most of the published metal catalyst systems are extremely sensitive to hydrolysis. The traditional aluminum alkoxide catalyst solution may contain the corresponding alcohol. The product ester can also be used as a non-interfering solvent system. Aprotic solvents such as CH_2Cl_2 are readily tolerated. Cooling is usually necessary, since the reaction is exothermic, and side reactions often occur at higher temperatures. Generally the choice of solvent depends on the exact catalyst system, and in several cases the solvent can be completely excluded. The heterogeneous Tishchenko reaction is usually run under vacuum, except when supercritical CO_2 is used as the reaction medium. The pretreatment temperature of a heterogeneous catalyst can also greatly affect the efficiency of the reaction.

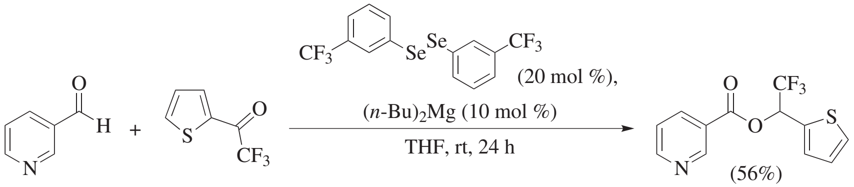
The aldol–Tishchenko reaction is similarly carried out under an inert atmosphere and dry conditions. Control between an aldol reaction and an aldol–Tishchenko reaction can be exerted by means of an excess of aldehyde and by the temperature. A traditional metal enolate mediated aldol reaction run at −78° can be directed to give an aldol–Tishchenko product by treating the enolate with an excess of aldehyde, and subsequently stirring the reaction mixture at ambient temperature. Several modern catalyst systems for the aldol–Tishchenko reaction tolerate ambient temperatures, although temperatures are frequently kept between −20° and 0° to avoid the thermodynamic ester migration. Reactions are usually run in mildly polar or aromatic solvents such as CH_2Cl_2, THF, or toluene. Evans–Tishchenko reactions are usually carried out in anhydrous THF at 0° to −10°, frequently with protection from light. The reactions can be performed by either adding samarium diiodide directly into the reaction mixture, or by preforming the samarium(III) pinacol adduct species and using it as the catalyst (see Scheme 9 in “Mechanism and Stereochemistry”).

EXPERIMENTAL PROCEDURES

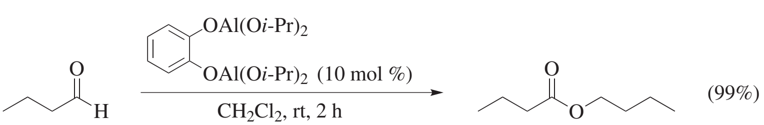


Benzyl Benzoate (Alkali Metal Catalyzed Tishchenko Reaction).[39] Three grams (0.13 mol) of metallic sodium was dissolved by warming for 0.5 hours in 70 g (0.65 mol) of pure benzyl alcohol, and after the mixture was cooled to rt, the solution was added gradually, with thorough mixing, to 454 g (4.3 mol) of benzaldehyde (which must contain less than 1% of benzoic acid). The temperature was kept slightly below 50–60°. A pasty gelatinous mass resulted. After about 0.5 h the temperature of the mixture was no longer rising; it was then warmed on a water bath for 1– 2 h, with occasional shaking. The cooled reaction product was treated with 200 mL of water, the layer of oil was separated, washed once with a second portion of water, and distilled under reduced pressure. The first fraction contained benzyl alcohol together with unchanged aldehyde, as well as a small quantity of water. The product boiled at 184–185° (15 mm Hg), and analysis by saponification showed it to be 99% pure.

The yield was 410–420 g (90–93%): mp 19.4°; IR (NaCl) 1720, 1452, 1376, 1314, 1272, 1110, 1070, 1026, 751, 712 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 8.08 (d, 2H), 7.56 (t, lH), 7.46–7.32 (m, 7H), 5.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 136.0, 133.0, 130.1, 129.7, 128.6, 128.4, 128.2, 128.1, 66.7. (Data from Ref. 61).

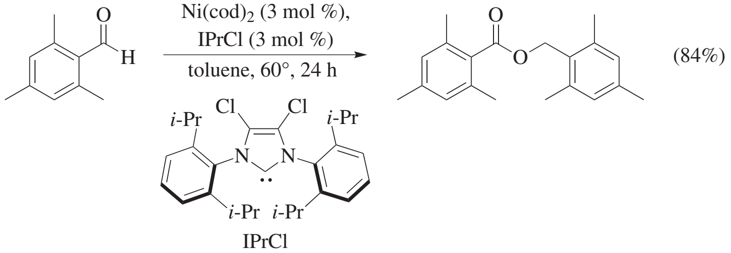


2,2,2-Trifluoro-1-(thiophen-2-yl)ethyl Nicotinate (Mg/Selenide Catalyzed Selective Crossed Tishchenko Reaction).[146] To a dry flask charged with 3 Å molecular sieves, a magnetic stirrer and bis(3-trifluoromethyl)phenyl diselenide (0.48 mmol, 0.123 mL, 20 mol %) under a strict atmosphere of argon was added THF (0.5 mL). To this orange solution was added di-*n*-butylmagnesium (1 M solution in heptane, 0.24 mmol, 0.24 mL) dropwise while stirring. To the resulting pale yellow solution, 2-trifluoroacetylthiophene (2.4 mmol, 0.308 mL) was added, then 3-pyridinecarboxaldehyde (2.4 mmol, 0.226 mL) and the mixture was stirred at rt for 24 h. The reaction mixture was diluted with EtOAc and concentrated in vacuo. The resulting product was purified by column chromatography using SiO_2 and eluting in gradient 0–10% EtOAc in *n*-hexane to give the title compound as a pale yellow oil (0.388 g, 56%): IR (neat) 1741, 1591, 1421, 1259, 1132, 1032, 908, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (br s, 1H), 8.87 (br s, 1H), 8.37 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 4.2 Hz, 1H), 7.38 (d, J = 3.6 Hz, 1H), 7.09 (dd, J = 3.6, 1.2 Hz, 1H), 6.74 (q, J = 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 153.8, 150.8, 137.1, 131.4, 129.3, 127.8, 126.6, 124.2, 123.1, 122.6 (q, J = 278.9 Hz), 68.3 (q, J = 35.0 Hz); ^{19}F (376.5 MHz, $CDCl_3$) δ −76.54; HRMS–EI (*m/z*): M$^+$ calcd for $C_{12}H_8F_3NO_2S$, 287.0228; found, 287.0238.

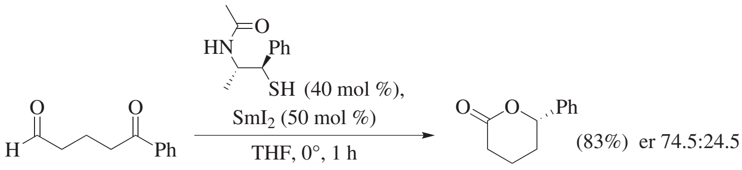


***n*-Butyl Butyrate (Aluminum-Catalyzed Tishchenko Reaction).**[160] Under an inert argon atmosphere catechol (13.2 mg, 0.12 mmol) was added to an oven-dried Schlenk flask equipped with a stirring bar. To the flask was added 1 mL of dry CH_2Cl_2 (freshly distilled over CaH_2). The reaction flask was then carefully degassed and a 2 M toluene solution of Me_3Al (0.12 mL, 0.24 mmol) was added followed by stirring at rt for 30 min. 2-Propanol (0.037 mL, 0.48 mmol; freshly distilled over CaH_2) was added, and the mixture was stirred an additional 15 min to give the catalyst. The reaction was initiated by adding freshly distilled *n*-butyraldehyde (1.1 mL, 12 mmol) dropwise into the reaction flask containing the catalyst (under argon). The resulting mixture was stirred at rt for 2 h, quenched by adding 5 mL of HCl (0.5 M in

H_2O) and extracted with Et_2O (3 × 10 mL). The combined extracts were dried over $MgSO_4$. Purification by flash chromatography (SiO_2, hexane/EtOAc = 4:1) gave *n*-butyl butyrate as a colorless oil (845 mg, 99%): IR (NaC1) 2965, 2875, 1740, 1460, 1255, 1180, 1093 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.08 (t, 2H), 2.28 (t, 2H), 1.68 (m, 4H), 1.38 (sext, 2H), 0.95 (t, 3H), 0.94 (t, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 64.1, 36.3, 30.7, 19.2, 18.5, 13.8, 13.7. (Data from Ref. 61).

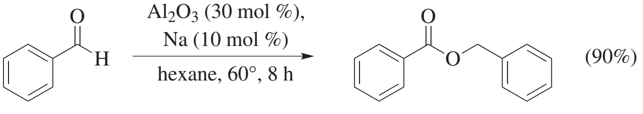


2,4,6-Trimethylbenzyl 2,4,6-Trimethylbenzoate (Transition Metal Catalyzed Tishchenko Reaction).[177] To a solution of $Ni(cod)_2$ (11.0 mg, 0.040 mmol) and IPrCl (18.3 mg, 0.040 mmol) in 2 mL of toluene was added 2,4,6-trimethylbenzaldehyde (202.1 mg, 1.36 mmol) under an inert atmosphere at room temperature. The reaction mixture was stirred at 60° for 24 h. Isolation by silica gel chrotmatography (EtOAc) gave the title product as a yellow oil (170.3 mg, 84%): ^1H NMR (400 MHz, $CDCl_3$) δ 6.88 (s, 2H, Ar*H*), 6.82 (s, 2H, Ar*H*), 5.40 (s, 2H, OC*H2*Ar), 2.40 (s, 6H, C*H3*), 2.27 (s, 6H, C*H3*), 2.26 (s, 6H, C*H3*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 139.1, 138.5, 138.2, 134.9, 131.3, 129.1, 128.8, 128.3, 61.4, 21.1, 21.0, 19.7, 19.6. HRMS (*m/z*): calcd for $C_{20}H_{24}O_2$, 296.1776; found, 296.1774.

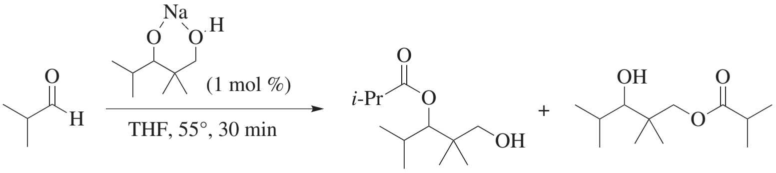


(*S*)-6-Phenyltetrahydro-2*H*-pyran-2-one (Enantioselective Lanthanoid-Catalyzed Intramolecular Tishchenko Reaction).[182] Under an atmosphere of argon, *N*-[(1*R*,2*S*)-1-mercapto-1-phenylpropan-2-yl]acetamide (84 mg, 0.4 mmol) was added to a deep blue SmI_2 (0.5 mmol) solution freshly prepared from samarium (80 mg) and 1,2-diiodoethane (140 mg) in THF (15 mL). The mixture was stirred for 5 min at rt, and a THF solution (5 mL) of 5-oxo-5-phenylpentanal (176 mg, 1.0 mmol) was added dropwise. The mixture was stirred for 1 h, and then filtered through a short silica gel column by eluting with EtOAc/hexane (1:1). The filtrate was concentrated by rotary evaporation to give (*S*)-6-phenyltetrahydro-2*H*-pyran-2-one (146 mg, 83%): $R_f = 0.19$ (hexane/EtOAc = 4:1); IR (neat) 1726 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.38–7.29 (m, 5H), 5.33 (dd, *J* = 10.2, 3.7 Hz, 1H), 2.80–2.48 (m, 2H), 2.12–2.03 (m, 1H), 1.99–1.71 (m, 3H); ^{13}C NMR (50 MHz,

$CDCl_3$) δ 171.3 (C), 139.7 (C), 128.6 (CH), 128.2 (CH), 125.7 (CH), 81.6 (CH), 30.5 (CH_2), 29.5 (CH_2), 18.6 (CH_2); MS *m/z* (% relative intensity): 176 (M^+, 55), 132 (11), 104 (100); HRMS (*m/z*): M^+ calcd for $C_{11}H_{12}O_2$, 176.0837; found, 176.0847. The enantiomeric ratio was determined to be 74.5:25.5 in favor of the (*S*)-isomer by chiral stationary phase HPLC analysis: t_R (*S*) 13.4 min, t_R (*R*) 15.9 min (Chiralcel OB, 10% *i*-PrOH in hexane, 2 mL/min, 254 nm).



Benzyl Benzoate (Tishchenko Reaction with a Heterogeneous Catalyst).[83] Alumina (3.5 g, 0.034 mmol) was first dried in an oven at 450° for 12 h, then placed in a 100-mL Schlenk tube with a glass-covered magnetic stir bar and heated at 200° under vacuum (1 mm Hg). After 30 min the Schlenk tube was filled with argon, and sodium metal (0.25 g, 0.011 mol) was added. As soon as the sodium metal had melted, the mixture was stirred vigorously. The homogeneous, free-flowing, violet–black powder was allowed to cool to rt, then covered with hexane (30 mL). Benzaldehyde (11.7 g, 0.11 mol) was added and the reaction mixture was stirred vigorously at 60°. The progress of the reaction was followed by GC analysis and the reaction mixture was filtered after 8 h. The greenish Al_2O_3 cake was washed once with 10 mL of dry ether to free it from adsorbed benzyl benzoate. Concentration followed by short-path distillation (90°, 1 mm Hg) yielded benzyl benzoate (10.5 g, 90%). See above for spectral data from Ref. 61.

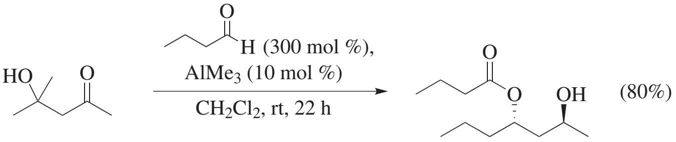


118 **119**

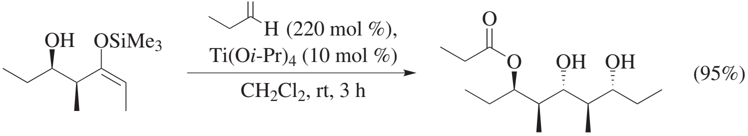
118 + **119** (92%), **118/119** = 35:65

1-Hydroxy-2,2,4-trimethylpentan-3-yl 2-Methylpropionate and 3-Hydroxy-2,2,4-trimethylpentyl 2-Methylpropionate (Alkali Metal Catalyzed Aldol–Tishchenko Reaction).[217] A solution of sodium 3-hydroxy-2,2,4-trimethylpentan-1-olate (1 M in THF, 5.0 mL, 0.5 mmol, 1 mol %) was placed in a reactor under argon. Isobutyraldehyde (3.6 g, 50 mmol, 100 mol %) was added over 2 min. The reaction was exothermic; the internal temperature was allowed to rise to 55° and kept at that temperature with external cooling. At the end of the reaction, external heating was used to keep the temperature at 55° (±3°). The mixture was stirred for 30 min and quenched with 3 mL of 2 M HCl. The reaction mixture was taken up with 15 mL of CH_2Cl_2, the water phase was saturated with NaCl, and the layers were separated. The water phase was extracted with CH_2Cl_2 (3 × 10 mL).

All organic phases were combined, dried over Na_2SO_4, filtered, and the CH_2Cl_2 was evaporated. The product mixture was analyzed by ^1H NMR spectroscopy. The products were separated by column chromatography (SiO_2, hexane/EtOAc = 90:10). The combined yield of the two products was 3.32 g (92%), **118/119** = 35:65. Ester **118**: R_f = 0.29 (hexane/EtOAc = 9:1); ^1H NMR (200 MHz, $CDCl_3$) δ 4.76 (d, *J* = 2.8 Hz, 1H), 3.13 (dd, *J* = 11.6 Hz, 2H), 2.65 (sept, *J* = 7.0 Hz, 1H), 2.07 (sept-*d*, *J* = 6.8, 2.7 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 6H), 1.02 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 178.3, 79.2, 69.9, 40.0, 34.5, 28.3, 22.9, 22.2, 19.6, 19.3, 17.7; MS–CI (NH_3) (*m*/*z*): $[M + NH_4]^+$ 234, $[M + H]^+$ 217. Ester **119**: R_f = 0.21 (EtOAc/hexane = 1:9); ^1H NMR (200 MHz, $CDCl_3$) δ 3.91 (dd, *J* = 10.9 Hz, 2H), 3.21 (d, *J* = 2.6 Hz, 1H), 2.54 (sept, *J* = 7.0 Hz, 1H), 1.88 (sept-*d*, *J* = 6.8, 2.3 Hz, 1H), 1.15 (d, *J* = 7.0 Hz, 6H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.93 (s, 3H), 0.92 (s, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 177.2, 79.4, 71.3, 39.3, 34.1, 28.6, 23.5, 22.0, 20.4, 19.0, 19.0, 16.7; MS–CI (NH_3) (*m*/*z*): $[M + NH_4]^+$ 234, $[M + H]^+$ 217.

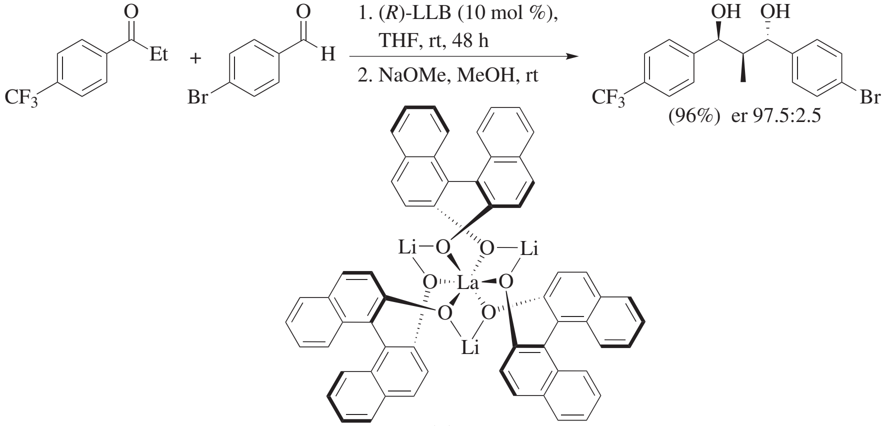


(2*S,4*S**)-2-Hydroxy-4-heptyl Butyrate (Aluminum-Catalyzed Tandem Aldol-Transfer–Tishchenko Reaction).**[247] Trimethylaluminum in toluene (0.1 mL, 0.2 mmol, 10 mol %) was added at rt under argon to dry CH_2Cl_2 (1 mL). To the solution was simultaneously added butanal (0.54 mL, 6 mmol, 300 mol %) and 4-hydroxy-4-methyl-2-pentanone (0.25 mL, 2 mmol, 100 mol %) by syringe. After stirring for 22 h, the reaction mixture was poured into aq HCl solution (0.5 M, 5 mL) and extracted with Et_2O (3 × 10 mL). The combined extracts were dried over $MgSO_4$. Evaporation of the solvent and purification of the residual oil by flash chromatography (SiO_2, hexane/EtOAc = 4:1) gave (2*S**,4*S**)-2-hydroxy-4-heptyl butyrate (324 mg, 80%) as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$, 20°) δ 5.10–4.97 (m, 1H), 3.65–3.56 (m, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.7–1.2 (m, 8H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 174.5, 71.2, 63.2, 44.6, 36.9, 36.3, 22.8, 18.7, 18.5, 13.8, 13.6.



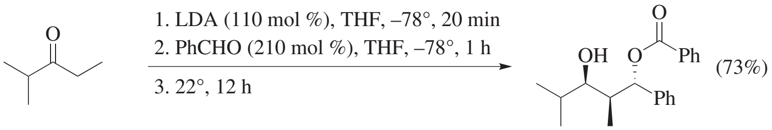
(3*R,4*R**,5*R**,6*R**,7*R**)-5,7-Dihydroxy-4,6-dimethylnonan-3-yl Propionate (Transition Metal Catalyzed Aldol–Tishchenko Reaction).**[263,265] To a stirred solution of tetraisopropoxytitanium (29 mg, 0.1 mmol) and propionaldehyde (2.2 mmol) in CH_2Cl_2 (10 mL) under argon was added by syringe a solution of

(3*R**,4*S**,5*E*)-4-methyl-5-(trimethylsilyloxy)hept-5-en-3-ol (1 mmol) in CH_2Cl_2 (7 mL). The mixture was stirred at rt until the enol silane had disappeared (TLC monitoring, ~3 h). After quenching with saturated aq NaCl (5 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with water (10 mL) and concentrated under vacuum. The crude ester was purified by flash chromatography (SiO_2, hexane/Et_2O = 1:1) to give the title compound as a colorless oil (247 mg, 95%): ^1H NMR (200 MHz, C_6D_6) δ 4.98 (ddd, J = 9.1, 5.8, 3.5 Hz, $CH_3CH_2C\mathit{H}O(CO)Et$, 1H), 3.62 (dd, J = 5.9, 5.0 Hz, $C\mathit{H}OH$, 1H), 3.48 (m, CH_3CH_2-$C\mathit{H}OH$, 1H), 2.08 (q, J = 6.8 Hz, $CH_3C\mathit{H}_2CO$, 2H), 1.60–1.30 (m, 6H), 1.12 (d, J = 6.8 Hz, $CHC\mathit{H}_3$, 3H), 1.02 (d, J = 6.8 Hz, $CHC\mathit{H}_3$, 3H), 0.96 (t, J = 6.8 Hz, $C\mathit{H}_3CH_2CO$, 3H), 0.83 (t, J = 7.0 Hz, $C\mathit{H}_3CH_2$, 3H), 0.82 (t, J = 7.0 Hz, $C\mathit{H}_3CH_2$, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, Me_4Si) δ 174.4 (C=O), 76.9 ($\mathit{C}HOCOEt$), 76.8 (CHOH), 76.1 (CHOH), 39.6 [$\mathit{C}H(CH_3)$], 39.3 [$\mathit{C}H(CH_3)$], 28.5 (CH_2), 27.8 (CH_2), 23.3 (CH_2), 10.7 (CH_3), 10.5 (CH_3), 10.4 (CH_3), 9.4 (CH_3), 6.6 (CH_3); MS *m/z* (% relative intensity): 261 ($[M + H]^+$, 14), 231 (8), 191 (38), 173 (80), 157 (55), 139 (52), 117 (90), 99 (80), 86 (100). Anal Calcd. for $C_{14}H_{28}O_4$: C, 64.6; H, 10.8. Found: C, 64.3; H, 10.6.

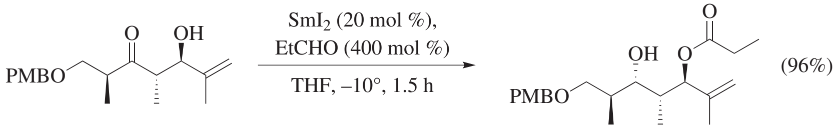


(*R*)-LLB

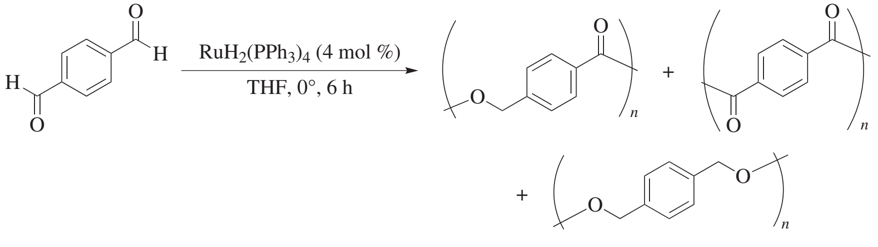
(1*S*,2*S*,3*S*)-1-(4-Bromophenyl)-2-methyl-3-(4-trifluoromethylphenyl) propane-1,3-diol (Lanthanoid-Catalyzed Aldol–Tishchenko Reaction).[104,256] A solution of (*R*)-LLB (0.2 M based on lanthanum metal, 0.25 mL, 0.05 mmol) was slowly added to a mixture of 1-(4-trifluoromethylphenyl)propan-1-one (101 mg, 0.50 mmol) and 4-bromobenzaldehyde (231 mg, 1.25 mmol) in THF (0.25 mL) at 4°. After stirring for 48 h at rt, the reaction mixture was diluted with Et_2O (5 mL) and quenched with 1 M aq HCl (2 mL). The aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. After concentration under vacuum, the residue was purified by column chromatography (SiO_2, hexane/Et_2O = 5:1 to 4:1) to afford the 4-bromobenzoic ester of the title product as a colorless oil. The product was dissolved in MeOH (3 mL), NaOMe (27 mg, 0.5 mmol) was added, and the resulting mixture was stirred until the starting material was consumed. The reaction mixture was diluted with EtOAc (20 mL), and washed with water (5 mL). The aqueous layer was extracted twice with EtOAc (2 x 10 mL) and the combined organic layers were washed with brine (10 mL) and dried over sodium sulfate. After concentration under vacuum, the residue was purified by flash chromatography (SiO_2, hexane/acetone = 10:1 to 8:1) to give the title product (96% yield for two steps, 98:2 er): $[\alpha]_D^{23}$ + 9.02 (*c* 0.820, $CHCl_3$); IR (neat) 3594, 3387, 3053, 2985, 1618, 1486, 1419, 1326, 1265, 1166 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 5.08 (br-s, 1H), 4.70 (dd, *J* = 6.3, 4 Hz, 1H), 3.16 (d, *J* = 4 Hz, 1H), 2.86 (d, *J* = 4 Hz, 1H), 2.17–2.09 (m, 1H), 0.75 (d, *J* = 7.45 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.3, 142.1, 131.5, 129.2 (q, $J_{C\text{-}F}$ = 32.4 Hz), 127.7, 126.1, 124.9 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.1 (q, $J_{C\text{-}F}$ = 274.1 Hz), 121.4, 77.1, 73.6, 45.4, 11.1; MS–ESI (*m/z*): $[M + Na]^+$ 413, 411. The enantiomeric ratio was determined by chiral stationary-phase HPLC analysis, t_R 16.5 min (minor) and 23.8 min (major) (Daicel Chiralpak AD-H, *i*-PrOH/hexane = 5/95, 1 mL/min, 254 nm). Anal. Calcd for $C_{17}H_{16}BrF_3O_2$: C, 52.46; H, 4.14. Found: C, 52.18; H, 3.91.



(1*S,2*S**,3*R**)-3-Hydroxy-2,4-dimethyl-1-phenylpentyl Benzoate (Lithium Enolate Mediated Aldol–Tishchenko Reaction).**[227] Freshly distilled diisopropylamine (4.4 mmol, 120 mol %) was added to anhydrous THF (10 mL). To the solution was added *n*-BuLi in hexanes (1.2 M, 4.3 mmol, 110 mol %) at 0°. The resulting mixture was stirred at 0° for 10 min, then cooled to −78°. 2-Methyl-3-pentanone (3.8 mmol, 100 mol %) was added dropwise, and the resulting mixture was stirred for 20 min at −78°. Benzaldehyde (7.9 mmol, 210 mol %) was added dropwise over 1 min and the resulting mixture was stirred at −78° for 1 h, then warmed to 22° for 12 h. The reaction was quenched with saturated aq $NaHCO_3$ (20 mL) and the mixture was extracted with CH_2Cl_2. The organic phases were filtered through cotton and concentrated under vacuum. The product was purified by flash chromatography over SiO_2 (hexane/EtOAc = 90:10) to give the 1,3-diol monoester (900 mg, 73%): IR (neat) 3491, 2939, 1694, 1025 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.4 Hz, 2H), 7.57 (m, 1H), 7.46 (m, 2H), 7.28 (m, 5H), 5.33 (dd, *J* = 9.6, 1.2 Hz, 1H), 4.13 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.96 (d, *J* = 3.9 Hz, 1H), 2.14 (m, 1H), 2.08 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.72 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 167.1, 145.4, 133.8, 131.6, 130.3, 129.5, 128.8, 128.0, 127.9, 79.3, 76.3, 43.0, 31.3, 19.8, 19.4, 10.8; HRMS–CI (*m/z*): $[M + H]^+$ calcd. for $C_{20}H_{25}O_3$, 313.1803; found, 313.1801. Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found C, 76.73; H, 7.80.



(3*R*,4*R*,5*S*,6*S*)-5-Hydroxy-7-(4-methoxybenzyloxy)-2,4,6-trimethylhept-1-ene-3-yl Propionate (Samarium-Catalyzed Evans–Tishchenko Reaction).[116] To a stirred solution of (2*R*,4*R*,5*S*)-1-(4-methoxybenzyloxy)-5-hydroxy-2,4,6-trimethyl-6-hepten-3-one (22.6 g, 73.8 mmol) and propionaldehyde (21.3 mL, 295 mmol) in THF (230 mL) at −10° was added, dropwise, a solution of SmI_2 (150 mL, 0.1 M in THF, 15 mmol) such that the deep blue SmI_2 was decolorized to pale yellow. After 1.5 h at −10° the mixture was partitioned between aq $NaHCO_3$ (200 mL) and Et_2O (3 × 200 mL). The combined organic phases were dried over $MgSO_4$ and evaporated under vacuum to give the crude product (26 g, ∼100%) as a colorless oil, which was used without further purification in a subsequent reaction. On a smaller scale (19 mmol) the product was purified by flash chromatography (SiO_2, hexane/EtOAc = 3:1) to give the title product in 96% yield: R_f 0.30 (hexane/EtOAc = 3:1); $[\alpha]_D^{20}$ + 29.0 (*c* 2.8, $CHCl_3$); IR ($CHCl_3$) 3486, 3009, 2979, 2939, 1727 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.22 (d, *J* = 9.8 Hz, 1H), 5.02 (s, 1H), 4.95 (s, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 3.78 (s, 3H), 3.54–3.47 (m, 3H), 3.27 (d, *J* = 2.0 Hz, 1H), 2.37–2.32 (m, 2H), 1.94–1.83 (m, 2H), 1.70 (s, 3H), 1.13 (t, *J* = 7.6 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 174.0, 159.2, 130.2, 129.2, 115.6, 113.8, 79.2, 75.1, 73.0, 72.7, 55.3, 36.4, 36.2, 27.8, 17.5, 13.6, 9.2, 8.3; MS–CI (NH_3) (*m/z*): $[M + NH_4]^+$ 382 (14), $[M + H]^+$ 365 (32); HRMS–CI (*m/z*): $[M + H]^+$ calcd. for $C_{21}H_{32}O_5$, 365.2328; found, 365.2328.



(95%) all products

Polyterephthalaldehyde (Polymerization of a Dialdehyde).[65] To a THF solution (4 mL) of $RuH_2(PPh_3)_4$ (0.070 g, 0.061 mmol, 4 mol %) was added terephthalaldehyde (0.20 g, 1.5 mmol). After stirring the reaction mixture at 0° for 6 h, the solution was poured into methanol (300 mL) to give a light-brown solid that was collected by filtration and dried under vacuum (0.19 g, 95%): IR (KBr) 3058, 2948, 2878, 1717, 1266, 1099 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 8.1 and 7.5

(d, $J = 14$ Hz, 4H), 5.42 and 5.37 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 165.7, 165.4, 165.3, 141.2, 140.9, 136.2, 135.9, 133.9, 133.6, 130.3, 129.7, 129.6, 128.5, 66.7, 66.3, 65.9. Anal. Calcd for $(C_8H_6O_2)_n$: C, 71.6; H, 4.5. Found: C, 70.7; H, 4.3.

TABULAR SURVEY

The literature has been searched using SciFinder and Beilstein databases and covers the period to April 2014. The tables are organized by substrate. Tables 1A-1J list classical Tishchenko reactions and Tables 2A-2H deal with aldol–Tishchenko reactions. The titles can be found in the "Table of Contents". Table 2G, Tishchenko Reactions of Preformed β-Hydroxy Ketones, lists the widely used Evans–Tishchenko reactions with samarium iodide as the catalyst as well as Tishchenko reactions of preformed β-hydroxy ketones that use other catalyst systems. Table 3 deals with oxidations of aldehydes using the Evans–Tishchenko reaction and Table 4 with tandem reactions.

Substrates are listed in the order of increasing carbon count. Protecting groups, chiral auxiliaries, simple sustituents on heteroatoms, and linkers and solid supports are excluded from the carbon count. The substrates in Table 1F, "Tishchenko Reactions Involving Two Different Aldehydes", are present in a 1:1 ratio unless otherwise stated. In those subsets of Table 2 that involve two substrates, the one used in excess is listed second. Substrates, such as acetone dimer, that first undergo a retro-aldol reaction, are assigned the carbon counts of the monomers. Reactions that involve the same substrate are listed in the order of catalyst systems used: alkali metal, alkaline earth metal, aluminum, transition-metal, lanthanoid, actinoid, and miscellaneous systems.

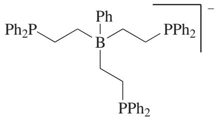
A dash enclosed in parentheses [(—)] signifies that the product was isolated but no yield was reported.

The following abbreviations (not included in "*The Journal of Organic Chemistry* Standard Abbreviations and Acronymns") are used in the Tabular Survey:

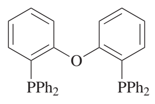
ALO	alumina (reference catalysts of the Catalysis Society of Japan)
BINOL	1,1′-binaphthol
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BOM	benzyloxymethyl
Cp*	1,2,3,4,5-pentamethylcyclopentadienyl
Cp″	1,2,3,4-tetramethylcyclopentadienyl
cym	cymene
dcpe	1,2-bis(dicyclohexylphosphino)ethane
DEIPS	diethylisopropylsilyl
DMB	3,4-dimethoxybenzyl
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppe-*p*-CF_3	1,2-bis(bis(4-trifluoromethyl)phenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane

dpppe	1,5-bis(diphenylphosphino)pentane
DTBP	2,6-di-*tert*-butylpyridine
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
IPrCl	1,3-bis(2,6-diisopropylphenyl)-4,5-dichloroimidazol-2-ylidene
LLB	$[LaLi_3(binol)_3]$
MW	microwaves
Na–TPP	sodium tripolyphosphate
NMI	*N*-methylimidazole
$PhBP_3$	tris(diphenyl phosphinomethyl)phenylborate
PMP	*p*-methoxyphenyl
PNB	*p*-nitrobenzoyl
PyNO	pyridine *N*-oxide
pz	pyrazole
SBA-15	mesoporous silicate
sc	supercritical
SEM	2-trimethylsilylethoxymethoxy
SDS	sodium dodecylsulfate
SIPr	1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene
TBDPS	*tert*-butyldiphenylsilyl
TES	triethylsilyl
TIPDS	tetraisopropyldisiloxane
TN	turnover number
TPPTS	triphenylphosphine-3,3′,3′′-trisulfonic acid trisodium salt
TS	titanium silicalite

CHART 1. LIGANDS AND CHIRAL THIOLS USED IN TABLES



$PhBP_3$



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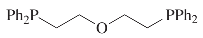
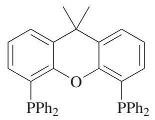
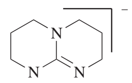


POP'



Xantphos



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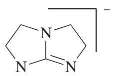
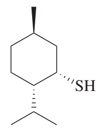


tbo



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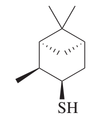

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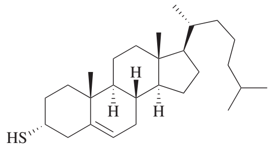

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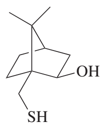

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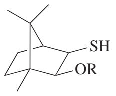
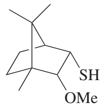


	R
5	H
6	Me
7	t-BuCH$_2$



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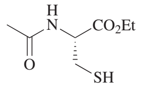

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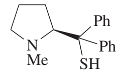

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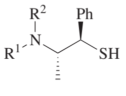
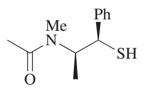


	R^1	R^2
11	—(CH$_2$)$_4$—	
12	Bn	Bn
13	Me	Et
14	Ac	H
15	Bz	H
16	Ts	H
17	Ac	Me
18	Ac	Bn
19	Bz	Me



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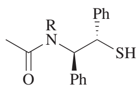
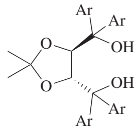
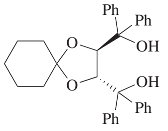


	R
21	H
22	Bn



	Ar
23	Ph
24	1-naphthyl
25	3,5-Me$_2$C$_6$H$_3$



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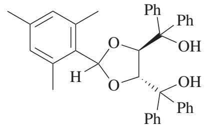

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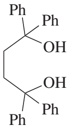

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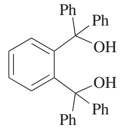

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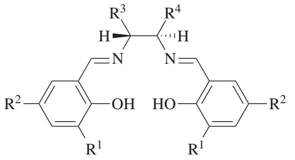
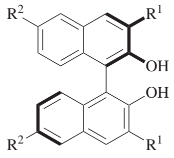
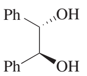


	R^1	R^2	R^3	R^4
30	t-Bu	t-Bu	—(CH$_2$)$_4$—	
31	t-Bu	H	—(CH$_2$)$_4$—	
32	Me	H	—(CH$_2$)$_4$—	
33	1-adamantyl	Me	—(CH$_2$)$_4$—	
34	t-Bu	t-Bu	Ph	Ph
35	1-adamantyl	Me	Ph	Ph



	R^1	R^2
36	H	H
37	Br	H
38	H	Br
39	Ph	H
40	4-t-BuC$_6$H$_4$	H
41	2-MeOC$_6$H$_4$	H
42	2,4-(MeO)$_2$C$_6$H$_3$	H
43	2-MeO-3,5-(t-Bu)$_2$C$_6$H$_2$	H
44	2-EtC$_6$H$_4$	H
45	2-MeOC$_6$H$_4$CH$_2$	H



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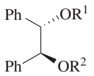
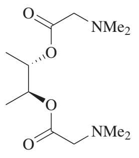


	R^1	R^2
47	Me$_2$NCH$_2$CH$_2$	Me$_2$NCH$_2$CH$_2$
48	Me$_2$NCH$_2$CH$_2$	H
49	Me$_2$NCH$_2$CO	H
50	Me$_2$NCH$_2$CO	Ac
51	Me$_2$NCH$_2$CO	Me$_2$NCH$_2$CO
52	Ac	Ac
53	CONMe$_2$	CONMe$_2$
54	CONMe$_2$	H



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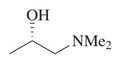

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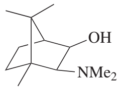

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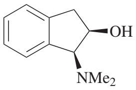

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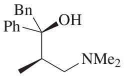

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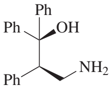

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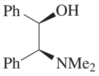

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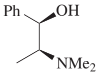

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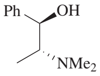

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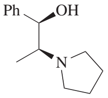

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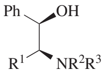
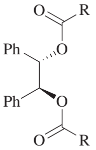
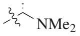
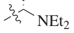
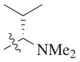
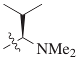
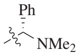
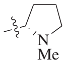
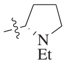
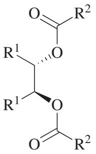
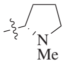
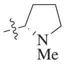
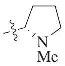
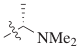


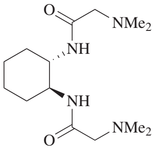
	R^1	R^2	R^3
65	Me	H	H
66	Me	H	Me
67	Me	Me	Me
68	Me	Et	Et
69	Me	Pr	Pr
70	Me	Bu	Bu
71	Ph	—$(CH_2)_4$—	
72	Me	—$(CH_2)_5$—	



	R
73	Et
74	$MeOCH_2$
75	
76	
77	
78	
79	
80	
81	



	R^1	R^2
82	Cy	Me_2NCH_2
83	4-FC_6H_4	
84	4-$MeOC_6H_4$	
85	4-*t*-BuC_6H_4	
86	1-naphthyl	



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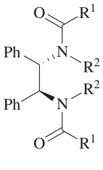
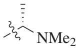
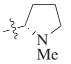
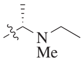
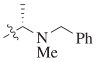
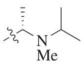
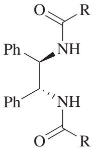
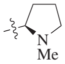
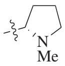
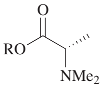


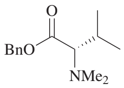
	R^1	R^2
88	Me_2NCH_2	H
89	Me_2NCH_2	Me
90		H
91		H
92		H
93		H
94		H



	R
95	
96	



	R
97	Bn
98	4-$MeC_6H_4CH_2$
99	4-$MeOC_6H_4CH_2$
100	4-$FC_6H_4CH_2$
101	2,4,6-$Me_3C_6H_2CH_2$
102	2,4,6-(*i*-Pr)$_3C_6H_2CH_2$
103	1-$C_{10}H_7CH_2$
104	$(Ph)_2CH$
105	Me
106	*t*-Bu



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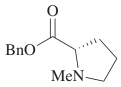

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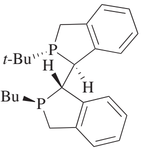
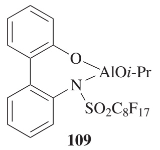


108a

CHART 2. CATALYSTS USED IN TABLES



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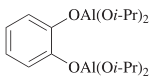

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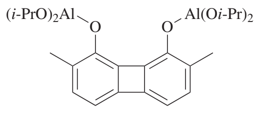

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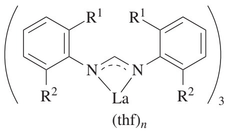
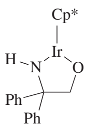


	R^1	R^2	*n*
112	Me	H	2
113	Me	Me	1
114	Et	Et	0



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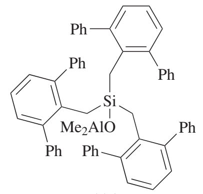

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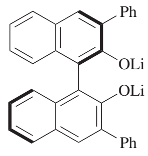

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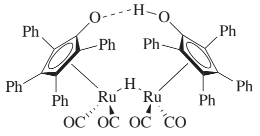

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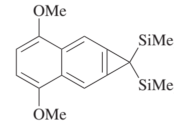

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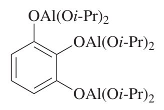

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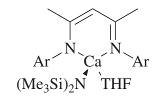
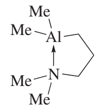


Ar = 2,6-diisopropylphenyl

121



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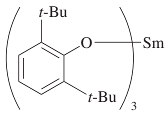

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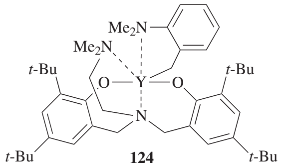

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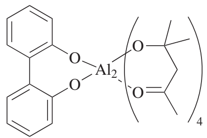

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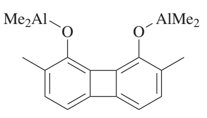

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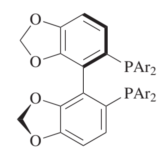
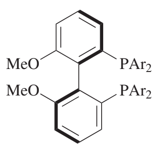
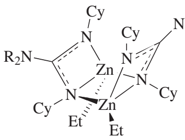


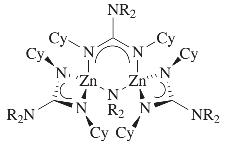
127 Ar = 3,5-(*t*-Bu)2-4MeOC6H2
(*R*) - DTBM-SEGPHOS



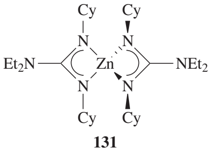
128 Ar = 3,4,5-(MeO)3C6H2



	NR_2
129a	piperidyl
129b	NBn_2
129c	NEt_2



	NR_2
130a	piperidyl
130b	NBn_2



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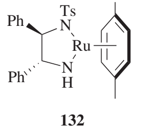

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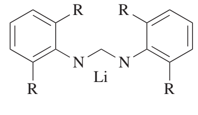


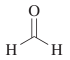
133 R = *i*-Pr

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES

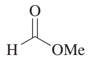
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C$_1$

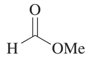


Catalyst (*x* mol %)



Catalyst	*x*	Solvent	Temp (°)	Time (h)		Refs.
Mg(OMe)$_2$	"cat."	—	—	—	(—)	2, 4
Al(OMe)$_3$[a]	"cat."	—	—	—	(84)	4, 2
RuCl$_2$[P(OMe)$_3$]$_4$	0.2	MeNO$_2$	65	20	(1)[b]	63
Cu wire	—	—	150–180	—	(—)	312
TS-1 MS	—	—, dark	rt	1	(~100)	313

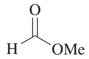
Metal oxide[c]



82

Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)	
W	100	300	(0)	W–Fe	90:10	230	(5)	Mo–Co	90:10	300	(0)
W–V	90:10	300	(0)	W–Sn	90:10	300	(20)	Mo–Bi	90:10	300	(0)
W–P	90:10	300	(0)	Mo	100	300	(0)	Mo–V	90:10	300	(0)
W–K	90:10	300	(0)	Mo–K	90:10	300	(0)	Mo–P	90:10	300	(3)
W–Ni	90:10	300	(0)	Mo–Ni	90:10	300	(1)	Mo–Ti	90:10	270	(3)
W–Ti	90:10	230	(8)	Mo–Fe	90:10	300	(1)	Mo–Sn	90:10	220	(11)

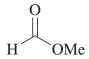
Metal oxide[c]



82

Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)	
Sn	100	180	(32)	Sn–W	50:50	180	(38)	Ti–K	94:6	275	(5)
Sn–Mo	70:30	150	(49)	Sn–W	30:70	180	(26)	Ti–V	90:10	210	(13)
Sn–V	90:10	180	(17)	Sn–P	90:10	220	(9)	Fe	100	260	(21)
Sn–V	80:20	180	(18)	Sn–K	90:10	220	(8)	Fe–Mo	98:2	260	(15)
Sn–V	60:40	180	(8)	Ti	100	275	(10)	Fe–P	98:2	260	(23)
Sn–V	60:40	160	(21)	Ti–Mo	90:10	275	(3)	Fe–K	99:1	260	(30)
Sn–W	90:10	180	(32)	Ti–W	93:7	275	(3)	Fe–W	90:10	230	(24)
Sn–W	70:30	180	(47)	Ti–P	96:4	275	(1)	Fe–V	98:2	210	(23)

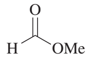
Metal oxide[c]



82

Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)		Metals	Ratio	Temp (°)	
V	100	260	(3)	U–K	90:10	300	(6)	Bi–Mo	90:10	200	(5)
V–Mo	90:10	260	(1)	Al	100	225	(20)	Bi–Mo	50:50	250	(3)
V–K	90:10	260	(3)	Al–Mo	90:10	225	(3)	Bi–K	90:10	200	(1)
V–Fe	90:10	230	(4)	Al–K	90:10	225	(13)	Cu	100	180	(1)
V–Ni	90:10	230	(7)	Zn	100	275	(1)	Cu–Mo	90:10	225	(4)
V–Sn	90:10	230	(7)	Zn–Mo	90:10	275	(1)	Mn	100	240	(7)
V–Ti	90:10	200	(12)	Zn–K	90:10	275	(0)	Cr	100	250	(1)
U	100	300	(6)	Bi	100	200	(4)	Mg	100	275	(0)
U–Mo	90:10	300	(4)								

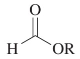
Catalyst, 200–250°



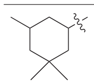
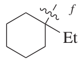
314

Catalyst		Catalyst	
Li$_2$CO$_3$	(0)	ZnO	(95)
Li$_2$O	(0)	SnO	(72)
Na$_2$CO$_3$	(0)	CdO	(61)
Na$_2$O	(0)	PbO	(23)
NaOH	(0)	Bi$_2$O$_3$	(3)
CaO	(2)	CoO	(0)
SrO	(0)	NiO	(21)
BaO	(0)	CuO	(0)
Ba(OH)$_2$	(0)	Nd$_2$O$_3$	(3)

ROMgBr, THF, heat



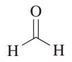
44

R		R	
n-C$_7$H$_{15}$[d]	(63)	 [d]	(82)
n-C$_7$H$_{15}$[e]	(74)		
CyCH$_2$[e]	(60)		
Bn[d]	(76)	Ph(CH$_2$)$_3$[e]	(69)
 [f]	(75)	PhC(=CH$_2$)CH$_2$[e]	(63)
		PhCMe$_2$(CH$_2$)$_2$[d]	(85)

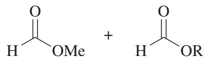
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_1



trans-ROIr(CO)$(PPh_3)_2$ (20 mol %), THF, rt, 2 d

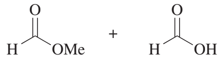


I + **II**

R	I[g]	II[h]
Me	(39)	(90)
n-Pr	(39)	(90)
i-Pr	(39)	(90)
t-Bu	(39)	(90)

315, 316

$FeAlPO_4$–5 MS,[i] –23° to rt, 70 min

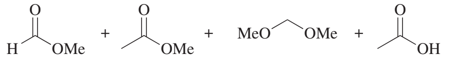


I + **II**

I + **II** (100)

317

Catalyst (0.2 mol %), $MeNO_2$, 65°, 20 h

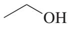


I + **II** + **III** + **IV**

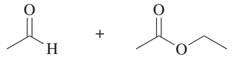
Catalyst	I–IV	I/II/III/IV
$RuCl(SnCl_3)[P(OMe)_3]_4$	(3)[g]	5:45:25:25
$Ru(SnCl_3)_2[P(OMe)_3]_4$	(5)[g]	6:43:30:21

63

C_2



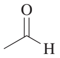
Catalyst



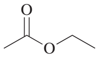
I + **II**

Catalyst	Temp (°)	I/II[j]
CaO	220	100:0
TiO_2	200	93:2[k]
Fe_3O_4	175	89:6[k]
SiO_2	300	75:8[l]
Fe_2O_3	160	56:44

318

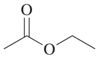


Catalyst (*x* mol %)



Catalyst	*x*	Additive	Solvent	Temp (°)	Time		Refs.
$Al(OEt)_3$	4	—	—	—	—	(69)	2, 4
$Al(OEt)_3$	4	$ZnCl_2$	—	—	10 min	(97)	16
$Al(OEt)_3$	7	—	—	—	—	(90)	16
$Al(OEt)_3$	2.9	—	xylene	—	—	(93)	16
$Al(OEt)_3$	5	$HgCl_2$ (21 mol %)	Et_2O	rt	24 h	(68)	17
$Al(OEt)_3$	5	$HgCl_2$ (63 mol %)	Et_2O	rt	24 h	(82)	17
$Al(OEt)_3$	"cat."	—	—	10 to rt	25 h	(—)	21
$Al(OEt)_3$	"cat."	—	—	8–10	1 h	(94)[m]	38
Al(O*i*-Pr)$_3$	5	—	xylene	rt	24 h	(97)	17
Al(O*n*-Bu)$_3$	5	—	xylene	rt	24 h	(95)	17
Al(O*n*-Bu)$_3$	"cat."	$AlCl_3$	xylene	—	—	(86)	19
109	1	—	toluene/heptane	0 to rt	2 h	(99)	161
111	0.5	—	toluene/heptane	0 to rt	2.5 h	(91)	161, 158
$ZnCrO_3$	"cat."	H_2 (21 MPa)	—	360	–	(10)[n]	319
$RuH_2(PPh_3)_4$	0.2	—	vacuum	20	40 min	(70)	57
$RuH_2(PPh_3)_4$	0.2	—	vacuum	0	40 min	(94)	57
$RuH_2(PPh_3)_4$	0.2	—	vacuum	–20	2 h	(0)	57
$Ti(OEt)_4$	5	—	xylene	rt	24 h	(41)	17
$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(68)	320
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	—	C_6D_6	70	48 h	(99)	67

$Al(OEt)_3$ (*x* wt %)

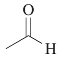
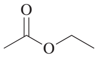
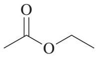
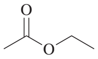
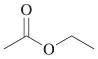
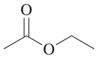
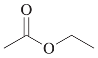
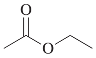
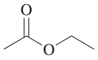
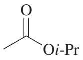
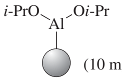
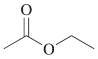
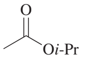
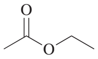
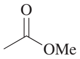


x	
5	(39)
10	(57)
15	(69)
20	(62)
25	(63)

2, 4

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

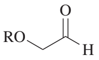
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2 	Al(OEt)$_3$ (4 mol %), promoter, xylene, rt, 24 h	 Promoter — (53) MeOH (17) EtOH (26) *i*-PrOH (37) *n*-BuOH (44) *i*-BuOH (44) Promoter 2-methylbutan-2-ol (46) EtOH + $CaCl_2$ (57) EtOH + $HgCl_2$ (55) EtOH + $AlCl_3$ (65) Al(OEt)$_3$^{o} (75)	16
	Al(OEt)$_3$ (4 mol %), promoter, xylene, rt, 24 h	 Promoter $HgCl_2$ (0.025 g) (62) $HgCl_2$ (0.05 g) (69) $HgCl_2$ (0.075 g) (87) EtOH + $ZnCl_2$ (80)	16
	Al(OEt)$_3$ (5 mol %), rt, 24 h	 Solvent CCl_4 (100) heptane (91) xylenes (65) Et_2O/benzene (67) $CHCl_3$ (72)	17
	Al(OEt)$_3$ (5 mol %), $AlCl_3$ (*x* mol %), Et_2O, rt, 24 h	 x^p 14 (73) 21 (84) 28 (88) 35 (40) 63 (15)	17
	Al(OEt)$_3$ (5 mol %), $ZnCl_2$ (*x* mol %), Et_2O, rt, 24 h	 x^p 8.3 (80) 21 (87) 52 (93) 63 (93)	17
	Al(OEt)$_3$ (5 mol %), $FeCl_3$ (*x* mol %), Et_2O, rt, 24 h	 x^p 5.6 (60) 21 (84) 28 (80) 35 (40) 63 (10)	17
	Al(OEt)$_3$ (5 mol %), promoter, Et_2O, BuOH, 25°, 24 h	 Promoter — (39) $FeCl_3$ (75) $AlCl_3$ (64) $ZnCl_2$ (75) $CuCl_2$ (70) $HgCl_2$ (65)	17
	Al(O*i*-Pr)$_3$ (5 mol %), hexane, 20°	 **I** +  **II** Time (min) / **I** / **II** 2 (0) (1) 5 (2) (4) 10 (10) (6) 30 (19) (10) 40 (22) (13) 60 (26) (14) 90 (32) (16)	27
	 (10 mg/mL), C_6D_6, rt, 48 h	 +  (—)	321
	● = metal-organic framework prepared from 2-aminoterephthalic acid and $AlCl_3$•6H_2O in DMF at 130°		
	trans-MeOIr(CO)(PPh$_3$)$_2$ (4 mol %), THF, rt, 5 d	 (37)^g +  (75)^h	315, 316

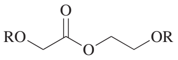
Aldehyde | Conditions | Product(s) and Yield(s) (%) | Refs.

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

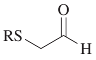
C_2



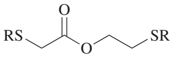
Catalyst (x mol %)



R	Catalyst	x	Solvent(s)	Temp (°)	Time (h)		Refs.
TBS	**109**	2	toluene/hexane	rt	2	(81)	161
CH_2=CH_2CH_2	$AlEt_3$	3	CH_2Cl_2	rt	54	(96)	214
CH_2=CH_2CH_2	$AlEt_3$	3	CH_2Cl_2	0	120	(79)	214
CH_2=CH_2CH_2	$AlEt_3$	3	CH_2Cl_2	–10	265	(69)	214
Bn	DIBAL-H	10	pentane	0 to rt	8	(52)	157, 156
Tr	DIBAL-H	10	pentane	0 to rt	6	(83)	157, 156



$AlEt_3$ (x mol %), solvent, –78°



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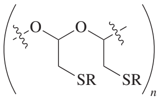
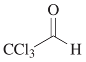


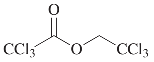
main product

213

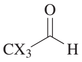
R	Solvent	x	Time (d)	
Me	—	1.5	1	(7)
Me	toluene	1	1	(12)
Et	—	1.4	1	(7)
Et	toluene	1	1	(6)
Et	THF	4	2d	(2)



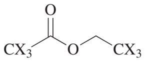
Catalyst (x mol %)



Catalyst	x	Solvent	Temp (°)	Time		Refs.
$AlEt_3$	3	C_6H_6	30	1 h	(84)	28
$AlEt_2Cl$	3	C_6H_6	30	1 h	(94)	28
$Al(OEt)_3$	3	C_6H_6	30	1 h	(2)	28
$Al(OEt)_3$	5	—	0 to rt	48 h	(26)	93
Al(O*i*-Pr)$_3$	3	C_6H_6	30	1 h	(<1)	28
Al(O*i*-Pr)$_3$	6	CH_2Cl_2	45 to rt	3 h	(13)	26
Al(O*t*-Bu)$_3$	3	C_6H_6	30	1 h	(0)	28
Al(O*t*-Bu)$_3$	10	C_6H_6	60	24 h	(5)	29
Al(O*t*-Bu)$_3$	100	heptane	30	13 d	(0)	32
Al(O*t*-Bu)$_3$	10	heptane	80	10 h	(<1)	32
$Al(OCH_2CCl_3)_3$	3	C_6H_6	30	1 h	(99)	28
$Al(OCH_2CHCl_2)_3$	3	C_6H_6	30	1 h	(7)	28
$Al(OCH_2CH_2Cl)_3$	3	C_6H_6	30	1 h	(1)	28
$Al(OCH_2CBr_3)_3$	3	C_6H_6	30	1 h	(50)	28
$Al[OCH(CH_2Cl)_2]_3$	3	C_6H_6	30	1 h	(92)	28
$Al(OSiMe_3)_3$	100	heptane	30	13 d	(71)	32
$Al(OSiMe_3)_3$	10	heptane	80	10 h	(29)	32

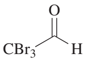


$Al(OEt)_3$ (cat.), benzene

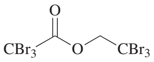


X	
Cl	(—)
Br	(—)

5, 3



Catalyst (3 mol %), benzene, 30°, 1 h



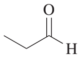
Catalyst	
$Al(OEt)_3$	(0)
$Al(OCH_2CBr_3)_3$	(98)

28

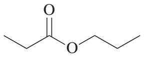
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

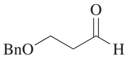
C$_3$



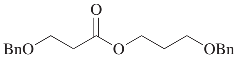
Catalyst (*x* mol %)



Catalyst	*x*	Additive	Solvent	Temp (°)	Time		Refs.
Al(OEt)$_3$	5	—	CCl$_4$	rt	24 h	(100)	17
Al(OPr)$_3$	"cat."	—	—	rt	2 months	(8)	5, 3
RuH$_2$(PPh$_3$)$_4$	0.08	—	—	rt	2 h	(46)	52
RuH$_2$(PPh$_3$)$_4$	0.36	—	—	rt	2 h	(71)	52
RuH$_2$(PPh$_3$)$_3$	1.4	—	vacuum	85	3 h	(96)	57
RuH$_2$(PPh$_3$)$_3$	0.4	—	vacuum	20	2 h	(95)	57, 52
RuH$_2$(PPh$_3$)$_3$	0.4	PPh$_3$	vacuum	20	2 h	(9)	57, 52
RuCl(SiMe$_3$)(CO)(PPh$_3$)$_2$	5	—	C$_6$D$_6$	70	2 d	(99)	67
RuH$_2$(CO)(PPh$_3$)$_3$	1.7	—	vacuum	90	3 h	(77)	57
RuHCl(PPh$_3$)$_3$	1.9	—	vacuum	85	1.5 h	(45)	57
RuHCl(PPh$_3$)$_3$	0.6	—	—	"heat"	7 h	(60)	174
RuHCl(CO)(PPh$_3$)$_3$	0.8	—	vacuum	85	1.5 h	(29)	57
RuH(η^2-CH=CMeCO$_2$Et)(PPh$_3$)$_3$	1.2	—	vacuum	85	4 h	(98)	57
Ru(C$_2$H$_4$)(PPh$_3$)$_3$	1.0	—	vacuum	90	2 h	(91)	57
RuCl$_2$(PPh$_3$)$_3$	1.1	—	vacuum	85	3 h	(0)	57
Rh[PhBP$_3$]H$_2$(MeCN)	1	—	C$_6$D$_6$	rt	1 min	(99)[q]	320

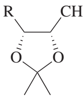


DIBAL-H (10 mol %), pentane,
0° to rt, 10 h

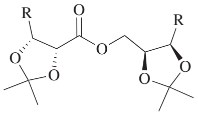


(61) 157, 156

C$_{3–5}$

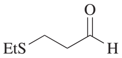


DIBAL-H (10 mol %), pentane,
0° to rt

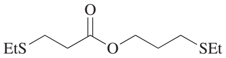


R	Time (h)		Refs.
H	10	(60)	157, 156
CH$_2$=CH	8	(71)	

C$_3$



AlEt$_3$ (2 mol %), additive,
toluene, –78°, 24 h



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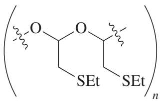
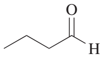


main product

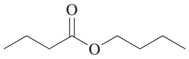
213

Additive	
t-BuOH	(10)
EtSH	(4)

C$_4$



Catalyst (*x* mol %)



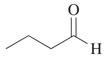
Catalyst	*x*	Solvent	Temp (°)	Time		Refs.
Al(OEt)$_3$	2.5	—	10 to rt	25 h	(75)	21
Al(OEt)$_3$	2	—	0 to rt	48 h	(82)	93
Al(OCH$_2$CBr$_3$)$_3$	3	C$_6$H$_6$	30	1 h	(92)	28
Al(O*i*-Pr)$_3$	3	C$_6$H$_6$	30	1 h	(26)	28
Al(O*i*-Pr)$_3$	—	CCl$_4$	20	—	(94)	90
Al(O*i*-Pr)$_3$	—	CCl$_4$	"heat"	—	(60)	90
Al(O*i*-Pr)$_3$	5 wt %	—	rt	24 h	(80)	91
Al(O*t*-Bu)$_3$	—	CCl$_4$	20	—	(90)	90
Al(O*n*-Bu)$_3$	"cat."	—	25–35	—	(91)	322
110	1	CH$_2$Cl$_2$	rt	0.5 h	(49)	160
110	1	CH$_2$Cl$_2$	rt	1 h	(77)	160
110	1	CH$_2$Cl$_2$	rt	2 h	(99)	160
120	0.7	CH$_2$Cl$_2$	rt	0.5 h	(62)	160
120	0.7	CH$_2$Cl$_2$	rt	1 h	(70)	160
Rh[PhBP$_3$]H$_2$(MeCN)	1	C$_6$D$_6$	rt	1 min	(99)[q]	320
Cp$_2$ZrH$_2$	5	—	0	0.5 h	(60)	61
Cp$_2$HfH$_2$	5	—	0	0.5 h	(78)	61
112	0.5	C$_6$D$_6$	rt	1 min	(16)[r]	184
SmI$_2$	1	THF	rt	6 h	(100)	179
La[N(SiMe$_3$)$_2$]$_3$	1	C$_6$D$_6$	–78 to 21	1 d	(45)[r]	74, 72
B(OH)$_3$	—	—	250	6 h	(10)	195

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

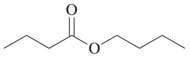
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_4

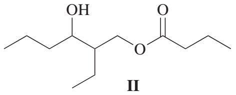


Catalyst, heptane



I

+



II

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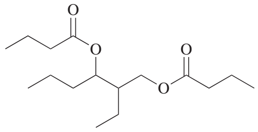
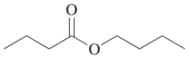


III

154

Catalyst	Temp (°)	Time	**I**	**II**	**III**
Al(O*t*-Bu)$_3$	20	6 d	(82)	(<1)	(3)
Al(O*t*-Bu)$_3$	80	6 h	(63)	(7)	(7)
Al(OSiMe$_3$)$_3$	20	24 h	(74)	(1)	(5)
Al(OSiMe$_3$)$_3$	20	6 d	(72)	(3)	(6)
Al(OSiMe$_3$)$_3$	8	6 h	(16)	(37)	(13)

Et_2AlO*s*-Bu, heptane, 1 h



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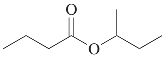
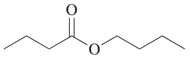


II

Temp (°)	**I**	**II**
–65	(6)	(10)
–40	(3)	(14)
–20	(10)	(20)
0	(7)	(16)
20	(7)	(14)
40	(4)	(5)

148

(*i*-Bu)$_2$AlOEt



I

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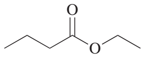
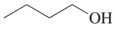


II

+

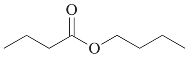


III

Temp (°)	**I**	**II**	**III**
–65 to –55	(0)	(12)	(2)
–45 to –35	(2)	(12)	(3)
–25 to –15	(10)	(30)	(21)
0	(23)	(47)	(26)
20	(20)	(39)	(38)

323

RuH$_2$(PPh$_3$)$_4$ (*x* mol %),
vacuum

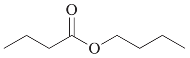


57

x	Additive	Solvent	Temp (°)	Time (h)	
0.8	—	none	100	2	(90)
0.9	—	none	20	2	(98)
0.2	—	none	20	2	(78)
0.3^s	—	none	20	2	(83)
0.5^s	—	none	20	2	(85)
0.6^s	—	none	20	2	(87)
0.7^s	—	none	20	2	(92)
0.3	*n*-BuOH	none	20	2	(28)
0.3	*n*-PrCO$_2$H	none	20	2	(0)
0.3	—	none	0	2	(99)
0.2	N$_2$	none	0	2	(90)

x	Additive	Solvent	Temp (°)	Time (h)	
0.3	H$_2$ (2 atm)	none	0	2	(71)
0.1	—	none	0	0.5	(98)
0.1	—	none	0	2	(88)
0.05	—	none	0	2	(89)
0.3	—	hexane	0	2	(91)
0.3	—	toluene	0	2	(90)
0.3	—	THF	0	2	(100)
0.2	—	pyridine	0	2	(14)
0.3	—	none	–10	2	(93)
0.3	—	none	–20	2	(61)
0.2	—	none	–30	2	(1)

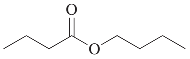
RuH$_2$(PPh$_3$)$_4$ (*x* mol %)



x	Temp (°)	Time (h)	
0.3	rt	1	(65)
0.4	rt	2	(84)
0.8	rt	2	(95)
0.2	100	2.5	(71)

52

Metal complex (*x* mol %), vacuum



57

Metal Complex	Temp (°)	Time (h)	
Ru(CO)$_3$(PPh$_3$)$_2$	90	3	(0)
[RuH(PPh$_3$)$_4$][PF$_6$]	20	5	(43)
RhH(PPh$_3$)$_4$	100	1.5	(5)
FeH$_2$(N$_2$)(PEtPh$_2$)$_3$	85	1	(<1)
CoH(N$_2$)(PPh$_3$)$_3$	20	6	(0)

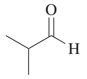
Metal Complex	Temp (°)	Time (h)	
MoH$_4$(dppe)$_2$	100	2	(0)
MoH$_4$(PMePh$_2$)$_4$	85	1	(0)
Mo(C$_2$H$_4$)(dppe)$_2$	85	1	(0)
Pd(C$_2$H$_5$)$_2$(PMePh$_2$)$_2$	0	4	(0)
Pt(C$_2$H$_5$)(acac)(PPh$_3$)$_2$	20	6	(0)

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

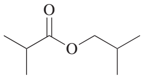
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_4

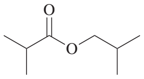


Catalyst (x mol %)

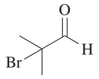


Catalyst	x	Additive	Solvent	Temp (°)	Time		Refs.
$Mg[Al(OEt)_4]_2$	—	—	—	rt	1 d	(57)	91
$Mg[Al(Oi\text{-}Pr)_4]_2$	—	—	—	rt	1 d	(56)	91
$Mg[Al(OBu)_4]_2$	—	—	—	rt	1 d	(50)	91
DIBAL-H	10	—	pentane	0 to rt	4 h	(83)	157, 156
$Al(OEt)_3$	"cat."	—	—	—	—	(85)	5, 3
$Al(Oi\text{-}Pr)_3$	5 wt %	—	—	rt	1 d	(75)	91
$Al(Oi\text{-}Bu)_3$	"cat."	—	—	5–80	—	(96)	18
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	—	C_6D_6	70	2 d	(97)	67
$RuH_2(PPh_3)_4$	0.4	—	vacuum	20	4.5 h	(71)	57, 52
$Rh[PhBP_3]H_2(MeCN)$	1	—	C_6D_6	rt	1 min	(99)[q]	320
η^2-CpTi(O*i*-Pr)$_2$	20	PhCN	Et_2O	–70 to –30	0.5 h	(50)[t]	324
Rh(η^3-CH_2Bz)$(PPh_3)_2$	2	—	C_6D_6	rt	0.5 h	(11)	64
Rh(η^3-$CH_2CH{=}CH_2$)$(PPh_3)_2$	1	H_2	C_6D_6	rt	—	(8)	64
Cp_2ZrH_2	5	—	—	0	0.5 h	(92)	61
Cp_2HfH_2	5	—	—	0	0.5 h	(92)	61
118	0.005	HCO_2H (10 mol %)	—	65	11 h	(50)	59
$La[N(SiMe_3)_2]_3$	1	—	C_6D_6	21	1 d	(84)	74, 72
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(100)	73
$B(OH)_3$	—	—	—	250	6 h	(77)	195

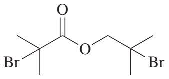
$Al(Oi\text{-}Bu)_3$ (x mol %)



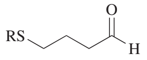
x	Temp (°)	Time (min)		Refs.
3	5	60	(79)	33
5	5	60	(91)	
3	15	60	(86)	
5	15	60	(90)	
3	25	30	(80)	
3	25	45	(79)	



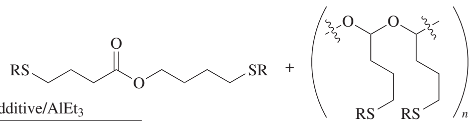
$Al(OEt)_3$ (cat.), benzene, 1 week



(—) 5, 3



$AlEt_3$, toluene, –78°, 24 h



main product

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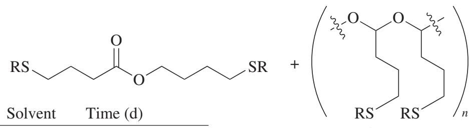
R	Additive	Additive/$AlEt_3$	
Me	H_2O	0.5	(2)
Me	H_2O	1	(<1)
Me	H_2O	2	(<1)
Et	Na-TPP	1	(4)
Et	Na-TPP	0.5	(8)

$AlEt_3$ (x mol %), –78°



main product

213

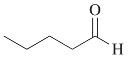
R	x	Solvent	Time (d)	
Me	1.7	—	1	(1)
Me	3.0	—	1	(0)
Me	1	toluene	1	(2)
Me	2	CH_2Cl_2	1	(15)
Me	4	THF	2	(3)
Et	1.0	—	1	(0)
Et	1.9	—	1	(0)

R	x	Solvent	Time (d)	
Et	3.8	—	1	(18)
Et	1	toluene	1	(6)
Et	2	CH_2Cl_2	1	(3)
Et	4	THF	2	(4)
Ph	1.5	—	1	(5)
Ph	1	toluene	1	(6)

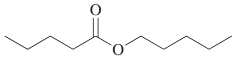
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

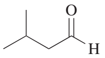
C_5



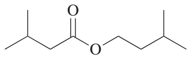
Catalyst (x mol %)



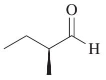
Catalyst	x	Additive	Solvent	Temp (°)	Time		Refs.
$Al(OEt)_3$	5	—	CCl_4	25	24 h	(84)	17
Al(O*n*-$C_5H_{11})_3$	"cat."	—	—	5–80	—	(96)	18
$RuH_2(PPh_3)_4$	0.6	—	vacuum	85	2 h	(43)	57, 52
118	0.005	HCO_2H (10 mol %)	—	65	5.5 h	(100)	59
$Rh[PhBP_3]H_2(MeCN)$	1	—	C_6D_6	rt	1 min	(99)[q]	320



Catalyst (x mol %)

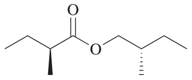


Catalyst	x	Solvent	Temp (°)	Time		Refs.
Al(O*i*-$C_5H_{11})_3$	"cat."	—	—	—	(—)	5, 3
Al(O*i*-$C_5H_{11})_3$	"cat."	—	5–80	—	(94)	18
$RuH_2(PPh_3)_4$	0.7	vacuum	85	3 h	(68)	57
$Rh[PhBP_3]H_2(MeCN)$	1	C_6D_6	rt	1 min	(99)[q]	52
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	C_6D_6	70	2 d	(99)	320
						67

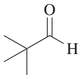


er = 94:6

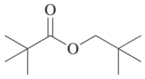
Al[(*S*)-O*s*-Bu]$_3$ (er = 94:6; 2.5 mol %),
0°, 1 h; rt, 40 min; 80°, 30 min



(60) er = 60:40[u] 20



Catalyst(s) (x mol %)

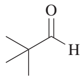


Catalyst(s)	x	Additive	Solvent	Temp (°)	Time		Refs.
$LiWO_2$	"cat."	—	THF	75	24 h	(79)	225
KH	5	—	C_6H_6	23	2	(93)	140
KH	5	18-c-6 (5 mol %)	C_6H_6	23	15 min	(93)[v]	140
$Ca[N(SiMe_3)_2]_2(thf)_2$	2	—	C_6H_6	rt	24 h	(96)[v]	51
$Mg(hpp)[N(SiMe_3)_2]$	1	—	C_6D_6	rt	24 h	(83)	325
DIBAL-H	10	—	pentane	0 to rt	5 h	(95)	157, 156
110	1	H_2	CH_2Cl_2	rt	2 h	(63)	160
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	H_2	C_6D_6	70	2 d	(0)	67
$Rh(\eta^3\text{-}CH_2Bz)(PPh_3)_2$	2	HCO_2H (10 mol %)	C_6D_6	rt	0.5 h	(0)	64
$Rh(\eta^3\text{-}CH_2CH{=}CH_2)(PPh_3)_2$	2	—	C_6D_6	rt	—	(0)	64
118	0.007	—	—	65	23 h	(40)	59
Cp_2ZrH_2	5	—	—	17	0.5 h	(62)	61
Cp_2HfH_2	5	—	—	0	0.5 h	(84)	61
$Ni(cod)_2$, IPrCl	1, 1	—	toluene	60	1 h	(99)	177
$La[N(SiMe_3)_2]_3$	1	—	C_6D_6	21	1 d	(80)	74, 72
La_2(*t*-$Bu_2pz)_6$	5	—	C_6D_6	21	—	(96)	73
EtNdI[w]	—	—	THF	65	20 h	(37)	69
$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	60	3 d	(100)	71, 70
$Cp^*{}_2NdCH(SiMe_3)_2$	1	—	C_6H_6	60	3 d	(46)	71, 70
112	0.5	—	C_6D_6	rt	4 h	(91)	184
113	0.5	—	C_6D_6	rt	10 h	(90)	184
114	0.5	—	C_6D_6	rt	10 h	(86)	184
SrO	"cat."	—	—	80	30 min	(70)	70
$KF–Al_2O_3$	"cat."	—	—	80	4 h	(8)	70

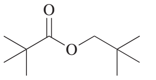
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_5



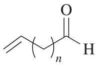
Catalyst, 50°, 5 h



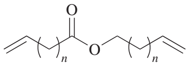
Catalyst	
KF (8.2 mmol/g) / Al_2O_3	(41)
KF (4.6 mmol/g) / Al_2O_3	(23)
KF	(0)
γ-Al_2O_3	(1)
MgO	(55)
CaO	(88)
$Mg(OH)_2$	(0)
$Ca(OH)_2$	(0)
KOH (4.5 mmol/g) / Al_2O_3	(0)
KOH (1.2 mmol/g) / Al_2O_3	(0)
RbOH / Al_2O_3	(0)

85

$C_{5–19}$



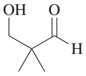
DIBAL-H (10 mol %), pentane, 0° to rt



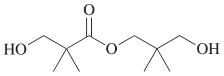
n	Time (h)	
2	12	(45)
3	12	(41)
4	8	(68)
5	8	(62)
8	5	(76)
11	6	(67)
12	8	(72)
13	8	(74)
16	10	(62)

157

C_5

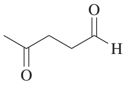


No catalyst, neat

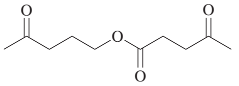


Temp (°)	Time (h)	
88	30	(47)
132	30	(94)

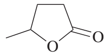
221



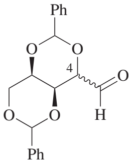
$RuHCl(CO)(PPh_3)_3$ (10 mol %), toluene, 120°, 40 h



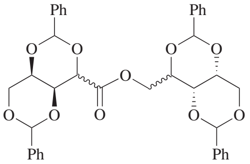
(55) +



(32) 167

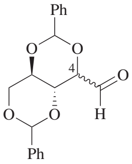


Al(O*i*-Pr)$_3$ (*x* mol %), $CHCl_3$

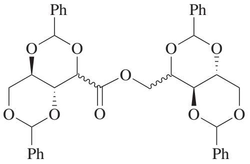


Config.	*x*	Temp (°)	Time (h)	
(*R*)	5	70	15	(83)
(*S*)	10	50	20	(76)

151



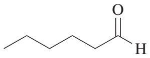
Al(O*i*-Pr)$_3$ (5 mol %), $CHCl_3$



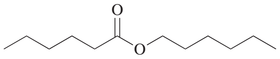
Config.	Temp (°)	Time (h)	
(*R*)	70	15	(92)
(*S*)	20	72	(71)

151

C_6



Catalyst (*x* mol %)



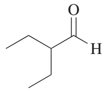
Catalyst	*x*	Additive	Solvent(s)	Temp (°)	Time		Refs.
KH	3	18-c-6 (3 mol %)	C_6H_6	23	3 h	(0)^x	140
Al(O*i*-Pr)$_3$	5 wt %	—	—	rt	1 d	(60)	91
109	0.5	—	toluene/hexane	rt	30 min	(86)	161
109	1	—	toluene/hexane	rt	1 h	(88)	161
111	1	—	toluene	21	0.2 h	(93)	158
111	0.5	—	toluene	21	0.25 h	(92)	158
111	0.3	—	toluene	21	0.25 h	(86)	158
111	0.2	—	toluene	21	0.25 h	(75)	158
116	1	—	toluene	21	30 min	(80)	162
$RuH_2(PPh_3)_4$	1.3	—	vacuum	85	3 h	(44)	57, 52
$Rh[PhBP_3]H_2(MeCN)$	1	—	C_6D_6	rt	1 min	(99)^q	320
Cp_2ZrH_2	5	—	—	17	30 min	(42)	61
Cp_2HfH_2	5	—	—	0	30 min	(57)	61

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

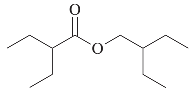
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

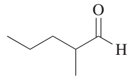
C_6



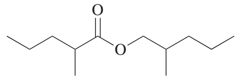
Catalyst (*x* amount)



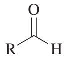
Catalyst	*x*	Solvent	Temp (°)	Time (d)		Refs.
$Mg[Al(OEt)_4)]_2$	—	—	0 to rt	1	(57)	91
$Mg[Al(Oi\text{-}Pr)_4)]_2$	—	—	rt	1	(59)	91
$Mg[Al(OBu)_4)]_2$	—	—	rt	1	(58)	91
$Al(OEt)_3$	3 mol %	—	rt	2	(70)	93
$Al(Oi\text{-}Pr)_3$	5 wt %	—	rt	1	(60)	91



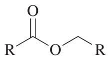
Catalyst (*x* mol %)



Catalyst	*x*	Solvent	Temp (°)	Time (h)		Refs.
110	1	CH_2Cl_2	rt	2	(89)	160
Cp_2ZrH_2	5	—	0	0.5	(64)	61
Cp_2HfH_2	5	—	0	0.5	(92)	61

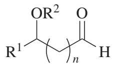


DIBAL-H (10 mol %), pentane,
0° to rt

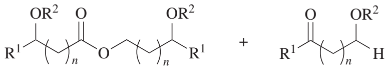


R	Time (h)		Refs.
$I(CH_2)_5$	12	(22)	157, 156
$Br(CH_2)_5$	5	(70)	
$MeO_2C(CH_2)_4$	12	(33)	
$(MeO)_2CH(CH_2)_4$	8	(32)	

$C_{6–11}$



DIBAL-H (10 mol %), pentane,
0° to rt, 13 h

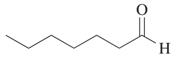


I **II**

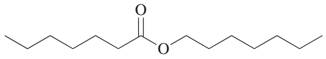
157

n	R^1	R^2	**I**	**II**
0	*t*-Bu	TBS	(0)	(0)
0	Cy	TBS	(0)	(45)
0	Cy	Ac	(31)	(10)
0	Ph	TBS	(37)	(26)
0	$Ph(CH_2)_3$	TBS	(0)	(78)
1	$Ph(CH_2)_2$	TBS	(52)	(29)

C_7

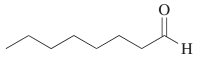


Catalyst (*x* mol %)

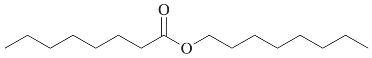


Catalyst	*x*	Solvent	Temp (°)	Time		Refs.
$Al(OEt)_3$	"cat."	—	rt	3 d	(—)	5, 3
$Al(OEt)_3$	5	CCl_4	25	24 h	(100)	17
DIBAL-H	10	pentane	0 to rt	5 h	(77)	157, 156
$Rh(\eta^3\text{-}CH_2Bz)(PPh_3)_2$	2	C_6D_6	rt	30 min	(87)	64
$Rh(\eta^3\text{-}CH_2CH{=}CH_2)(PPh_3)_2$	1	C_6D_6	rt	—	(86)	64
SmI_2	1	THF	rt	6	(100)	179

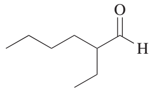
C_8



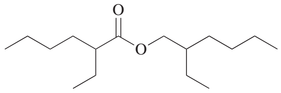
See table.



Catalyst	Amount	Solvent	Temp (°)	Time		Refs.
$Al(OEt)_3$	5 wt %	—	rt	48	(69)	93
110	1 mol %	CH_2Cl_2	rt	2	(83)	160



$Al(OR)_3$ (*x* mol %)



21

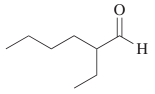
R	*x*	Solvent	Temp (°)	Time (h)	
Et	8	product ^{y}	50	2	(69)
Et	8	product ^{y}	40	16	(39)
i-Pr	8	benzene	45	40	(55)
i-Pr	15	benzene	45	40	(44)
2-ethylhexyl	6	2-ethylhexanol	50	22	(87)

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

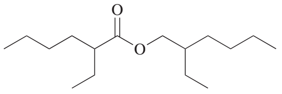
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_8

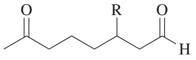


See table.

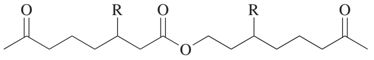


Catalyst(s)	Amount	Solvent	Temp (°)	Time		Refs.
$Mg[Al(OEt)_4)]_2$	—	—	rt	1 d	(75)	91
$Mg[Al(Oi\text{-}Pr)_4)]_2$	—	—	rt	1 d	(69)	91
$Mg[Al(OBu)_4)]_2$	—	—	rt	1 d	(75)	91
$Al(Oi\text{-}Pr)_3$	5 wt %	—	rt	1 d	(75)	91
110	1 mol %	CH_2Cl_2	rt	2 h	(86)	160
$Ni(cod)_2$, IPrCl	2, 2 mol %	toluene	60	1 h	(94)	177
$B(OH)_3$	—	—	250	6 h	(47)	195

C_{8-9}

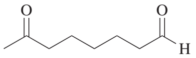


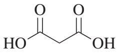
$Al(Oi\text{-}Pr)_3$ (5 mol %), petroleum ether, rt, 48 h

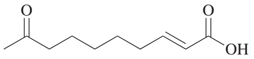


R		Refs.
H	(70)	326
Me	(72)	327

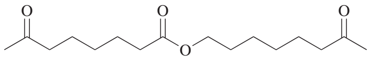
C_8



1. , piperidine, pyridine, 20°, 48 h
2. 60°, 2 h
3. 115°, time

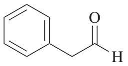


I

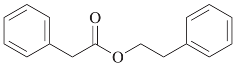
\+ 

II

Time (h)	I	II	Refs.
2	(42)	(43)	200
4	(33)	(34)	

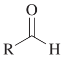


See table.

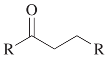


Catalyst	Amount	Additive	Solvent	Temp (°)	Time (h)		Refs.
$Al(OEt)_3$	5 wt %	—	—	rt	48	(32)	93, 59
118	0.017 mol %	HCO_2H (10 mol %)	—	65	7	(90)	

C_{8-15}

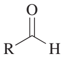


DIBAL-H (10 mol %), pentane, 0° to rt

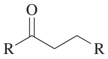


R	Time (h)		Refs.
$MeO_2C(CH_2)_6$	12	(61)	157, 156
$(MeO)_2CH(CH_2)_6$	12	(50)	
$HC{\equiv}C(CH_2)_6$	14	(62)	
$Ac(CH_2)_8$	18	(33)	
$PhC{\equiv}C(CH_2)_6$	7	(51)	

C_{9-12}

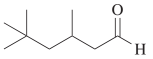


118 (x mol %), HCO_2H (10 mol %), 65°

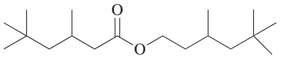


R	x	Time (h)		Refs.
$n\text{-}C_8H_{17}$	0.01	2	(95)	59
$n\text{-}C_9H_{19}$	0.017	3	(97)	
$n\text{-}C_{11}H_{23}$	0.01	5	(100)	

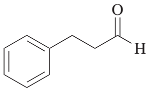
C_9



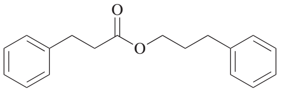
$Ni(cod)_2$ (1 mol %), IPrCl (1 mol %), toluene, 60°, 1 h



(96) 177



Catalyst (x amount)



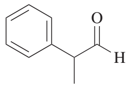
Catalyst	x	Solvent	Temp (°)	Time (h)		Refs.
$Mg[Al(OEt)_4]_2$	"cat."	—	0 to rt	48	(69)	93
$Al(OEt)_3$	5 wt %	—	rt	48	(66)	93
DIBAL-H	10 mol %	pentane	0 to rt	5	(77)	157, 156
116	1 mol %	toluene	21	2	(80)	162
115	1 mol %	MeCN	rt	13	(91)	68

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

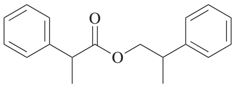
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_9

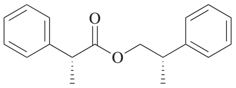


Catalyst (*x* mol %)

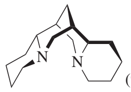


Catalyst	*x*	Additive(s)	Solvent(s)	Temp (°)	Time (h)		Refs.
109	1	—	toluene/hexane	rt	0.5	(89)	161
110	1	—	CH_2Cl_2	rt	2	(87)	160
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20	(56)	328

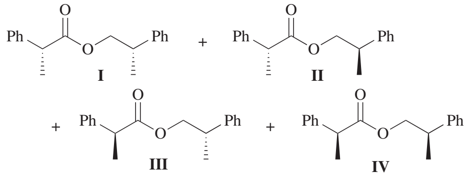
Al[(*R*)-BINOL]Me_2 (2 mol %), toluene



Temp		er	Refs.
–78°	(0)	—	49
0°	(100)	58.5:41.5[z]	



(9 mol %), EtMgBr (7.5 mol %)



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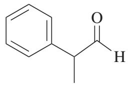
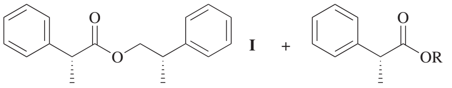
Solvent	Temp (°)	Time (h)	**I–IV**	**I/II/III/IV**	er (**I**, **IV**)	er (**II**, **III**)
toluene	–7	3	(89)	35:25:21:19	64:36	54:46
toluene	–40	3	(98)	34:23:23:19	64:36	50:50
THF	–78	3	(78)	42:25:19:13	76:34	56.5:43.5
THF	0	3	(88)	35:22:21:22	60.5:39.5	52:48
Et_2O	–78	3	(86)	38:27:19:16	71:29	58.5:41.5
CH_2Cl_2	–78	3	(63)	34:23:20:23	59:41	54:46
hexane	–78	3	(85)	32:27:20:21	60:40	56.5:43.5
1,2-diethoxyethane	–78	3	(79)	46:22:19:13	77.5:22.5	54:46
THF	–78	0.16	(16)	55:20:15:10	83.5:16.5	57.5:42.5
THF	–78	0.5	(34)	49:23:17:11	82:18	57:43
THF	–78	1	(46)	44:25:19:12	77.5:22.5	56.5:43.5
THF	–78	2	(67)	43:25:19:13	76.5:23.5	56.5:43.5
THF	–78	3	(0)[aa]	—	—	—



$Al(OR)_3$ (*x* mol %)



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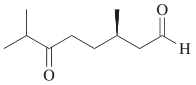
R	*x*	Solvent	Temp (°)	Time (h)	**I**	**II**	er (Acid)[bb]	er (Alcohol)[bb]
(*R*,*S*,*S*)-menthyl	17.5	CH_2Cl_2	–78	4	(46)	(10)	51.15:48.85	69.3:30.7
(*R*,*S*,*S*)-menthyl	17.5[cc]	CH_2Cl_2	–78	4	(44)	(—)	50.8:49.2	60:40
(*R*,*S*,*S*)-menthyl	17.5[cc]	CH_2Cl_2	–7°	24	(49)	(1)	50.75:49.25	42.4:57.6[dd]
(*R*,*S*,*S*)-menthyl	17.5[cc]	CH_2Cl_2	–78	24	(35)	(—)	50.05:49.95	52.1:48.9
(*R*,*S*,*S*)-menthyl	17.5	CH_2Cl_2	–78	24	(25)	(63)	—	—
(*R*,*S*,*S*)-menthyl	17.5	CH_2Cl_2	–30	24	(31)	(8)	50.6:49.4	66.1:33.9
(*R*,*S*,*S*)-menthyl	17.5[cc]	CH_2Cl_2	–30	4	(61)	(—)	49.9:50.1[dd]	57.6:42.4
(*R*,*S*,*S*)-menthyl	17.5	CH_2Cl_2	25	4	(25)	(6)	50.25:49.75	56.65:43.35
(*R*,*S*,*S*)-menthyl	17.5[cc]	CH_2Cl_2	25	4	(57)	(—)	50.05:49.955	52.35:47.65
(*R*,*S*,*S*)-menthyl	11.0	CH_2Cl_2	–78	4	(28)	(3)	0.45:49.55	64.75:35.25
(*R*,*S*,*S*)-menthyl	11.0[cc]	CH_2Cl_2	–78	4	(63)	(—)	50.1:49.9	60.25:39.75
(*R*,*S*,*S*)-menthyl	0.5	CH_2Cl_2	–78	24	(25)	(2)	50.1:49.9	55.7:44.3
(*R*,*S*,*S*)-menthyl	0.5[cc]	CH_2Cl_2	–78	24	(68)	(—)	—	52.15:47.85
(*R*,*S*,*S*)-menthyl	5.0	THF	–78	24	(59)	(1)	50.3:49.7	57.35:42.65
(*R*,*S*,*S*)-menthyl	5.0	toluene	–78	24	(89)	(2)	50.1:49.9	57.55:42.45
(*R*,*S*,*S*)-menthyl	5.0	CH_2Cl_2 / (*S*)-2-methylbutanol	–78	24	(21)	(31)	50.1:49.9	65.25:34.75
(*R*,*S*,*S*)-menthyl	5.0[cc]	CH_2Cl_2 / (*S*)-2-methylbutanol	–78	24	(59)	(8)	50.05:49.95	55.5:44.5
(*S*)-2-methylbutyl	20.0	CH_2Cl_2	20	48	(19)	(25)	50.2:49.8	51.2:48.8
(*S*)-2-methylbutyl	20.0[cc]	CH_2Cl_2	20	48	(8)	(59)	50.05:49.95	50.55:49.45
(*S*)-2-methylbutyl	20.0[cc]	CH_2Cl_2	20	48	(72)	(24)	—	—
(*R*)-2-butyl	0.5	CH_2Cl_2	20	24	(72)	(—)	—	—
(*R*)-2-butyl	2.5	CH_2Cl_2	–78	24	(77)	(—)	50.1:49.9	50.3:49.7
(*R*,*R*,*R*)-2-bornanyl	17.5	CH_2Cl_2	–78	24	(96)	(9)	50.75:49.25	61.15:38.85
(*R*,*R*,*R*)-2-bornanyl	5.0	CH_2Cl_2	–78	24	(99)	(3)	50.4:49.6	60:40

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

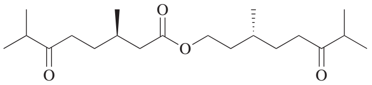
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

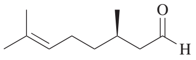
C_{10}



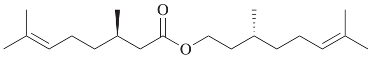
Al(O*i*-Pr)$_3$ (5 mol %),
petroleum ether, rt, 48 h



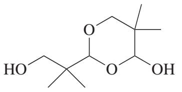
(70) 329



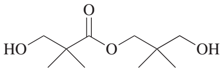
See table.



Catalyst	Amount	Solvent	Temp (°)	Time (h)		Refs.
DIBAL-H	10 mol %	pentane	0 to rt	5	(77)	157, 156
Al(OEt)$_3$	5 wt %	—	rt	48	(75)	93



Catalyst (*x* mol %)



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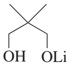
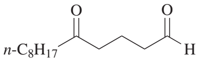
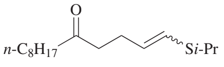
Catalyst	*x*	Solvent	Temp (°)	Time	
LiOH	—	MTBE	32	6 h	(70)
	5	THF	0	25 min	(92)

C_{13}

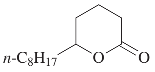


Catalyst (*x* mol %),
i-PrSH (*y* mol %), THF, rt



I

or



II

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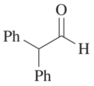
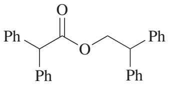
Catalyst	*x*	*y*	
SmI$_2$	50	40	(94) **II**
SmI$_3$	110	100	(87) **I**
SmI$_3$	10	100	(79) **I**

C_{14}

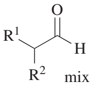


Cat. **112** (1 mol %), C_6D_6, 60°, 20 h



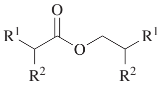
(80) 184

$C_{15–19}$



mixture of all isomers

Al(OEt)$_3$ (cat.), rt



(86–88) 330

C$_{15}$

R^1	R^2
n-C_7H_{15}	*n*-C_6H_{13}
n-C_8H_{17}	*n*-C_5H_{11}
n-C_9H_{19}	*n*-Bu
n-$C_{10}H_{21}$	*n*-Pr
n-$C_{11}H_{23}$	Et
n-$C_{12}H_{25}$	Me
n-$C_{13}H_{27}$	H

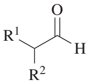
C$_{17}$

R^1	R^2
n-C_8H_{17}	*n*-C_7H_{15}
n-C_9H_{19}	*n*-C_6H_{13}
n-$C_{10}H_{21}$	*n*-C_5H_{11}
n-$C_{11}H_{23}$	*n*-Bu
n-$C_{12}H_{25}$	*n*-Pr
n-$C_{13}H_{27}$	Et
n-$C_{14}H_{29}$	Me
n-$C_{15}H_{31}$	H

C$_{19}$

R^1	R^2
n-C_9H_{19}	*n*-C_8H_{17}
n-$C_{10}H_{21}$	*n*-C_7H_{15}
n-$C_{11}H_{23}$	*n*-C_6H_{13}
n-$C_{12}H_{25}$	*n*-C_5H_{11}
n-$C_{13}H_{27}$	*n*-Bu
n-$C_{14}H_{29}$	*n*-Pr
n-$C_{15}H_{31}$	Et
n-$C_{16}H_{33}$	Me
n-$C_{17}H_{35}$	H

$C_{17–19}$



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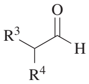
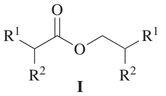


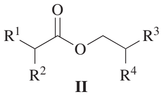
mixture of all isomers

Al(OEt)$_3$ (cat.), rt



I

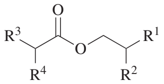
+



II

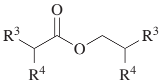
330

+



III

+



IV

I + **II** + **III** + **IV** (86–88)

R^1	R^2	R^3	R^4
n-C_8H_{17}	*n*-C_7H_{15}	*n*-C_9H_{19}	*n*-C_8H_{17}
n-C_9H_{19}	*n*-C_6H_{13}	*n*-$C_{10}H_{21}$	*n*-C_7H_{15}
n-$C_{10}H_{21}$	*n*-C_5H_{11}	*n*-$C_{11}H_{23}$	*n*-C_6H_{13}
n-$C_{11}H_{23}$	*n*-Bu	*n*-$C_{12}H_{25}$	*n*-C_5H_{11}
n-$C_{12}H_{25}$	*n*-Pr	*n*-$C_{13}H_{27}$	*n*-Bu
n-$C_{13}H_{27}$	Et	*n*-$C_{14}H_{29}$	*n*-Pr
n-$C_{14}H_{29}$	Me	*n*-$C_{15}H_{31}$	Et
n-$C_{15}H_{31}$	H	*n*-$C_{16}H_{33}$	Me
		n-$C_{17}H_{35}$	H

TABLE 1A. TISHCHENKO REACTIONS OF ALIPHATIC ALDEHYDES (*Continued*)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

[a] The starting material was paraformaldehyde.

[b] The yield is based on the amount of catalyst.

[c] Both single and binary metal oxides were used.

[d] The alkoxide was prepared by deprotonating the corresponding alcohol with EtMgBr.

[e] The alkoxide was prepared by adding the proper Grignard reagent to formaldehyde.

[f] The alkoxide was prepared by adding EtMgBr to cyclohexanone.

[g] The yield is calculated from the turnover number given in the original reference.

[h] The yield is based on the amount of catalyst.

[i] H_2O was present in the reaction system.

[j] The composition of the product mixture was determined at a low conversion (< 2%).

[k] Acetone was produced in the reaction.

[l] Methanol and crotonaldehyde were also produced in the reaction.

[m] Two parallel reactors were used.

[n] The number indicates the weight percentage of ethyl acetate in the product mixture.

[o] The amount of added Al(OEt)$_3$ was equal to that of the original catalytic amount.

[p] The number indicates the molar percentage based on the Al(OEt)$_3$ catalyst.

[q] The number is the conversion.

[r] Trimeric aldol-Tishchenko by-products were present.

[s] Fresh catalyst was added into the system of the entry above when no more ester was being formed.

[t] The reaction was a competition experiment between PhCN and *i*-PrCHO, and thus gave a complex mixture of products. The main product is shown.

[u] The optical purity was determined on the acid and alcohol after hydrolysis.

[v] The yield was determined by NMR spectroscopy.

[w] The catalyst was prepared in situ.

[x] The aldol condensation product was formed in 90% yield.

[y] A small amount of the preformed product ester was used as a solvent for the catalyst, and the yields were determined by quantifying the unreacted aldehyde.

[z] The reaction yielded also an (*SS*)/(*RR*) diastereomeric pair with an ee of 0%.

[aa] Sparteine was omitted from the reaction.

[bb] The values were measured after alkaline saponification.

[cc] The catalyst was recycled from the previous entry.

[dd] The product was the opposite enantiomer than indicated by the structure.

TABLE 1B. TISHCHENKO REACTIONS OF α,β-UNSATURATED ALDEHYDES

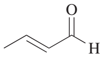
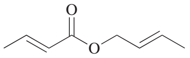
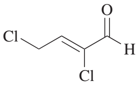
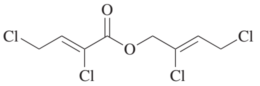
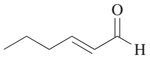
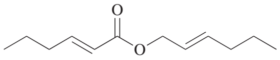
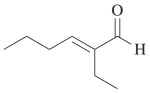
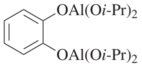
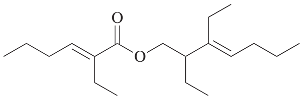
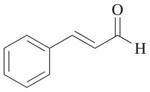
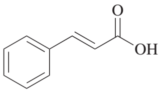
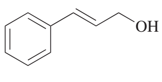
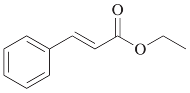
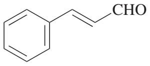
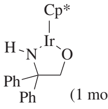
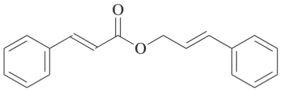
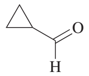
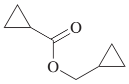
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	Rh[PhBP$_3$]H$_2$(MeCN) (1 mol %), C_6D_6, rt, 1 min	 (<1)	320
	Al(O*i*-Pr)$_3$ (10 mol %), 35° to rt, 3 h	 (43)	329
C_6			
	Rh[PhBP$_3$]H$_2$(MeCN) (1 mol %), C_6D_6, rt, 1 min	 (<1)	320
C_8			
	 OAl(O*i*-Pr)$_2$ OAl(O*i*-Pr)$_2$ (1 mol %), CH_2Cl_2, rt, 2 h	 (3)	160
C_9			
	1. Al(OEt)$_3$ (cat.), Et_2O, rt, 1 d 2. heat, several d	 (—) +  (41) +  (—)	331
	 (1 mol %), K_2CO_3, MeCN, rt, 18 h	 (34)	68

TABLE 1C. TISHCHENKO REACTIONS OF ALICYCLIC ALDEHYDES

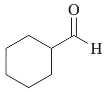
Aldehyde	Conditions	Product(s) and Yield(s) (%)		Refs.

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

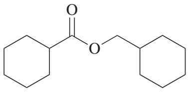
C_4

	NaOMe, MeOH, 80°, 96 h		(4)	332, 333

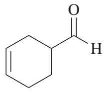
C_7



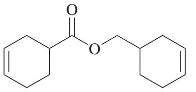
Catalyst(s) (x mol %)



Catalyst(s)	x	Additive(s)	Solvent(s)	Temp (°)	Time		Refs.
KH	5	18-c-6 (5 mol %)	toluene	80	10 h	(45)	140
Mg(hpp)[N(SiMe$_3$)$_2$]	1	—	C_6D_6	rt	24 h	(75)	325
BnSH, PhMgBr	20, 20	—	THF	65	48 h	(63)	144
Bn$_2$Se$_2$, Bu$_2$Mg	10, 5	—	THF	rt	24 h	(98)	146
Ca[N(SiMe$_3$)$_2$]$_2$(thf)$_2$	5	—	C_6H_6	rt	24 h	(82)	51
109	0.5	—	toluene/hexane	rt	0.5 h	(93)	161
DIBAL-H	10	—	pentane	0–rt	5 h	(93)	157, 156
110	1	—	CH_2Cl_2	rt	2 h	(96)	160
111	1	—	toluene	21	0.2 h	(98)	158
111	0.5	—	toluene	21	0.25 h	(99)	158
111	0.3	—	toluene	21	0.25 h	(98)	158
111	0.2	—	toluene	21	0.25 h	(98)	158
Cp$_2$ZnH$_2$	5	—	—	0	0.5 h	(79)	61
Cp$_2$HfH$_2$	5	—	—	0	0.5 h	(80)	61
Ni(cod)$_2$, IPrCl	1, 1	—	toluene	60	1 h	(99)	177
Rh[PhBP$_3$]H$_2$(MeCN)	1	—	toluene	rt	10 min	(88)	320
[RuCl$_2$(*p*-cym)]$_2$	1.25	P(C$_6$H$_4$-4-OMe)$_3$ (2.5 mol %), HCO$_2$Na	dioxane	80	20 h	(76)	328
OsH$_6$[P(*i*-Pr)$_3$]$_2$	1	—	—	"heat"	0.5 h	(98)	66
OsH$_2$(CO)$_2$[P(*i*-Pr$_3$)]$_2$	1	—	—	"heat"	22 h	(92)	66
OsH$_3$(κ^3-O$_2$CCy)[P(*i*-Pr)$_3$]$_2$	1	—	—	"heat"	22 h	(76)	66
La[N(SiMe$_3$)$_2$]$_3$	1	—	C_6D_6	21	24 h	(80)	74, 72
La$_2$(*t*-Bu$_2$pz)$_6$	5	—	C_6D_6	21	—	(100)	73
La(OPr-*i*)$_3$	1	—	C_6H_6	60	2 d	(84)	71
Cp*$_2$LaCH(SiMe$_3$)$_2$	1	—	C_6H_6	rt	3 d	(95)	71, 70
Cp*$_2$Sm(thf)$_2$	10	—	toluene	0, 25	0.5 h, 2.5 h	(99)	185
112	1	—	C_6D_6	rt	4 min	(100)	184
113	1	—	C_6D_6	rt	4 min	(100)	184
114	1	—	C_6D_6	rt	4 min	(100)	184
Yb$_2$Na$_8$(OCH$_2$CH$_2$NMe$_2$)$_{12}$(OH)$_2$	1	—	toluene	60	12 h	(81)	334



Catalyst (x mol %)



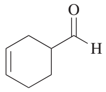
Catalyst	x	Additive	Solvent(s)	Temp (°)	Time (h)		Refs.
109	0.5	—	toluene/hexane	rt	0.5	(95)	161
111	1	—	toluene	21	0.2	(98)	158
111	0.5	—	toluene	21	0.25	(99)	158
111	0.3	—	toluene	21	0.25	(86)	158
Al(O*i*-Pr)$_3$	"cat."	—	—	50	—	(95)	22
115	1	K$_2$CO$_3$	MeCN	rt	39	(90)	68
La[N(SiMe$_3$)$_2$]$_3$	1	—	C_6D_6	21	24	(75)	74, 72
La$_2$(*t*-Bu$_2$pz)$_6$	5	—	C_6D_6	21	—	(100)	73
B(OH)$_3$	—	—	—	250	6	(55)	195

TABLE 1C. TISHCHENKO REACTIONS OF ALICYCLIC ALDEHYDES (*Continued*)

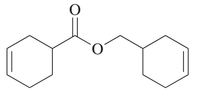
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7



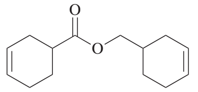
Al(O*i*-Pr)$_3$ (1.5 mol %),[a]
slow addition



22

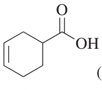
Temp (°)	Time after Addition (min)	
70	0	(96)
70	20	(97)
70	40	(98)
90	0	(83)
90	10	(88)
90	20	(92)
90	100	(95)
110	0	(58)
110	20	(59)
110	40	(61)
110	100	(61)

Catalyst (5 mol %)

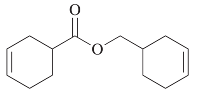


61

Catalyst	Temp (°)	Time (h)	
Cp_2ZrH_2	0	0.5	(90)
Cp_2HfH_2	0	0.5	(87)
Cp_2ZrHCl	0	0.5	(9)
Cp_2ZrHCl	17	8	(94)
Cp_2HfHCl	0	0.5	(67)
Cp_2ZrCl_2	0	0.5	(0)
Cp_2HfCl_2	0	0.5	(0)
Cp_2ZrCl_2 + *n*-BuLi (1 eq)	0	0.5	(80)
Cp_2ZrCl_2 + *n*-BuLi (2 eq)	0	0.5	(93)
Cp_2HfCl_2 + *n*-BuLi (1 eq)	0	0.5	(89)
Cp_2HfCl_2 + *n*-BuLi (2 eq)	0	0.5	(95)
Cp_2TiCl_2 + *n*-BuLi (2 eq)	0	0.5	(6)



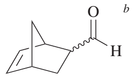
(0.5 mol %),
Al(O*i*-Pr)$_3$ (1.5 mol %),[a]
slow addition



22

Temp (°)	Time after Addition (min)	
50	0	(61)
50	10	(90)
50	20	(95)
50	40	(95)
50	70	(98)
50	120	(99)
60	0	(78)
60	10	(86)
60	20	(90)
60	40	(91)
60	70	(95)
70	0	(37)
70	10	(62)
70	20	(63)
70	70	(63)
70	120	(64)

C_8



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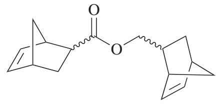

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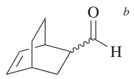
335

C_9



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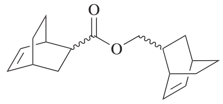
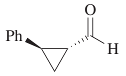
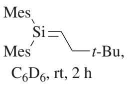


(—)

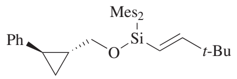
335

C_{10}





C_6D_6, rt, 2 h



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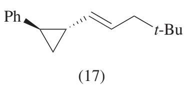

(17)

203

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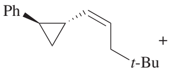

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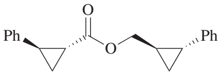

(17)

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[a] A small amount of the preformed product ester was used as the solvent for the catalyst, and the yields were determined by quantifying the unreacted aldehyde.

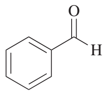
[b] The C-2 configuration was not indicated.

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES

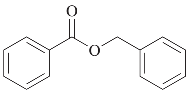
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7



Catalyst(s) (*x* mol %)



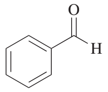
Catalyst(s)	*x*	Additive	Solvent(s)	Temp	Time		
Li_3N	"cat."	—	CCl_4	"heat"	—	(56)	40
LiBr	50	—	Et_3N	rt	2 d	(96)	45
$LiN(SiMe_3)_2$	5	—	toluene	rt	90 h	(<5)	140
$BuLi/Al_2O_3$	10, 30	—	hexane	60°	12 h	(94)	83
Na	10	—	hexane[a]	"heat"	5 h	(92)	43
Na, Al_2O_3	10, 30	—	hexane	60°	8 h	(90)	83
NaH	10	—	—	high-speed ball milling, rt	0.5 h	(98)	336
NaH	1	—	toluene	rt	18 h	(95)	139
NaH	5	—	toluene	rt	18 h	(94)	139
NaH	—	—	C_6H_6	80°	5 h[b]	(92)[c]	136
$NaN(SiMe_3)_2$	5	—	toluene	rt	60 h	(85)	140
$NaN(SiMe_3)_2$	2.5	—	toluene	60°	12 h	(88)	140
NaOMe[d]	—	—	MeOH	"heat"	—	(38)	1
NaO*t*-Bu	5	—	toluene	rt	9 h	(86)	140
NaOBn[d]	—	—	BnOH	"heat"	—	(75)	1
NaOBn[d]	—	—	BnOH	50–60°	2.5 h	(93)	39
KH	1	—	toluene	rt	1.3 h	(97)	140
KH	1	—	none	rt	1 h	(97)	140
KH	1	18-c-6 (1 mol %)	C_6H_6	rt	5 min	(97)	140
$KN(SiMe_3)_2$	5	—	toluene	rt	7 h	(86)	140
$KN(SiMe_3)_2$	2.5	—	toluene	60°	2 h	(90)	140
$KN(SiMe_3)_2$	2	18-c-6 (2 mol %)	C_6H_6	rt	8 h	(91)	140
KO*t*-Bu	1	—	toluene	rt	1.5 h	(96)	140
KO*t*-Bu	1	18-c-6 (1 mol %)	C_6H_6	rt	10 min	(96)	140
KOPh	—	—	—	100°	18 h	(30)	337
C_8K	50 (based on K)	—	—	20°	—	(3)[e]	338
C_8K	50 (based on K)	—	—	45°	—	(25)[e]	338
C_8K	50 (based on K)	—	—	65°	—	(25)[e]	338
EtMgBr	25	—	Et_2O	rt, "heat"	10 h, 4 h	(17)	46
121	1	—	C_6D_6	rt	2 h	(—)[f]	51
133	1	—	none	110°	1 h	(95)	339
$Mg[Al(OEt)_4]_2$	"cat."	—	—	0° to rt	48 h	(57)	93
$Ca[N(SiMe_3)_2]_2(thf)_2$	0.1	—	C_6H_6	rt	88 h	(63)	51
$Ca[N(SiMe_3)_2]_2(thf)_2$	0.2	—	C_6H_6	rt	48 h	(74)	51
$Ca[N(SiMe_3)_2]_2(thf)_2$	1	—	C_6D_6	rt	24 h	(97)	51
$Sr[N(SiMe_3)_2]_2(thf)_2$	1	—	C_6D_6	rt	24 h	(78)	51
$Ba[N(SiMe_3)_2]_2(thf)_2$	1	—	C_6D_6	rt	24 h	(86)	51
$Mg(hpp)[N(SiMe_3)_2]$	1	—	C_6D_6	rt	2 h	(86)	325
$Mg(hpp)[N(SiMe_3)_2]$	10	—	C_6D_6	rt	1 h	(64)	325
$Mg(tbo)[N(SiMe_3)_2](THF)$	1	—	C_6D_6	rt	100 min	(48)	325
$Mg(tbo)[N(SiMe_3)_2](THF)$	10	—	C_6D_6	rt	1 h	(59)	325
$Al(OSiMe_3)_3$	—	—	heptane	20°	3 d	(0)	32
$Al(OEt)_3$	5	—	CCl_4	rt	24 h	(72)	17
$Al(OEt)_3$	"cat."	—	—	—	—	(88)	4, 2
$Al(Ot\text{-}Bu)_3$	—	—	heptane	20°	3 d	(98)	32, 154
$Al(Ot\text{-}Bu)_3$	—	—	benzene	20°	—	(90)	30
$Al(OBn)_3$	—	—	benzene	20°	—	(85)	30
109	2	—	toluene/hexane	rt	5 h	(68)	161
111	1	—	toluene	21°	5 h	(67)	158
116	1	—	toluene	21°	5 h	(92)	162
116	2	—	toluene	21°	5 h	(95)	162
122	—	—	pentane	80° (pressure tube)	5 h	(91)	340
$B(OH)_3$	—	—	—	250°	6 h	(31)	195
Bn_2Se_2, Bu_2Mg	2.5, 1.25	—	THF	rt	24 h	(99)	146

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

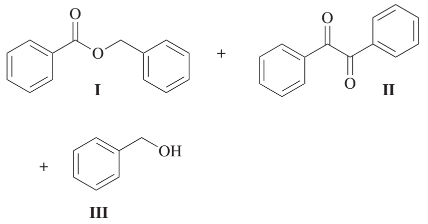
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7



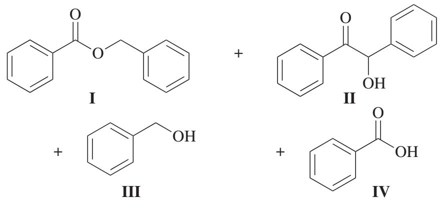
LiWO$_2$ (x mol %), THF, 72 h



225

x	Temp (°)	**I**	**II**	**III**
100	60	(5)	(16)	(22)
50	60	(28)	(7)	(10)
20	60	(60)	(4)	(8)
10	60	(76)	(<1)	(5)
5	60	(89)	(0)	(<1)
5	75	(98)	—	—
20	40	(23)	—	—
20	50	(34)	—	—
20	75	(66)	—	—

KH (110 mol %),
18-crown-6 (x mol %), THF, rt



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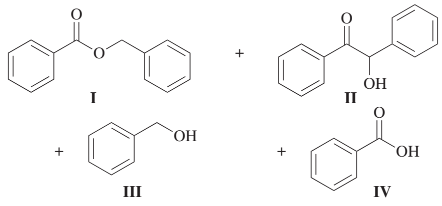
x	Time (h)	**I**	**II**	**III**	**IV**	x	Time (h)	**I**	**II**	**III**	**IV**
1.0	2	(61)	(—)	(33)	(4)	2.8	10	(27)	(31)	(29)	(10)
2.8*	2	(60)	(7)	(17)	(—)	5.7	10	(23)	(28)	(34)	(11)
2.8*	2	(70)	(7)	(24)	(—)	1.0	24	(42)	(2)	(43)	(10)
3.8	2	(—)	(12)	(75)	(13)	2.8*	24	(8)	(38)	(36)	(16)
1.0	5	(59)	(—)	(33)	(5)	2.8*	24	(13)	(38)	(29)	(10)
2.8*	5	(40)	(20)	(20)	(14)	3.8	24	(—)	(21)	(55)	(10)
2.8*	5	(51)	(20)	(28)	(14)	(—)	48	(26)	(—)	(58)	(10)
3.8	5	(—)	(17)	(70)	(8)	1.0	48	(7)	(—)	(70)	(22)
1.0	10	(33)	(9)	(38)	(9)	2.8	48	(—)	(47)	(14)	(10)
						3.8	48	(—)	(38)	(50)	(10)

*Identical conditions for which no explanation of the different product distributions is provided.

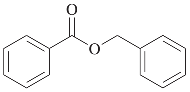
Catalyst (x mol %), THF, rt



138

Catalyst	x	Additive	Time (h)	**I**	**II**	**III**	**IV**
NaH	110	—	48	(62)	(—)	(12)	(12)
NaOBn	50	—	48	(70)	(—)	(3)	(20)
KH	110	PhCO$_2$Me (110 mol %)	24	(61)	(14)	(—)	(21)

KO$_2$ (14 mol %), Et$_3$SiH,
18-c-6 (17 mol %), 40°, 30 min



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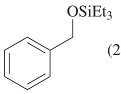


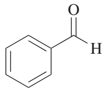
(29) 199

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

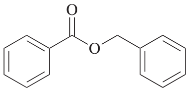
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7



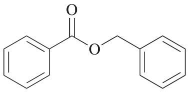
Metal oxide.



Metal Oxide	Temp (°)	Time	
MgO	180	3 h	(~40)
CaO	180	2.5 h	(90)
SrO	180	40 min	(100)
BaO	180	20 min	(100)
BaO	138	20 min	(95)
BaO	128	30 min	(100)
BaO	118	2 h	(100)

76

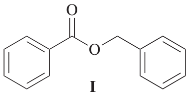
Catalyst, 50°



Catalyst	Time (h)	
KF / Al_2O_3	20	(99)
KF / Al_2O_3	3	(94)
KNH_2 / Al_2O_3	3	(76)
K_2CO_3 / Al_2O_3	3	(23)
KOH / Al_2O_3	3	(1)
Al_2O_3	3	(0)

84

Catalyst, Et_3SiH, 30°



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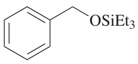
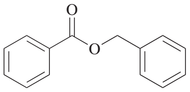


II

86

Catalyst	Solvent	Time (h)	**I + II**	**I/II**
KF / Al_2O_3	DMF	20	(100)	0:100
KF / Al_2O_3	DMF	1	(100)	0:100
KF / Al_2O_3	hexane	20	(99)	99:1
KF / Al_2O_3	THF	20	(88)	99:1
KF / Al_2O_3	—	20	(99)	99:1
K_2CO_3 / Al_2O_3	DMF	20	(99)	0:100
KNH_2 / Al_2O_3	DMF	20	(60)	0:100
MgO	DMF	20	(44)	16:84
CaO	DMF	20	(14)	50:50

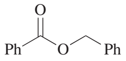
Metal oxide (MO)



MO	Temp (°)	Time (min)	
MgO^g	40	3	(7)^h
MgO^g	70	6	(46)^h
MgO^g	70	7	(58)^h
MgO	70	3	(32)
CaO^g	40	1	(9)^h

81, 192

PhMgBr (x mol %), RSH,
THF (y M), 65°



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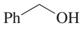

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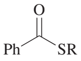

III

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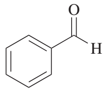
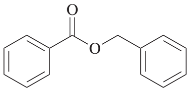
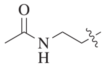
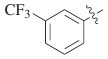
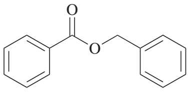
R	x	y	Time (h)	**I**^{i}	**II**^{i}	**II**^{i}
Ph	5	0.90	48	(48)	(6)	(0)
Cy	5	0.90	48	(48)	(5)	(0)
Bn	5	0.90	48	(87)	(4)	(0)
Bn	5	0.68	72	(71)	(5)	(0)
Bn	20	0.34	24	(98)	(1)	(0)
Bn	10	0.68	72	(100)	(0)	(0)
4-*t*-$BuC_6H_4CH_2$	5	0.90	48	(66)	(6)	(0)
4-*t*-$BuC_6H_4CH_2$	5	0.68	72	(23)	(7)	(4)
4-*t*-$BuC_6H_4CH_2$	10	0.68	72	(89)	(6)	(2)
4-*t*-$BuC_6H_4CH_2$	10	1.0	24	(97)	(2)	(1)

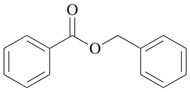
TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*			
C_7			
	RSH (x mol %), PhMgBr (x mol %), MW, THF (y M), 110°		145

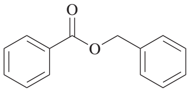
R	x	y	Time (min)	
4-t-$BuC_6H_4CH_2$	10	0.68	10	(70)
4-t-$BuC_6H_4CH_2$	10	1.0	10	(85)
4-t-$BuC_6H_4CH_2$	10	1.2	10	(83)
4-t-$BuC_6H_4CH_2$	10	1.2	30	(82)
4-t-$BuC_6H_4CH_2$	10	1.8	10	(85)
4-t-$BuC_6H_4CH_2$	5	1.8	10	(85)
4-t-$BuC_6H_4CH_2$	5	1.8	30	(92)
4-t-$BuC_6H_4CH_2$	5	2.0	30	(91)
	10	0.68	10	(64)
	10	0.68	10	(28)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Al(OBn)_3$ (2 mol %), $Al(Ot$-$Bu)_3$ (2 mol %), additive, benzene, 20°		31

Additive	Time (min)		Additive	Time (min)	
—	100	(6)	H_2NSO_3H	100	(7)
$PhCO_2H$	100	(74)	$PhCH_2OH$	100	(5)
$MeCO_2H$	100	(75)	H_2O	100	(5)
4-$O_2NC_6H_4OH$	100	(31)	$PhCO_2Na$	100	(4)
C_6H_5OH	100	(5)	$MeCO_2Na$	100	(6)
4-TsOH	100	(8)	Ac_2O^j	50	(81)
2,4-$Me_2C_6H_3SO_3H$	100	(5)	Bz_2O^j	100	(57)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$ROAlMe_2$ (x mol %), toluene, 21°, 5 h		162

R	x	
$(2,6$-$Ph_2C_6H_3CH_2)_3Si$	2	(95)
$(2,6$-$Ph_2C_6H_3CH_2)_3Si$	1	(92)
Ph_3Si	2	(15)
Ph_3Si	1	(<1)
Et_3Si	2	(6)
Et_3Si	1	(<1)
Bn_3Si	2	(<1)
Bn_3Si	1	(<1)
t-$BuPh_2Si$	2	(8)
t-$BuPh_2Si$	1	(<1)

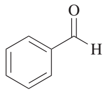
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst(s) (x mol %)		

Catalyst(s)	x	Additive	Solvent	Temp (°)	Time		Refs.
$MnPh_2PCy_3$	1	—	—	rt	1 d	(89)	55
$Fe(OBn)_2(bpy)$	0.5	—	—	80	6 h	(63)	56
$Na_2Fe(CO)_4$	3	—	THF	rt	40 h	(95)	54
$Na_2Fe(CO)_4$	3	—	THF/N-methylpyrrolidinone	rt	20 h	(92)	54
$K_2Fe(CO)_4$	20	18-c-6	THF	60	6 h	(71)	62
$Ni(cod)_2$, IPrCl	1,1	—	toluene	60	3 h	(99)	177
$Zn(OEt)_2$	20	—	—	"heat"	2 h	(43)	164
$Zn(Oi$-$Pr)_2$	30	—	—	"heat"	4 h	(16)	164
Cp_2ZrH_2	5	—	—	17	0.5 h	(7)	61
Cp_2HfH_2	5	—	—	17	0.5 h	(9)	61
$RuH_2(PPh_3)_4$	0.8	—	vacuum	20	2 h	(23)	57, 52
$RuH_2(PMe_3)_4$	25–30	—	$C_6D_5CD_3$	–20	16 d	(0)	166
$RuH_2(PMe_3)_4$	25–30	—	C_6D_6	rt	6 d	(56)	166
$RuH_2(PMe_3)_4$	25–30	—	C_6D_6	100	5 h	(63)	166

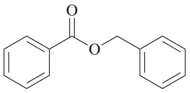
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7

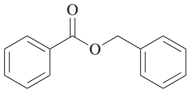


Catalyst(s) (*x* mol %)



Catalyst(s)	*x*	Additive	Solvent	Temp (°)	Time		Refs.
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	—	C_6D_6	70	2 d	(0)	67
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(92)	328
118	0.02	HCO_2H	—	65	10 h	(80)	59
118	0.02	HCO_2H	—	100	4.5 h	(90)	59
$RhH(PPh_3)_4$	8	—	C_6H_6	50	4 h	(90)	58
$RhH(PPh_3)_4$	16	—	C_6H_6	50	1 h	(89)	58
$RhH(PPh_3)_4$	25	—	C_6H_6	30	4 h	(82)	58
$RhH(PPh_3)_4$	25	—	C_6H_6	50	4 h	(89)	58
$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(81)	320
$Rh(\eta^3\text{-}CH_2C(O)Ph)(PPh_3)_2$	0.2	—	C_6D_6	rt	30 min	(2)	64
$Rh(\eta^3\text{-}CH_2C(O)Ph)(PPh_3)_2$	1	—	C_6D_6	rt	30 min	(17)	64
$Rh(\eta^3\text{-}CH_2C(O)Ph)(PPh_3)_2$	2	—	C_6D_6	rt	30 min	(94)	64
$Rh(\eta^3\text{-}CH_2CH{=}CH_2)(PPh_3)_2$	0.2	H_2	C_6D_6	rt	—	(0)	64
$Rh(\eta^3\text{-}CH_2CH{=}CH_2)(PPh_3)_2$	1	H_2	C_6D_6	rt	—	(94)	64
$Rh(\eta^3\text{-}CH_2CH{=}CH_2)(PPh_3)_2$	2	H_2	C_6D_6	rt	—	(95)	64
$OsH_6[P(i\text{-}Pr)_3]_2$	1	—	—	"heat"	75 h	(20)	66
$OsH_2(CO)_2[P(i\text{-}Pr)_3]_2$	1	—	—	"heat"	141 h	(92)	66
115	1	K_2CO_3	MeCN	rt	12 h	(86)	68
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(100)	73
$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	rt	3 d	(94)	71
$Sm[N(SiMe_3)_2]_3$	2.5	—	hexane/toluene	—	24 h	(85)	194
$Sm[N(SiMe_3)_2]_3\text{–}SiO_2$	1	—	toluene	rt	24 h	(57)	193
$YN(SiMe_3)_2]_3\text{–}SiO_2$	1	—	toluene	rt	24 h	(31)	193
$[SBA\text{–}15]Sm[N(SiMe_3)_2]_x$	2.5	—	hexane/toluene	—	24 h	(80)	194
$Cp^*{}_2ThMe_2$	1	—	C_6D_6	rt	48 h	(65)	188
$Th(NEtMe)_4$	1	—	C_6D_6	rt	48 h	(85)	188
$Me_2SiCp''{}_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or C_6D_6CD	rt	24 h	(96)	187
$Me_2SiCp''{}_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or C_6D_6CD	rt	6 h	(49)[k]	187

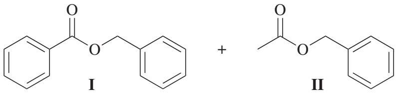
$K_2Fe(CO)_4$ (*x* mol %) 18-crown-6, THF, 60°



x	Time (h)	
2	40	(46)
7	6	(72)
10	24	(63)
20	7	(71)
100	4	(80)

62

1. $Na_2Fe(CO)_4$, THF, rt, time
2. MeI, 5 h

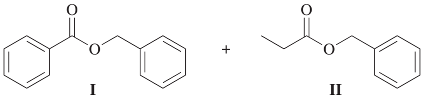


I + **II**

Time (h)	**I + II**	**I/II**
4	(80)	88:12
5	(88)	85:15

54

1. $Na_2Fe(CO)_4$, THF, rt, 5 h
2. EtI, 5 h

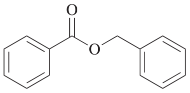


I + **II**

I + II (79), **I/II** 89:11

54

$Ni(cod)_2$ (*x* mol %), ligand, toluene-d_8



x	Ligand / (mol %)	Temp (°)	Time (h)	
10	PCy_3 / 20	100	24	(90)
2	IPr / 2	60	6	(99)
2	IPrCl /2	60	1.5	(99)
1	IPrCl / 1	60	3	(99)

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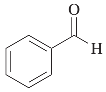
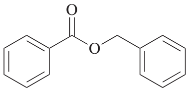
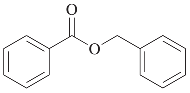
TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

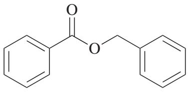
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	CuO*t*-Bu, ligand, THF, rt, 48 h		53

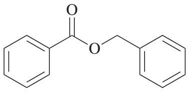
Ligand	
$P(n\text{-}Bu)_3$	(83)
PPh_3	(68)
t-BuNC	(61)
$P(OMe)_3$	(49)
C_5H_5N	(30)
Et_3N	(27)
CO	(0)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$[RuCl_2(p\text{-cym})]_2$ (1.25 mol %), ligand (2.5 mol %), HCO_2Na, dioxane, 80°		328

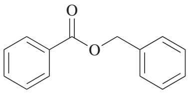
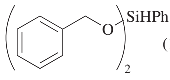
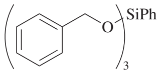
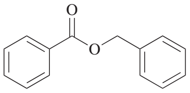
Ligand	
PPh_3	(84)
$P(4\text{-}CF_3C_6H_4)_3$	(58)
$P[3,5\text{-}(CF_3)_2C_6H_3]_3$	(33)
$P(4\text{-}ClC_6H_4)_3$	(71)
$P(4\text{-}MeOC_6H_4)_3$	(76)
$CyPPh_2$	(93)
Cy_2PPh	(94)
PCy_3	(75)
BINAP	(84)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst (*x* mol %), no solvent, 80°, 12 h		341

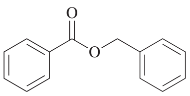
Catalyst	*x*	
129a	5	(95)
129b	5	(92)
129c	1	(80)
129c	2.5	(93)
129c	5	(98)
130a	5	(80)
130b	5	(78)
131	5	(96)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst (1 mol %), rt		

Catalyst	Additive	Solvent	Time		Refs.
SmI_2	—	THF	6 h	(100)	179
$Cp^*{}_2NdCH(SiMe_3)_2$	$PhMe_2SiH$	C_6H_6	3 d	(90)	71
$Cp^*{}_2NdCH(SiMe_3)_2$	—	C_6H_6	3 d	(88)	71, 70
112	—	C_6D_6	0.5 h	(99)	184
113	—	C_6D_6	0.75 h	(99)	184
114	—	C_6D_6	1 h	(99)	184
123	—	C_6D_6	—	(70)	74

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$PhSiH_3$, $Cp^*{}_2NdCH(SiMe_3)_2$ (1 mol %), benzene, rt, 30 min	 (12) +  (11) +  (12)	71
	Catalyst (1 mol %), toluene, 60°, 2 h		334

Catalyst	
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	(93)
$Pr_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	(75)
$Nd_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	(83)
$Sm_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	(69)
$Y_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	(81)
$Nd(OCH_2CH_2NMe_2)_3$	(0)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$ (*x* mol %), toluene, 2 h		334

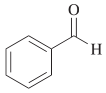
x	Temp (°)	
2	20	(91)
1	20	(78)
0.5	20	(40)
0.1	60	(0)
1	60	(93)
0.5	60	(84)

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

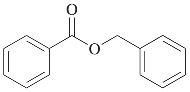
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7

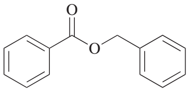


Cat. **124** (x mol %), toluene



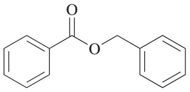
x	Temp (°)	Time (h)		Refs.
1	60	0.5	(72)	165
1	60	2	(81)	
1	60	4	(82)	
1	rt	10	(83)	
2	rt	2	(53)	
2	40	2	(80)	
2	60	2	(84)	
2	80	2	(77)	
2	100	2	(78)	
4	60	2	(93)	

$EtLnI^{I}$ (x mol %), THF, 20 h

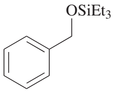


Ln	x	Temp (°)		Refs.
Pr	100	65	(32)	69
Pr	20	65	(40)	
Nd	100	65	(40)	
Nd	20	65	(23)	
Sm	100	65	(30)	
Sm	20	rt	(58)	

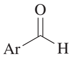
Et_3SiH, KO_2 (14 mol %),
18-c-6 (7 mol %), 40°, 30 min



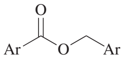
(69) +



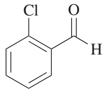
(29) 199



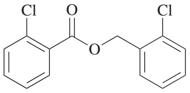
Catalyst (x mol %)



Ar	Catalyst	x	Additive(s)	Solvent	Temp (°)	Time		Refs.
3-FC_6H_4	NaH	10	—	toluene	high-speed ball milling, rt	0.5 h	(91)	336
3-FC_6H_4	LiBr	50	—	Et_3N	rt	2 d	(95)	45
4-FC_6H_4	NaH	5	—	toluene	rt	18 h	(95)	139
4-FC_6H_4	KH	5	—	toluene	80	1 h	(84)	140
4-FC_6H_4	KO*t*-Bu	5	—	toluene	80	1 h	(80)	140
4-FC_6H_4	$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(87)	73
4-FC_6H_4	$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	rt	3 d	(95)	71
4-FC_6H_4	$La[N(SiMe_3)_2]_3$	5	—	—	21	1 d	(66)	74
2,3,4,5-F_4C_6H	$[RuCl_2(p\text{-}cym)]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(84)	328



Catalyst(s) (x mol %)



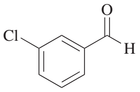
Catalyst(s)	x	Additive	Solvent(s)	Temp (°)	Time (h)		Refs.
NaH	5	—	toluene	95	18	(95)	139
KH	2	18-c-6 (2 mol %)	C_6H_6	23	0.33	(95)	140
KO*t*-Bu	2	—	toluene	23	24	(92)	140
BnSH, PhMgBr	20, 20	—	THF	60	18	(93)	144
109	2	—	toluene/hexane	rt	5	(88)	161
111	1	—	toluene	21	5	(88)	158
129c	5	—	none	80	12	(96)	341
133	1	—	none	80	4	(49)	339
$Cp^*{}_2ThMe_2$	1	—	C_6D_6	rt	48	(50)	188
$Th(NEtMe)_4$	1	—	C_6D_6	rt	48	(95)	187
$Me_2SiCp''{}_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24 h	(89)	187

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

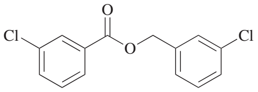
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

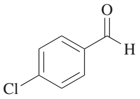
C_7



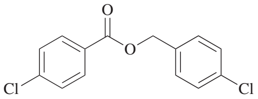
Catalyst(s) (x mol %)



Catalyst(s)	x	Additive	Solvent(s)	Temp	Time (h)		Refs.
NaH	5	—	toluene	95°	18	(88)	139
BnSH, PhMgBr	10,10	—	THF	65°	18	(94)	144
Bn_2Se_2, Bu_2Mg	2,5, 1.25	3 Å MS	THF	rt	24	(99)	146
$Cp^{*}_{2}ThMe_2$	1	—	C_6D_6	rt	48	(57)	188
$Th(NEtMe)_4$	1	—	C_6D_6	rt	48	(96)	187
$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24	(95)	187

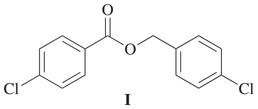


Catalyst(s) (x mol %)



Catalyst(s)	x	Additive	Solvent(s)	Temp (°)	Time (h)		Refs.
Na	"cat."	—	THF	rt, 50–55	1, 3	(60)[m]	342
Na	"cat."	—	THF	55	5	(60)	342
LiBr	50	—	Et_3N	rt	48	(80)	45
NaH	10	—	—	high-speed ball milling, rt	0.5	(92)	336
NaH	5	—	toluene	rt	18	(95)	139
KH	2	18-c-6 (2 mol %)	C_6H_6	rt	1.5	(92)	140
$KN(SiMe_3)_2$	5	—	toluene	60	2	(86)	140
KO*t*-Bu	2	—	toluene	rt	18	(94)	140
KO*t*-Bu	2	—	toluene	80	1	(94)	140
BnSH, PhMgBr	10, 10	—	THF	65	12	(92)	144
124	1	—	toluene	60	2	(74)	165
$Na_2Fe(CO)_4$	3	—	THF	rt	20	(90)	54
$K_2Fe(CO)_4$	30	18-c-6	THF	60	4	(69)	62
115	1	K_2CO_3	MeCN	rt	13	(93)	68
118	0.02	HCO_2H	—	100	5	(75)	59
129c	5	—	none	80	12 h	(98)	341
133	1	—	THF	rt	24 h	(73)	339
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(22)	73
$Cp^{*}_{2}LaCH(SiMe_3)_2$	1	—	C_6H_6	rt	48	(89)	71
EtNdI[l]	100	—	THF	65	20	(40)	69
$Sm[N(SiMe_3)_2]_3$	2.5	—	hexane/toluene	—	24	(85)	194
$La[N(SiMe_3)_2]_3$	5	—	—	21	24	(47)	74
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	20	12	(64)	334
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	60	2	(74)	334
$Cp^{*}_{2}ThMe_2$	1	—	C_6D_6	rt	48	(60)	188
$Th(NEtMe)_4$	1	—	C_6D_6	rt	48	(97)	187
$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24	(98)	187
$[SBA\text{–}15]Sm[N(SiMe_3)_2]_x$	2.5	—	hexane/toluene	—	24	(82)	194

Ce/Hg amalgam,
$C_6H_5CH_2I$, 0°, 2 h



I

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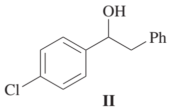


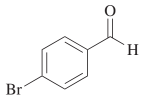
II

I + **II** (77), **I**/**II** = 55:45

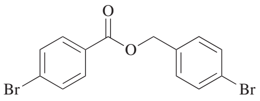
343

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

C_7

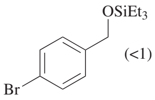


Catalyst (*x* mol %)



Catalyst	*x*	Additive(s)	Solvent(s)	Temp (°)	Time (h)		
LiBr	50	—	Et_3N	rt	48	(97)	45
NaH	10	—	—	high speed ball milling, rt	2	(91)	336
NaH	5	—	toluene	rt	18	(93)	139
KH	1	18-c-6 (1 mol %)	toluene	rt	0.33	(95)	140
$KN(SiMe)_2$	3	—	toluene	60	2	(85)	140
KO*t*-Bu	2	—	toluene	rt	1.5	(93)	140
$Ca[N(SiMe_3)_2]_2(thf)_2$	5	—	C_6H_6	rt	24	(70)	51
124	1	—	toluene	60	2	(90)	165
115	1	K_2CO_3	MeCN	rt	18	(89)	68
129c	5	—	none	80	12	(98)	341
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20	(74)	328
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(16)	73
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	20	12	(57)	334
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	60	2	(81)	334
$La[N(SiMe_3)_2]_3$	5	—	—	21	24	(71)	74

Et_3SiH, KO_2 (14 mol %),
18-c-6 (7 mol %), 40°, 30 min



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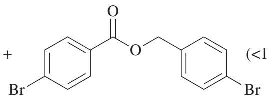

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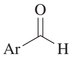
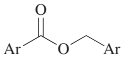
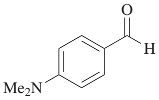


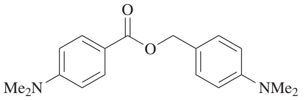
Catalyst (*x* mol %)



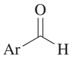
Ar	Catalyst	*x*	Additives	Solvent	Temp	Time (h)		
2-F-6-ClC_6H_3	$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80°	20	(80)	328
2-Cl-6-FC_6H_3	$Ca[N(SiMe_3)_2]_2(thf)_2$	5	—	C_6H_6	rt	96	(40)	51



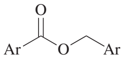
Catalyst (*x* mol %)



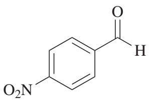
Catalyst	*x*	Solvent	Temp	Time (h)		
Na	10	hexane[a]	"heat"	12	(86)	43
$La[N(SiMe_3)_2]_3$	5	—	21°	24	(35)	74



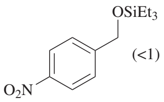
Catalyst (*x* mol %)



Ar	Catalyst	*x*	Additive	Solvent	Temp	Time (h)		
2-$O_2NC_6H_4$	$Al(OEt)_3$	"cat."	—	C_6H_6	—	—	(—)	5, 3
2-$O_2NC_6H_4$	$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24	(—)	187
3-$O_2NC_6H_4$	$Al(OEt)_3$	"cat."	—	C_6H_6	—	—	(—)	5, 3
3-$O_2NC_6H_4$	$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24	(98)	187
4-$O_2NC_6H_4$	$LiWO_2$	20	—	THF	60°	72	(77)	225
4-$O_2NC_6H_4$	$NaNH_2$	60	Me_2SO_2 (50 mol %)	DMF	rt	24	(55)	201
4-$O_2NC_6H_4$	$Al(OEt)_3$	"cat."	—	C_6H_6	—	—	(—)	5, 3
4-$O_2NC_6H_4$	BnSH, PhMgBr	10, 10	—	THF	65°	18	(90)	144
4-$O_2NC_6H_4$	**115**	1	K_2CO_3	MeCN	rt	18	(88)	68
4-$O_2NC_6H_4$	**133**	1	—	THF	rt	24	(76)	339
4-$O_2NC_6H_4$	$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	20°	12	(51)	334
4-$O_2NC_6H_4$	$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	6	(51)	187



Et_3SiH, KO_2 (14 mol %),
18-c-6 (7 mol %), 40°, 30 min



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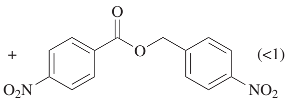

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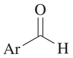
TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

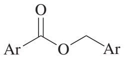
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

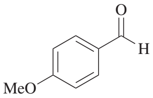
C_7



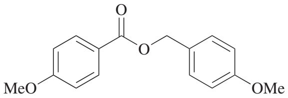
Catalyst (*x* mol %)



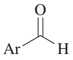
Ar	Catalyst	*x*	Additive(s)	Solvent	Temp (°)	Time (h)		Refs.
2-$MeOC_6H_4$	Na	"cat."	—	THF	rt, 50–55	1, 3	(65)	342
2-$MeOC_6H_4$	Na	"cat."	—	THF	85	100	(65)	342
2-$MeOC_6H_4$	BnSH, PhMgBr	20, 20	—	THF	65	96	(56)	144
2-$MeOC_6H_4$	$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20	(75)	328
3-$MeOC_6H_4$	LiBr	50	—	Et_3N	rt	48	(95)	45
3-$MeOC_6H_4$	$Ca[N(SiMe_3)_2]_2(thf)_2$	3	—	C_6H_6	rt	24	(72)	51



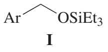
Catalyst(s) (*x* mol %)



Catalyst(s)	*x*	Additive(s)	Solvent	Temp (°)	Time		Refs.
$LiWO_2$	5	—	THF	60	3 d	(32)	225
$LiWO_2$	20	—	THF	60	3 d	(31)	225
Na	10	—	hexane[a]	"heat"	8 h	(88)	43
NaH	10	—	—	high-speed ball milling, rt	16 h	(97)	336
NaH	5	—	toluene	95	18 h	(94)	139
KH	1	18-c-6 (1 mol %)	C_6H_6	rt	2.5 h	(97)	140
KO*t*-Bu	2	—	toluene	rt	24 h	(92)	140
BnSH, PhMgBr	20, 20	—	THF	65	2 d	(92)	144
Bn_2Se_2, Bu_2Mg	10, 5	3 Å MS	THF	rt	24 h	(91)	146
$Ca[N(SiMe_3)_2]_2(thf)_2$	5	—	C_6H_6	rt	4 d	(10)	51
$Na_2Fe(CO)_4$	3	—	—	rt	50 h	(0)	54
$Na_2Fe(CO)_4$	3	—	—	60	20 h	(76)	54
$K_2Fe(CO)_4$	20	18-c-6	THF	60	45 h	(8)	62
129c	5	—	none	80	12 h	(75)	341
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(88)	328
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(95)[n]	328
$[RuCl_2(p\text{-cym})]_2$	1.25	Cy_2PPh (2.5 mol %), HCO_2Na	dioxane	80	20 h	(59)[n]	328
124	1	—	toluene	60	2 h	(<1)	165
124	5	—	toluene	60	2 h	(83)	165
124	5	—	toluene	60	4 h	(86)	165
$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(—)	320
118	0.02	HCO_2H	—	100	24 h	(50)	59
$Ni(cod)_2$, IPrCl	2, 2	—	toluene	60	2 h	(95)	177
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(0)	73
$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	60	2 d	(95)	71
$La[N(SiMe_3)_2]_3$	5	—	—	21	24 h	(86)	74
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	20	12 h	(80)	334
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	60	2 h	(90)	334
EtNdI[l]	100	—	THF	65	20 h	(11)	69
$Me_2SiCp''{}_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_5CD_3$	rt	24 h	(39)	187
133	1	—	none	80	4 H	(74)	339



Et_3SiH (*x* eq), KO_2 (*y* mol %), 18-c-6 (7 mol %)



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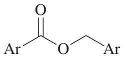


II

199

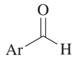
Ar	*x*	*y*	Solvent	Temp (°)	Time (h)	**I**	**II**
2-$MeOC_6H_4$	—	14	—	40	0.5	(86)	(0)
3-$MeOC_6H_4$	—	14	—	40	0.5	(1)	(2)
4-$MeOC_6H_4$	—	14	—	40	0.5	(90)	(0)
4-$MeOC_6H_4$	1	7	benzene	rt	20	(62)	(16)
4-$MeOC_6H_4$	1	14	benzene	rt	20	(72)	(28)
4-$MeOC_6H_4$	1	14	benzene	40	1	(75)	(25)
4-$MeOC_6H_4$	1	14	benzene	40	1	(86)	(14)
4-$MeOC_6H_4$	1.5	14	benzene	40	1	(100)	(0)
4-$MeOC_6H_4$	1.5	14	THF	40	1	(100)	(0)
4-$MeOC_6H_4$	1.5	14	hexane	40	1	(95)	(5)

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

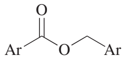
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

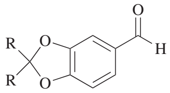
C_7



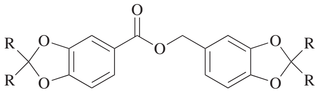
Catalyst (*x* mol %)



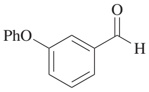
Ar	Catalyst	*x*	Solvent(s)	Temp (°)	Time (h)		Refs.
2,3-$(MeO)_2C_6H_3$	$Sm[N(SiMe_3)_2]_3$	2.5	hexane/toluene	—	24	(10)	194
2,3-$(MeO)_2C_6H_3$	$[SBA\text{–}15]Sm[N(SiMe_3)_2]_x$	2.5	hexane/toluene	—	24	(5)	194
3,4-$(MeO)_2C_6H_3$	Na	10	hexane[a]	"heat"	10	(95)	43



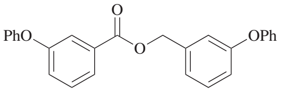
Catalyst (*x* mol %)



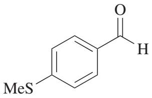
R	Catalyst	*x*	Additives	Solvent(s)	Temp (°)	Time (h)		Refs.
H	Na	10	—	hexane[a]	"heat"	10	(92)	43
F	$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20	(73)	328



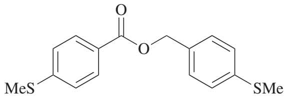
Cat. **118** (*x* mol %), HCO_2H, 100°



x	Time (h)		Refs.
0.02	7	(60)	59
0.1	3.5	(95)	

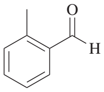


Catalyst (*x* mol %)

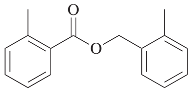


Catalyst	*x*	Additive	Solvent	Temp (°)	Time (h)		Refs.
NaH	10	—	—	high-speed ball milling, rt	2	(93)	336
115	1	K_2CO_3	MeCN	rt	18	(89)	68
$La_2(t\text{-}Bu_2pz)_6$	5	—	C_6D_6	21	—	(0)	73
$La[N(SiMe_3)_2]_3$	5	—	—	21	24	(84)	74

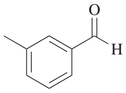
C_8



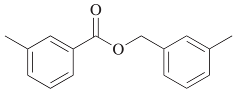
Catalyst (*x* mol %)



Catalyst	*x*	Solvent	Temp	Time		Refs.
BnSH, PhMgBr	20, 20	THF	65°	4 d	(87)	144
$Rh[PhBP_3]H_2(MeCN)$	1	toluene	rt	10 min	(81)	320
$Cp^*_2ThMe_2$	1	C_6D_6	rt	48 h	(10)	188
$Th(NEtMe)_4$	1	C_6D_6	rt	48 h	(55)	188
$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	C_6D_6 or $C_6D_6CD_3$	rt	24 h	(70)	187



Catalyst (*x* mol %)



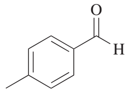
Catalyst	*x*	Solvent	Temp	Time		Refs.
LiBr	50	Et_3N	rt	2 d	(81)	45
NaH	10	—	high-speed ball milling, rt	2 h	(86)	336
$Cp^*_2ThMe_2$	1	C_6D_6	rt	2 d	(20)	188
$Th(NEtMe)_4$	1	C_6D_6	rt	2 d	(75)	188
$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	C_6D_6 or $C_6D_6CD_3$	rt	24 h	(94)	187

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

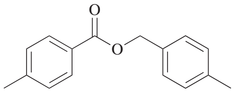
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_7

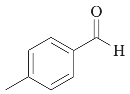


Catalyst (x mol %)

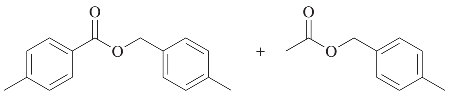


Catalyst	x	Additive(s)	Solvent(s)	Temp (°)	Time		Refs.
Li_3N	"cat."	—	CCl_4	"heat"	—	(55)	40
$LiWO_2$	5	—	THF	60	3 d	(79)	225
$LiWO_2$	20	—	THF	60	3 d	(40)	225
Na	10	—	hexane[a]	"heat"	5 h	(88)	43
NaH	10	—	—	high-speed ball milling, rt	2 h	(69)	336
NaH	5	—	toluene	rt	18 h	(85)	139
$Na_2Fe(CO)_4$	3	—	THF	rt	50 h	(73)	54
$K_2Fe(CO)_4$	20	18-c-6	THF	60	4 h	(14)	62
115	1	K_2CO_3	MeCN	rt	22 h	(97)	68
129c	5	—	none	80	12 h	(88)	341
133	1	—	none	80	4 h	(86)	339
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(87)	328
$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(75)	320
$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	60	2 d	(88)	71
EtNdI[l]	100	—	THF	65	20 h	(40)	69
$Sm[N(SiMe_3)_2]_3$	2.5	—	hexane/toluene	—	24 h	(82)	194
$[SBA\text{–}15]Sm[N(SiMe_3)_2]_x$	2.5	—	hexane/toluene	—	24 h	(78)	194
$La[N(SiMe_3)_2]_3$	5	—	—	21	24 h	(78)	74
$Cp^*{}_2ThMe_2$	1	—	C_6D_6	rt	2 d	(25)	188
$Th(NEtMe)_4$	1	—	C_6D_6	rt	2 d	(82)	188
$Me_2SiCp''{}_2Th(n\text{-Bu})_2$	1	—	C_6D_6 or $C_6D_6CD_3$	rt	24 h	(74)	187

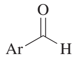
C_8



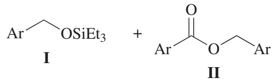
1. $Na_2Fe(CO)_4$, THF, rt, 6 h
2. MeI, 6 h



I **I + II** (80), **I/II** 88:12 **II** 54



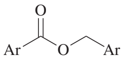
Et_3SiH, KO_2 (14 mol %), 18-c-6 (7 mol %), 40°, 30 min



I + **II**

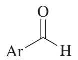
Ar	**I**	**II**	Refs.
2-MeOC_6H_4	(<1)	(<1)	199
3-MeOC_6H_4	(56)	(32)	

Catalyst(s) (x mol %)

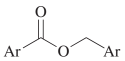


Ar	Catalyst(s)	x	Additive(s)	Solvent	Temp (°)	Time		Refs.
$2\text{-CF}_3C_6H_4$	$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(82)	328
$3\text{-CF}_3C_6H_4$	$Ca[N(SiMe_3)_2]_2(thf)_2$	3	—	C_6H_6	rt	24 h	(87)	51
$4\text{-CF}_3C_6H_4$	$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(65)	328
$4\text{-CF}_3C_6H_4$	$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(92)	320
$4\text{-CF}_3C_6H_4$	$Ni(cod)_2$, IPrCl	10,10	—	toluene	60	4 h	(82)	177
$4\text{-CF}_3C_6H_4$	**119**	—	t-BuOK	THF	–70 to rt	—	(40)	202

C_{8-13}

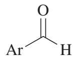


Catalyst(s) (x mol %)

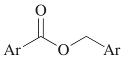


Ar	Catalyst(s)	x	Additive	Solvent	Temp (°)	Time (h)		Refs.
4-NCC_6H_4	$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	rt	1	(96)	71
4-NCC_6H_4	$La[N(SiMe_3)_2]$	5	—	—	21	24	(80)	74
4-NCC_6H_4	$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	20	12	(76)	334
4-NCC_6H_4	$Me_2SiCp''{}_2Th(n\text{-Bu})_2$	1	—	C_6D_6 or $C_6D_5CD_3$	rt	24	(98)	187
$4\text{-MeO}_2CC_6H_4$	$Ni(cod)_2$, IPrCl	2, 2	—	toluene	80	3	(99)	177
$3\text{-CH}_2\text{=CHC}_6H_4$	Bn_2Se_2, Bu_2Mg	5, 2.5	3 Å MS	THF	rt	24	(93)	146
4-PhC_6H_4	NaH	5	—	toluene	95	18	(93)	139
4-PhC_6H_4	$Ca[N(SiMe_3)_2]_2(thf)_2$	2.5	—	C_6H_6	rt	24	(74)	51

C_{9-15}



$Ni(cod)_2$ (x mol %), IPrCl (x mol %), toluene



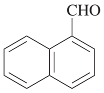
Ar	x	Temp (°)	Time (h)		Refs.
$2,4\text{-Me}_2C_6H_3$	1	60	3	(99)	177
$3,5\text{-Me}_2C_6H_3$	1	60	3	(99)	
$2,4,6\text{-Me}_3C_6H_2$	3	60	24	(84)	
$3,5\text{-}(t\text{-Bu})_2C_6H_3$	2	80	2	(99)	

TABLE 1D. TISHCHENKO REACTIONS OF AROMATIC ALDEHYDES (*Continued*)

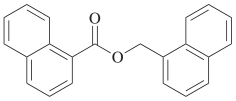
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

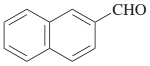
C_{11}



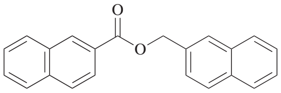
Catalyst(s) (*x* mol %), THF, rt



Catalyst(s)	*x*	Additive	Time (h)		Refs.
Bn_2Se_2, Bu_2Mg	5, 2.5	3 Å MS	24	(84)[o]	146
$Na_2Fe(CO)_4$	3	—	40	(72)	54



Catalyst(s) (*x* mol %), THF, rt



Catalyst(s)	*x*	Solvent	Temp (°)	Time (h)		Refs.
LiBr	50	Et_3N	rt	48	(92)	45
NaH	10	—	high-speed ball milling, rt	16	(91)	336
$Ni(cod)_2$, IPrCl	3, 3	toluene	60	2	(82)	17
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	toluene	60	2	(76)	334

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[a] The solvent contained 1 mol % of biphenyl. Without biphenyl the reaction took a longer time to reach completion.

[b] The temperature was raised to 80° gradually over 45 minutes.

[c] In this procedure 5 mol % of NaH was used. When a stoichiometric amount of NaH was used, the reaction gave a yield of 87%.

[d] The catalyst was prepared by dissolving metallic sodium in the corresponding alcohol.

[e] The product was a mixture of several compounds, and the Tishchenko product was present only when a substoichiometric amount of C_8K was used.

[f] Benzyl benzoate was the major product but no yield was determined.

[g] The metal oxide was ^{18}O-enriched.

[h] The product also contained ^{18}O-enriched benzyl benzoate.

[i] The reactions were monitored by ^1H NMR spectroscopy with (*E*)-stilbene as internal standard

[j] The catalyst was $Al(OBn)_3$ alone.

[k] The catalyst was recycled from the previous entry.

[l] The catalyst was prepared in situ.

[m] When THF was omitted the yield was 50%.

[n] The number is the conversion.

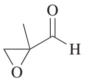
[o] The yield was determined by ^1H NMR spectroscopy using an internal standard.

TABLE 1E. TISHCHENKO REACTIONS OF HETEROCYCLIC ALDEHYDES

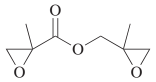
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_4

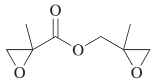


NaH (cat.), benzene,
20°, 30 h



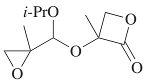
(—) 210

Al(O*i*-Pr)₃ (*x* mol %),
benzene, 20°, 120 h



I

+

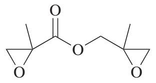


II

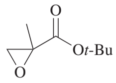
x	**I/II**[a]
2.5	58:42
5	13:78
7.5	7:93
10	5:95

210

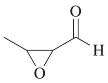
Al(O*t*-Bu)$_3$ (2.5 mol %),
benzene, 20°, 100 min



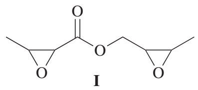
(14) +



(4) 344

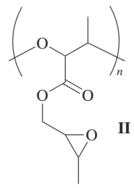


Al(O*i*-Pr)$_3$, (*x* mol %)



I

+



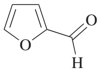
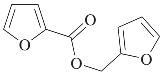
II

Temp (°)	*x*	Time (d)	**I**	**II**	Refs.
20	0.10	15	(—)	(—)	208
20	0.22	15	(33)	(13)	
20	0.50	15	(48)	(38)	
20	0.50	21	(—)	(—)	
20	0.50	45	(—)	(—)	
20	0.50	125	(37)	(62)	
20	1.02	15	(36)	(58)	
50	0.25	6.7	(35)	(19)	
50	0.50	6.7	(47)	(33)	
50	0.50	21	(43)	(57)	
50	0.50	45	(22)	(78)	
50	1.03	6.7	(33)	(64)	

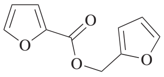
TABLE 1E. TISHCHENKO REACTIONS OF HETEROCYCLIC ALDEHYDES (*Continued*)

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

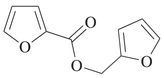
C_5

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst(s) (x mol %)		

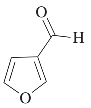
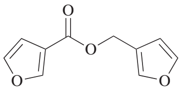
Catalyst(s)	x	Additive(s)	Solvent(s)	Temp (°)	Time		
Na	10	—	hexane[b]	"heat"	15 h	(82)	43
NaH	10	—	—	high-speed ball milling, rt	2 h	(69)	336
NaH	10	—	toluene	95	18 h	(74)	139
2-furylCH_2ONa[c]	—	—	C_6H_6	heat[d]	—	(78)	135
NaOPh[e]	"cat."	—	C_6H_6	"heat"	—	(—)[f]	42
KH	5	—	toluene	80	1.2 h	(83)	140
KO*t*-Bu	5	—	toluene	80	1.5 h	(79)	140
$Al(OEt)_3$	5	—	CCl_4	25	24 h	(13)	17
$Na_2Fe(CO)_4$	20	—	THF	25	20 h	(0)	54
$K_2Fe(CO)_4$	33	18-c-6	THF	60	24 h	(3)	62
Bn_2Se_2, Bu_2Mg_2	20, 10	3 Å MS	THF	60	24 h	(63)	146
118	0.1	HCO_2H (10 mol %)	—	100	6 h	(80)	59
129c	5	—	none	80	12 h	(35)	341
Rh(η^3-$CH_2C(O)Ph$)$(PPh_3)_2$	1	—	C_6D_6	rt	1 h	(13)	64
Rh(η^3-$CH_2C(O)Ph$)$(PPh_3)_2$	2	—	C_6D_6	rt	1 h	(45)	64
Rh(η^3-$CH_2CH{=}CH_2$)$(PPh_3)_2$	1	H_2	C_6D_6	rt	—	(97)	64
$Rh[PhBP_3]H_2(MeCN)$	1	—	toluene	rt	10 min	(91)	320
$Ni(cod)_2$, IPrCl	2, 2	—	toluene	60	4 h	(62)	177
$[RuCl_2(p\text{-cym})]_2$	1.25	$CyPPh_2$ (2.5 mol %), HCO_2Na	dioxane	80	20 h	(45)	328
$Sm[N(SiMe_3)_2]_3$	2.5	—	hexane/toluene	—	24 h	(45)	194
$La[N(SiMe_3)_2]_3$	1	—	—	21	24 h	(36)	74, 72
$Cp^*{}_2LaCH(SiMe_3)_2$	1	—	C_6H_6	60	3 d	(77)	71, 70
$Yb_2Na_8(OCH_2CH_2NMe_2)_{12}(OH)_2$	1	—	toluene	60	12 h	(39)	334
112	0.5	—	C_6D_6	rt	120 h	(45)	184
112	0.5	—	C_6D_6	60	16 h	(79)	184
$Me_2SiCp''_2Th(n\text{-}Bu)_2$	1	—	C_6D_6 or $C_6D_5CD_3$	60	48 h	(42)	187
$[SBA\text{–}15]Sm[N(SiMe_3)_2]_x$	2.5	—	hexane/toluene	—	24 h	(30)	194

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	See table.		77

Metal Oxide	Temp (°)	Time (h)	
MgO	80	4	(<1)
CaO	80	4	(61)
CaO	80	6	(78)
SrO	80	4	(83)
SrO	80	6	(95)
SrO	50	12	(70)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Metal oxide, 80°, 4 h	 (0)	77

Metal Oxide	Metal Oxide
BaO	hydrotalcite (Mg/Al = 2)
La_2O_3	KF-Al_2O_3
ZrO_2	KOH-Al_2O_3
γ-Al_2O_3	

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	Metal oxide (cat.), 262°, 4 h		345

Metal Oxide	
MgO	(10)
CaO	(36)
SrO	(90)
BaO	(3)

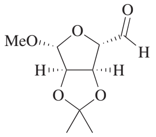
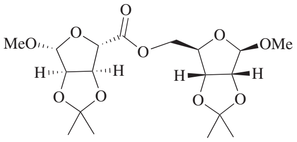
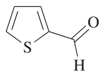
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	DIBAL-H (10 mol %), pentane, 0° to rt, 8 h	 (71)	157, 156

TABLE 1E. TISHCHENKO REACTIONS OF HETEROCYCLIC ALDEHYDES (*Continued*)

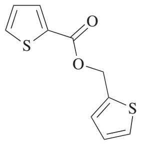
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_5

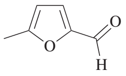
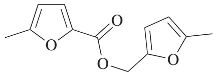


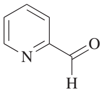
Catalyst(s) (x mol %)



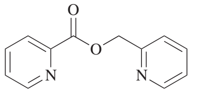
Catalyst(s)	x	Additive	Solvent	Temp (°)	Time (h)		
LiBr	50	—	Et_3N	rt	48	(66)	45
NaH	10	—	—	high-speed ball milling, rt	2	(70)	336
NaH	5	—	toluene	95	18	(78)	139
KO*t*-Bu	2	—	toluene	rt	24	(88)	140
Bn_2Se_2, Bu_2Mg	5, 2.5	3 Å MS	THF	rt	24	(96)	146
112	0.5	—	C_6D_6	rt	120	(88)	184
114	0.5	—	C_6D_6	rt	120	(77)	184
114	0.5	—	C_6D_6	60	16	(88)	184
$Cp^*_2LaCH(SiMe_3)_2$	1	—	C_6H_6	60	72	(100)	71, 70
$Cp^*_2NdCH(SiMe_3)_2$	1	—	C_6H_6	60	72	(31)	71, 70
119	—	*t*-BuOK	THF	–70 to rt	—	(45)	202

C_6

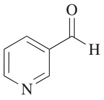
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	$La[N(SiMe_3)_2]_3$ (5 mol %), C_6D_6, 21°, 1 d	 (28)	74



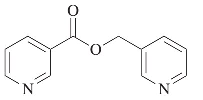
Catalyst (x mol %)



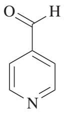
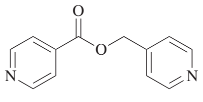
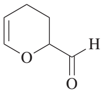
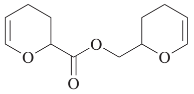
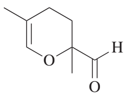
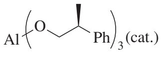
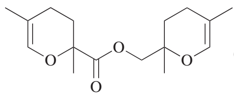
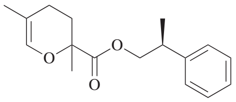
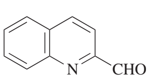
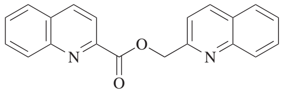
Catalyst	x	Solvent	Temp (°)	Time (h)		
NaH	10	toluene	95	18	(77)	139
129c	5	none	80	12	(54)	341



Catalyst(s) (x mol %)



Catalyst	x	Additive	Solvent	Temp (°)	Time (h)		
NaH	10	—	toluene	95	18	(88)	139
LiBr	50	—	Et_3N	rt	48	(80)	45
NaH	10	—	—	high-speed ball milling, rt	0.5	(80)	336
Bn_2Se_2, Bu_2Mg	5, 2.5	3 Å MS	THF	rt	24	(95)	146
$La[N(SiMe_3)_2]_3$	5	—	—	21	24	(37)	74

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaH (10 mol %), toluene, 95°, 18 h	 (87)	139
	$Al(Oi\text{-}Pr)_3$ (2 mol %), 35° to rt, 1 d	 (78)	34, 35
C_8			
	 (cat.)	 (—) +  (—)	36
C_{10}			
	NaH (10 mol %), toluene, 95°, 18 h	 (86)	139

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[a] The product was a mixture of two diastereomers whose exact structures were not elucidated.

[b] The solvent contained 1 mol % of biphenyl. Without biphenyl the reaction took a longer time to reach completion.

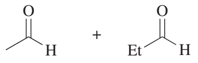
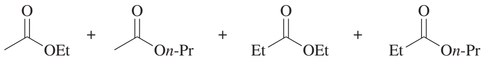
[c] The catalyst was prepared by dissolving metallic sodium in the corresponding alcohol.

[d] Furfural was added gradually into the catalyst solution with no external heating, refluxing was maintained by the developing heat of the reaction.

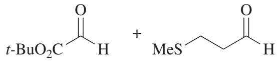
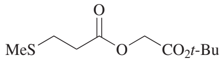
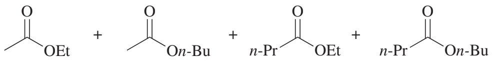
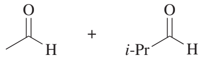
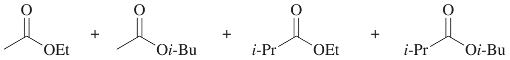
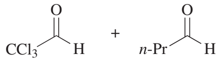
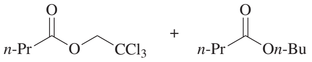
[e] The catalyst was prepared by dissolving anhydrous NaOH in phenol.

[f] No yield or experimental conditions were given in the reference, but a possibility for quantitative isolation was mentioned.

TABLE 1F. TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_2 + C_3$			
	Catalyst (x mol %)	 **I** + **II** + **III** + **IV**	

Catalyst	x	Solvent	Temp (°)	Time (d)	**I–IV**	**I/II/III/IV**	Refs.
$RuH_2(PPh_3)_4$	0.9	vacuum	rt	—	(74)	21:11:40:28	57
$RuCl(SiMe_3)(CO)(PPh_3)_2$	5	C_6D_6	70	3	(70)	35:25:20:20	67

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Rh(dppe)ClO_4$, CH_2=CHCO*t*-Bu, $ClCH_2CH_2Cl$, MeCN, rt, then 70°, 18 h	 (86)	346
$C_2 + C_4$			
	$RuH_2(PPh_3)_4$ (0.4 mol %), vacuum, rt	 **I** + **II** + **III** + **IV** **I–IV** (71), **I/II/III/IV** = 49:21:8:22	57
	$RuH_2(PPh_3)_4$ (0.9 mol %), vacuum, rt	 **I** + **II** + **III** + **IV** **I–IV** (31), **I/II/III/IV** = 24:49:11:16	57
 **I** + **II**	$Al(Oi-Pr)_3$ (2.5 mol %), CCl_4, 0° to rt, 1 d	 **III** + **IV** **I/II** 1:3: **III**[a] (45), **IV** (63) **I/II** 1:1: **III**[a] (45), **IV** (48)	90

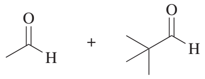
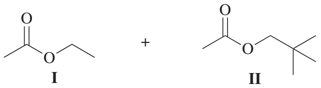
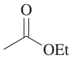
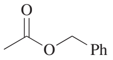
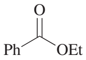
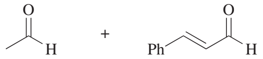
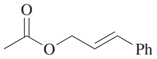
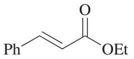
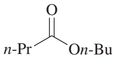
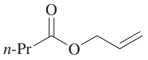
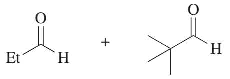
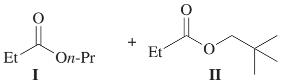
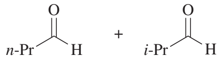
Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_2 + C_5$			
	$RuCl(SiMe_3)(CO)(PPh_3)_2$ (5 mol %), C_6D_6, 70°, 2 d	 **I** + **II** **I** + **II** (100), **I/II** = 62:38	67
$C_2 + C_7$			
 **I** **I/II** = 2:1 **II**	$Al(Oi-Pr)_3$ (2.5 mol %), CCl_4, 0° to rt, 1 d	 (57) +  (57)[b] +  (1)[b]	90
$C_2 + C_9$			
	$Al(OEt)_3$ (cat.), Et_2O, 5 d	 (—) +  (—)	331
$C_3 + C_4$			
 **I** **I/II** = 1:5 **II**	$Al(Oi-Pr)_3$ (2.5 mol %), CCl_4, 0° to rt, 1 d	 (42) +  (66)[c] **III** **IV**	90
$C_3 + C_5$			
	$RuCl(SiMe_3)(CO)(PPh_3)_2$, C_6D_6, 70°, 2 d	 **I** + **II** **I** + **II** (100), **I/II** = 66:34	67

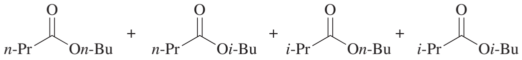
TABLE 1F. TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES (*Continued*)

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.

$C_4 + C_4$



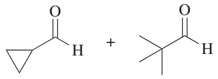
Catalyst (*x* mol %), rt



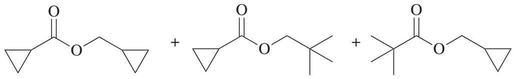
I **II** **III** **IV**

Catalyst	*x*	Solvent	Time (min)	**I–IV**	**I/II/III/IV**	Refs.
$RuH_2(PPh_3)_4$	1.5	vacuum	—	(90)	27:51^{d}:22	57
Cp_2ZrH_2	5	—	30	(76)	21:33:17:29	61
Cp_2ZrClH	5	—	30	(70)	23:33:17:27	61

$C_4 + C_5$



Metal oxide (cat.), 80°, 4 h

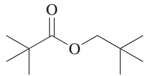


I **II** **III**

79

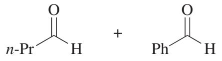
Metal Oxide	**I–IV**	**I/II/III/IV**
MgO	(39)	15:64:3:18
CaO	(58)	12:45:9:34
SrO	(87)	20:34:12:34
BaO	(0)	—

\+

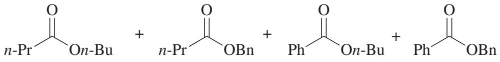


IV

$C_4 + C_7$



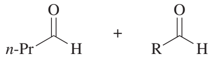
$RuH_2(PPh_3)_4$ (0.7 mol %), vacuum, rt



I **II** **III** **IV**

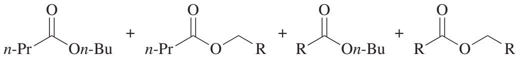
I–IV (48), **I/II/III/IV** = 1:3:22:74

57



I **II**

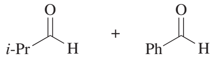
Catalyst (5 mol %), rt, 0.5 h



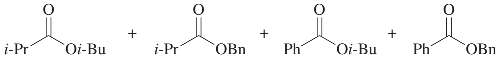
III **IV** **V** **VI**

61

R	**I/II**	Catalyst	**III–VI**	**I/II/III/IV**
Cy	1:1	Cp_2ZrH_2	(66)	15:38:13:34
Cy	1:1	Cp_2ZrClH	(88)	25:43:12:20
Ph	1:1	Cp_2ZrH_2	(58)	38:59:0:3
Ph	1:2	Cp_2ZrH_2	(71)	22:71:3:4
Ph	1:1	Cp_2ZrClH	(58)	44:54:0:2
Ph	1:2	Cp_2ZrClH	(76)	26:71:0:3



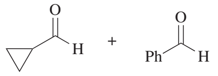
$RuH_2(PPh_3)_4$ (0.7 mol %), vacuum, rt



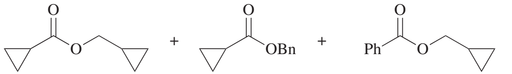
I **II** **III** **IV**

I–IV (44), **I/II/III/IV** = 2:6:36:56

57



Metal oxide (cat.), 80°, 4 h

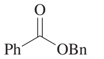


I **II** **III**

79

Metal Oxide	**I– IV**	**I/II/III/IV**
MgO	(37)	16:41:11:32
CaO	(85)	15:19:33:33
SrO	(97)	23:18:34:25
BaO	trace	—

\+

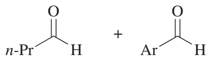


IV

TABLE 1F. TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES (*Continued*)

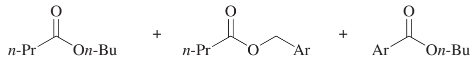
Aldehydes | Conditions | Product(s) and Yield(s) (%) | Refs.

$C_4 + C_{5–9}$



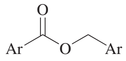
I + **II**

Al(O*i*-Pr)$_3$ (2.5 mol %), CCl_4, 0° to rt, 1 d



III + **IV** + **V**

Ar	**I/II**	**III**	**IV**	**V**	**VI**
2-furyl	1:1	(26)	(32)	(1)	(—)
Ph	2.5:1	(68)	(70)^b	(5)^b	(47)^e
3-$O_2NC_6H_4$	2.9:1	(70)	(68)^f	(10)^f	(—)
PhCH=CH	4.1:1	(69)	(59)^g	(—)	(—)

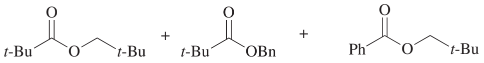
+ 

VI

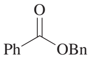
Refs. 90

$C_5 + C_7$

Catalyst, 80°, 4 h



I + **II** + **III**

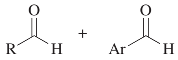
+ 

IV

Catalyst	**I–IV**	**I/II/III/IV**
MgO	(73)	25:16:38:21
CaO	(98)	23:27:29:21
SrO	(100)	23:34:24:19
BaO	(~7)	14:43:29:14
La_2O_3	(<3)	—
ZrO_2	(0)	—
ZnO	(0)	—
γ-Al_2O_3	(<3)	—
hydrotalcite	(<3)	—
KF / Al_2O_3	(<4)	—
KOH / Al_2O_3	(0)	—

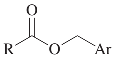
Refs. 79

$C_{5–7} + C_7$



1:1

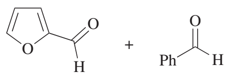
4-*t*-Bu$C_6H_4CH_2SH$ (20 mol %), Bu_2Mg (10 mol %), THF, 65°



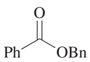
R	Ar	Time (h)	
t-Bu	2-BrC_6H_4	24	(63)
t-Bu	2-Br-4-PhSC_6H_3	24	(62)
2-furyl	2-MeOC_6H_4	24	(16)^h
2-thienyl	2-MeOC_6H_4	24	(38)^h
3-thienyl	2-MeOC_6H_4	24	(71)
3-thienyl	2-Br-5-MeOC_6H_3	24	(95)
3-thienyl	2-Br-4,5-(MeO)$_2C_6H_2$	24	(99)
4-pyridyl	2-MeOC_6H_4	36	(63)
4-pyridyl	2-Br-5-FC_6H_3	24	(69)
4-pyridyl	2-TsO-5-BrC_6H_3	24	(72)
c-C_6H_{11}	2-BrC_6H_4	24	(58)^i

Refs. 147

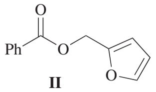
$C_5 + C_7$



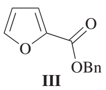
Catalyst (2.5 mol %), hexane, 48 h



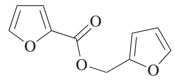
I

+ 

II

+ 

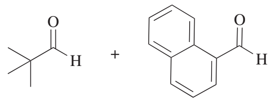
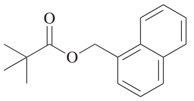
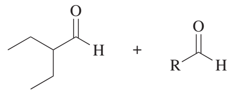
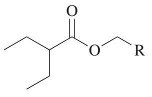
III

+ 

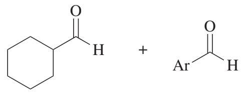
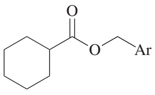
IV

Catalyst	Cosolvent	**I–IV**	**I/II/III/IV**
Sm[N(SiMe_3)$_2$]$_3$	toluene	(—)	33:36:17:14
[SBA–15]Sm[N(SiMe_3)$_2$]	none	(—)	27:53:7:13

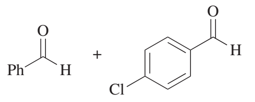
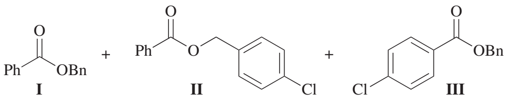
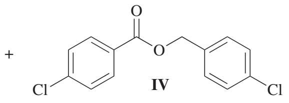
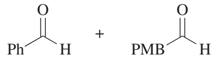
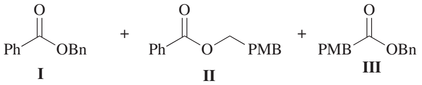
Refs. 194

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_5 + C_{11}$			
	$Ni(cod)_2$ (10 mol %), SIPr (10 mol %), toluene, rt, 12 h	 (65)	178
$C_6 + C_{11–15}$			
	$Ni(cod)_2$ (*x* mol %), SIPr (*x* mol %), toluene		178

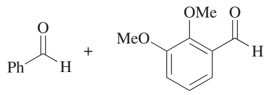
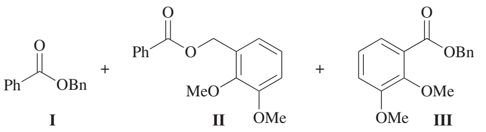
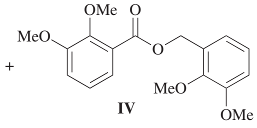
R	*x*	Temp	Time (h)	
1-naphthyl	10	rt	12	(65)
3,5-(*t*-Bu)$_2C_6H_3$	4	40°	4	(83)

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_{7–15}$			
	$Ni(cod)_2$ (*x* mol %), SIPr (*x* mol %), toluene		178

Ar	*x*	Temp (°)	Time (h)	
Ph	2	40	4	(84)
4-MeOC_6H_4	2	40	4	(82)
2,4-$Me_2C_6H_3$	4	40	4	(88)
3,5-$Me_2C_6H_3$	2	40	4	(85)
2,4,6-$Me_3C_6H_2$	4	40	4	(57)
1-naphthyl	2	50	2	(47)
2-naphthyl	4	50	2	(83)
3,5-(*t*-Bu)$_2C_6H_3$	2	40	4	(81)

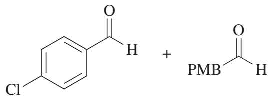
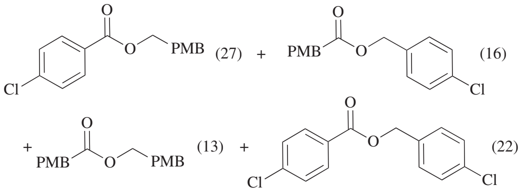
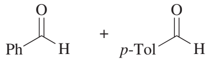
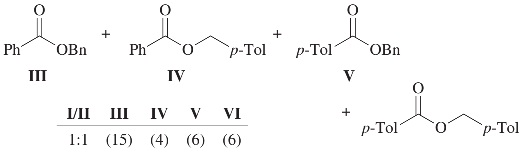
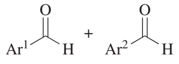
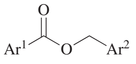
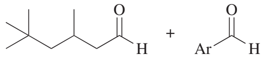
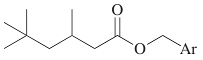
Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_7$			
	Al(O*i*-Pr)$_3$ (cat.), benzene, 20°	  **I–IV** (48) **I/II/III/IV =** 23:30:19:28	30
	Catalyst (*x* mol %)		

Catalyst	*x*	Solvent	Temp (°)	Time (h)	**I + II + III**	**I/II/III**	
Al(O*t*-Bu)$_3$	"cat."	C_6H_6	20	—	(60)	63:37:trace	30
$Na_2Fe(CO)_4$	6	THF	25	40	(56)	61:0:39	54

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst (2.5 mol %), hexane, toluene, 48 h	 	194

Catalyst	**I–IV**	**I/II/III/IV**
Sm[N(SiMe_3)$_2$]$_3$	(—)	49:51:0.3:0
[SBA–15]Sm[N(SiMe_3)$_2$]$_x$	(—)	33:67:0:0

TABLE 1F. TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES (*Continued*)

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_7$			
	4-*t*-$BuC_6H_4CH_2SH$ (20 mol %), Bu_2Mg (10 mol %), THF, 65°		147
$C_7 + C_8$			
 **I** **II**	$Cp^*{}_2ThMe_2$ (1 mol %), C_6D_6, rt, 48 h	 **III** **IV** **V** **VI**	188
$C_{7-8} + C_{7-8}$			
	4-*t*-$BuC_6H_4CH_2SH$ (20 mol %), Bu_2Mg (10 mol %), THF, 65°, 24 h		147
$C_9 + C_{9-11}$			
	$Ni(cod)_2$ (4 mol %), SIPr (4 mol %), toluene		178

I/II	III	IV	V	VI
1:1	(15)	(4)	(6)	(6)
2:1	(25)	(2)	(5)	(5)
1:2	(9)	(6)	(6)	(6)

Ar^1	Ar^2	
Ph	2-$MeOC_6H_4$	(73)
4-ClC_6H_4	2-ClC_6H_4	(78)
4-ClC_6H_4	2-BrC_6H_4	(94)
4-ClC_6H_4	2-Br-5-$MeOC_6H_3$	(93)
4-ClC_6H_4	2-$MeOC_6H_4$	(88)
4-ClC_6H_4	2-$TsOC_6H_4$	(93)
4-ClC_6H_4	2-$PhSC_6H_4$	(71)
4-ClC_6H_4	2-MeC_6H_4	(64)
4-ClC_6H_4	2-$CF_3C_6H_4$	(80)
4-$MeOC_6H_4$	2-$MeOC_6H_4$	(69)
4-$(EtO)_2CHC_6H_4$	2-Br-5-$BnOC_6H_3$	(92)

Ar	Temp (°)	Time (h)	
2,4-$Me_2C_6H_3$	40	4	(66)
1-naphthyl	50	2	(66)

---

[a] The yield is based on trichloroacetaldehyde.

[b] The yield is based on benzaldehyde.

[c] The yield is based on acrolein.

[d] The number refers to the sum of isomers **II** and **III**, which were not separated.

[e] Only benzyl benzoate was formed when a 1:1 ratio of aldehydes was used.

[f] The yield is based on 3-nitrobenzaldehyde.

[g] The yield is based on cinnamaldehyde.

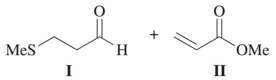
[h] The yield was determined by NMR spectroscopy.

[i] The yield was 72% when 2 equivalents of 2-bromobenzaldehyde were used.

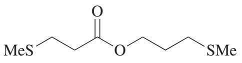
TABLE 1G. TISHCHENKO REACTIONS OF ALDEHYDES WITH MISCELLANEOUS SUBSTRATES

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

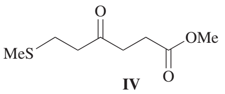
$C_3 + C_3$


I + II

Rh complex (10 mol %), H_2, acetone-d_6


III

+


IV

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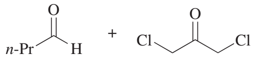
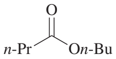
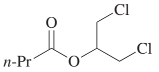
I/II	Rh Complex	Temp (°)	Time (h)	III	IV
1:1	$[Rh(DPEphos)(C_3D_6O)_2][BAr^F{}_4]$	22	20	(7)	(93)
1:1	$[Rh(POP')(C_3D_6O)_2][BAr^F{}_4]$	22	165	(44)	(6)
1:1	$[Rh(Xantphos)(C_3D_6O)_2][BAr^F{}_4]$	22	145	(20)	(10)
1:1	$[Rh(dppe)(C_3D_6O)_2][BAr^F{}_4]$	22	60	(8)	(91)
1:1	$[Rh(dppp)(C_3D_6O)_2][BAr^F{}_4]$	22	10	(62)	(38)
1:1	$[Rh(dppb)(C_3D_6O)_2][BAr^F{}_4]$	22	8	(50)	(50)
1:1	$[Rh(dpppe)(C_3D_6O)_2][BAr^F{}_4]$	22	6	(87)	(13)
1:1	$[Rh(dpppe)(C_3D_6O)_2][BAr^F{}_4]$	40	0.5	(83)	(17)
1:1	$[Rh(dpppe)(C_3D_6O)_2][BAr^F{}_4]$	55	0.1	(81)	(19)
1:5	$[Rh(dpppe)(C_3D_6O)_2][BAr^F{}_4]$	18	15	(46)	(30)

$C_4 + C_3$



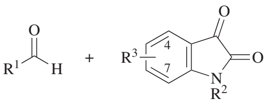
$Al(Oi\text{-}Pr)_3$ (10 mol %), CCl_4, 24–16°, 1 d

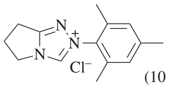

(62) +

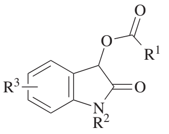

(24)[a]

90

$C_{4-11} + C_{8-10}$




(10 mol %), t-BuOK (20 mol %), toluene, 100°



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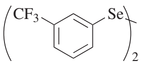
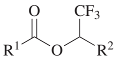
R^1	R^2	R^3	Time (min)		R^1	R^2	R^3	Time (min)	
n-Pr	Bn	H	15	(57)	$2\text{-}FC_6H_4$	Bn	H	30	(79)
2-furyl	Bn	H	15	(81)	$4\text{-}FC_6H_4$	Bn	H	15	(91)
2-thienyl	Bn	H	15	(99)	$2\text{-}ClC_6H_4$	Bn	H	120	(26)
$c\text{-}C_6H_{11}$	Bn	H	15	(69)	$3\text{-}ClC_6H_4$	Bn	H	15	(95)
Ph	H	H	15	(80)	$4\text{-}ClC_6H_4$	Bn	H	15	(86)
Ph	Bz	H	120	complex mixture	$4\text{-}BrC_6H_4$	Bn	H	15	(83)
Ph	Bn	H	15	(93)	$4\text{-}IC_6H_4$	Bn	H	15	(81)
Ph	Bn	5-F	15	(90)	$4\text{-}O_2NC_6H_4$	Bn	H	120	low conversion
Ph	Bn	5-Cl	15	(77)	$3\text{-}MeOC_6H_4$	Bn	H	15	(91)
Ph	Bn	7-Cl	15	(85)	$4\text{-}MeOC_6H_4$	Bn	H	15	(90)
Ph	Bn	5-Me	15	(85)	$4\text{-}MeC_6H_4$	Bn	H	15	(92)
Ph	Bn	7-Me	15	(91)	$4\text{-}NCC_6H_4$	Bn	H	15	(75)
Ph	Bn	$4,6\text{-}Me_2$	120	low conversion	2-Np	Bn	H	15	(92)

$C_{5-11} + C_{5-7}$


(x mol %), Bu_2Mg (y mol %), 3 Å MS, THF, rt, 24 h



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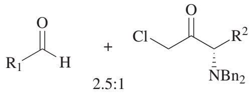
R^1	R^2	x	
2-furyl	Ph	20	(96)
2-thienyl	Ph	10	(95)
3-pyridyl	2-thienyl	20	(56)
3-pyridyl	Ph	20	(80)
3-pyridyl	$4\text{-}FC_6H_4$	20	(63)[b]
Ph	$4\text{-}FC_6H_4$	20	(90)
Ph	$4\text{-}MeC_6H_4$	10	(95)
Ph	$4\text{-}CF_3C_6H_4$	20	(93)
$4\text{-}FC_6H_4$	Ph	20	(87)
$3\text{-}MeOC_6H_4$	Ph	20	(94)
$4\text{-}NCC_6H_4$	Ph	20	(73)
$3\text{-}H_2C{=}CHC_6H_4$	Ph	20	(84)
1-Np	Ph	20	(87)

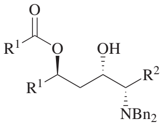
TABLE 1G. TISHCHENKO REACTIONS OF ALDEHYDES WITH MISCELLANEOUS SUBSTRATES (*Continued*)

Substrates | Conditions | Product(s) and Yield(s) (%) | Refs.

$C_{5–14} + C_{4–10}$

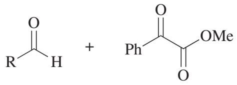


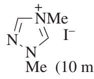
SmI$_2$ (3 eq), THF, –78°, 1 h; to rt



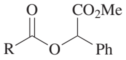
R^1	R^2		dr	Refs.
i-Bu	Me	(81)	2.5:1	244
i-Bu	*i*-Bu	(90)	3:1	
i-Bu	Bn	(90)	1.5:1	
c-C$_6$H$_{11}$	Me	(80)	3:1	
c-C$_6$H$_{11}$	*i*-Bu	(88)	3.5:1	
c-C$_6$H$_{11}$	Bn	(85)	2.5:1	
n-C$_7$H$_{15}$	Me	(80)	2.5:1	
n-C$_7$H$_{15}$	*i*-Bu	(91)	3:1	
n-C$_7$H$_{15}$	Bn	(79)	1.7:1	
n-C$_{13}$H$_{27}$	Me	(83)	2.5:1	

$C_{5–11} + C_8$



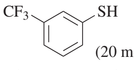


(10 mol %), DBU, CH$_2$Cl$_2$, rt^c

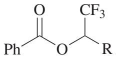


R		Refs.
2-furyl	(73)	196
Ph	(78)	
4-FC$_6$H$_4$	(71)	
4-MeOC$_6$H$_4$	(77)	
4-MeC$_6$H$_4$	(72)	
PhCH$_2$CH$_2$	(0)	
2-Np	(70)	

$C_7 + C_{6–9}$

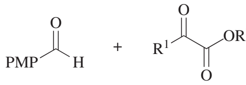


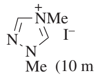
(20 mol %), PhMgBr (20 mol %), THF



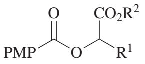
R	Temp (°)	Time		Refs.
2-thienyl	65	40 h	(78)	144
2-thienyl	MW (110)	3 min	(51)^b	145
Ph	MW (110)	3 min	(82)	145
3-FC$_6$H$_4$	MW (110)	3 min	(63)	145
3-FC$_6$H$_4$	65	40 h	(94)	144
4-ClC$_6$H$_4$	65	30 h	(91)	144
4-ClC$_6$H$_4$	MW (110)	3 min	(81)	145
4-BrC$_6$H$_4$	65	30 h	(93)	144
4-BrC$_6$H$_4$	MW (110)	3 min	(81)	145
3-CF$_3$C$_6$H$_4$	65	40	(80)	144

$C_7 + C_{6–12}$



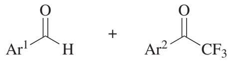


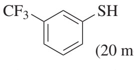
(10 mol %), DBU, CH$_2$Cl$_2$, rt^c



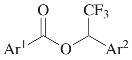
R^1	R^2		Refs.
2-thienyl	Et	(73)	196
Ph	Me	(77)	
4-ClC$_6$H$_4$	Et	(81)	
4-BrC$_6$H$_4$	Et	(87)	
3-MeOC$_6$H$_4$	Et	(72)	
2-Np	Et	(78)	

$C_{7–10} + C_8$



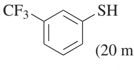


(20 mol %), PhMgBr (20 mol %), THF

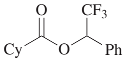


Ar^1	Ar^2	Temp (°)	Time (h)		Refs.
4-FC$_6$H$_4$	Ph	MW (110)	3	(76)	145
3-ClC$_6$H$_4$	Ph	MW (110)	2	(73)	145
3-ClC$_6$H$_4$	Ph	65	24	(87)	144
3-ClC$_6$H$_4$	4-ClC$_6$H$_4$	MW (110)	3	(83)	145
3-O$_2$NC$_6$H$_4$	Ph	65	24	(46)	144
4-MeOC$_6$H$_4$	Ph	65	67	(92)	144
2,4,6-Me$_3$C$_6$H$_2$	Ph	MW (110)	3	(0)	145

$C_7 + C_8$

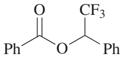


(20 mol %), PhMgBr (20 mol %), MW, THF, 110°, 3 min



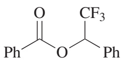
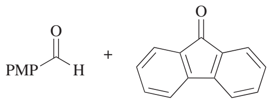
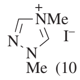
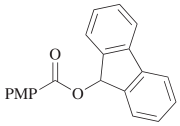
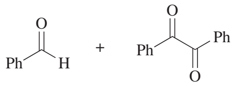
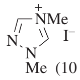
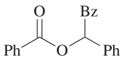
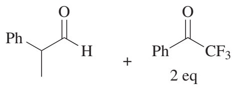
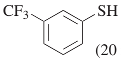
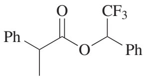
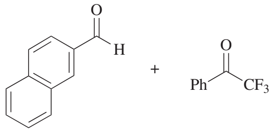
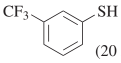
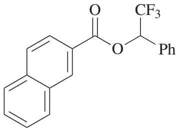
(56) 145

PhMgBr (*x* mol %), RSH, THF, 65°, 24 h



R	*x*	Time (h)		Refs.
Cy	20	4	(6)	144
Cy	20	24	(25)	
4-*t*-BuC$_6$H$_4$CH$_2$	20	4	(11)	
4-*t*-BuC$_6$H$_4$CH$_2$	20	24	(37)	
MeCONH(CH$_2$)$_2$	20	4	(32)	
MeCONH(CH$_2$)$_2$	20	24	(65)	
Ph	20	4	(48)	
Ph	20	24	(90)	
3-CF$_3$C$_6$H$_4$	20	4	(75)	
3-CF$_3$C$_6$H$_4$	20	24	(96)	
3-CF$_3$C$_6$H$_4$	10	90	(91)	

TABLE 1G. TISHCHENKO REACTIONS OF ALDEHYDES WITH MISCELLANEOUS SUBSTRATES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_8$			
	R_2Se_2 (*x* mol %), Bu_2Mg (*y* mol %), 3 Å MS, THF, rt, 24 h	 R, *x*, *y* Ph 10 5 (70) 3-$CF_3C_6H_4$ 10 5 (92) Bn 20 10 (39)	146
$C_7 + C_{13}$			
	 (10 mol %), DBU, CH_2Cl_2, rt[c]	 (0)	196
$C_7 + C_{14}$			
	 (10 mol %), DBU, CH_2Cl_2, rt[c]	 (83)	196
$C_9 + C_8$			
 2 eq	 (20 mol %), PhMgBr (20 mol %), MW, THF, 110°, 3 min	 (34)[d]	145
$C_{11} + C_8$			
	 (20 mol %), PhMgBr (20 mol %), THF	 Temp (°) Time 65 24 h (86) MW, 110 3 min (68)	144 145

[a] The yield is based on 1,3-dichloroacetone.

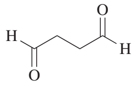
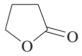
[b] The yield was determined by ^1H NMR spectroscopy.

[c] The reaction times given for the series was 9 h or until TLC showed complete consumption of the aldehyde.

[d] The product was a 4:1 mixture of diastereomers.

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS

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

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	Catalyst (*x* mol %)		

Catalyst	*x*	Solvent	Temp (°)	Time (h)		Refs.
$[Rh(dppe)(acetone)_2]ClO_4$	2	Me_2CO	34	—	(—)	348
$[Rh(dcpe)(acetone)_2]ClO_4$	2	Me_2CO	34	—	(—)	348
$RuHCl(CO)(PPh_3)_3$	1	toluene	110	5	(40)[a]	167

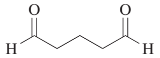
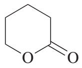
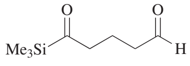
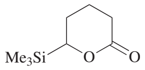
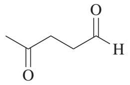
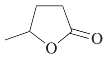
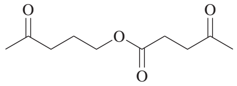
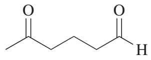
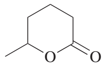
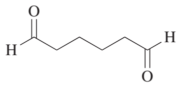
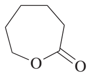
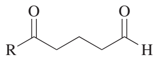
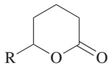
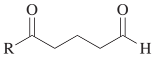
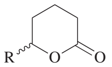
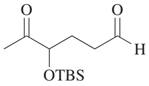
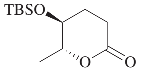
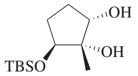
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	$RuHCl(CO)(PPh_3)_3$ (5 mol %), toluene, 90°, 10 h	 (70)[a]	167
	SmI_2, MeOH, THF, rt , 5 min	 (79)	183
	$RuHCl(CO)(PPh_3)_3$ (10 mol %), toluene, 120°, 40 h	 (32) +  (55)	167
C_6			
	SmI_2Ot-Bu, THF, rt	 (~10)[b]	180
	$RuHCl(CO)(PPh_3)_3$ (10 mol %), toluene, 110°, 20 h	 (49)[a]	167
$C_{6–13}$			
	SmI_2 (50 mol %), *i*-PrSH (40 mol %),[c] THF, rt, 1 h	 R Me (99) Et (91) *t*-Bu (91) Cy (96) R *n*-C_6H_{13} (99) Ph (99) $PhCH_2$ (99) *n*-C_8H_{17} (94)	182, 181

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

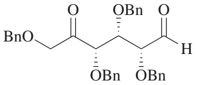
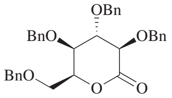
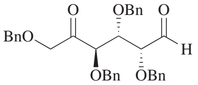
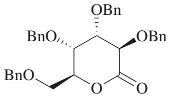
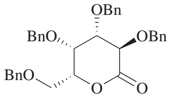
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

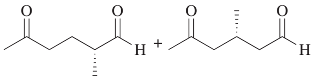
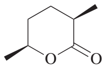
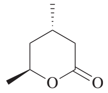
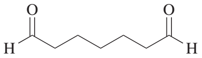
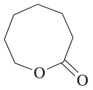
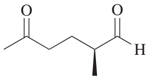
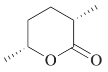
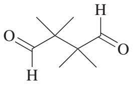
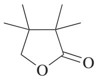
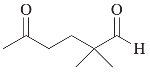
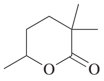
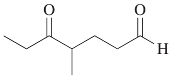
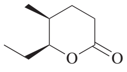
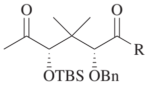
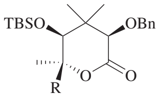
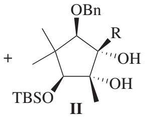
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{6-23}$			
	SmI$_2$ (50 mol %), **19** (40 mol %), THF, 0°, 1 h		182

R		er
Me	(84)	73.5:26.5 (*R*)
t-Bu	(73)	72:28 (—)
Cy	(74)	71.5:28.5 (—)
n-C$_6$H$_{13}$	(80)	70:30 (*R*)
Ph	(83)	74.5:25.5 (*S*)
2-MeOC$_6$H$_4$	(74)	74.5:25.5 (—)
PhCH$_2$	(73)	74:26 (—)
n-C$_8$H$_{17}$	(75)	84:16 (*R*)
n-C$_{11}$H$_{23}$	(75)	87:13 (*R*)
n-C$_{14}$H$_{29}$	(76)	81.5:18.5 (—)
n-C$_{18}$H$_{37}$	(84)	82.5:17.5 (—)

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$			
	Catalyst, rt	 **I** +  **II**	180

Catalyst	Solvent(s)	I	II
SmI$_2$	MeOH + THF/hexane (1:1)	(41)	(35)
SmI$_2$O*t*-Bu	THF	(75)	(0)

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. SmI$_2$O*t*-Bu, THF, rt, 12 h 2. TFA, CH$_2$Cl$_2$, 0°, 30 min	 (76)[d]	280
	1. SmI$_2$O*t*-Bu, THF, rt, 12 h 2. TFA, CH$_2$Cl$_2$, 0°, 30 min	 +  (78)[d,e]	280

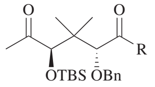
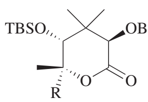
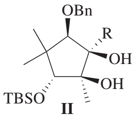
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_7$			
	SmI$_2$ (50 mol %), *i*-PrSH (40 mol %),[c] THF, 0°	 **I** +  **II** **I** + **II** (—), **I/II** = 1:1	182
	RuHCl(CO)(PPh$_3$)$_3$, toluene	 (7) + dimeric cyclic esters (13)	167
	SmI$_2$ (50 mol %), *i*-PrSH (40 mol %),[c] THF, rt	 (76)	182
C$_8$			
	[Rh(dcpe)(acetone)$_2$]ClO$_4$ (6 mol %), acetone, 34°	 (—)	348
	SmI$_2$ (50 mol %), *i*-PrSH (40 mol %), THF, rt, 1 h	 (80)	182, 181
	SmI$_2$ (50 mol %), *i*-PrSH (40 mol %), THF, rt	 (88)	182, 181
	Catalyst, rt	 **I** +  **II**	180

R	Catalyst	Solvent(s)	I	II
H	SmI$_2$	MeOH/THF/hexane	(65)	(18)
H	SmI$_2$O*t*-Bu	THF	(89)	(0)
D	SmI$_2$	THF	(20)	(67)

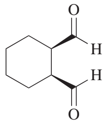
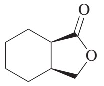
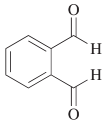
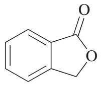
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

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

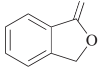
C$_8$

	Catalyst, rt	 **I** +  **II**	180

R	Catalyst	Solvent(s)	I	II
H	SmI$_2$	MeOH/THF/hexane	(62)	(21)
H	SmI$_2$O*t*-Bu	THF	(75)	(0)
D	SmI$_2$	THF	(16)	(62)

	[Rh(dcpe)(acetone)$_2$]ClO$_4$ (7 mol %), acetone, 34°	 (—)	348
	Catalyst (*x* mol %)		

Catalyst	*x*	Additive	Solvent(s)	Temp (°)	Time (h)		Refs.
NaH	5	—	toluene	rt	24	(96)	139
NaH	10	—	—	high-speed ball milling, rt	2	(93)	336
LiBr	50	—	Et$_3$N	rt	48	(96)	45
KO*t*-Bu	5	—	toluene	80	1.5	(77)	140
Ca[N(SiMe$_3$)$_2$]$_2$(thf)$_2$	1	—	C$_6$H$_6$	rt	24	(81)	51
111	0.5	—	toluene	21	0.25	(70)	158
111	1	—	toluene	21	0.25	(83)	158
116	1	—	toluene	21	0.5	(99)	162
K$_2$Fe(CO)$_4$	7	18-c-6	THF	60	22	(17)	62
RhH(CO)(PPh$_3$)$_3$	5	—	EtOH	"heat"	360	(49)	349
RhCl$_3$•3H$_2$O	10	PPh$_3$, Na$_2$CO$_3$	EtOH	"heat"	2.3	(74)	349
[Rh(dcpe)(acetone)$_2$]ClO$_4$	—	—	Me$_2$CO	34	—	$(100)^f$	348
[Rh(dppe)(acetone)$_2$]ClO$_4$	—	—	Me$_2$CO	34	—	$(100)^f$	348
[Rh(dppe-*p*-CF$_3$)(acetone)$_2$]ClO$_4$	—	—	Me$_2$CO	34	—	$(100)^f$	348
[Rh(dppp)(acetone)$_2$]ClO$_4$	—	—	Me$_2$CO	34	—	$(100)^f$	348
[Rh(dppb)(acetone)$_2$]ClO$_4$	—	—	Me$_2$CO	34	—	$(100)^f$	348
[RhCl(cod)]$_2$	5	dppp (10 mol %)	xylene	100	24	(91)	169
Cp*$_2$LaCH(SiMe$_3$)$_2$	1	—	C$_6$H$_6$	60	24	(94)	71
La[N(SiMe$_3$)$_2$]$_3$	1	—	pentane/hexane (1:1)	21	24	(85)	74, 72
La$_2$(*t*-Bu$_2$pz)$_6$	5	—	C$_6$D$_6$	21	—	(100)	73
112	1	—	C$_6$D$_6$	rt	1	(100)	184
[SBA–15]Sm[N(SiMe$_3$)$_2$]$_x$	2.5	—	hexane/toluene	—	24	(100)	194

	Catalyst (*x* mol %), benzene, 40°		80, 78

Catalyst	*x*	Time	
MgO	25	1 h	(15)
MgO	125	15 min	(91)
MgO	125	15 min	$(87)^g$
CaO	18	1 h	(59)
CaO	89	15 min	(100)
SrO	10	1 h	(15)
SrO	48	15 min	(86)
BaO	7	1 h	(0)

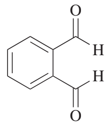
Catalyst	*x*	Time	
ALO-1A	50	4 h	(83)
ALO-2	50	4 h	(99)
ALO-3	50	4 h	(68)
ALO-4	10	1 h	(8)
ALO-4	50	4 h	(93)
ALO-4	50	4 h	(62)
ALO-5a	50	4 h	(98)

Catalyst	*x*	Time	
KF/Al$_2$O$_3^h$	10	1 h	(5)
KF/Al$_2$O$_3^h$	50	4 h	(35)
KOH/Al$_2$O$_3^i$	10	1 h	(3)
KOH/Al$_2$O$_3^i$	50	4 h	(53)
hydrotalcite	2	1 h	(0)
La$_2$O$_3$	3	1 h	(1)
ZrO$_2$	8	1 h	(0)
ZnO	12	1 h	(0)

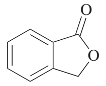
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_8



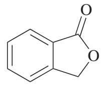
Catalyst, CO_2 (sc), 8 MPa, 40°



Catalyst	Time (h)	
CaO	2	(1)
ALO-2	4	(64)
ALO-3	2	(1)
ALO-4	4	(15)
meso Al_2O_3	4	(59)
meso Al_2O_3 / SO_4^{2-} (0.23 wt%)[j]	2	(66)
meso Al_2O_3 / SO_4^{2-} (0.48 wt%)[j]	2	(62)
meso Al_2O_3 / SO_4^{2-} (1.30 wt%)[k]	4	(81)
meso Al_2O_3 / SO_4^{2-}	2	(56)

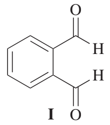
87, 88, 89

meso Al_2O_3 / SO_4^{2-} (1.30 wt %),[j] 8 MPa, 40°, 15 min



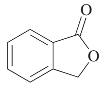
Solvent	
benzene	(38)
THF	(40)
CO_2 (sc)	(31)
CO_2 (sc)/benzene	(48)
CO_2 (sc)/THF	(58)
CO_2 (sc)/AcOH	(1)
CO_2 (sc)/MeOH	(6)

87, 88, 89



I

Catalyst (*x* mol %), toluene, 90°, 5 h

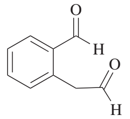


II

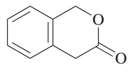
Catalyst	*x*	**II**[l]	**I**[l]
$RuHCl(CO)(PPh_3)_3$	0.5	(94)	(6)
$RuHCl(CO)(PPh_3)_3$	1.0	(99)	(trace)
$RuH_2(PPh_3)_4$	0.5	(5)	(95)
$RuH_2(CO)(PPh_3)_3$	0.5	(1)	(95)
$RuH(NO)(PPh_3)_3$	0.5	(19)	(76)

167

C_9

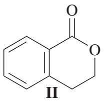


$RuHCl(CO)(PPh_3)_3$ (5 mol %), toluene, 120°, 40 h



I

\+

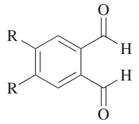


II

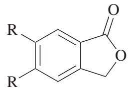
I + **II** (99), **I/II** = 1:1.1[l]

167

C_{8-10}



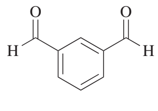
meso Al_2O_3 / SO_4^{2-} (1.30 wt %),[j] CO_2 (sc), 10 MPa, 80°, 24 h



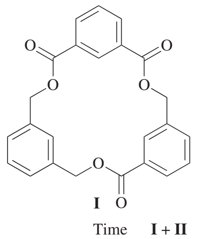
R	
Cl	(40)
Me	(60)

89

C_8

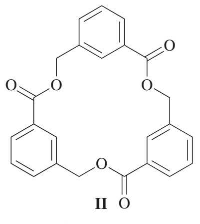


$Cp^*{}_2LaCH(SiMe_3)_2$ (1 mol %), benzene, 60°



I

\+

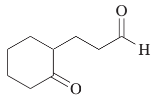


II

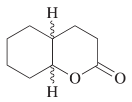
Time	**I** + **II**	**I/II**	(**I** + **II**)/Polymer
3 h	—	—	19:81
24 h	—	—	47:53
4 d	—	—	53:47
7 d	(86)	96:4	80:20

71

C_9



See table.



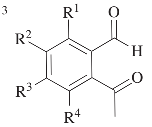
Catalyst	*x*	Additive	Solvent	Temp (°)	Time (h)		*cis*:*trans*	Refs.
(*i*-Bu)$_2$AlOMe	—	—	toluene	–60 to rt	—	(85)	15:85	155
SmI_2	50	*i*-PrSH (40 mol %)	THF	25	1	(70)	4:96	182, 181

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

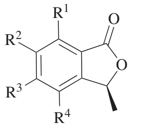
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

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

C_{9-13}



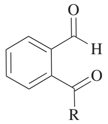
$[Rh(cod)Cl]_2$ (*x* mol %), **108a** (5 mol %), additive (5 mol %), toluene, 100°



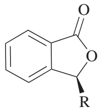
172

R^1	R^2	R^3	R^4	*x*	Additive	Time (d)		er
H	H	H	H	5	$AgNO_3$	1	(97)	98.5:1.5
H	Cl	H	H	5	$AgNO_3$	1	(67)	97.5:2.5
H	O_2N	H	H	5	$AgNO_3$	1	(94)	96.5:3.5
H	H	MeO	H	10	$AgNO_3$	3	(84)[k]	98:2
MeO	H	H	H	5	$AgNO_3$	1	(5)	—
MeO	H	H	H	10	none	3	(78)	98.5:1.5
H	H	H	Me	5	$AgNO_3$	1	(<5)	—
H	H	Me	H	5	$AgNO_3$	2	(88)	98:2
H	Me	H	H	5	$AgNO_3$	2	(91)	96:4
H	MeO_2C	H	H	5	$AgNO_3$	1	(94)	97.5:2.5
H	*t*-Bu	H	H	5	$AgNO_3$	2	(84)	99:1

C_{9-15}



$Rh(cod)Cl]_2$ (*x* mol %), **108a** (*y* mol %), AgY (*z* mol %), toluene, 1 d



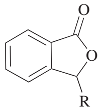
172

R	*x*	*y*	Y	*z*	Temp (°)	Time (d)		er
Me	5	5	NO_3	5	100	1	(97)	98.5:1.5
Et	3.5	7	NO_3	7	100	2.5	(94)	98:2
i-Pr	7.5	15	NO_3	15	75	3.5	(83)	98.5:1.5
n-Bu	5	10	NO_3	10	75	3	(93)	98.5:1.5
Ph	5	10	OMs	10	90	3	(81)	96.5:3.5
$4\text{-}O_2NC_6H_4$	5	10	OTf	10	75	3	(92)	98:2
$4\text{-}O_2NC_6H_4$	5	10	OMs	10	90	3	(25)	—
$4\text{-}MeOC_6H_4$	5	10	OMs	10	90	3	(93)	98:2
$4\text{-}MeC_6H_4$	5	10	OMs	10	90	3	(88)	96:4
$4\text{-}MeC_6H_4$	5	10	NO_3	10	90	3	(22)	94.5:5.5
$4\text{-}MeC_6H_4$	5	10	OTf	10	90	3	(48)	56.5:43.5

A: NaCN (10 mol %), DMSO, 50°, 4 h

or

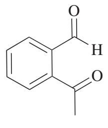
B: DMSO, *h*ν (350 nm), rt, 3 d



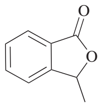
R	Conditions **A**	Conditions **B**
Me	(70)	(71)
Et	(74)	(75)
4-pyridyl	(72)	(74)
Ph	(70)	(81)
$4\text{-}BrC_6H_4$	(61)	(83)
$4\text{-}O_2NC_6H_4$	(62)	(75)
$2\text{-}HOC_6H_4$	(73)	(85)
$4\text{-}MeOC_6H_4$	(65)	(78)
$4\text{-}MeC_6H_4$	(63)	(79)

198

C_9



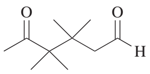
$RuHCl(CO)(PPh_3)_3$ (5 mol %), toluene, 120°, 40 h



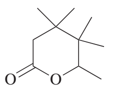
(91)

167

C_{10}

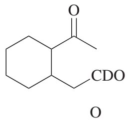


(*i*-Bu)$_2$AlOMe, toluene, –60° to rt

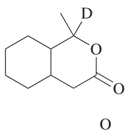


(85)

155

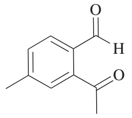


(*i*-Bu)$_2$AlOMe, toluene, –60° to rt

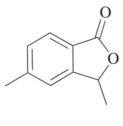


(—)

155



Catalyst **132** (5 mol %), *i*-PrOH (3 eq), EtOAc, 22°, 24 h



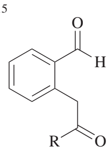
(55%) er 95:5

350

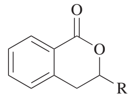
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_{10–15}$

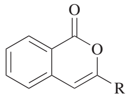


115 (5 mol %), *t*-BuOH,
heat, 16 h



I

+

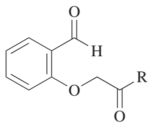


II

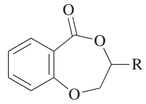
R	**I + II**	**I/II**
Me	(98)	71:29
Ph	(92)	49:51

176

$C_{10–19}$



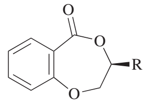
Rh(dppp)$_2$(BF$_4$)$_2$ (2.5 mol %),
CH_2Cl_2, rt



R	Time (h)	
Me	10	(>99)
i-Pr	3.7	(95)
n-Bu	9	(94)
t-Bu	3.5	(94)
2-furyl	20	(78)
Ph	4	(94)
4-FC$_6$H$_4$	1.2	(96)
4-ClC$_6$H$_4$	3.5	(95)
4-MeOC$_6$H$_4$	12	(89)
4-MeC$_6$H$_4$	5	(>99)
4-CF$_3$C$_6$H$_4$	1.2	(>99)
4-MeO$_2$CC$_6$H$_4$	15	(98)
Bn	9	(92)
2-benzothienyl	20	(37)
2-Np	4.5	(91)

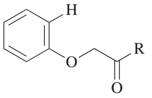
171

Cat. **127** (5 mol %), CH_2Cl_2, rt



I

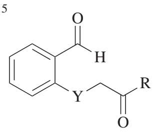
+



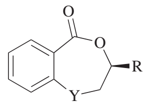
II

R	Time (d)	**I**	er **I**	**II**	Refs.
Me	2	(91)	99.5:0.5	(6)	171, 170
i-Pr	1.5	(98)	>99.5:0.5	(0)	171, 170
n-Bu	2	(99)	>99.5:0.5	(0)	171, 170
t-Bu	1.5	(94)	>99.5:0.5	(0)	171, 170
2-furyl	5^{m}	(7)	—	(41)	171
Ph	3	(92)	99.5:0.5	(7)	171, 170
4-FC$_6$H$_4$	3	(84)	99.5:0.5	(7)	171
4-ClC$_6$H$_4$	2	(89)	99.5:0.5	(7)	171, 170
4-MeOC$_6$H$_4$	6	(14)	66:34	(9)	171
4-MeC$_6$H$_4$	6	(50)	99.5:0.5	(8)	171
4-CF$_3$C$_6$H$_4$	2	(97)	99.5:0.5	(1)	171
4-MeO$_2$CC$_6$H$_4$	2	(98)	99.5:0.5	(1.5)	171
Bn	3.5	(93)	>99.5:0.5	(0)	171, 170
2-benzothienyl	4^{m}	(0)	—	(73)	171
2-Np	2	(85)	99.5:0.5	(9)	171, 170

$C_{10–15}$



Catalyst (2 mol %), CH_2Cl_2



173

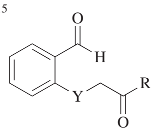
Y	R	Catalyst	Temp (°)	Time		er
NMe	Me	**128**	–35	—	(85)	87.5:12.5
NMe	*n*-Bu	**128**	–35	—	(86)	96.5:3.5
NMe	*t*-Bu	**128**	–35	—	(90)	75:25

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

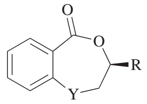
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*
Continued from previous page.

$C_{10–15}$



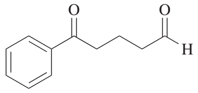
Catalyst (2 mol %), CH_2Cl_2



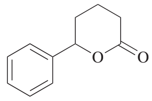
173

Y	R	Catalyst	Temp (°)	Time		er
NMe	Ph	**128**	–35	8 h	(91)	92.5:7.5
NMe	Ph	**128**	rt	—	(91)	88.5:11.5
NMe	Ph	**127**	rt	<5 min	(>99)[n]	86:14
NMs	Ph	**127**	rt	—	(0)[o]	—
NTs	Ph	**127**	rt	—	(0)[o]	—
O	Ph	**127**	rt	8 h	(36)	99.5:0.5
S	Ph	**127**	rt	2 h	(>99)[n]	99.5:0.5

C_{11}



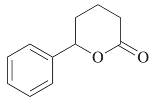
SmI$_2$ (*x* mol %),
i-PrOH (*y* mol %),
i-PrSH (*z* mol %),
THF, rt, 30 min



x	*y*	*z*	
50	50	0	(0)
50	50	50	(53)
50	0	40	(99)
20	0	10	(100)
10	0	20	(27)
10	0	5	(0)

182

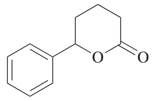
SmI$_2$ (*x* mol %),
(RS)$_2$ (*y* mol %),
THF, rt°, 1 h



R	*x*	*y*	
Me	42	20	(67)
i-Pr	42	20	(68)
Ph	42	20	(100)
Ph	12	5	(100)

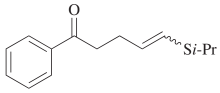
182

Lewis acid(s) (*x* mol %),
i-PrSH (*y* mol %), THF, rt



I

or



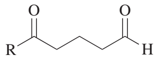
II

182

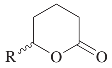
Lewis Acid(s)	*x*	*y*	**I**	**II**
SmI$_2$	40	40	(99)	(—)
SmI$_3$	110	100	(—)	(85)
SmI$_3$	10	100	(—)	(75)
SmI$_2$ + SmI$_3$	25 + 25	20	(69)	(—)
SmI$_2$ + SmI$_3$	50 + 50	20	(99)	(—)
SmF$_3$	50	50	(0)	(0)

Lewis Acid	*x*	*y*	**I**	**II**
SmCl$_3$	50	50	(0)	(0)
SmBr$_3$	50	50	(0)	(0)
Sm(OAc)$_3$	50	50	(0)	(0)
Sm(OTf)$_3$	50	50	(0)	(0)
Sm(O*i*-Pr)$_3$	50	50	(0)	(0)

$C_{11–13}$



1. Chiral alcohol,
   catalyst (*x* mol %), THF, rt, 1 h
2. Hydrolysis
3. Lactonization



182

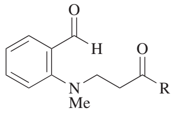
R	Chiral Alcohol	Catalyst	*x*		er	
Ph	(–)-menthol	SmI$_2$	100	(65)	92:8	(*S*)
Ph	(–)-8-Ph-menthol	SmI$_2$	100	(77)	86:14	(*S*)
Ph	(+)-neomenthol	SmI$_2$	100	(70)	60.5:39.5	(*R*)
Ph	(–)-menthol	SmI$_3$	20	(65)[p]	89:11	(*S*)
n-C$_8$H$_{17}$	(–)-menthol	SmI$_2$	100	(89)	86:14	(*S*)
n-C$_8$H$_{17}$	(–)-menthol	SmI$_3$	20	(58)[p]	65.5:34.5	(*S*)

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

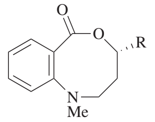
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

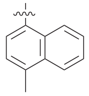
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

C_{11-21}



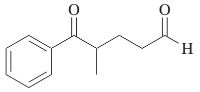
Catalyst **127** (x mol %), CH_2Cl_2, rt, 30 h



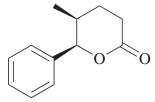
R	x		er
Me	1	(92)	99:1^{q}
Et	1	(91)	98:2^{q}
Ph	2	(95)	98:2
4-FC_6H_5	5	(99)	94:6
4-ClC_6H_5	5	(98)	98.5:1.5
4-BrC_6H_5	5	(94)	99.5:1.5
4-$MeOC_6H_5$	5	(84)	97.5:2.5
4-MeC_6H_5	5	(90)	99.5:0.5
	5	(92)	98.5:1.5

173

C_{12}

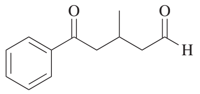


SmI_2 (80 mol %), *i*-PrSH (50 mol %), THF, 25°, 1 h

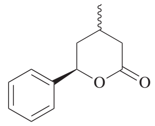


(94)

182, 181

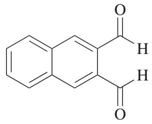


SmI_2 (100 mol %), *i*-PrSH (90 mol %), THF, 1 h

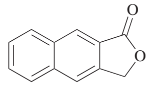


Temp		*cis*:*trans*
0°	(90)	94:6
rt	(97)	77:23

182, 181

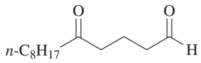


See table.

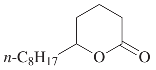


Catalyst	Amount	Solvent	Temp (°)	Time (h)		Refs.
[Rh(dcpe)(acetone)$_2$]ClO_4	1 mol %	Me_2CO	34	—	(—)	348
[Rh(dppe)(acetone)$_2$]ClO_4	1 mol %	Me_2CO	34	—	(—)	348
$RuHCl(CO)(PPh_3)_3$	2 mol %	toluene	110	5	(94)	167
meso Al_2O_3 / $SO_4^{2-\,j}$	1.3 wt %	CO_2 (sc, 10 MPa)	80	24	(31)	89
meso Al_2O_3 / $SO_4^{2-\,j}$	1.3 wt %	CO_2 (sc, 10 MPa) + THF	80	24	(60)	89
CaO	—	C_6H_6	40	2	(21)	80
CaO	—	C_6H_6	60	2	(94)	80
ALO-4	—	C_6H_6	40	20	(74)	80
ALO-4	—	C_6H_6	60	20	(100)	80

C_{13}

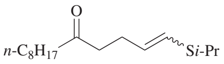


Catalyst (x mol %), additive (y mol %), THF, rt



I

or



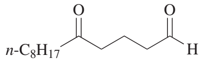
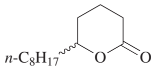
II

182

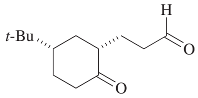
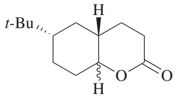
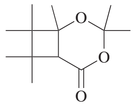
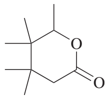
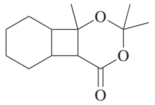
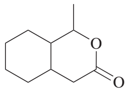
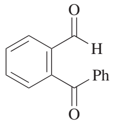
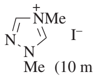
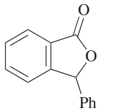
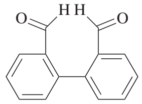
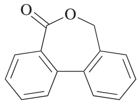
Catalyst	x	Additive	y	Time (h)	**I**	**II**
SmI_2	85	$(MeS)_2$	40	1	(87)	(0)
SmI_2	42	(*i*-PrS)$_2$	20	1	(56)	(0)
SmI_2	42	$(PhS)_2$	20	1	(100)	(0)
SmI_2	50	*i*-PrSH	40	—	(94)	(0)
SmI_3	110	*i*-PrSH	100	—	(0)	(87)
SmI_3	10	*i*-PrSH	100	—	(0)	(79)

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

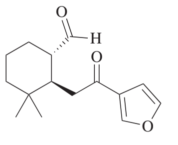
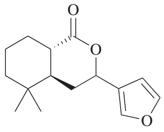
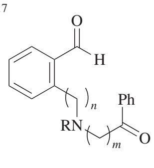
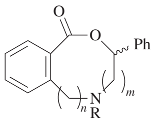
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			
	Chiral thiol (40 mol %), SmI_2 (50 mol %), THF, 0°, 1 h		182

Chiral Thiol		er		Chiral Thiol		er	
1	(37)	59:41	(*S*)	**12**	(71)	60.6:39.5	(*R*)
2	(99)	60:40	(*R*)	**13**	(99)	64.5:35.5	(*R*)
3	(80)	57:43	(*R*)	**14**	(75)	84:16	(*R*)
4	(99)	69:31	(*R*)	**15**	(64)	72.5:27.5	(*R*)
5	(83)	72:28	(*R*)	**16**	(90)	63.5:36.5	(*R*)
6	(99)	61:39	(*R*)	**17**	(86)	76:24	(*R*)
7	(73)	61:39	(*R*)	**18**	(68)	65.5:35.5	(*R*)
8	(53)	56:44	(*S*)	**19**	(70)	76.5:23.5	(*R*)
9	(99)	62:38	(*R*)	**20**	(87)	69.5:30.5	(*R*)
10	(79)	55:45	(*R*)	**21**	(63)	76.5:23.5	(*S*)
11	(74)	62.5:37.5	(*R*)	**22**	(76)	67:33	(*S*)

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 racemic	SmI_2 (40 mol %), *i*-PrSH (35 mol %), THF, rt, 1 h	 (91) *cis*/*trans* = 19:81	182, 181
	1. DIBAL-H, toluene, –60° 2. MeOH, –60° to rt	 (86)	155
	1. DIBAL-H, toluene, –60° 2. MeOH, –60° to rt	 (54)	155
C_{14}			
	 (10 mol %), DBU, CH_2Cl_2, rt^r	 (60)	196
	Catalyst (*x* mol %)		

Catalyst	*x*	Additive(s)		Temp (°)	Time (h)		Refs.
$RhH(CO)(PPh_3)_3$	5	none	EtOH	"heat"	360	(72)	349
$RhCl_3{\bullet}3H_2O$	10	PPh_3, Na_2CO_3	EtOH	"heat"	2	(93)	349
$RuHCl(CO)(PPh_3)_3$	1	none	toluene	110	5	(97)	167

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	(*i*-Bu)$_2$AlOMe, toluene, 0° to rt, 4 h	 (96)	281
$C_{16–17}$			
	Catalyst **127** (*x* mol %), CH_2Cl_2		173

n	*m*	R	*x*	Temp (°)	
1	1	Ph	10	60	(0)
1	2	Ph	—	—	(0)
0	3	Me	—	—	(0)

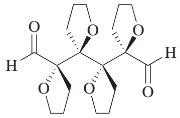
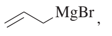
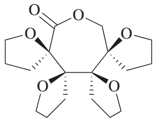
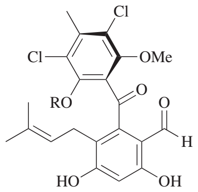
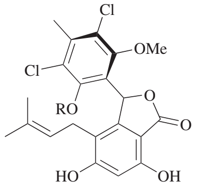
Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}			
	, THF, Et_2O, 0° to rt, 1 h	 (65)	143

TABLE 1H. INTRAMOLECULAR TISHCHENKO REACTIONS (*Continued*)

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

Aldehyde(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20} 	See table.		198

R	Conditions	
H	NaCN (10 mol %), DMSO, 50°, 4 h	(62)
H	DMSO, *h*ν (350 nm), 6 d	(80)
Me	LiSEt (4 eq), DMF, 70°, 4 h	(13)

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[a] The yield was determined by ^{1}H-NMR spectroscopy.

[b] Aldol products were isolated from the product mixture.

[c] The catalyst mixture was activated by premixing an aliquot of SmI_2/*i*-PrSH with the substrate and re-inserting it into the mixture.

[d] The yield is given over three steps, including the preparation of the starting material via Swern oxidation of the corresponding diol.

[e] The product was a mixture of the two stereoisomers that could not be separated.

[f] The number is the % conversion.

[g] THF was used as solvent.

[h] KF loading was 8.2 mmol/g.

[i] KOH loading was 1.2 mmol/g.

[j] The alumina was synthesized using H_2SO_4 as the sulfate source.

[k] The alumina was synthesized using $Al_2(SO_2)_3$ as the sulfate source.

[l] The ratio was determined by ^{1}H-NMR spectroscopy.

[m] The reaction was carried out at 90° in a sealed tube.

[n] The number is the % conversion as determined by ^{1}HNMR spectroscopy.

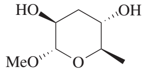
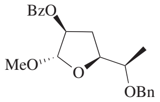
[o] Starting material was recovered quantitatively.

[p] The reaction mixture was treated with TFA in CH_2Cl_2 directly after the first step to effect the lactonization.

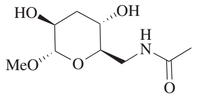
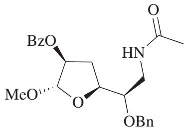
[q] The text shows the (*R*) configuration as reproduced in this entry, whereas the (*S*) configuration is shown in the Supporting Information.

[r] The reaction times given are 9 hours or until TLC showed complete consumption of the aldehyde.

TABLE 1I. TISHCHENKO-TYPE CARBOHYDRATE REARRANGEMENTS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	Lewis acid, PhCHO		278, 277

Lewis acid	Solvent	Temp	Time	
$ZnCl_2$	—	35°	3 d	(70)[a]
$TiCl_4$	1,4-dioxane	rt	1 d	(70)
$AlCl_3$	1,4-dioxane	rt	30 min	(95)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	$ZnCl_2$, $AlCl_3$, PhCHO, 3 h	 (—)	279

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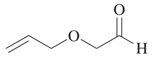
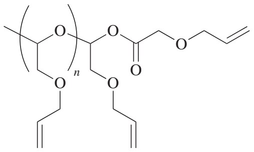
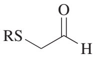
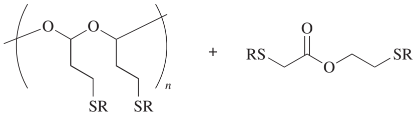
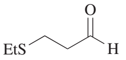
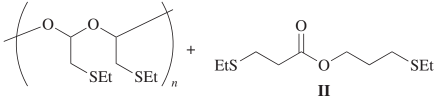
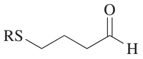
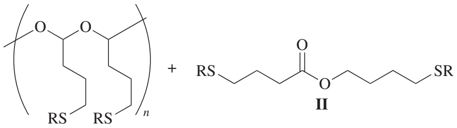
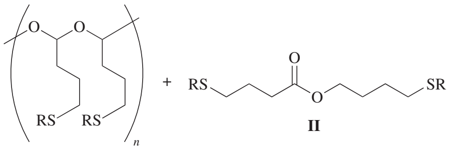
[a] The reaction was also done with the L-form of the hexopyranoside.

TABLE 1J. THE TISHCHENKO REACTION IN POLYMER CHEMISTRY

<table>
<tr><th>Substrate(s)</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_2</td><td></td><td></td><td></td></tr>
<tr><td></td><td>AlEt$_3$ (3 mol %), CH$_2$Cl$_2$</td><td><table><tr><th>Temp (°)</th><th>Time (h)</th><th></th></tr><tr><td>0</td><td>120</td><td>(20)</td></tr><tr><td>–10</td><td>265</td><td>(30)</td></tr><tr><td>–20</td><td>120</td><td>(12)</td></tr><tr><td>–45</td><td>120</td><td>(62)</td></tr><tr><td>–78</td><td>72</td><td>(50)</td></tr></table></td><td>214</td></tr>
<tr><td></td><td>AlEt$_3$ (x mol %), –78°</td><td>
I (main product) II<table><tr><th>R</th><th>x</th><th>Solvent</th><th>Time (d)</th><th>I</th><th>II</th></tr><tr><td>Me</td><td>1.5</td><td>—</td><td>1</td><td>(—)</td><td>(7)</td></tr><tr><td>Me</td><td>1</td><td>toluene</td><td>1</td><td>(—)</td><td>(12)</td></tr><tr><td>Et</td><td>1.4</td><td>—</td><td>1</td><td>(—)</td><td>(7)</td></tr><tr><td>Et</td><td>1</td><td>toluene</td><td>1</td><td>(—)</td><td>(6)</td></tr><tr><td>Et</td><td>4</td><td>THF</td><td>2</td><td>(—)</td><td>(2)</td></tr></table></td><td>213</td></tr>
<tr><td>C_3</td><td></td><td></td><td></td></tr>
<tr><td></td><td>AlEt$_3$ (2 mol %), toluene, –78°, 24 h<table><tr><th>Additive</th><th>I</th><th>II</th></tr><tr><td><i>t</i>-BuOH</td><td>(—)</td><td>(10)</td></tr><tr><td>EtSH</td><td>(—)</td><td>(4)</td></tr></table></td><td>
I (main product) II</td><td>213</td></tr>
</table>

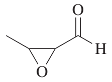
<table>
<tr><th>Substrate(s)</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_4</td><td></td><td></td><td></td></tr>
<tr><td></td><td>AlEt$_3$, toluene, –78°, 24 h<table><tr><th>R</th><th>Additive</th><th>Additive/AlEt$_3$</th><th>I</th><th>II</th></tr><tr><td>Me</td><td>H$_2$O</td><td>0.5</td><td>(—)</td><td>(2)</td></tr><tr><td>Me</td><td>H$_2$O</td><td>1</td><td>(—)</td><td>(<1)</td></tr><tr><td>Me</td><td>H$_2$O</td><td>2</td><td>(—)</td><td>(<1)</td></tr><tr><td>Et</td><td>Na-TPP</td><td>1</td><td>(—)</td><td>(4)</td></tr><tr><td>Et</td><td>Na-TPP</td><td>0.5</td><td>(—)</td><td>(8)</td></tr></table></td><td>
I (main product) II</td><td>213</td></tr>
<tr><td></td><td>AlEt$_3$ (x mol %), –78°</td><td>
I (main product) II</td><td>213</td></tr>
</table>

R	x	Solvent	Time (d)	**I**	**II**
Me	1.7	—	1	(—)	(1)
Me	3.0	—	1	(—)	(0)
Me	1	toluene	1	(—)	(2)
Me	2	CH$_2$Cl$_2$	1	(—)	(15)
Me	4	THF	2	(—)	(3)
Et	1.0	—	1	(—)	(0)
Et	1.9	—	1	(—)	(0)
Et	3.8	—	1	(—)	(18)
Et	1	toluene	1	(—)	(6)
Et	2	CH$_2$Cl$_2$	1	(—)	(3)
Et	4	THF	2	(—)	(4)
Ph	1.5	—	1	(—)	(5)
Ph	1	toluene	1	(—)	(6)

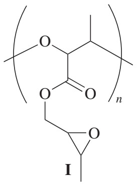
TABLE 1J. THE TISHCHENKO REACTION IN POLYMER CHEMISTRY (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

C_4

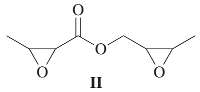


Al(OPr-*i*)$_3$, (*x* mol %)



I

+



II

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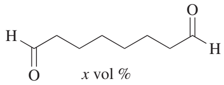
Temp (°)	*x*	Time (h)	**I**	**II**
20	0.10	360	(—)	(—)
20	0.22	360	(13)	(33)
20	0.50	360	(38)	(48)
20	0.50	500	(—)	(—)
20	0.50	1080	(—)	(—)
20	0.50	3000	(62)	(37)

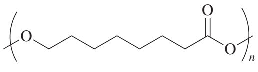
Temp (°)	*x*	Time (h)	**I**	**II**
20	1.02	360	(58)	(36)
50	0.25	160	(19)	(35)
50	0.50	160	(33)	(47)
50	0.50	500	(57)	(43)
50	0.50	1080	(78)	(22)
50	1.03	160	(64)	(33)

C_8



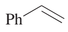
x vol %

Al(OPr-*i*)$_3$ (*y* mol %), CCl$_4$, 19 h

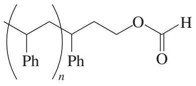


x	*y*	
9	6	(23)
33	6	(53)
40	3	(53)
40	3	(55)

23

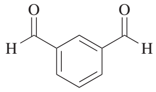


1. Li–naphthalene (*x* mol %), THF (*y* M)
2. HCHO, slow addition

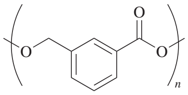


x	y	Temp (°)	
0.3	0.50	–70	(83)
0.3	0.42	–32	(87)
0.2	0.50	25	(88)
0.2	0.14	–21	(98)
3	0.50	–30	(88)
3	0.14	–25	(90)

212

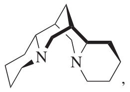


Al(OEt)$_3$ (3 mol %), 95°, 2 h



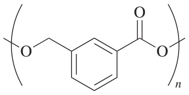
(91)

204



,

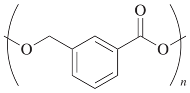
EtMgBr (*x* mol %), toluene, CH$_2$Cl$_2$, 0–30°, 18 h



x	
2	(1)
4	(4)

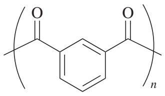
48

RuH$_2$(PPh$_3$)$_4$ (4 mol %), THF, 0°, 6 h



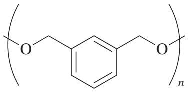
I

+



II

+

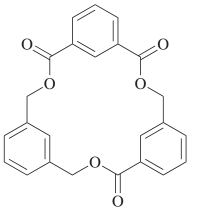


III

I + **II** + **III** (49)

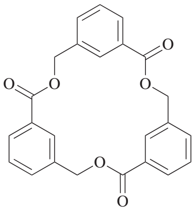
65

Cp*$_2$LaCH(SiMe$_3$)$_2$ (1 mol %), benzene, 60°



I

+



II

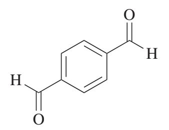
71

Time	Polymer	**I** + **II**	**I**/**II**
3 h	(81)	(19)	—
24 h	(53)	(47)	—
4 d	(47)	(53)	—
7 d	(20)	(86)	96:4

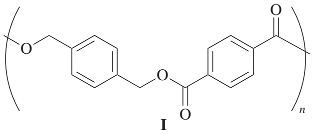
TABLE 1J. THE TISHCHENKO REACTION IN POLYMER CHEMISTRY (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

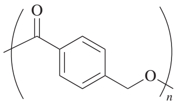
C_8



$Al(OEt)_3$ (3 mol %), 120°, 6 h



I

+ 

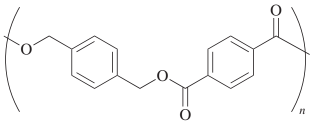
II

I + **II** (100)

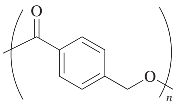
204

Catalyst (2 mol %), cyclohexane, 80°, 1 d

Catalyst	**I + II**
$AlEt_3$	(90)
$Al(i\text{-}Bu)_3$	(90)
$Al(i\text{-}Pr)_3$	(60)
$AlEt_2Br$	(60)
$Al_2Me_3Br_3$	(30)
$ZnEt_2$	(80)



I

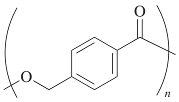
+ 

II

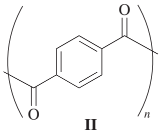
205

$RuH_2(PPh_3)_4$ (x mol %), THF, 6 h

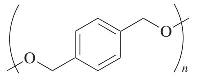
x	Temp (°)	**I + II + III**
4	0	(95)
2	0	(75)
1	0	(0)
4	–20	(55)
2	20	(11)



I

+ 

II

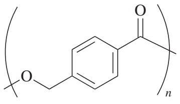
+ 

III

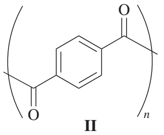
65

SmI_2 (x mol %), THF, 24 h

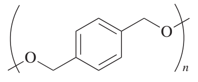
x	Temp (°)	**I + II + III**
5	20	(81)
10	20	(83)
10	0	(25)
10	50	(62)



I

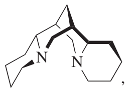
+ 

II

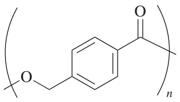
+ 

III

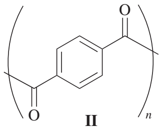
65



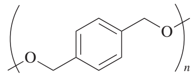
, EtMgBr (x mol %)



I

+ 

II

+ 

III

48

x	Solvent(s)	Temp (°)	Time (h)	**I + II + III**
2	THF	0	28	(0)
2	THF	30	28	(8)
2	$CHCl_3$	0	28	(67)
2	$CHCl_3$	30	28	(80)
4	$CHCl_3$	50	18	(53)
2	$CHCl_3$	30	118	(0)[a]
2	CH_2Cl_2	30	18	(53)
4	CH_2Cl_2	30	18	(65)
2	$CHCl_3$/THF (7:3)	25	18	(9)
2	$CHCl_3$/THF (7:3)	50	18	(74)
2	$CHCl_3$/THF (7:3)	50	18	(71)
2	$CHCl_3$/THF (7:3)	60	118	(82)
2	CH_2Cl_2/THF (9:1)	40	118	(53)
2	$CHCl_3$/THF (9:1)	60	118	(85)

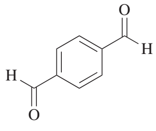
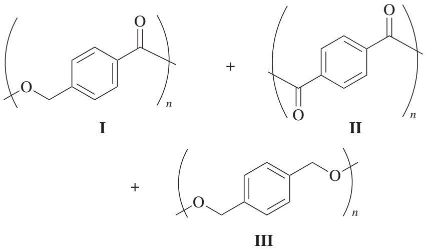
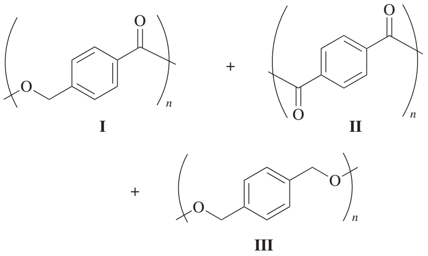
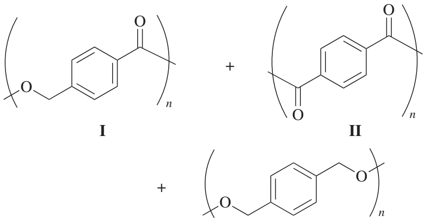
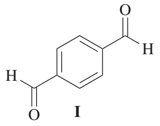
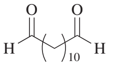
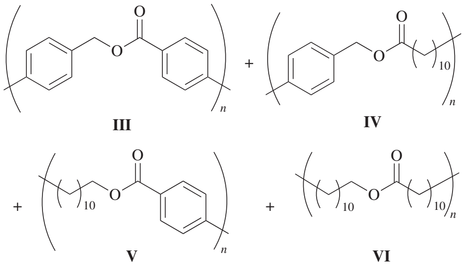
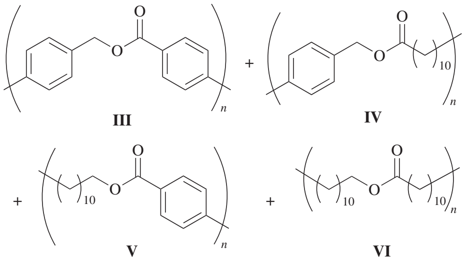
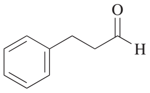
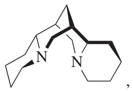
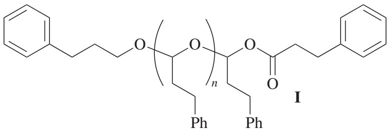
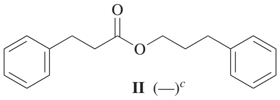
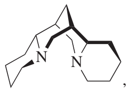
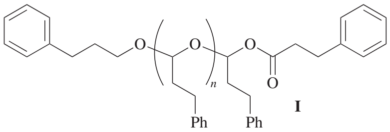
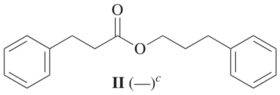
<table>
<tr><th>Substrate(s)</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td>C_8
</td><td>Al(O<i>i</i>-Pr)$_3$ (2 mol %),
CH$_2$Cl$_2$, 18 h<table><tr><th>Temp (°)</th><th>I + II + III</th></tr><tr><td>0</td><td>(0)</td></tr><tr><td>30</td><td>(68)</td></tr></table></td><td></td><td>48</td></tr>
<tr><td></td><td>Al[(<i>R</i>)-BINOL]Me$_2$ (2 mol %),
CH$_2$Cl$_2$, 18 h<table><tr><th>Temp (°)</th><th>I + II + III</th></tr><tr><td>0</td><td>(0)</td></tr><tr><td>30</td><td>(83)</td></tr></table></td><td></td><td>48</td></tr>
<tr><td></td><td>Cp*$_2$NdCH(SiMe$_3$)$_2$ (1 mol %),
benzene, 60°, 7 d</td><td>
I + II + III (97)</td><td>71</td></tr>
<tr><td>$C_8 + C_{12}$
 I
+
 II</td><td>RuH$_2$(PPh$_3$)$_4$ (<i>x</i> mol %),
THF, 0°, 21 h<table><tr><th>I/II</th><th><i>x</i></th><th>III–VI</th><th>III/IV/V/VI</th></tr><tr><td>1:1</td><td>4</td><td>(46)</td><td>12:43:5:40</td></tr><tr><td>1:1</td><td>6</td><td>(63)</td><td>24:38:3:35</td></tr><tr><td>2:1</td><td>4</td><td>(82)</td><td>52:31:2:15</td></tr><tr><td>4:1</td><td>4</td><td>(51)</td><td>69:25:2:4</td></tr><tr><td>1:2</td><td>4</td><td>(0)</td><td>—</td></tr></table></td><td></td><td>65</td></tr>
<tr><td></td><td>1. SmI$_2$ (10 mol %), THF,
rt, 40 min
2. PhCHO,^{b} THF, rt, 1 h<table><tr><th>I/II</th><th>III–VI</th><th>III/IV/V/VI</th></tr><tr><td>1:4</td><td>(69)</td><td>8:32:5:55</td></tr><tr><td>1:2</td><td>(40)</td><td>8:44:3:45</td></tr><tr><td>1:1</td><td>(30)</td><td>15:60:3:22</td></tr><tr><td>2:1</td><td>(16)</td><td>39:46:4:11</td></tr><tr><td>4:1</td><td>(19)</td><td>66:28:2:4</td></tr></table></td><td></td><td>211</td></tr>
</table>

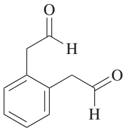
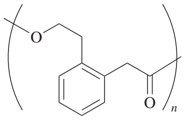
TABLE 1J. THE TISHCHENKO REACTION IN POLYMER CHEMISTRY (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	 , EtMgBr (2 mol %), toluene	 **I** +  **II** (—)[c]	47

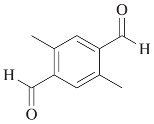
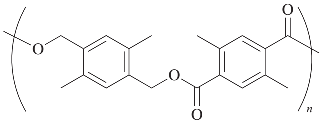
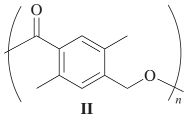
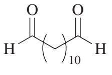
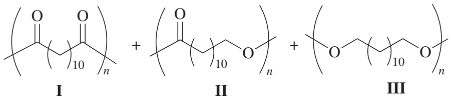
Concentration (M)	Temp(°)	Time (h)	**I**	$[\alpha]^{25}_{365}$
7.5	–78	2	(36)	–46.0
2.5	–78	2	(39)	–55.6
0.75	–78	2	(44)	–33.0
2.5	–98	2	(13)	–42.7
2.5	–78	100	(14)[a]	—

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , initiator (2 mol %), toluene –78°, 2 h	 **I** +  **II** (—)[c]	47

Initiator	**I**	$[\alpha]^{25}_{365}$
t-BuMgBr	(36)	–54.3
PhMgBr	(48)	–55.3
$Ph(CH_2)_2OMgBr$	(46)	–49.0
CyMgBr	(42)	41.0
CyMgCl	(41)	–43.0
n-$C_8H_{17}MgBr$	(49)	–46.0
n-$C_8H_{17}MgBr$	(48)[d]	–48.8
n-BuLi	(—)	—

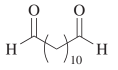
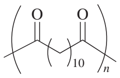
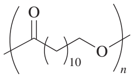
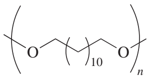
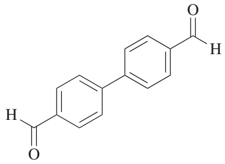
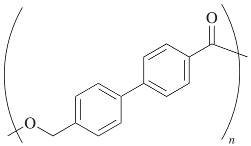
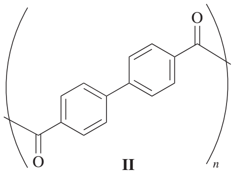
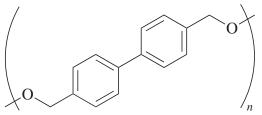
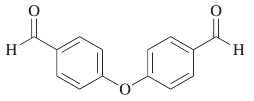
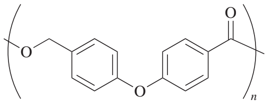
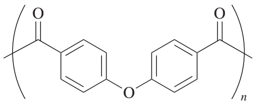
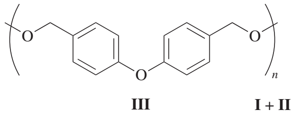
Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	Catalyst(s) (5 mol %)		206

Catalyst(s)	Temp (°)	Time (h)	
$AlEt_3$	20	20	(43)
$AlEt_3$	0	19	(71)
$AlEt_3$	0 to –78	19	(83)
$AlEt_3$/PhNHCOMe	–78	20	(42)
AlEt/$TiCl_4$	–78	15	(20)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Al(OEt)_3$ (4 mol %), 110°, 8 h	 **I** +  **I** + **II** (41) **II**	204
C_{12}			
	$RuH_2(PPh_3)_4$ (*x* mol %), THF, 2 h	 **I** **II** **III**	65

x	Temp (°)	**I** + **II** + **III**
6	0	(80)
10	0	(75)
3	20	(0)

TABLE 1J. THE TISHCHENKO REACTION IN POLYMER CHEMISTRY (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	1. SmI_2 (10 mol %), THF, rt, 45 min 2. PhCHO,[b] THF, rt, 1 h	 **I** +  **II** +  **III** **I** + **II** + **III** (65)	211
C_{14} 	$Al(OEt)_3$ (4 mol %), 180°, 0.5 h	 **I** +  **II** +  **III** **I** + **II** + **III** (90)	204
	$Cp^*{}_2LaCH(SiMe_3)_2$ (1 mol %), benzene, 60°, 7 d	 **I** +  **II** +  **III** **I** + **II** + **III** (86)	71

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[a] Only EtMgBr was used as the catalyst.

[b] The benzaldehyde added terminated the polymerization by end-capping the chain via the Tishchenko reaction.

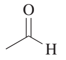
[c] The reaction yielded a MeOH-soluble main fraction consisting mostly of 3-phenylpropyl-3-phenylpropanoate, but the yield was not determined.

[d] The polymerization was terminated with MeOD.

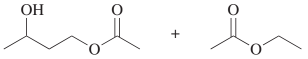
TABLE 2A. ALDOL-TISHCHENKO REACTIONS INVOLVING A SINGLE ALDEHYDE

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

C_2



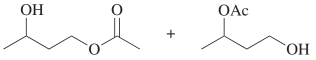
Catalyst (x amount)



I **II**

Catalyst	x	Solvent	Temp (°)	Time (h)	I	II	Refs.
$Mg[B(OMe)_4]_2$	2 mol %	Et_2O	15–45	—	(70)	(15)	216
$Mg[B(OMe)_4]_2$	5 mol %	MeOH	15–45	—	(50)	(15)	216
$Mg[Al(OEt)_4]_2{}^a$	5 wt %	—	rt	24	(53)	(0)	92
$Mg[Al(OEt)_4]_2$	5 wt %	—	rt	24	(24)	(0)	91
$Mg[Al(Oi\text{-}Pr)_4]_2$	5 wt %	—	rt	24	(24)	(0)	91
$Mg[Al(OBu)_4]_2$	5 wt %	—	rt	24	(24)	(0)	91
$Al(OEt)_3$	"cat."	—	—	—	(—)	(—)	4, 2

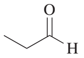
Catalyst (x mol %), 1 h



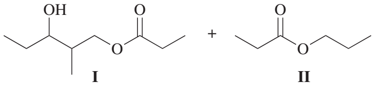
I **II** 238

Catalyst	x	Solvent	Temp (°)	I + II	I/II
$Cp^*{}_2Sm(thf)_2$	3	toluene	rt	(86)	81:19
$Cp^*{}_2Yb(thf)_2$	3	toluene	rt	(59)	73:27
$Cp^*{}_2Sm(thf)_2$	1.5	toluene	rt	(84)	77:23
$Cp^*{}_2Sm(thf)_2$	3	toluene	0	(63)	80:20
SmI_2	3	THF	50	(74)	51:49
$Sm(Oi\text{-}Pr)_3$	3	THF	rt	(70)	75:25
$Sm(OTf)_3$	3	THF	rt	(—)	—
SmI_3	3	THF	50	(—)	—

C_3



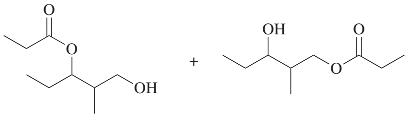
Catalyst (x amount)



I **II**

Catalyst	x	Solvent	Temp (°)	Time (h)	I	II	Refs.
$Mg[Al(OEt)_4]_2$	5 wt %	—	rt	24	(65)	(0)	91
$Mg[Al(Oi\text{-}Pr)_4]_2$	5 wt %	—	rt	24	(61)	(0)	91
$Ca[B(OMe)_4]_2$	5 mol %	MeOH	15–45	—	$(31)^b$	(0)	216
$Ca[B(OMe)_4]_2$	5 mol %	Et_2O	15–45	—	(61)	(10)	216
$Ca[B(OMe)_4]_2$	5 mol %	C_6H_6	15–45	—	$(0)^b$	(0)	216

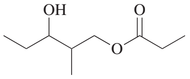
Catalyst (x mol %)



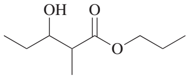
I **II**

Catalyst	x	Solvent	Temp (°)	Time (h)	I+II	I:II	Refs.
PhOMgBr	10	HMPA	40	2	(72)	—	219
$2,4,6\text{-}Me_3C_6H_2OMgBr$	—	HMPA	0	24	(94)	33:67	220, 218
$Cp^*{}_2Sm(thf)_2$	3	toluene	rt	1	(82)	27:73	238

$Al(On\text{-}Pr)_3$ ("cat."), 2 months



$(—)^c$ +

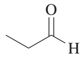


(—) 5, 3

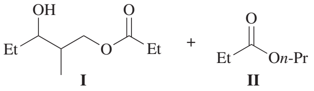
TABLE 2A. ALDOL-TISHCHENKO REACTIONS INVOLVING A SINGLE ALDEHYDE (*Continued*)

Aldehyde | Conditions | Product(s) and Yield(s) (%) | Refs.

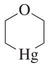
C_3



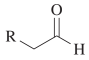
$Mg[B(OMe)_4]_2$ (x mol %), 15–45°, 2 h



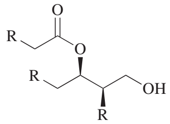
Refs. 216

x	Solvent	Additive	I	II
2	MeOH	—	(10)^d	(0)
5	C_6H_6	—	(70)	(14)
5	cyclohexane	—	(52)^d	(11)
5	Et_2O	—	(69)	(16)
5^e	Et_2O	—	(69)	(15)
5^f	Et_2O	—	(52)^g	(10)
5^e	Et_2O	$HgCl_2$	(43)^g	(20)
5^e	Et_2O	Hg	(70)^g	(10)
5^e	Et_2O		(60)^g	(13)
8^f	Et_2O	—	(17)^g	(13)

$C_{3–4} + C_7$

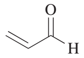


$LiClO_4$, Et_3N, rt

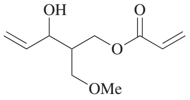


R	
Me	(31)
Et	(22)

Refs. 231



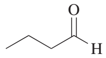
$Mg[B(OMe)_4]_2$ (10 mol %), Et_2O, 20–50°, 24 h



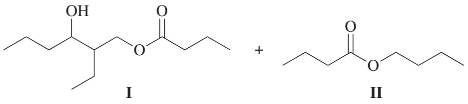
(46)

Refs. 216

C_4

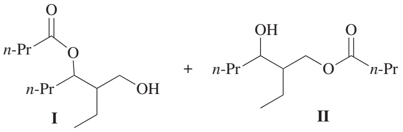


Catalyst (x amount)



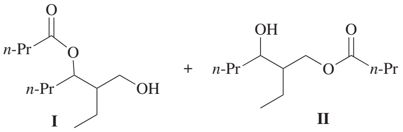
Catalyst	x	Solvent	Temp (°)	Time (h)	I	II	Refs.
$Mg(OMe)_2$	5 mol %	Et_2O	20–50	2	(55)	(13)	216
$Mg(OEt)_2$	5 wt %	—	0 to rt	48	(32)	(7)	93
$Mg[B(OMe)_4]_2$	5 mol %	Et_2O	20–50	2	(68)	(17)	216
$Na_2Mg(OEt)_4$	5 wt %	—	0 to rt	48	(41)	(3)	93
$Mg[Al(OEt)_4]_2$	5 wt %	—	0 to rt	48	(44)	(26)	93
$Mg[Al(OEt)_4]_2$	5 wt %	—	rt	24	(55)	(0)	91
$Mg[Al(Oi\text{-}Pr)_4]_2$	5 wt %	—	rt	24	(45)	(0)	91
$Mg[Al(OBu)_4]_2$	5 wt %	—	rt	24	(42)	(0)	91
$Mg[Al(OBu)_4]_2$	—	—	rt	24	(45)	(0)	92
$Ca(OEt)_2$	5 wt %	—	0 to rt	48	(50)	(7)	93
$Ca[B(OMe)_4]_2$	5 mol %	THF	20–50	2	(48)	(15)	216
$Ca[Al(OEt)_4]_2$	5 wt %	—	0 to rt	48	(23)	(15)	93

Catalyst (x mol %)



Catalyst	x	Additive	Solvent	Temp (°)	Time (h)	I+II	I/II	Refs.
PhOMgBr	10	—	HMPA	40	3	(72)	—	219
$2,4,6\text{-}Me_3C_6H_2OMgBr$	—	—	HMPA	0	2	(95)	33:67	220, 218
$Fe_3(CO)_{12}$^{h}	1.5	—	pyridine	80	15	(93)	30:70	224
$Fe_3(CO)_{12}$^{h}	0.3	pyridine *N*-oxide	C_6H_6	80	15	(91)	90:10	224
$Cp^*{}_2Sm(thf)_2$	3	—	toluene	rt	1	(87)	24:76	238

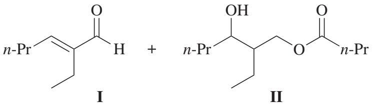
$LiWO_2$ (x mol %), THF, 24 h



x	Temp (°)	I + II	I/II
5	30	(38)	—
5	40	(43)	1:2
5	55	(46)	—
5	75	(50)	—
10	30	(51)	—
20	30	(59)	—
33	30	(65)	—

Refs. 225

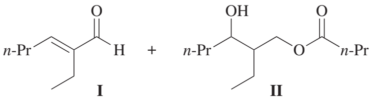
$2,4,6\text{-}Me_3C_6H_2OM$, C_6H_6, 40°, 2 h



M	I	II
Li	(11)	(45)
Na	(18)	(20)

Refs. 220

MgBrOMes (x mol %), 40°



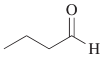
Solvent	x	Time (h)	I	II
C_6H_6	100	3	(90)	(0)
C_6H_6	50	3	(85)	(5)
C_6H_6	20	3	(24)	(67)
C_6H_6	10	24	(16)	(78)
C_6H_6	5	24	(8)	(84)
none	2	2	(4)	(49)

Refs. 220, 218

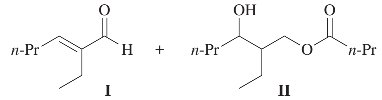
TABLE 2A. ALDOL-TISHCHENKO REACTIONS INVOLVING A SINGLE ALDEHYDE (*Continued*)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

C_4



Mg(OR)$_2$ (x mol %), 40°

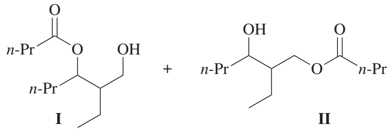


220, 218

R	x	Solvent	Time	I	II
Ph	100	C_6H_6	4 h	(85)	(6)
Ph	20	C_6H_6	8 h	(49)	(40)
Ph	5	C_6H_6	24 h	(51)	(33)
2,4,6-Me$_3$C$_6$H$_2$	100	C_6H_6	1 h	(19)	(63)
2,4,6-Me$_3$C$_6$H$_2$	20	C_6H_6	1 h	(19)	(73)

R	x	Solvent	Time	I	II
2,4,6-Me$_3$C$_6$H$_2$	10	C_6H_6	1 h	(16)	(80)
2,4,6-Me$_3$C$_6$H$_2$	5	C_6H_6	1 h	(10)	(84)
2,4,6-Me$_3$C$_6$H$_2$	2	none	5 min	(10)	(58)
2,6-(t-Bu)$_2$C$_6$H$_3$	100	C_6H_6	6 h	(70)	(12)
2,6-(t-Bu)$_2$C$_6$H$_3$	5	C_6H_6	32 h	(<1)	(<1)

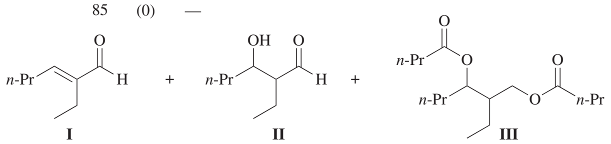
Catalyst^h (x mol %),
C_6H_6, 80°, 15 h



224

Catalyst	Additive	x	I + II	I/II
Fe$_3$(CO)$_{12}$	pyridine *N*-oxide	1	(95)	9:1
Et$_3$NH[HFe$_3$(CO)$_{11}$]	—	1.5	(89)	3:7
Na$_2$Fe$_2$(CO)$_8$	—	25	(55)	6:4
Na$_2$Fe(CO)$_4$	—	38	(15)	5:5
Na$_2$Fe(CO)$_4$	—	85	(0)	—

Catalyst

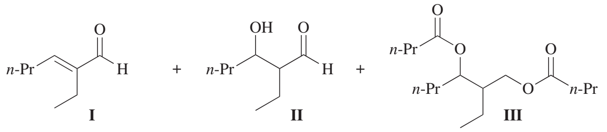


190

Catalyst	Temp (°)	Time (h)	I + II + III	I/II/III
MgO	50	1	(52)	3:74:23
MgO	0	1	(35)	2:82:16
CaO	0	1	(41)	3:40:57
γ-Al$_2$O$_3$	50	2	(33)	19:59:21
Na/Al$_2$O$_3$	50	0.5	(28)	5:92:3

Catalyst	Temp (°)	Time (h)	I + II + III	I/II/III
K/Al$_2$O$_3$	50	0.5	(50)	4:94:2
Rb/Al$_2$O$_3$	50	0.5	(53)	3:96:1
MgO/Al$_2$O$_3$	50	2	(37)	10:59:31
MgO/Al$_2$O$_3$^{i}	50	2	(31)	11:61:28

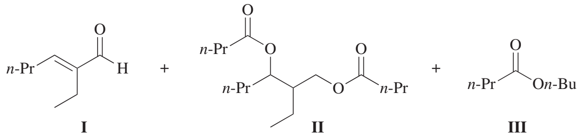
Alkali ion-exchanged or
ion-added Zeolite (Z), 50°, 5 h



190

Ion-Exchanged Z	Ion-Added Z	I + II + III	I/II/III
NaZ	—	(2)	17:73:10
KZ	—	(2)	14:79:7
RbZ	—	(4)	7:87:6
—	Na/NaZ	(63)	13:81:6
—	K/KZ	(62)	16:79:5
—	Rb/RbZ	(53)	13:82:5

See table.

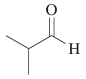


351

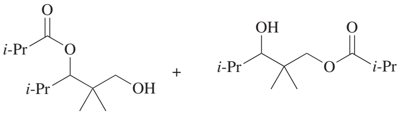
Catalyst	Temp (°)	Time (h)	I	II	III
FSM-16	120	24	(14)	(1)	(<1)
CuCl/Py-FSM-16	120	24	(14)	(2)	(<1)
CuCl/Py-FSM-16	120	72	(44)	(5)	(<1)
MgO	50	1	(25)	(19)	(5)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

C_4



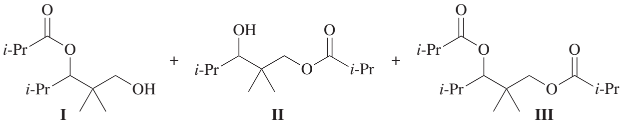
Catalyst (*x* mol %)



I **II**

Catalyst	*x*	Additive	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	Refs.
LiO*t*-Bu	10	—	THF	55	0.5	(69)	40:60	217
NaOAc	—	—	—	180	100	(26)	0:100	95
NaO*i*-Bu	1	—	*i*-BuOH	"heat"	1	(30)	39:61	215
PhOMgBr	"cat."	—	DMSO	rt	—	(—)	40:60[j]	133
Al(O*i*-Bu)$_3$	"cat."	—	—	—	—	(—)[c]	0:100	5, 3
Fe$_3$(CO)$_{12}$[h]	2	—	pyridine	80	15	(64)	60:40	224
Fe$_3$(CO)$_{12}$[h]	0.3	pyridine *N*-oxide	C_6H_6	80	15	(83)	90:10	224
SmI$_2$	1	—	THF	rt	6	(—)	—	179

LiWO$_2$ (*x* mol %), THF, 24 h

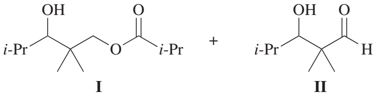


I **II** **III**

225

x	Temp (°)	**I + II**	**I/II**	**III**
0.5	30	(38)	—	(0)
5	30	(50)	—	(35)
5	40	(55)	1:2	(38)
5	55	(55)	—	(36)

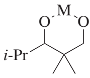
K$_2$CO$_3$ (aq)



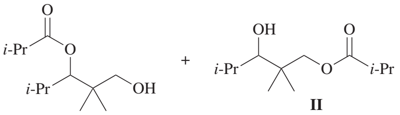
I **II**

Temp (°)	Time	**I**	**II**
130	40 h	(41)	(7)
100	60 h	(36)[k]	(—)
65	60 h	(87)[l]	(16)
60	55 h	(43)	(24)
40	75 h	(38)	(0)
rt	16 d	(12)	(42)
rt	28 d	(65)[l]	(15)

98



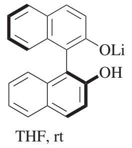
(10 mol %), 55°



I **II**

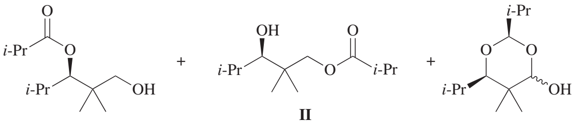
217

M	Solvent	Time (min)	**I + II**[m]	**I/II**
Li	hexane	40	(73)	38:62
Li	hexane	30	(87)	44:56
Li	THF	20	(77)	41:59
Li	hexane	60	(65)	40:60
Li	THF	30	(77)	34:66
Na	THF	30	(92)	35:65
Na	THF	20	(76)	40:60
K	THF	30	(41)	37:63



(*x* mol %),

THF, rt

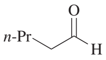


I **II** **III**

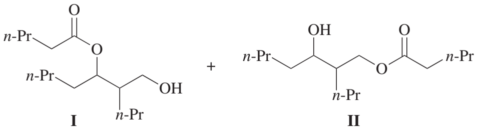
101

x	Time (h)	**I**	er **I**	**II**	er **II**	**III**	er **III**
"cat."	2	(6)	59.5:40.5	(0)	—	(10)	—
"cat."	12	(17)	57.5:42.5	(1)	—	(32)	63:37
"cat."	50	(24)	51:49	(11)	—	(56)	61.5:38.5
"cat."	143	(17)	49:51[n]	(21)	66.5:35.5	(59)	60.5:39.5
10	214	(24)	52:48	(28)	59.5:40.5	(43)	59.5:40.5

C_5



Catalyst (*x* amount)



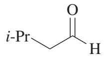
I **II**

Catalyst	*x*	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	Refs.
PhOMgBr	10 mol %	HMPA	40	2	(92)	—	219
2,4,6-Me$_3$C$_6$H$_2$OMgBr	—	HMPA	0	24	(92)	33:67	220, 218
Mg[Al(OEt)$_4$]$_2$	5 wt %	—	rt	24	(63)	0:100	91
Mg[Al(O*i*-Pr)$_4$]$_2$	5 wt %	—	rt	24	(57)	0:100	91
Cp*$_2$Sm(thf)$_2$	3 mol %	toluene	rt	1	(95)	30:70	238

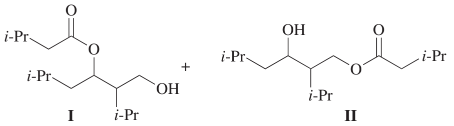
TABLE 2A. ALDOL-TISHCHENKO REACTIONS INVOLVING A SINGLE ALDEHYDE (*Continued*)

Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

C_5

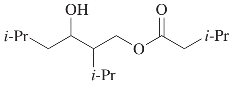


Catalyst (*x* amount)

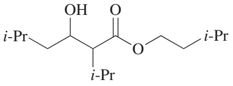


Catalyst	*x*	Additive	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	Refs.
$Mg[Al(OEt)_4]_2$	5 wt %	—	—	rt	24	(52)	0:100	91
$Fe_3(CO)_{12}{}^h$	2 mol %	—	pyridine	80	15	(50)	40:60	224
$Fe_3(CO)_{12}{}^h$	0.3 mol %	pyridine *N*-oxide	C_6H_6	80	15	(33)	80:20	224
$Cp^*{}_2Sm(thf)_2$	3 mol %	—	toluene	rt	1	(71)	14:86	238

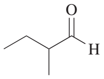
$Al(Oi\text{-}C_5H_{11})_3$ ("cat.")



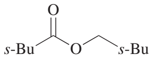
(—)[c] +



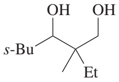
(—) 5, 3



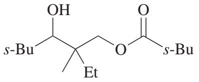
See table.



I +

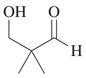


II +



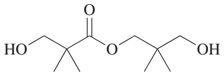
III 99

Catalyst	Solvent	Temp (°)	Time (h)	**I**	**II**	**III**
Na	—	10–120	2	(18)	(—)	(32)
NaOEt	EtOH	—	—	(—)	(—)	(—)
KOH	—	0; rt; "heat"	0.5; 15; 0.5	(0)	(60)	(0)



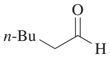
[p]

$Ca(OH)_2$ (3 mol %), 40 min

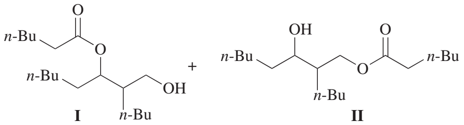


(75) 94

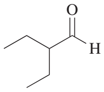
C_6



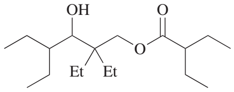
Catalyst (*x* amount)



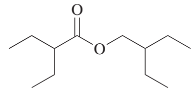
Catalyst	*x*	Solvent	Temp (°)	Time (h)	**I + II**	**I/II**	Refs.
PhOMgBr	10 mol %	HMPA	40	2	(91)	—	219
$2,4,6\text{-}Me_3C_6H_2OMgBr$	—	HMPA	0	24	(90)	33:67	220, 218
$Mg[Al(OEt)_4]_2$	5 wt %	—	rt	24	(63)[o]	0:100	91
$Mg[Al(Oi\text{-}Pr)_4]_2$	5 wt %	—	rt	24	(61)[o]	0:100	91
$Cp^*{}_2Sm(thf)_2$	3 mol %	toluene	rt	1	(51)	18:82	238



Catalyst (5 wt %), 0° to rt, 48 h

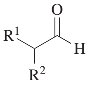


I +

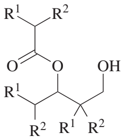


II 93

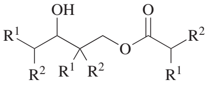
Catalyst	**I**	**II**
$Mg[Al(OEt)_4]_2$	(6)	(54)
$Ca(OEt)_2$	(4)	(51)
$Ca[Al(OEt)_4]_2$	(—)	(—)



$Fe_3(CO)_{12}{}^h$ (*x* mol %), 80°, 15 h



I +



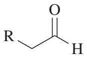
II 224

R^1	R^2	*x*	Additive	Solvent	**I + II**	**I/II**
Et	Et	10	—	pyridine	(0)	—
Et	Et	10	pyridine *N*-oxide	C_6H_6	(0)	—
Me	*n*-Pr	2	—	pyridine	(44)	6:4
Me	*n*-Pr	0.3	pyridine *N*-oxide	C_6H_6	(12)	8:2

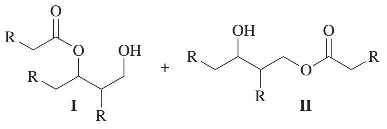
TABLE 2A. ALDOL-TISHCHENKO REACTIONS INVOLVING A SINGLE ALDEHYDE (*Continued*)

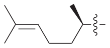
Aldehyde	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{6-11}



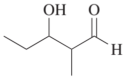
i-PrOZnEt (20 mol %), THF, 0° to rt



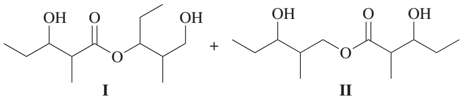
R	Time (h)	I + II
$Br(CH_2)_4$	20	(87)
$MeO_2C(CH_2)_3$	24	(50)
$(MeO)_2CH(CH_2)_3$	22	(72)
$MeO_2C(CH_2)_5$	24	(68)
Bn	18	(91)
$H_2C{=}CH(CH_2)_5$	18	(84)
$(MeO)_2CH(CH_2)_5$	20	(73)
	14	(56)
$MeCO(CH_2)_7$	15	(50)

Refs. 233

C_6



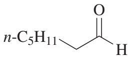
110°, 16 h



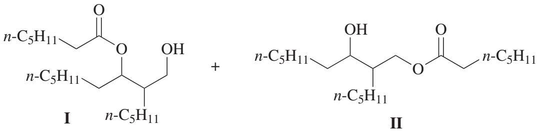
I + **II** (44), **I/II** = 70:30

Refs. 94

C_7

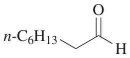


Catalyst (*x* amount)

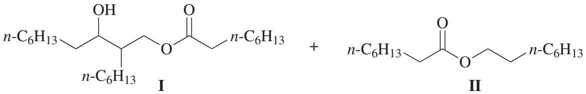


Catalyst	*x*	Solvent	Temp (°)	Time (h)	I + II	I/II	Refs.
$LiWO_2$	5 mol %	THF	30	24	(0)	—	225
$LiWO_2$	5 mol %	THF	40	24	(93)	42:58	225
PhOMgBr	10 mol %	HMPA	40	5	(73)	—	219
$2,4,6\text{-}Me_3C_6H_2OMgBr$	—	HMPA	0	24	(96)	33:67	220, 218
$Mg[Al(OEt)_4]_2$	5 wt %	—	rt	24	(51)	0:100	91
$Mg[Al(OBu)_4]_2$	5 wt %	—	rt	24	(51)	0:100	91
i-PrOZnEt	20 mol %	THF	0 to rt	12	(90)	—	233

C_8



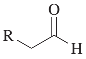
Catalyst (5 wt %), 0° to rt, 48 h



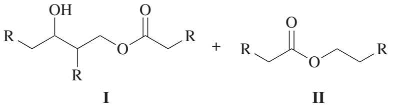
Catalyst	I	II
$Mg(OEt)_2$	(28)	(3)
$Mg[Al(OEt)_4]_2$	(43)	(20)
$Ca(OEt)_2$	(40)	(13)
$Ca[Al(OEt)_4]_2$	(21)	(12)

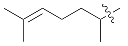
Refs. 93

C_{8-10}



$Mg[Al(OEt)_4]_2$ (5 wt %), 0° to rt, 48 h



R	I	II
Ph	(—)	(20)
	(46)	(33)

Refs. 93

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[a] The reference gives the catalyst as $Mg(AlEt_4)_2$ but we believe this to be a typographical error, since the authors' other works (Refs. 91 & 93) do not support this.

[b] The reaction also gave the aldol condensation product.

[c] The 1,3-diol monoester was a side product from a traditional Tishchenko reaction.

[d] The reaction also gave the aldol condensation product, (*E*)-2-methylpent-2-enal.

[e] The Mg used in the preparation of the catalyst was activated with iodine.

[f] The Mg used in the preparation of the catalyst was activated with mercury.

[g] A portion of the 1,3-diol monoester formed a diester with boronic acid.

[h] The catalyst was activated by heating in the solvent at 80° prior to the addition of the aldehyde.

[i] The magnesia-alumina catalyst was prepared from hydrotalcite (Mg/Al = 2:1).

[j] The secondary ester was formed first, and the ratio was 82:18. The equilibrium reaches the given ratio of 40:60 over time.

[k] Part of the reaction mixture was lost.

[l] Anhydrous K_2CO_3 was used.

[m] The reaction gave also the corresponding diol, diester, and aldoxan.

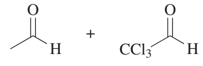
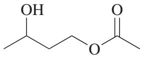
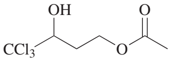
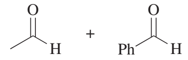
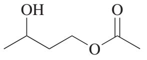
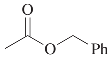
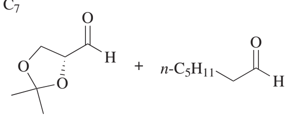
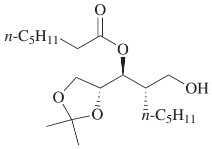
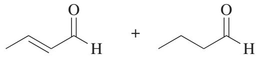
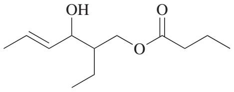
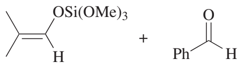
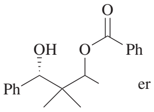
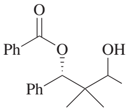
[n] The enantioselectivity for the major isomer changed from (*S*) to (*R*) over time.

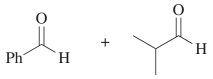
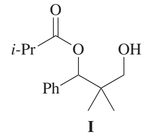
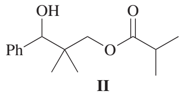
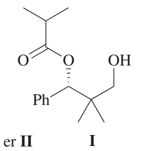
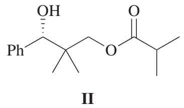
[o] The conversion was 50% and the yield is calculated based on reacted aldehyde.

[p] The starting material was prepared in situ from isobutyraldehyde and formaldehyde. The yield is based on the original amount of isobutyraldehyde.

TABLE 2B. ALDOL-TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES

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

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_2 + C_2$			
	$Mg[Al(OEt)_4]_2$ (5 wt %), 0° to rt, 48 h	 (22.5) +  (5.5)[a]	93
$C_2 + C_7$			
	$Mg[Al(OEt)_4]_2$ (5 wt %), 0° to rt, 48 h	 (37) +  (7.8)	93
$C_3 + C_7$			
	SmI_2 (30 mol %), 4 Å MS, THF, 0°	 (85)	134
$C_4 + C_4$			
	$Mg[Al(OEt)_4]_2$ (5 wt %), rt, 1 d	 (15)	91
$C_4 + C_7$			
	Cat. **117** (10 mol %), THF, –23°, 24 h	 (50) er 95.5:4.5 +  (20) er 95.5:4.5	255

Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_4$			
	LiO*i*-Pr (20 mol %), Et_2O, rt, 12 h	 +  **I** + **II** (84)	237
	$Y_5O(Oi\text{-}Pr)_{13}$ (2 mol %), ligand (13 mol %), CH_2Cl_2, 4 Å MS, 5 h	 + 	103

Ligand	**I** + **II**	**I**/**II**	er **II**
30	(44)	1:3.4	78.5:21.5
31	(36)	1:3.0	80:20
32	(54)	1:1.6	57:43
33	(42)	1:3.2	82.5:17.5
34	(48)	1:3.3	83:17
35	(70)	1:>15	87:13

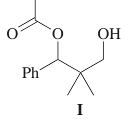
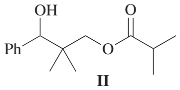
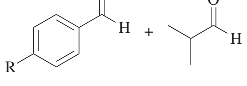
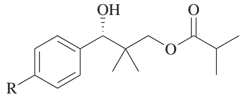
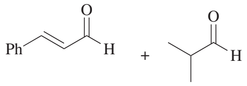
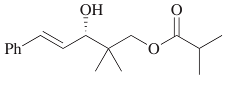
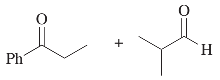
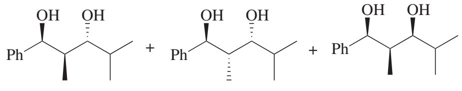
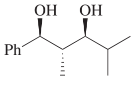
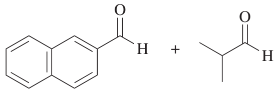
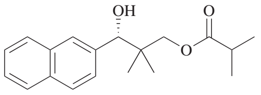
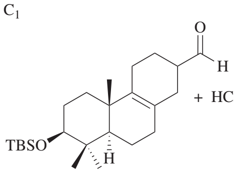
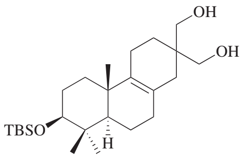
Aldehydes	Conditions	Product(s) and Yield(s) (%)	Refs.
	$Ti(Oi\text{-}Pr)_4$ (20 mol %), BuLi, Et_2O, rt, 12 h	 +  **I** + **II** (68)	237
	$Y_5O(Oi\text{-}Pr)_{13}$ (2 mol %), **35** (13 mol %), CH_2Cl_2, 4 Å MS	 R: Br (55) er 85:15 R: MeO (21) er 86:14	103

TABLE 2B. ALDOL-TISHCHENKO REACTIONS INVOLVING TWO DIFFERENT ALDEHYDES (*Continued*)

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

<table>
<tr><th>Aldehydes</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td colspan="4">$C_9 + C_4$</td></tr>
<tr><td></td><td>$Y_5O(Oi\text{-}Pr)_{13}$ (2 mol %),
35 (13 mol %), CH_2Cl_2, 4 Å MS</td><td> (50) er 55:45</td><td>103</td></tr>
<tr><td></td><td>1. Catalyst (20 mol %),
Et$_2$O, rt, 15 h
2. NaOH, MeOH, rt, 12 h</td><td>
I II III
<table><tr><th>Catalyst</th><th>I</th><th>I/II/III/IV</th></tr><tr><td>$Mg(Oi\text{-}Pr)_2$</td><td>(14)</td><td>4:1:0.1:0.2</td></tr><tr><td>$Ca(OMe)_2$</td><td>(8)</td><td>32:1:0.5:0.5</td></tr><tr><td>$Zr(Ot\text{-}Bu)_4$</td><td>(14)</td><td>5:1:0.2:0.2</td></tr><tr><td>$Cu(Oi\text{-}Pr)_2$</td><td>(8)</td><td>49:1:<0.1:<0.1</td></tr><tr><td>$Zn(Ot\text{-}Bu)_2$</td><td>(7)</td><td>19:1:0.5:<0.2</td></tr></table>+ 
IV</td><td>237</td></tr>
<tr><td colspan="4">$C_{11} + C_4$</td></tr>
<tr><td></td><td>$Y_5O(Oi\text{-}Pr)_{13}$ (2 mol %),
35 (13 mol %), CH_2Cl_2,
4 Å MS</td><td> (50) er 82:18</td><td>103</td></tr>
<tr><td colspan="4">$C_{18} + C_1$</td></tr>
<tr><td> + HCHO (aq)</td><td>1. Na_2CO_3, MeOH, CH_2Cl_2, heat
2. $NaBH_4$, MeOH</td><td> (87)</td><td>352</td></tr>
</table>

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[a] In a table footnote the value of 9.3 is given.

TABLE 2C. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY ALDEHYDES

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

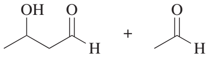
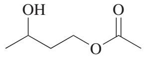
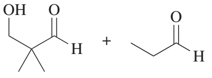
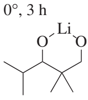
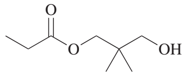
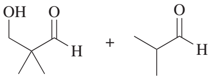
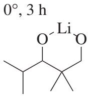
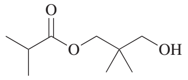
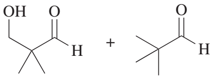
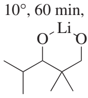
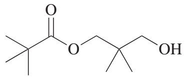
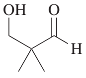
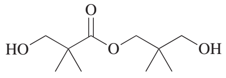
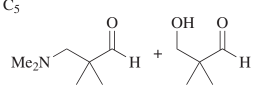
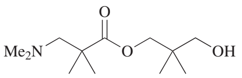
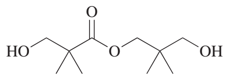
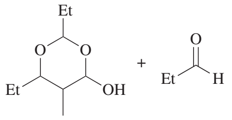
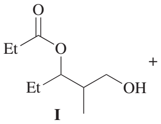
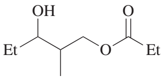
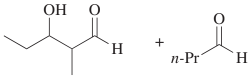
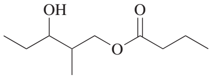
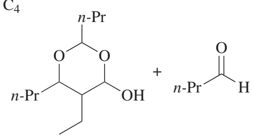
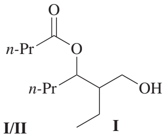
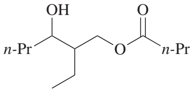
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_4 + C_2$			
	$Mg[B(OMe)_4]_2$ (10 mol %), Et$_2$O, –78°; 10°, 1 h; 50°, 2 h	 (74)	216
$C_5 + C_3$			
	1. EtCHO, heat, 3 h 2. 0°, 3 h 3.  (30 mol %), THF, 0°, 15 min	 (41)	142
$C_5 + C_4$			
	1. *i*-PrCHO, 65°, 3 h 2. 0°, 3 h 3.  (30 mol %), THF, 0°, 45 min	 (86)	142
$C_5 + C_5$			
	1. *t*-BuCHO, 65°, 3 h 2. 0°, 3 h 3. 10°, 60 min, vacuum 4.  (30 mol %), THF, 0°, 60 min	 (60)	142
 [a]	$Ca(OH)_2$ (3 mol %), 40 min	 (75)	94

TABLE 2C. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY ALDEHYDES (*Continued*)

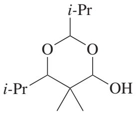
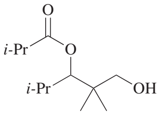
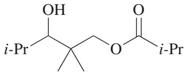
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_5 + C_5$			
	125°, 6 h	 (10) +  (15)^b	94
$C_6 + C_3$			
	See table.	 **I** +  **II**	94

Temp (°)	Time	**I + II**	**I/II**
110	20 h	(39)	50:50
120	20 min	(5)	99:1
120	40 min	(9)	95:5
120	80 min	(16)	86:14
120	160 min	(33)	79:21
120	300 min	(48)	66:33

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6 + C_4$			
	Mg[B(OMe)$_4$]$_2$ (10 mol %), Et$_2$O, –78°; 10°, 1 h; 50°, 2 h	 (72)	216
$C_8 + C_4$			
	See table.	 **I** +  **II**	94

Temp (°)	Time	**I + II**	**I/II**
120	20 min	(7)	97:3
120	40 min	(12)	94:6
120	80 min	(21)	85:15
120	160 min	(36)	76:24
120	320 min	(53)	61:39
200	6 h	(43)	60:40

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	Lewasorb A 50, 45°	 **I** +  **II**	94

Time (min)	**I + II**	**I/II**
15	(14)	98:2
30	(25)	97:3
60	(42)	92:8
90	(54)	87:13
180	(69)	74:26
300	(82)	40:60

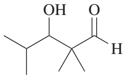
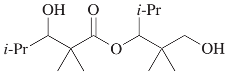
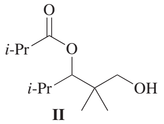
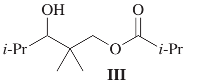
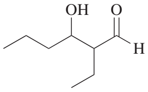
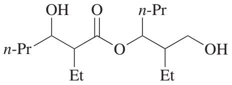
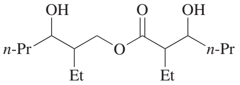
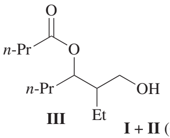
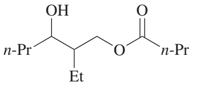
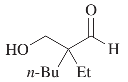
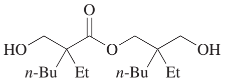
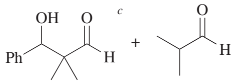
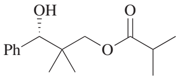
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_8 + C_8$			
	120°, 16 h	 **I** +  **II** +  **III** **I** (18), **II + III** (37)	94
	120°, 14 h	 **I** +  **II** +  **III** +  **IV** **I + II** (65), **I/II** = 90:10 **III + IV** (10)	94

TABLE 2C. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY ALDEHYDES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_9 + C_9$			
	$Ca(OH)_2$ (7 mol %), 80–100°, 80 min	 (83)	94
$C_{11} + C_4$			
 ^{c}	$Y_5O(Oi\text{-}Pr)_{13}$ (2 mol %), **35** (13 mol %), CH_2Cl_2, 4 Å MS	 (38) er 88:12	103

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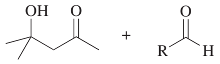
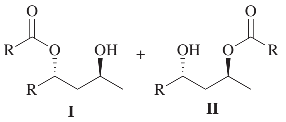
[a] The starting material was prepared in situ from isobutyraldehyde and formaldehyde. The yield is based on the original amount of isobutyraldehyde.

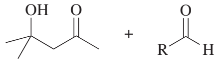
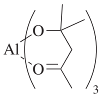
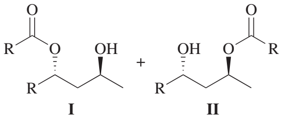
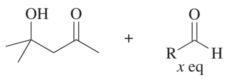
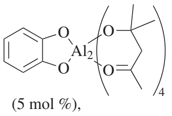
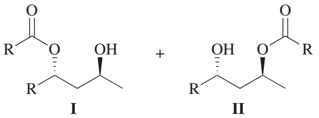
[b] The yield is based on 3-hydroxy-2,2-dimethylpropanal, of which an excess was used.

[c] The starting material was racemic and contaminated with 15% PhCHO.

TABLE 2D. ALDOL-TISHCHENKO REACTIONS OF DIALKYL KETONES

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_3 + C_{2\text{–}8}$			
 *x* eq	$AlMe_3$ (*y* mol %), CH_2Cl_2, rt, 22 h		245

R	*x*	*y*	**I + II**
Me	3	10	(68)
Et	3	10	(73)
n-Pr	2	1	(<1)[a]
n-Pr	2	5	(48)
n-Pr	2	10	(56)
n-Pr	3	5	(35)
n-Pr	3	10	(80)
i-Pr	3	10	(59)
2-pentyl	3	10	(81)
Cy	3	10	(74)
n-C_7H_{15}	3	10	(79)
n-(1-Br)-C_7H_{14}	3	10	(0)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_3 + C_{3\text{–}8}$			
	 (10 mol %), CH_2Cl_2, rt		247
 *x* eq	 (5 mol %), additive (*y* mol %), CH_2Cl_2, rt		247

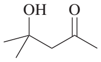
R	Time (h)	**I + II**	**I/II**
Et	22	(73)	3:1
n-Pr	21	(80)	5:1
i-Pr	22	(59)	—
2-pentyl	22	(81)	—
Cy	22	(74)	4:1
n-C_7H_{15}	22	(79)	4:1

R	*x*	Additive	*y*	Time (h)	**I + II**	**I/II**
Et	3	$AlMe_3$	5	18	(72)	3:2
n-Pr	2	—	—	20	(39)	—
n-Pr	4	—	—	20	(47)	—
n-Pr	3	$AlMe_3$	5	20	(67)	4:1
n-Pr	3	$AlMe_3$	10	20	(58)	4:1
i-Pr	3	$AlMe_3$	5	20	(72)	—
2-pentyl	3	$AlMe_3$	5	20	(81)	—
Cy	3	$AlMe_3$	5	21	(80)	4:1
n-C_7H_{15}	3	$AlMe_3$	5	21	(61)	4:1

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_3 + C_{3–9}$



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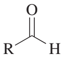
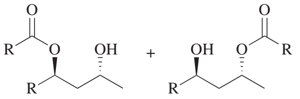


$Zr(Ot\text{-}Bu)_4$ (10 mol %), THF, –20°, 48 h

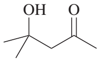


I + II

R	I + II	I/II
Et	(75)	3:1
i-Pr	(85)	9:1
c-C_6H_{11}	(70)	22:1
n-C_6H_{13}	(89)	2:1
$BnCH_2$	(75)	1:1

246

$C_3 + C_4$



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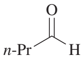
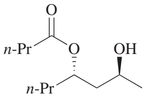
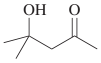


Cat. **125** (5 mol %), CH_2Cl_2, rt



Time (h)	
24	(49)
48	(67)
72	(69)

247



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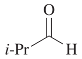
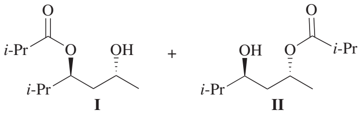


Catalyst (10 mol %)



I + II

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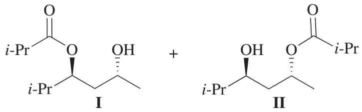
Catalyst	Solvent	Temp (°)	Time (h)	I + II	I/II
$Zr(Oi\text{-}Pr)_4$	THF	0	24	(5)	—
$Hf(Ot\text{-}Bu)_4$	THF	–20	17	(64)	—
$Ti(Oi\text{-}Pr)_4$	CH_2Cl_2	rt	24	(0)	—
$Ti(Ot\text{-}Bu)_4$	CH_2Cl_2	rt	24	(5)	—
$Y_5O(Ot\text{-}Bu)_{13}$	CH_2Cl_2	–20	1	(89)	10:1
$ZnEt_2$	THF	0	24	(9)	—

$Zr(Ot\text{-}Bu)_4$ (10 mol %), CH_2Cl_2

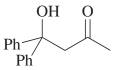


I + II

249

Solvent	Temp (°)	Time (h)	I + II	I/II
CH_2Cl_2	0	2	(84)	11:1
CH_2Cl_2	–20	4	(87)	10:1
CH_2Cl_2	–50	24	(55)	16:1
CH_2Cl_2	–65	40	(5)	—
CH_2Cl_2	–78	24	(0)	—
THF	0	2	(84)	5:1

Solvent	Temp (°)	Time (h)	I + II	I/II
Et_2O	0	2	(90)	5:1
toluene	0	2	(87)	6:1
DMF	0	2	(55)	14:1
MeCN	0	2	(84)	1:1
$CHCl_3$	0	2	(0)	—



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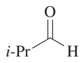
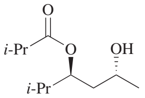
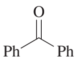


$Zr(Ot\text{-}Bu)_4$, THF, –20°, 70 min



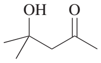
(23) +



(70)

249

$C_3 + C_{4–7}$



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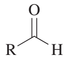
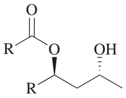


$Zr(Ot\text{-}Bu)_4$ (10 mol %), ligand, CH_2Cl_2



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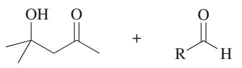
R	Ligand	Temp(°)	Time (h)		er
i-Pr	**23**	0	3	(80)	70:30
i-Pr	**24**	0	3	(84)	70.5:29.5
i-Pr	**25**	0	3	(79)	73.5:26.5
i-Pr	**25**	–20	40	(28)	64:36
i-Pr	**26**	0	3	(78)	65:35
i-Pr	**27**	0	3	(73)	69:31

R	Ligand	Temp(°)	Time (h)		er
i-Pr	**36**	0	3	(31)	64:36
i-Pr	**37**	0	3	(62)	50:50
i-Pr	**38**	0	3	(35)	62.5:37.5
i-Pr	**39**	0	3	(89)	64:36
Cy	**25**	0	3	(86)	76:24
n-C_6H_{13}	**25**	0	3	(86)	62.6:37.5

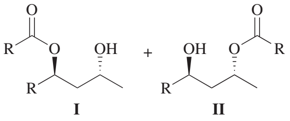
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_3 + C_{4–7}$



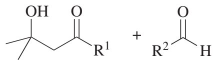
Zr(O*t*-Bu)$_4$ (10 mol %), ligand, CH_2Cl_2, 0°



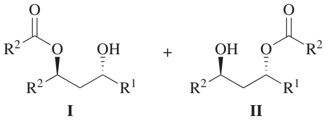
R	Ligand	I + II	I/II
i-Pr	**28**	(26)	20:1
i-Pr	**29**	(79)	20:1
n-C_6H_{13}	none	(72)	1:1
n-C_6H_{13}	**28**	(31)	20:1
n-C_6H_{13}	**29**	(91)	5:1

249

$C_{3–6} + C_{4–7}$



Zr(O*t*-Bu)$_4$ (10 mol %), **29**, CH_2Cl_2, 0°, 3 h



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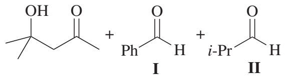
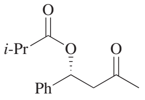
R^1	R^2	I + I	I/II
Me	*i*-Bu	(87)	20:1
Me	1-ethylpropyl	(72)	20:1
Me	Cy	(86)	20:1
i-Pr	*i*-Pr	(94)	—
i-Pr	*n*-C_6H_{13}	(86)	5:1
t-Bu	*i*-Pr	(84)	7:1
t-Bu	Ph	(86)	20:1
t-Bu	1-ethylpropyl	(86)	20:1
t-Bu	Cy	(75)	20:1
t-Bu	*n*-C_6H_{13}	(88)	15:1
t-Bu	*c*-C_3H_5	(70)	13:1
Ph	*n*-C_6H_{13}	(79)	10:1
Ph	*i*-Pr	(75)	14:1
2-$MeOC_6H_4$	*i*-Pr	(90)	12:1
2-$MeOC_6H_4$	*n*-C_6H_{13}	(89)	12:1

$C_3 + C_7 + C_4$



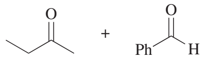
1. **I**, Zr(O*t*-Bu)$_4$ (10 mol %), CH_2Cl_2, –20°, 24 h
2. **II**, Zr(O*t*-Bu)$_4$ (10 mol %), CH_2Cl_2, –20°, 30 min



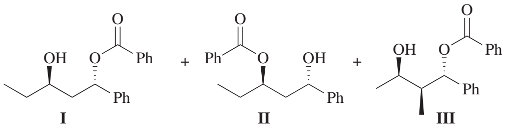
(48)

249

$C_4 + C_7$



Catalyst (30 mol %), 4 Å MS, THF, 0°



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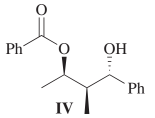
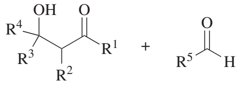
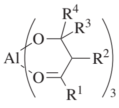
Catalyst	Time (h)	I–IV	I/II/III/IV
SmI_2	2	(83)	49:4:40:7
SmI_3	14	(82)	0:50:0:50

\+

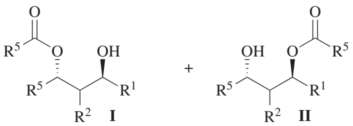


$C_{4–5} + C_{3–4}$





(10 mol %), CH_2Cl_2, rt



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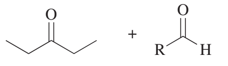
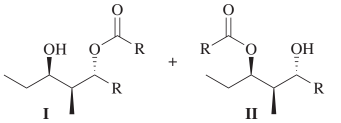
R^1	R^2	R^3	R^4	R^5	Time (h)	I + II	I/II
Et	Br	Me	Me	Et	20	(71)	—[b]
i-Pr	H	Me	*i*-Pr	*n*-Pr	23	(62)	5:2
i-Pr	H	Me	*i*-Pr	*i*-Pr	21	(64)	—[c]
Et	Me	Et	Et	Et	20	(53)	—[c]
Et	Me	Et	Et	*n*-Pr	22	(72)	4:3

$C_5 + C_{3–7}$



Catalyst (30 mol %), 4 Å MS, THF



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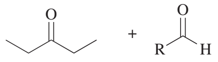
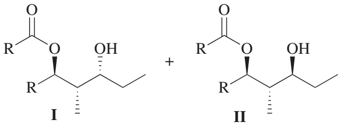
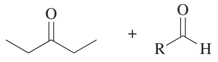
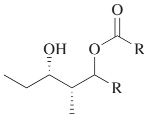
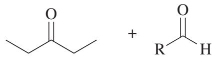
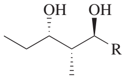
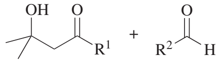
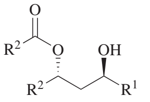
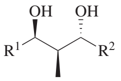
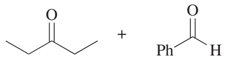
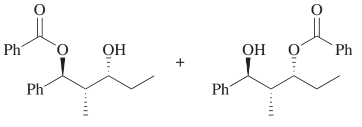
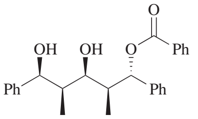
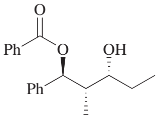
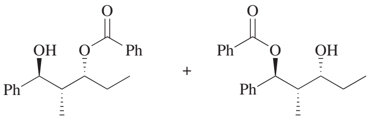
R	Catalyst	Temp (°)	Time (h)	I + II	I/II
Et	SmI_2	0	0.5	(79)	100:0
i-Pr	SmI_2	rt	2	(78)	64:36
Ph	SmI_2	0	1	(86)	90:10
Ph	SmI_2	rt	2	(88)	14:86
Ph	SmI_3	0	14	(85)	100:0

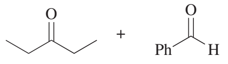
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_5 + C_{4–7}$			
	$BuTi(Oi\text{-}Pr)_4Li$ (20 mol %),[d] $t\text{-}BuOCH_2CH_2OMe$, rt, 24 h	 R | I + II | I/II *n*-Pr | (79) | 99:1 *i*-Pr | (86) | 98:2 *t*-Bu | (84) | 98:2 Ph | (63) | 97:3	236
$C_5 + C_5$			
	1. Aldehyde, SmI_2 (60 mol %), THF, rt, 1 h 2. Ketone, 0°, 1 h	 R 3-furyl (68) 2-thienyl (63) 3-thienyl (61)	272
$C_5 + C_{5–9}$			
	1. Cat. **117** (10 mol %), THF, 0°, 48 h 2. NaOMe, MeOH	 R | | er *t*-Bu | (0) | — Ph | (81) | 96.5:3.5 $4\text{-}BrC_6H_4$ | (80) | 94:6 $4\text{-}MeOC_6H_4$ | (87) | 97.5:2.5 $4\text{-}MeC_6H_4$ | (81) | 97.5:2.5 $PhCH_2CH_2$ | (0) | — PhCH=CH | (61) | 97:3	253 253, 252 253, 252 253, 252 253, 252 253 253, 252
$C_{5–6} + C_{4–7}$			
	$Zr(Ot\text{-}Bu)_4$ (10 mol %), **23**, CH_2Cl_2, 0°, 3 h	 R^1 | R^2 | | er *i*-Pr | *i*-Pr | (82) | 72:28 *i*-Pr | $n\text{-}C_6H_{13}$ | (86) | 65:35 *t*-Bu | *i*-Pr | (84) | 78.5:21.5 *t*-Bu | 2-ethylpropyl | (69) | 73.5:26.5 *t*-Bu | Cy | (75) | 75:25 *t*-Bu | $n\text{-}C_6H_{13}$ | (88) | 71:29	248
$C_{5–9} + C_{4–7}$			
	1. LiO*i*-Pr (15 mol %), Et_2O, rt, 15 h 2. NaOH, MeOH, rt, 12 h	 R^1 | R^2 | | dr Et | *i*-Pr | (61) | 5:1 *i*-Pr | *i*-Pr | (55) | 95:5 *i*-Pr | Ph | (45) | 6:1 Ph | *i*-Pr | (74) | 96:4	237
$C_5 + C_7$			
	Cat. **117** (10 mol %), THF, rt, 3 h	 (44) er 92.5:7.5 (23) er 92.5:7.5	253
	1. LDA, THF, –78° 2. Aldehyde, –22°, 5 h	 (81)[e]	227
	$Yb(OTf)_3$ (20 mol %), **46**, $EtN(i\text{-}Pr)_2$, rt, 20 h	 Solvent | | er THF | (59) | 56:44 CH_2Cl_2 | (17) | 46:54 dioxane | (58) | 54.5:45.5 Me_2O | (35) | 54.5:45.5 MeCN | (—) | — Et_2O | (18) | 52.5:47.5	258
	$Yb(OTf)_3$ (1 eq), **46** (1 eq), $EtN(i\text{-}Pr)_2$ (2 eq), THF, rt, 4 h	 (6) 100% de, er 87.5:22.5 (68) 98% de, er 59:41	258

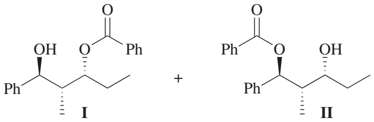
Substrates | Conditions | Product(s) and Yield(s) (%) | Refs.

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

$C_5 + C_7$



Yb(OTf)$_3$ (20 mol %), **46**, base (x mol %), THF, rt, 20 h



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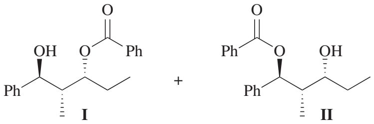
Base	*x*	**I**	er **I**	**II**	er **II**
Et$_3$N	20	(38)	21.5:78.5	(51)	53.5:46.5
Et$_3$N	40	(9)	41.5:58.5	(68)	55.5:45.5
EtN(*i*-Pr)$_2$	20	(36)	21:79	(56)	53.5:46.5
EtN(*i*-Pr)$_2$	40	(8)	31:69	(57)	55.5:45.5

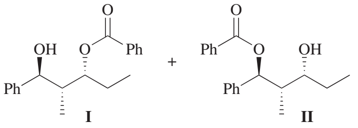
Base	*x*	**I**	er **I**	**II**	er **II**
NMI	20	(18)	17:83	(60)	54:46
NMI	40	(15)	21:79	(62)	50:50
BuLi	20	(4)	25:75	(42)	50:50
BuLi	40	(0)	—	(56)	61.5:38.5

Yb(OTf)$_3$ (x mol %), ligand, THF



Ligand	*x*	Additive	Temp	Time (h)	**I + II**	**I/II**	er	Refs.
47	10	—	rt	20	(0)	—	—	260
47	20	—	rt	20	(75)	1:2	50:50	260
48	20	—	rt	20	(—)	—	—	260
49	20	—	rt	20	(74)	1:3.3	52.5:48.5	260
50	20	—	rt	20	(62)	1:7	53.5:46.5	260
51	20	—	rt	2	(96)	2:1	62:38	260
51	20	—	–20°	4	(90)	3:1	55:45	260
51	10	—	rt	4	(97)	2:3	62:38	260
51	10	—	40°	4	(90)	—	60:40	260
52	20	EtN(*i*-Pr)$_2$	rt	20	(13)	1:0	50:50	260
53	20	—	rt	20	(—)	—	—	260
54	20	—	rt	20	(—)	—	—	260
55	10	—	rt	20	(84)	2:1	50:50	260
56	20	—	rt	20	(34)	—	54.5:44.5	259
57	20	—	rt	20	(20)	—	48.5:51.5	259
58	20	—	rt	20	(16)	—	53.5:6.5	259
59	20	—	rt	20	(90)	—	50:50	259
60	20	—	rt	20	(23)	—	50:50	259
61	20	—	rt	20	(70)	—	54:46	259
62	20	—	rt	20	(69)	—	55:45	259
63	20	—	rt	20	(—)	—	—	259
cinchonidine	20	—	rt	20	(83)	—	50:50	259

Catalyst (10 mol %), **51**, THF, rt



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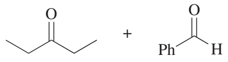
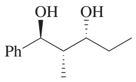
Catalyst	**I + II**	dr	er
Sc(OTf)$_3$	(—)	—	—
La(OTf)$_3$	(—)	—	—
Pr(OTf)$_3$	(15)	70:30	54:46
Sm(OTf)$_3$	(35)	60:40	54:46
Eu(OTf)$_3$	(62)	64:36	55:45

Catalyst	**I + II**	dr	er
Dy(OTf)$_3$	(83)	90:10	57.5:42.5
Er(OTf)$_3$	(94)	97.5:2.5	60:40
Yb(OTf)$_3$	(97)	99.5:0.5	62:38
Y(OTf)$_3$	(95)	96.5:3.5	53.5:6.5
In(OTf)$_3$	(—)	—	—

TABLE 2D. ALDOL-TISHCHENKO REACTIONS OF DIALKYL KETONES (*Continued*)

<table>
<tr><th>Substrates</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td colspan="4">Please refer to the charts preceding the tables for structures indicated by the bold numbers.</td></tr>
<tr><td>$C_5 + C_7$
</td><td>1. Yb(OTf)$_3$ (x mol %), ligand, THF, rt
2. NaOMe, MeOH, rt</td><td>
<table>
<tr><th>x</th><th>Ligand</th><th></th><th>er</th></tr>
<tr><td>20</td><td>73</td><td>(0)</td><td>—</td></tr>
<tr><td>20</td><td>74</td><td>(0)</td><td>—</td></tr>
<tr><td>20</td><td>75</td><td>(95)</td><td>70:30</td></tr>
<tr><td>20</td><td>76</td><td>(68)</td><td>50:50</td></tr>
<tr><td>20</td><td>77</td><td>(98)</td><td>50:50</td></tr>
<tr><td>20</td><td>78</td><td>(97)</td><td>50:50</td></tr>
<tr><td>20</td><td>79</td><td>(70)</td><td>54.5:45.5</td></tr>
<tr><td>20</td><td>80</td><td>(98)</td><td>70:30</td></tr>
<tr><td>20</td><td>81</td><td>(66)</td><td>50:50</td></tr>
<tr><td>20</td><td>82</td><td>(15)</td><td>52.5:47.5</td></tr>
<tr><td>20</td><td>83</td><td>(55)</td><td>61.5:38.5</td></tr>
<tr><td>20</td><td>84</td><td>(35)</td><td>57:43</td></tr>
<tr><td>20</td><td>85</td><td>(13)</td><td>63.5:36.5</td></tr>
<tr><td>20</td><td>86</td><td>(92)</td><td>65:35</td></tr>
<tr><td>20</td><td>87</td><td>(23)</td><td>50:50</td></tr>
<tr><td>20</td><td>88</td><td>(42)</td><td>65:35</td></tr>
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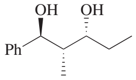
<tr><td>20</td><td>90</td><td>(46)</td><td>70:30</td></tr>
<tr><td>20</td><td>91</td><td>(51)</td><td>75:25</td></tr>
<tr><td>30</td><td>91</td><td>(97)</td><td>75:25</td></tr>
<tr><td>20</td><td>92</td><td>(91)</td><td>73:27</td></tr>
<tr><td>10</td><td>92</td><td>(54)</td><td>73:27</td></tr>
<tr><td>10</td><td>92[f]</td><td>(72)</td><td>73:27</td></tr>
<tr><td>20</td><td>93</td><td>(95)</td><td>55:45</td></tr>
<tr><td>20</td><td>94</td><td>(55)</td><td>55:45</td></tr>
</table></td><td>261</td></tr>
<tr><td></td><td>1. Yb(OTf)$_3$ (x mol %), ligand, THF, rt
2. NaOMe, MeOH, rt</td><td>
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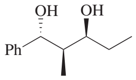
<tr><td>20</td><td>98</td><td>(98)</td><td>72:28</td></tr>
<tr><td>20</td><td>99</td><td>(—)</td><td>—</td></tr>
<tr><td>20</td><td>100</td><td>(—)</td><td>—</td></tr>
<tr><td>15</td><td>101</td><td>(92)</td><td>75:25</td></tr>
<tr><td>15</td><td>102</td><td>(50)</td><td>66:34</td></tr>
<tr><td>15</td><td>103</td><td>(93)</td><td>72:28</td></tr>
<tr><td>20</td><td>104</td><td>(93)</td><td>73:27</td></tr>
<tr><td>15</td><td>105</td><td>(96)</td><td>64:36</td></tr>
<tr><td>15</td><td>106</td><td>(77)</td><td>61:39</td></tr>
<tr><td>15</td><td>107</td><td>(95)</td><td>54:46</td></tr>
<tr><td>15</td><td>108</td><td>(50)</td><td>62:38</td></tr>
</table></td><td>262</td></tr>
<tr><td></td><td>1. Yb(OTf)$_3$ (20 mol %), ligand, THF, rt
2. NaOMe, MeOH, rt</td><td>
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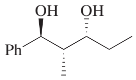
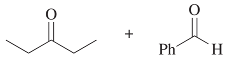
<tr><td>95</td><td>(50)</td><td>74:26</td></tr>
<tr><td>96</td><td>(0)</td><td>—</td></tr>
</table></td><td>261</td></tr>
<tr><td></td><td>1. Yb(OTf)$_3$ (x mol %), 97, rt
2. NaOMe, MeOH, rt</td><td>
<table>
<tr><th>Solvent</th><th>x</th><th>Yb/97</th><th></th><th>er</th></tr>
<tr><td>THF</td><td>20</td><td>1:1</td><td>(85)</td><td>58:42</td></tr>
<tr><td>THF</td><td>20</td><td>1:2</td><td>(93)</td><td>68:32</td></tr>
<tr><td>THF</td><td>20</td><td>1:3</td><td>(93)</td><td>71:29</td></tr>
<tr><td>THF</td><td>20</td><td>1:4</td><td>(98)</td><td>72.5:27.5</td></tr>
<tr><td>THF</td><td>10</td><td>1:4</td><td>(92)</td><td>72.5:27.5</td></tr>
<tr><td>THF</td><td>15</td><td>1:4</td><td>(50)</td><td>72.5:27.5</td></tr>
<tr><td>MeCN</td><td>20</td><td>1:4</td><td>(70)</td><td>53:47</td></tr>
<tr><td>dioxane</td><td>20</td><td>1:4</td><td>(75)</td><td>63:37</td></tr>
</table></td><td>262</td></tr>
</table>

TABLE 2D. ALDOL-TISHCHENKO REACTIONS OF DIALKYL KETONES (*Continued*)

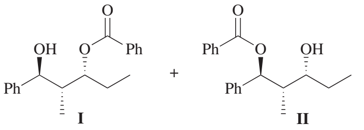
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_5 + C_7$



Yb(OTf)$_3$ (x mol %), **64**, rt, 20 h

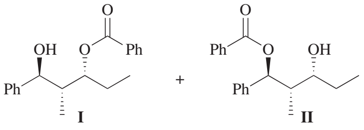


259, 105

Solvent	x	Yb/**64**	**I** + **II**	er
THF	20	1:1	(0)	—
THF	20	1:2	(88)	71:29
THF	20	1:3	(76)	77.5:22.5
THF	20	1:4	(86)	81:19
THF	10	1:5	(60)	77.5:22.5
THF	20	1:5	(86)	80.5:19.5
THF	20	1:10	(83)	75:25

Solvent	x	Yb/**64**	**I** + **II**	er
CH_2Cl_2	20	1:2	(0)	—
dioxane	10	1:2	(35)	76:24
MeCN	20	1:2	(16)	67.5:32.5
DME	20	1:2	(66)	80:20
DME	20	1:4	(82)	88:12
DME	10	1:4	(33)	83.5:16.5

Yb(OTf)$_3$ (20 mol %), ligand, rt, 20 h

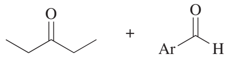


105

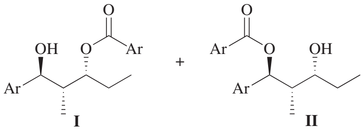
Ligand	Solvent	Yb/Ligand	**I** + **II**	er
65	THF	1:2	(—)	—
66	THF	1:2	(—)	—
67	THF	1:2	(69)	55:45
67	THF	1:4	(70)	57:43
67	DME	1:4	(55)	60:40
68	DME	1:4	(46)	77.5:22.5

Ligand	Solvent	Yb/Ligand	**I** + **II**	er
69	DME	1:4	(17)	75:25
70	DME	1:4	(46)	76.5:23.5
71	DME	1:4	(50)	82.5:17.5
72	DME	1:4	(55)	76:24
ent-**64**	DME	1:4	(75)	15:85

$C_5 + C_{7-8}$



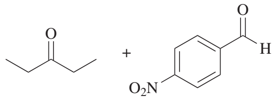
Yb(OTf)$_3$ (20 mol %), **46**, EtN(i-Pr)$_2$, THF, rt, 20 h



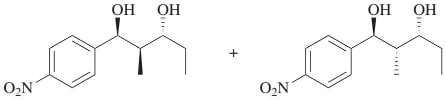
258

Ar	**I**	er **I**	**II**	er **II**
4-ClC$_6$H$_4$	(38)	23.5:76.5	(58)	69:31
4-FC$_6$H$_4$	(51)	34:64	(30)	62:38
4-MeOC$_6$H$_4$	(2)	—	(45)	59:41
4-MeC$_6$H$_4$	(10)	87:13	(64)	58.5:41.5

$C_5 + C_7$



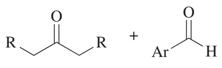
1. Yb(OTf)$_3$ (20 mol %), **64**, DME, rt, 20 h
2. NaOMe, MeOH



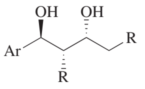
(28) er 56:44 (14) er 57:43

105

$C_{5-7} + C_{7-11}$



1. Yb(OTf)$_3$ (x mol %), **91**, THF, rt
2. NaOMe, MeOH, rt



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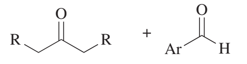
R	Ar	x		er
Me	4-MeC$_6$H$_4$	40	(98)	78:22
Me	4-MeOC$_6$H$_4$	20	(26)	82:18
Me	4-MeOC$_6$H$_4$	30	(75)	82:18
Me	4-MeOC$_6$H$_4$	40	(98)	82:18
Me	4-t-BuC$_6$H$_4$	40	(96)	78:22
Et	4-MeC$_6$H$_4$	40	(69)	78:22
Et	4-MeOC$_6$H$_4$	40	(44)	75:25

TABLE 2D. ALDOL-TISHCHENKO REACTIONS OF DIALKYL KETONES (*Continued*)

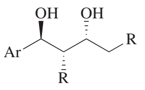
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_{5-7} + C_{7-11}$

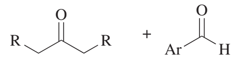


1. $Yb(OTf)_3$ (20 mol %), **64**, DME, rt, 20 h
2. NaOMe, MeOH

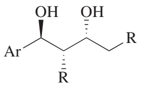


R	Ar		er	Refs.
Me	Ph	(77)	87.5:12.5	105
Me	4-$MeOC_6H_4$	(60)	93:7	
Me	4-MeC_6H_4	(76)	90:10	
Me	4-ClC_6H_4	(76)	76.5:23.5	
Me	4-BrC_6H_4	(75)	77.5:22.5	
Me	2-naphthyl	(67)	85:15	
Et	Ph	(77)	82.5:17.5	
Et	4-$MeOC_6H_4$	(25)	90:10	

$C_{5-9} + C_{7-8}$

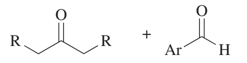


1. $Yb(OTf)_3$ (*x* mol %), **92**, THF, rt
2. NaOMe, MeOH, rt

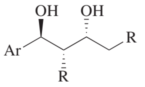


R	Ar	*x*		er	Refs.
Me	4-BrC_6H_4	20	(84)	65:35	261
Et	Ph	20	(74)	78:22	
n-Pr	Ph	20	(95)	77:23	
n-Pr	4-MeC_6H_4	30	(54)	76:24	

$C_{5-17} + C_7$

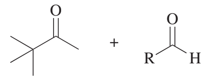


1. $Yb(OTf)_3$ (15 mol %), **101**, THF, rt, 16 h
2. NaOMe, MeOH, rt

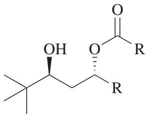


R	Ar		er	Refs.
Me	4-$MeOC_6H_4$	(75)	76:24	262
Me	4-ClC_6H_4	(92)[g]	70:30	
n-Pr	Ph	(93)	70:30	
n-Pr	4-ClC_6H_4	(75)	68:32	
i-Pr	Ph	(0)	—	
n-C_7H_{15}	Ph	(35)	72:28	

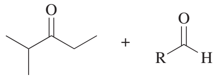
$C_6 + C_{4-7}$



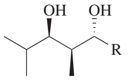
Catalyst (30 mol %), 4 Å MS, THF, 0°



R	Catalyst	Time (h)		Refs.
i-Pr	SmI_2	4	(80)	134
Ph	SmI_2	4	(80)	
Ph	SmI_3	14	(78)	

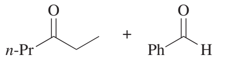


1. Base, THF, –78°
2. RCHO, –78°, 1 h
3. 22°, 12 h
4. NaOH, MeOH

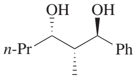


R	Base			dr	Refs.
i-Pr	LHMDS		(56)	87:13	227
Ph	LDA	(73)[h]	(72)	99:1	

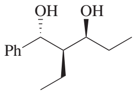
$C_6 + C_7$



1. Cat. **117** (10 mol %), THF, –10°, 48 h
2. NaOMe, MeOH

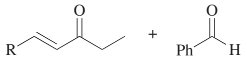


(70) er 97:3 +

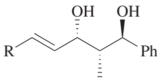


(16) er 98.5:1.5 253

$C_{6-11} + C_7$

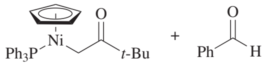


1. Cat. **117** (10 mol %), THF, temp, 48 h
2. NaOMe, MeOH

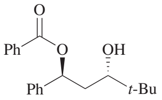


R	Temp		er	Refs.
Me	0°	(80)	93.5:6.5	252, 253
Ph	rt	(91)	85:15	253

$C_6 + C_7$

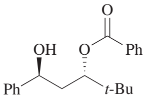


Toluene, 0°, 7 h



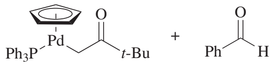
I

+

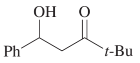


II

I + **II** (60),[i] **I**/**II** = 45:55 100

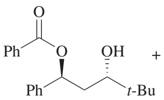


C_6D_6, 45°, 3 d



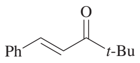
I

+



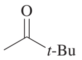
II

+



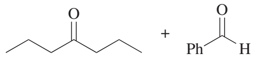
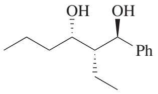
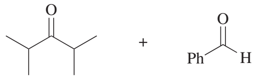
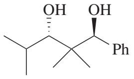
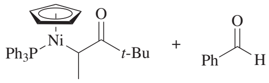
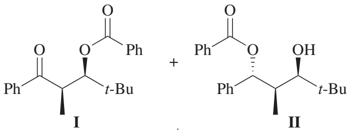
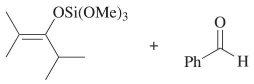
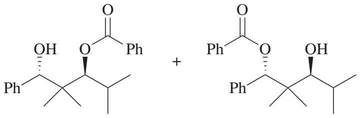
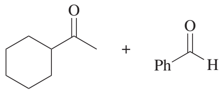
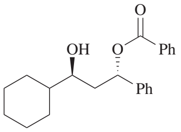
III 100

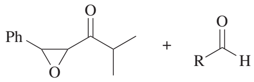
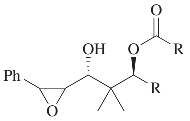
I–**IV** (100),[i] **I**/**II**/**III**/**IV** = 25:22:3:50 +



IV

TABLE 2D. ALDOL-TISHCHENKO REACTIONS OF DIALKYL KETONES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_7 + C_7$			
	1. Cat. **117**, (10 mol %), THF, 0°, 48 h 2. NaOMe, MeOH	 (71) er 96.5:3.5	253, 252
	1. Cat. **117**, (10 mol %), THF, rt, 48 h 2. NaOMe, MeOH	 (0)	253
	Toluene, rt, 72 h	 **I + II** (99),[i] **I/II** = 55:45	100
	Cat. **117** (10 mol %), THF, rt , 24 h	 (66) er 80:20 + (10) er 80:20	255
$C_8 + C_7$			
	Catalyst (30 mol %), 4 Å MS, THF, 0°	 Catalyst / Time (h) SmI_2 3 (80) SmI_3 8 (84)	134

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{12} + C_{2–8}$			
	1. LTMP, THF, –78° 2. RCHO, rt, 1 d	 R Me (46) Ph (63) 4-$MeOC_6H_4$ (56) 4-ClC_6H_4 (74) 4-BrC_6H_4 (71) 4-MeC_6H_4 (60)	226

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[a] The reaction time was 138 hours.

[b] The product was a 65:35 mixture of diastereomers.

[c] The product was a 1:1 mixture of diastereomers.

[d] The catalyst was prepared in situ.

[e] The product was a mixture of stereoisomers with a ratio of 86:6:5:3, with the major isomer presented in the entry.

[f] The aldol-Tishchenko reaction was carried out at 40°.

[g] After one recrystallization the yield was reported to be 60-65% with an er of 99:1.

[h] The yield was determined before the hydrolysis step.

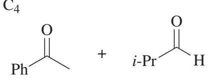
[i] The yield is based on the metal enolate.

TABLE 2E. ALDOL-TISHCHENKO REACTIONS OF ALKYL ARYL KETONES

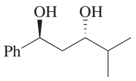
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_8 + C_4$

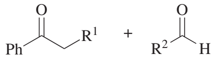


1. $Mg(Oi\text{-}Pr)_2$ (20 mol %), Et_2O, rt, 15 h
2. NaOH, MeOH, rt, 12 h

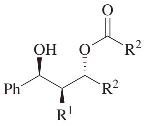


(29) — 237

$C_{8–15} + C_{3–7}$



Catalyst (30 mol %), 4 Å MS, THF, 0°



R^1	R^2	Catalyst	Temp (°)	Time (h)	
H	Et	SmI_2	rt	2	(68)[a]
H	*i*-Pr	SmI_2	0	2	(72)
H	Ph	SmI_2	0	2	(84)
H	Ph	SmI_3	0	6	(80)
Me	Ph	SmI_2	0	4	(90)
Me	Ph	SmI_3	0	10	(90)
Bn	Ph	SmI_2	0	4	(88)
Bn	Ph	SmI_3	0	10	(87)

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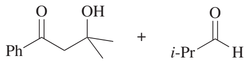
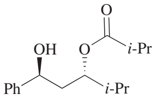
$C_8 + C_4$



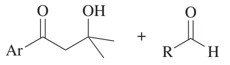
$Zr(Ot\text{-}Bu)_4$ (10 mol %), ligand, CH_2Cl_2, 0°, 2 h



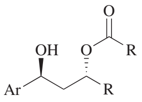
Ligand		er
39	(89)	55.5:44.5
40	(88)	63:37
41	(90)	80:20
42	(75)	78.5:21.5
43	(95)	53.5:46.5
44	(91)	50:50
45	(71)	54:46

107

$C_{8–9} + C_{4–7}$



$Zr(Ot\text{-}Bu)_4$ (10 mol %), **41**, CH_2Cl_2, 0°, 2 h



Ar	R		er
Ph	*i*-Pr	(90)	80:20
Ph	*i*-Bu	(89)	71:29
Ph	Cy	(87)	77:23
Ph	*n*-C_6H_{13}	(82)	70.5:29.5
4-$MeOC_6H_4$	Cy	(71)	80:20
3-MeC_6H_4	2-ethylpropyl	(68)	74.5:25.5
3-MeC_6H_4	Cy	(85)	76.5:23.5
4-MeC_6H_4	*i*-Pr	(50)	75:25
4-MeC_6H_4	Cy	(81)	78:22

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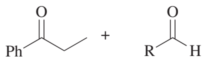
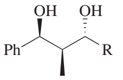
$C_9 + C_{2–4}$



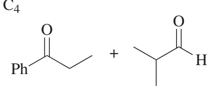
1. LDA, THF, –78°
2. RCHO, –78°, 1 h
3. 22°, 12 h
4. NaOH, MeOH



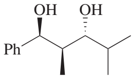
R			dr
Me	(—)	(41)	98:2
Et	(76)[b]	(64)	98:2
i-Pr	(69)[b]	(62)	99:1

227

$C_9 + C_4$

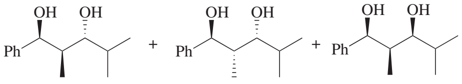


1. $LiOi\text{-}Pr$ (15 mol %), Et_2O, rt, 15 h
2. NaOH, MeOH, rt, 12 h

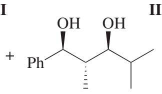


(74) dr 96:4 — 237

1. Catalyst (20 mol %), Et_2O, rt, 15 h
2. NaOH, MeOH, rt, 12 h



I + II + III



\+ IV

Catalyst	I	I/II/III/IV
$LiOi\text{-}Pr$[c]	(54)	28:1:0.3:0.3
$LiOi\text{-}Pr$	(37)	99:1:0.1:0.3
$NaOt\text{-}Bu$	(68)	98:1:2.2:0.9
$Mg(Oi\text{-}Pr)_2$	(14)	4:1:0.1:0.2
$Ca(OMe)_2$	(8)	32:1:0.5:0.5
$Zr(Ot\text{-}Bu)_4$	(14)	5:1:0.2:0.2
$Cu(Oi\text{-}Pr)_2$	(8)	49:1:<0.1:<0.1
$Zn(Ot\text{-}Bu)_2$	(7)	19:1:0.5:<0.2
$Sm(Oi\text{-}Pr)_3$	(23)	4:1:0.2:0.2
$Yb(Oi\text{-}Pr)_3$	(6)	2:1:0.1:0.2

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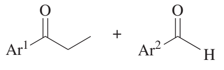
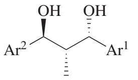
$C_9 + C_{7–11}$



1. $Yb(OTf)_3$ (20 mol %), **64**, DME, rt, 20 h
2. NaOMe, MeOH



Ar^1	Ar^2		er
Ph	Ph	(85)	86.5:13.5
Ph	4-$MeOC_6H_4$	(45)	87.5:12.5
Ph	4-ClC_6H_4	(70)	80:20
Ph	2-naphthyl	(72)	85:15
4-ClC_6H_4	Ph	(89)	86:14
4-ClC_6H_4	4-$MeOC_6H_4$	(92)	89:11

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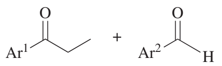
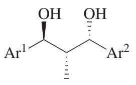
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

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

$C_9 + C_7$



1. $Yb(OTf)_3$ (20 mol %), **92**, THF, rt
2. NaOMe, MeOH, rt



Ar^1	Ar^2		er
Ph	Ph	(79)	75:25
Ph	4-$MeOC_6H_4$	(53)	68:32
4-ClC_6H_4	Ph	(87)	69:31
4-$MeOC_6H_4$	Ph	(44)	77:23

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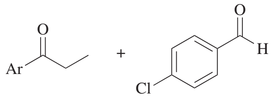
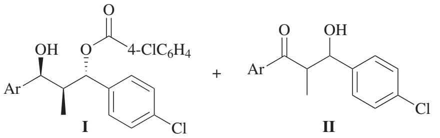
$C_{9-10} + C_7$



Catalyst (10 mol %), THF, rt



I + II

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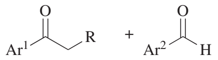
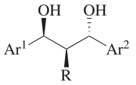
Ar	Catalyst	Additive	Time (h)	**I + II**	**I**/**II**	er **I**
Ph	(*R*)-LLB*	—	48	(20)	1:1	82:18
Ph	(*R*)-LLB	LiI	48	(75)	1:1	80:20
Ph	(*R*)-LLB	$LiBF_4$	48	(50)	1:1	72:28
Ph	(*R*)-LLB	$LiClO_4$	48	(78)	1:1	82:18
Ph	(*R*)-LLB	LiOTf	48	(60)	1:1	89:11
Ph	(*R*)-LLB	$LiPF_6$	48	(73)	1:1	82:18
Ph	(*R*)-LLB	NaOTf	48	(70)	1:1	81:19
Ph	(*R*)-LLB	KOTf	48	(65)	1:1	86.5:13.5
Ph	(*R*)-LLB	CuOTf	48	(40)	>10:1	54.5:5.5
Ph	(*R*)-LLB	AgOTf	48	(42)	9:1	64:36
Ph	$La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:6)	—	48	(60)	1:1	93:7
4-$CF_3C_6H_4$	(*R*)-LLB	LiOTf	24	(89)	>98:2	96.5:3.5
4-$CF_3C_6H_4$	$La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:6)	—	24	(75)	>98:2	94:6
4-$CF_3C_6H_4$	$La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:5.6)	—	24	(80)	>98:2	96.5:3.5

* (*R*)-LLB = La(O*i*-Pr)$_3$/(*R*)-BINOL/BuLi (1:3:3)

$C_{9-12} + C_{5-11}$



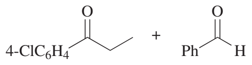
1. $La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:5.6) (10 mol %), THF, rt
2. NaOMe, MeOH, rt, 1 h



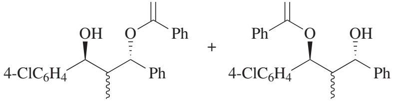
256, 104

Ar^1	R	Ar^2	Time (h)		er
3,5-$F_2C_6H_3$	Me	4-ClC_6H_4	48	(77)	93.5:6.5
3-ClC_6H_4	Me	4-ClC_6H_4	48	(60)	92:8
3,4-$Cl_2C_6H_3$	Me	4-ClC_6H_4	48	(81)	94:6
3,5-$Cl_2C_6H_3$	Me	4-ClC_6H_4	48	(73)	92.5:7.5
4-BrC_6H_4	Me	4-BrC_6H_4	48	(70)	92.5:7.5
4-$CF_3C_6H_4$	Me	3-furyl	84	(77)	91.5:8.5
4-$CF_3C_6H_4$	Me	3-thienyl	84	(82)	97:3
4-$CF_3C_6H_4$	Me	Ph	84	(95)	95.5:4.5
4-$CF_3C_6H_4$	Me	4-FC_6H_4	72	(85)	96:4
4-$CF_3C_6H_4$	Me	4-ClC_6H_4	60	(95)	96.5:3.5
4-$CF_3C_6H_4$	Me	4-BrC_6H_4	48	(96)	97.5:2.5
4-$CF_3C_6H_4$	Me	4-MeC_6H_4	94	(67)	96:4
4-$CF_3C_6H_4$	Me	3-BrC_6H_4	48	(92)	93:7
4-$CF_3C_6H_4$	Me	3-$MeOC_6H_4$	72	(65)	92.5:7.5
4-$CF_3C_6H_4$	Me	2-naphthyl	80	(67)	94:6
4-$CF_3C_6H_4$	Et	4-BrC_6H_4	90	(90)	94:6
4-$CF_3C_6H_4$	Pr	4-BrC_6H_4	90	(88)	93.5:6.5

$C_9 + C_7$



$Yb(OTf)_3$ (*x* mol %), **51**, THF, rt, 4 h



I + **II**

x	**I + II**	er
5	(63)	—
10	(98)	59.5:40.5

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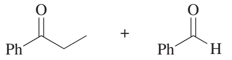
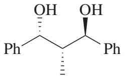


1. Cat. **117**, (10 mol %), THF, rt, 48 h
2. NaOMe, MeOH



(60) er 86:12

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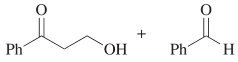
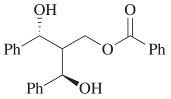
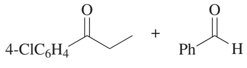
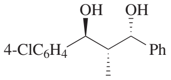
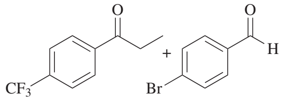
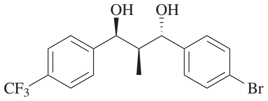
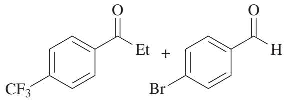
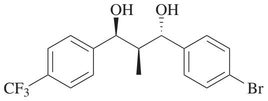
TABLE 2E. ALDOL-TISHCHENKO REACTIONS OF ALKYL ARYL KETONES (*Continued*)

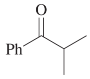
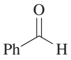
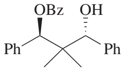
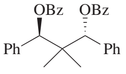
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_9 + C_7$			
	Cat. **117** (10 mol %), THF, −45°, 24 h	 (93) er 95:5	254
	1. $Yb(OTf)_3$ (15 mol %), **101**, THF, rt, 16 h 2. NaOMe, MeOH, rt	 (95) er 70:30	262
$C_{10} + C_7$			
	1. Catalyst (10 mol %), THF, rt, 48 h 2. NaOMe, MeOH, rt, 1 h		256

Catalyst		er
(*R*)-LLB	(75)	89.5:10.5
(*R*)-LLB/LiOTf (1:3)	(92)	94:4
$La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:6)	(87)	96:4
$La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:5.6)	(96)	97.5:2.5
(*R*)-$[La_2Li_4(BINOL)_5]_2$	(83)	79.5:20.5
(*R*)-$[La_2Li_4(BINOL)_5]_2$/LiOTf (1:6)	(92)	90:10
(*R*)-$[La_2Li_4(BINOL)_5]_2$/(*R*)-BINOL/BuLi (1:1:2)	(79)	90.5:9.5
(*R*)-$[La_2Li_4(BINOL)_5]_2$/(*R*)-BINOL/BuLi/LiOTf (1:1:2:6)	$(90)^d$	96:4
(*R*)-$[La_2Li_4(BINOL)_5]_2$/(*R*)-BINOL/BuLi/LiOTf (1:1:2:6)	$(93)^e$	95:5
(*R*)-$[La_2Li_4(BINOL)_5]_2$/(*R*)-BINOL/BuLi/LiOTf (1:1:3:6)	$(98)^e$	67:33
(*R*)-LLB/(*R*)-BINOL/BuLi/LiOTf (1:0.5:1:3)	$(82)^e$	84:16
(*R*)-LLB/(*R*)-BINOL/BuLi/LiOTf (1:5:4:3)	$(88)^e$	62:38

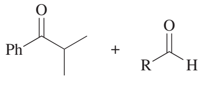
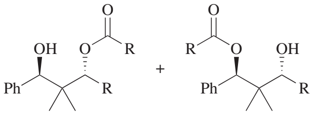
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. $La(OTf)_3$/(*R*)-BINOL/BuLi (1:3:5.6) (10 mol %), THF (*x* M), rt 2. NaOMe, MeOH		256

x		er
1.0	(96)	97.5:2.5
0.7	(82)	93:7
0.5	(66)	89:11
0.2	(22)	88.5:11.5

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 **I** +  **II**	Base (*x* mol %), THF, 15 h	 **III** +  **IV**	353

I/II	Base	*x**	Temp	I	II
1:2.5	LiOEt or LiO*i*-Pr	100	rt	(0)	(0)
1:2.5	LiO*t*-Bu	10	rt	(9)	(0)
1:2.5	LiO*t*-Bu	20	rt	(18)	(0)
1:2.5	LiO*t*-Bu	100	rt	(71)	(0)
1:4.5	LiO*t*-Bu	100	rt	(79)	(0)
1:2.5	NaO*i*-Pr	100	rt	(13)	(<5)
1:2.5	NaO*t*-Bu	20	rt	(5)	(8)
1:2.5	NaO*t*-Bu	100	rt	(28)	(34)
1:4.5	NaO*t*-Bu	100	rt	(0)	(94)
1:2.5	KOH	100	reflux	(0)	(0)

* The percentage is relative to **I**.

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{10} + C_{7–8}$			
	LDA, THF, rt		132

R	
Ph	(—)
4-MeC_6H_4	(—)

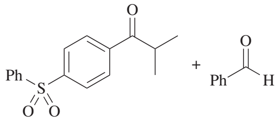
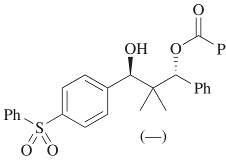
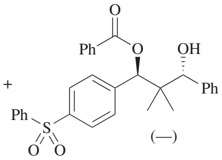
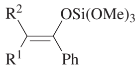
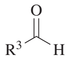
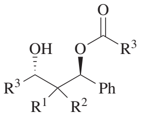
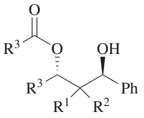
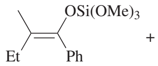
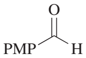
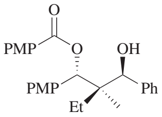
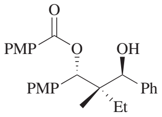
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{10} + C_7$			
	Lithium-9-benzylfluorene, THF, rt	 (—) +  (—)	132

TABLE 2E. ALDOL-TISHCHENKO REACTIONS OF ALKYL ARYL KETONES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{10-13} + C_{7-9}$			
 + 	Cat. **117** (10 mol %), THF	 **I** +  **II**	255

R^1	R^2	R^3	(*E*)/(*Z*)	Temp (°)	Time (h)	**I**	er **I**	**II**	er **II**
Me	Me	*c*-C_6H_{11}	—	–23	24	(0)	—	(71)	65:35
Me	Me	Ph	—	–23	6	(0)	—	(92)	94:6
Et	Me	Ph	5.3:1	–23	6	(16)	96.5:3.5	(82)	96.5:3.5
Et	Me	Ph	1.2:1	–23	6	(16)	94:4	(79)	94:4
—$(CH_2)_5$—		Ph	—	rt	24	(0)	—	(70)	85.5:14.5
Me	Me	4-Br_6H_4	—	–23	6	(0)	—	(88)	93:7
Me	Me	4-$MeOC_6H_4$	—	–23	24	(0)	—	(80)	97.5:2.5
Me	Me	$PhCH_2CH_2$	—	–23	24	(0)	—	(34)	64:36
Me	Me	(*E*)-PhCH=CH	—	–23	24	(0)	—	(51)	65:35

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{11} + C_7$			
 + 	Cat. **117** (10 mol %), THF, –23°, 24 h	 **I** +  **II** **I** + **II** (82), **I**/**II** = 6.5:1	255

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[a] Both the 1-*O* ester and 3-*O* ester were formed in a ratio of 3:1.

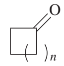
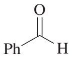
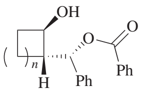
[b] The yield was determined before the hydrolysis step.

[c] The catalyst was prepared in situ.

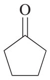
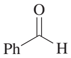
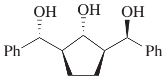
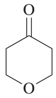
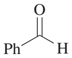
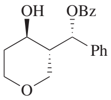
[d] LiOTf was added to the catalyst system before the addition of *n*-BuLi

[e] LiOTf was added to the catalyst system after the addition of *n*-BuLi

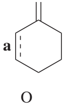
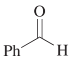
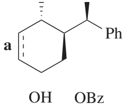
TABLE 2F. ALDOL-TISHCHENKO REACTIONS OF CYCLIC KETONES

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{4-6} + C_7$			
 + 	Catalyst (30 mol %), 4 Å MS, THF		134

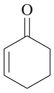
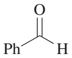
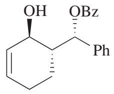
n	Catalyst	Time (h)	
1	SmI_2	1	(80)
1	SmI_3	4	(81)
2	SmI_2	2	(85)
2	SmI_3	6	(87)
3	SmI_2	3	(88)
3	SmI_3	8	(89)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_5 + C_7$			
 + 	1. Cat. **117** (10 mol %), THF, 0°, 48 h 2. $Me_2C(OMe)_2$, PPTS 3. Separation 4. NaOMe, MeOH	 (65) er 99.5:0.5	253, 252
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°		134

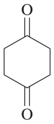
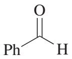
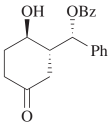
Catalyst	Time (h)	
SmI_2	4	(84)
SmI_3	13	(81)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6 + C_7$			
 + 	1. Cat. **117** (10 mol %), THF, temp, 48 h 2. NaOMe, MeOH		253, 252

Bond **a**	Temp (°)		er
single	0	(91)	95:5
double	–23	(88)	92:5:7.5

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°		134

Catalyst	Time (h)	
SmI_2	5	(92)
SmI_3	14	(89)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°		134

Catalyst	Time (h)	
SmI_2	4	(80)
SmI_3	10	(90)

TABLE 2F. ALDOL-TISHCHENKO REACTIONS OF CYCLIC KETONES (*Continued*)

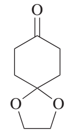
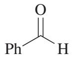
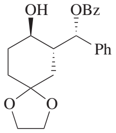
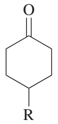
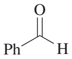
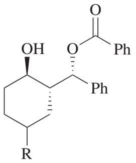
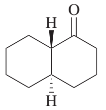
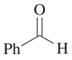
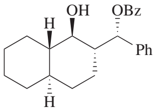
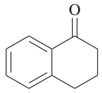
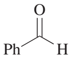
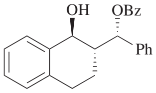
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*			
$C_6 + C_7$			
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°	 Catalyst, Time (h) SmI_2 5 (93) SmI_3 10 (89)	134
$C_{7-10} + C_7$			
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°	 R, Catalyst, Time (h) Me SmI_2 3 (95) Me SmI_3 8 (91) *t*-Bu SmI_2 4 (85) *t*-Bu SmI_3 12 (84)	134
$C_{10} + C_7$			
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°	 Catalyst, Time (h) SmI_2 6 (81) SmI_3 12 (79)	134
 + 	Catalyst (30 mol %), 4 Å MS, THF, 0°	 Catalyst, Time (h) SmI_2 2 (77) SmI_3 6 (77)	134

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES

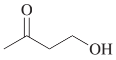
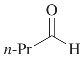
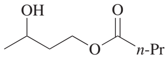
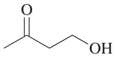
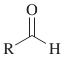
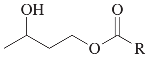
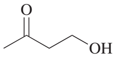
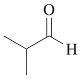
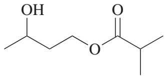
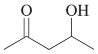
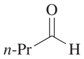
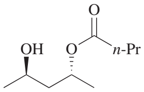
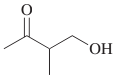
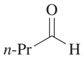
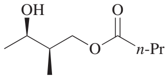
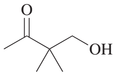
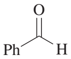
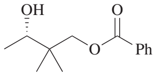
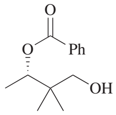
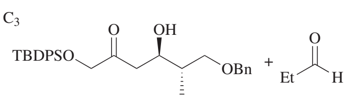
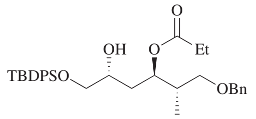
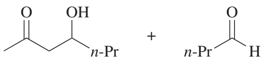
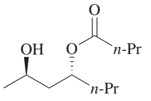
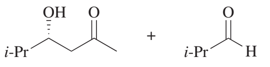
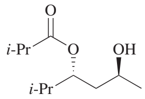
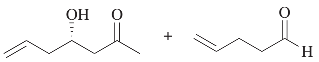
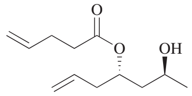
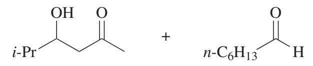
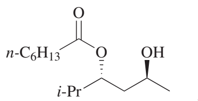
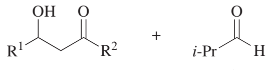
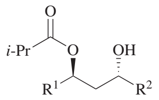
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
Please refer to the charts preceding the tables for structures indicated by the ***bold*** *numbers.*			
$C_4 + C_4$			
 + 	Catalyst (*x* mol %), THF, rt	 Catalyst, *x*, Time (h) Cp_2ZrH_2 5 5 (80) Cp_2ZrHCl 5 5 (26) Cp_2ZrHCl 20 24 (70) Cp_2ZrCl_2/*n*-BuLi 5 24 (68) Cp_2ZrCl_2 5 5 (—)	234
$C_4 + C_{4-8}$			
 + 	Cp_2ZrH_2 (5 mol %), THF, rt, 5 h	 R *i*-Pr (95) $CH_2CH{=}CH_2$ (0) Cy (55) Ph (0) *n*-C_7H_{15} (98) $BnCH_2$ (80)	234
$C_4 + C_4$			
 + 	$Sc(OTf)_3$ (10 mol %), THF, rt, 2.5 h	 (95)	235
$C_5 + C_4$			
 + 	Cp_2ZrH_2 (5 mol %), THF, rt	 (99) *anti*/*syn* = 97:3	234
 + 	Cp_2ZrH_2 (5 mol %), THF, rt	 (92) *syn*/*anti* = 95:5	234
$C_6 + C_7$			
 + 	Cat. **117**, (10 mol %), THF, –40°, 6 h	 +  (91) er 99.5:0.5	254

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

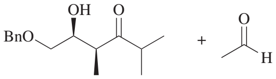
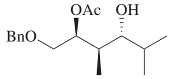
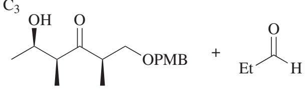
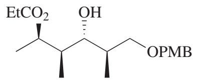
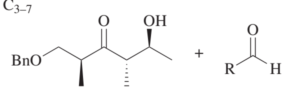
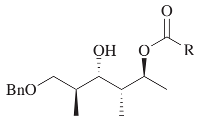
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_3$			
	SmI_2 (20 mol %), THF, –10°, 3.5 h	 (90)	124
$C_7 + C_4$			
	Cp_2ZrH_2 (5 mol %), THF, rt, 5 h	 (99) *anti/syn* = 84:16	234
	Zr(O*t*-Bu)$_4$ (10 mol %), ligand, CH_2Cl_2, 0°		

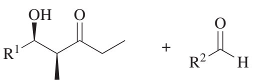
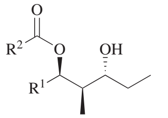
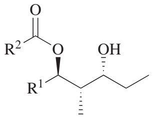
Config.	er	Ligand		er	Refs.
(*R*)	95.5:4.5	**23**	(82)	95.5:4.5	248, 251
(*R,S*)	—	none	(75)	—	248

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_7 + C_5$			
	1. PhCHO, SmI_2 (30 mol %), THF, 0°, 30 min[a] 2. 4-Pentenal, 0° 3. Substrate, 0°	 (85), dr >95:5	123
$C_7 + C_7$			
	Zr(O*t*-Bu)$_4$ (10 mol %), CH_2Cl_2, 0°	 (85)	249
$C_{7–15} + C_4$			
 1.5 eq	Zr(O*t*-Bu)$_4$ (5 mol %), toluene, –30°		251

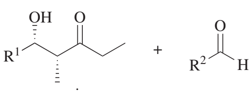
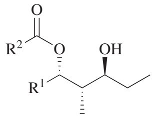
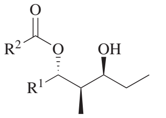
R^1	R^2	
i-Pr	Me	(82)
i-Pr	Et	(80)
i-Pr	*t*-Bu	(75)
CH=CH_2	Ph	(61)
n-C_6H_{13}	Et	(87)
i-Pr	Ph	(90)
t-Bu	Ph	(28)
t-Bu	Ph	(79)[b]
n-C_6H_{13}	*t*-Bu	(86)
n-C_6H_{13}	Ph	(81)
Ph	Ph	(85)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_8 + C_2$			
	SmI_2 (60 mol %), THF, –10°, 1.5 h	 (0)	108
$C_8 + C_3$			
	SmI_2 (20 mol %), THF, –30°; –20° to –10°, 3 h	 (98) dr >95:5	354
$C_8 + C_{3–7}$			
	SmI_2 (cat.), THF, –10°		

R	Time (h)		Refs.
Et	1.5	(—)	288
Ph	1	(94)	285, 286

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{8–14} + C_{3–7}$			
 racemic	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$, cinchonine, CH_2Cl_2, rt	 **I** +  **II**	257

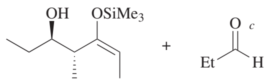
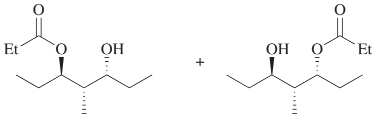
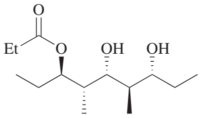
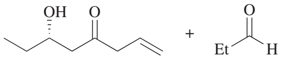
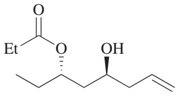
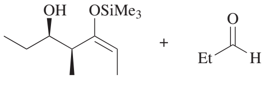
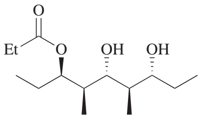
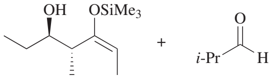
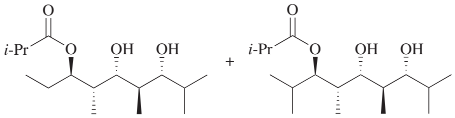
R^1	R^2	**I**	er **I**	**II**	er **II**
Et	Et	(50)	59:41	(45)	71:29
n-Pr	*i*-Pr	(28)	60:40	(13)	69:31
i-Pr	*i*-Pr	(23)	68:32	(29)	81:19
Cy	Cy	(27)	71:29	(17)	89:11
Ph$(CH_2)_2$	*i*-Pr	(10)	55:45	(7)	65:35

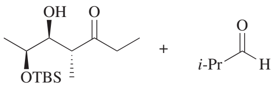
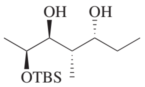
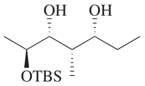
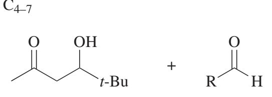
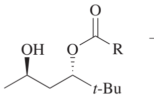
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 racemic	[(*S*)-BINOL]Ti(O*t*-Bu)$_2$, cinchonidine, CH_2Cl_2, rt	 **I** +  **II**	257

R^1	R^2	**I**	er **I**	**II**	er **II**
Et	Et	(28)	61:39	(37)	72:28
n-Pr	*i*-Pr	(25)	64:36	(26)	66:34
i-Pr	*i*-Pr	(45)	74:26	(19)	84:16
Cy	Cy	(22)	70:30	(17)	80:20
Ph$(CH_2)_2$	*i*-Pr	(8)	60:40	(10)	68:32

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_8 + C_3$			
	$TiCl_2(Oi\text{-}Pr)_2$ (20 mol %), CH_2Cl_2, rt, 2 h	 **I** **I** + **II** (95), **I**/**II** = 1:1 **II**	263
	$Ti(Oi\text{-}Pr)_4$ (10 mol %), CH_2Cl_2, rt, 3 h	 (95)	263
	SmI_2 (20 mol %), THF, −10°, 2 h	 (95)	355
	$Ti(Oi\text{-}Pr)_4$ (10 mol %), CH_2Cl_2, rt, 3 h	 (95)	263
$C_8 + C_4$			
	$Ti(Oi\text{-}Pr)_4$ (10 mol %), CH_2Cl_2, rt	 **I** **I** + **II** (95), **I**/**II** = 70:30 **II**	265

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. $Ti(Ot\text{-}Bu)_4$, CH_2Cl_2, rt, 3 d 2. NaOMe, MeOH	 (76)	257
	1. $Ti(Ot\text{-}Bu)_4$, CH_2Cl_2, rt, 5 d 2. NaOMe, MeOH	 (65)	257
$C_8 + C_{4–7}$			
	Catalyst (*x* mol %), THF	 (99)	

R	Catalyst	*x*	Temp (°)	Time (h)	*anti/syn*	Refs.
n-Pr	Cp_2ZrH_2	5	rt	5	91:9	234
Ph	SmI_2	50	–10	2	—	356

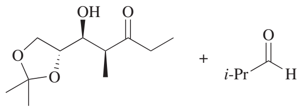
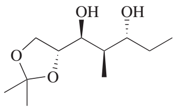
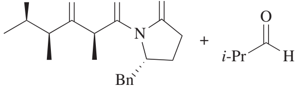
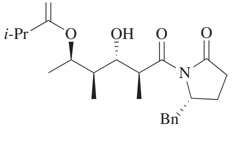
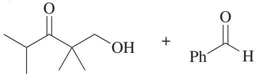
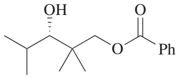
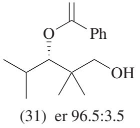
$C_8 + C_4$			
	1. $Ti(Ot\text{-}Bu)_4$, CH_2Cl_2, rt, 4 d 2. NaOMe, MeOH	 (73)	257
	*i*-PrCHO, SmI_2 (30 mol %), THF, −10°, 45 min	 (81) dr >99:1	108
$C_8 + C_7$			
	Cat. **117** (10 mol %), THF, rt, 4 h	 (64) er 96.5:3.5 +  (31) er 96.5:3.5	254

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

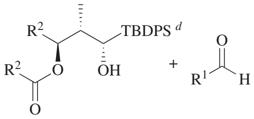
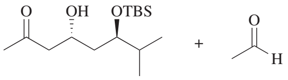
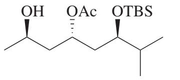
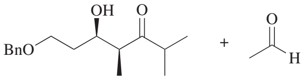
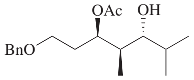
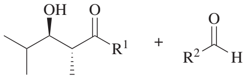
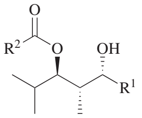
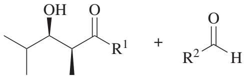
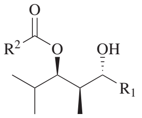
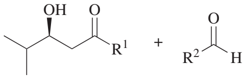
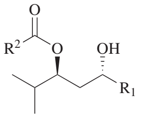
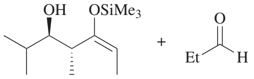
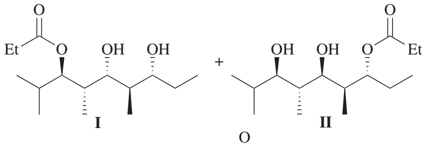
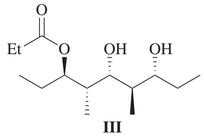
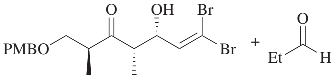
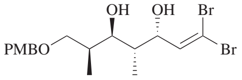
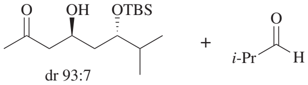
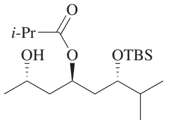
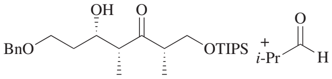
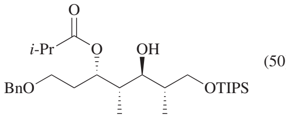
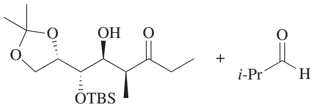
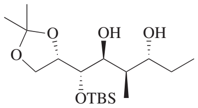
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
C_{8-10} + C_7			
 2.5 eq	LiHMDS (2 eq), THF, –78°, 30 min; to 0°, 4 h	 R^1 / R^2 t-Bu / 4-BrC$_6$H$_4$ (81) Ph / Ph (85) Ph / 4-BrC$_6$H$_4$ (78) Ph / 4-O$_2$NC$_6$H$_4$ (82)	357
C_9 + C_2			
	SmI$_2$ (20 mol %),THF, 0°, 20 min	 (79)	358
	SmI$_2$ (15 mol %), THF, –10°, 45 min	 (88) dr >99:1	108
C_{9-10} + C_{2-7}			
	SmI$_2$ (15 mol %), THF, –10°, 45 min	 R^1 / R^2 / / *anti/syn* Et / Me / (86) / >99:1 *i*-Pr / Ph / (95) / >99:1	108
C_{9-10} + C_{2-4}			
	SmI$_2$ (15 mol %), THF, –10°, 45 min	 R^1 / R^2 / / *anti/syn* Et / *i*-Pr / (95) / >99:1 *i*-Pr / Me / (85) / >99:1	108
C_{9-12} + C_{2-7}			
	SmI$_2$ (15 mol %), THF, –10°, 45 min	 R^1 / R^2 / / *anti/syn* *i*-Pr / Me / (85) / >99:1 *i*-Pr / Ph / (99) / >99:1 Cy / Me / (96) / >99:1 Cy / *i*-Pr / (95) / >99:1 Cy / Ph / (94) / >99:1	108
C_9 + C_3			
	Ti(O*i*-Pr)$_4$ (10 mol %), CH$_2$Cl$_2$	 Temp (°) / I–III / I/II/III rt / (95) / 40:40:20 0 / (95) / 48:48:4 + 	265, 264
	1. SmI$_2$ (1 eq), THF, –20°, 18 h 2. K$_2$CO$_3$, MeOH, rt, 1h	 (94) dr >20:1	359
C_9 + C_4			
 dr 93:7	SmI$_2$ (15 mol %), THF, –10°, 1 h	 (61) dr 89:11	360
	SmI$_2$ (20 mol %), THF, 0°, 2.5 h	 (50)	361
	1. Ti(O*t*-Bu)$_4$, CH$_2$Cl$_2$, rt, 5 d 2. NaOMe, MeOH	 (61)	257

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

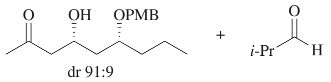
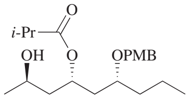
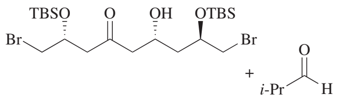
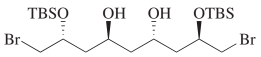
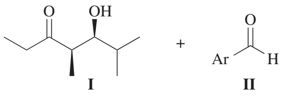
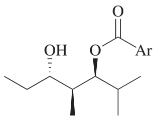
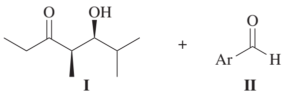
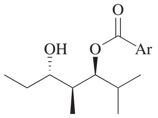
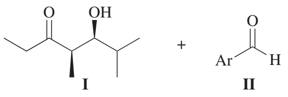
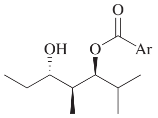
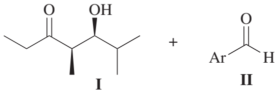
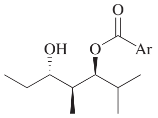
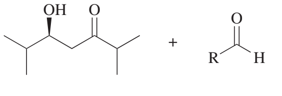
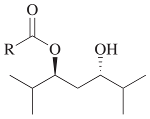
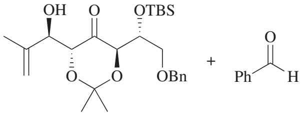
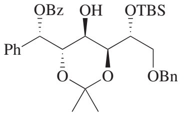
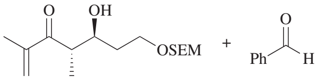
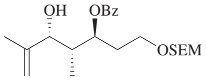
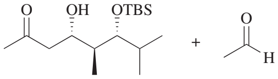
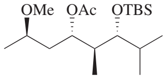
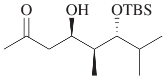
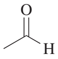
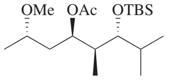
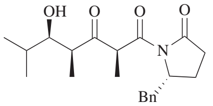
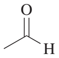
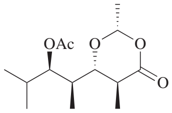
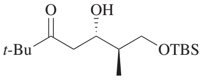
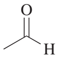
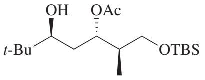
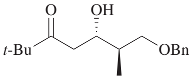
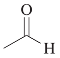
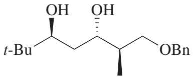
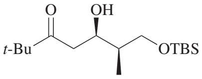
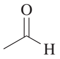
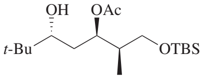
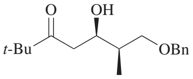
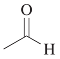
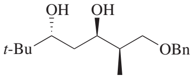
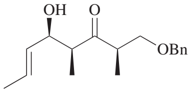
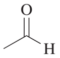
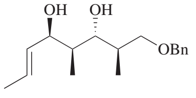
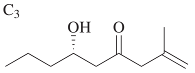
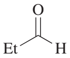
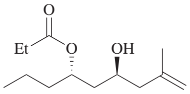
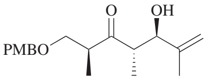
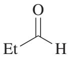
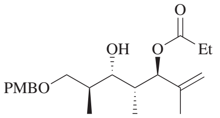
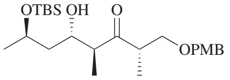
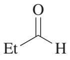
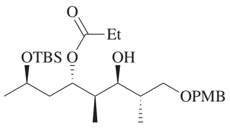
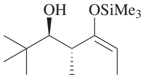
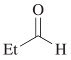
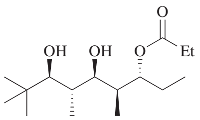
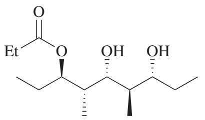
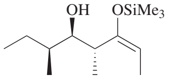
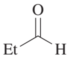
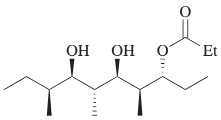
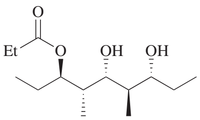
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_9 + C_4$			
 dr 91:9	SmI_2 (15 mol %), THF, –10°, 1 h	 (59) dr 89:11	360
	1. SmI_2 (75 mol %), THF, –25°, 20 min 2. DIBAL-H, CH_2Cl_2, –78 to –35°, 40 min	 (70) de >95%	296
$C_9 + C_5$			
	1. **II**, SmI_2 (2 eq), THF, rt, 30 min^a 2. **I**, –15°, 1 h	 Ar — dr 2-furyl (98) >95:5 3-furyl (99) >95:5 2-thienyl (99) >95:5 3-thienyl (99) >95:5	272
$C_9 + C_{5–6}$			
	1. **II**, SmI_2 (10 mol %), THF, rt, 30 min^a 2. **I**, rt, 1 h	 Ar — dr 2-furyl (69) 92:8 3-furyl (63) 89:11 2-thienyl (47) 89:11 3-thienyl (61) 90:10 2-pyridyl (11) — 3-pyridyl (99) 96:4 4-pyridyl (99) 90:10	272
	1. PhCHO, SmI_2 (10 mol %), THF, rt, 30 min^a 2. **I**, **II**, rt, 1 h	 Ar — dr 2-furyl (12) 92:8 3-furyl (62) 90:10 2-thienyl (39) 90:10 3-thienyl (23) 89:11 2-pyridyl (13) — 3-pyridyl (99) 95:5 4-pyridyl (93) 91:9	272
$C_9 + C_{5–9}$			
	1. PhCHO, SmI_2 (2 eq), THF, rt, 30 min^a 2. **I**, **II**, –15°, 1 h	 Ar — dr 2-furyl (99) 91:9 3-furyl (98) >95:5 2-thienyl (99) 91:9 3-thienyl (99) >95:5 5-nitro-2-furyl (93) >95:5 5-bromo-2-furyl (90) 94:6 5-phenyl-2-furyl (92) >95:5 5-bromo-2-thienyl (99) >95:5 3-benzo[*b*]thienyl (95) 92:8 3-(*N*-Boc)indolyl (90) 90:10	272
$C_9 + C_{6–7}$			
	1. Cat. **126** (5 mol %), toluene, 0–21°, 30 min 2. RCHO, 21°, 6 h	 R — *anti*/*syn* *n*-C_5H_{11} (92) 96:4 Ph (99) 99:1	158
$C_9 + C_7$			
	SmI_2 (cat.), THF, 0°	 (—)	117
	SmI_2 (cat.), THF, –10°	 (93)	114
$C_{10} + C_2$			
	1. SmI_2 (20 mol %), THF, 0°, 15 min 2. MeOTf, DTBMP, DCE, rt, 10 h	 (49)	362, 358

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{10} + C_2$			
 + 	1. SmI$_2$ (20 mol %), THF, 0°, 10 min 2. MeOTf, DTBMP, DCE, rt, 8 h	 (62)	362, 358
 + 	SmI$_2$ (30 mol %), THF, –10°, 2.5 h	 (70) *anti*/*syn* >99:1	108
 + 	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (95)	362
 + 	1. SmI$_2$ (20 mol %), THF, 0°, 30 min 2. NaOH, MeOH	 (33)	362
 + 	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (92)	362
 + 	1. SmI$_2$ (20 mol %), THF, 0°, 30 min 2. NaOH, MeOH	 (74)	362
 + 	1. SmI$_2$ (2 mol %), THF, –20°, 3 h 2. K$_2$CO$_3$, MeOH/H$_2$O, rt, 30 min	 $(70)^e$ single isomer	363
$C_{10} + C_3$			
 + 	SmI$_2$ (40 mol %), THF, –10°, 2 h	 (95)	364
 + 	SmI$_2$ (20 mol %), THF, –10°, 1.5 h	 (96) dr >97:3	116, 289
 + 	SmI$_2$ (8 mol %), THF, –20° to –10°, 2 h	 (80) dr >95:5	365
 + 	Ti(O*i*-Pr)$_4$ (10 mol %), CH$_2$Cl$_2$	 **I** +  **II**	265, 264

Temp (°)	I + II	I/II
rt	(95)	70:30
0	(95)	95:5

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 + 	Ti(O*i*-Pr)$_4$ (10 mol %), CH$_2$Cl$_2$	 **I** +  **II**	265

Temp	I + II	I/II
rt	(95)	70:30
0°	(95)	95:5

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

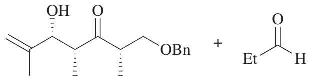
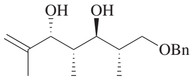
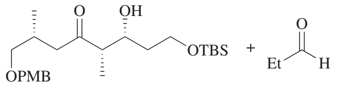
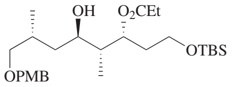
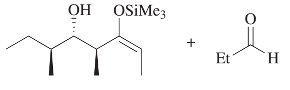
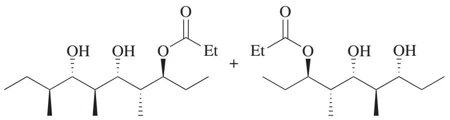
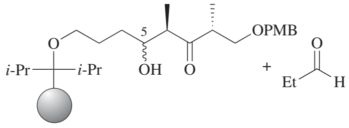
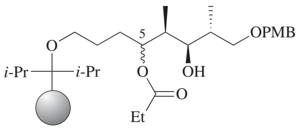
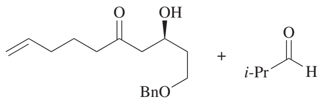
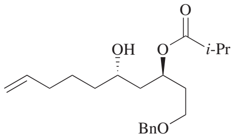
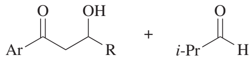
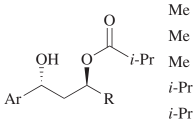
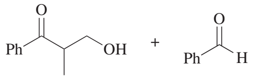
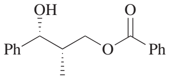
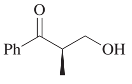
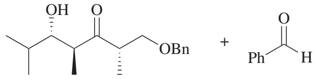
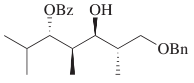
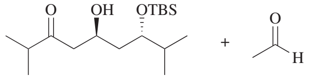
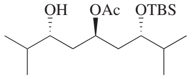
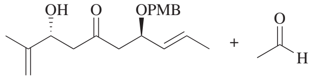
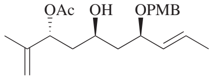
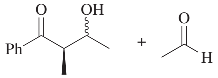
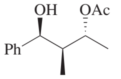
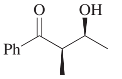
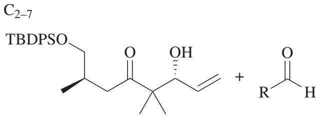
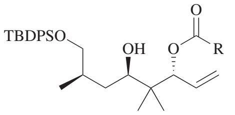
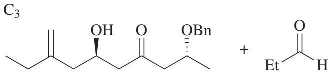
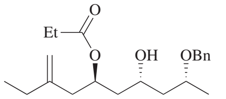
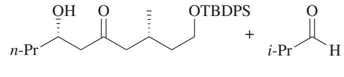
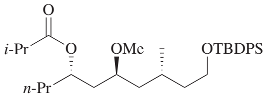
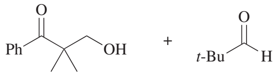
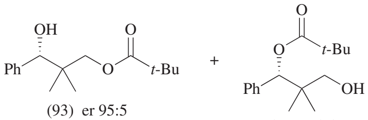
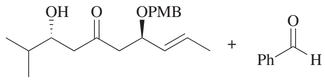
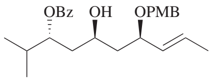
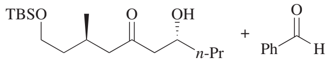
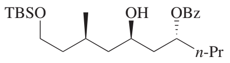
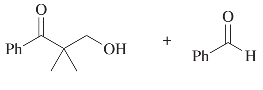
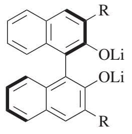
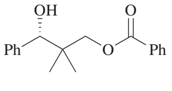
<table>
<tr><th>Substrates</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td colspan="4">Please refer to the charts preceding the tables for structures indicated by the bold numbers.</td></tr>
<tr><td colspan="4">$C_{10} + C_3$</td></tr>
<tr><td></td><td>1. SmI_2 (30 mol %), THF, 0°, 1 h
2. K_2CO_3, MeOH, rt, 12 h</td><td> (65) dr 95:5</td><td>366</td></tr>
<tr><td></td><td>SmI_2 (50 mol %), THF, –30°, 2 h</td><td> (>86)</td><td>367</td></tr>
<tr><td></td><td>Ti(Oi-Pr)$_4$ (10 mol %), CH_2Cl_2</td><td>
I + II
<table>
<tr><th>Temp</th><th>I + II</th><th>I/II</th></tr>
<tr><td>rt</td><td>(95)</td><td>70:30</td></tr>
<tr><td>0°</td><td>(95)</td><td>95:5</td></tr>
</table></td><td>265</td></tr>
<tr><td></td><td>SmI_2 (cat.), THF, –10° to 0°, 20 h</td><td>
<table>
<tr><th>C5</th><th></th></tr>
<tr><td>(R)</td><td>(—)</td></tr>
<tr><td>(S)</td><td>(67)^f</td></tr>
</table></td><td>368</td></tr>
<tr><td colspan="4">$C_{10} + C_4$</td></tr>
<tr><td></td><td>Zr(Ot-Bu)$_4$ (10 mol %),
toluene, –78°, 8 h</td><td> (83)</td><td>369</td></tr>
<tr><td colspan="4">$C_{10-17} + C_4$</td></tr>
<tr><td></td><td>Sc(OTf)$_3$ (10 mol %), THF, –10°</td><td>
<table>
<tr><th>R</th><th>Ar</th><th>Time (h)</th><th></th><th>dr</th></tr>
<tr><td>Me</td><td>Ph</td><td>48</td><td>(83)</td><td>>97.5:2.5</td></tr>
<tr><td>Me</td><td>4-ClC$_6$H$_4$</td><td>48</td><td>(93)</td><td>88:12</td></tr>
<tr><td>Me</td><td>4-MeOC$_6$H$_4$</td><td>120</td><td>(57)</td><td>94:6</td></tr>
<tr><td>i-Pr</td><td>Ph</td><td>48</td><td>(93)</td><td>>97.5:2.5</td></tr>
<tr><td>i-Pr</td><td>4-ClC$_6$H$_4$</td><td>48</td><td>(55)</td><td>89:11</td></tr>
<tr><td>i-Pr</td><td>4-MeOC$_6$H$_4$</td><td>120</td><td>(38)</td><td>90:10</td></tr>
<tr><td>BnCH$_2$</td><td>Ph</td><td>72</td><td>(17)</td><td>>97.5:2.5</td></tr>
<tr><td>BnCH$_2$</td><td>4-ClC$_6$H$_4$</td><td>72</td><td>(40)</td><td>94:6</td></tr>
<tr><td>BnCH$_2$</td><td>4-MeOC$_6$H$_4$</td><td>120</td><td>(59)</td><td>97:3</td></tr>
</table></td><td>235</td></tr>
<tr><td colspan="4">$C_{10} + C_7$</td></tr>
<tr><td></td><td>Cat. 117 (10 mol %), THF,
–45°, 24 h</td><td> (48) er 93:7
+
 (42) er 94:6</td><td>254</td></tr>
<tr><td></td><td>SmI_2 (cat.), THF, 3°, 16 h</td><td> (86)</td><td>370</td></tr>
<tr><td colspan="4">$C_{11} + C_2$</td></tr>
<tr><td></td><td>SmI_2 (40 mol %),THF, 0°, 30 min</td><td> (76)</td><td>358</td></tr>
<tr><td></td><td>SmI_2 (cat.), THF, –20°, 2–4 h</td><td> (64) dr 98.5:1.5</td><td>371</td></tr>
<tr><td>
anti/syn = 1:1</td><td>SmI_2 (15 mol %), THF, –10°</td><td> (—) +  (—)</td><td>372</td></tr>
</table>

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{11} + C_{2–7}$			
	SmI_2 (15 mol %), THF, –10°, 10 min	 R: Me (45) Ph (60)	373
$C_{11} + C_3$			
	SmI_2 (30 mol %), THF, –20°, 16 h	 (90), dr >97:3	374, 375
$C_{11} + C_4$			
	1. Zr(O*t*-Bu)$_4$, toluene, –78° 2. Me_3OBF_4, Proton Sponge, 4 Å MS, CH_2Cl_2, rt	 (90)	376
$C_{11} + C_5$			
	Cat. **117** (10 mol %), THF, 0°, 1 h	 (93) er 95:5 + (5) er 95:5	254
$C_{11} + C_7$			
	SmI_2 (cat.), THF, –20°, 2–4 h	 (96) dr 98.5:1.5	371
	SmI_2 (1 eq), THF, –10°, 12 h	 (91)	377, 378

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	 (10 mol %)		254

R	Solvent	Temp	Time (h)		er
H	THF	rt	24	(36)	51:49
Br	THF	rt	24	(76)	91.5:8.5
Me	THF	rt	24	(91)	89.5:10.5
Ph	THF	rt	0.5	(82)	98:2
Ph	THF	–40°	0.5	(87)	99.5:0.5
Ph	THF	–78°	48	(56)	99.5:0.5
Ph	Et_2O	rt	0.5	(73)	78:22
Ph	toluene	rt	0.5	(63)	81.5:18.5
4-MeC_6H_4	THF	rt	0.5	(80)	94.5:5.5
3,5-$Me_2C_6H_3$	THF	rt	0.5	(84)	60:40

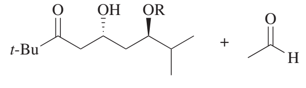
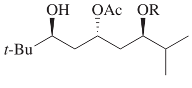
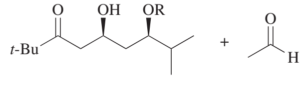
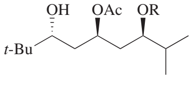
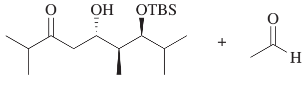
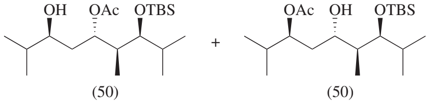
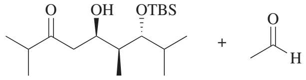
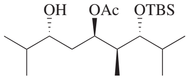
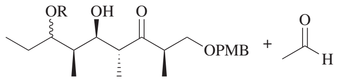
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{12} + C_2$			
	SmI_2 (20 mol %), THF, 0°, 30 min	 R: TBS (94) Bn (—)^g	358 362
	SmI_2 (20 mol %), THF, 0°, 30 min	 R: TBS (—)^g Bn (—)^g	362
	SmI_2 (20 mol %), THF, 0°, 2 h	 (50) + (50)	362, 358
	SmI_2 (20 mol %), THF, 0°, 10 min	 (70)	362, 358

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

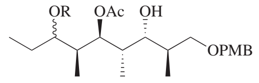
Substrates | Conditions | Product(s) and Yield(s) (%) | Refs.

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

$C_{12} + C_2$



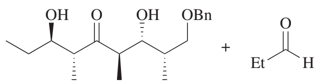
SmI$_2$ (*x* mol %),
THF, –20° to 0°



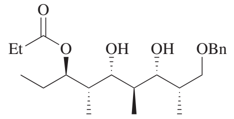
R	*x*	Time (h)	
BnOSi(*i*-Pr)$_2$	60	19	(87)[h]
●—OSi(*i*-Pr)$_2$	100	18	(100)[i]

379

$C_{12} + C_3$



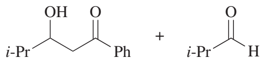
Ti(O*i*-Pr)$_4$ (10 mol %),
CH$_2$Cl$_2$, rt



(85)[j]

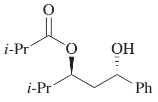
102

$C_{12} + C_4$



x eq

Zr(O*t*-Bu)$_4$ (*y* mol %), –30°



x	*y*	Solvent	Time (min)	
2.5	10	toluene	10	(92)
1.5	5	toluene	30	(90)
2.5	10	CH$_2$Cl$_2$	30	(90)
1.5	5	CH$_2$Cl$_2$	30	(51)
2.5	10	THF	30	(88)
1.5	5	THF	30	(19)

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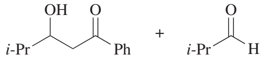
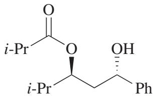


Catalyst (5 mol %),
toluene, –30°, 30 min



Catalyst		*anti*/*syn*
Zr(O*i*-Pr)$_4$	(10)	—
Hf(O*t*-Bu)$_4$	(85)	—
Y(O*i*-Pr)$_3$	(51)	10:1
Ti(O*i*-Pr)$_4$	(—)	—

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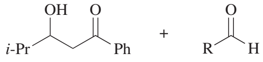
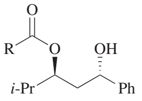
$C_{12} + C_7$

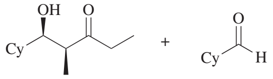


Zr(O*t*-Bu)$_4$ (cat.),
toluene, –30°



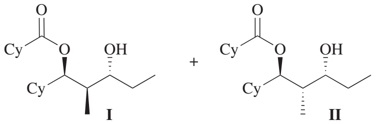
R	
n-C$_6$H$_{13}$	(87)
Ph	(19)

251



racemic

Catalyst,
[(*R*)-BINOL]Ti(O*t*-Bu)$_2$,
CH$_2$Cl$_2$, rt



Catalyst	**I**	er	**II**	er
cinchonine	(27)	71:29	(17)	89:11
cinchonidine	(30)	65:35	(11)	69:31

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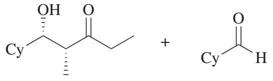
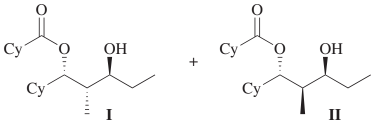


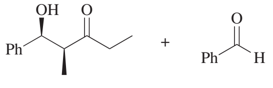
racemic

Catalyst,
[(*S*)-BINOL]Ti(O*t*-Bu)$_2$,
CH$_2$Cl$_2$, rt

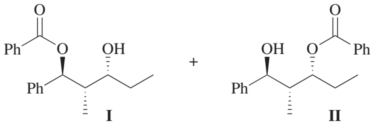


Catalyst	**I**	er	**II**	er
cinchonine	(27)	60.5:39.5	(16)	63:37
cinchonidine	(22)	70:30	(15)	80:20

257



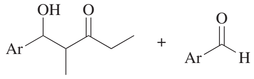
BuTi(O*i*-Pr)$_4$Li[k] (10 mol %),
t-BuOCH$_2$CH$_2$OMe,
rt, 24 h



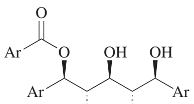
I + **II** (—), **I**/**II** = 10:90

236

$C_{12–14} + C_{7–9}$



Ti(O*t*-Bu)$_4$, cinchonine, rt



Ar		er
Ph	(52)	99:1
4-O$_2$NC$_6$H$_4$	(36)	98.5:1.5
4-MeOC$_6$H$_4$	(61)	98:2
2,4-(MeO)$_2$C$_6$H$_3$	(—)	—
4-MeC$_6$H$_4$	(72)	99:1
2,4-Me$_2$C$_6$H$_3$	(—)	—

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TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

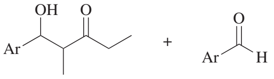
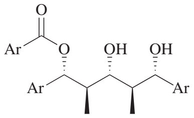
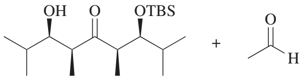
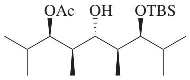
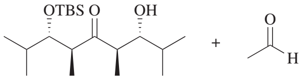
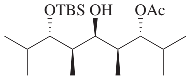
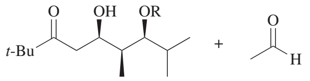
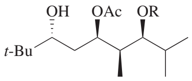
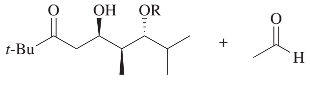
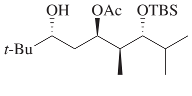
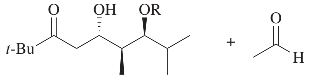
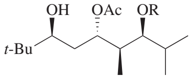
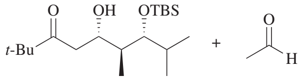
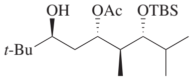
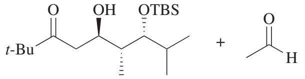
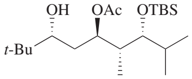
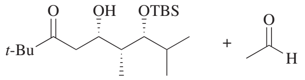
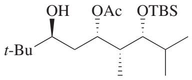
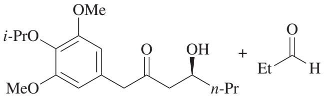
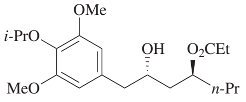
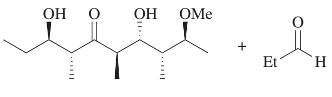
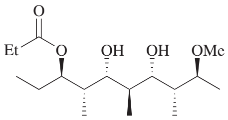
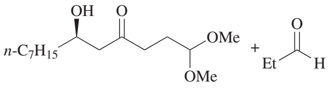
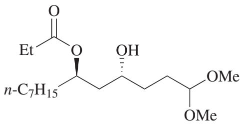
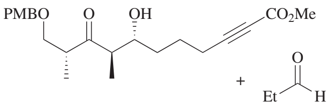
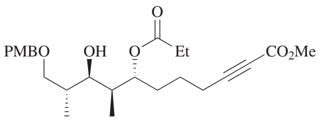
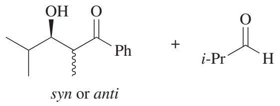
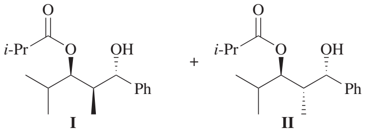
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-14} + C_{7-9}			
	Ti(O*t*-Bu)$_4$, cinchonidine, rt	 Ar — — er Ph (59) 98.5:1.5 4-MeOC$_6$H$_4$ (65) 99:1 2,4-(MeO)$_2$C$_6$H$_3$ (—) — 4-O$_2$NC$_6$H$_4$ (32) 99:1 4-MeC$_6$H$_4$ (61) 99:1 2,4-Me$_2$C$_6$H$_3$ (—) —	106
C_{13} + C_2			
	SmI$_2$ (40 mol %), THF, –10°, 1.5 h	 (95)	108
	SmI$_2$ (40 mol %), THF, 0°, 2 h	 (95)	268
 R = TBS, TMS, TES, TIPS, Bn	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (—)^g	362
	SmI$_2$ (20 mol %), THF, 0°, 30 min	 R TBS (93) Bn (—)^g	362, 358
	SmI$_2$ (20 mol %), THF, 0°, 30 min	 R TBS (—)^g TMS (—)^g TES (—)^g TIPS (—)^g Bn (92)	362
	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (92)	362, 358
	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (93)	362, 358
	SmI$_2$ (20 mol %), THF, 0°, 30 min	 (95)	362, 358
C_{13} + C_3			
	SmI$_2$ (50 mol %), THF, –10°, 4 h	 (90)	380
	Ti(O*i*-Pr)$_4$, CH$_2$Cl$_2$, 0°	 (—)	102
	SmI$_2$ (30 mol %), THF, –15°, 2 h	 (93) dr >97.5:2.5	381, 382
	SmI$_2$ (15 mol %), THF, 0°, 15 min	 (77) de >95%	383

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

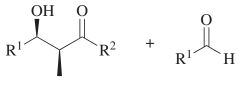
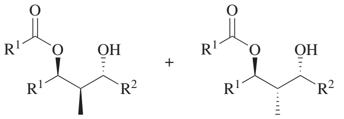
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

$C_{13} + C_4$

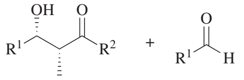
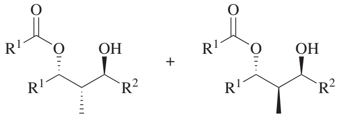
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 *syn* or *anti*	Zr(O*t*-Bu)$_4$, toluene	 **I** + **II**	251

	Temp (°)	**I + II**	**I/II**
syn	–30	(83)	70:30
syn	–50	(79)	82:18
anti	–30	(88)	45:55

$C_{13–16} + C_{4–7}$

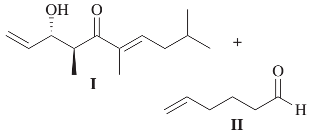
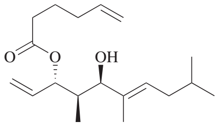
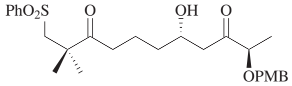
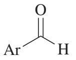
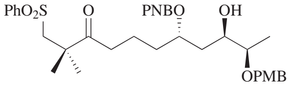
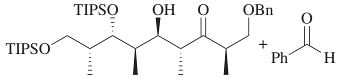
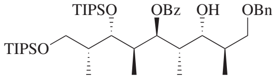
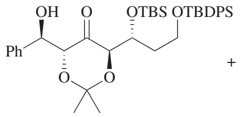
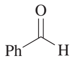
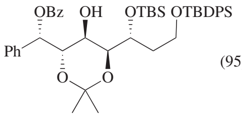
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 racemic	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$, cinchonine, CH$_2$Cl$_2$, rt	 **I** + **II**	257

R^1	R^2	**I**	er	**II**	er
i-Pr	Ph	(30)	70:30	(11)	93:7
Cy	*i*-Pr	(40)	76:24	(29)	80:20
Cy	*t*-Bu	(—)	—	(—)	—
Cy	Ph	(28)	77:23	(12)	90:10

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 racemic	[(*S*)-BINOL]Ti(O*t*-Bu)$_2$, cinchonidine, CH$_2$Cl$_2$, rt	 **I** + **II**	257

R^1	R^2	**I**	er	**II**	er
i-Pr	Ph	(25)	77:23	(14)	89:11
Cy	*i*-Pr	(55)	71:29	(29)	77:23
Cy	Ph	(26)	78:22	(20)	86:24

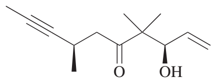
$C_{13} + C_7$

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 **I** + **II**	1. PhCHO, SmI$_2$ (30 mol %), THF, 0°, 30 min^a 2. **II**, 0°, 30 min 3. **I**, 0°, 30 min	 (93) dr >90:10	123
 + Ar = 4-O$_2$NC$_6$H$_4$ 	SmI$_2$ (25 mol %), THF, 0°, 5.5 h	 (76) dr >95:5	112, 113
	SmI$_2$ (30 mol %), THF, –10°, 2 h	 (76)	384
 + 	SmI$_2$ (60 mol %), THF, 0°	 (95)	117

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

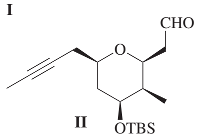
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*

$C_{13} + C_{12}$



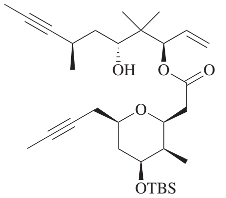
I

+



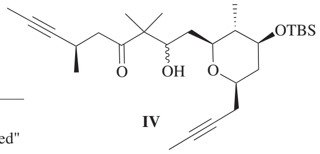
II

SmI_2 (*x* mol %), THF



III

+

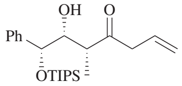


IV

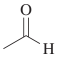
291

I/II	*x*	Temp (°)	Time (h)	III	IV
—	35	–10	—		~1:1
1:1.3	50	–50	1	(68)	"mostly suppressed"

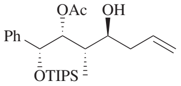
$C_{14} + C_2$



+



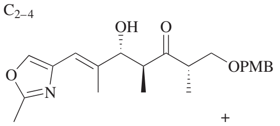
SmI_2 (20 mol %), THF, 0°, 1 h



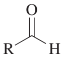
(96)

385

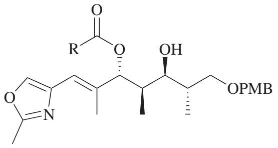
$C_{14} + C_{2–4}$



+



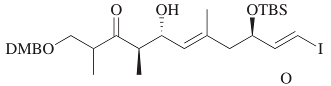
SmI_2 (30 mol %), THF, –20°, 15 min



R	
Me	(96)
i-Pr	(86)

386, 387

$C_{14} + C_3$



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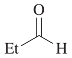
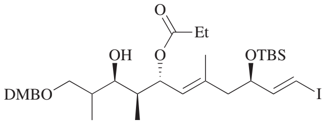


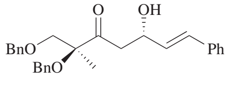
SmI_2 (50 mol %), THF, –20°, 1 h



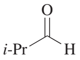
(95)

388

$C_{14} + C_4$

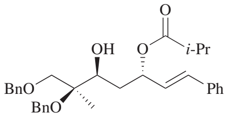


+



5 eq

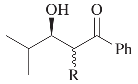
SmI_2 (0.15 eq), THF, –10°



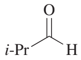
(87) >20:1 dr

389

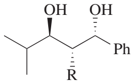
$C_{14–15} + C_4$



+



1. Catalyst, titanium complex, CH_2Cl_2, rt, time
2. Hydrolysis

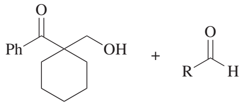
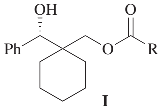
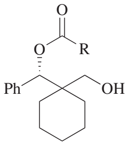
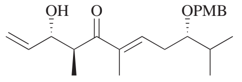
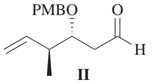
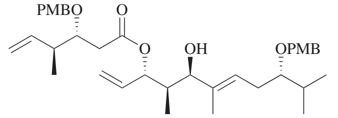
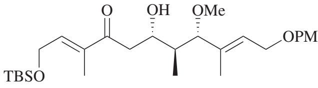
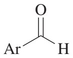
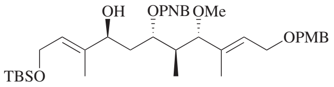
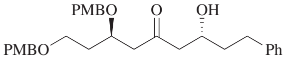
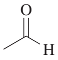
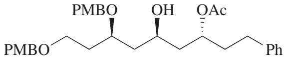
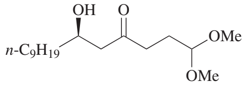
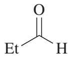
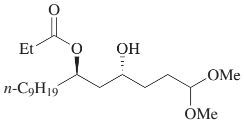
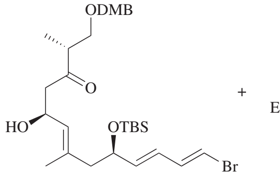


257

R	Config.	Catalyst	Titanium complex	Time (d)		er
Et	*syn*	—	Ti(O*t*-Bu)$_4$	3	(55)	—
Et	*syn*	cinchonine	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$	6	(53)	94:6
Et	*anti*	—	Ti(O*t*-Bu)$_4$	1	(57)	—
Et	*anti*	cinchonine	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$	3	(54)	90:10
i-Pr	*syn*	—	Ti(O*t*-Bu)$_4$	7	(51)	—
i-Pr	*syn*	cinchonine	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$	7	(48)	91.5:8.5
i-Pr	*anti*	—	Ti(O*t*-Bu)$_4$	3	(49)	—
i-Pr	*anti*	cinchonine	[(*R*)-BINOL]Ti(O*t*-Bu)$_2$	4	(52)	90.5:9.5

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

<table>
<tr><th>Substrates</th><th>Conditions</th><th>Product(s) and Yield(s) (%)</th><th>Refs.</th></tr>
<tr><td colspan="4">$C_{14} + C_{5–7}$</td></tr>
<tr><td></td><td>Cat. 117 (10 mol %), THF
<table><tr><th>R</th><th>Temp (°)</th><th>Time (h)</th><th>I</th><th>I er</th><th>II</th></tr><tr><td><i>t</i>-Bu</td><td>0</td><td>4</td><td>(82)</td><td>91.5:8.5</td><td>(13)</td></tr><tr><td>Ph</td><td>–40</td><td>0.5</td><td>(96)</td><td>99:1</td><td>(0)</td></tr></table></td><td>
I
+

II</td><td>254</td></tr>
<tr><td colspan="4">$C_{14} + C_7$</td></tr>
<tr><td>
I
+

II</td><td>1. PhCHO, SmI_2 (30 mol %), THF, 0°, 30 min[a]
2. II, 0°, 30 min
3. I, 0°, 30 min</td><td>
(96)</td><td>123</td></tr>
<tr><td>
Ar = 4-$O_2NC_6H_4$ +
</td><td>SmI_2 (1 eq), THF, 0°, 1.5 h</td><td>
(86)</td><td>119</td></tr>
<tr><td colspan="4">$C_{15} + C_2$</td></tr>
<tr><td>
+
</td><td>SmI_2 (10 mol %), THF, –10°, 15 min</td><td>
(64)</td><td>390</td></tr>
<tr><td colspan="4">$C_{15} + C_3$</td></tr>
<tr><td>
+
</td><td>SmI_2 (40 mol %), THF, –15°, 2 h</td><td>
(93)</td><td>391</td></tr>
<tr><td>
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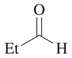
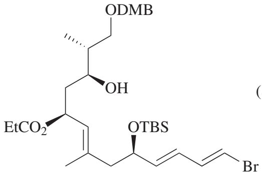
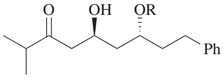
</td><td>SmI_2 (50 mol %), THF, –10°, 1 h</td><td>
(80) dr = 95:5</td><td>392, 393</td></tr>
<tr><td colspan="4">$C_{16} + C_2$</td></tr>
<tr><td>
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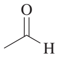
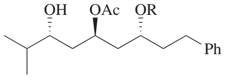
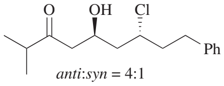
</td><td>SmI_2 (20 mol %), THF, 0°</td><td>
<table><tr><th>R</th><th>Time (min)</th><th></th></tr><tr><td>TBS[l]</td><td>20</td><td>(84)</td></tr><tr><td>Ac</td><td>10</td><td>(94)</td></tr></table></td><td>358</td></tr>
<tr><td>
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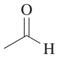
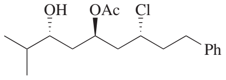
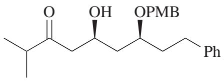
</td><td>SmI_2 (20 mol %), THF, 0°, 30 min</td><td>
(51) + unspecified products (30)</td><td>358</td></tr>
<tr><td>
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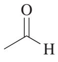
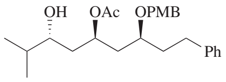
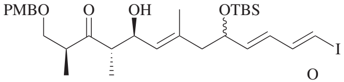
</td><td>SmI_2 (20 mol %), THF, 0°, 30 min</td><td>
(83)</td><td>358</td></tr>
<tr><td colspan="4">$C_{16} + C_3$</td></tr>
<tr><td>
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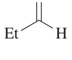
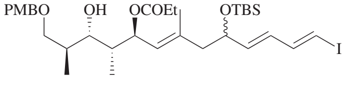
</td><td>SmI_2 (cat.), THF, –20° to –10°, 2h</td><td>
(92) dr >97:3</td><td>115</td></tr>
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TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

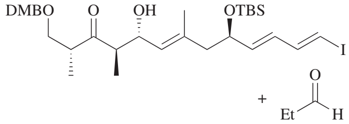
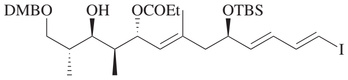
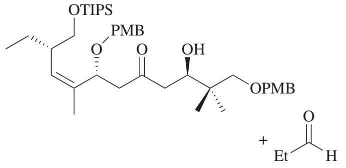
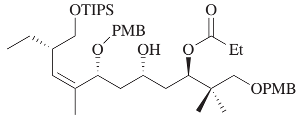
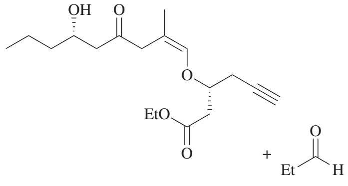
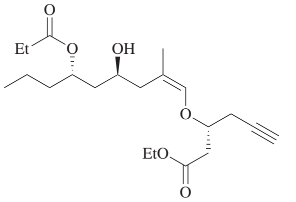
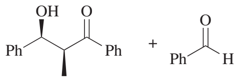
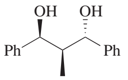
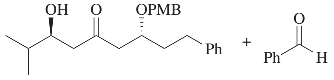
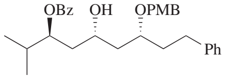
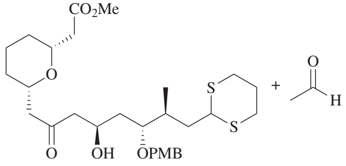
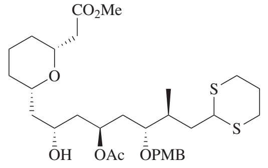
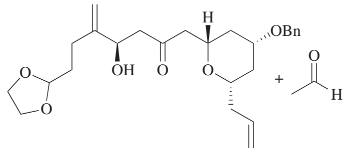
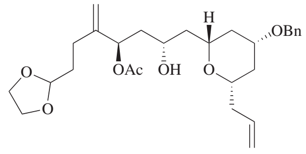
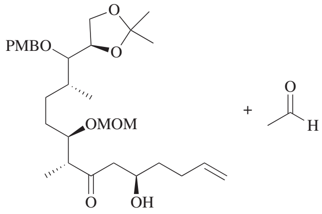
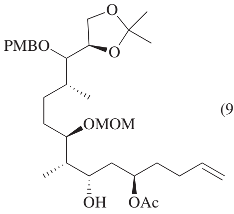
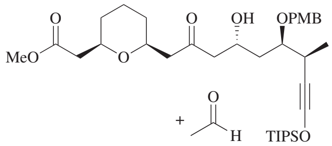
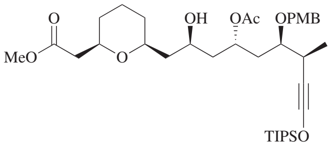
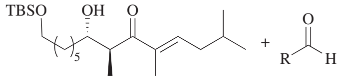
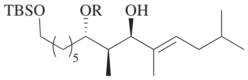
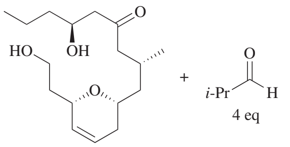
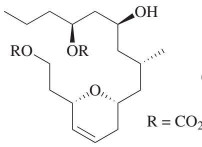
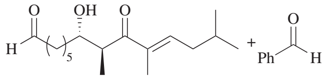
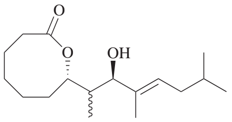
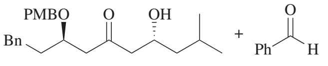
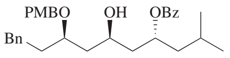
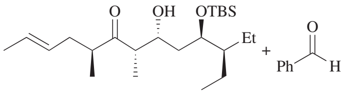
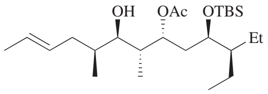
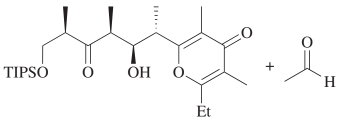
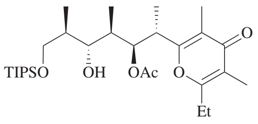
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{16} + C_3$			
	SmI_2 (cat.), THF, –20°	 (79)[m] dr = 98:2	297
	SmI_2 (cat.), THF	 (88)	394
	SmI_2 (40 mol %), THF, –10°, 4 h	 (77)	395, 396
$C_{16} + C_7$			
 racemic	1. $Yb(OTf)_3$ (20 mol %), **64**, DME, rt, 20 h 2. NaOMe, MeOH	 (68) er 85:15	105
	SmI_2 (30 mol %), THF, –10°, 1 h; rt, 30 min	 (94)	388
$C_{17} + C_2$			
	SmI_2 (15 mol %), THF, –11°, 30 min; –11°, 70 min	 (94%) dr 90:10	397
	SmI_2 (30 mol %), THF, –10°, 15 min	 (93) dr >95:5	398, 399
	SmI_2 (10 mol %), THF, –10°, 1.5 h	 (99)	400, 401
	SmI_2 (15 mol %), THF, –10°	 (98)	402

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{17} + C_{2-7}$			
	SmI_2 (60 mol %), THF, 0°, 10 min	 R: Me (70) Ph (70)	111
$C_{17} + C_4$			
	Zr(O*t*-Bu)$_4$, (13 mol %), PhMe, –55°, 6 h; to rt	 (85) R = CO_2*i*-Pr	403
$C_{17} + C_7$			
	1. SmI_2 (30 mol %), THF[a] 2. β-hydroxy ketone, 0°, 10 min	 (30)[n]	111
	SmI_2 (30 mol %), THF, –10°, 1 h	 (60)	390
	SmI_2 (40 mol %), THF, –15°, 1 h	 (90) dr 98:2	404
$C_{18} + C_2$			
	SmI_2 (1.25 eq), THF, –10°, 1 h; –26°, 16 h	 (100)	405, 406

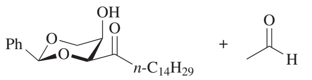
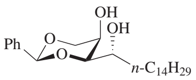
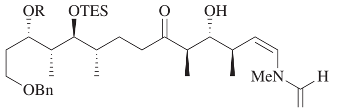
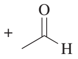
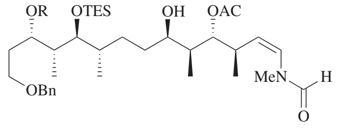
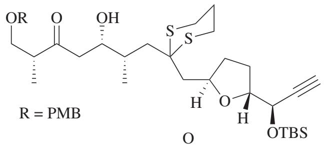
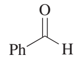
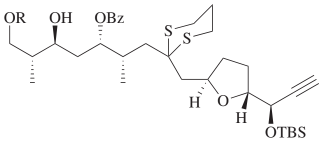
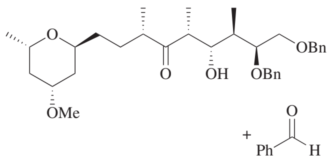
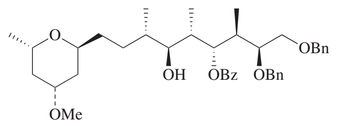
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. SmI_2 (10 mol %), THF, –10°, 2 h 2. NaOMe, MeOH, CH_2Cl_2, 12 h	 (80)	269
 R = CO*i*-Pr 	SmI_2 (cat.), THF, –5°, 2.5 h	 (50)	361
$C_{18} + C_7$			
 R = PMB 	SmI_2 (25 mol %), THF, –10°, 15 min	 (94) dr 11:1	407
	SmI_2 (30 mol %), THF, –10°, 1 h	 (89)	408, 110

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

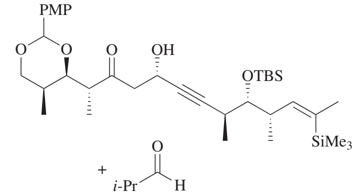
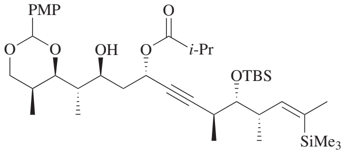
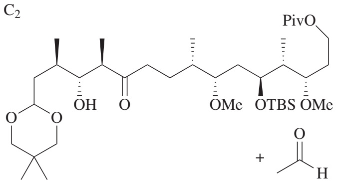
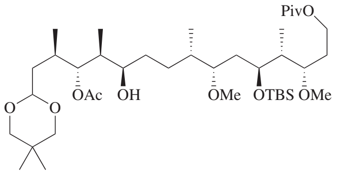
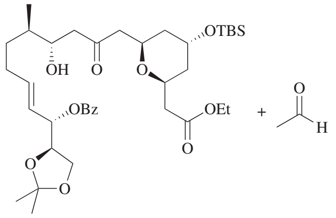
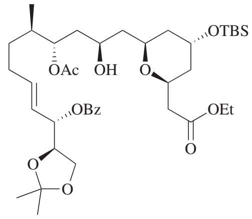
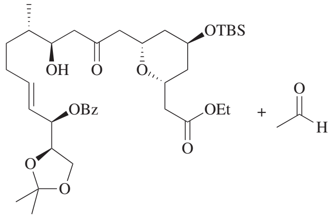
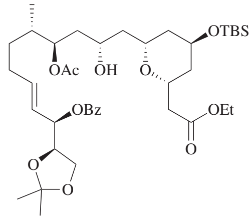
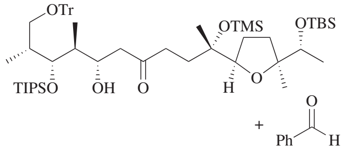
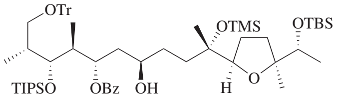
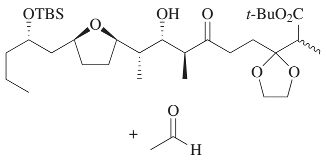
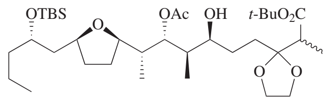
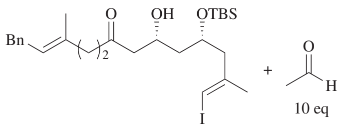
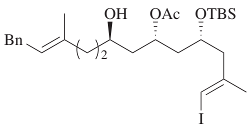
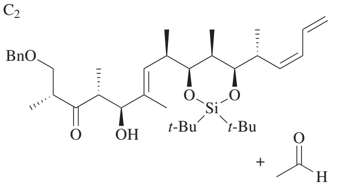
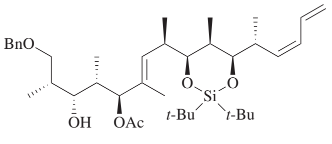
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{19} + C_4$			
	SmI_2 (30 mol %), THF, –10°, 4 h	 (95)	121, 290
$C_{20} + C_2$			
	SmI_2 (30 mol %), THF, –10°, 20 min	 (91)	409
	SmI_2 (30 mol %), THF, –10°, 4 h	 (85)	302
	SmI_2 (cat.), THF	 (0)	302
$C_{20} + C_7$			
	SmI_2 (26 mol %), THF, –10°, 30 min	 (90)	410
$C_{21} + C_2$			
	SmI_2 (cat.), THF, –10°	 (59)	411
	SmI_2 (10 eq), THF, –10°, 1 h	 (100) crude	412
$C_{22} + C_2$			
	SmI_2 (cat.), THF, 0°, 1 h	 (87) dr >97:3	413

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

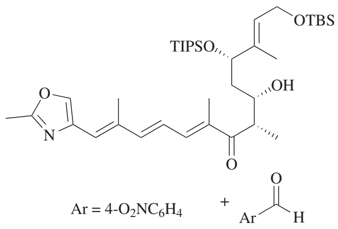
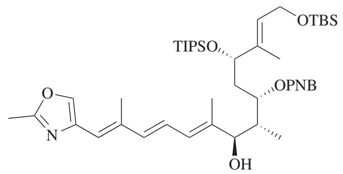
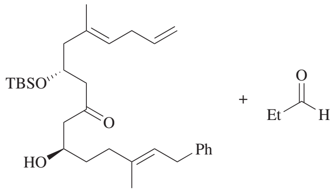
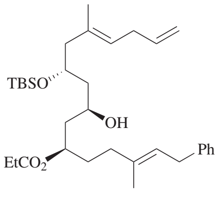
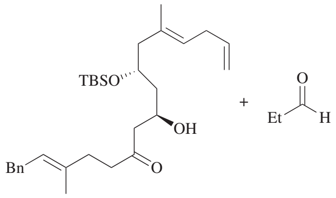
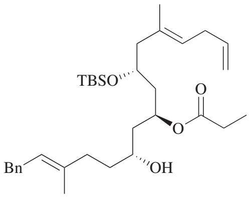
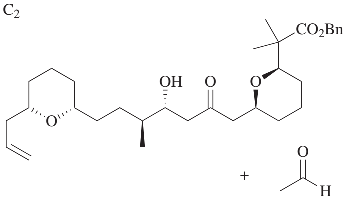
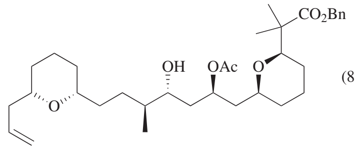
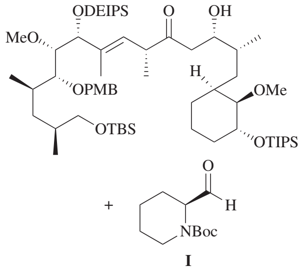
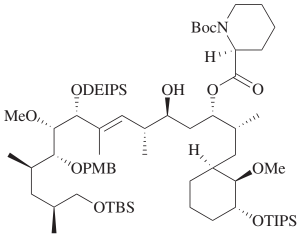
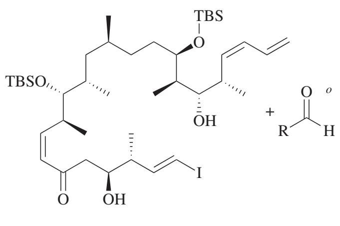
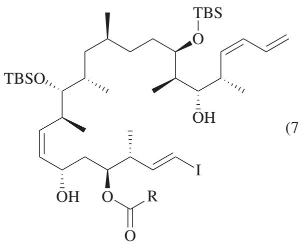
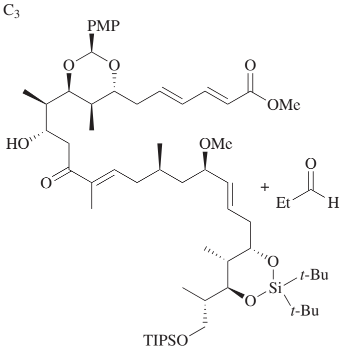
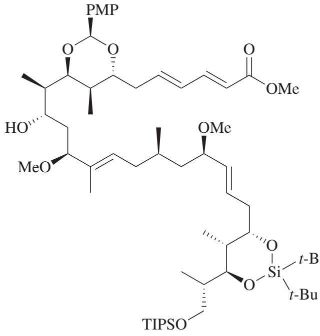
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
*Please refer to the charts preceding the tables for structures indicated by the **bold** numbers.*			
$C_{22} + C_7$			
 Ar = 4-$O_2NC_6H_4$	SmI_2 (30 mol %), THF, –10°, 3.5 h	 (83)	293, 292
$C_{24} + C_3$			
	SmI_2 (30 mol %), THF, –20°, 50 min	 (90) dr >24:1	414
	SmI_2 (35 mol %), THF, –20°, 1 h	 (93) dr >20:1	415
$C_{25} + C_2$			
	SmI_2 (30 mol %), THF, –10° to 0°, 8 h	 (82)	416
$C_{26} + C_6$			
 **I**	1. PhCHO, SmI_2 (30 mol %), THF, 0° [a] 2. **I**, –10°, 30 min	 (95) dr >20:1	109
$C_{29} + C_x$			
	SmI_2 (cat.)	 (70) dr 5:1	417

TABLE 2G. TISHCHENKO REACTIONS OF PREFORMED β-HYDROXY KETONES (*Continued*)

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

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{33} + C_3$			
	1. SmI_2 (cat.), THF, 0°, 3 h 2. MeOTf, DTBP, CH_2Cl_2, 20°, 2 h 3. K_2CO_3, MeOH, 20°	 (70)	418

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[a] This step produces the pinacol adduct of the aldehyde and samarium, $(RCHO)_2SmI•SmI_3$, which is assumed to be the active catalyst.

[b] The amount of catalyst was changed from 5 mol % to 10 mol %, and the amount of aldehyde from 1.5 eq to 2.5 eq.

[c] A stoichiometric amount of aldehyde was used.

[d] The proposed mechanism involves a series of retro-aldol reaction, aldol condensation with R^2CHO, and Tishchenko reaction. (027a)

[e] The yield is for the three steps of aldol reaction, Evans-Tishchenko reaction, and hydrolysis.

[f] The number denotes the yield after subsequent hydrolysis and release from solid support.

[g] No yield was given; the crude product was used without purification.

[h] The product was a 1:1.4 mixture of epimers with respect to the *O*-silyl-functionalized carbon.

[i] The reaction was run twice to achieve complete conversion.

[j] The yield includes three further steps.

[k] The catalyst was prepared in situ.

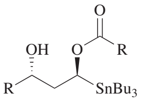
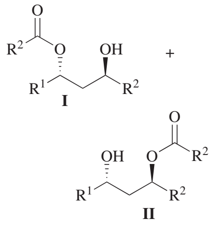
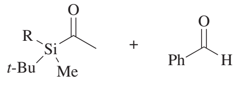
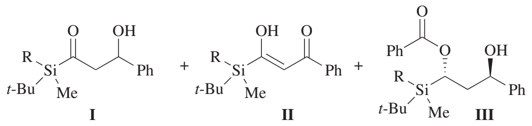
[l] The starting material was a mixture of diastereomers.

[m] The number denotes the yield after subsequent *O*-silylation, ester hydrolysis, and *O*-methylation steps.

[n] The product was a mixture of inseparable diastereomers due to the epimerization of the starting material under the reaction conditions.

[o] The nature of R was not specified.

TABLE 2H. ALDOL-TISHCHENKO REACTIONS OF MISCELLANEOUS SUBSTRATES

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_1 + C_{4-7}$			
	1. *t*-BuLi, Et_2O, –50°, 10 min 2. CO (1 atm), –78°, 2 h 3. RCHO, –78° to 20°, 12 h		229
$C_2 + C_{3-11}$			
	1. LDA, THF, –40°, 0.5 h 2. R^2CHO, 0°, 1 h	 I + II	228
$C_2 + C_7$			
	LDA, THF, –78° to rt	 I + II + III	419

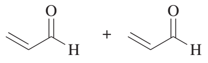
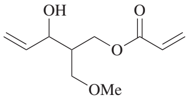
R	
i-Pr	(69)
Ph	(71)

R^1	R^2	I + II	I/II
$SiMe_3$	Et	(81)	99:1
$SiMe_2Ph$	Et	(32)	99:1
$SiMe_2t$-Bu	Et	(—)[a]	—
$SiMe_3$	*t*-Bu	(34)	75:25
$SiMe_3$	Cy	(48)	68:32
$SiMe_3$	Ph	(62)	99:1
$SiMe_3$	Ph	(33)[b]	99:1
$SiMe_3$	$4-MeOC_6H_4$	(—)[a]	—
$SiMe_3$	$4-NCC_6H_4$	(58)	99:1
$SiMe_3$	*n*-C_7H_{15}	(64)	99:1
$SiMe_3$	1-naphthyl	(45)	99:1

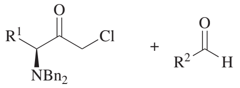
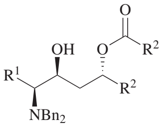
R	I	II	III
$BnOCH_2$	(0)	(35)	(32)
Me	(60)	(20)	(10)

TABLE 2H. ALDOL-TISHCHENKO REACTIONS OF MISCELLANEOUS SUBSTRATES (*Continued*)

$C_3 + C_3$

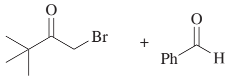
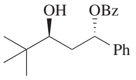
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\mathrm{Mg[B(OMe)_4]_2}$ (10 mol %), $\mathrm{Et_2O}$, 20–50°, 24 h	 (46)	216

$C_{4–10} + C_{5–14}$

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\mathrm{SmI_2}$ (3 eq), THF, –78°, 1 h; to rt		244

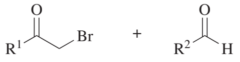
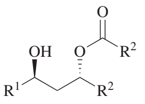
R^1	R^2		dr
Me	*i*-Bu	(81)	71:29
Me	*c*-C_6H_{11}	(80)	75:25
Me	*n*-C_7H_{15}	(80)	71:29
Me	*n*-$C_{13}H_{27}$	(83)	71:29
i-Bu	*i*-Bu	(90)	75:25
i-Bu	*c*-C_6H_{11}	(88)	78:22
i-Bu	*n*-C_7H_{15}	(91)	75:25
Bn	*i*-Bu	(90)	60:40
Bn	*c*-C_6H_{11}	(85)	71:29
Bn	*n*-C_7H_{15}	(79)	63:27

$C_6 + C_7$

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\mathrm{NdI_3}$, additive, THF, rt		242

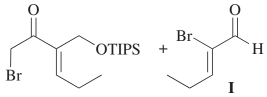
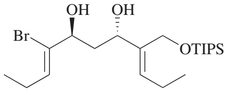
Additive	Time (h)	
CuI	3	(82)
$\mathrm{SbI_3}$	18	(81)
$\mathrm{Sc(OTf)_3}$	18	(69)

$C_{6–8} + C_7$

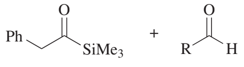
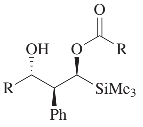
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\mathrm{NdBr_3}$, NaI, THF, 50°, 24 h		242

R^1	R^2		dr
t-Bu	Ph	(58)	>95:5
Ph	Ph	(79)	>95:5
Ph	4-$O_2NC_6H_4$	(77)	>95:5
3-BrC_6H_4	Ph	(77)	>95:5

$C_7 + C_5$

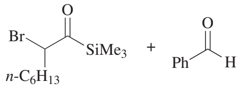
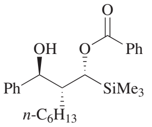
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
 **I**	1. $\mathrm{SmI_2}$, **I**, THF, 0° 2. MeCHO, 0°, 4 h 3. $\mathrm{K_2CO_3}$, MeOH, rt, 6 h	 (96)	243

$C_8 + C_{3–11}$

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. LDA, THF, –40°, 0.5 h 2. RCHO, 0°, 1 h		228

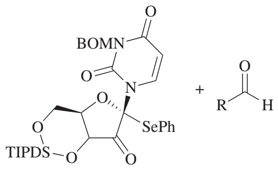
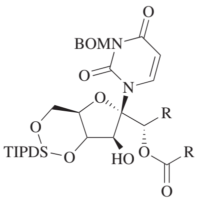
R		R	
Et	(77)	Ph	(62)
i-Pr	(58)	4-$MeOC_6H_4$	(31)
t-Bu	(0)	4-NCC_6H_4	(15)
3-furyl	(42)	*n*-C_7H_{15}	(58)
Cy	(46)	1-naphthyl	(24)

$C_8 + C_7$

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	Catalyst		232

Catalyst	
Zn dust	(80)
$\mathrm{ZnEt_2}$	(87)
$\mathrm{GaMe_3}$	(95)

$C_9 + C_{2–7}$

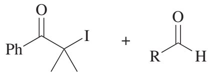
Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
	$\mathrm{SmI_2}$, THF, 3 h		241

R	Temp (°)	
Me	–78 to –10	(83)
i-Pr	–78 to –10	(55)^c
Ph	–78 to rt	(74)

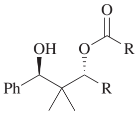
TABLE 2H. ALDOL-TISHCHENKO REACTIONS OF MISCELLANEOUS SUBSTRATES (*Continued*)

Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.

$C_{10} + C_{2-7}$



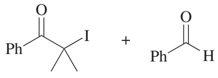
1. n-BuLi, Et_2O, 0°, 5 min
2. RCHO, 0°, 15 min



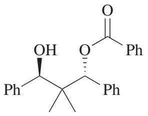
R	
Me	(55)
i-Pr	(65)
Ph	(79)

230

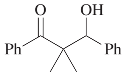
$C_{10} + C_7$



1. Et_2Zn, Et_2O, 0°, 5 min
2. PhCHO, 0°, 15 min



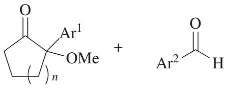
(32) +



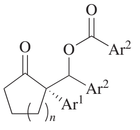
(32)

230

$C_{11-12} + C_7$



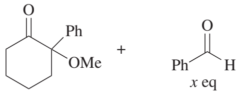
SmI_2, HMPA, THF, rt



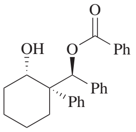
n	Ar^1	Ar^2	
1	Ph	$4\text{-}MeOC_6H_4$	(94)
1	Ph	$4\text{-}O_2NC_6H_4$	(93)
1	Ph	$4\text{-}BrC_6H_4$	(84)
1	Ph	$4\text{-}ClC_6H_4$	(85)
1	$4\text{-}BrC_6H_4$	Ph	(92)
1	$4\text{-}ClC_6H_4$	Ph	(75)
1	$4\text{-}MeC_6H_4$	Ph	(98)
2	Ph	Ph	(72)

420

$C_{12} + C_7$



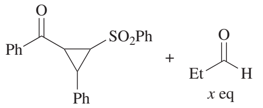
SmI_2, additive, THF



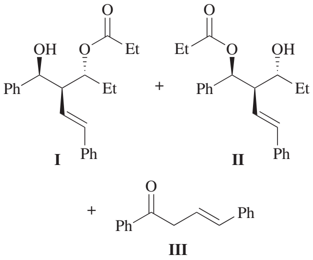
x	Additive	Temp (°)	
2	—	0	(86)
2	—	rt	(84)
3	—	rt	(88)
3	HMPA (2 eq)	rt	(95)

420

$C_{16} + C_3$



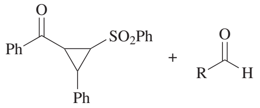
SmI_2, THF, –78° to rt



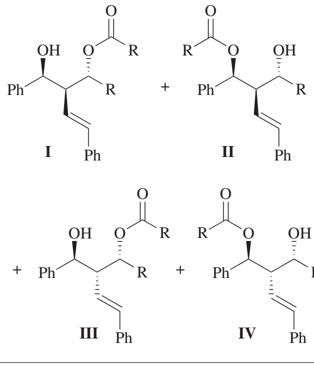
x	Time (h)	**I–III**	**I/II/III**
10	5	(74)	59:41:0
10	5	(52)	69:21:10
1.5	1	(66)	74:11:15
2.0	1	(76)	80:16:4
3.0	1	(85)	80:20:0
3.0	5	(77)	62:38:0
4.0	1	(79)	77:23:0

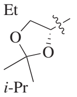
240

$C_{16} + C_{3-8}$



SmI_2, THF, –78° to rt, 1 h



R	**I–IV**	**I/II/III/IV**
Et	(85)	80:20:0:0
	(43)[d]	12:0:88:0
i-Pr	(78)	42:4:41:13
n-Bu	(85)	74:26:0:0
i-Bu	(69)	80:20:0:0
Ph	(56)	50:50:0:0
$4\text{-}ClC_6H_4$	(55)	38:62:0:0
$4\text{-}BrC_6H_4$	(32)	31:69:0:0
$4\text{-}MeOC_6H_4$	(36)	83:17:0:0
$4\text{-}MeC_6H_4$	(53)	51:49:0:0
$n\text{-}C_7H_{15}$	(89)	70:30:0:0

240

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[a] The reaction gave a complex mixture of products.

[b] One equivalent of aldehyde was used.

[c] A cyclic hemiketal was formed as a side product in 41% yield.

[d] The reaction was run at room temperature.

TABLE 3. OXIDATION OF ALDEHYDES WITH THE EVANS-TISHCHENKO REACTION

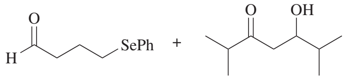
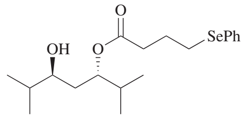
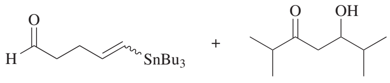
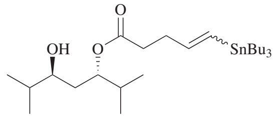
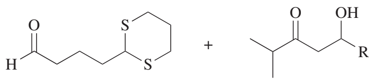
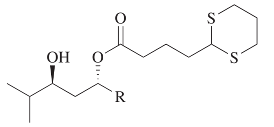
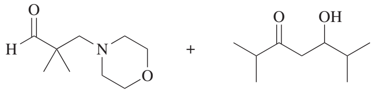
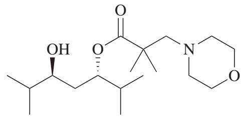
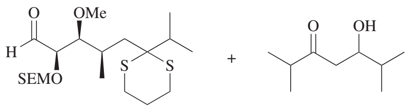
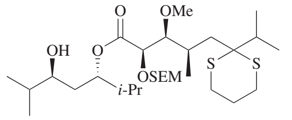
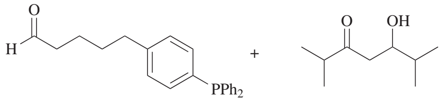
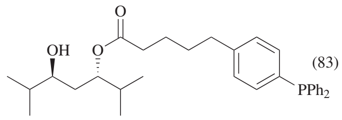
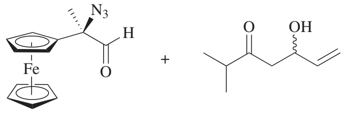
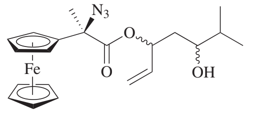
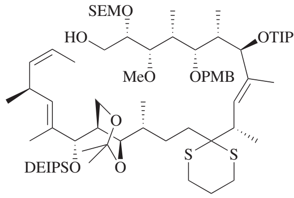
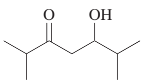
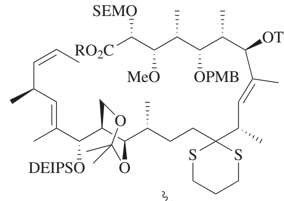
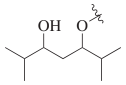
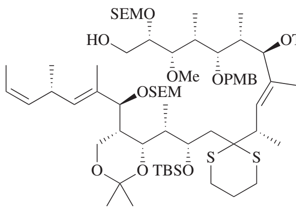
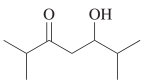
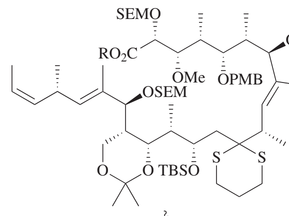
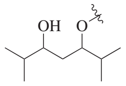
	Substrates	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4		SmI_2 (20 mol %), THF, –15°, 1 h	 (86)	421
C_5		SmI_2 (20 mol %), THF, –10°, 1 h	 (88)	421
		SmI_2 (20 mol %), THF, –10°		421
		R, Time (min)		
		Me, 60	(67)	
		Et, 45	(78)	
		$CH{=}CH_2$, 45	(75)	
		i-Pr, 60	(89)	
		Ph, 60	(85)	
		$4\text{-}MeOC_6H_4$, 15	(80)	
C_9		SmI_2 (20 mol %), THF, –10° to 0°, 1.5 h	 (80)	421
C_{10}		SmI_2 (24 mol %), THF, –10°, 1 h	 (96)	120, 421
C_{11}		SmI_2 (20 mol %), THF, –10º, 1 h	 (83)	421
C_{13}		SmI_2 (1 eq), THF, –10°, 3 h	 (85)	422
C_{31}	 +  I	1. SO_3•py, DMSO, $(i\text{-}Pr)_2EtN$, CH_2Cl_2, –15°, 45 min, slow addition 2. I, SmI_2 (35 mol %), THF, –10° to rt, 90 min	 (75) R = 	118, 120
	 +  I	1. SO_3•py, DMSO, $(i\text{-}Pr)_2EtN$, CH_2Cl_2, 0°, 30 min 2. I, SmI_2 (35 mol %), THF, –10°, 1 h	 (75) R = 	122

TABLE 4. TANDEM REACTIONS

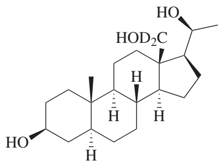
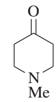
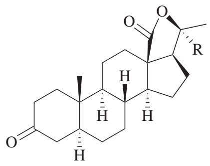
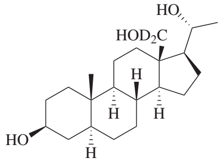
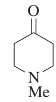
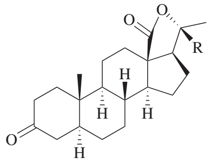
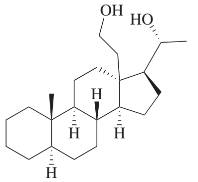
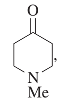
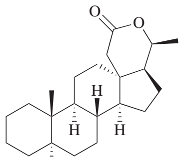
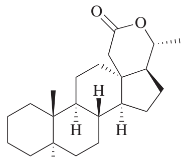
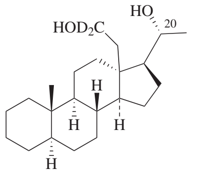
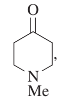
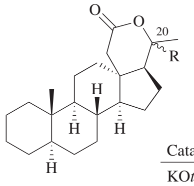
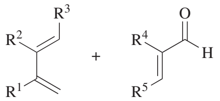
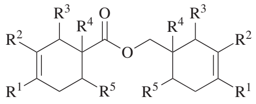
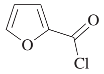
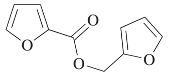
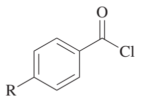
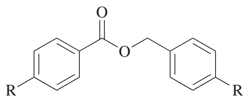
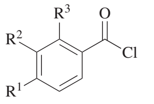
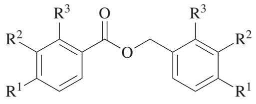
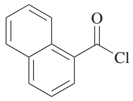
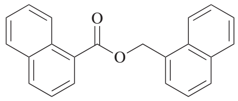
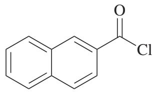
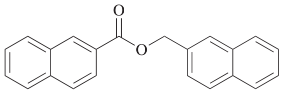
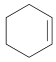
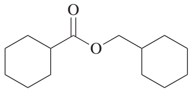
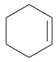
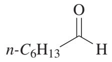
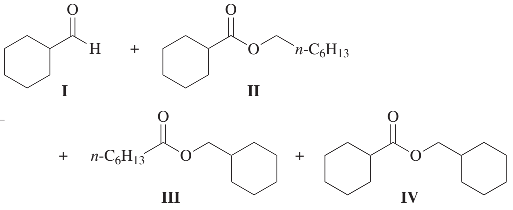
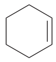
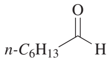
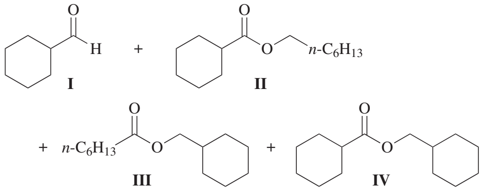
Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
Tandem Oppenauer–Tishchenko Reactions			
C_{21}			
	 , KO*t*-Bu, xylene, 11 h	 R **I** H **II** D **I** + **II** (23), **I/II** = 82:18	423
	 , KO*t*-Bu, xylene, 11 h	 R **I** H **II** D **I** + **II** (23), **I/II** = 82:18	423
C_{22}			
	 , catalyst, xylene Catalyst / Time (h) / **I** + **II** / **I/II** KO*t*-Bu / 8 / (80) / 45:55 Al(O*t*-Bu)$_3$ / 6 / (93) / 81:19	 **I** +  **II**	423
	 , catalyst, xylene	 R **I** H **II** D Catalyst / Time (h) / **I** + **II** / C20 (*R*)/(*S*) / **I/II** KO*t*-Bu / 12 / (84) / 56:44 / 52:48 Al(O*t*-Bu)$_3$ / 5 / (76) / 16:84 / 20:80	423
Tandem Diels–Alder–Tishchenko Reactions			
C_{3-6}			
	AlEt$_3$, TiCl$_4$, heptane, rt, 5 h, slow addition	 configurations undefined R^1 / R^2 / R^3 / R^4 / R^5 H / H / H / H / H / (20) Me / H / H / H / H / (25) H / H / Me / H / H / (13) H / H / H / Me / H / (4) H / H / H / H / Me / (0) Me / Me / H / H / H / (21)	163
Tandem Rosenmund–Tishchenko Reactions			
C_5			
	RuHCl(PPh$_3$)$_3$ (5 mol %), H$_2$ (1 atm), 2,4,6-collidine, toluene, 55°, 21 h	 (10)	60
C_7			
	RuHCl(PPh$_3$)$_3$ (5 mol %), H$_2$ (1 atm), 2,4,6-collidine, toluene, 55°	 R / Time (h) H / 20 / (85) Cl / 15 / (53) OMe / 19 / (57) NO$_2$ / 24 / (67)	60
C_{7-8}			
	RuCl$_2$(PPh$_3$)$_3$ (5 mol %), H$_2$ (1 atm), 2,4,6-collidine, toluene, 55°	 R^1 / R^2 / R^3 / Time (h) H / H / H / 19 / (75) Cl / H / H / 20 / (52) MeO / H / H / 22 / (25) Me / H / H / 20 / (85) H / Me / H / 21 / (77) H / H / Me / 20 / (52)	60
C_{11}			
	Catalyst (5 mol %), H$_2$ (1 atm), 2,4,6-collidine, toluene, 55°	 Catalyst / Time (h) RuHCl(PPh$_3$)$_3$ / 15 / (55) RuCl$_2$(PPh$_3$)$_3$ / 24 / (55)	60

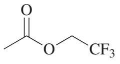
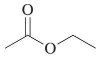
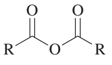
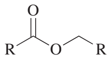
TABLE 4. TANDEM REACTIONS (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	$RuCl_2(PPh_3)_3$ (5 mol %), H_2 (1 atm), 2,4,6-collidine, toluene, 55°, 24 h	 (61)	60
Tandem Hydroformylation–Tishchenko Reactions			
C_6			
 + $(HCHO)_n$	$Ru_3(CO)_{12}$ (0.1 mol %), CO (20 atm), 200°, 48 h	 (51)^a	175
 + 	$Ru_3(CO)_{12}$ (x mol %), CO (20 atm)		175

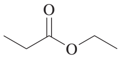
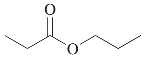
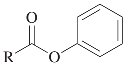
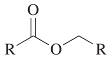
x	Temp (°)	Time (h)	**I**	**II + III**	**IV**
0.125	180	24	(5)	(2)	(0)
0.25	180	24	(5)	(1)	(0)
0.125	200	24	(20)	(2)	(3)
0.25	200	12	(19)	(2)	(1)
0.25	200	24	(29)	(3)	(6)
0.5	200	24	(7)	(4)	(15)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 + 	$Ru_3(CO)_{12}$ (cat.), gas (x atm), 24 h		175

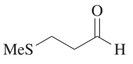
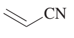
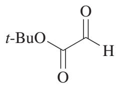
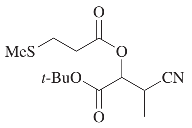
Gas	x	Temp (°)	**I**	**II + III**	**IV**
CO	20	200	(29)	(3)	(6)
CO	50	200	(29)	(5)	(6)
CO	80	200	(8)	(2)	(1)
Ar	50	200	(2)	(4)	(3)
Ar	50	150	(7)	(3)	(2)
N_2	50	200	(6)	(4)	(5)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
Tandem Ester C–O Bond Cleavage–Tishchenko Reactions			
C_4			
	$CoH(N_2)(PPh_3)_3$ (5 mol %), toluene, 20°, 48 h	 (30)^b	424
$C_{4–8}$			
	$CoH(N_2)(PPh_3)_3$, toluene, rt, 1 d		424

R	Substrate/Co	
Me	1:1	(23)^b
Et	2:1	(28)^b
n-Pr	1.9:1	(30)^b

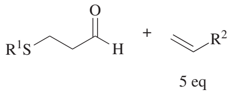
Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	$CoH(N_2)(PPh_3)_3$ (cat.), toluene 20°, 72 h	 (12)^b	424
$C_{8–13}$			
	$CoH(N_2)(PPh_3)_3$ (cat.), toluene, rt		424

R	Time (h)	
Me	48	(40)^b
CF_3	1	(31)^b
Et	72	(33)^b
n-Pr	24	(38)^b
Ph	24	(28)^b

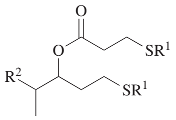
Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
Tandem Reductive Aldol Coupling–Tishchenko Reactions			
$C_3 + C_3 + C_2$			
 +  +  1:3:1	$Rh(dppe)ClO_4$, $ClCH_2CH_2Cl$, MeCN, rt, then 70°, 16 h	 (60) dr 1.4:1	425

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

$C_3 + C_{3-9}$

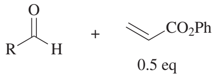


Rh(dppe)ClO$_4$ (10 mol %), ClCH$_2$CH$_2$Cl, rt; then 70°, 16 h

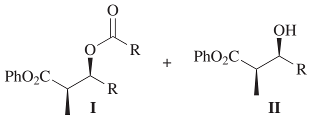


R^1	R^2		dr	Refs.
Me	CN	(88)	2.3:1	425
Me	COMe	(73)	—	346
Et	CN	(79)	3.3:1	425
Et	CO$_2$Ph	(67)	3.3:1	425
Et	COMe	(73)	1.4:1	425
Et	COPh	(74)	3.3:1	425
Ph	CN	(78)	2.5:1	425

$C_{3-7} + C_3$



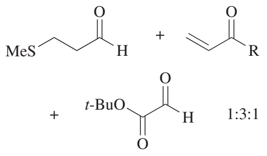
1. [codRhBinap]BF$_4$ 2.1 mmol), silane (21 mmol), ClCH$_2$CH$_2$Cl, rt, 24 h
2. HF/MeCN, rt, 45 min



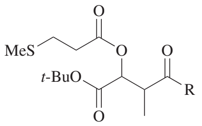
426

R	Silane	I	dr	er	II	dr	er
Et	(EtO)Me$_2$SiH	(29)	—	89:11	(0)	—	—
Et	EtMeSiH	(42)	—	91:9	(23)	—	91:9
Et	PhMe$_2$SiH	(40)	—	90:10	(18)	—	90:10
Ph	PhMe$_2$SiH	(10)	3:1	86:14	(44)	3:1	86:14

$C_3 + C_{4-11} + C_2$

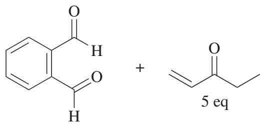


Rh(dppe)ClO$_4$, ClCH$_2$CH$_2$Cl, MeCN, rt, then 70°, 18 h

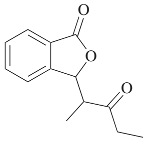


R		dr	Refs.
MeO	(0)[c]	—	346
PhO	(54)	2.3:1	346
Me	(92)	3:1	346
Et	(94)	2.2:1	346
i-Pr	(96)	2:1	346
t-Bu	(0)[d]	—	346
2-furyl	(83)	2.7:1	346
2-thienyl	(91)	2.7:1	346
n-C$_5$H$_{11}$	(77)	2.1:1	346
Ph	(99)	2.1:1	425, 346
(*E*)-PhCH=CH	(92)	2.3:1	346

$C_8 + C_5$



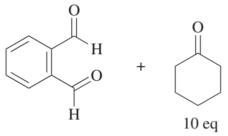
RuHCl(CO)(PPh$_3$)$_3$ (10 mol %), toluene, 90°, 5 h



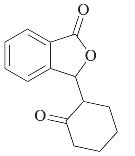
(79) dr 2:1

167

$C_8 + C_6$



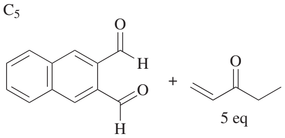
RuHCl(CO)(PPh$_3$)$_3$ (10 mol %), toluene, 90°, 5 h



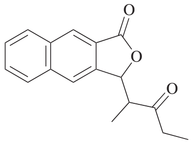
(45) dr 4:4

167

$C_{12} + C_5$



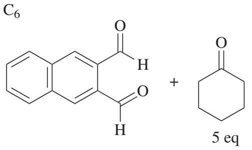
RuHCl(CO)(PPh$_3$)$_3$ (10 mol %), toluene, 90°, 5 h



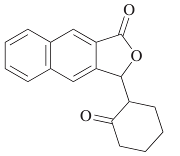
(43) dr 1.9:1

167

$C_{12} + C_6$



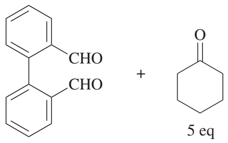
RuHCl(CO)(PPh$_3$)$_3$ (10 mol %), toluene, 90°, 5 h



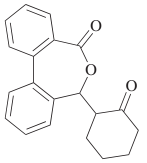
(60) dr 3.6:1

167

$C_{14} + C_6$



RuHCl(CO)(PPh$_3$)$_3$ (10 mol %), toluene, 90°, 5 h



(44) dr 2.8:1

167

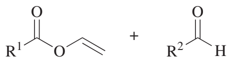
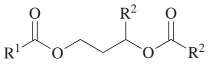
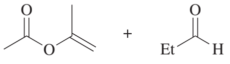
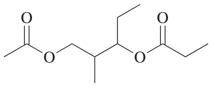
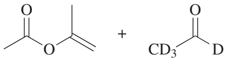
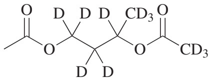
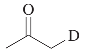
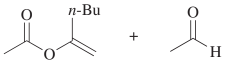
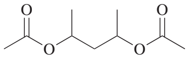
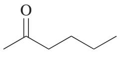
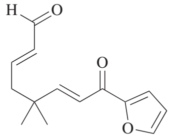
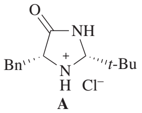
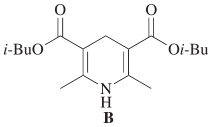
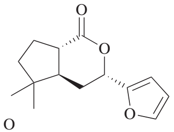
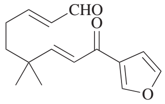
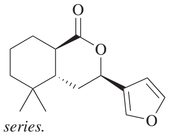
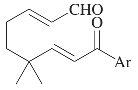
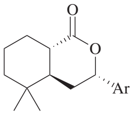
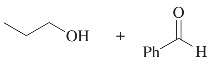
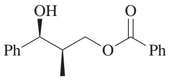
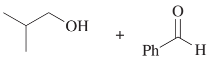
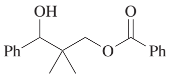
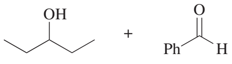
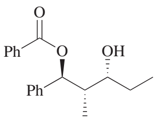
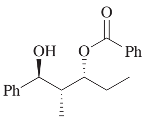
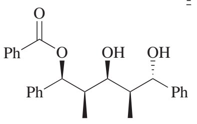
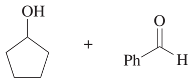
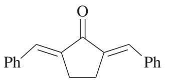
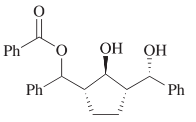
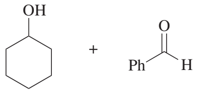
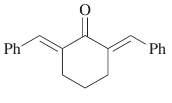
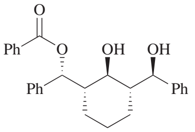
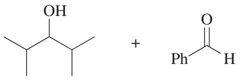
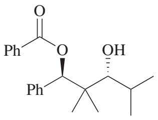
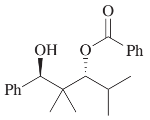
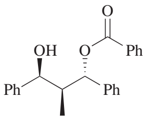
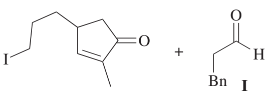
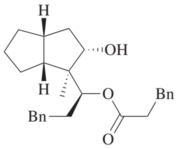
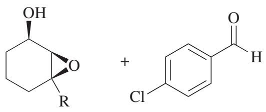
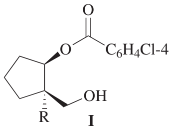
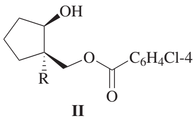
Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
Coupling of Vinyl Esters and Aldehydes Followed by the Tishchenko Reaction			
C_{4-8} 	1. $Cp^*{}_2Sm(thf)_2$ (10 mol %), toluene, 0°, 0.5 h 2. rt, 2.5 h	 R^1 R^2 Me Me (80) Me n-Pr (42) Me i-Pr (70) Me t-Bu $(—)^e$ Me c-C_6H_{11} (77) Me Ph (77) CH_2=CH Ph (71) MeCH=CH Ph (68) n-C_5H_{11} Ph (98)	185
C_5 	1. $Cp^*{}_2Sm(thf)_2$ (10 mol %), toluene, 0°, 0.5 h 2. rt, 2.5 h	 (78)	185
	1. $Cp^*{}_2Sm(thf)_2$ (10 mol %), toluene, 0°, 0.5 h 2. rt, 2.5 h	 $(46)^f$ +  (—)	185
C_8 	1. $Cp^*{}_2Sm(thf)_2$ (10 mol %), toluene, 0°, 0.5 h 2. rt, 2.5 h	 (57) +  (60)	185
Reductive Michael–Tishchenko Cascade Reactions			
C_{14} 	1. **A** (20 mol %), **B**, dioxane, 22°, 72 h 2. Sm(O*i*-Pr)$_3$ (1.2 eq), 4 h  **A**  **B**	 (30)	281
C_{15} 	1. **A** (20 mol %), **B**, dioxane, 22°, 72 h 2. Sm(O*i*-Pr)$_3$ (1.2 eq), 4 h	 (43)	281
*Structures of **A** and **B** are in the first entry of this series.*			
C_{15-17} 	1. **A** (20 mol %), **B**, dioxane, 22°, 72 h 2. Sm(O*i*-Pr)$_3$ (1.2 eq), 4 h	 Ar 2-furyl (42) 3-furyl (48) 2-thienyl (40) Ph (30)	281
*Structures of **A** and **B** are in the first entry of this series.*			
Tandem Oxidation–Aldol–Tishchenko Sequence			
C_3 	$LiClO_4$, Et_3N, rt	 (5)	231
C_4 	$LiClO_4$, Et_3N, rt	 (12)	231
C_5 	$LiClO_4$, Et_3N, rt	 (5) +  (7) +  (23)	231

TABLE 4. TANDEM REACTIONS (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	$LiClO_4$, Et_3N, rt	 (58) +  (2)	231
C_6			
	$LiClO_4$, Et_3N, rt	 (53) +  (2)	231
C_7			
	$LiClO_4$, Et_3N, rt	 (15) +  (12)	231
C_9			
	$LiClO_4$, Et_3N, rt	 (18)	231
Tandem Barbier–Aldol–Tishchenko Reaction			
	1. SmI_2, THF, DMPU, rt 2. **I**, rt, 30–60 min	 (81)	239
Tandem Semipinacol–Evans–Tishchenko Reactions			
$C_{8–13}$			
	SmI_2 (*x* mol %)	 **I** +  **II**	274

R	Solvent	*x*	Temp (°)	Time (h)	**I** + **II**	**I/II**
Et	toluene	30	80	1	(75)	80:20
Et	toluene	20	80	2.5	(55)	67:33
Et	DCE	30	70	1.5	(73)	99:1
Et	THF	30	"heat"	8	(58)	19:81
Et	MeCN	30	70	4	(65)	50:50
allyl	DCE	30	70	1	(82)	1:99
n-Bu	DCE	30	70	2	(76)	98:2
Ph	DCE	30	65	1.5	(63)	90:10
Ph	DCE	30	65	3	(63)	45:55
Ph	DCE	30	85	1	(62)	72:28
Bn	DCE	30	70	2.5	(82)	60:40

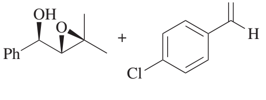
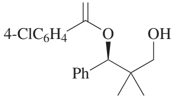
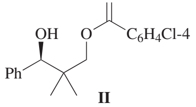
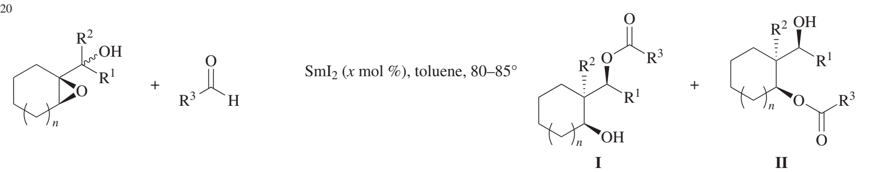
C_{11}			
	SmI_2 (30 mol %), DCE, rt, 2 h	 **I** +  **II** **I** + **II** (89), **I/II** 1:99	274

TABLE 4. TANDEM REACTIONS (*Continued*)

Substrate(s)	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{11-20}



SmI_2 (*x* mol %), toluene, 80–85°

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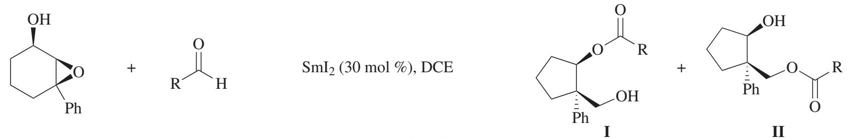
syn/*anti*	*n*	R^1	R^2	R^3	*x*	Time (h)	**I + II**	**I/II**
91:9	1	Me	$c\text{-}C_3H_5$	$4\text{-}ClC_6H_4$	30	4	(78)	93:7
60:40	1	Me	2-thienyl	$4\text{-}ClC_6H_4$	25	4	(83)	0:100
80:20	0	Me	Ph	$4\text{-}ClC_6H_4$	30	7	(85)	74:26
70:30	1	Me	Ph	Ph	15	4	(96)	100:0
61:39	1	Et	Ph	Ph	15	4	(92)	100:0
87:13	1	*i*-Pr	Ph	Ph	20	6	(92)	100:0
56:44	1	allyl	Ph	Ph	30	8	(70)	100:0
73:21	1	*n*-Bu	Ph	Ph	30	6	(78)	100:0
—	1	Ph	Ph	Ph	10	4	(95)	100:0
70:30	0	Bn	Ph	Ph	30	6	(88)	44:56
100:0	1	Bn	Ph	Ph	30	2	(95)	0:100

C_{12}



SmI_2 (30 mol %), DCE

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R	Temp (°)	Time (h)	**I + II**	**I/II**
n-Pr	60	3.5	(56)	24:76
i-Pr	60	3.5	(41)	98:2
2-furyl	60	4.5	(0)	—
Cy	60	3	(50)	85:15
Ph	65	3	(47)	72:28
$2\text{-}ClC_6H_4$	65	4	(11)	80:20
$3\text{-}ClC_6H_4$	65	2	(60)	60:40
$4\text{-}ClC_6H_4$	65	1.5	(63)	90:10
$2\text{-}FC_6H_4$	60	7	(40)	63:27
$4\text{-}O_2NC_6H_4$	60	0.25	(55)	82:18
$2\text{-}MeC_6H_4$	60	2	(2)	99:1
$3\text{-}MeC_6H_4$	60	4	(17)	99:1
$4\text{-}MeC_6H_4$	60	5	(7)	99:1
$3\text{-}MeOC_6H_4$	60	3.5	(52)	80:20
$4\text{-}MeOC_6H_4$	60	2	(<1)	—
$4\text{-}CF_3C_6H_4$	60	1.5	(62)	98:2

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[a] The yield is based on the initial amount of paraformaldehyde.

[b] The yield is based on the cobalt complex.

[c] The hydroacylation product $MeSCH_2CH_2COCH_2CH_2CO_2Me$ was formed in 76% yield.

[d] The Tishchenko product $MeSCH_2CH_2CO_2CH_2CO_2t\text{-}Bu$ was formed in 86% yield. See Table 1F, $C_2 + C_3$.

[e] The reaction gave a complex mixture of products.

[f] The yield is given for a reaction between undeuterated acetaldehyde and isopropenyl acetate.

REFERENCES

[1] Claisen, L. *Chem. Ber.* **1887**, *20*, 646.
[2] Tishchenko, V. E. *J. Russ. Phys. Chem. Soc.* **1906**, *38*, 355.
[3] Tishchenko, V. E. *J. Russ. Phys. Chem. Soc.* **1906**, *38*, 482.
[4] Tishchenko, V. E. *Chem. Zentralbl.* **1906**, *77*, 1309.
[5] Tishchenko, V. E. *Chem. Zentralbl.* **1906**, *77*, 1552.
[6] Cannizzaro, S. *Liebigs Ann. Chem.* **1853**, *88*, 129.
[7] Geissman, T. A. *Org. React.* **1944**, *2*, 94.
[8] Meerwein, H.; Schmidt, R. *Liebigs Ann. Chem.* **1925**, *444*, 221.
[9] Verley, A. *Bull. Soc. Chim. France* **1925**, *37*, 537.
[10] Verley, A. *Bull. Soc. Chim. France* **1925**, *37*, 871.
[11] Verley, A. *Bull. Soc. Chim. France* **1927**, *41*, 788.
[12] Ponndorf, W. *Angew. Chem.* **1926**, *39*, 138.
[13] Wilds, A. L. *Org. React.* **1944**, *2*, 178.
[14] Oppenauer, R. *Recl. Trav. Chim. Pays-Bas* **1937**, *56*, 137.
[15] Djerassi, C. *Org. React.* **1951**, *6*, 207.
[16] Child, W. C.; Adkins, H. *J. Am. Chem. Soc.* **1923**, *45*, 3013.
[17] Child, W. C.; Adkins, H. *J. Am. Chem. Soc.* **1925**, *47*, 798.
[18] Danilov, S. N. *Trans. State Inst. Applied Chem. (Moscow)* **1927**, 66.
[19] Batalin, V. S.; Nikitina, M. K.; Rivkin, S. M.; Sekretareva, E. V. *Zh. Prikl. Khim.* **1936**, *9*, 1820.
[20] Baker, R. H.; Linn, L. E. *J. Am. Chem. Soc.* **1949**, *71*, 1399.
[21] Häusermann, M. *Helv. Chim. Acta* **1951**, *34*, 2172.
[22] Hawkins, E. G. E.; Long, D. J. G.; Major, F. W. *J. Chem. Soc.* **1955**, 1462.
[23] Koral, J. N.; Smolin, E. M. *J. Polym. Sci. A* **1963**, *1*, 2831.
[24] Yu, C.-Y.; Huang, C.-T. *Huaxue Xuebao* **1964**, *30*, 348.
[25] Gosteva, O. K.; Libina, S. L.; Rivkina, E. G. *Plasticheskie Massy* **1965**, 55.
[26] Kopp, E.; Smidt, J. *Liebigs Ann. Chem.* **1966**, *693*, 117.
[27] Ogata, Y.; Kawasaki, A.; Kishi, I. *Tetrahedron* **1967**, *23*, 825.
[28] Saegusa, T.; Ueshima, T. *J. Org. Chem.* **1968**, *33*, 3310.
[29] Saegusa, T.; Ueshima, T.; Kauchi, K.; Kitagawa, S. *J. Org. Chem.* **1968**, *33*, 3657.
[30] Ogata, Y.; Kawasaki, A. *Tetrahedron* **1969**, *25*, 929.
[31] Ogata, Y.; Kawasaki, A. *Tetrahedron* **1969**, *25*, 2845.
[32] Saegusa, T.; Ueshima, T.; Kitagawa, S. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 248.
[33] Gavrilova, V. M.; Rudkovskii, D. M.; Trifel, A. G. *Zh. Prikl. Khim.* **1972**, *45*, 1320.
[34] Okada, M.; Sumimoto, H.; Tajima, I. *Macromolecules* **1977**, *10*, 505.
[35] Sumimoto, H.; Hashimoto, K. *Macromolecules* **1977**, *10*, 1327.
[36] Maślińska-Solich, J.; Rudnicka, I.; Jedliński, Z. J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3034.
[37] Ulrich, D.; Jankowski, H. *Chem. Tech.(Leipzig)* **1988**, *40*, 393.
[38] Liu, Y.; Wang, D.; Han, Z.; Chang, Q. *Huaxue Yu Nianhe* **1993**, 160.
[39] Kamm, O.; Kamm, W. F. *Org. Synth. Coll. Vol. 1* **1941**, 104.
[40] Morris, J. M.; Dunmire, R. B.; Koenig, P. E.; Newkome, G. R. *J. Org. Chem.* **1972**, *37*, 1244.
[41] Klecan, T.; Rybczyk, M.; Jedliński, Z. *Rocz. Chem.* **1974**, *48*, 701.
[42] Isăcescu, D. A.; Avramescu, F. *Rev. Roum. Chim.* **1978**, *6*, 873.
[43] Pasha, M. A.; Ravindranath, B. *Indian J. Chem. Sect. B.* **1985**, *24*, 1068.
[44] Bunce, R. A.; Shellhammer, A. *Org. Prep. Proced. Int.* **1987**, *19*, 161.
[45] Mojtahedi, M. M.; Akbarzadeh, E.; Sharifi, R.; Abaee, M. S. *Org. Lett.* **2007**, *9*, 2791.
[46] Terentiev, A. P. Z. *Anorg. Allg. Chem.* **1927**, *159*, 226.
[47] Choi, S.-H.; Yashima, E.; Okamoto, Y. *Macromolecules* **1996**, *29*, 1880.
[48] Choi, S.-H.; Yashima, E.; Okamoto, Y. *Polymer J.* (Tokyo) **1997**, *29*, 261.
[49] Choi, S.-H.; Yashima, E.; Okamoto, Y. *Enantiomer* **1997**, *2*, 105.
[50] Yashima, E.; Okamoto, Y. Japanese Patent 10, 120,770 (**1998**).
[51] Crimmin, M. R.; Barrett, A. G. M.; Hill, M. S.; Procopiou, P. A. *Org. Lett.* **2007**, *9*, 331.
[52] Horino, H.; Ito, T.:, Yamamoto, A. *Chem. Lett.* **1978**, 17.
[53] Tsuda, T.; Habu, H., Saegusa, T. *J. Chem. Soc., Chem. Commun.* **1974**, 620.
[54] Yamashita, M.; Watanabe, Y.; Mitsudo, T.; Takegami, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3597.
[55] Maruyama, K.; Ito, T.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 849.
[56] Komiya, S.; Tane-ichi, S.; Yamamoto, A.; Yamamoto, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 673.
[57] Ito, T.; Horino, H.; Koshiro, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 504.
[58] Massoui, M.; Beaupère, D.; Nadjo, L.; Uzan, R. *J. Organomet. Chem.* **1983**, *259*, 345.

[59] Menashe, N.; Shvo, Y. *Organometallics* **1991**, *10*, 3885.
[60] Grushin, V. V.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5159.
[61] Morita, K.-I.; Nishiyama, Y.; Ishii, Y. *Organometallics* **1993**, *12*, 3748.
[62] Yamashita, M.; Ohishi, T. *Appl. Organomet. Chem.* **1993**, *7*, 357.
[63] Yamakawa, T.; Hiroi, M.; Shinoda, S. *J. Chem. Soc., Dalton Trans.* **1994**, 2265.
[64] Slough, G. A.; Ashbaugh, J. R.; Zannoni, L. A. *Organometallics* **1994**, *13*, 3587.
[65] Yamaguchi, I.; Kimishima, T.; Osakada, K.; Yamamoto, T. *J. Polym. Sci., Part A* **1997**, *35*, 1265.
[66] Barrio, P.; Esteruelas, M. A.; Oñate, E. *Organometallics* **2004**, *23*, 1340.
[67] Sorkau, A.; Schwarzer, K.; Wagner, C.; Poetsch, E.; Steinborn, D. *J. Mol. Catal. A* **2004**, *224*, 105.
[68] Suzuki, T.; Yamada, T.; Matsuo, T.; Watanabe, K.; Katoh, T. *Synlett* **2005**, 1450.
[69] Yokoo, K.; Mine, N.; Taniguchi, H.; Fujiwara, Y. *J. Organomet. Chem.* **1985**, *279*, C19.
[70] Onozawa, S.; Sakakura, T.; Tanaka, M. *Chem. Lett.* **1994**, 531.
[71] Onozawa, S.; Sakakura, T.; Tanaka, M.; Shiro, M. *Tetrahedron* **1996**, *52*, 4291.
[72] Berberich, H.; Roesky, P. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 1569.
[73] Deacon, G. B.; Gitlits, A.; Roesky, P. W.; Bürgstein, M. R.; Lim, K. C.; Skelton, B. W.; White, A. H. *Chem.—Eur. J.* **2001**, *7*, 127.
[74] Bürgstein, M. R.; Berberich, H.; Roesky, P. W. *Chem.—Eur. J.* **2001**, *7*, 3078.
[75] Saito, K.; Tanabe, K. *Nippon Kagaku Kaishi* **1974**, 1014.
[76] Tanabe, K.; Saito, K. *J. Catal.* **1974**, *35*, 247.
[77] Seki, T.; Akutsu, K.; Hattori, H. *Chem. Commun.* **2001**, 1000.
[78] Seki, T.; Hattori, H. *Chem. Commun.* **2001**, 2510.
[79] Seki, T.; Kabashima, H.; Akutsu, K.; Tachikawa, H.; Hattori, H. *J. Catal.* **2001**, *204*, 393.
[80] Seki, T.; Tachikawa, H.; Yamada, T.; Hattori, H. *J. Catal.* **2003**, *217*, 117.
[81] Tsuji, H.; Hattori, H. *ChemPhysChem* **2004**, *5*, 733.
[82] Ai, M. *J. Catal.* **1983**, *83*, 141.
[83] Scott, F.; van Heerden, F. R.; Raubenheimer, H. G. *J. Chem. Res. (S)* **1994**, 144.
[84] Handa, H.; Baba, T.; Sugisawa, H.; Ono, Y. *J. Mol. Catal. A* **1998**, *134*, 171.
[85] Kabashima, H.; Tsuji, H.; Nakata, S.; Tanaka, Y.; Hattori, H. *Appl. Catal. A* **2000**, *194–195*, 227.
[86] Kawanami, Y.; Yuasa, H.; Toriyama, F.; Yoshida, S.; Baba, T. *Catal. Commun.* **2003**, *4*, 455.
[87] Seki. T.; Onaka, M. *Chem. Lett.* **2005**, *34*, 262.
[88] Seki, T.; Onaka, M. *Catal. Surv. Asia* **2006**, *10*, 138.
[89] Seki, T.; Onaka, M. *J. Phys. Chem. B* **2006**, *110*, 1240.
[90] Lin, I.; Day, A. R. *J. Am. Chem. Soc.* **1952**, *74*, 5133.
[91] Kulpinski, M. S.; Nord, F. F. *J. Org. Chem.* **1943**, *8*, 256.
[92] Villani, F. J.; Nord, F. F. *J. Am. Chem. Soc.* **1946**, *68*, 1674.
[93] Villani, F. J.; Nord, F. F. *J. Am. Chem. Soc.* **1947**, *69*, 2605.
[94] Fouquet, G.; Merger, F.; Platz, R. *Liebigs. Ann. Chem.* **1979**, 1591.
[95] Brauchbar, M.; Kohn, L. *Monatsh. Chem.* **1898**, *19*, 16.
[96] Franke, A.; Kohn, L. *Monatsh. Chem.* **1898**, *19*, 354.
[97] Morgenstern, M. *Monatsh. Chem.* **1903**, *24*, 579.
[98] Kirchbaum, F. M. A. *Monatsh. Chem.* **1904**, *25*, 249.
[99] Neustädter, V. *Monatsh. Chem.* **1906**, *27*, 879.
[100] Burkhardt, E. R.; Bergman, R. G.; Heathcock, C. H. *Organometallics* **1990**, *9*, 30.
[101] Loog, O.; Mäeorg, U. *Tetrahedron: Asymmetry* **1999**, *10*, 2411.
[102] Delas, C.; Blacque, O.; Moïse, C. *Tetrahedron Lett.* **2000**, *41*, 8269.
[103] Mascarenhas, C. M.; Miller, S. P.; White, P. S.; Morken, J. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 601.
[104] Gnadadesikan, V.; Horiuchi, Y.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7782.
[105] Mlynarski, J.; Rakiel, B.; Stodulski, M.; Suszczyńska, A.; Frelek, J. *Chem.—Eur. J.* **2006**, *12*, 8158.
[106] Rohr, K.; Herre, R.; Mahrwald, R. *Org. Lett.* **2005**, *7*, 4499.
[107] Schneider, C.; Hansch, M.; Sreekumar, P. *Tetrahedron: Asymmetry* **2006**, *17*, 2738.
[108] Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447.
[109] Romo, D.; Meyer, S. D.; Johnson, D. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 7906.
[110] Richter, P. K.; Tomaszewski, M. J.; Miller, R. A.; Patron, A. P.; Nicolaou, K. C. *J. Chem. Soc., Chem. Commun.* **1994**, 1151.
[111] Hulme, A. N.; Howells, G. E. *Tetrahedron Lett.* **1997**, *38*, 8245.
[112] Evans, D. A.; Carter, P. J.; Carreira, E. M.; Prunet, J. A.; Charette, A. B.; Lautens, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2354.
[113] Evans, D. A.; Carter, P. J.; Carreira, E. M.; Prunet, J. A.; Charette, A. B.; Lautens, M. *J. Am. Chem. Soc.* **1999**, *121*, 7540.

[114] Schöning, K.-U.; Hayashi, R. K.; Powell, D. R.; Kirschning, A. *Tetrahedron: Asymmetry* **1999**, *10*, 817.
[115] Paterson, I.; Davies, R. D. M.; Marquez, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 603.
[116] Paterson, I.; Florence, G. J.; Gerlach, K.; Scott, J. P.; Sereinig, N. *J. Am. Chem. Soc.* **2001**, *123*, 9535.
[117] Enders, D.; Ince, S. J.; Bonnekessel, M.; Runsink, J.; Raabe, G. *Synlett* **2002**, 962.
[118] Smith, A. B., III; Adams, C. M.; Lodise Barbosa, S. A.; Degnan, A. P. *J. Am. Chem. Soc.* **2003**, *125*, 350.
[119] Jiang, Y.; Hong, J.; Burke, S. D. *Org. Lett.* **2004**, *6*, 1445.
[120] Smith, A. B., III; Adams, C. M.; Lodise Barbosa, S. A.; Degnan, A. P. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 12042.
[121] Arefolov, A.; Panek, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 5596.
[122] Smith, A. B., III; Lee, D. *J. Am. Chem. Soc.* **2007**, *129*, 10957.
[123] Aird, J. I.; Hulme, A. N.; White, J. W. *Org. Lett.* **2007**, *9*, 631.
[124] Saibaba, V.; Sampath, A.; Mukkanti, K.; Iqbal, J.; Das, P. *Synthesis* **2007**, 2797.
[125] Törmäkangas, O. P.; Koskinen, A. M. P. *Recent Res. Devel. Org. Chem.* **2001**, *5*, 225.
[126] Mahrwald, R. *Curr. Org. Chem.* **2003**, *7*, 1713.
[127] Mahrwald, R. In *Modern Aldol Reactions Vol. 2*; Mahrwald, R., Ed.; Wiley-VCH: Weinheim, 2004; pp 327–343.
[128] Mlynarski, J. *Eur. J. Org. Chem.* **2006**, 4779.
[129] Seki, T.; Nakajo, T.; Onaka, M. *Chem. Lett.* **2006**, *35*, 824.
[130] Shibasaki, M.; Ohshima, T. In *Asymmetric Synthesis*, 2nd ed.; Christmann, M., Bräse, S., Eds.; Wiley-VCH: Weinheim, 2007; pp 149–154.
[131] Ralston, K. J.; Hulme, A. N. *Synthesis* **2012**, 2310.
[132] Abu-Hasanayn, F.; Streitwieser, A. *J. Org. Chem.* **1998**, *63*, 2954.
[133] Peterson, J.; Timotheus, H.; Mäeorg, U. *Proc. Estonian. Acad. Sci. Chem.* **1997**, *46*, 93.
[134] Lu, L.; Chang, H.-Y.; Fang, J.-M. *J. Org. Chem.* **1999**, *64*, 843.
[135] Nielsen, E. R. *J. Am. Chem. Soc.* **1944**, *66*, 1230.
[136] Swamer, F. W.; Hauser, C. R. *J. Am. Chem. Soc.* **1946**, *68*, 2647.
[137] Lewis, G. E. *J. Org. Chem.* **1965**, *30*, 2433.
[138] Govindan, M.; Pinnick, H. W. *J. Org. Chem.* **1981**, *46*, 5011.
[139] Werner, T.; Koch, J. *Eur. J. Org. Chem.* **2010**, 6904.
[140] Rajesh, K.; Berke, H. *Adv. Synth. Cat.* **2013**, *355*, 901.
[141] Törmäkangas, O. P.; Koskinen, A. M. P. *Tetrahedron Lett.* **2001**, *42*, 2743.
[142] Törmäkangas, O. P.; Saarenketo, P.; Koskinen, A. M. P. *Org. Process Res. Devel.* **2002**, *6*, 125.
[143] Paquette, L. A.; Ohmori, N.; Lowinger, T. B; Rogers, R. D. *J. Org. Chem.* **2000**, *65*, 4303.
[144] Cronin, L.; Manoni, F.; O'Connor, C. J.; Connon, S. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 3045.
[145] O'Connor, C. J.; Manoni, F.; Curran, S. P.; Connon, S. J. *New. J. Chem.* **2011**, *35*, 551.
[146] Curran, S. P.; Connon, S. *J. Org. Lett.* **2012**, *14*, 1074.
[147] Curran, S. P.; Connon, S. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 10866.
[148] Saegusa, T.; Hirota, K.; Hirasawa, E.; Fujii. H. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 967.
[149] Okada, M.; Sumimoto, H.; Tajima, H. *Macromolecules* **1977**, *10*, 505.
[150] Sumimoto, H.; Hashimoto, K. *Macromolecules* **1977**, *10*, 1327.
[151] Zinner, H.; Reck, R. *Carbohydr. Res.* **1971**, *16*, 459.
[152] Dworzak, R. *Monatsh. Chem.* **1926**, *47*, 11.
[153] Labriola, R. A. *An. Asoc. Quim. Argent.* **1935**, *23*, 32B.
[154] Saegusa, T.; Kitagawa, S.; Ueshima, T. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 1960.
[155] Lange, G. L.; Organ, M. G. *Synlett* **1991**, 665.
[156] Hon, Y.-S.; Chang, C.-P.; Wong, Y.-C. *Tetrahedron Lett.* **2004**, *45*, 3313.
[157] Hon, Y.-S.; Wong, Y.-C.; Chang, C.-P.; Hsieh, C.-H. *Tetrahedron* **2007**, *63*, 11325.
[158] Ooi, T.; Miura, T.; Takaya, K.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 7695.
[159] Ooi, T.; Miura, T.; Itagaki, Y.; Ichikawa, H.; Maruoka, K. *Synthesis* **2002**, 279.
[160] Simpura, I.; Nevalainen, V. *Tetrahedron* **2001**, *57*, 9867.
[161] Ooi, T.; Ohmatsu, K.; Sasaki, K.; Miura, T.; Maruoka, K. *Tetrahedron Lett.* **2003**, *44*, 3191.
[162] Shirakawa, S.; Takai, J.; Sasaki, K.; Miura, T.; Maruoka, K. *Heterocycles* **2003**, *59*, 57.
[163] Lutz, E. F. *J. Org. Chem.* **1963**, *28*, 912.
[164] Neunhoeffer, O.; Ruske, E. *Chem. Ber.* **1961**, *94*, 623.
[165] Pang, M.; Yao, Y.; Zhang, Y.; Shen, Q. *Chin. Sci. Bull.* **2008**, *53*, 1978.
[166] Ozawa, F.; Yamagami, I.; Yamamoto, A. *J. Organomet. Chem.* **1994**, *473*, 265.
[167] Omura, S.; Fukuyama, T.; Murakami, Y.; Okamoto, H.; Ryu, I. *Chem. Commun.* **2009**, 6741.

168 Washington, J.; McDonald, R.; Takats, J.; Menashe, N.; Reshef, D.; Svho, Y. *Organometallics* **1995**, *14*, 3996.
169 Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Chem. Commun.* **2005**, 3295.
170 Shen, Z.; Khan, H. A.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 2916.
171 Shen, Z.; Dornan, P. K.; Khan, H. A.; Woo, T. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 1077.
172 Phan, D. H. T.; Kim, B.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 15608.
173 Khan, H. A.; Kou, K. G. M.; Dong, V. M. *Chem. Sci.* **2011**, *2*, 407.
174 Isnard, P.; Denise, B.; Sneeden, R. P. A.; Cognion, J. M.; Durual, P. *J. Organomet. Chem.* **1982**, *240*, 285.
175 Kondo, T.; Akazome, M.; Tsuji, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286.
176 Suzuki, T.; Yamada, T.; Watanabe, K.; Katoh, T. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2583.
177 Ogoshi, S.; Hoshimoto, Y.; Ohashi, M. *Chem. Commun.* **2010**, *46*, 3354.
178 Hoshimoto, Y.; Ohashi, M.; Ogoshi, S. *J. Am. Chem. Soc.* **2011**, *133*, 4668.
179 Collin, J.; Namy, J.-L.; Kagan, H. B. *Nouv. J. Chim.* **1986**, *10*, 229.
180 Uenishi, J.; Masuda, S.; Wakabayashi, S. *Tetrahedron Lett.* **1991**, *32*, 5097.
181 Hsu, J.-L.; Chen, C.-T.; Fang, J.-M. *Org. Lett.* **1999**, *1*, 1989.
182 Hsu, J.-L.; Fang, J.-M. *J. Org. Chem.* **2001**, *66*, 8573.
183 Chuang, T.-H.; Fang, J.-M.; Jiaang, W.-T.; Tsai, Y.-M. *J. Org. Chem.* **1996**, *61*, 1794.
184 Zuyls, A.; Roesky, P. W.; Deacon, G. B.; Konstas, K.; Junk, P. C. *Eur. J. Org. Chem.* **2008**, 693.
185 Takeno, M.; Kikuchi, S.; Morita, K.-I.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1995**, *60*, 4974.
186 Barnea, E.; Eisen, M. S. *Coord. Chem. Rev.* **2006**, *250*, 855.
187 Sharma, M.; Andrea, T.; Brookes, N. J.; Yates, B. F.; Eisen, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 1341.
188 Andrea, T.; Barnea, E.; Eisen, M. S. *J. Am. Chem. Soc.* **2008**, *130*, 2454.
189 Hattori, H. *Chem. Rev.* **1995**, *95*, 537.
190 Tsuji, H.; Yagi, F.; Hattori, H.; Kita, H. *J. Catal.* **1994**, *148*, 759.
191 Idriss, H.; Seebauer, E. G. *Catal. Lett.* **2000**, *66*, 139.
192 Tsuji, H.; Hattori, H. *Catal. Today* **2006**, *116*, 239.
193 Gauvin, R. M.; Chenal, T.; Hassan, R. A.; Addad, A.; Mortreux, A. *J. Mol. Catal. A* **2006**, *257*, 31.
194 Chen, Y.; Zhu, Z.; Zhang, J.; Shen, J.; Zhou, X. *J. Organomet. Chem.* **2005**, *690*, 3783.
195 Stapp, P. R. *J. Org. Chem.* **1973**, *38*, 1433.
196 Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 4558.
197 Du, D.; Lu, Y.; Jin, J.; Tang, W.; Lu, T. *Tetrahedron* **2011**, *67*, 7557.
198 Gerbino, D. C.; Augner, D.; Slavov, N.; Schmalz, H.-G. *Org. Lett.* **2012**, *14*, 2338.
199 Le Bideau, F.; Coradin, T.; Gourier, D.; Hénique, J.; Samuel, E. *Tetrahedron Lett.* **2000**, *41*, 5215.
200 Ishmuratov, G. Yu.; Yakovleva, M. P.; Botsman, L. P.; Ishmuratova, N. M.; Muslukhov, R. R.; Khambalova, G. V.; Tolstikov, G. A. *Chem. Nat. Comp. (Engl. Transl.)* **2003**, *39*, 28; *Khim. Prir. Soedin.* **2003**, *39*, 24.
201 Selvaraj, S.; Dhanabalan, A.; Perumal, S.; Arumugam, N. *Phosphorus Sulfur Silicone*, *Relat. Elem.* **1988**, *39*, 217.
202 Halton, B.; Boese, R.; Dixon, G. M. *Eur. J. Org. Chem.* **2003**, 4507.
203 Milnes, K. A.; Baines, K. M. *Organometallics* **2007**, *26*, 2392.
204 Mitin, Yu. V.; Sazanov, Yu. N.; Vlasov, G. P.; Koton, M. M. *Vysokomol. Soedin.* **1960**, *2*, 716.
205 Sweeny, W. *J. Appl. Polym. Sci. 1963*, 7, **1983**.
206 Tagami, S.; Kunitake, T. *Makromol. Chem.* **1974**, *175*, 3367.
207 Furukawa, J.; Saegusa, T.; Fujii, H. *Makromol. Chem.* **1961**, *44*, 398.
208 Jedliński, Z.; Majnusz, J. *Makromol. Chem.* **1972**, *155*, 111.
209 Jedliński, Z.; Rybczyk, M.; Majnusz, J.; Janik, S. *Makromol. Chem.* **1975**, *176*, 905.
210 Jedliński, Z.; Kowalczuk, M. *J. Org. Chem.* **1979**, *44*, 222.
211 Yamaguchi, I.; Kimishima, T.; Osakada, K.; Yamamoto, T. *J. Polym. Sci., Part A* **1997**, *35*, 2821.
212 Carter, J. H.; Michelotti, F. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1964**, *5*, 614.
213 Yamamoto, N.; Yamashita, I. *Polym. J.* **1972**, *3*, 704.
214 Hashimoto, K.; Sumitomo, H.; Kitao, O. *J. Polym. Sci., Polym. Chem. Ed.* **1975**, *13*, 1257.
215 Schwenk, U.; Becker, A. *Liebigs Ann. Chem.* **1972**, *756*, 162.
216 Hesse, G.; Maurer, M. *Liebigs Ann. Chem.* **1962**, *658*, 21.
217 Törmäkangas, O. P.; Koskinen, A. M. P. *Org. Process Res. Devel.* **2001**, *5*, 421.
218 Casnati, G.; Pochini, A.; Salerno, G.; Ungaro, R. *Tetrahedron Lett.* **1974**, *15*, 959.
219 Pochini, A.; Salerno, G.; Ungaro, R. *Synthesis* **1975**, 164.
220 Casnati, G.; Pochini, A.; Salerno, G.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1527.
221 Finch, G. K.; *J. Org. Chem.* **1960**, *25*, 2219.
222 Späth, E.; Lorenz, R.; Freund, E. *Chem. Ber.* **1943**, *76*, 57.

[223] Späth, E.; Lorenz, R.; Freund, E. *Chem. Ber.* **1943**, *76*, 1196.

[224] Ito, K.; Kamiyama, N.; Nakanishi, S.; Otsuji, Y. *Chem. Lett.* **1983**, *12*, 657.

[225] Villacorta, G. M.; San Filippo, J. *J. Org. Chem.* **1983**, *48*, 1151.

[226] Baramee, A.; Chaichit, N.; Intawee, P.; Thebtaranonth, C.; Thebtaranonth, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 1016.

[227] Bodnar, P. M.; Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 5674.

[228] Honda, M.; Iwamoto, R.; Nogami, Y.; Segi, M. *Chem. Lett.* **2005**, *34*, 466.

[229] Iwamoto, K.; Chatani, N.; Murai, S. *J. Organomet. Chem.* **1999**, *574*, 171.

[230] Aoki, Y.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1995**, *24*, 463.

[231] Markert, M.; Mahrwald, R. *Synthesis* **2004**, 1429.

[232] Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1995**, *36*, 5353.

[233] Hon, Y.-S.; Chang, C.-P. *Tetrahedron* **2005**, *61*, 5267.

[234] Umekawa, Y.; Sakaguchi, S., Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 3409.

[235] Gillespie, K. M.; Munslow, I. J.; Scott, P. *Tetrahedron Lett.* **1999**, *40*, 9371.

[236] Mahrwald, R.; Costisella, B. *Synthesis* **1996**, 1087.

[237] Mascarenhas, C. M.; Duffey, M. O.; Liu, S.-Y.; Morken, J. P. *Org. Lett.* **1999**, *1*, 1427.

[238] Miyano, A.; Tashiro, D.; Kawasaki, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **1998**, *39*, 6901.

[239] Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317.

[240] Reutrakul, V.; Jaratjaroonphong, J.; Tuchinda, P.; Kuhakarn, C.; Kongsaeree, P.; Prabpai, S.; Pohmakotr, M. *Tetrahedron Lett.* **2006**, *47*, 4753.

[241] Kodama, T.; Shuto, S.; Ichikawa, S.; Matsuda, A. *J. Org. Chem.* **2002**, *67*, 7706.

[242] Kirsch, S. F.; Liébert, C. *Eur. J. Org. Chem.* **2007**, 3711.

[243] Shotwell, J. B.; Krygowski, E. S.; Hines, J.; Koh, B.; Huntsman, E. W. D.; Choi, H. W.; Schneekloth, J. S. Jr.; Wood, J. L.; Crews, C. M. *Org. Lett.* **2002**, *4*, 3087.

[244] Rodríguez-Solla, H.; Concellón, C.; Tuya, P.; García-Granda, S.; Díaz, M. R. *Adv. Synth. Catal.* **2012**, *354*, 1679.

[245] Simpura, I.; Nevalainen, V. *Tetrahedron Lett.* **2001**, *42*, 3905.

[246] Schneider, C.; Hansch, M. *Chem. Commun.* **2001**, 1218.

[247] Simpura, I.; Nevalainen, V. *Tetrahedron* **2003**, *59*, 7535.

[248] Schneider, C.; Hansch, M. *Synlett* **2003**, 837.

[249] Schneider, C.; Hansch, M.; Weide, T. *Chem.—Eur. J.* **2005**, *11*, 3011.

[250] Loog, O.; Mäeorg, U. *Proc. Estonian Acad. Sci. Chem.* **1998**, *47*, 193.

[251] Schneider, C.; Klapa, K.; Hansch, M. *Synlett* **2005**, 91.

[252] Ichibakase, T.; Nakajima, M. *Org. Lett.* **2011**, *13*, 1579.

[253] Ichibakase, T.; Nakajima, M. *Synthesis* **2012**, 3145.

[254] Ichibakase, T.; Nakatsu, M.; Nakajima, M. *Molecules* **2011**, *16*, 5008.

[255] Ichibakase, T.; Keneko, T.; Orito, Y.; Kotani, S.; Nakajima, M. *Tetrahedron*, **2012**, *68*, 4210.

[256] Horiuchi, Y.; Gnadadesikan, V.; Ohshima, T.; Masu, H.; Katagiri, K.; Sei, Y.; Yamaguchi, K.; Shibasaki, M. *Chem.—Eur. J.* **2005**, *11*, 5195.

[257] Rohr, K.; Herre, R.; Mahrwald, R. *J. Org. Chem.* **2009**, *74*, 3744.

[258] Mlynarski, J.; Mitura, M. *Tetrahedron Lett.* **2004**, *45*, 7549.

[259] Mlynarski, J.; Jankowska, J.; Rakiel, B. *Chem. Commun.* **2005**, 4854.

[260] Mlynarski, J.; Jankowska, J.; Rakiel, B. *Tetrahedron: Asymmetry* **2005**, *16*, 1521.

[261] Stodulski, M.; Jazwinski, J.; Mlynarski, J. *Eur. J. Org. Chem.* **2008**, 5553.

[262] Stodulski, M.; Mamińska, A.; Mlynarski, J. *Tetrahedron: Asymmetry* **2011**, *22*, 464.

[263] Delas, C.; Moïse, C. *Synthesis* **2000**, 251.

[264] Delas, C.; Moïse, C. C. R. *Hebd. Sceance Acad. Sci. IIc* **2000**, *3*, 17.

[265] Delas, C.; Blacque, O.; Moïse, C. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2265.

[266] Szymoniak, J.; Lefranc, H.; Moïse, C. *J. Org. Chem.* **1996**, *61*, 3926.

[267] Szymoniak, J.; Thery, N.; Moïse, C. *Synlett* **1997**, 1239.

[268] Evans, D. S.; Ng, H. P.; Clark, J. S.; Rieger, D. L. *Tetrahedron* **1992**, *48*, 2127.

[269] Wild, R.; Schmidt, R. R. *Tetrahedron: Asymmetry* **1994**, *5*, 2195.

[270] Deng, L.-S.; Huang, X.-P.; Zhao, G. *J. Org. Chem.* **2006**, *71*, 4625.

[271] Sun, B.; Xu, X. *Tetrahedron Lett.* **2006**, *47*, 299.

[272] Dorgan, P. D.; Durrani, J.; Cases-Thomas, M. J.; Hulme, A. N. *J. Org. Chem.* **2010**, *75*, 7475.

[273] Fan, C.-A.; Wang, B.-M.; Tu, Y.-Q.; Song, Z.-L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3877.

[274] Fan. C.-A.; Hu, X.-D.; Tu, Y.-Q.; Wang, B.-M.; Song, Z.-L. *Chem.—Eur. J.* **2003**, *9*, 4301.

[275] Starck, D. In *Encyclopedia of Chemical Processing and Design*, 1st ed.; McKetta, J. J., Ed.; Marcel Dekker: New York, **1984**; Vol. 20, p 63.

[276] Weissermel, K.; Arpe, H.-J. In *Industrial Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, 1997; p 187.

[277] Florent, J.-C.; Monneret, C.; Khuong-Huu, Q. *Tetrahedron Lett.* **1977**, *18*, 243.

[278] Florent, J.-C.; Monneret, C. *Carbohydr. Res.* **1980**, *81*, 225.

[279] Florent, J.-C.; Monneret, C. *Tetrahedron* **1981**, *37 Suppl.*, 9.

[280] Adinolfi, M.; Barone, G.; De Lorenzo, F.; Iadonisi, A. *Synlett* **1999**, 336.

[281] Michrowska, A.; List, B. *Nature Chem.* **2009**, *1*, 225.

[282] Hagemeyer, H. J., Jr.; Wright, H. N., Jr. U.S. Patent 3,091,632 (1963).

[283] Parsons, T. E. In *Kirk-Othmer: Encyclopedia of Chemical Technology*, 4th ed.; Kroschwitz, J. I., Howe-Grant, M., Eds.; John Wiley & Sons: New York, 1994; Vol. 14, p 726.

[284] Weissermel, K.; Arpe, H.-J. In *Industrial Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, 1997; p 213.

[285] Paterson, I.; Doughty, V. A.; McLeod, M. D.; Trieselmann, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1308.

[286] Paterson, I.; Steadman née Doughty, V. A.; McLeod, M. D.; Trieselmann, T. *Tetrahedron* **2011**, *67*, 10119.

[287] Smith, A. B., III; Freeze, B. S. *Tetrahedron* **2008**, *64*, 261.

[288] Paterson, I.; Florence, G. J. *Tetrahedron Lett.* **2000**, *41*, 6935.

[289] Paterson, I.; Florence, G. J.; Gerlach, K.; Scott, J. P. *Angew. Chem., Int. Ed.* **2000**, *39*, 377.

[290] Arefolov, A.; Panek, J. S. *Org. Lett.* **2002**, *4*, 2397.

[291] Brewitz, L.; Llaveria, J.; Yada, A.; Fürstner, A. *Chem.—Eur. J.* **2013**, *19*, 4532.

[292] Lafontaine, J. A.; Provencal, D. P.; Gardelli, C.; Leahy, J. W. *Tetrahedron Lett.* **1999**, *40*, 4145.

[293] Lafontaine, J. A.; Provencal, D. P.; Gardelli, C.; Leahy, J. W. *J. Org. Chem.* **2003**, *68*, 4215.

[294] Jiang, Y.; Hong, J.; Burke, S. D. *Org. Lett.* **2004**, *6*, 1445.

[295] Sinz, C. J.; Rychnovsky, S. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 3224.

[296] Sinz, C. J.; Rychnovsky, S. D. *Tetrahedron* **2002**, *58*, 6561.

[297] Paterson, I.; Davies, R. D. M.; Heimann, A. C.; Marquez, R.; Meyer, A. *Org. Lett.* **2003**, *5*, 4477.

[298] Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380.

[299] Hughes, D. L. *Org. React.* **1992**, *42*, 335.

[300] Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.

[301] Saksena, A. K.; Mangiaracina, P. *Tetrahedron Lett.* **1983**, *24*, 273.

[302] Fettes, A.; Carreira, E. M. *J. Org. Chem.* **2003**, *68*, 9274.

[303] Bode, S. E.; Wolberg, M.; Müller, M. *Synthesis* **2006**, 557.

[304] Anwar, S.; Davis, A. P. *Tetrahedron* **1988**, *44*, 3761.

[305] Keck, G. E.; Wager, C. A.; Sell, T.; Wager, T. T. *J. Org. Chem.* **1999**, *64*, 2172.

[306] Keck, G. E.; Wager, C. A. *Org. Lett.* **2000**, *2*, 2307.

[307] Chopade, P. R.; Davis, T. A.; Prasad, E.; Flowers, R. A., II *Org. Lett.* **2004**, *6*, 2685.

[308] Davis, T. A.; Chopade, P. R.; Hilmersson, G.; Flowers, R. A., II *Org. Lett.* **2005**, *7*, 119.

[309] Fradet, A.; Marechal, E. *Adv. Polym. Sci.* **1982**, *43*, 51.

[310] Shimasaki, K.; Aida, T.; Inoue, S. *Macromolecules* **1987**, *20*, 3076.

[311] Uyama, H.; Takeya, K.; Hoshi, N.; Kobayashi, S. *Macromolecules* **1995**, *28*, 7046.

[312] Miyazaki, E.; Yasumori, I. *Bull. Chem. Soc. Jap.* **1967**, *40*, 2012.

[313] Ulagappan, N.; Frei, H. *J. Phys. Chem. A* **2000**, *104*, 7834.

[314] Górski, A.; Kraśnicka, A. *J. Therm. Anal.* **1987**, *32*, 1243.

[315] Bernard, K. A.; Atwood, J. D. *Organometallics* **1989**, *8*, 795.

[316] Bernard, K. A.; Atwood, J. D. *Organometallics* **1988**, *7*, 235.

[317] Yeom, Y. H.; Ulagappan, N.; Frei, H. *J. Phys. Chem. A* **2002**, *106*, 3345.

[318] Idriss, H.; Seebauer, E. G. *J. Mol. Catal. A* **2000**, *152*, 201.

[319] Adkins, H.; Folkers, K; Kinsey, M. *J. Am. Chem. Soc.* **1931**, *53*, 2714.

[320] Tejel, C.; Ciriano, M. A.; Passarelli, V. *Chem.—Eur. J.* **2011**, *17*, 91.

[321] Bromberg, L.; Su, X.; Hatton, T. A. *Chem. Mater.* **2013**, *25* 1636.

[322] Terelak, K.; Trybula, S. *Przem. Chem.* **2004**, *83*, 331.

[323] Zakharkin, L. I.; Sorokina, L. P. *Zh. Obshch. Khim.* **1967**, *37*, 561.

[324] Cadoret, F.; Six, Y. *Tetrahedron Lett.* **2007**, *48*, 5491.

[325] Day, B. M.; Mansfield, N. E.; Coles, M. P.; Hitchcock, P. B. *Chem. Commun.* **2011**, *47*, 4995.

[326] Ishmuratov, G. Yu.; Yakovleva, M. P.; Mingaleeva, G. R.; Muslukhov, R. R.; Vyrypaev, E. M.; Galkin, E. G.; Ivanov, S. P.; Tolstikov, A. P. *Chem. Nat. Comp. (Engl. Transl.)* **2009**, *45*, 465; *Khim. Prir. Soedin.* **2009**, *45*, 395.

[327] Ishmuratov, G. Yu.; Mingaleeva, G. R.; Yakovleva, M. P.; Muslukhov, R. R.; Shakhanova, O. O.; Vyrypaev, E. M.; Tolstikov, A. P. *Chem. Nat. Comp. (Engl. Transl.)* **2011**, *47*, 1410; *Khim. Prir. Soedin.* **2011**, *47*, 1386.

[328] Simon, M.-O.; Darses, S. *Adv. Synth. Cat.* **2010**, *352*, 305.
[329] Ishmuratov, G. Yu.; Mingaleeva, G. R.; Yakovleva, M. P.; Muslukhov, R. R.; Vyrypaev, E. M.; Galkin, E. G.; Ivanov, S. P.; Tolstikov, A. P. *Chem. Nat. Comp. (Engl. Transl.)* **2009**, *45*, 470; *Khim. Prir. Soedin.* **2009**, *45*, 400.
[330] Bott, K. *Fette, Seifen, Anstrichm.* **1974**, *76*, 443.
[331] Endoh, C. *Recl. Trav. Chim. Pays-Bas* **1925**, *44*, 866.
[332] Van der Maeden, F. P. B.; Steinberg, H.; De Boer, Th. J. *Tetrahedron Lett.* **1967**, *18*, 4521.
[333] Van der Maeden, F. P. B.; Steinberg, H.; De Boer, Th. J. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 423.
[334] Li, L.; Sheng, H.; Xu, F.; Shen, Q. *Chin. J. Chem.* **2009**, *27*, 1127.
[335] Medved, T. M.; Christie, H. W. *J. Chem. Eng. Data* **1964**, *9*, 240.
[336] Waddell, D. C.; Mack, J. *Green Chem.* **2009**, *11*, 79.
[337] Kharasch, M. S.; Snyder, R. H. *J. Org. Chem.* **1949**, *14*, 819.
[338] Leeson, F.; Lundstedt, T.; Lejon, T. *J. Chemom.* **2006**, *20*, 386.
[339] Yao, J.; Liu, Q.; Wu, J.; Yuan, H.; Zhang, W.; Guo, Z.; Wei, X. *Shanxi Daxue Xuebao, Ziran Kexueban* **2013**, *36*, 92.
[340] Baidossi, W.; Rosenfeld, A.; Wassermann, B. C.; Schutte, S.; Schumann, H.; Blum, J. *Synthesis* **1996**, 1127.
[341] Li, J.; Shi, J.; Han, H.; Guo, Z.; Tong, H.; Wei, X.; Liu, D.; Lappert, M. F. *Organometallics* **2013**, *32*, 3721.
[342] Handlovits, C. E.; Louch, J. B. U.S. Patent *3*,387,020 (**1968**).
[343] Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.
[344] Jedliński, Z.; Kowalczuk, M.; Olaś, B. *Pol. J. Chem.* **1981**, *55*, 1329.
[345] Seki, T.; Hattori, H. *Catal. Surv. Asia* **2004**, *7*, 145.
[346] Osborne, J. D.; Willis, M. C. *Chem. Commun.* **2008**, 5025.
[347] Pawley, R. J.; Moxham, G. L.; Dallanegra, R.; Chaplin, A. B.; Brayshaw, S. K.; Weller, A. S.; Willis, M. C. *Organometallics* **2010**, *29*, 1717.
[348] Bergens, S. H.; Fairlie, D. P.; Bosnich, B. *Organometallics* **1990**, *9*, 566.
[349] Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S. *Tetrahedron* **1981**, *37*, 4313.
[350] Murphy, S. K.; Dong, V. M. *J. Am. Chem. Soc.* **2013**, *135*, 5553.
[351] Shishido, T.; Kawaguchi, T.; Iwashige, T.; Teramura, K.; Hitomi, Y.; Tanaka, T. *Catal. Lett.* **2010**, *140*, 121.
[352] Yajima, A.; Toda, K.; Okada, K.; Yamane, H.; Yamamoto, M.; Hasegawa, M.; Katsuta, R.; Nukada, T. *Tetrahedron Lett.* **2011**, *52*, 3212.
[353] Bhowmick, S.; Bhowmick, K. C. *Mendeleev Commun.* **2013**, *23*, 96.
[354] Paterson, I.; Fink, S. J.; Lee, L. Y. W.; Atkinson, S. J.; Blakey, S. B. *Org. Lett.* **2013**, *15*, 3118.
[355] Yang, Z.; Xie, X.; Jing, P.; Zhao, G.; Zheng, J.; Zhao, C.; She, X. *Org. Biomol. Chem.* **2011**, *9*, 984.
[356] Tello-Aburto, R.; Newar, T. D.; Maio, W. A. *J. Org. Chem.* **2012**, *77*, 6271.
[357] Reddy, G. P.; Murthy, A. S.; Reddy, J. S.; Das, S.; Roisnel, T.; Yadav, J. S.; Chandrasekhar, S.; Grée, R. *Tetrahedron Lett.* **2014**, *55*, 365.
[358] Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G. *J. Am. Chem. Soc.* **1996**, *118*, 4322.
[359] Paterson, I.; Paquet, T.; Dalby, S. M. *Org. Lett.* **2011**, *13*, 4398.
[360] Walleser, P.; Brückner, R. *Eur. J. Org. Chem.* **2010**, 4802.
[361] Paterson, I.; Blakey, S. B.; Cowden, C. J. *Tetrahedron Lett.* **2002**, *43*, 6005.
[362] Evans, D. A.; Allison, B. D.; Yang, M. G.; Masse, C. E. *J. Am. Chem. Soc.* **2001**, *123*, 10840.
[363] Pronin, S. V.; Martinez, A.; Kuznedelov, K.; Severinov, K.; Shuman, H. A.; Kozmin, S. A. *J. Am. Chem. Soc.* **2011**, *133*, 12172.
[364] Yang, Z.; Zhang, B.; Zhao, G.; Yang, J.; Xie, X.; She, X. *Org. Lett.* **2011**, *13*, 5916.
[365] Paterson, I.; Gibson, L. J.; Kan, S. B. *J. Org. Lett.* **2010**, *12*, 5530.
[366] Gregg, C.; Gunawan, C.; Ng, A. W. Y.; Wimala, S.; Wickremasinghe, S.; Rizzacasa, M. A. *Org. Lett.* **2013**, *15*, 516.
[367] Paterson, I.; Haslett, G. W. *Org. Lett.* **2013**, *15*, 1338.
[368] Paterson, I.; Donghi, M.; Gerlach, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3315.
[369] La Cruz, T. E.; Rychnovsky, S. D. *J. Org. Chem.* **2007**, *72*, 2602.
[370] Paterson, I.; Man, J. *Tetrahedron Lett.* **1997**, *38*, 695.
[371] Paterson, I.; Gibson, K. R.; Oballa, R. M. *Tetrahedron Lett.* **1996**, *37*, 8585.
[372] Morihata, K.; Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1995**, *36*, 5555.
[373] Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagornyy, P. A.; Robarge, L. A.; Wardrop, D. J.; White, J. D. *J. Org. Chem.* **2005**, *70*, 5449.

[374] Paterson, I.; Coster, M. J.; Chen, D. Y.-K.; Gibson, K. R.; Wallace, D. *J. Org. Biomol. Chem.* **2005**, *3*, 2410.
[375] Paterson, I.; Coster, M. *J. Tetrahedron Lett.* **2002**, *43*, 3285.
[376] Youngsaye, W.; Lowe, J. T.; Pohlki, F.; Ralifo, P.; Panek, J. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 9211.
[377] Custar, D. W.; Zabawa, T. P.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 804.
[378] Custar, D. W.; Zabawa, T. P.; Hines, J.; Crews, C. M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 12406.
[379] Paterson, I.; Temal-Laïb, T. *Org. Lett.* **2002**, *4*, 2473.
[380] Fang, B.; Xie, X.; Zhao, C.; Jing, P.; Li, H.; Wang, Z.; Gu, J.; She, X. *J. Org. Chem.* **2013**, *78*, 6338.
[381] Cohen, F.; Overman, L. E. *J. Am. Chem. Soc.* **2001**, *123*, 10782.
[382] Cohen, F.; Overman, L. E. *J. Am. Chem. Soc.* **2006**, *128*, 2604.
[383] Paterson, I.; Cowden, C. J.; Woodrow, W. D. *Tetrahedron Lett.* **1998**, *39*, 6037.
[384] Stenkamp, D.; Hoffmann, R. W.; Göttlich, R. *Eur. J. Org. Chem.* **1999**, 2929.
[385] Gardinier, K. M.; Leahy, J. W. *J. Org. Chem.* **1997**, *62*, 7098.
[386] Paterson, I.; Arnott, E. A. *Tetrahedron Lett.* **1998**, *39*, 7185.
[387] Paterson, I.; Luckhurst, C. A. *Tetrahedron Lett.* **2003**, *44*, 3749.
[388] Paterson, I.; Paquet, T. *Org. Lett.* **2010**, *12*, 2158.
[389] Cowper, N.; Azzi, S.; Dupont-Gadet, K.; Burch, J. D. *Tetrahedron Lett.* **2012**, *53*, 1837.
[390] Evans, D. A.; Côté, B.; Coleman, P. J.; Connell, B. T. *J. Am. Chem. Soc.* **2003**, *125*, 10893.
[391] Cohen, F.; Overman, L. E.; Ly Sakata, S. K. *Org. Lett.* **1999**, *1*, 2169.
[392] Paterson, I.; Findlay, A. D.; Florence, G. *J. Tetrahedron* **2007**, *63*, 5806.
[393] Paterson, I.; Findlay, A. D.; Florence, G. *J. Org. Lett.* **2006**, *8*, 2131.
[394] Paterson, I.; Di Francesco, M. E.; Kühn, T. *Org. Lett.* **2003**, *5*, 599.
[395] Tu, W.; Floreancig, P. E. *Angew. Chem., Int. Ed.* **2009**, *48*, 4567.
[396] Cui, Y.; Tu, W.; Floreancig, P. E. *Tetrahedron*, **2010**, *66*, 4867.
[397] Arlt, A.; Benson, S.; Schulthoff, S.; Gabor, B.; Fürstner, A. *Chem.—Eur. J.* **2013**, *19*, 3596.
[398] Kozmin, S. A. *Org. Lett.* **2001**, *3*, 755.
[399] Wang, Y.; Janjic, J.; Kozmin, S. A. *Pure Appl. Chem.* **2005**, *77*, 1161.
[400] Kim, Y. J.; Lee, D. *Org. Lett.* **2006**, *8*, 5219.
[401] Kim, Y. J.; Lee, D. *Org. Lett.* **2007**, *9*, 3859.
[402] O'Neil, G. W.; Ceccon, J:; Benson, S.; Collin, M.-P.; Fasching, B.; Fürstner, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9940.
[403] Raghavan, S.; Samanta, P.K. *Org. Lett.* **2012**, *14*, 2346.
[404] Enders, D.; Dhulut, S.; Steinbusch, D.; Herrbach, A. *Chem.—Eur. J.* **2007**, *13*, 3942.
[405] Paterson, I.; Chen, D. Y.-K.; Aceña, J. L.; Franklin, A. S. *Org. Lett.* **2000**, *2*, 1513.
[406] Paterson, I.; Franklin, A. S. *Tetrahedron Lett.* **1994**, *35*, 6925.
[407] Shotwell, J. B.; Roush, W. R. *Org. Lett.* **2004**, *6*, 3865.
[408] Nicolaou, K. C.; Patron, A. P.; Ajito, K.; Richter, P. K.; Khatuya, H.; Bertinato, P.; Miller, R. A.; Tomaszewski, M. J. *Chem.—Eur. J.* **1996**, *2*, 847.
[409] Matsunaga, S.; Liu, P.; Celatka, C. A.; Panek, J. S.; Fusetani, N. *J. Am. Chem. Soc.* **1999**, *121*, 5605.
[410] Lautens, M.; Colucci, J. T.; Hiebert, S.; Smith, N. D.; Bouchain, G. *Org. Lett.* **2002**, *4*, 1879.
[411] Lanners, S.; Norouzi-Arasi, H.; Salom-Roig, X. J.; Hanquet, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 7086.
[412] Tang, W.; Prusov, E. V. *Angew. Chem., Int. Ed.* **2012**, *51*, 3401.
[413] Paterson, I.; Schlapbach, A. *Synlett* **1995**, 498.
[414] Winter, P.; Hiller, W.; Christmann, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3396.
[415] Glaus, F.; Altmann, K.-H. *Angew. Chem., Int. Ed.* **2012**, *51*, 3405.
[416] Soltani, O.; De Brabander, J. K. *Org. Lett.* **2005**, *7*, 2791.
[417] Paterson, I.; Britton, R.; Delgado, O.; Gardner, N. M.; Meyer, A.; Naylor, G. J.; Poullennec, K. G. *Tetrahedron* **2010**, *66*, 6534.
[418] Paterson, I.; Woodrow, M. D.; Cowden, C. *J. Tetrahedron Lett.* **1998**, *39*, 6041.
[419] Huber, P.; Enev, V.; Linden, A.; Bienz, S. *Tetrahedron* **1995**, *51*, 3749.
[420] Sun, X.-W.; Xu, M.-H.; Lin, G.-Q. *Tetrahedron Lett.* **2009**, *50*, 3381.
[421] Smith, A. B., III; Lee, D.; Adams, C. M.; Kozlowski, M. C. *Org. Lett.* **2002**, *4*, 4539.
[422] Moreno, R. M.; Catasús, M.; Lopéz, C.; Moyano, A. *Eur. J. Org. Chem.* **2008**, 2388.
[423] Eignerová, L.; Kasal, A. *Collect. Czech. Chem. Commun.* **1976**, *41*, 1056.
[424] Hayashi, Y.; Yamamoto, T.; Yamamoto, A.; Komiya, S.; Kushi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 385.
[425] Willis, M. C.; Woodward, R. L. *J. Am. Chem. Soc.* **2005**, *127*, 18012.
[426] Russell, A. E.; Fuller, N. O.; Taylor, S. J.; Aurriset, P.; Morken, J. P. *Org. Lett.* **2004**, *6*, 2309.