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Chan–Lam coupling reaction
Dess–Martin oxidation Minisci reaction
Mitsunobu reaction
Negishi cross-coupling reaction Nicholas reaction
Nozaki–Hiyama–Kishi reaction
Overman rearrangement Petasis reaction

Jie Jack Li

Name Reactions

A Collection of Detailed Mechanisms and Synthetic Applications

Sixth Edition

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Dedicated to Prof. David R. Williams

Kurt Alder
1902–1958
Nobel Prize, 1950



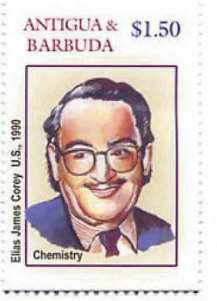
Eduard Buchner
1860–1917
Nobel Prize, 1907



Adolf von Baeyer
1835–1917
Nobel Prize, 1905



Elias James Corey
1928–
Nobel Prize, 1990



Derek H. R. Barton
1918–1999
Nobel Prize, 1969



Otto Paul Herman Diels
1876–1954
Nobel Prize, 1950



Emil Fisher
1852–1919
Nobel Prize, 1902



Victor Grignard
1871–1935
Nobel Prize, 1912



Hermann Staudinger
1881–1965
Nobel Prize, 1953



Robert Robinson
1886–1975
Nobel Prize, 1947



Georg Wittig
1897–1987
Nobel Prize, 1979



Otto Wallach
1847–1931
Nobel Prize, 1910



Karl Ziegler
1898–1973
Nobel Prize, 1963



Preface

Five years have elapsed since the fifth edition was published. Much has happened since then. The author has migrated from academia back to industry. I have taken out some name reactions from the fifth edition because the book was physically getting too heavy and unwieldy. This change allows more space to expand and update the more popular name reactions. All references have been updated to 2020 when available.

As in previous editions, each reaction is delineated by detailed, step-by-step, electron-pushing mechanism, supplemented with the original and the latest references, especially review articles. Now, with addition of many synthetic applications, it is not only an indispensable resource for senior undergraduate and graduate students to learn mechanisms and synthetic utility of name reactions and to prepare for their exams, but also a good reference book for all organic chemists in both industry and academia.

As always, I welcome your critique. Please send your comments to this email address: lijiejackli@hotmail.com.



March 1, 2020
San Mateo, California

Jie Jack Li

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Abbreviations and Acronyms

	Polymer support
1,10-phen	1,10-Phenanthroline
3CC	Three-component condensation
3CR	Three-component reaction
4CC	Four-component condensation
9-BBN	9-Borabicyclo[3.3.1]nonane
A	Adenosine
Ac	Acetyl
acac	Acetylacetonate
ACC	Acetyl-CoA carboxylase
ADDP	1,1′-(Azodicarbonyl)dipiperidine
AIBN	2,2′-Azobisisobutyronitrile
Alpine-borane®	*B*-Isopinocampheyl-9-borabicyclo[3.3.1]-nonane
AOM	*p*-Anisyloxymethyl = *p*-$MeOC_6H_4OCH_2$-
Ar	Aryl
ARA	Asymmetric reductive amination
ATH	Asymmetric transfer hydrogenation
ATPH	Tris(2,6-diphenyl)phenoxyaluminane
B**:**	Generic base
BBEDA	Bis-benzylidene ethylenediamine
bmim	1-Butyl-3-methylimidazolium
BINAP	2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl
BINOL	1,1′-Bi-2-naphthaol
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
BQ	Benzoquinone
BPR	Back pressure regulator
BT	Benzothiazole
Bz	Benzoyl

CAN	Cerium ammonium nitrate
CBS	Corey–Bakshi–Shibata reaction
Cbz	Benzyloxycarbonyl
CCB	Calcium channel blockers
CD4	Cluster of differentiation 4
CDK	Cyclin-dependent kinase
CFC	Continuous flow centrifugation
cod	1,5-Cyclooctadiene
COPC	Carbonyl–olefin [2 + 2] photocycloaddition
Cp	Cyclopentyl
CPME	Cyclopentyl methyl ether
CSA	Camphorsulfonic acid
CuTC	Copper thiophene-2-carboxylate
Cy	Cyclohexyl
DABCO	1,4-Diazabicyclo[2.2.2]octane
dba	Dibenzylideneacetone
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
o-DCB	*ortho*-Dichlorobenzene
DCC	1,3-Dicyclohexylcarbodiimide
DCE	Dichloroethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
de	Diastereoselctive excess
DEAD	Diethyl azodicarboxylate
DEL	DNA-encoded library
DET	Diethyl tartrate
Δ	Reaction heated under reflux
$(DHQ)_2$-PHAL	1,4-Bis(9-*O*-dihydroquinine)-phthalazine
$(DHQD)_2$-PHAL	1,4-Bis(9-*O*-dihydroquinidine)-phthalazine
DIAD	Diisopropyl azodidicarboxylate
DIBAL	Diisobutylaluminum hydride
DIC	*N,N′*-Diisopropylcarbodimide
DIPT	Diisopropyl tartrate
DIPEA	Diisopropylethylamine
DKR	Dynamic kinetic resolution
DLP	Dilauroyl peroxide
DMA	*N,N*-dimethylacetamide
DMAP	4-*N,N*-Dimethylaminopyridine
DME	1,2-Dimethoxyethane
DMF	*N,N*-Dimethylformamide
DMFDMA	*N,N*-Dimethylformamide dimethyl acetal
DMP	Dess–Martin periodinane
DMPU	*N,N′*-Dimethylpropyleneurea
DMS	Dimethylsulfide
DMSO	Dimethylsulfoxide
DMSY	Dimethylsulfoxonium methylide
DMT	Dimethoxytrityl

DPP-4	Dipeptidyl peptidase IV
DPPA	Diphenylphosphoryl azide
dppb	1,4-Bis(diphenylphosphino)butane
dppe	1,2-Bis(diphenylphosphino)ethane
dppf	1,1′-Bis(diphenylphosphino)ferrocene
dppp	1,3-Bis(diphenylphosphino)propane
dr	Diastereoselective ratio
DTBAD	Di-*tert*-butylazodicarbonate
DTBMP	2,6-Di-*tert*-butyl-4-methylpyridine
DTBP	Di-*tert*-butyl peroxide
E1	Unimolecular elimination
E1cB	2-Step, base-induced β-elimination *via* carbanion
E2	Bimolecular elimination
EAN	Ethylammonium nitrate
EDCI	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
EDDA	Ethylenediamine diacetate
EDG	Electron-donating group
EDTA	Ethylenediaminetetraacetic acid
ee	Enantiomeric excess
Ei	Two groups leave at about the same time and bond to each other as they are doing so.
EMC	Meerwein–Eschenmoser–Claisen
ERK	Extracellular signal-regulated kinase
Eq	Equivalent
Equiv	Equivalent
Et	Ethyl
EtOAc	Ethyl acetate
EWG	Electron-withdrawing group
FEP	Fluorinated ethylene propene
Fmoc	Fluorenylmethyloxycarbonyl protecting group
fod	1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate = Siever′s reagent
FVP	Flash vacuum pyrolysis
HCV	Hepatitis virus C
HFIP	Hexafluoroisopropanol
HKR	Hydrolytic kinetic resolution
HMDS	Hexamethyldisilazane
HMPA	Hexamethylphosphoramide
HMTA	Hexamethylenetetramine
HMTTA	1,1,4,7,10,10-Hexamethyltriethylenetetramine
HOMO	Highest occupied molecular orbital
IBDA	Iodosobenzene diacetate, also known as PIDA
IBX	*o*-Iodoxybenzoic acid
IDH1	Isocitrate dehydrogenase 1
IEDDA	Inverse-electron-demand Diels–Alder
Imd	Imidazole

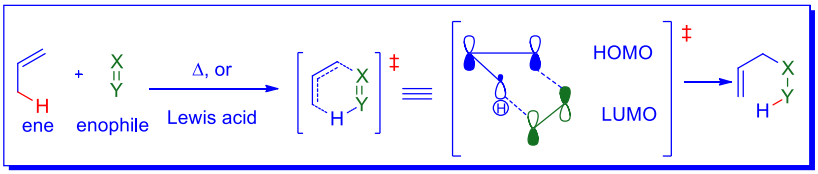
IMDA	Intramolecular Diels–Alder reaction
IPA	Isopropyl alcohol (Indian pale ale)
IPB	Insoluble polymer bound
IPr	Diidopropyl-phenylimidazolium derivative
JAK	Janus kinase
KHMDS	Potassium hexamethyldisilazide
LAH	Lithium aluminum hydride
LDA	Lithium diisopropylamide
LED	Light-emitting diode
LHMDS	Lithium hexamethyldisilazide
LUMO	Lowest unoccupied molecular orbital
LTMP	Lithium 2,2,6,6-tetramethylpiperidide
M	Metal
MBI	Mechanism-based inhibitors
m-CPBA	*m*-Chloroperoxybenzoic acid
MCRs	Multicomponent reactions
Mes	Mesityl
Mincle	Macrophage-inducible C-type lectin
MLCT	Metal to ligand charge transfer
MOM ether	Methoxymethyl ether
MPL	Medium pressure lamp
MPM	Methyl phenylmethyl
MPS	Morpholine-polysulfide
Ms	Methanesulfonyl (mesyl)
MS	Molecular sieves
MWI	Microwave irradiation
MTBE	Methyl tertiary butyl ether
MVK	Methyl vinyl ketone
NaDA	Sodium diisopropylamide
NBE	Norbornene
NBS	*N*-Bromosuccinimide
NCL	Native chemical ligation
NCS	*N*-Chlorosuccinimide
nbd	2,5-Norbornadiene
NBE	Norbornene
Nf	Nonafluorobutanesulfonyl
NFSI	*N*-Fluorobenzenesulfonimide
NHC	*N*-Heterocyclic carbene
NIS	*N*-Iodosuccinimide
NMM	*N*-Methyl morpholine
NMO	*N*-Methylmorpholine N-oxide (NMMO)
NMP	1-Methyl-2-pyrrolidinone
Nos	Nosylate = 4-nitrobenzenesulfonyl = Ns
NRI	Noradrenaline reuptake inhibitor
N-PSP	*N*-Phenylselenophthalimide
N-PSS	*N*-Phenylselenosuccinimide

Nu	Nucleophile
Nuc	Nucleophile
Ns	Nosylate
PAR-1	Protease activated receptor-1
PARP	Poly(ADP-ribosyl) polymerase
PCC	Pyridinium chlorochromate
PDC	Pyridinium dichromate
PDI	Phosphinyl dipeptide isostere
PE	Premature ejaculation
PEG	Polyethylene glycol
PEPPSI	Pyridine-enhanced pre-catalyst preparation, stabilization, and initiation
phen	1,10-Phenanthroline
PIDA	Phenyliodine diacetate (same as IBDA)
Pin	Pinacol
Piv	Pivaloyl
PNB	*p*-Nitrobenzyl
PMB	*para*-Methoxybenzyl
PPA	Polyphosphoric acid
PPSE	Trimethylsilyl polyphosphate
PPTS	Pyridinium *p*-toluenesulfonate
PT	Phenyltetrazolyl
PTADS	Tetrakis[(*R*)-(+)-N-(*p*-dodecylphenylsulfonyl)prolinato]
PTSA	*p*-Toluenesulfonic acid
$PyPh_2P$	Diphenyl 2-pyridylphosphine
Pyr	Pyridine
rac	Racemic
Red-Al	Sodium bis(methoxy-ethoxy)aluminum hydride (SMEAH)
rr	*r*egioisomeric *r*atio
Salen	*N,N*′-Disalicylidene-ethylenediamine
SET	Single-electron transfer
SIBX	Stabilized IBX
SM	Starting material
SMC	Sodium methyl carbonate
SMEAH	Sodium bis(methoxy-ethoxy)aluminum hydride: trade name Red-Al
S_N1	Unimolecular nucleophilic substitution
S_N2	Bimolecular nucleophilic substitution
S_NAr	Nucleophilic substitution on an aromatic ring
SSRI	Selective serotonin reuptake inhibitor
T3P	Propylphosphonic anhydride
TBABB	Tetra-*n*-butylammonium bibenzoate
TBAF	Tetra-*n*-butylammonium fluoride
TBAI	Tetra-*n*-butylammonium iodide
TBAO	1,3,3-Trimethyl-6-azabicyclo[3.2.1]octane

TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
TBHP	*tert*-Butyl hydroperoxide
TBS	*tert*-Butyldimethylsilyl
t-Bu	*tert*-Butyl
TDI	Thiophosphinyl dipeptide isostere
TDS	Thexyldimethylsilyl
TEA	Triethylamine
TEMPO	2,2,6,6-Tetramethylpiperidinyloxy
TEOC	Trimethysilylethoxycarbonyl
TES	Triethylsilyl
Tf	Trifluoromethanesulfonyl (triflate)
TFA	Trifluoroacetic acid
TFAA	Trifluoroacetic anhydride
TFE	Trifluoroethanol
TFEA	Trifluoroethyl trifluoroacetate
THF	Tetrahydrofuran
TFP	Tri-2-furylphosphine
TFPAA	Trifluoroperacetic acid
TIPS	Triisopropylsilyl
TMEDA	*N,N,N′,N′*-Tetramethylethylenediamine
TMG	1,1,3,3-Tetramethylguanidine
TMOF	Trimethyl orthoformate
TMP	Tetramethylpiperidine
TMS	Trimethylsilyl
TMSCl	Trimethylsilyl chloride
TMSCN	Trimethylsilyl cyanide
TMSI	Trimethylsilyl iodide
TMSOTf	Trimethylsilyl triflate
TMU	Tetramethylurea
Tol	Toluene or tolyl
Tol-BINAP	2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl
TosMIC	(*p*-Tolylsulfonyl)methyl isocyanide
TPPO	Triphenylphosphine oxide
TrxR	Thioredoxin reductase
Ts	Tosyl
TsO	Tosylate
TTBP	2,4,6-Tri-*tert*-butylpyrimidine
UHP	Urea-hydrogen peroxide
VAPOL	2,2′-Diphenyl-(4-biphen-anthrol)
VMR	Vinylogous Mannich reaction
WERSA	Water extract of rice straw ash

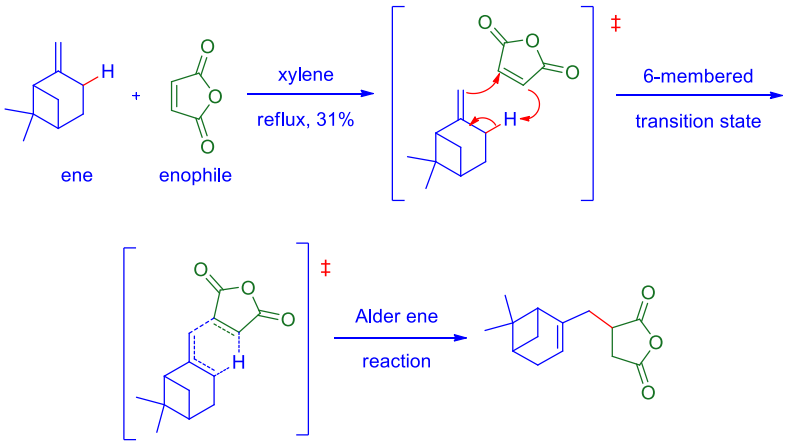
Alder Ene Reaction

The Alder ene reaction, also known as the hydro-allyl addition, is addition of an enophile to an alkene (ene) *via* allylic transposition. The four-electron system including an alkene π-bond and an allylic C–H σ-bond can participate in a pericyclic reaction in which the double bond shifts and new C–H and C–C σ-bonds are formed.

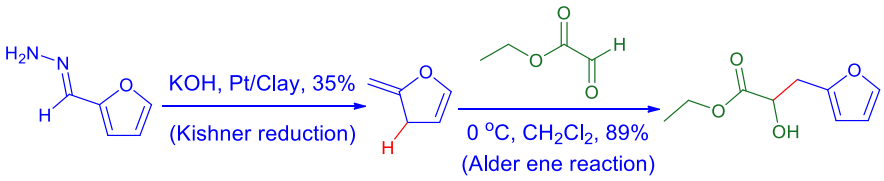


X=Y: C=C, C≡C, C=O, C=N, N=N, N=O, S=O, *etc*.

Example 1[5]

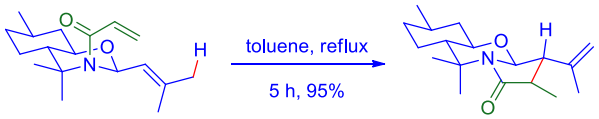


Example 2, Here the "ene" is a carbonyl of the aldehyde[7]

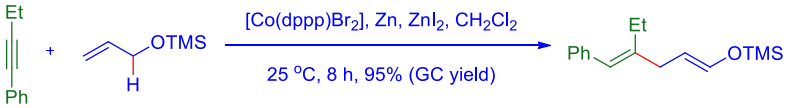


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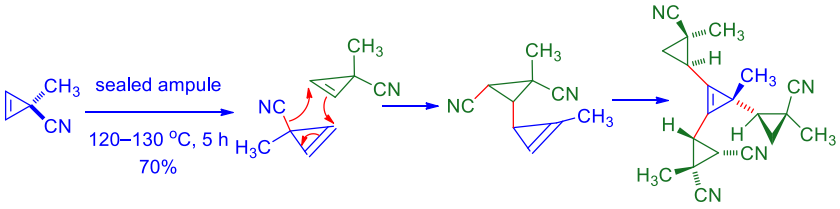
Example 3, Intramolecular Alder ene reaction[8]



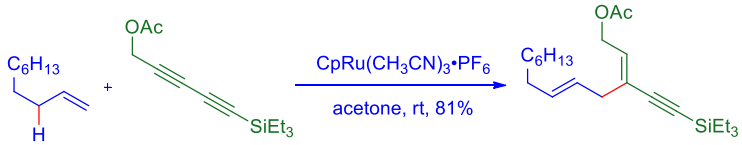
Example 4, Cobalt-catalyzed Alder ene reaction[9]



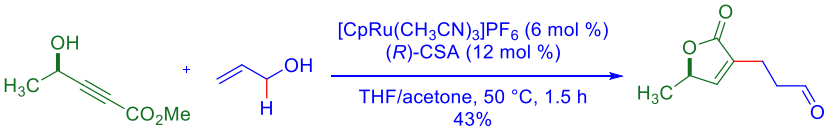
Example 5, Nitrile-migrating Alder ene reaction[10]



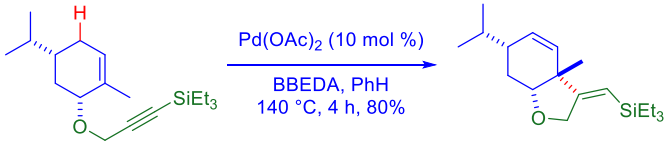
Example 6[11]



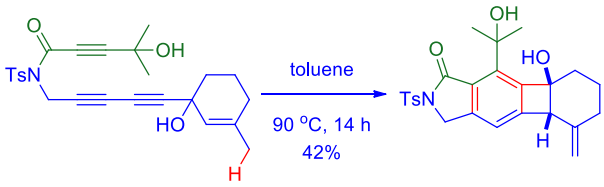
Example 7[13]



Example 8, Pd-catalyzed intramolecular Alder ene (BBEDA = bis-benzylidene ethylenediamine)[14]



Example 9, Alder ene driven by high steric strain and bond angle distortion[15]

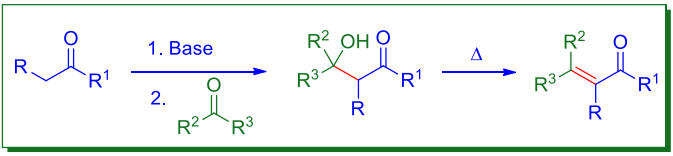


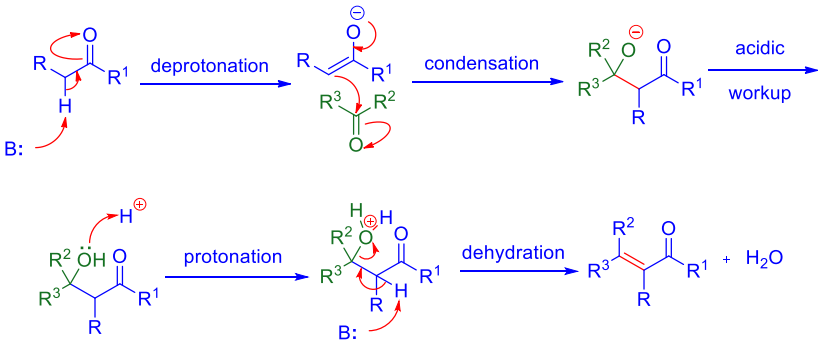
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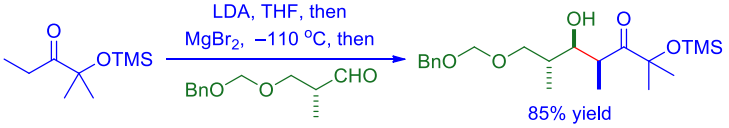
Aldol Condensation

The aldol condensation is the coupling of an enolate ion with a carbonyl compound to form a β-hydroxycarbonyl, and sometimes, followed by dehydration to give a conjugated enone. A simple case is addition of an enolate to an **ald**ehyde to afford an alcoh**ol**, thus the name **aldol**.

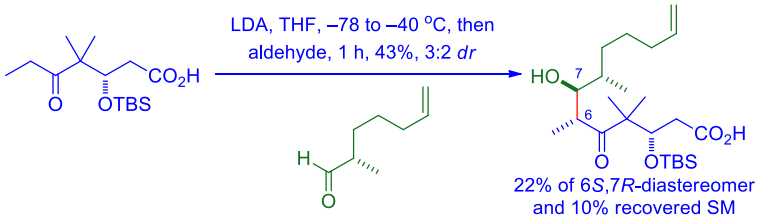




Example 1[3]

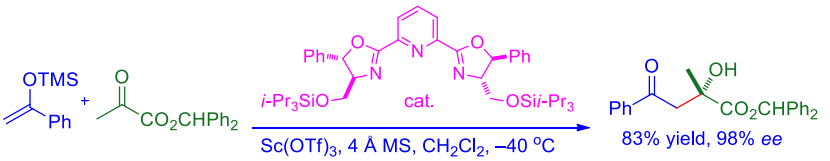


Example 2[8]

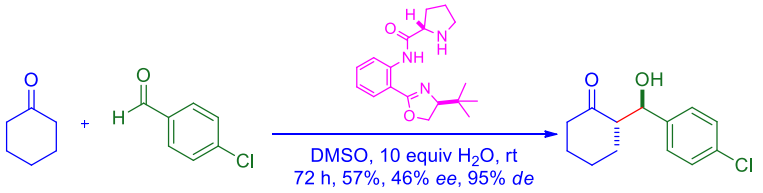


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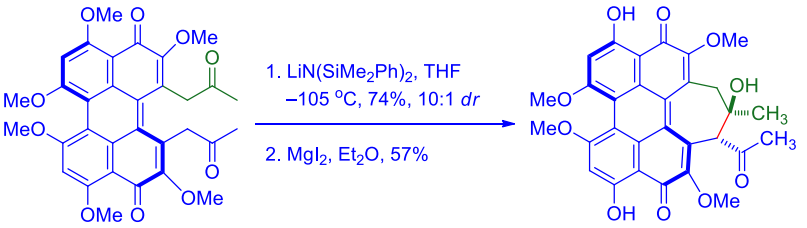
Example 3, Enantioselective Mukaiyama aldol reaction[10]



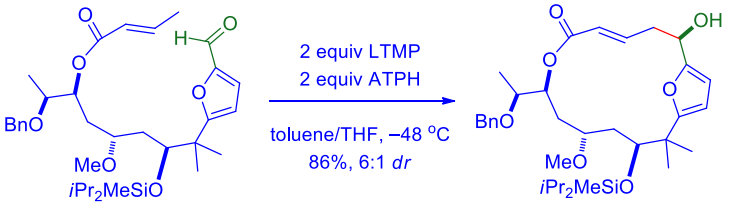
Example 4, Intermolecular aldol reaction using organocatalyst[12]



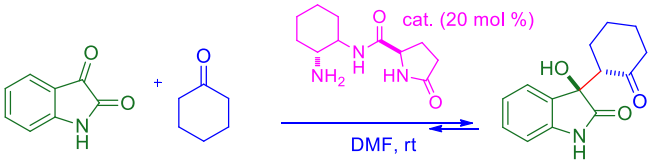
Example 5, Intramolecular aldol reaction[13]



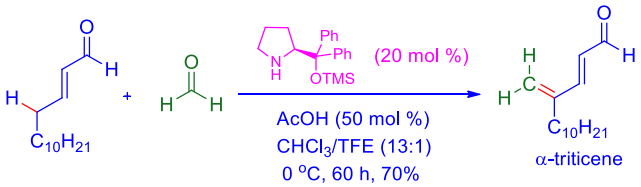
Example 6, Intramolecular vinylogous aldol reaction [ATPH = tris(2,6-diphenyl)phenoxyaluminane][14]



Example 7, A rare stereospecific retroaldol reaction[15]



Example 8, A rare intermolecular vinylogous aldol reaction, TFE = trifluoroethanol[16]

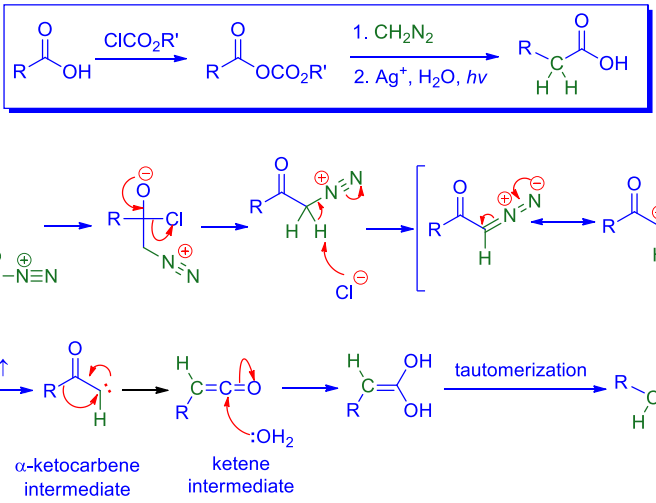


References

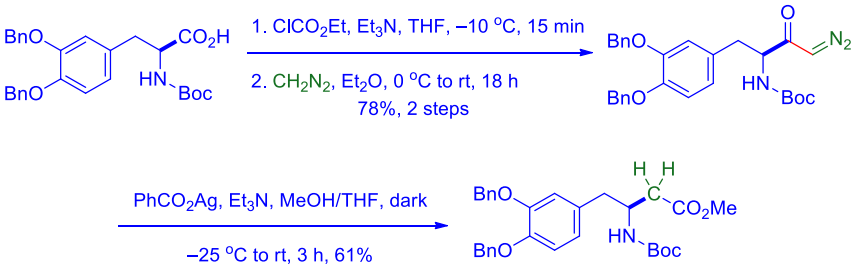
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Arndt–Eistert Homologation

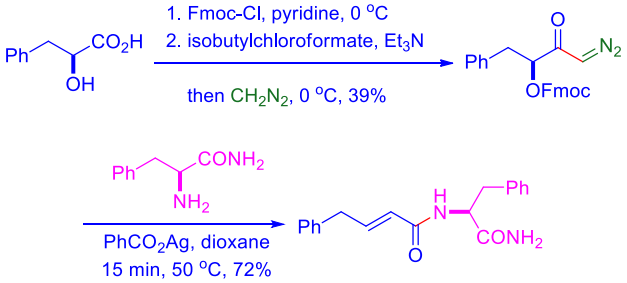
One-carbon homologation of carboxylic acids using diazomethane.



Example 1, Homologation of an amino acid[7]

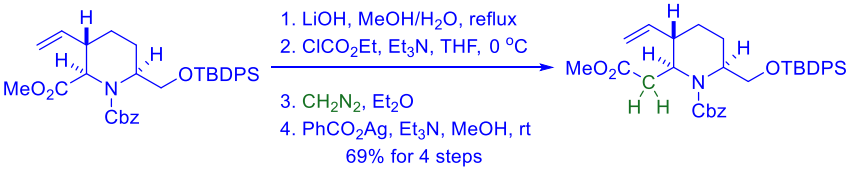


Example 2, An interesting variation[9]

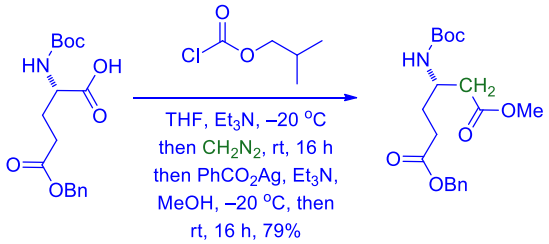


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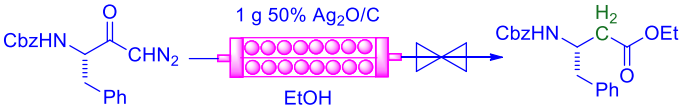
Example 3[10]



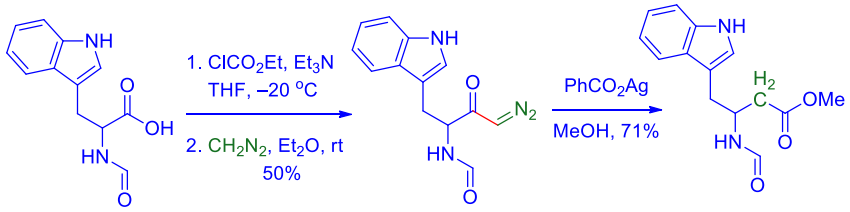
Example 4[10]



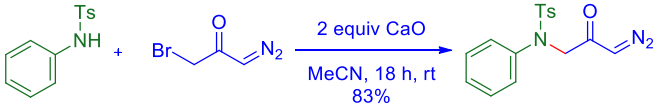
Example 5, Continuous flow silver-catalyzed Arndt–Eistert reaction/Wolff rearrangement[12]



Example 6, Arndt–Eistert reaction/Wolff rearrangement sequence[13]



Example 7, α-Arylamino diazoketones: reaction in the presence of diazoketones[14]

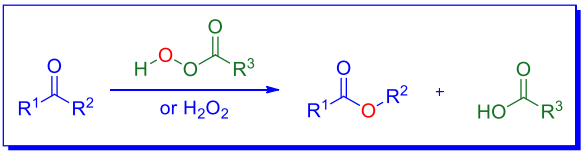


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Baeyer–Villiger Oxidation

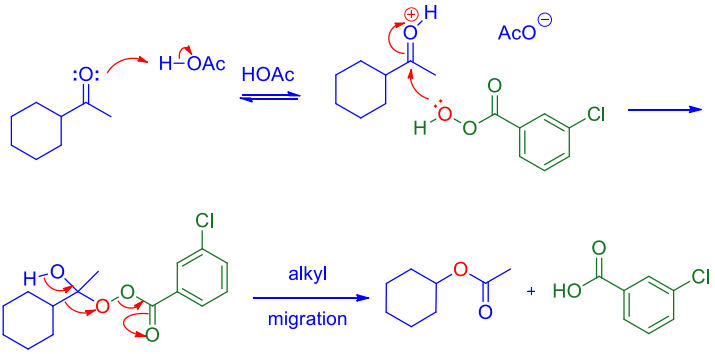
General scheme:



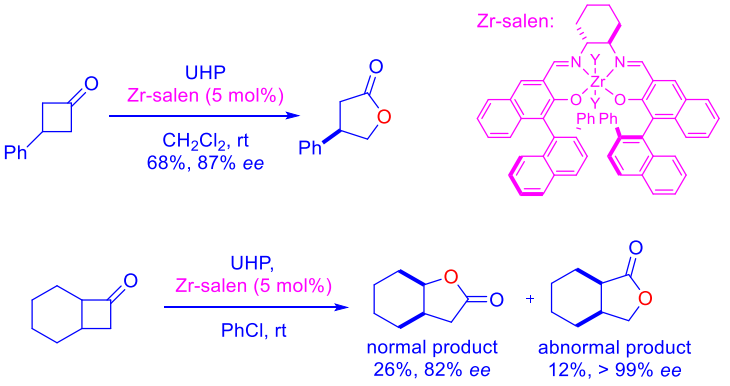
The most electron-rich alkyl group (more substituted carbon) migrates first.

The general migration order: tertiary alkyl > cyclohexyl > secondary alkyl > benzyl > phenyl > primary alkyl > methyl >> H.

For substituted aryls: *p*-MeO-Ar > *p*-Me-Ar > *p*-Cl-Ar > *p*-Br-Ar > *p*-O_2N-Ar

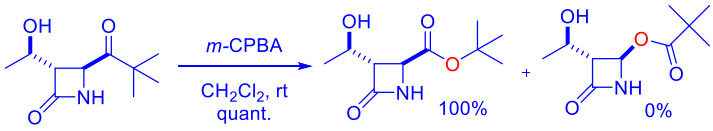


Example 1, UHP = urea hydrogen peroxide[4]

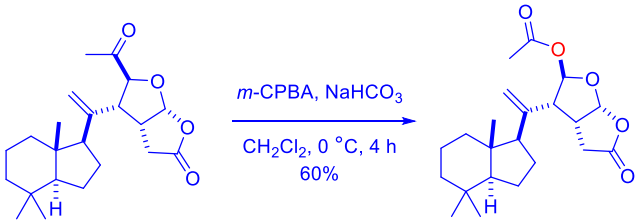


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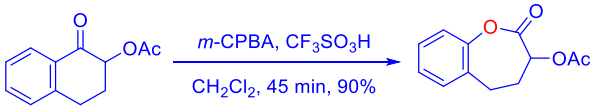
Example 2, Chemoselective over lactam[5]



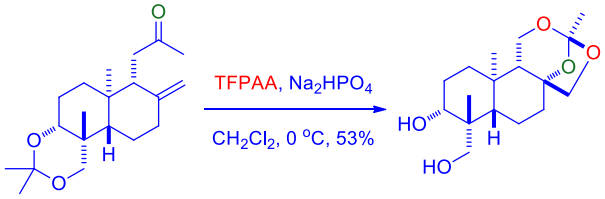
Example 3, Chemoselective over lactone[6]



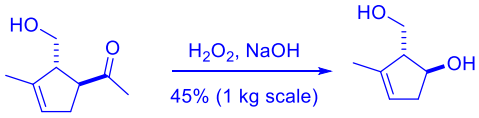
Example 4, Chemoselective over ester[8]



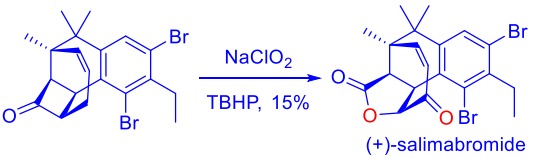
Example 5, A trifluoroperacetic acid (TFPAA)-mediated tandem reaction[11]



Example 6, A process route toward entecavir[12]



Example 7, One-pot Baeyer–Villiger oxidation/allylic oxidation[13]

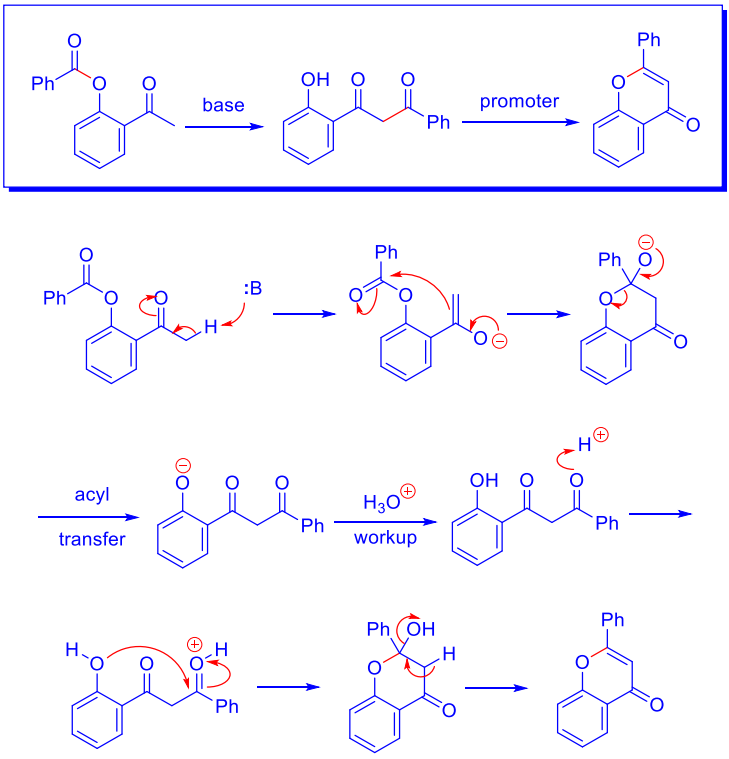


References

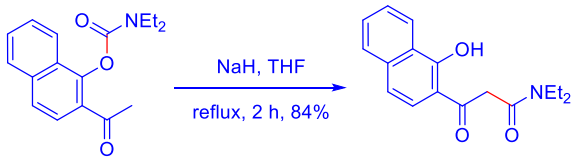
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Baker–Venkataraman Rearrangement

Base-catalyzed acyl transfer reaction that converts α-acyloxyketones to β-diketones, which are substrates for making flavones (flavonoids).

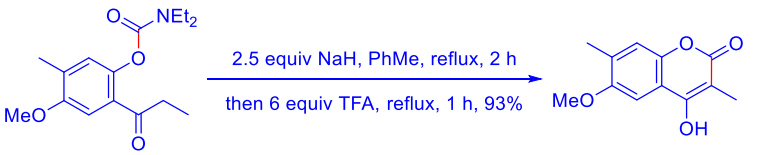


Example 1, Carbamoyl Baker–Venkataraman rearrangement[5]

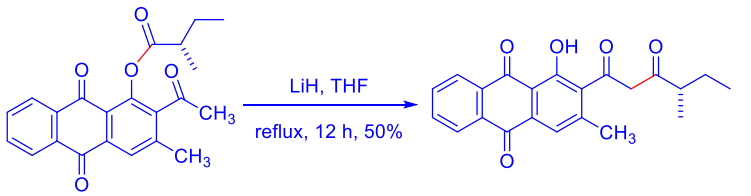


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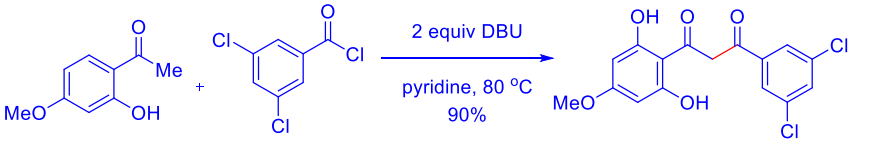
Example 2, Carbamoyl Baker–Venkataraman rearrangement, followed by cyclization[6]



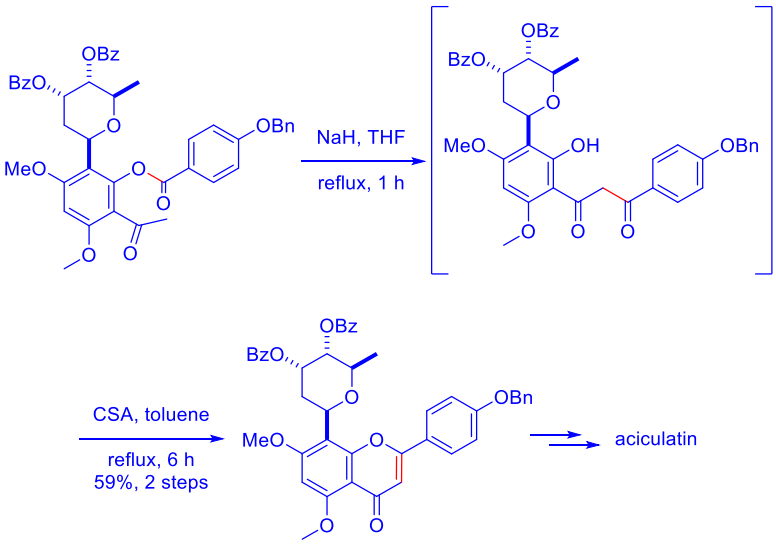
Example 3, Baker–Venkataraman rearrangement[9]



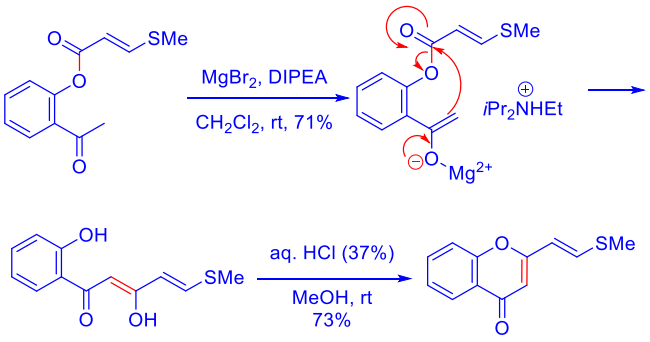
Example 4, Baker–Venkataraman rearrangement[10]



Example 5, In the presence of the *C*-aryl glycoside[11]



Example 6, Soft-enolization Baker–Venkataraman rearrangement[12]

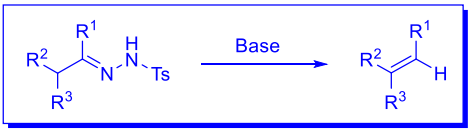


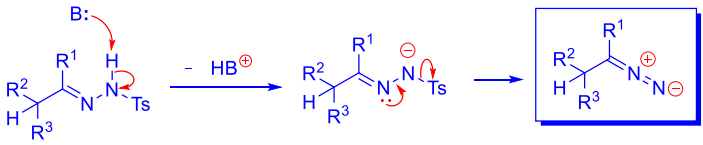
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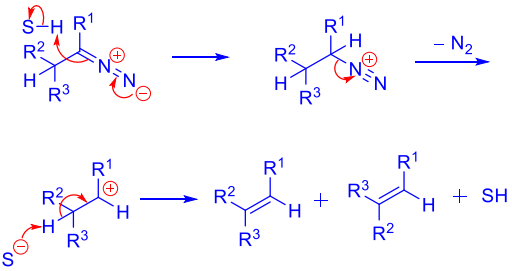
Bamford–Stevens Reaction

The Bamford–Stevens reaction and the Shapiro reaction share a similar mechanistic pathway. The former uses a base such as Na, NaOMe, LiH, NaH, $NaNH_2$, heat, *etc.*, whereas the latter employs bases such as alkyllithiums and Grignard reagents. As a result, the Bamford–Stevens reaction furnishes more-substituted olefins as the thermodynamic products, while the Shapiro reaction generally affords less-substituted olefins as the kinetic products.

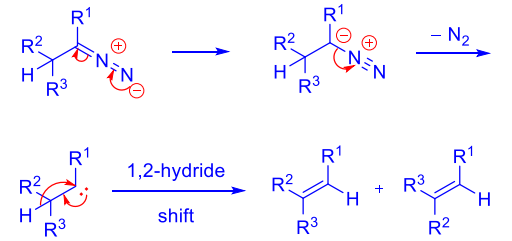




In protic solvent (S–H):

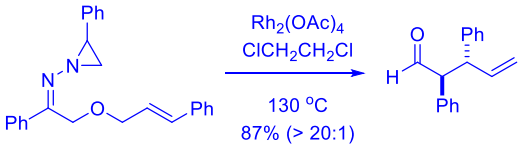


In aprotic solvent:

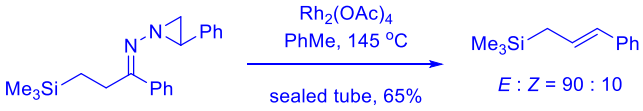


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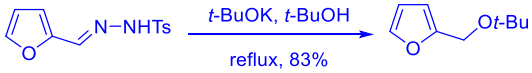
Example 1, Tandem Bamford–Stevens/thermal aliphatic Claisen rearrangement sequence[6]



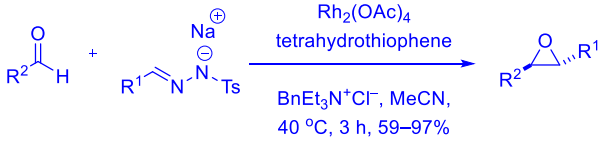
The starting material *N*-aziridinyl imine is also known as Eschenmoser hydrazone.
Example 2, Thermal Bamford–Stevens[6]



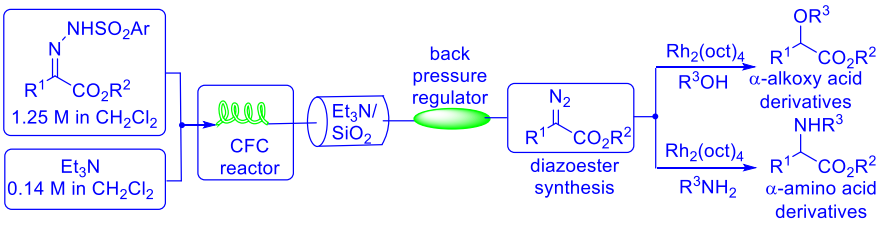
Example 3[7]



Example 4[8]

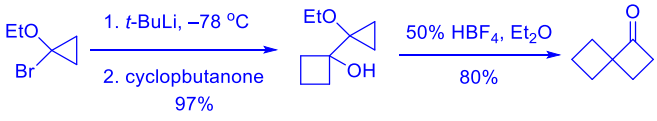


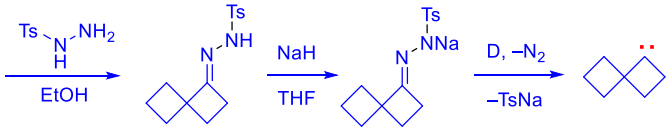
Example 5, Diazoesters from arylsulfonylhydrazones by means of in-flow Bamford–Stevens reactions[11]



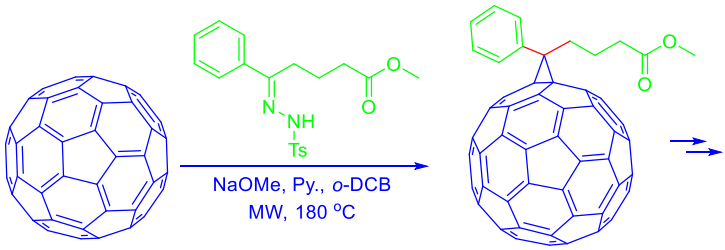
CFC = Continuous-Flow Centrifugation

Example 6, Synthesis of carbene precursor[12]





Example 7, Microwave-mediated synthesis of fullerene acceptors for organic photovoltaics[12]

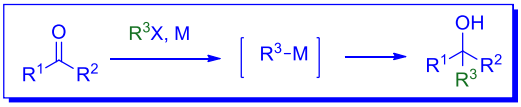


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Barbier Reaction

The Barbier reaction is an organic reaction between an alkyl halide and a carbonyl group as an electrophilic substrate in the presence of magnesium, aluminium, zinc, indium, tin or its salts. The reaction product is a primary, secondary or tertiary alcohol. *Cf.* Grignard reaction.



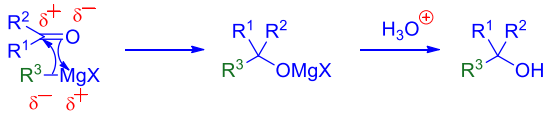
According to conventional wisdom,[3] the organometallic intermediate (M = Mg, Li, Sm, Zn, La, *etc*.) is generated *in situ*, which is intermediately trapped by the carbonyl compound. However, recent experimental and theoretical studies seem to suggest that the Barbier coupling reaction goes through a single electron transfer (SET) pathway.

Generation of the organometallic intermediate *in situ*:

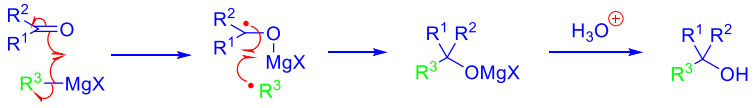


SET = single electron transfer

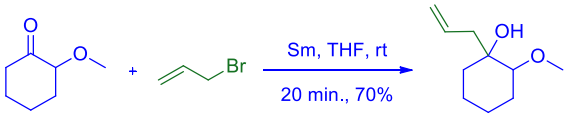
Ionic mechanism,



Single electron transfer (SET) mechanism:

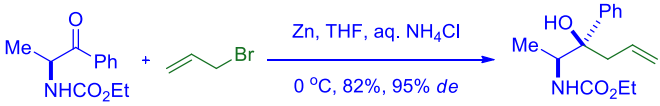


Example 1[6]

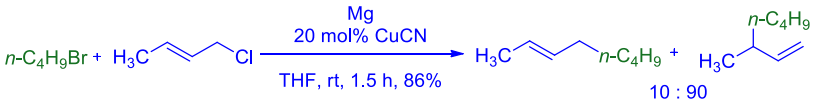


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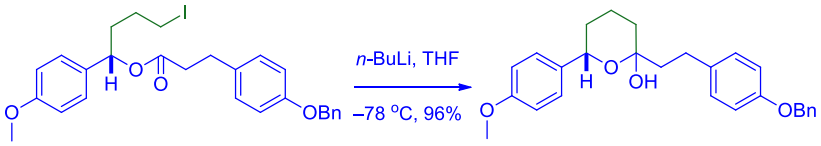
Example 2[9]



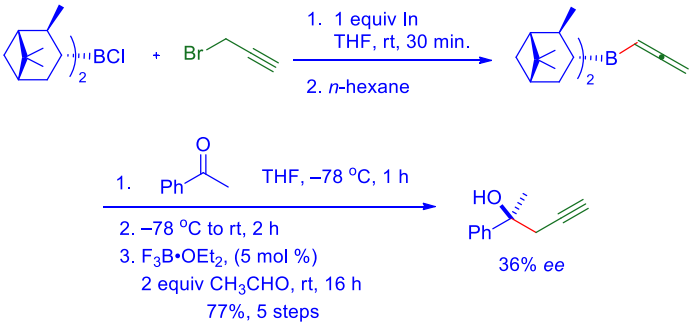
Example 3[10]



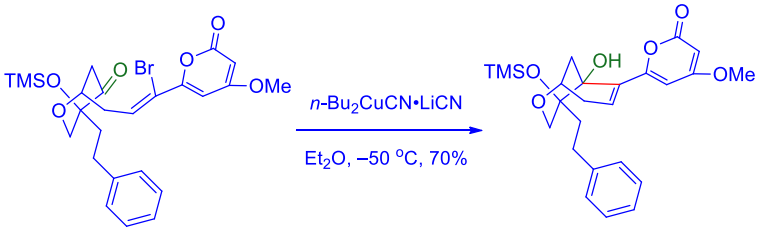
Example 4, Intramolecular Barbier reaction[11]



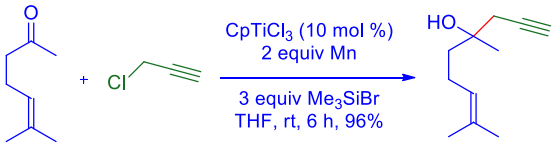
Example 5, The following whole sequence of 5 steps can also be carried out in one-pot[12]



Example 6, A cuprate Barbier protocol to overcome strain and sterical hindrance[13]

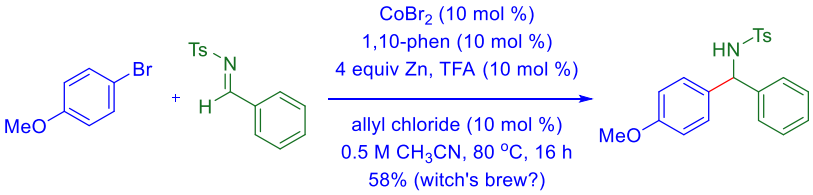


Example 7, $CpTiCl_2$ as an improved titanocene(III) catalyst[14]



Manganese dust reduces $CpTiCl_3$ to $CpTiCl_2$

Example 8, Co(I)-catalyzed Barbier reaction of an aromatic halide with an aromatic aldehyde or an imine[15]

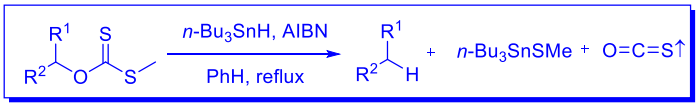


References

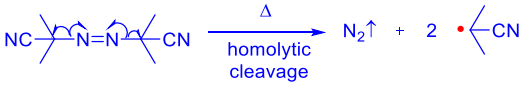
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Barton–McCombie Deoxygenation

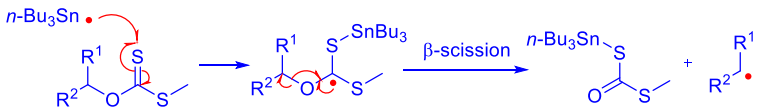
Deoxygenation of alcohols by means of radical scission of their corresponding thiocarbonyl derivatives.

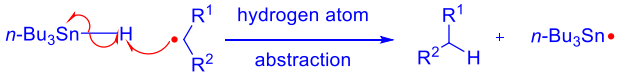


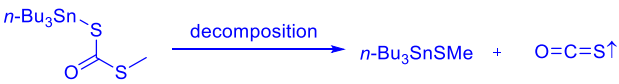
AIBN = 2,2′-azobisisobutyronitrile



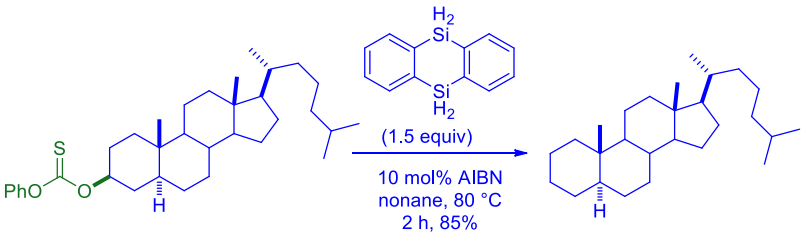






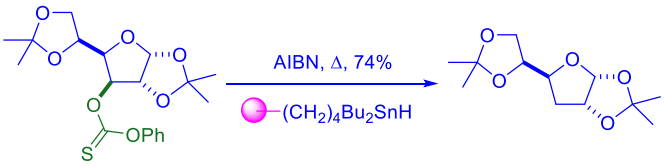


Example 1[2]

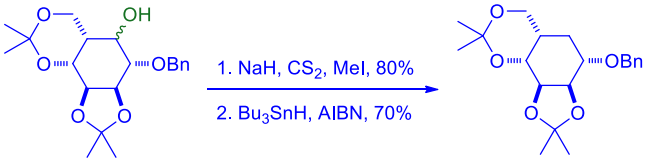


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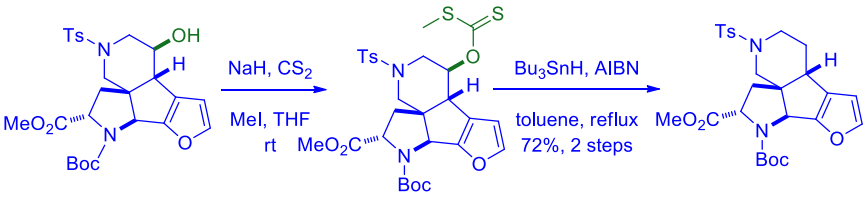
Example 2[5]



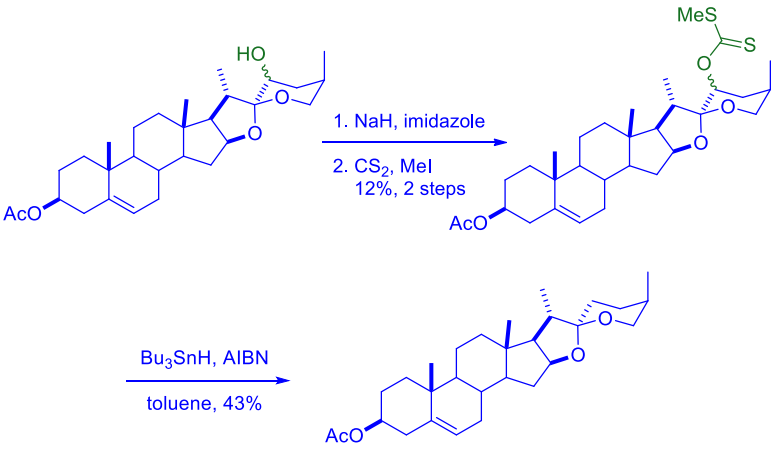
Example 3[6]



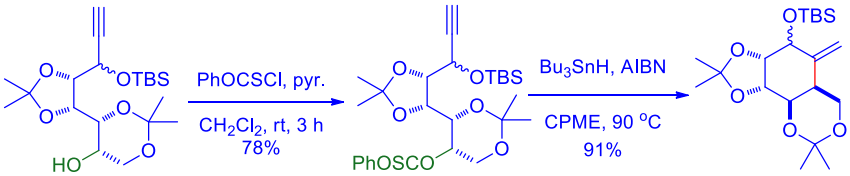
Example 4[7]



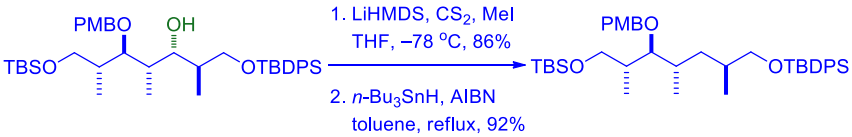
Example 5[8]



Example 6, CPME = cyclopentyl methyl ether[10]



Example 7[11]

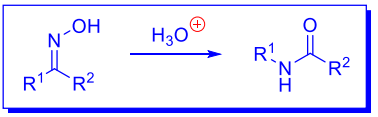


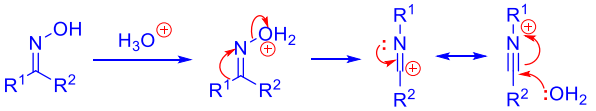
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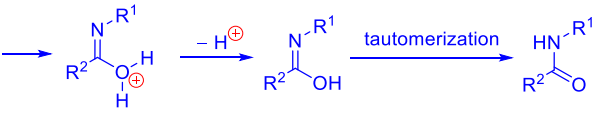
Beckmann Rearrangement

Acid-mediated isomerization of oximes to amides.
In protic acid:

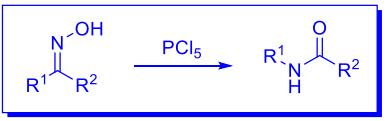


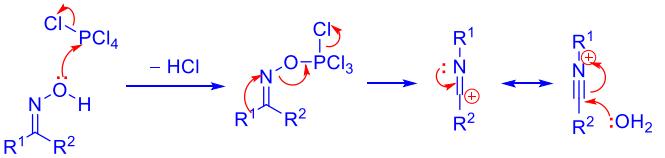


the substituent *trans* to the leaving group migrates

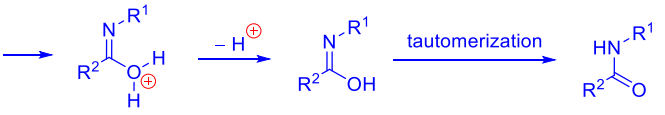


With PCl_5:

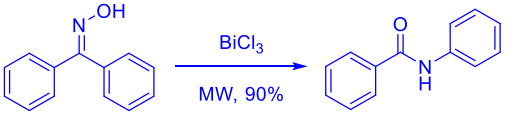




Again, the substituent *trans* to the leaving group migrates

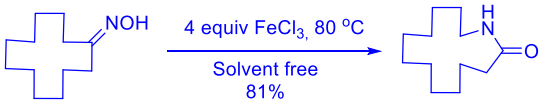


Example 1, Microwave (MW) reaction[3]

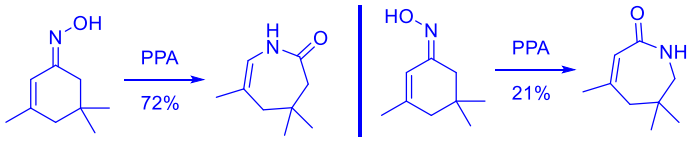


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Example 2[4]

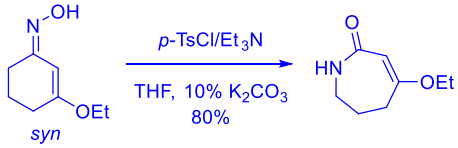


Example 3[6]

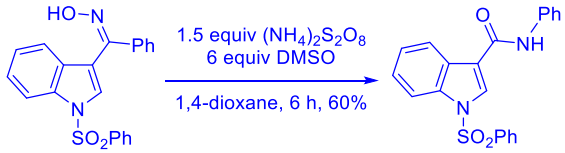


PPA = polyphosphoric acid

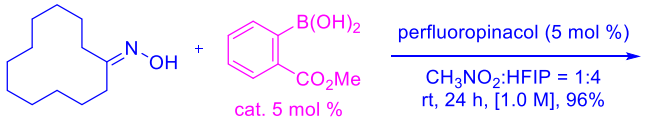
Example 4[8]



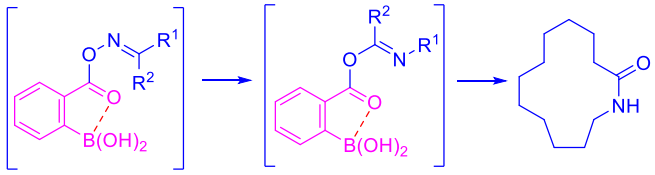
Example 5, Radical Beckmann rearrangement[11]



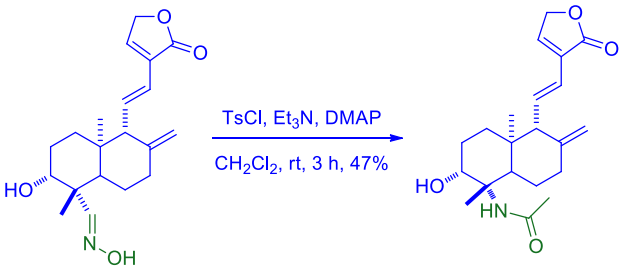
Example 6, Organocatalytic Beckmann rearrangement with a boronic acid/perfluoropinacol system under ambient conditions[142]



HFIP = hexafluoroisopropanol



Example 7, Novel androhrapholide Beckmann rearrangement derivatives[13]

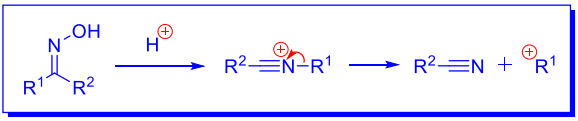


References

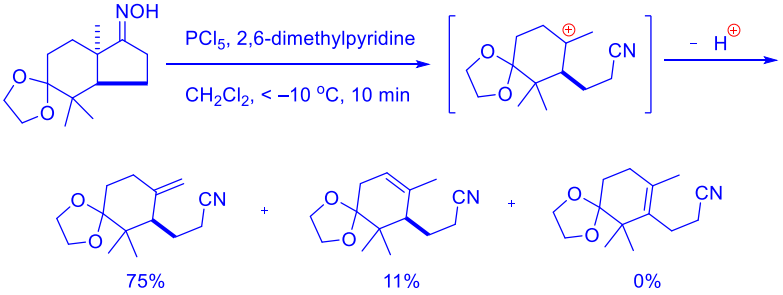
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Abnormal Beckmann Rearrangement

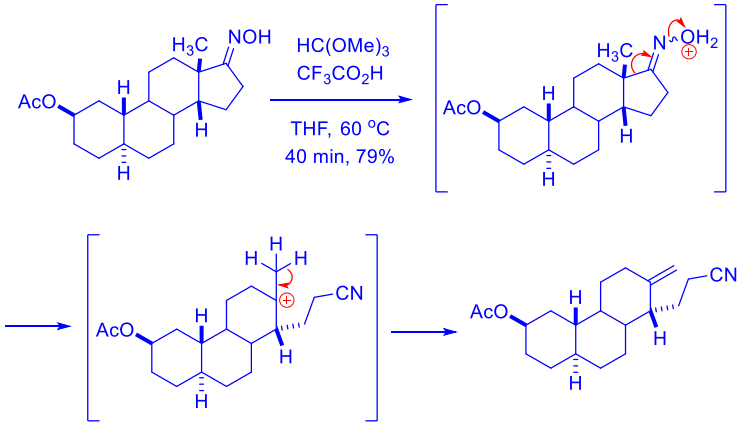
Takes place when the migrating fragment (e.g., R^1) departs from the intermediate, leaving a nitrile as a stable product.



Example 1[9]



Example 2[10]

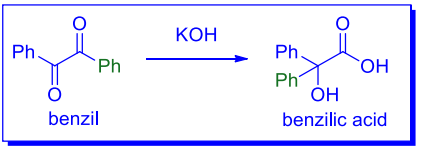


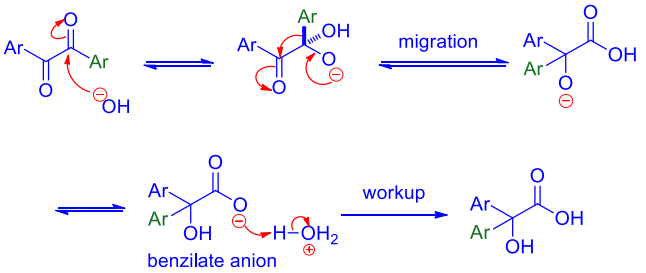
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Benzilic Acid Rearrangement

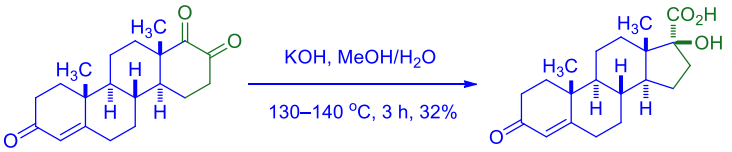
Rearrangement of benzil to benzilic acid *via* aryl migration.



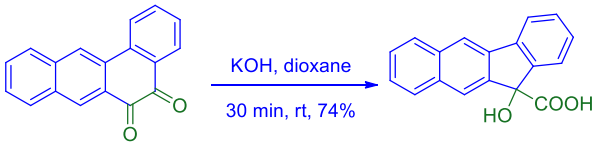


Final deprotonation (before workup) of the carboxylate to afford the benzilate anion drives the reaction forward.

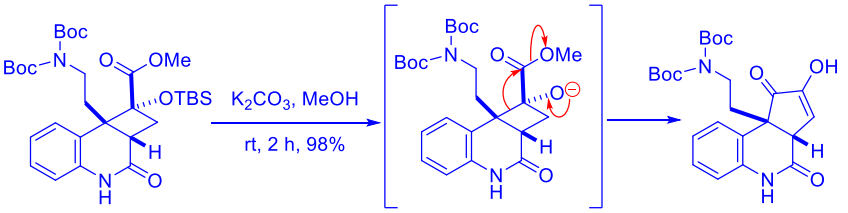
Example 1[3]



Example 2[6]

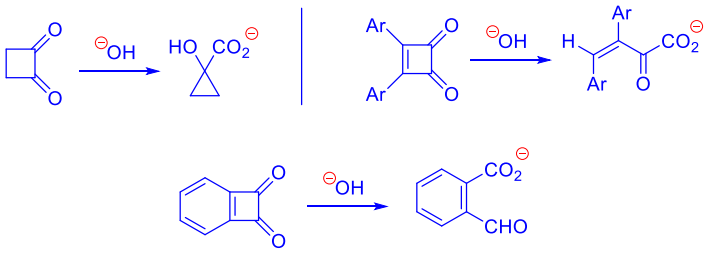


Example 3, Retro-benzilic acid rearrangement[7]

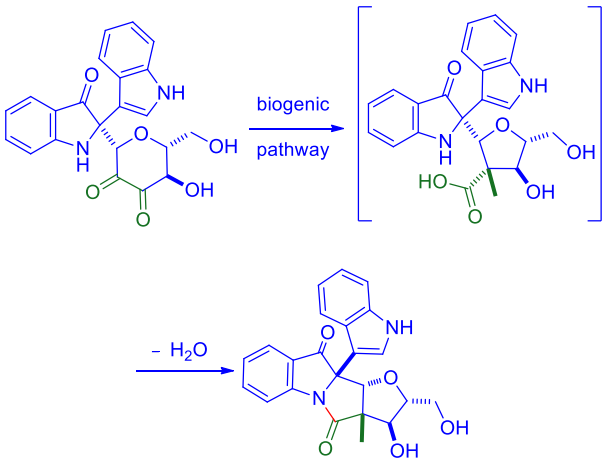


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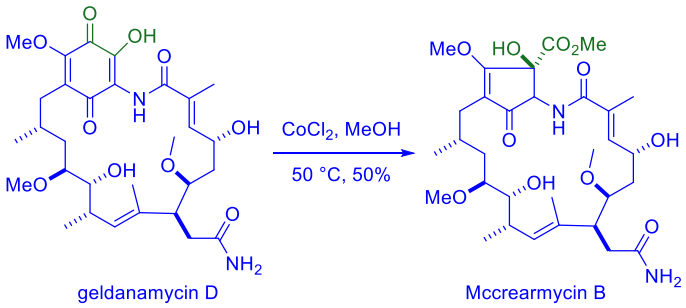
Example 4, Cyclobutane-1,2-diones (Computational Chemistry)[9]



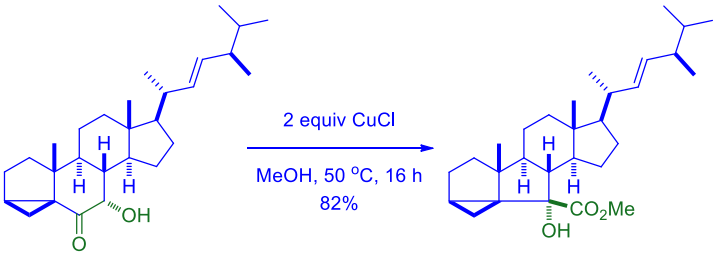
Example 5, Biomimetic benzilic acid rearrangement[10]



Example 6, Benzoquinone ansamycin converted to cyclopentenone-containing ansamycin macrolactam via the benzilic acid rearrangement[11]



Example 7, Biomimetic benzilic acid rearrangement[12]

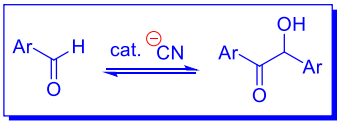


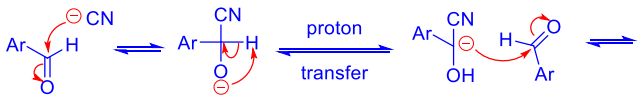
References

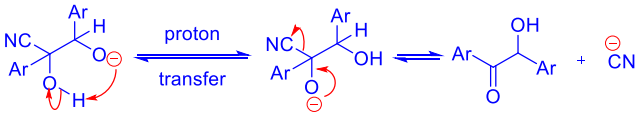
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Benzoin Condensation

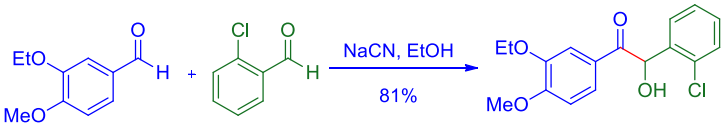
Cyanide-catalyzed condensation of aryl aldehyde to benzoin. Now cyanide is mostly replaced by thiazolium salts or *N*-heterocyclic carbenes. *Cf.* Stetter reaction.



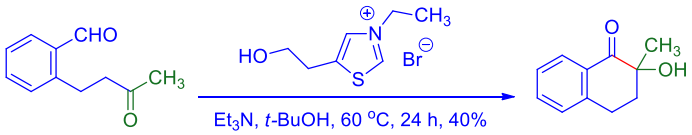




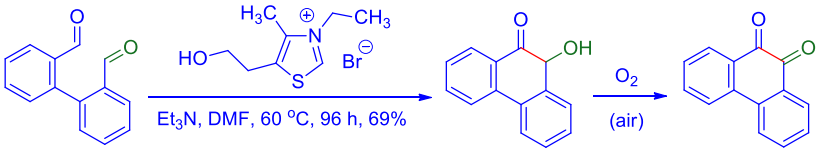
Example 1[2]



Example 2[7]

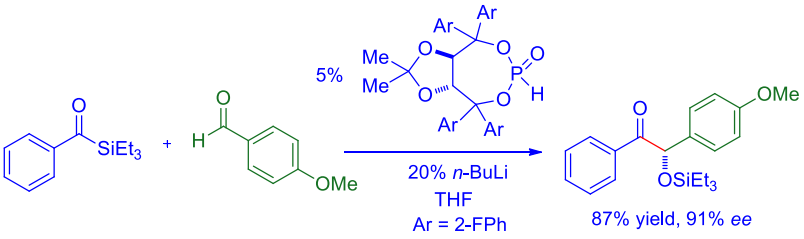


Example 3[7]

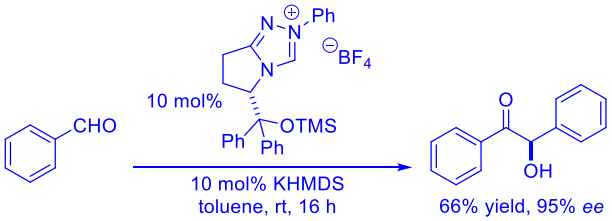


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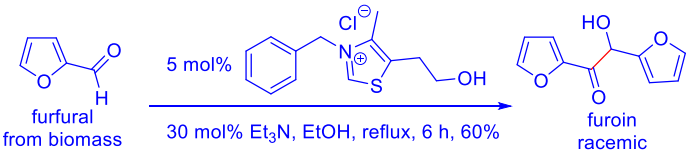
Example 4, With Brook rearrangement[9]



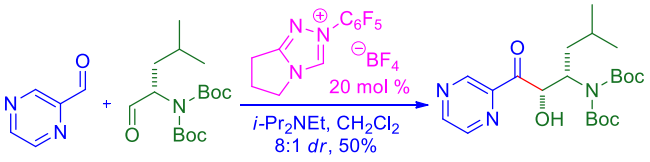
Example 5[10]



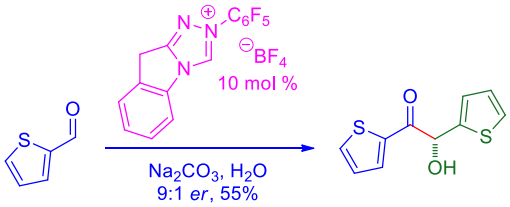
Example 6[12]



Example 7, *N*-Heterocyclic carbene (NHC)-catalyzed cross benzoin reaction resulting in substrate-controlled diastereoselectvity reversal[13]



Example 8, *N*-Heterocyclic carbene (NHC)-catalyzed asymmetric benzoin reaction in water[14]

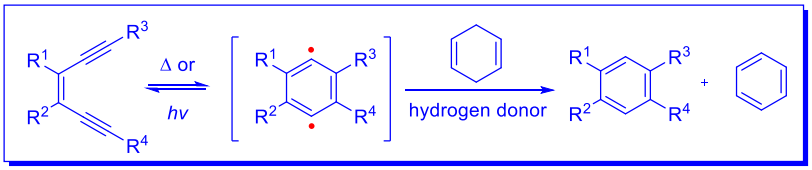


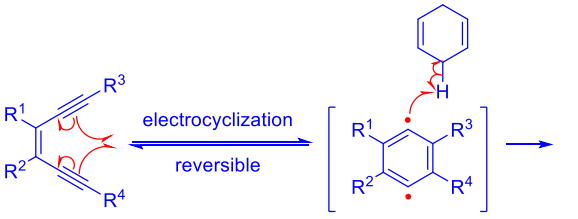
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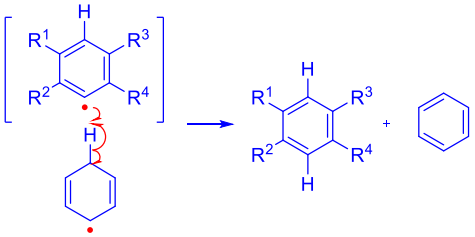
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Bergman Cyclization

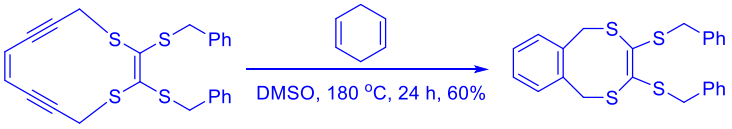
Formation of a substituted benzene through 1,4-benzenediyl diradical formation from enediyne *via* electrocyclization.



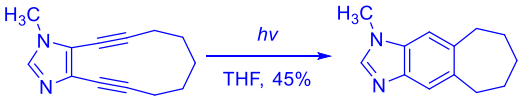




Example 1[6]

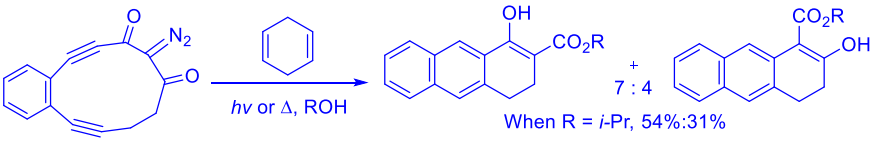


Example 2[7]

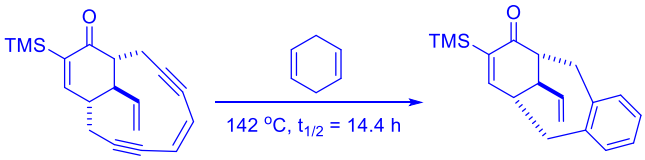


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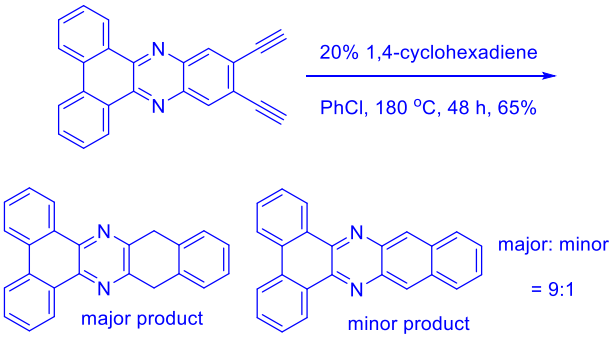
Example 3, Wolff rearrangement followed by Bergman cyclization[8]



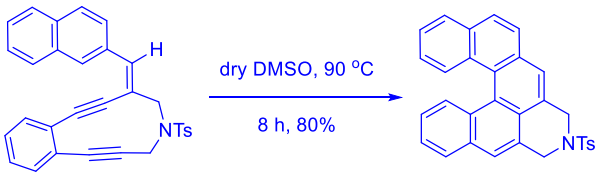
Example 4[10]



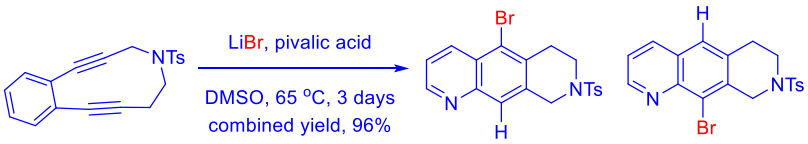
Example 5[12]



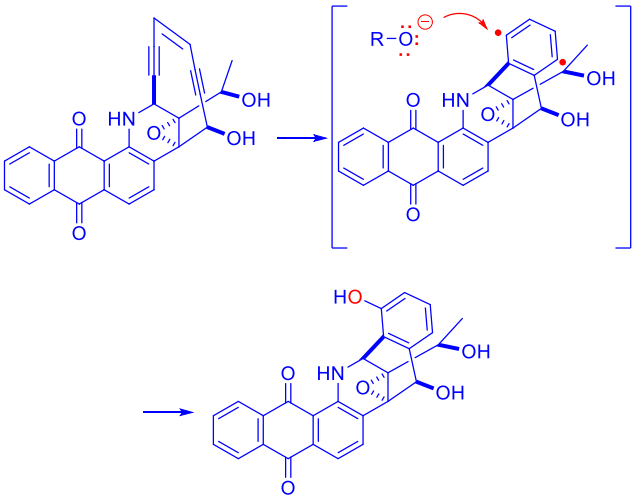
Example 5[13]



Example 6, Barrierless nucleophilic addition to *p*-benzynes[15]



Example 7, Barrierless nucleophilic addition to *p*-benzynes[14]

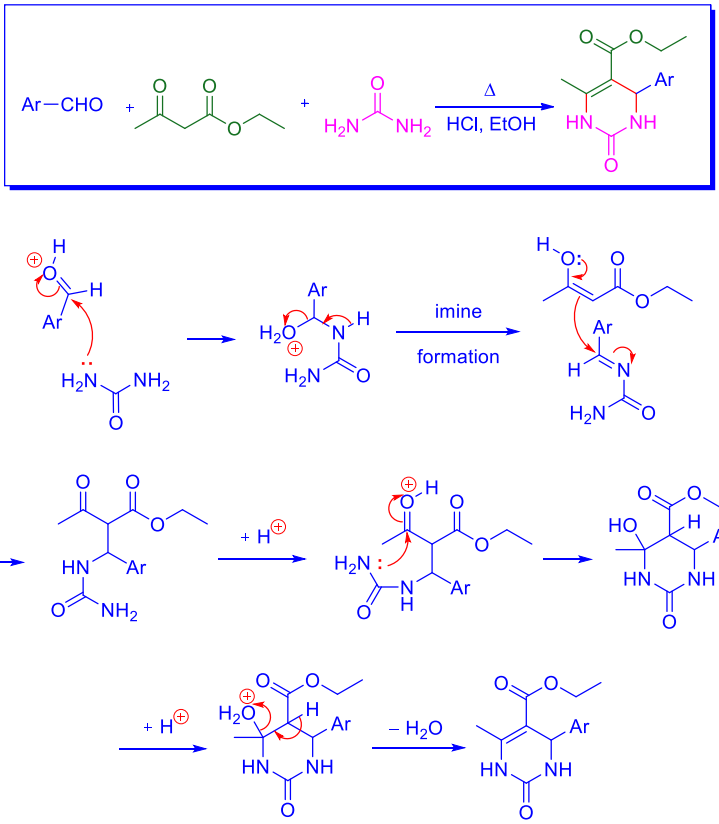


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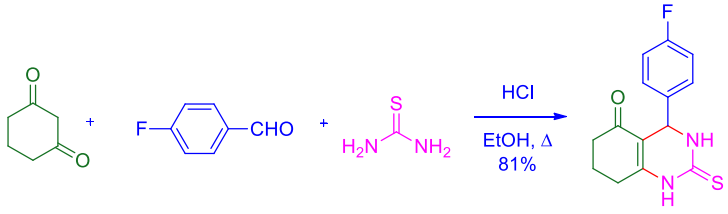
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Biginelli Reaction

Also known as Biginelli pyrimidone synthesis. One-pot condensation of an aromatic aldehyde, urea, and β-dicarbonyl compound in acidic ethanolic solution and expansion of such a condensation thereof. It belongs to a class of transformations called multicomponent reactions (MCRs).

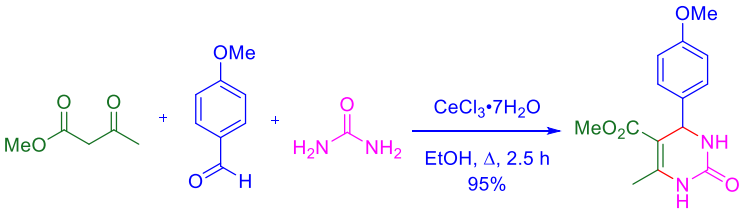


Example 1[4]

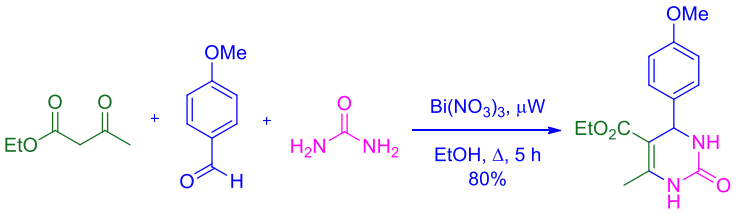


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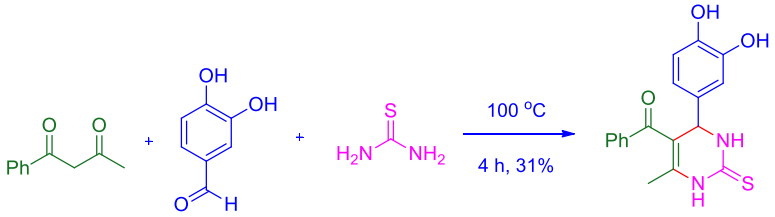
Example 2[5]



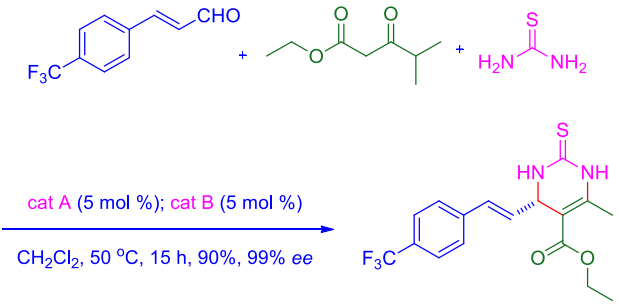
Example 3, Microwave (μW)-induced Biginelli condensation[9]



Example 3[10]

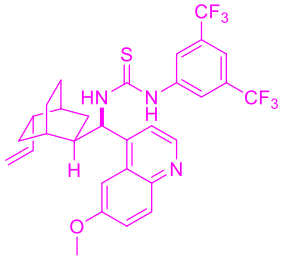


Example 4, Dual organocatalysis system[13]





cat A = *trans*-4,5-methanoproline



cat B = quinidine urea

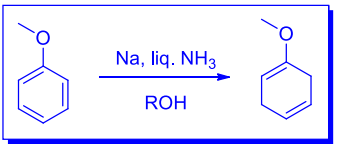
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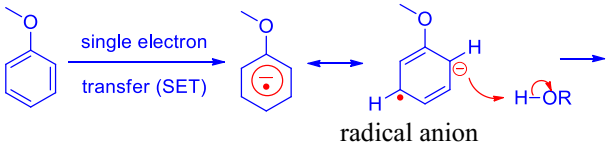
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Birch Reduction

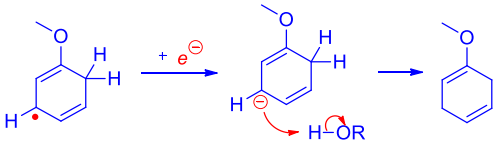
The Birch reduction is the 1,4-reduction of aromatics to their corresponding cyclohexadienes by alkali metals (Li, K, Na) dissolved in liquid ammonia in the presence of an alcohol.

Benzene ring bearing an electron-donating substituent:

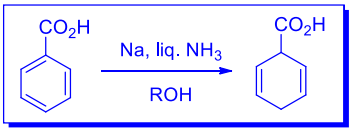


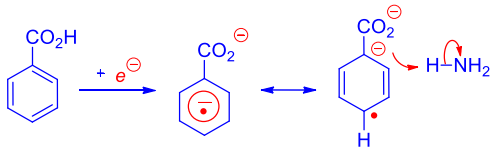


radical anion

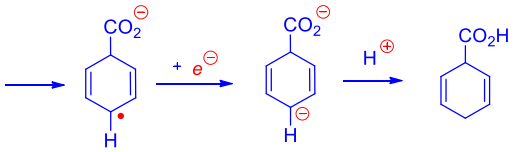


Benzene ring with an electron-withdrawing substituent:



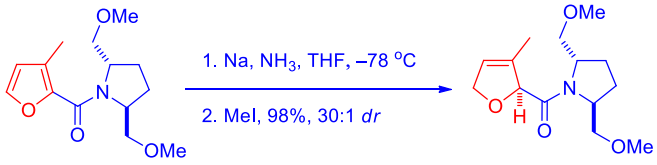


radical anion

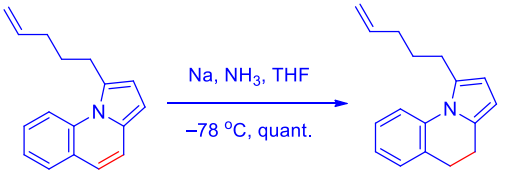


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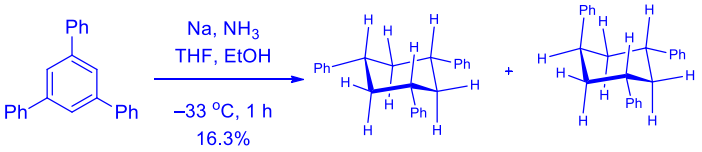
Example 1, Birch reductive alkylation[4]



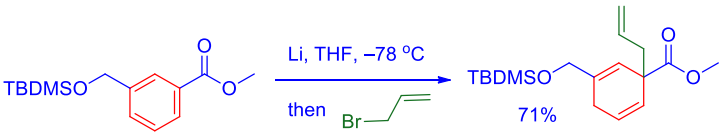
Example 2[7]



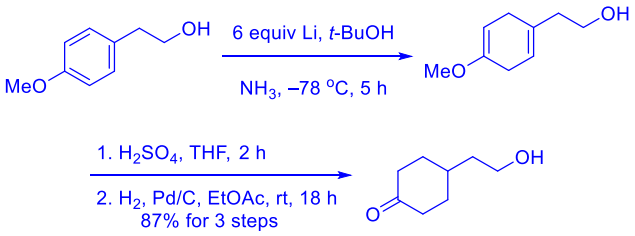
Example 3, Fully reduced products[8]



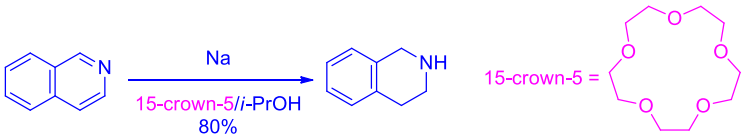
Example 4, Birch reductive alkylation[9]



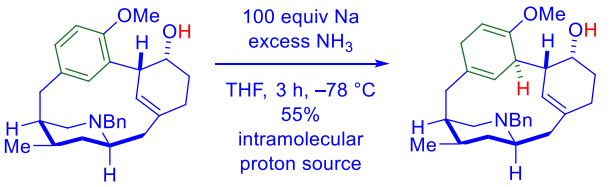
Example 5[10]



Example 6, Chemoselective ammonia-free Birch reduction[11]

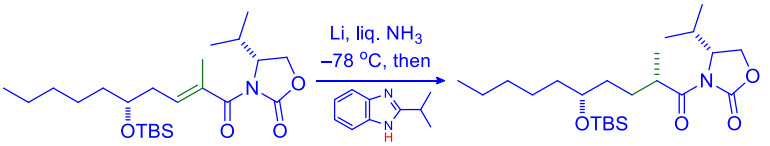


Example 7, Directed Birch reduction enabled by an intramolecular proton source[12]



The hydroxyl group serves as the intramolecular proton source.

Example 8, Birch reduction of α,β-unsaturated imide[13]

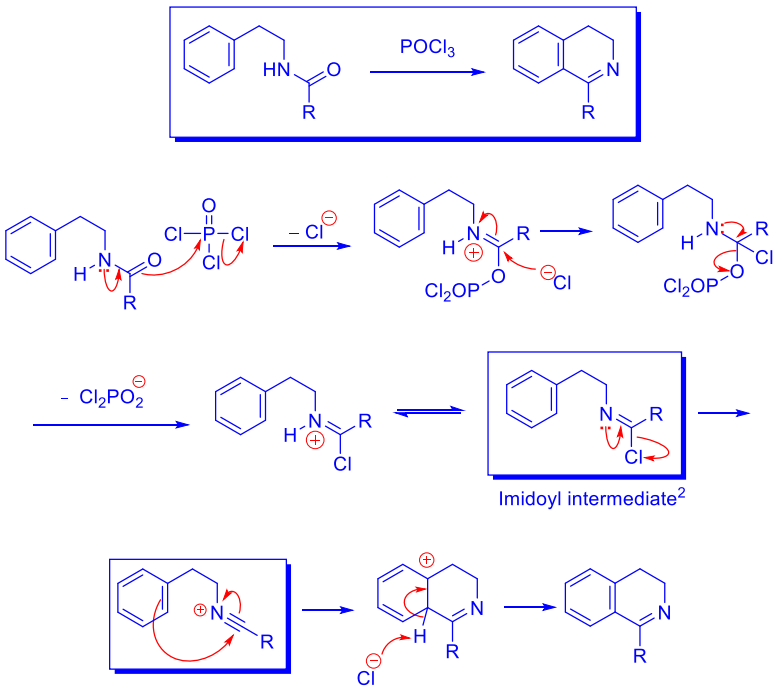


References

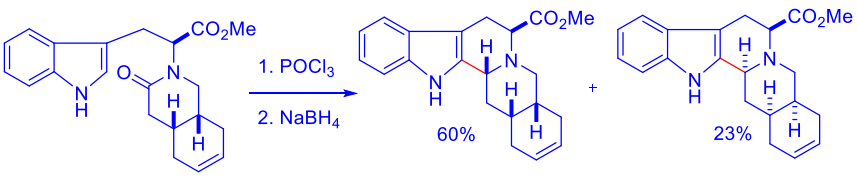
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Bischler–Napieralski Reaction

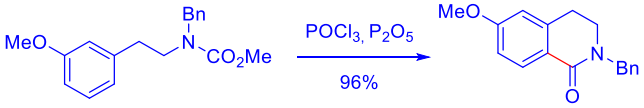
Dihydroisoquinolines from β-phenethylamides in refluxing phosphorus oxychloride.



Example 1[3]

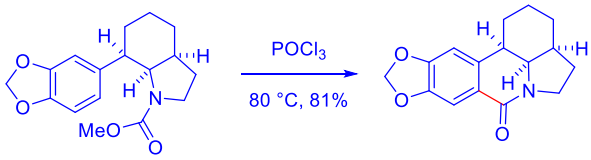


Example 2[5]

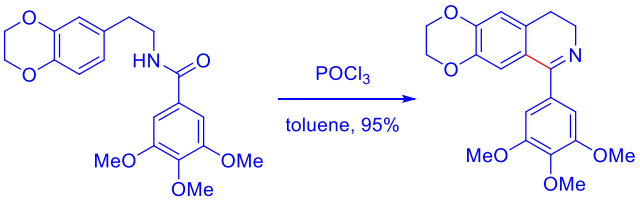


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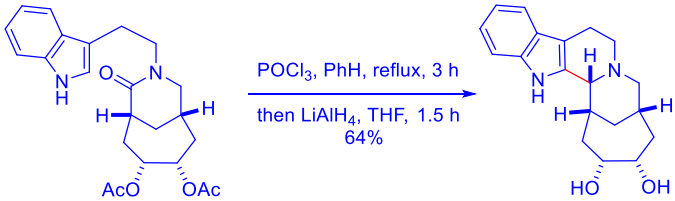
Example 3[7]



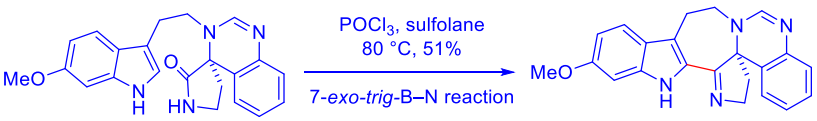
Example 4[8]



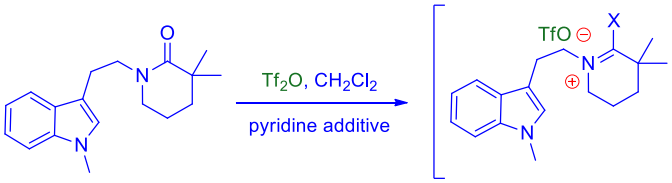
Example 5[10]

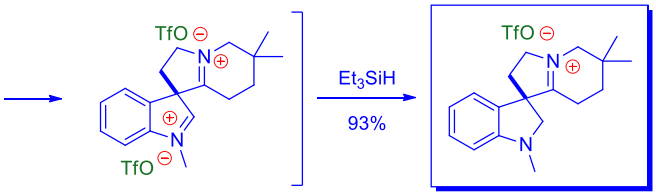


Example 6, An unprecedented Bischler–Napieralski (B–N) reaction[11]

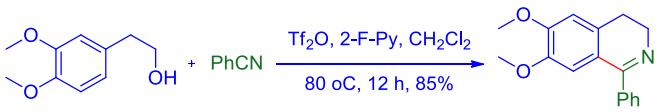


Example 7, Direct bservation of intermediates involved in the Bischler–Napieralski reaction[12]





Example 8, A new Bischler–Napieralski reaction[13]



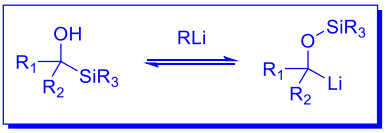
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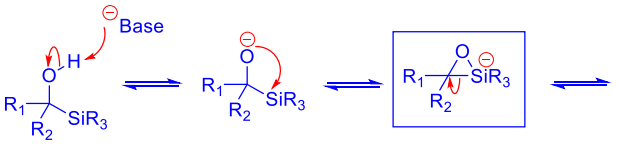
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Brook Rearrangement

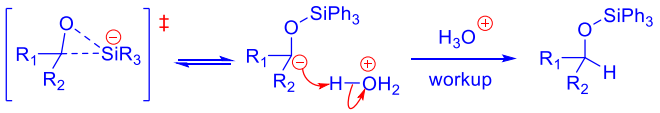
Rearrangement of α-silyl oxyanions to α-silyloxy carbanions *via* a reversible process involving a pentacoordinate silicon intermediate is known as the [1,2]-Brook rearrangement, or [1,2]-silyl migration.

[1,2]-Brook rearrangement

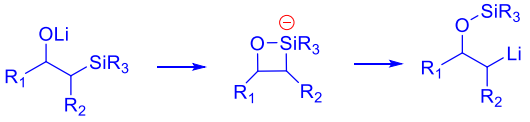




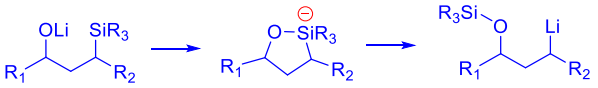
pentacoordinate silicon intermediate



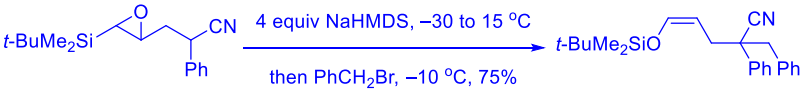
[1,3]-Brook rearrangement



[1,4]-Brook rearrangement

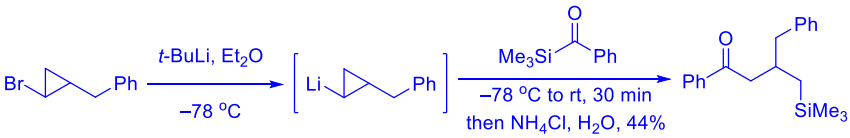


Example 1[6]

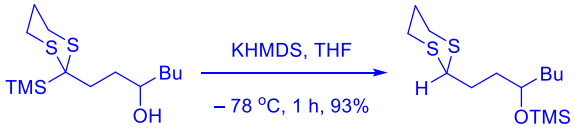


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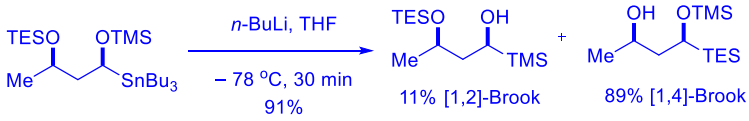
Example 2, [1,2]-Brook rearrangement followed by a retro-[1,5]-Brook rearrangement[8]



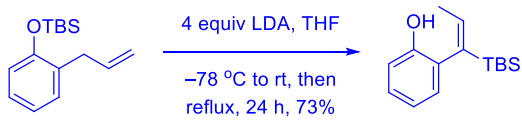
Example 3, [1,5]-Brook rearrangement[9]



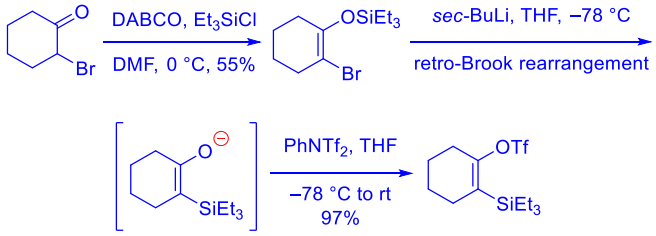
Example 4, Retro-[1,4]-Brook rearrangement[10]



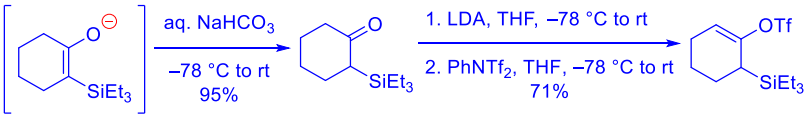
Example 5, Retro-Brook rearrangement[12]



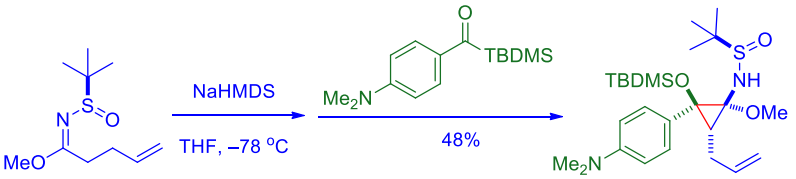
Example 6, Retro-Brook rearrangement[13]



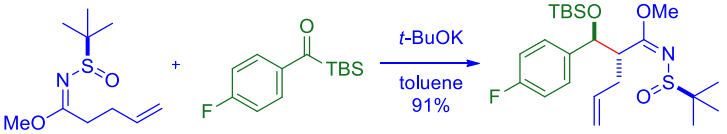
Alternatively:



Example 7, Cyclopropanes from Brook rearrangement[14]



Alternatively:

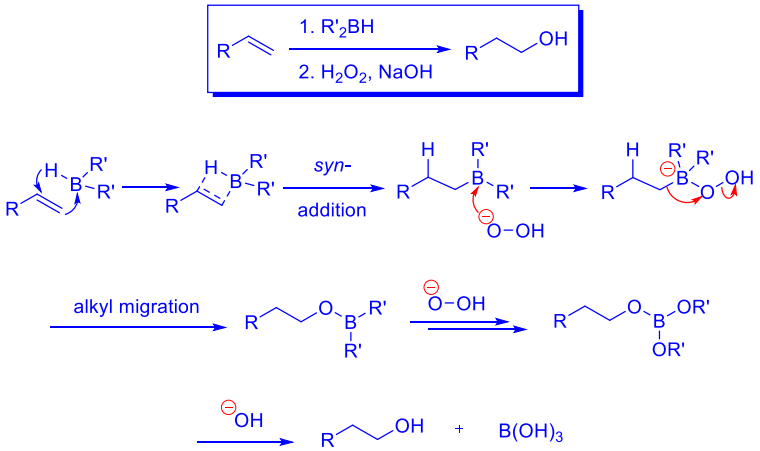


References

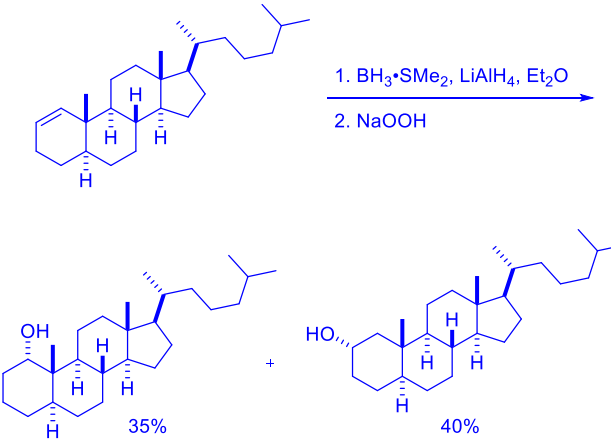
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Brown Hydroboration

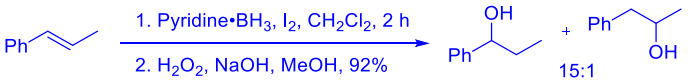
Addition of boranes to olefins followed by alkalinic oxidation of the organoborane adducts to afford alcohols. Regiochemistry follows anti-Markovnikov′s rule.



Example 1[2]

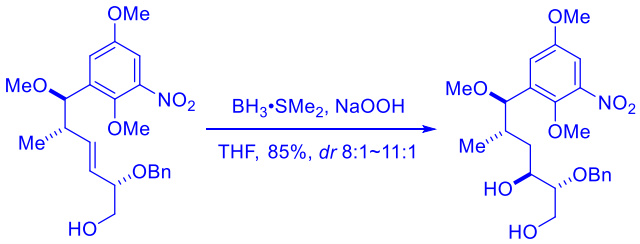


Example 2[7]

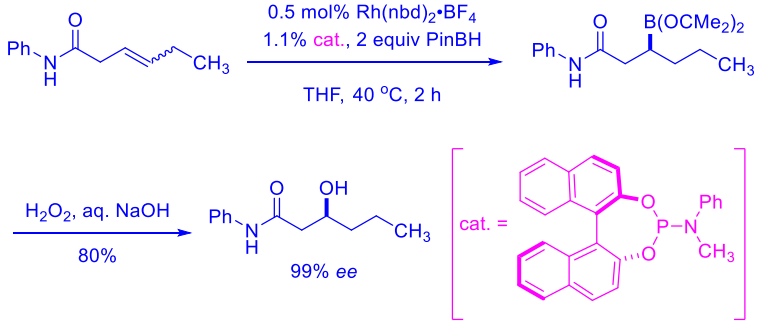


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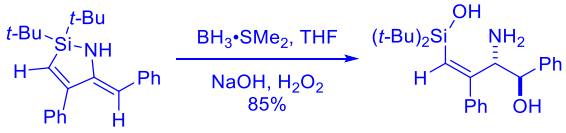
Example 3[8]



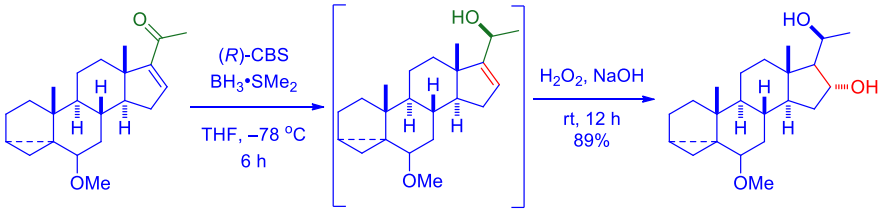
Example 4, Asymmetric hydroboration, nbd = 2,5-norbornadiene[10]



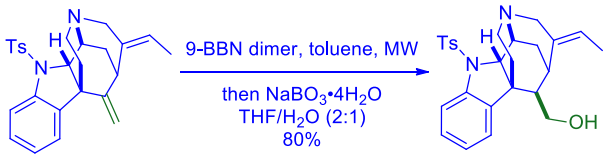
Example 5[11]



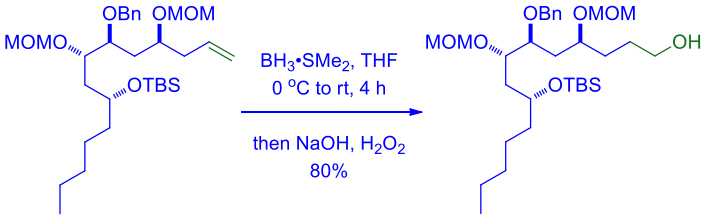
Example 6, Double whammy: One-pot CBS reduction/Brown hydroboration[12]



Example 7, The excellent diastereoselectivity of the Brown hydroboration likely resulted from complete shielding of the top face of the double bond by two piperidine rings[13]



Example 8, Simple, but get the job done[14]

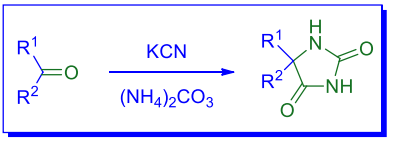


References

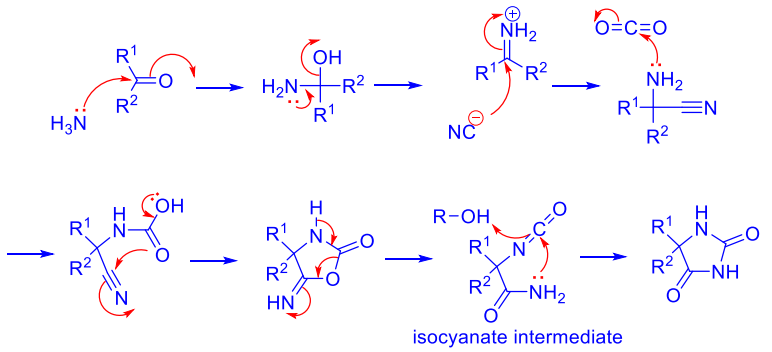
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Bucherer–Bergs Reaction

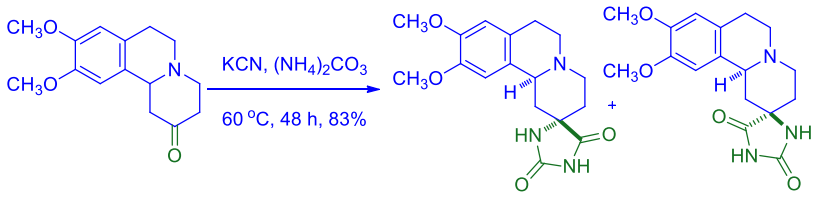
Formation of hydantoins from carbonyl compounds with potassium cyanide (KCN) and ammonium carbonate [$(NH_4)_2CO_3$] or from cyanohydrins and ammonium carbonate. It belongs to the category of multiple component reactions (MCRs).



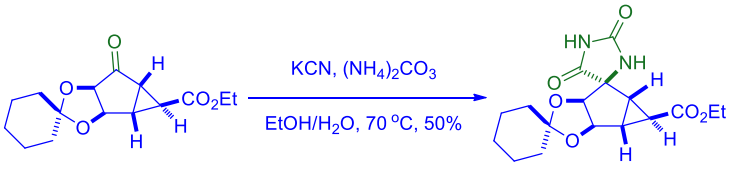
$(NH_4)_2CO_3 = 2\ NH_3 + CO_2 + H_2O$



Example 1[5]

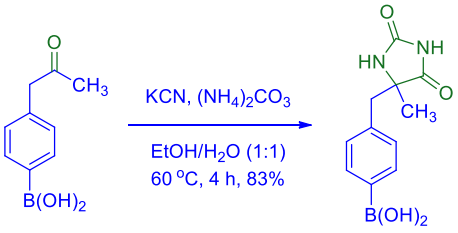


Example 2[6]

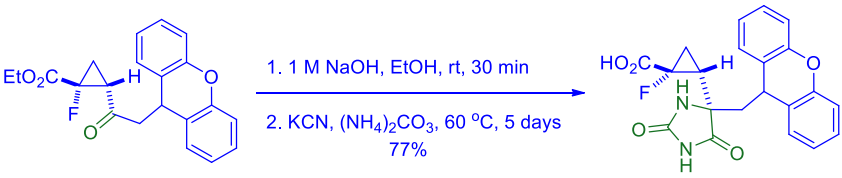


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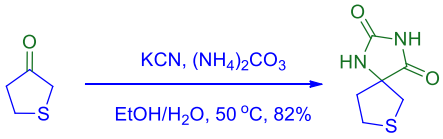
Example 3, In the presence of boronic acid[7]



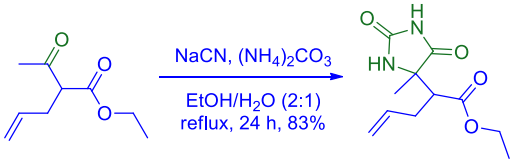
Example 4[9]



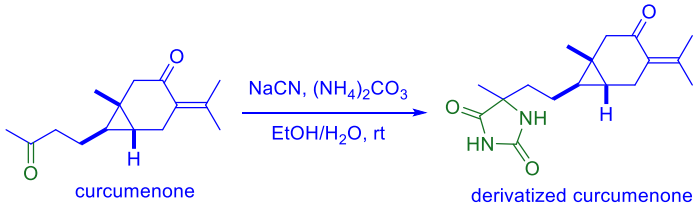
Example 5[11]



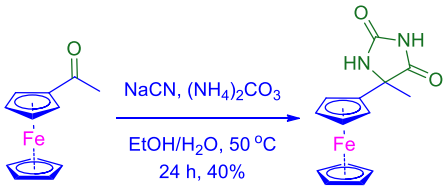
Example 6, From β-keto-ester[12]



Example 7, Derivatization of natural product extracts via the Bucherer–Bergs reaction[13]



Example 8, Ferrocenyl hydantoin[13]

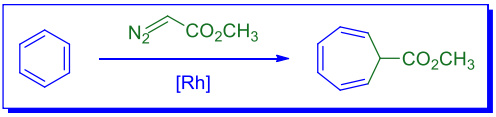


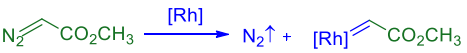
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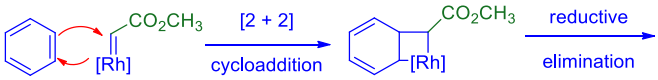
Büchner Ring Expansion

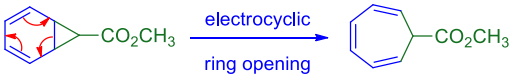
Reaction of a phenyl ring with a diazoacetic ester to give a cyclohepta-2,4,6-trienecarboxylic acid ester. Intramolecular Büchner reaction is more useful in synthesis. *Cf.* Pfau–Platter azulene synthesis.



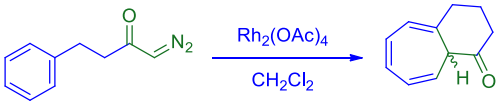


rhodium carbenoid

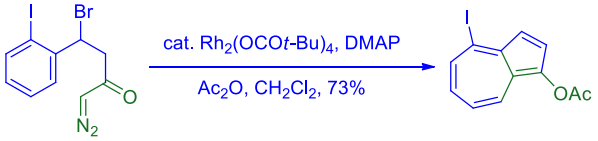




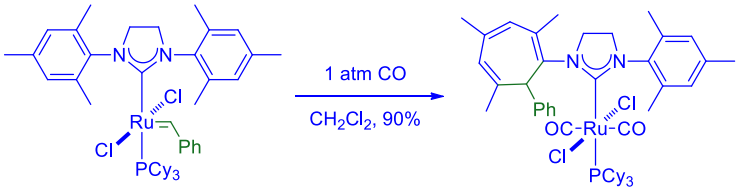
Example 1, Intramolecular Büchner reaction[7]



Example 2, Intramolecular Büchner reaction[8]

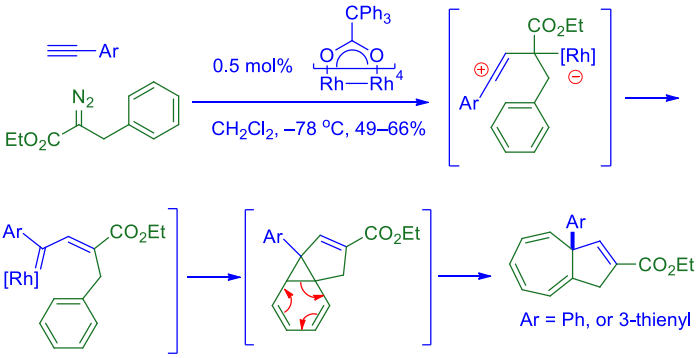


Example 3, Intramolecular Büchner reaction within the Grubbs′ catalyst[9]

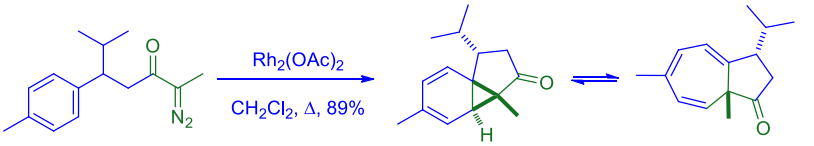


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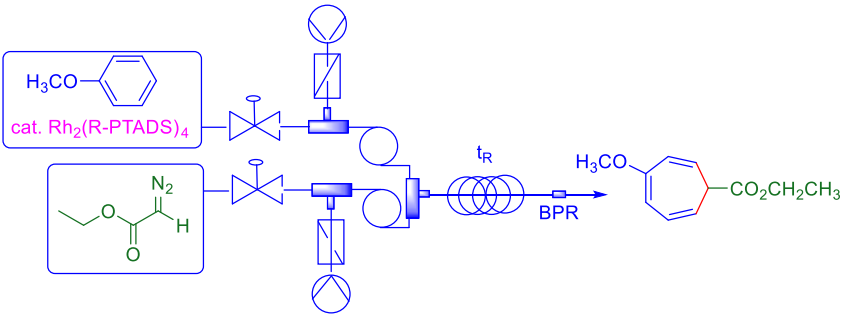
Example 4, Intermolecular Büchner reaction[10]



Example 5, Intramolecular Büchner ring expansion[12]

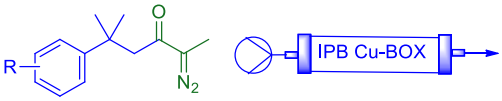


Example 6, regioselective and enantioselective intermolecular Büchner ring expansion in flow, PTADS = Tetrakis[(*R*)-(+)-N-(*p*-dodecylphenylsulfonyl)-prolinato][13]

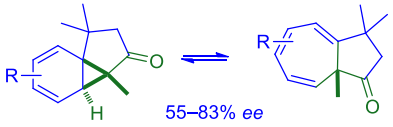


BPR = back pressure regulator

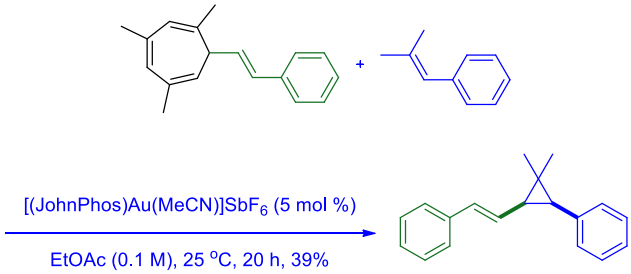
Example 7, Intermolecular Büchner ring expansion in flow[14]



IPB Cu-BOX = insoluble polymer bound Cu-bis(oxazoline) ligand



Example 8, Cyclopropanation by gold- or zinc-catalyzed retro-Büchner reaction at room temperature[15]

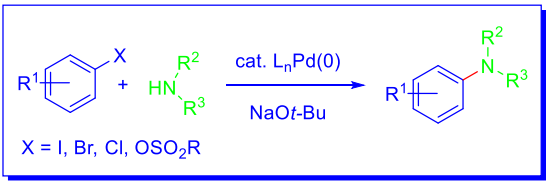


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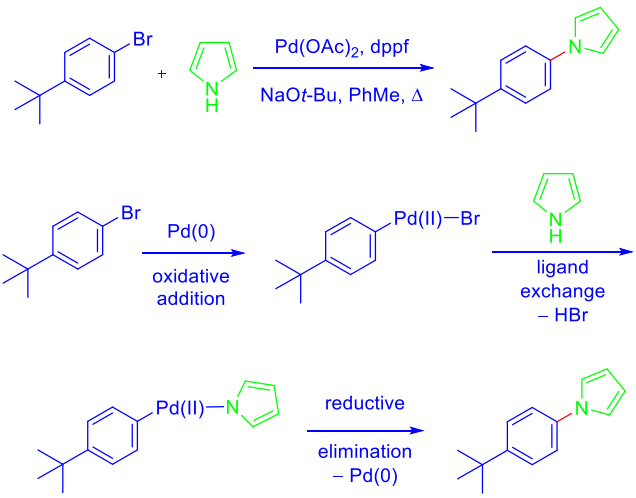
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Buchwald–Hartwig Amination

The Buchwald–Hartwig amination is an exceedingly general method for generating an aromatic amine from an aryl halide or an aryl sulfonates. The key feature of this methodology is the use of catalytic palladium modulated by various electron-rich ligands. Strong bases, such as sodium *tert*-butoxide, are essential for catalyst turnover.



Mechanism:



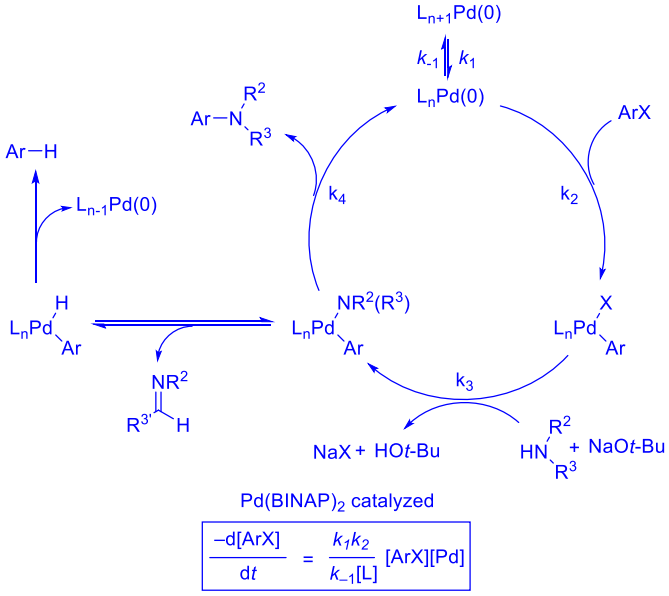
The catalytic cycle is shown on the next page.

Example 1[3]

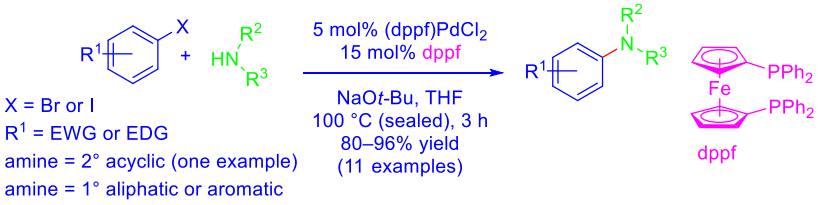


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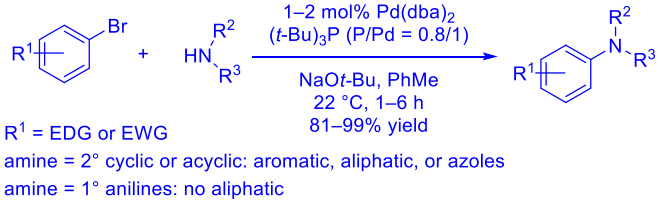
Catalytic cycle:



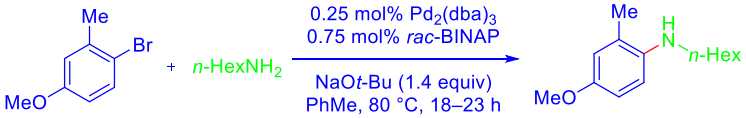
Example 2[4]



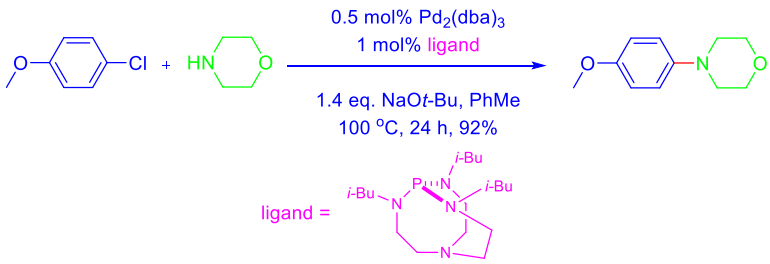
Example 3, Room temperature Buchwald–Hartwig amination[9]



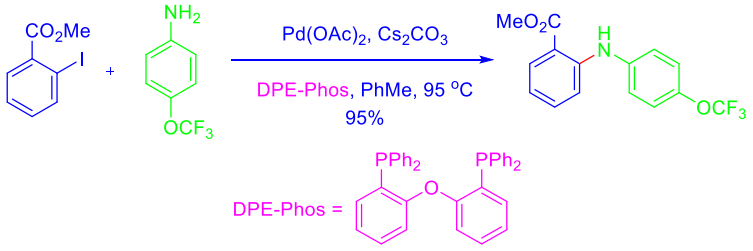
Example 4[10]



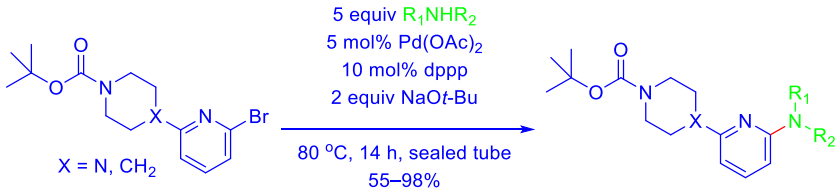
Example 5[11]



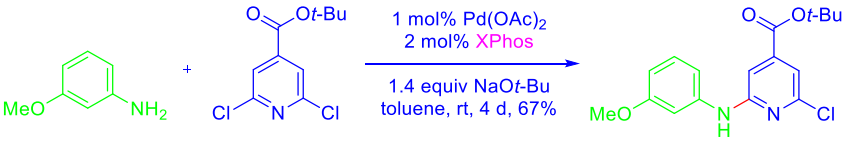
Example 6[12]

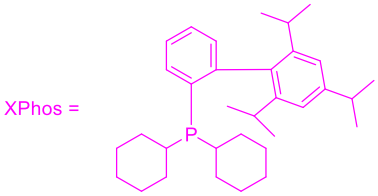


Example 7, Amination of volatile amines[14]

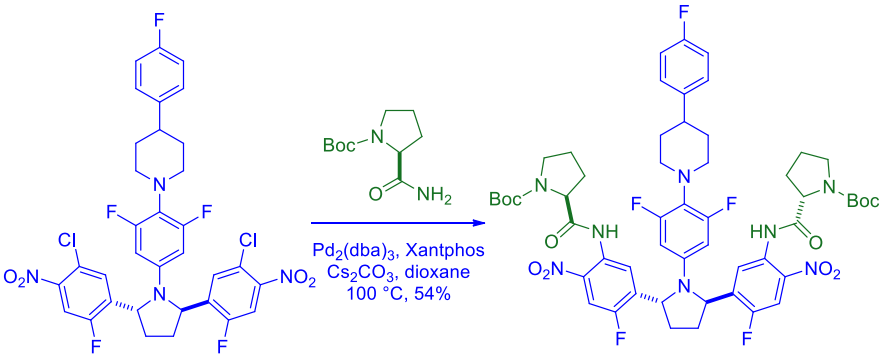


Example 8[15]





Example 9, In the sysnthesis of HCV NS5A polymerase inhibitor pibrentasvir. Coupling between an arylchloride and an amide[17]



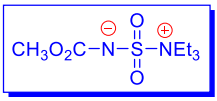
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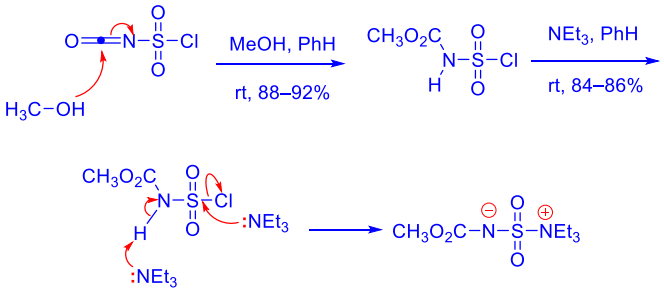
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Burgess reagent

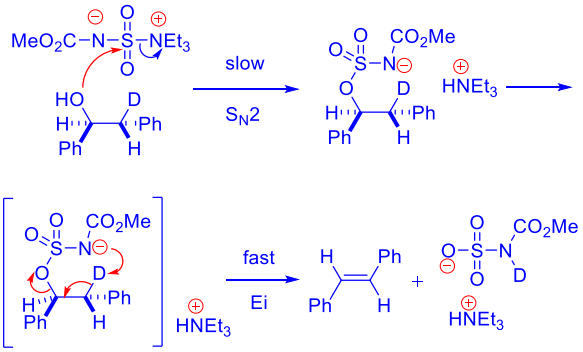
The Burgess reagent [methyl N-(triethylammoniumsulfonyl)carbamate], a neutral, white crystalline solid, is efficient at generating olefins from secondary and tertiary alcohols where the first-order thermolytic Ei (during the elimination—the two groups leave at about the same time and bond to each other concurrently) mechanism prevails.



Preparation[2]

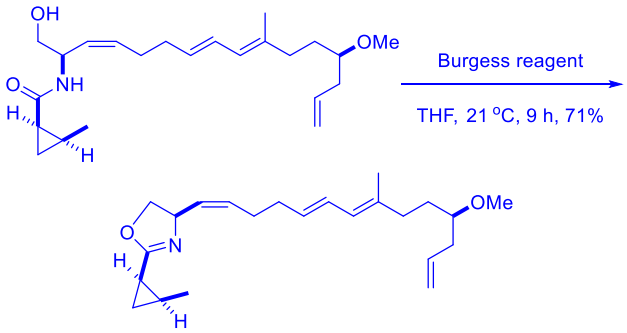


Mechanism of dehydration[5]

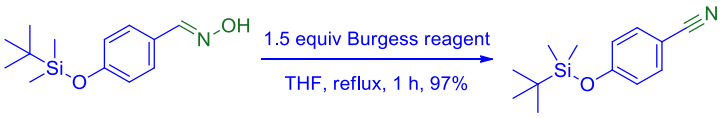


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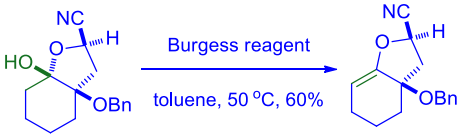
Example 1, On primary alcohols, the hydroxyl group does not eliminate but rather undergoes substitution[3]



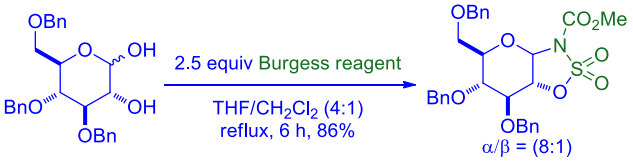
Example 2, Dehydration[6]



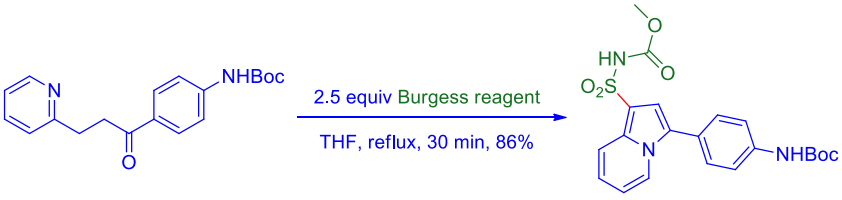
Example 3, Dehydration[7]



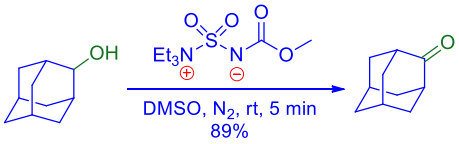
Example 4[8]



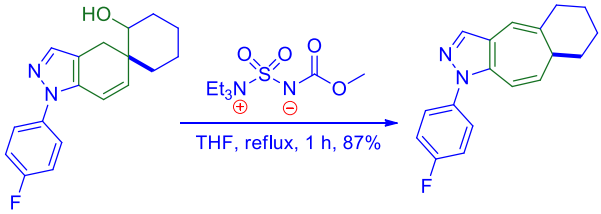
Example 5, Cyclodehydration followed by a novel carbamoylsulfonylation[10]



Example 6, Burgess reagent facilitates alcohol oxidation in DMSO[12]



Example 7, Burgess reagent-mediated ring expansion[13]



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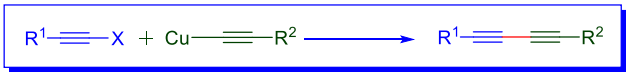
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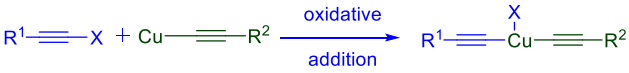
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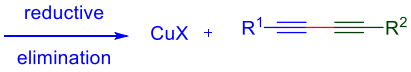
Cadiot–Chodkiewicz Coupling

Bis-acetylene synthesis from alkynyl halides and alkynyl copper reagents.
Cf. Castro–Stephens reaction.

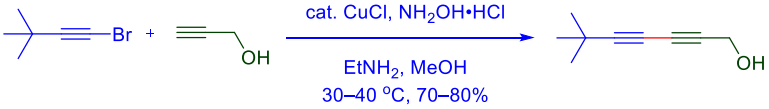




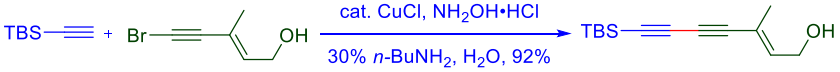
Cu(III) intermediate



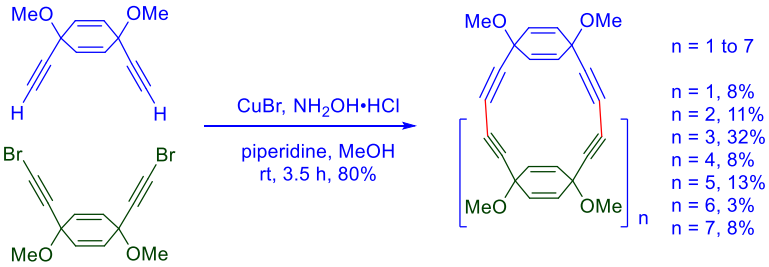
Example 1[3]



Example 2[7]

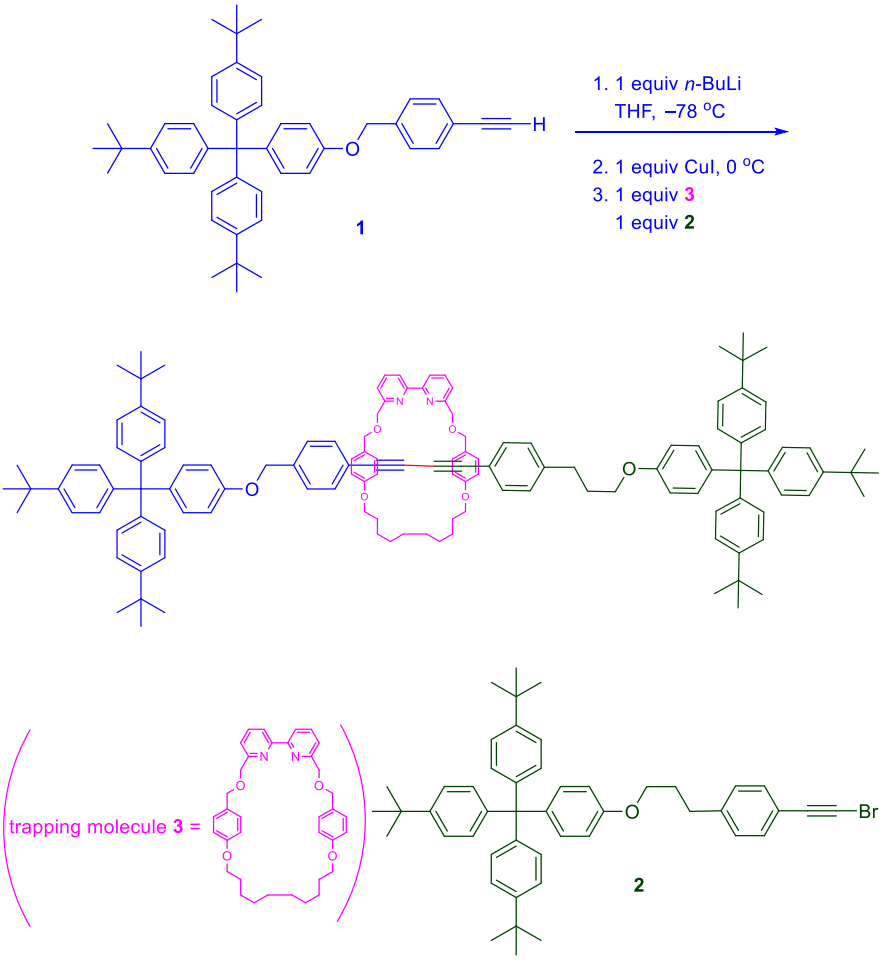


Example 3[9]

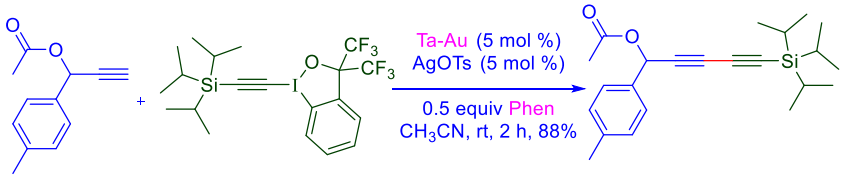


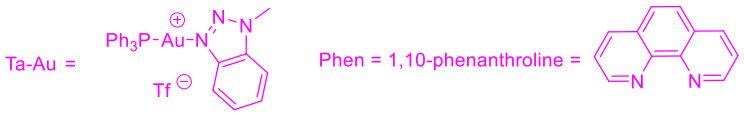
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Example 4, Cadiot–Chodkiewicz active template synthesis of rotaxanes and switchable molecular shuttles with weak intercomponent interactions[10]

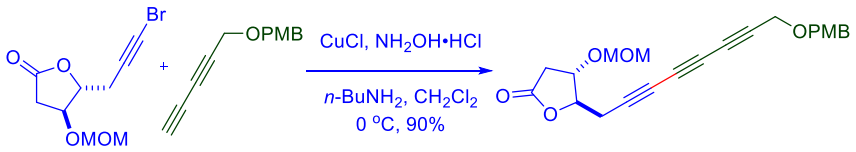


Example 5, Gold-catalyzed Cadiot–Chodkiewicz cross-coupling of terminal alkynes with alkynyl hypervalent iodine reagents[13]





Example 6, Cadiot–Chodkiewicz cross-coupling is superior to the Sonogashi coupling in this case:[14]

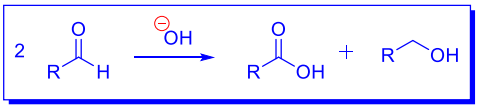


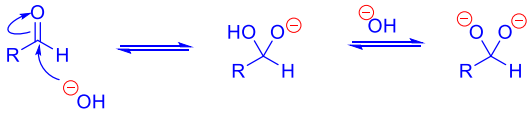
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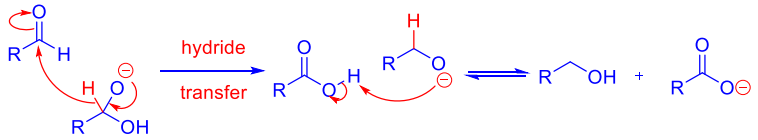
Cannizzaro Reaction

Base-induced disproportionation between two aldehydes to produce an alcohol and a carboxylic acid. If the starting material is an α-ketoaldehyde, an intramolecular Cannizzaro disproportionation reaction can also occur (see Examples 1, 5 and 6). Aldehydes are aromatic aldehydes, formaldehyde or other aliphatic aldehydes without α-hydrogen.



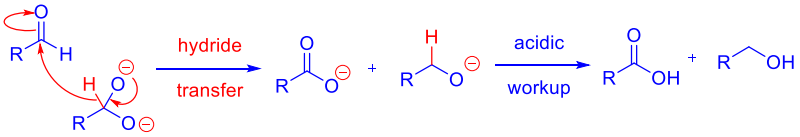


Pathway A:

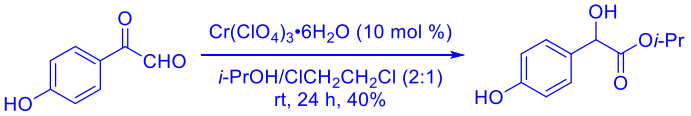


Final deprotonation of the carboxylic acid drives the reaction forward.

Pathway B:

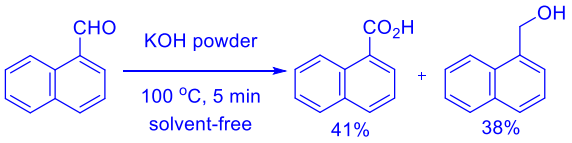


Example 1, Intramolecular Cannizzaro disproportionation reaction[3]

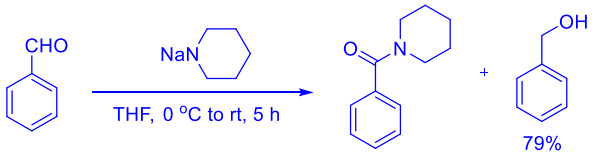


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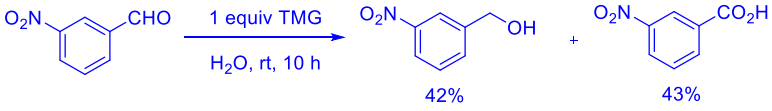
Example 2[4]



Example 3[6]

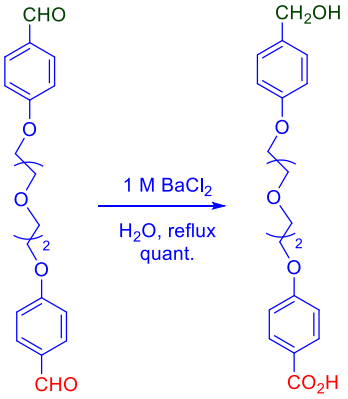


Example 4[8]

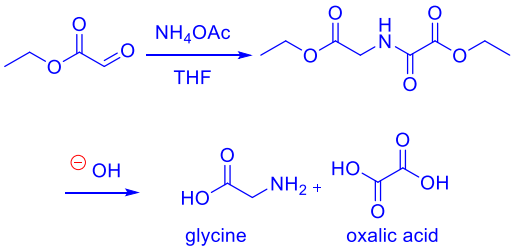


TMG = 1,1,3,3-tetramethylguanidine, an organic base

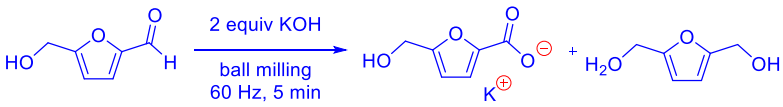
Example 5, Desymmetrization by intramolecular Cannizzaro reaction[9]



Example 6, Intramolecular aza-Cannizzaro reaction[11]



Example 7, Ball mill Cannizzaro reaction[12]



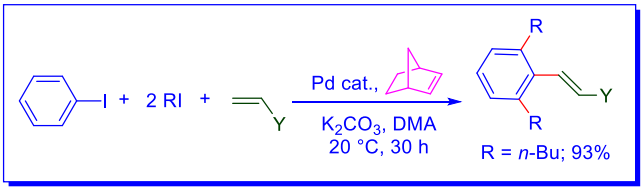
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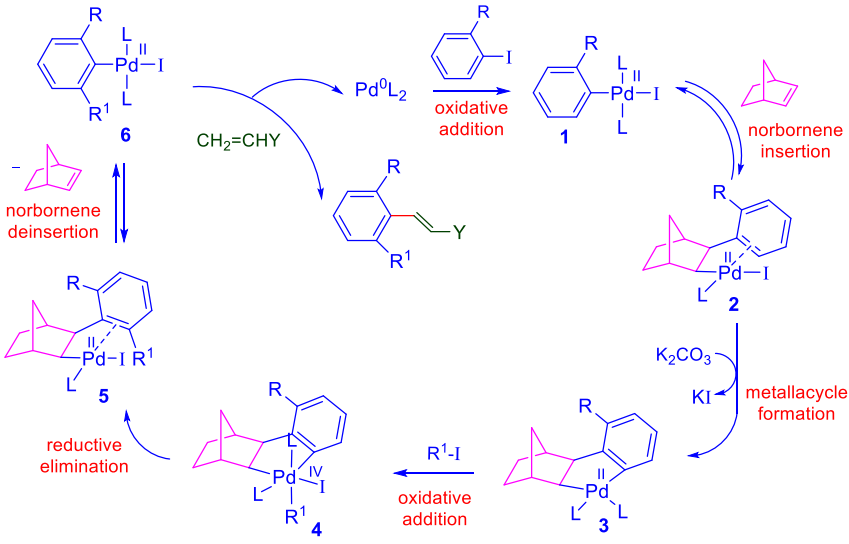
Catellani Reaction

Selective *ortho*-alkylation and -arylation of aryl iodides can be achieved by the cooperative catalytic action of palladium and norbornene.[1] The first reported case was the *ortho*-dialkylation of aryl iodides, followed by Heck reaction.[2] Here an aryl iodide with free *o*-positions reacts with an aliphatic iodide and a terminal olefin in the presence of palladium/norbornene (NBE) as catalyst and a base, to give a 2,6-substituted vinylarene. Analogously, an aryl iodide with one substituted *o*-position leads to a vinylarene containing two different *ortho* groups.[3]

Example 1, A three-component reaction allowing the construction of three adjacent C–C bonds through C–I and C–H activation.[2]



Mechanism for the reaction of an *o*-substitued aryl iodide: Pd(0), Pd(II) and Pd(IV) intermediates and catalytic role of palladium and norbornene.[1–3]

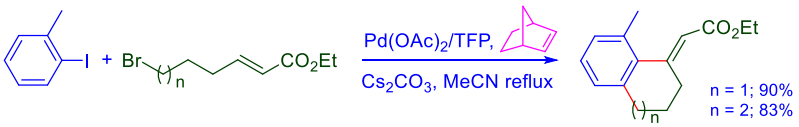


The mechanism involves initial oxidative addition of an *o*-substituted aryl iodide to Pd(0) followed by a stereoselective norbornene (NBE) insertion leading to the *cis*,*exo* complex **2**. β-Hydrogen elimination is prevented by geometric constraints, and a five-membered palladacycle (**3**) readily forms through intramolecu-

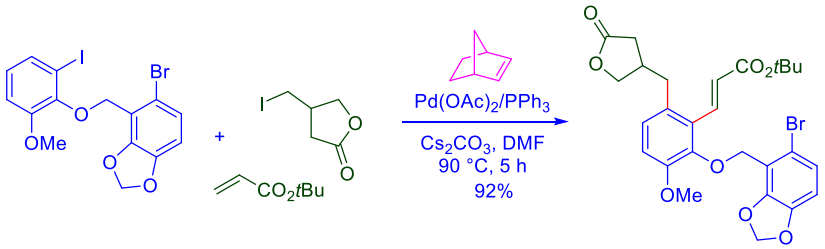
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lar C–H activation. Oxidative addition of an alkyl iodide to **3** affords a Pd(IV) intermediate (**4**) which undergoes reductive elimination by selective migration of the alkyl moiety onto the aromatic ring to form **5**. Norbornene deinsertion occurs spontaneously at this point, likely due to steric hindrance, giving 2,6-disubstituted phenylpalladium(II) species (**6**) which finally react with the terminal olefin to liberate the organic product and Pd(0). Alternatively the sequence can be terminated by other well-known reactions of the aryl-Pd bond such as the Suzuki or Sonogashira couplings, hydrogenolysis, amination, or cyanation. The described methodology can also be extended to ring-forming reactions.[1e] Thus, the reaction is very versatile and offers countless possibilities for building up many types of functionalized aromatic compounds.

Example 2, The synthesis of fused aromatic compounds through final intramolecular Heck reaction was first reported by the Lautens group.[4,1e]

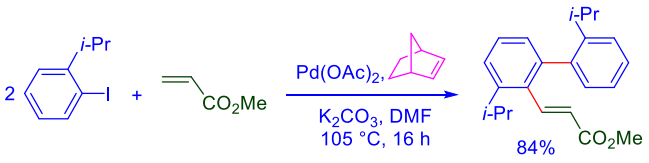


Example 3, The high tolerance to functional groups enabled a key step to the synthesis of a precursor of (+)-linoxepin by Lautens.[5]

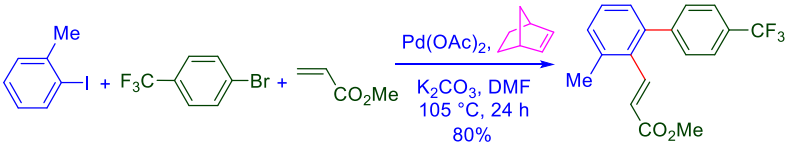


ortho-Arylation of an aryl iodide leading to the construction of a biaryl moiety is also possible, provided that the starting aryl iodide bears an *ortho* substituent. The *o*-substituent in palladacycles of type **3** is essential for selectively directing the attack of an aryl halide onto the aromatic site (*ortho* effect).[1,6]

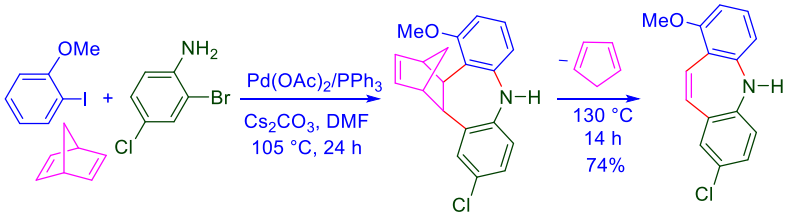
Example 4, Aryl-aryl coupling combined with Heck reaction.[7]



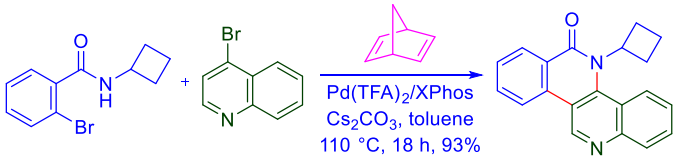
Example 5. The non symmetrical coupling of an aryl iodide bearing an *o*-electron-donating group, an aryl bromide containing an electron-withdrawing substituent, and a terminal olefin illustrates the importance of correctly tuning the electronic properties of the two aryl halides for selectivity control.[8]



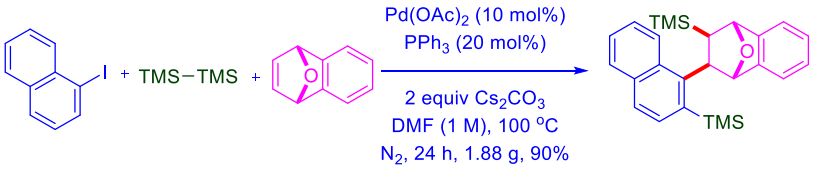
Example 6, Internal chelation to Pd(IV)[9] can cancel the *ortho* effect.[10]



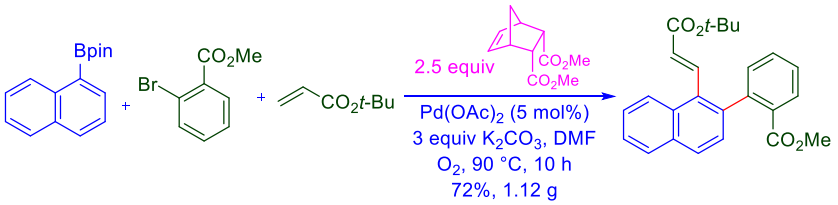
Example 7, Synthjesis of benzo[1,6]naphthyridinones[11]



Example 8, Iterative C–H bis-silylation[12]



Example 9, Borono-Catellani arylation for unsymmetrical biaryl synthesis[13,14]



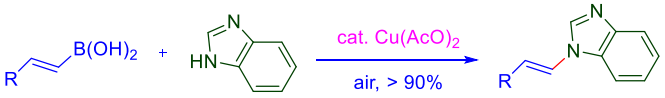
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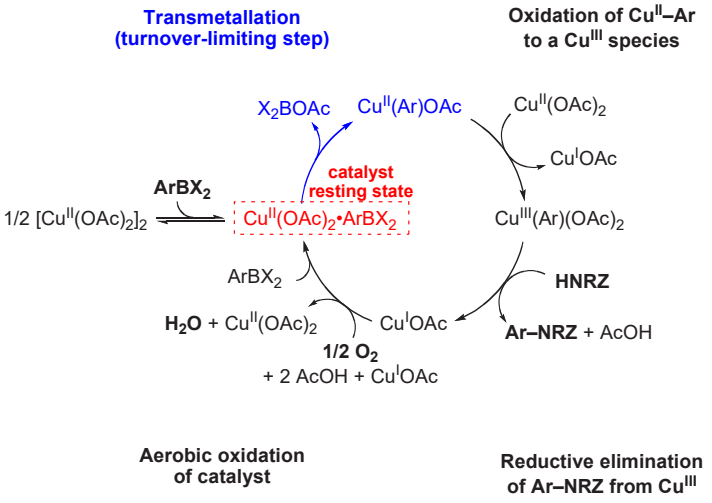
Chan–Lam C–X Coupling Reaction

Arylation, vinylation and alkylation of a wide range of NH/OH/SH substrates by oxidative cross-coupling with boronic acids in the presence of catalytic cupric acetate, weak base and in air (open-flask chemistry). The reaction works for amides, amines, amidines, anilines, azides, azoles, hydantoins, hydrazines, imides, imines, nitroso, pyrazinones, pyridines, purines, pyrimidines, sulfonamides, sulfinates, sulfoximines, ureas, alcohols, phenols, thiols, *etc*. The boronic acids can be replaced with siloxanes, stannanes or other organometalloids. The mild condition of this reaction is an advantage over Buchwald–Hartwig′s Pd-catalyzed cross-coupling using halides, though boronic acids are more expensive than halides. The Chan–Lam C–X bond cross-coupling reaction has emerged as a powerful and popular methodogy similar to Suzuki–Miyaura′s C–C bond cross-coupling reaction.



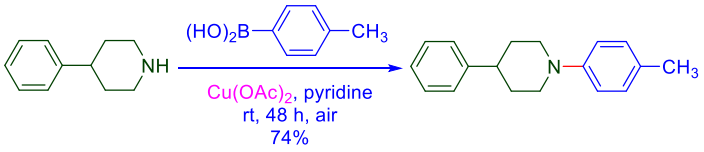


Proposed Mechanism:[4]

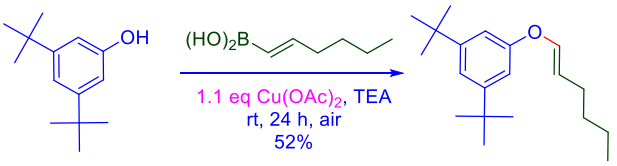


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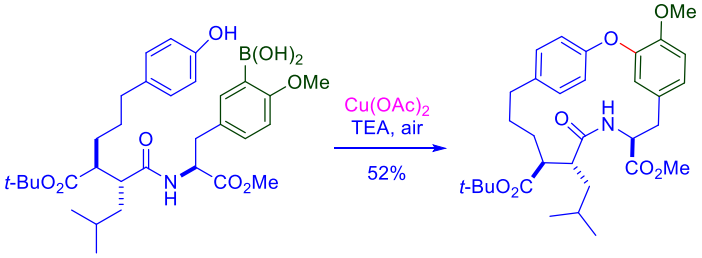
Example 1[1a,d]



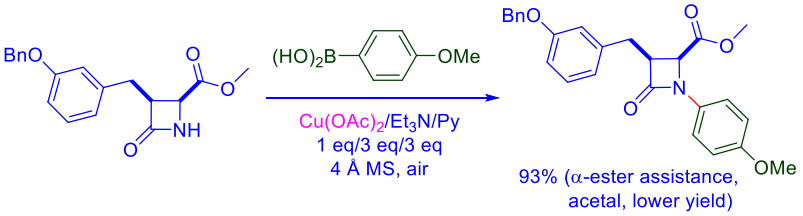
Example 2[5]



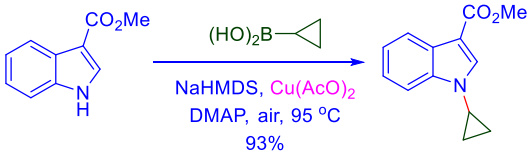
Example 3[6]



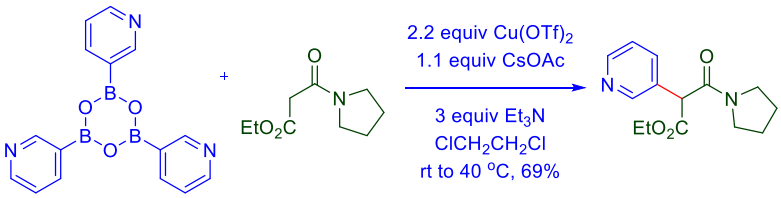
Example 4[14]



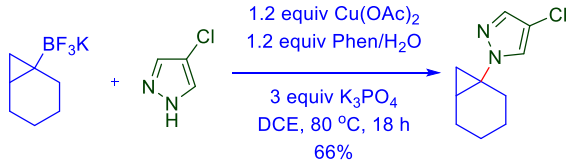
Example 5[15]



Example 6, Chan–Lam coupling between aryl boroxines and enolates as sp^3-carbon nucleophiles[18]



Example 7, Using tertiary trifluoroborates[20]



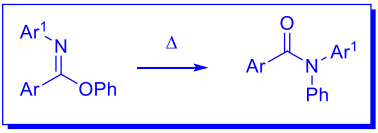
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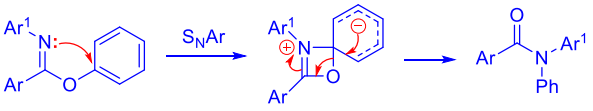
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Chapman Rearrangement

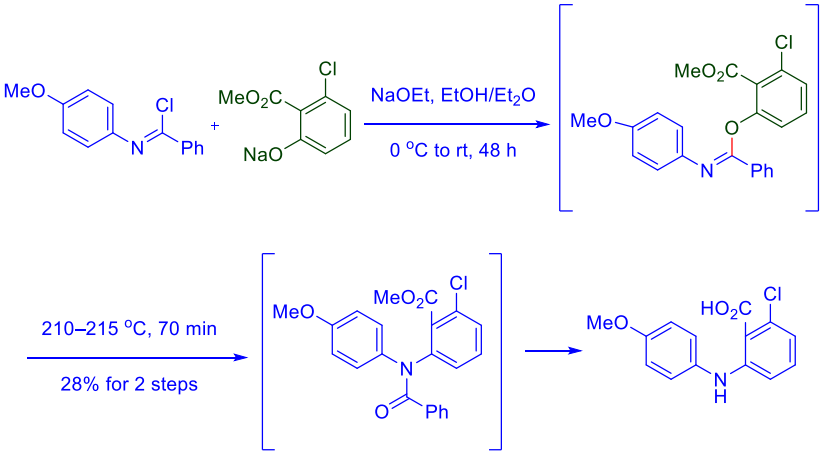
Thermal aryl rearrangement of *O*-aryliminoethers to amides.



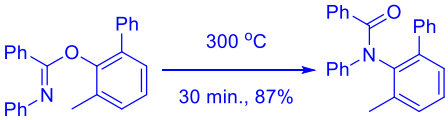
Mechanism:



Example 1[2]

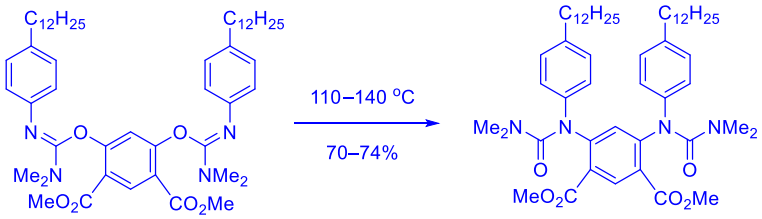


Example 2[4]

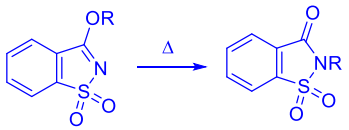


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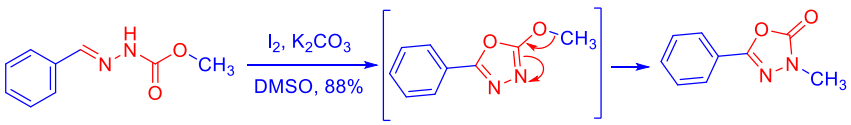
Example 3, Double Chapman rearrangement[9]



Example 4, Chapman-like thermal rearrangement[11]



Example 5, Chapman-like thermal rearrangement[12]

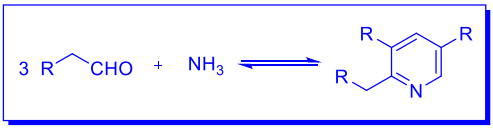


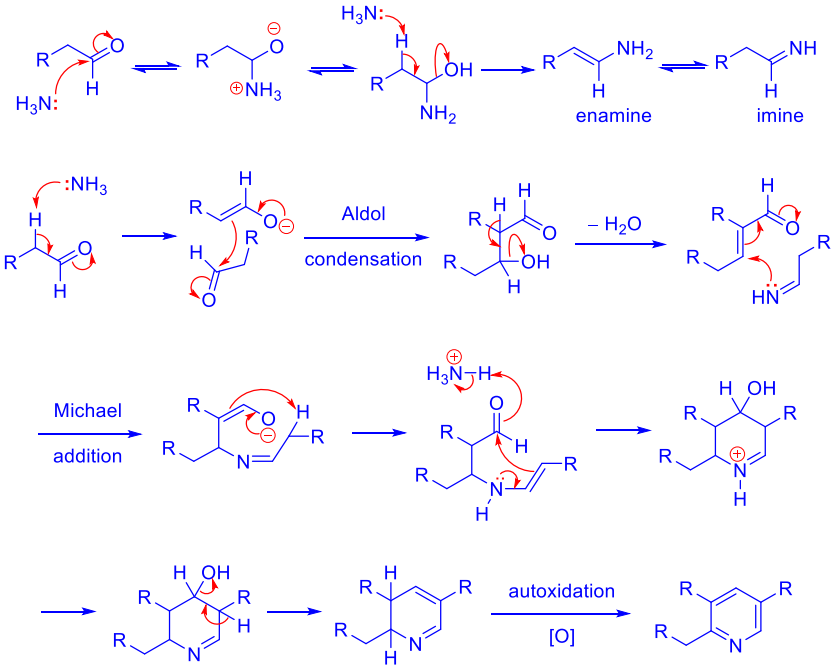
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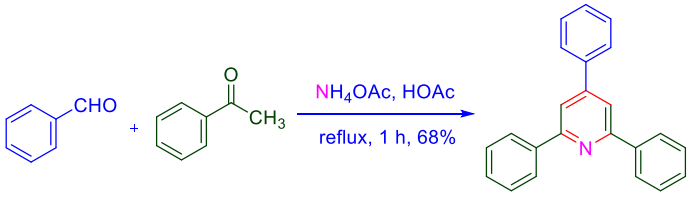
Chichibabin Pyridine Synthesis

Also known as the Chichibabin reaction. Condensation of aldehydes with ammonia to afford pyridines.



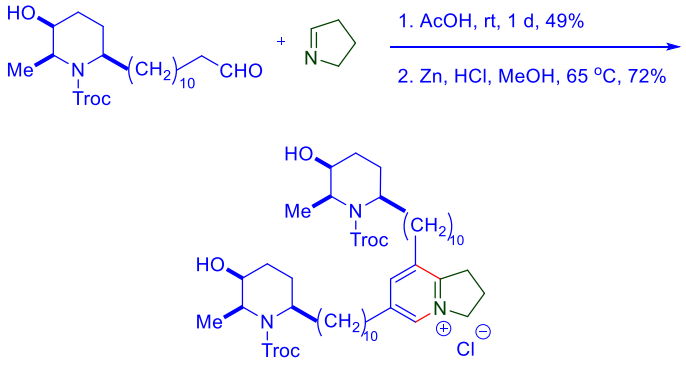


Example 1[3]

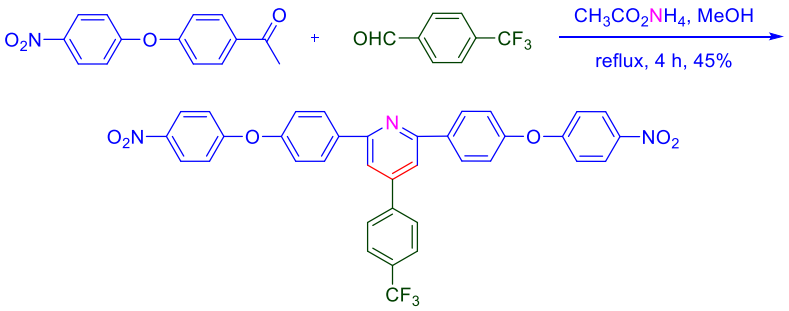


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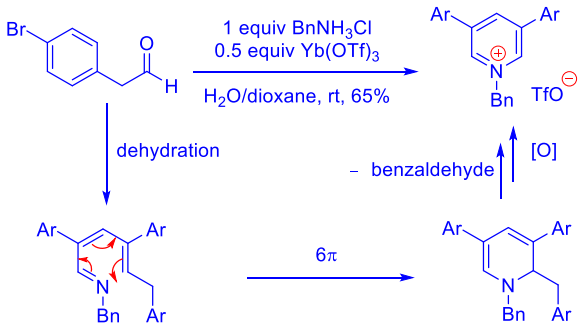
Example 2[7]



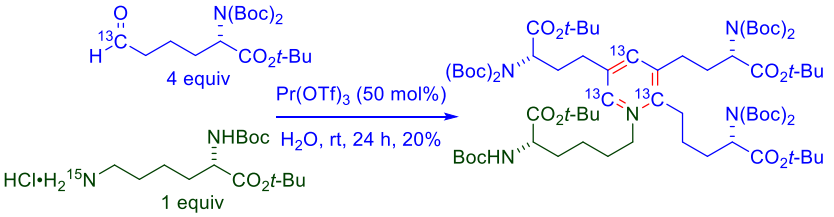
Example 3[8]



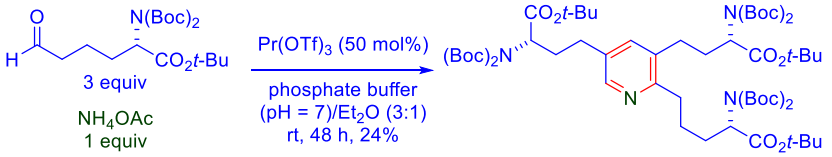
Example 4, An abnormal Chichibabin reaction[9]



Example 5, Radiolabeled Chichibabin reaction[11]



Example 6, Radiolabeled Chichibabin reaction[13]

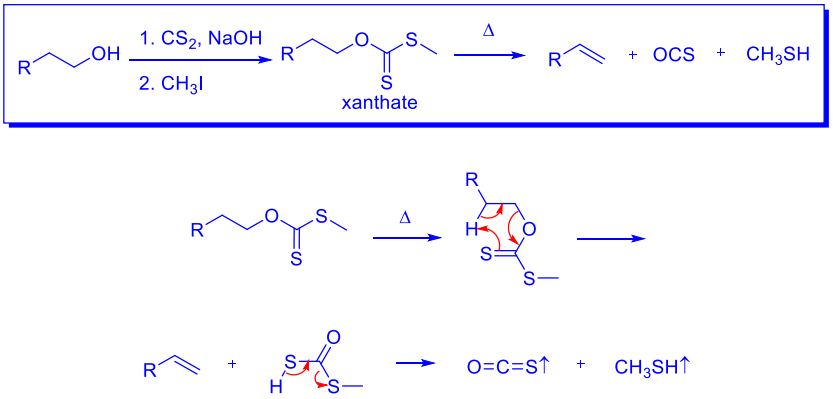


References

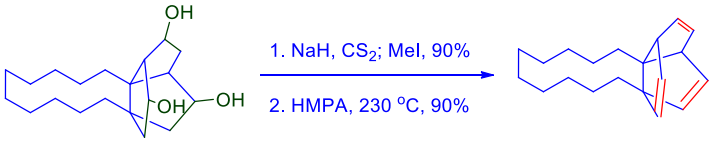
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Chugaev Elimination

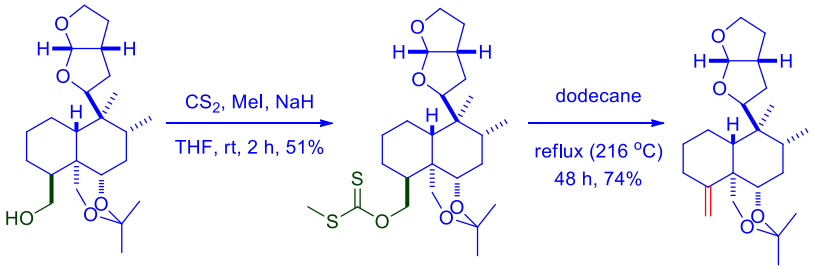
Thermal elimination of xanthates to olefins.



Example 1[4]

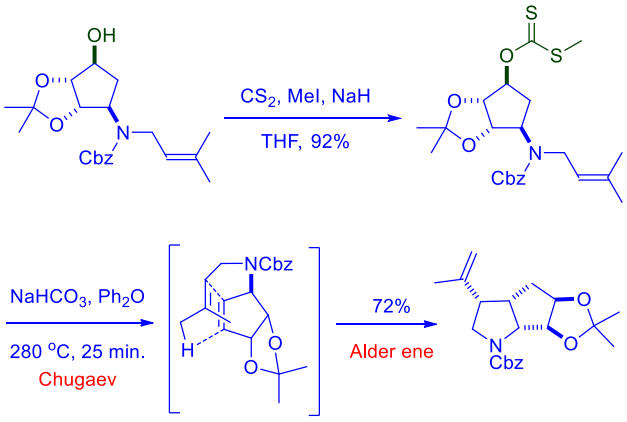


Example 2[5]

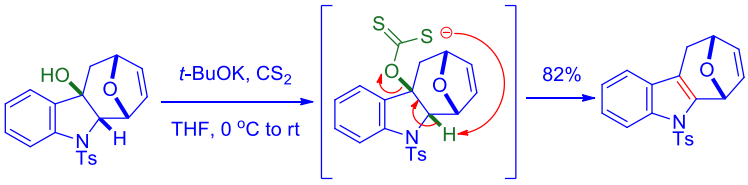


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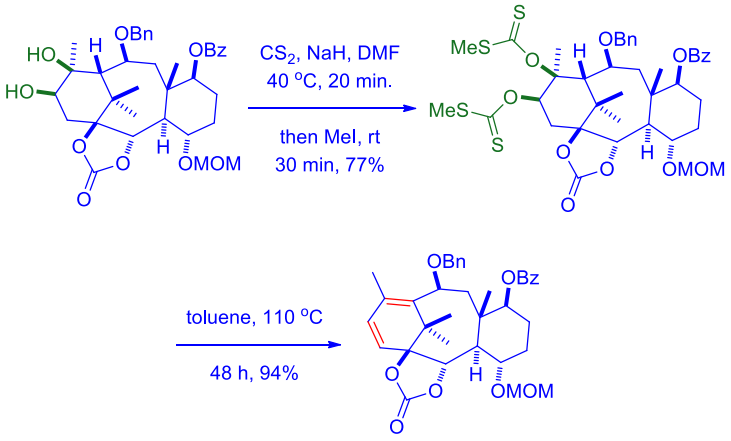
Example 3, Chugaev *syn*-elimination is followed by an intramolecular ene reaction[6]



Example 4, Aromatization via Chugaev elimination[10]



Example 5, Double Chugaev elimination[11]

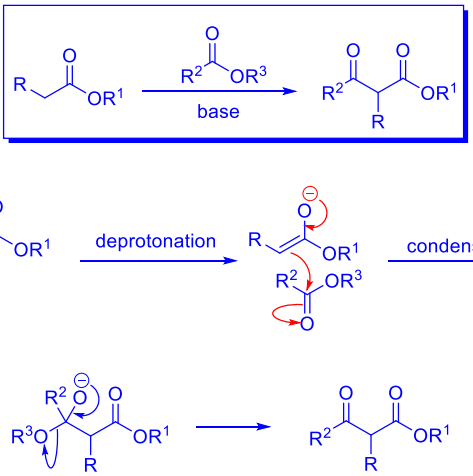


References

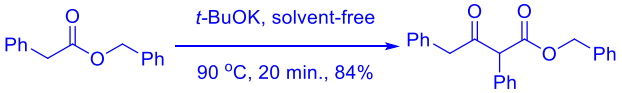
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Claisen Condensation

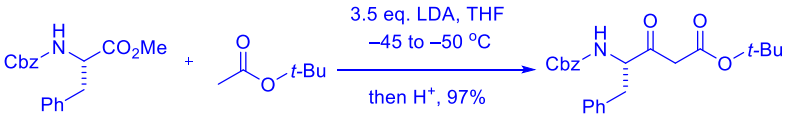
Base-catalyzed condensation of esters to afford β-keto esters.



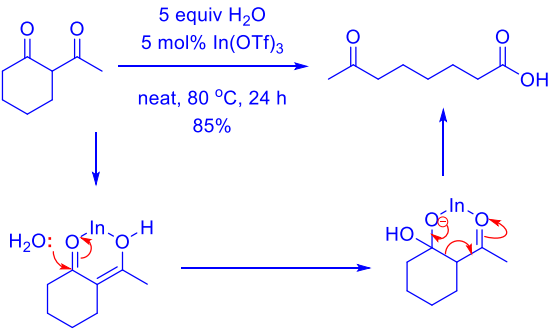
Example 1[4]



Example 2[6]

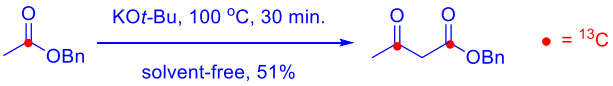


Example 3, Retro-Claisen condensation[9]

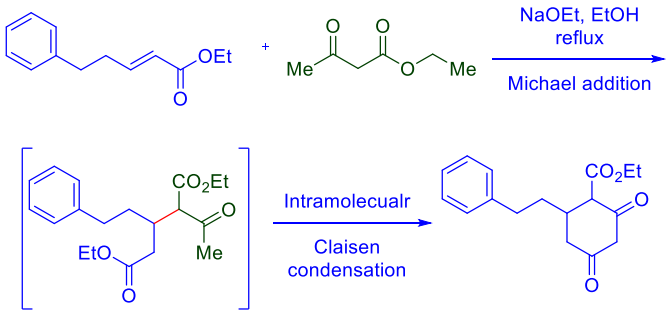


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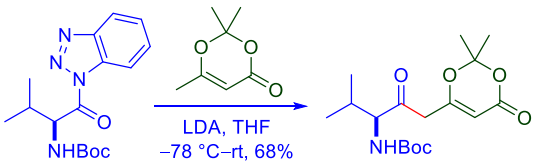
Example 4, Solvent-free Claisen condensation[10]



Example 5, Intramolecualar Claisen condensation (Dieckmann condensation)[11]



Example 6, Vinylogous Claisen condensation[12]



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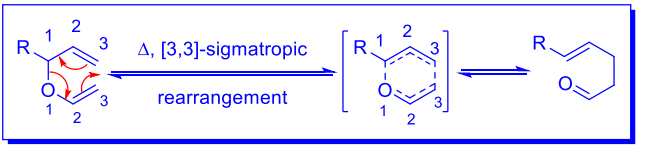
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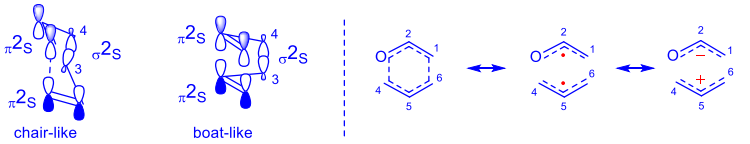
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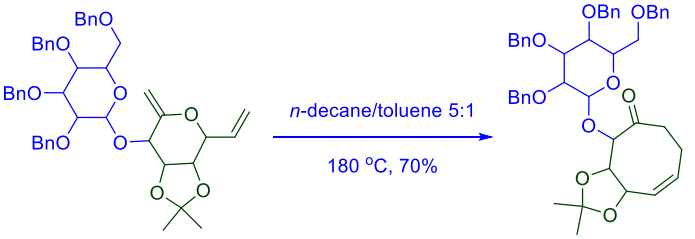
Claisen Rearrangement

The Claisen, *para*-Claisen rearrangements, Belluš–Claisen rearrangement; Corey–Claisen, Eschenmoser–Claisen rearrangement, Ireland–Claisen, Kazmaier–Claisen, Saucy–Claisen; orthoester Johnson–Claisen, along with the Carroll rearrangement, belong to the category of *[3,3]-sigmatropic rearrangements*. The Claisen rearrangement is a concerted process and the arrow pushing here is merely illustrative.

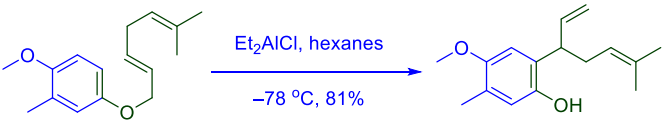




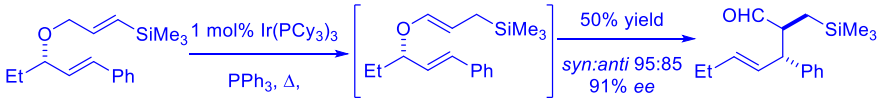
Example 1[7]



Example 2[8]

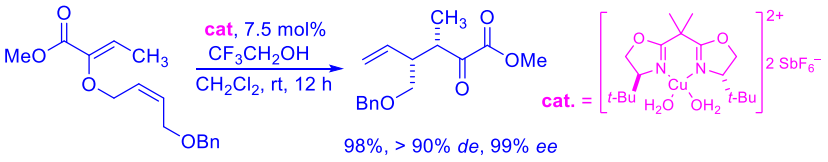


Example 3[9]

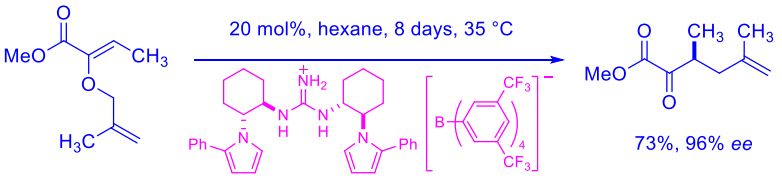


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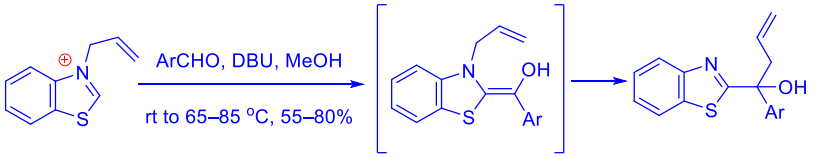
Example 4, Asymmetric Claisen rearrangement[10]



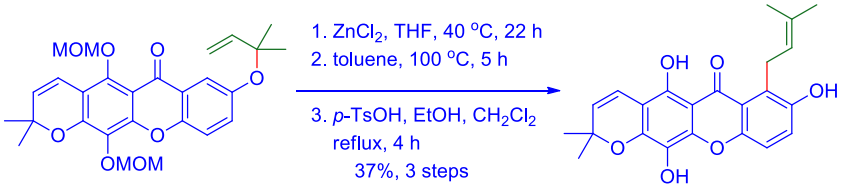
Example 5, Asymmetric Claisen rearrangement[11]



Example 6[13]



Example 7, Introduction of the prenyl group[14]



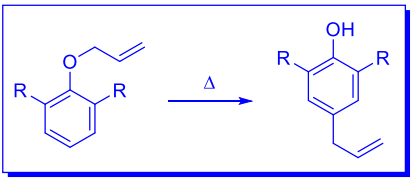
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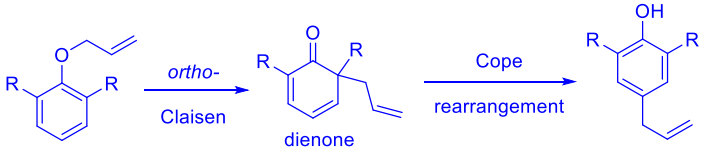
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para-*Claisen Rearrangement*

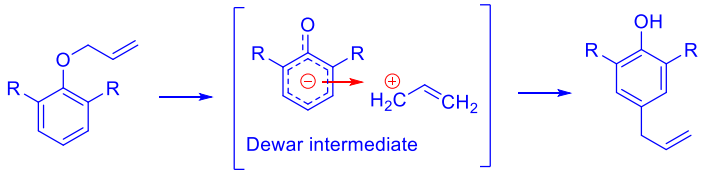
Further rearrangement of the normal *ortho*-Claisen rearrangement product gives the *para*-Claisen rearrangement product.



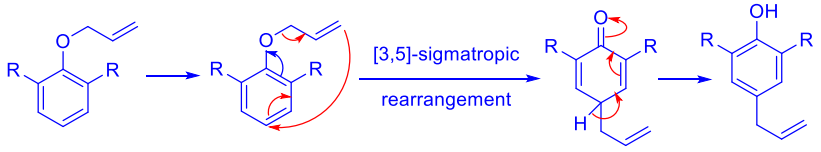
Mechanism 1:



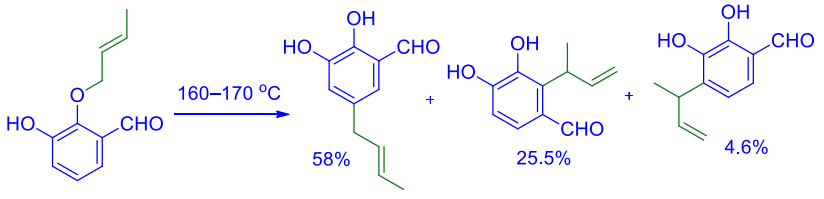
Mechanism 2:



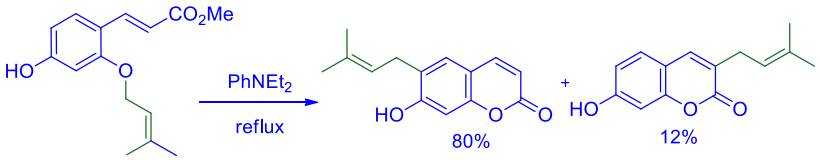
Mechanism 3:



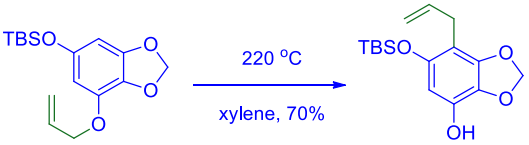
Example 1[6]



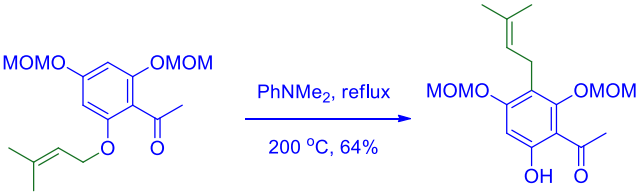
Example 2[7]



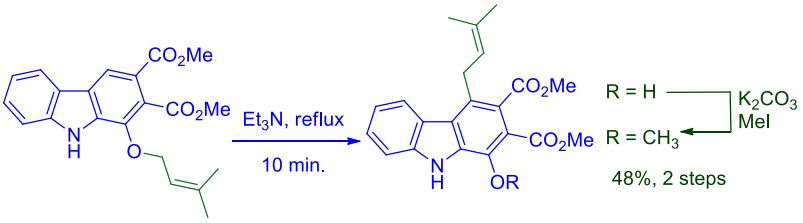
Example 3[8]



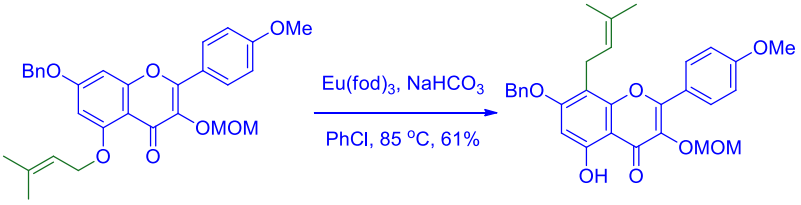
Example 4[10]



Example 5[11]



Example 6, fod = 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate = Siever′s reagent[12]

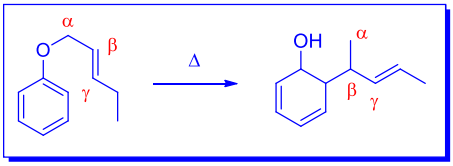


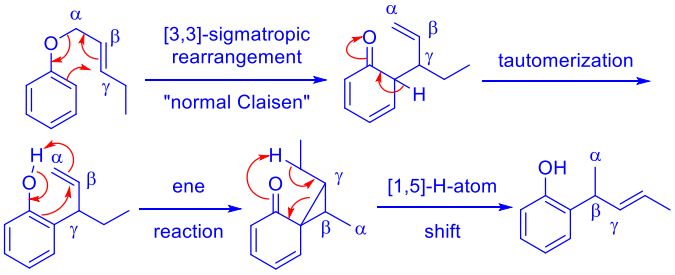
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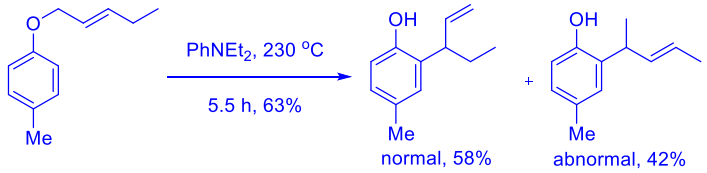
Abnormal Claisen Rearrangement

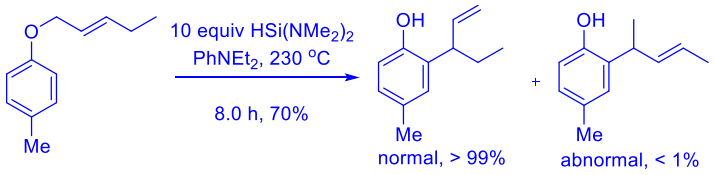
Further rearrangement of the normal Claisen rearrangement product with the β-carbon becoming attached to the ring.



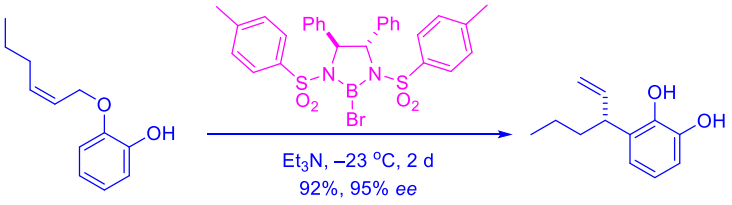


Example 1[3]

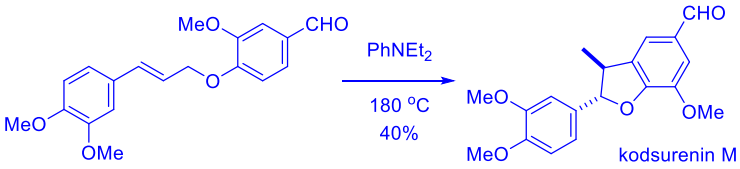




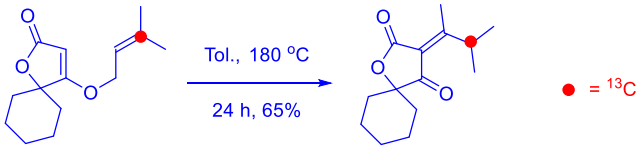
Example 2, Enantioselective aromatic Claisen rearrangement[4]



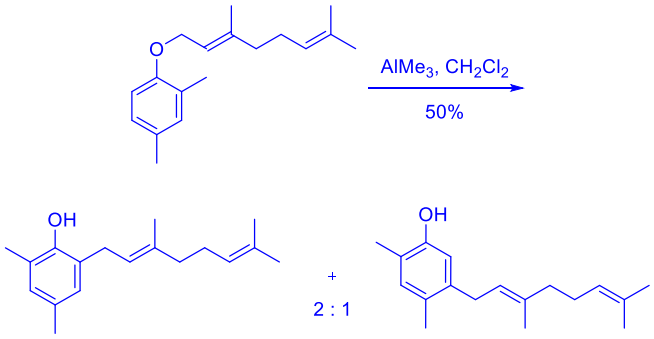
Example 3[5]



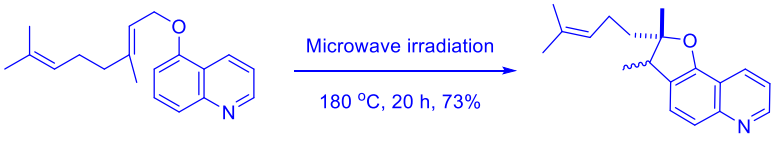
Example 4[6]



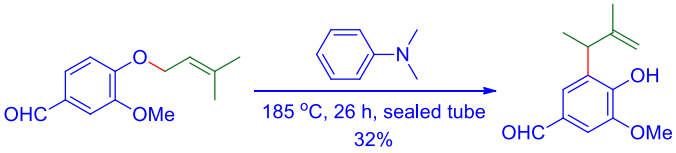
Example 5[7]



Example 6[10]



Example 7[11]

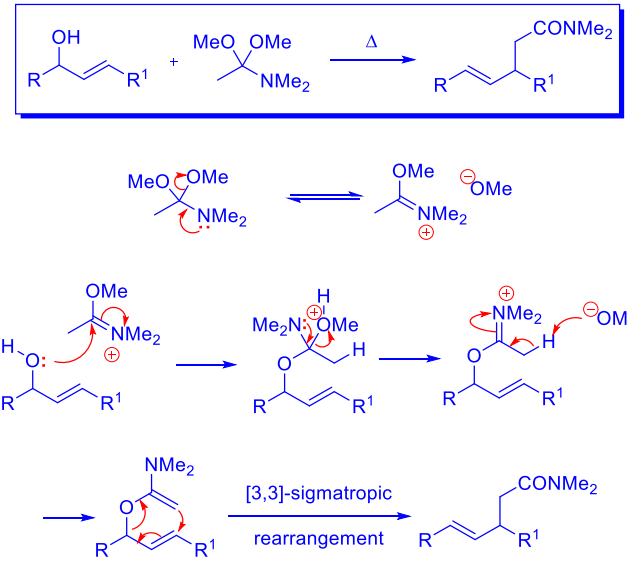


References

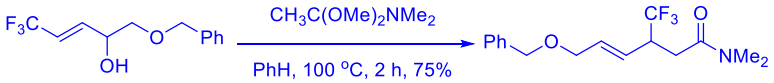
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Eschenmoser–Claisen Amide Acetal Rearrangement

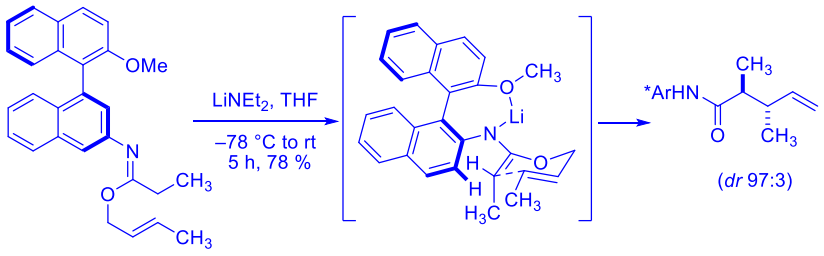
[3,3]-Sigmatropic rearrangement of *N,O*-ketene acetals to yield γ,δ-unsaturated amides. Since Eschenmoser was inspired by Meerwein′s observations on the interchange of amide, the Eschenmoser–Claisen rearrangement is sometimes known as the Meerwein–Eschenmoser–Claisen (MEC) rearrangement.



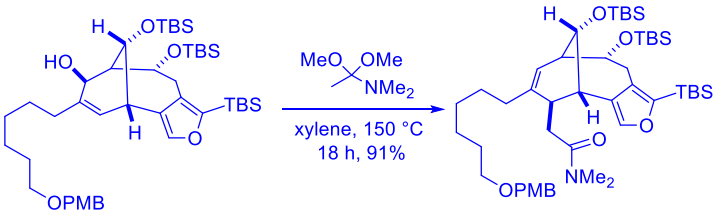
Example 1[4]



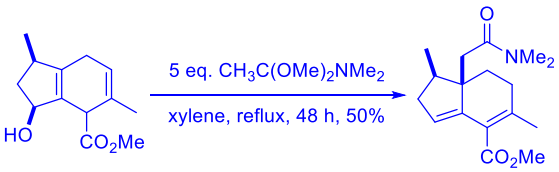
Example 2[5]



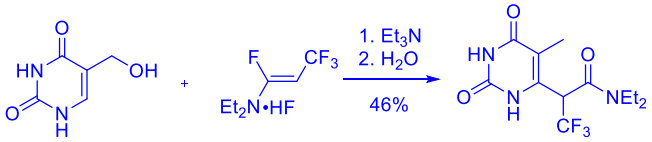
Example 3[6]



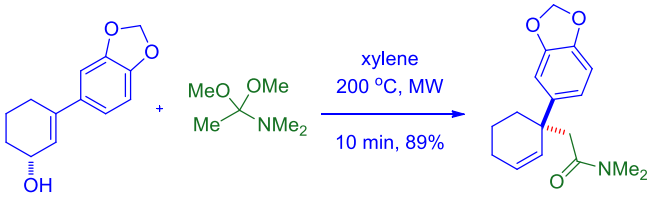
Example 4[8]



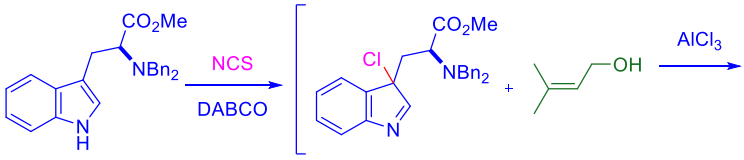
Example 5[9]

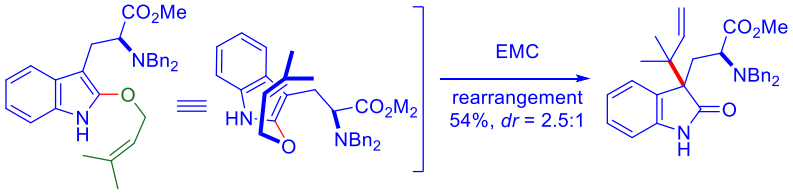


Example 6, Application in total synthesis[11]



Example 7, A one-pot diastereoselective Meerwein–Eschenmoser–Claisen (MEC) rearrangement[15]



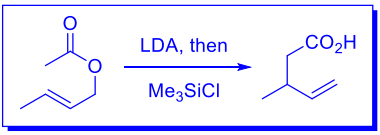


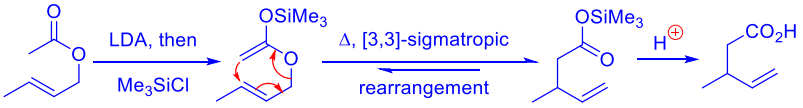
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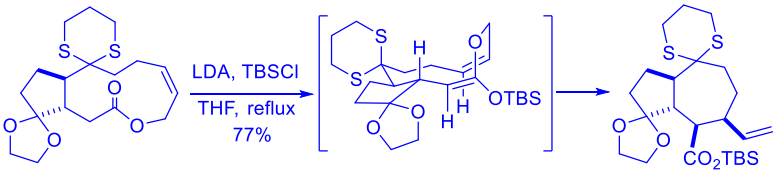
Ireland–Claisen (Silyl Ketene Acetal) Rearrangement

Rearrangement of allyl trimethylsilyl ketene acetal, prepared by reaction of allylic ester enolates with trimethylsilyl chloride, to yield γ,δ-unsaturated carboxylic acids. The Ireland–Claisen rearrangement seems to be advantageous to the other variants of the Claisen rearrangement in terms of *E/Z* geometry control and mild conditions.

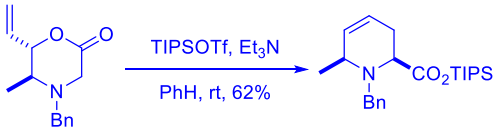




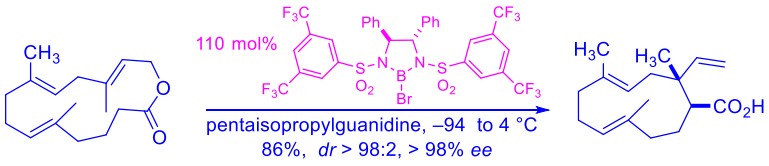
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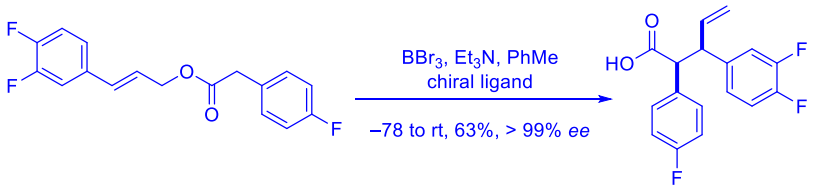
Example 2[3]



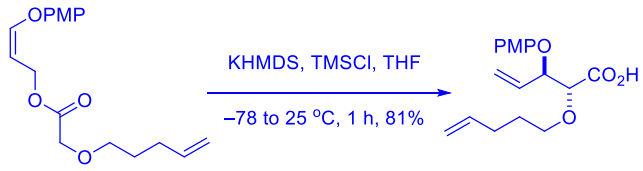
Example 3, Enantioselective ester enolate–Claisen Rearrangement[6]



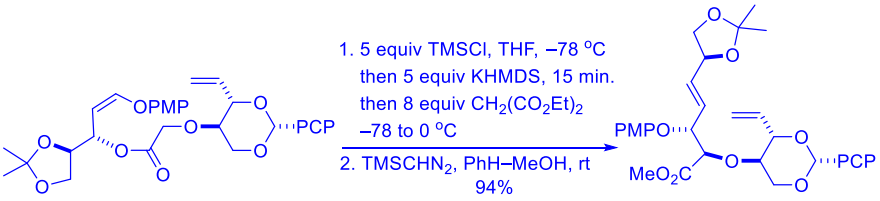
Example 4, A modified Ireland–Claisen rearrangement[8]



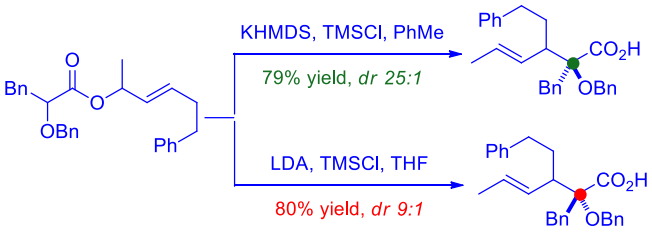
Example 5[9]



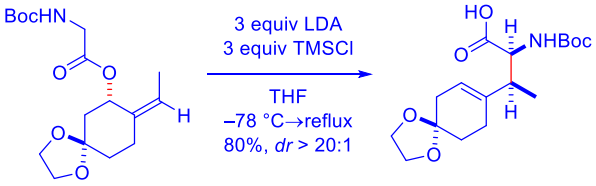
Example 6, Chirality-transferring Ireland–Claisen rearrangement[11]



Example 7, Stereodivergence in the Ireland–Claisen rearrangement of α-alkoxy esters[12]



Example 8, A highly diastereoselective Ireland–Claisen rearrangement[15]

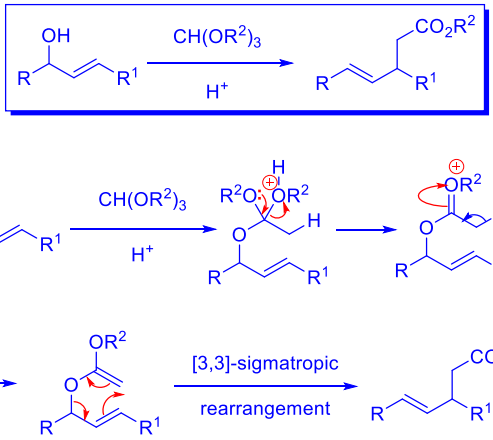


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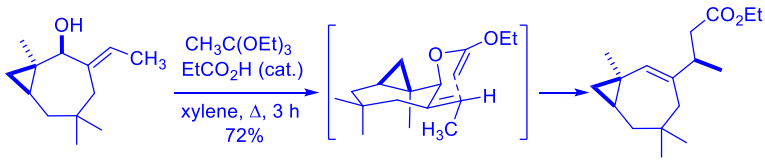
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Johnson–Claisen Orthoester Rearrangement

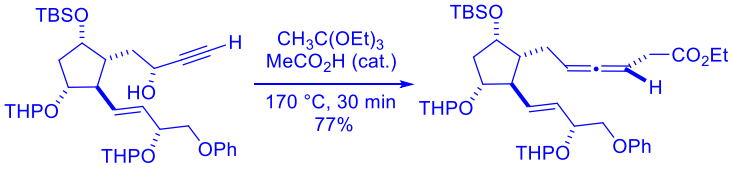
Heating of an allylic alcohol with an excess of trialkyl orthoacetate in the presence of trace amounts of a weak acid gives a mixed orthoester. Mechanistically, the orthoester loses alcohol to generate the ketene acetal, which undergoes [3,3]-sigmatropic rearrangement to give a γ,δ-unsaturated ester.



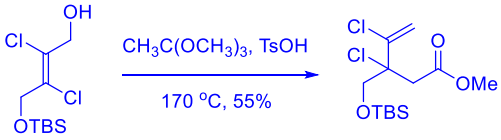
Example 1[2]



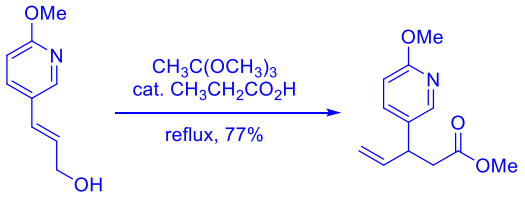
Example 2[3]



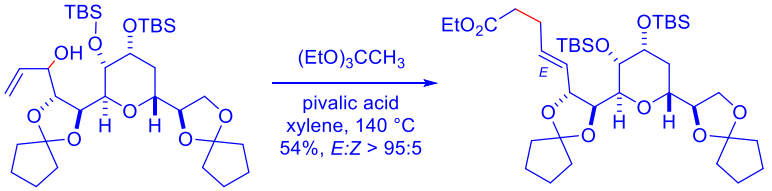
Example 3[4]



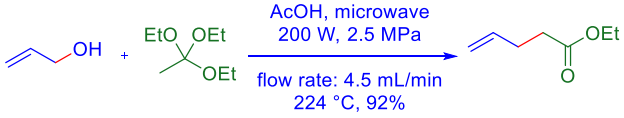
Example 4[9]



Example 5[10]



Example 6. Scalable microwave-assisted Johnson–Claisen rearrangement[11]



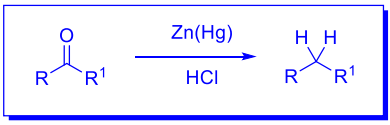
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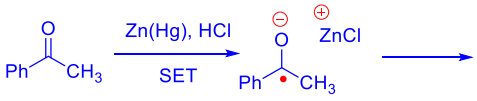
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Clemmensen Reduction

Reduction of aldehydes or ketones to the corresponding methylene compounds using amalgamated zinc in hydrochloric acid.



The zinc-carbenoid mechanism:[3]

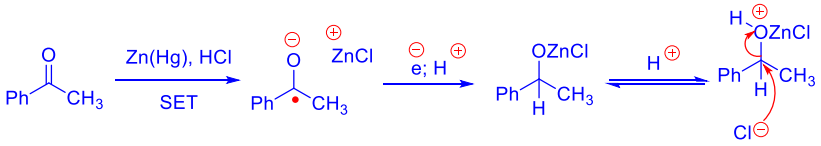


radical anion

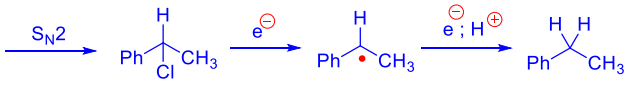


zinc-carbenoid

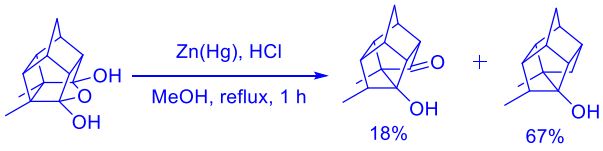
The radical anion mechanism:



radical anion

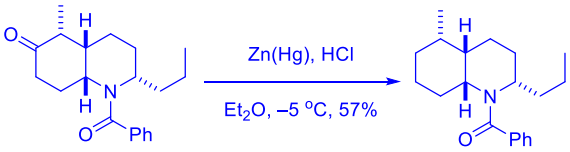


Example 1[5]

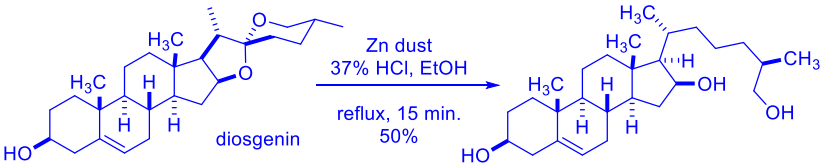


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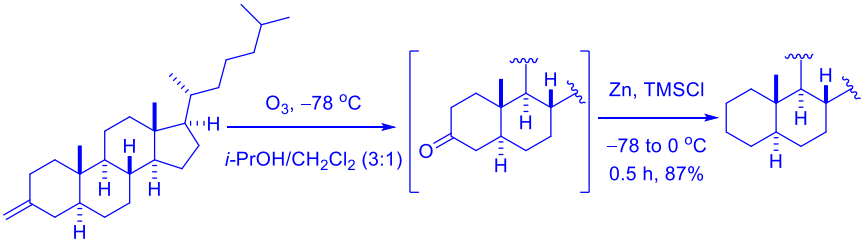
Example 2[6]



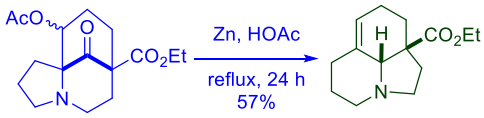
Example 3[7]



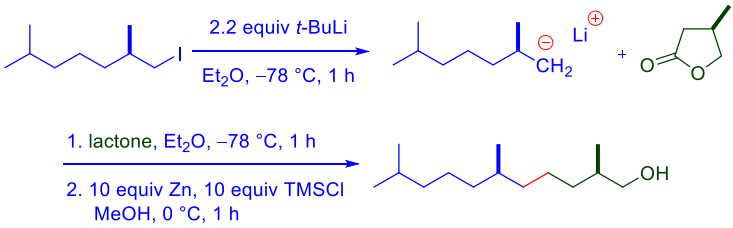
Example 4[9]



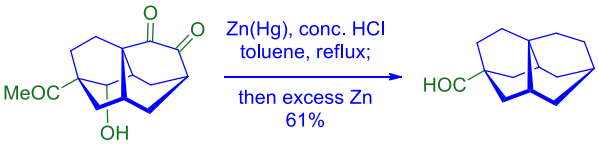
Example 5, Clemensen reductive rearrangement[10]



Example 6, Reuctive lactone alkylation[11]



Example 7, Toward the synthesis of dibarrelane[12]

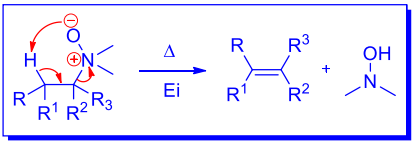


References

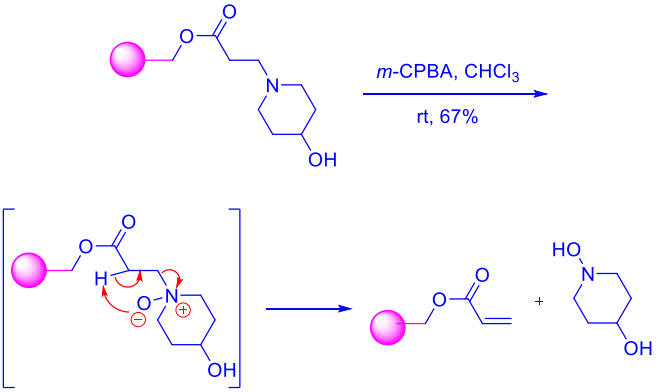
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Cope Elimination

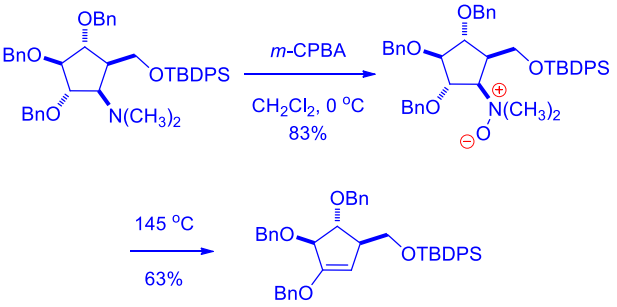
Thermal elimination of *N*-oxides to olefins and *N*-hydroxyl amines.



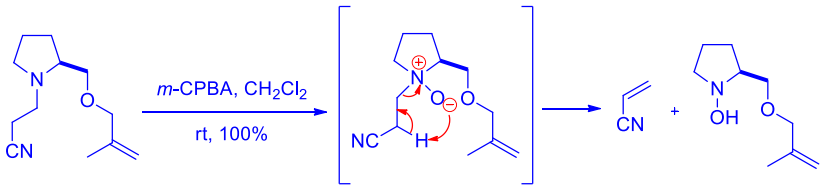
Example 1, Solid-phase Cope elimination[5]



Example 2[6]

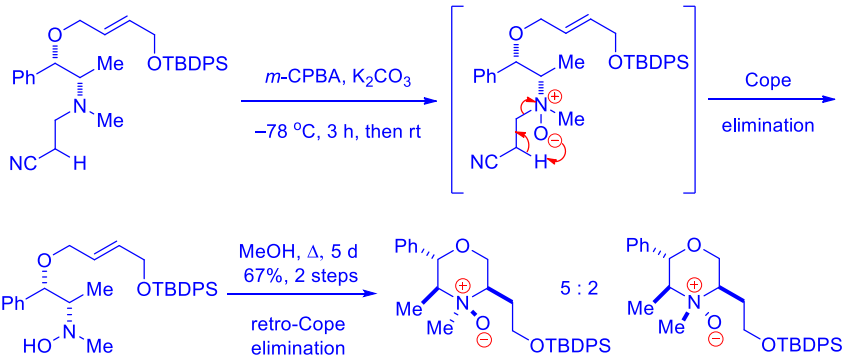


Example 3[8]

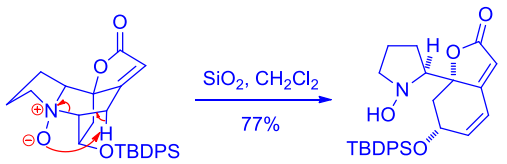


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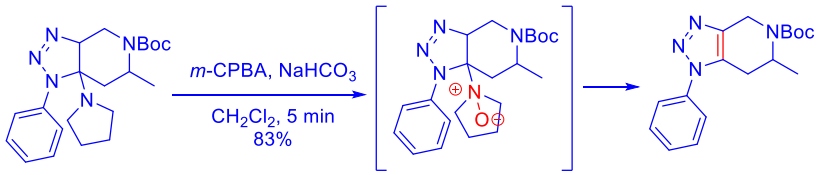
Example 4, Retro-Cope elimination[9]



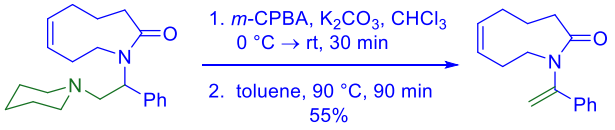
Example 5[12]



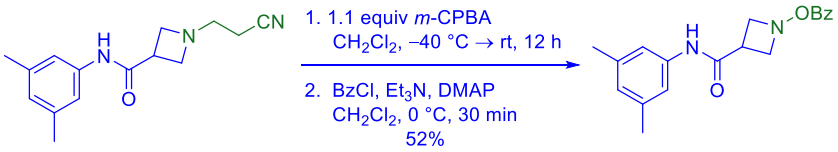
Example 6, Application in medicinal chemistry[13]



Example 7[13]



Example 8, Similar to Example 3[14]

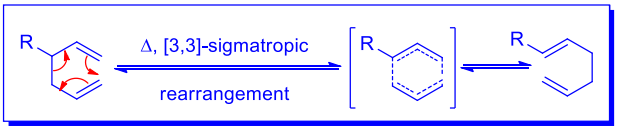


References

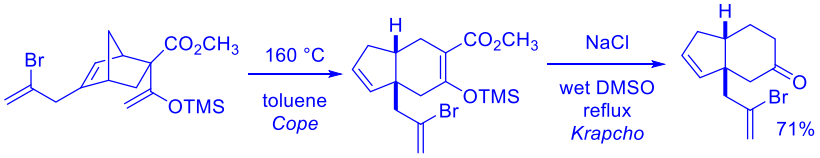
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Cope Rearrangement

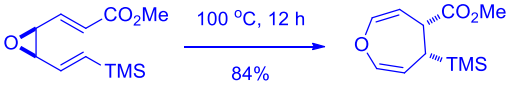
The Cope, aza-Cope, anionic oxy-Cope, and oxy-Cope rearrangements belong to the category of *[3,3]-sigmatropic rearrangements*. Since it is a concerted process, the arrow pushing here is only illustrative. This reaction is an equilibrium process. *Cf.* Claisen rearrangement.



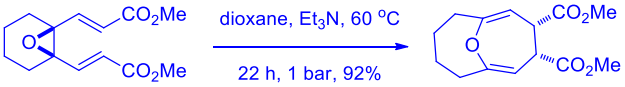
Example 1[4]



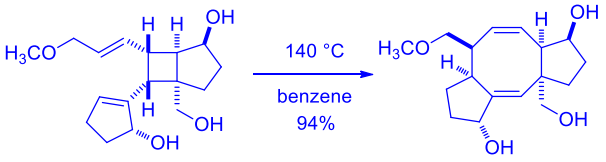
Example 2[6]



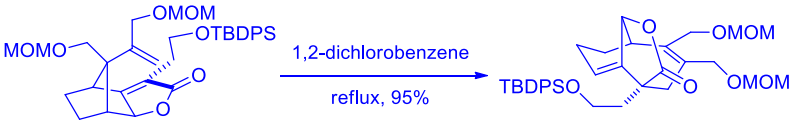
Example 3[9]



Example 4[10]

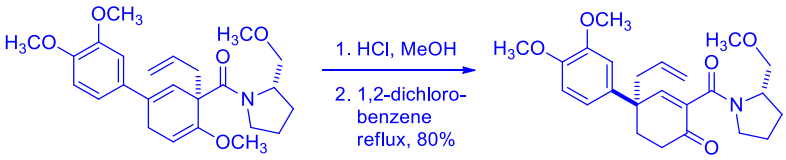


Example 5[11]

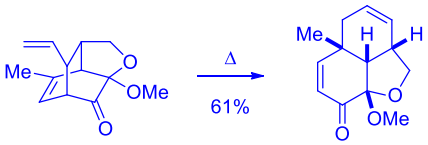


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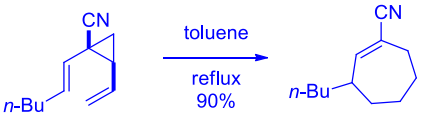
Example 6[12]



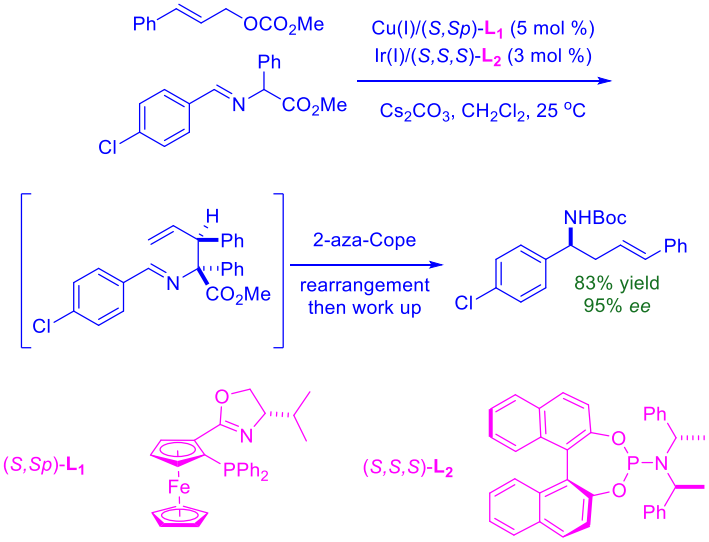
Example 7[14]



Example 8[15]



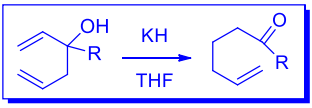
Example 9, Allylation, followed by 2-aza-Cope rearrangement[16]

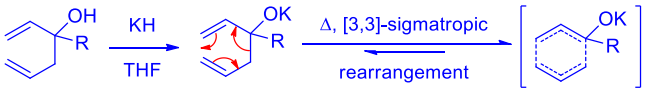


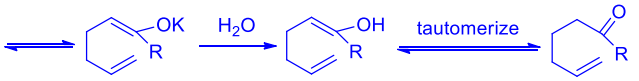
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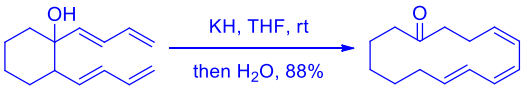
Anionic Oxy-Cope Rearrangement



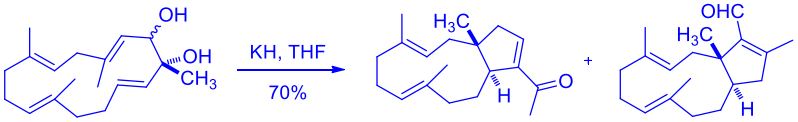




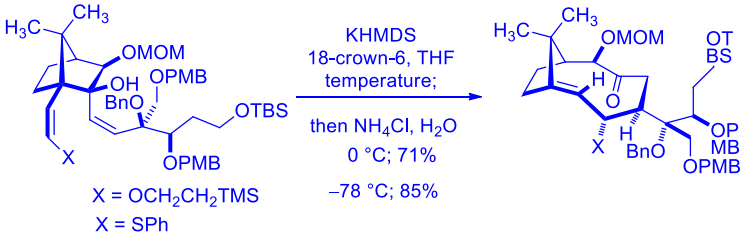
Example 1[1]



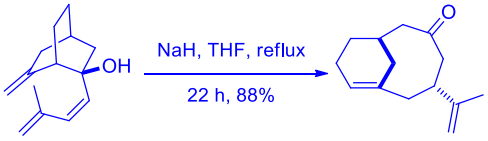
Example 2[4]



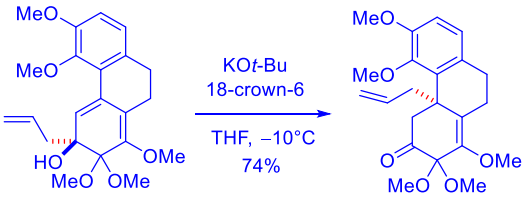
Example 3[5]



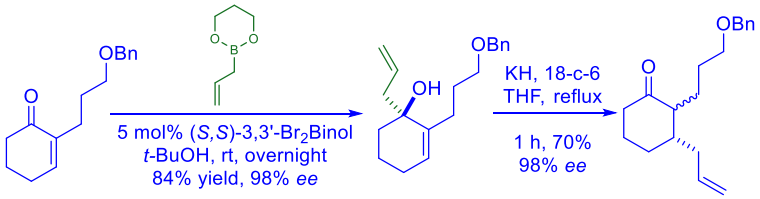
Example 4[8]



Example 5[9]



Example 6[11]

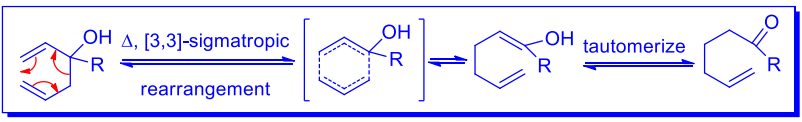


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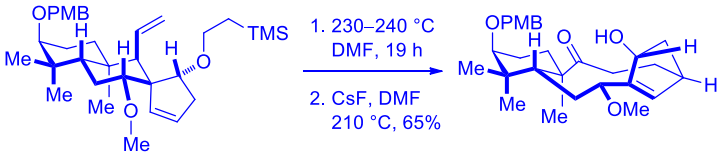
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Oxy-Cope Rearrangement

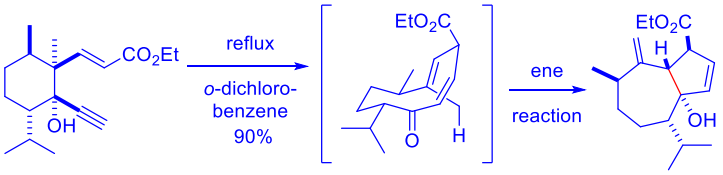
While the anionic oxy-Cope rearrangements work at low temperature, the oxy-Cope rearrangements require high temperature but provide a thermodynamic sink.



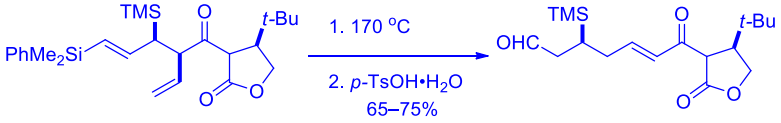
Example 1[2]



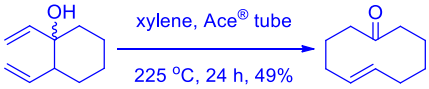
Example 2[3]



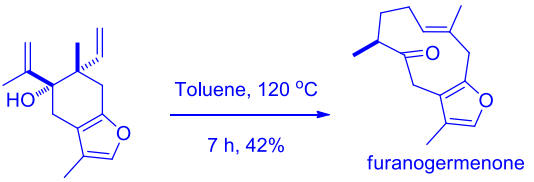
Example 3[4]



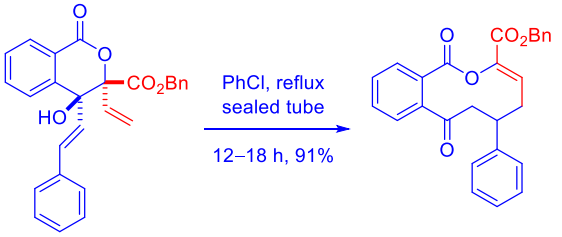
Example 4[6]



Example 5[8]



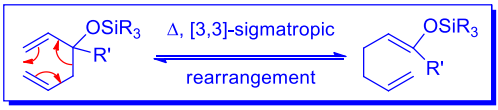
Example 6, Thermally induced oxy-Cope ring-expansion[8]



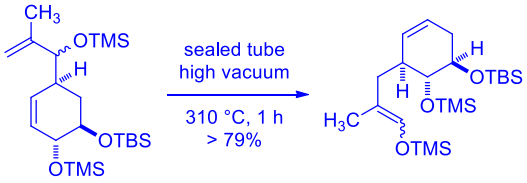
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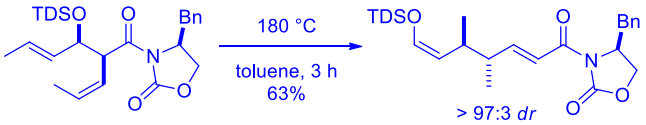
Siloxy-Cope Rearrangement



Example 1[1]

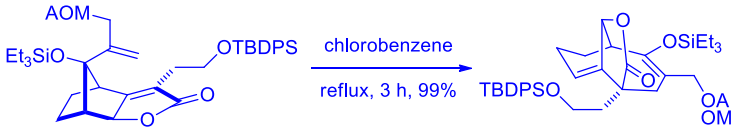


Example 2[2]



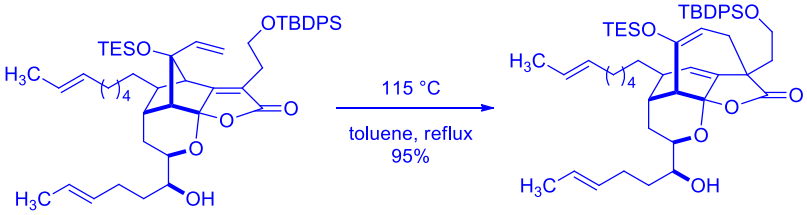
TDS = thexyldimethylsilyl

Example 3[3]

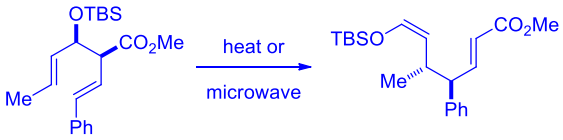


AOM = *p*-Anisyloxymethyl = *p*-$MeOC_6H_4OCH_2$-

Example 4[4]



Example 5, Tandem aldol reaction/siloxy-Cope rearrangement[6]

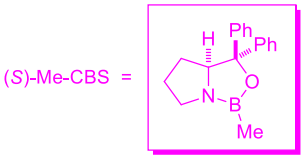


References

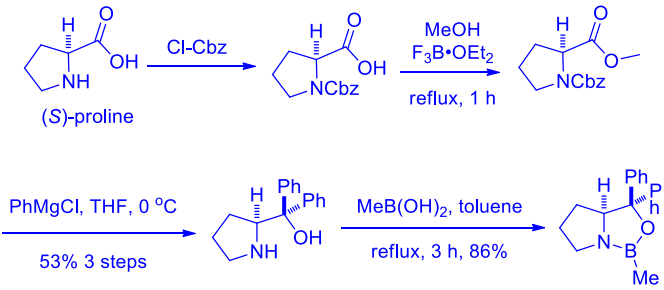
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Corey–Bakshi–Shibata (CBS) Reduction

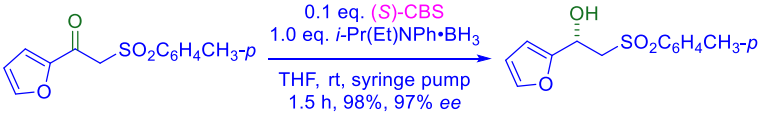
The CBS (Corey–Bakshi–Shibata) reagent is a chiral catalyst derived from proline. Also known as Corey's oxazaborolidine, it is used in enantioselective borane reduction of ketones, asymmetric Diels–Alder reactions and [3 + 2] cycloadditions.



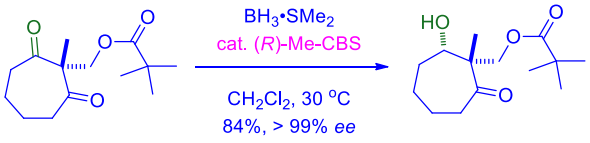
Preparation[1,3]



Example 1[6]

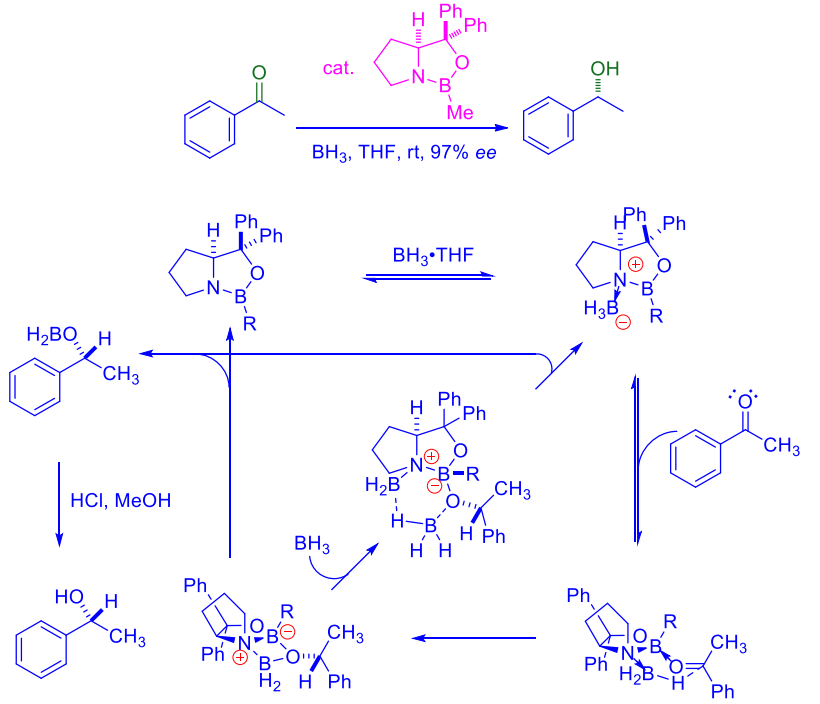


Example 2[9]

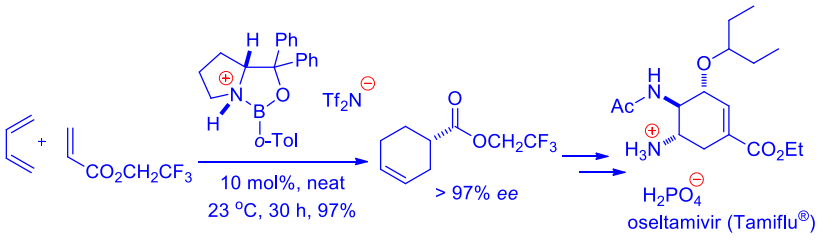


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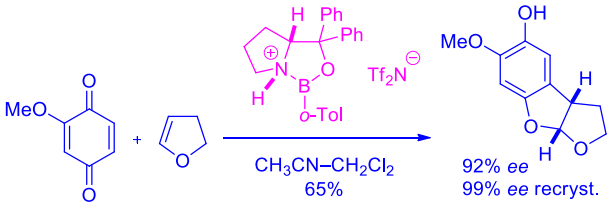
The mechanism and catalytic cycle:[1,3]



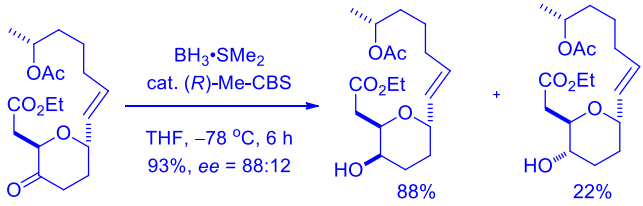
Example 3[11]



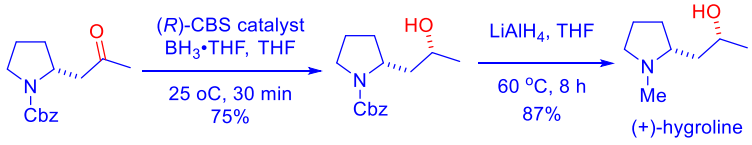
Example 4, Asymmetric [3 + 2]-cycloaddition[10]



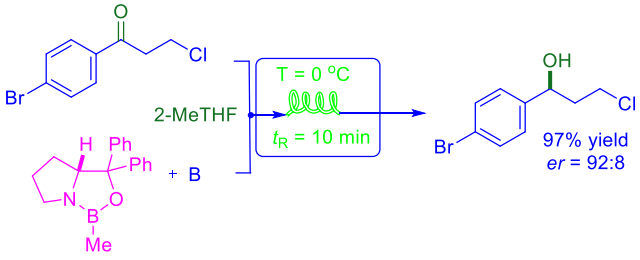
Example 5[13]



Example 6, Application in total synthesis of alkaloid[14]



Example 7, CBS reduction in flow microreactor system[15]



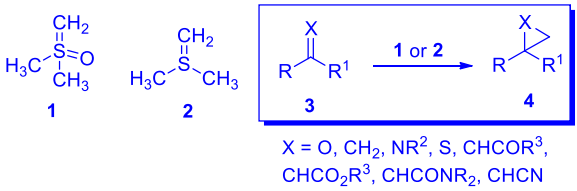
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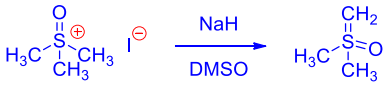
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Corey–Chaykovsky Reaction

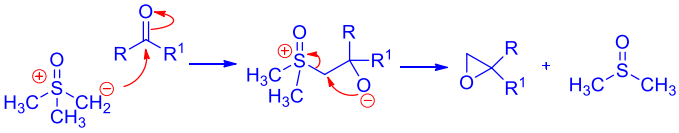
The Corey–Chaykovsky reaction entails the reaction of a sulfur ylide, either dimethylsulfoxonium methylide **1** (Corey′s ylide) or dimethylsulfonium methylide **2**, with electrophile **3** such as carbonyl, olefin, imine, or thiocarbonyl, to offer **4** as the corresponding epoxide, cyclopropane, aziridine, or thiirane.



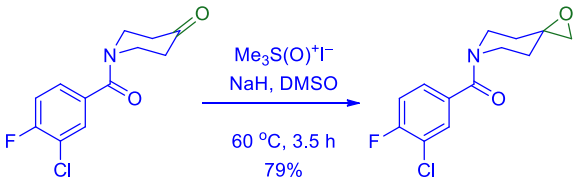
Preparation[1]



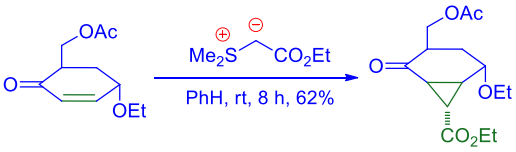
Mechanism[1]



Example 1, Epoxide from ketone[11]

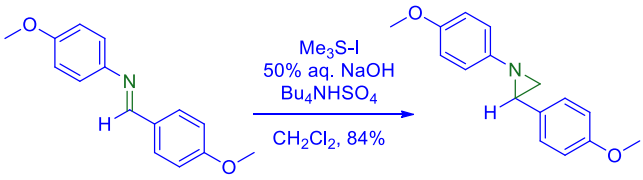


Example 2, Cyclopropane from olefin[9]

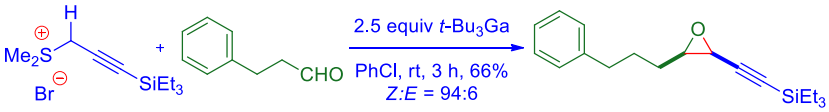


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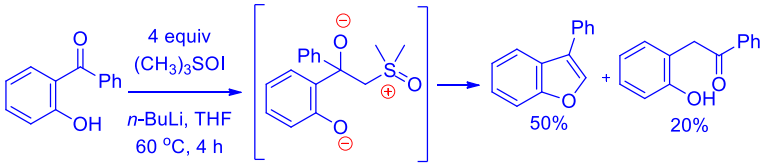
Example 3, Aziridine from aza-Corey–Chaykovsky reaction[9]



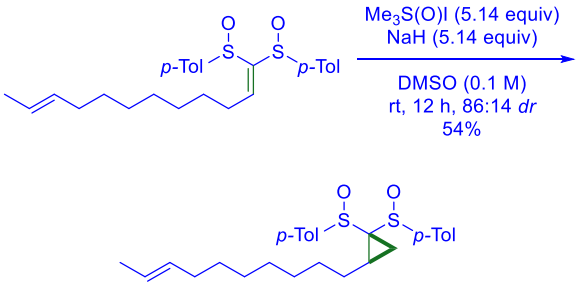
Example 4[12]



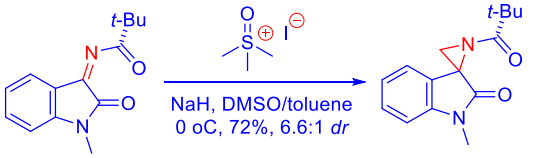
Example 5[13]



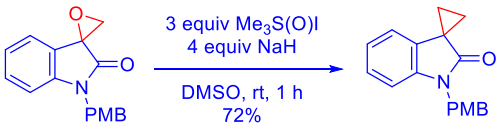
Example 6, Cyclopropane from olefin[14]



Example 7, Diastereoselective aziridination of ketimino ester[15]



Example 8, Corey–Chaykovsky reaction for one-pot access to spirocyclopropyl oxindoles[17]



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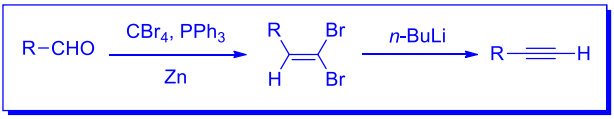
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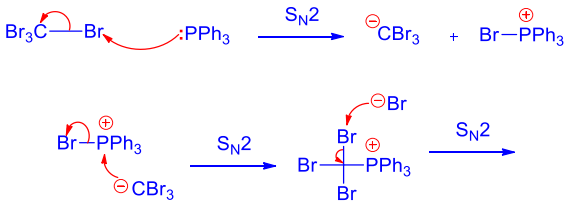
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Corey–Fuchs Reaction

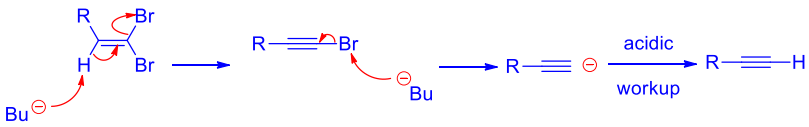
One-carbon homologation of an aldehyde to dibromoolefin, which is then treated with *n*-BuLi to produce a terminal alkyne.



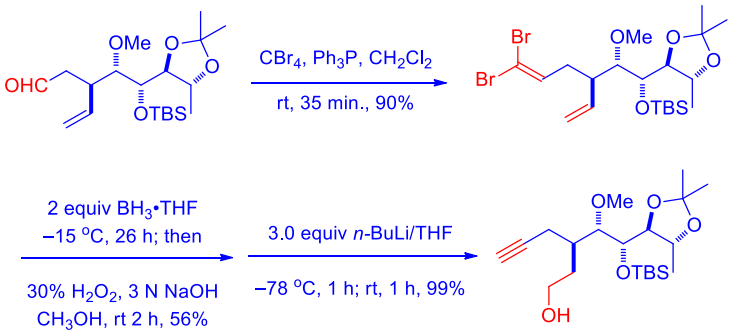


Wittig reaction



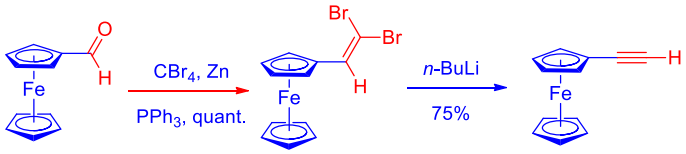


Example 1[3]

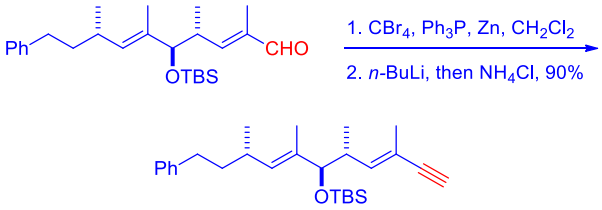


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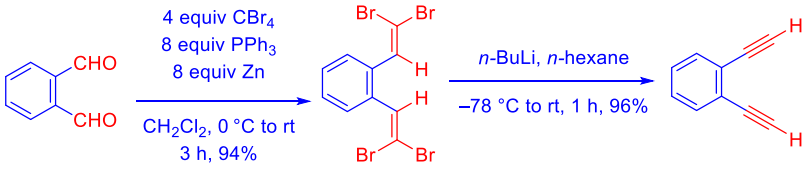
Example 2[7]



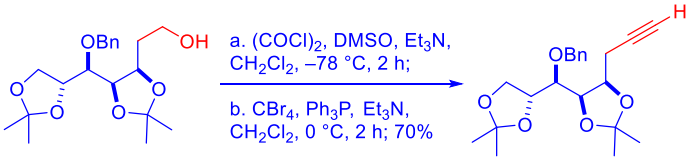
Example 3[8]



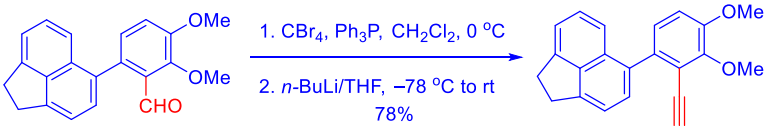
Example 4[10]



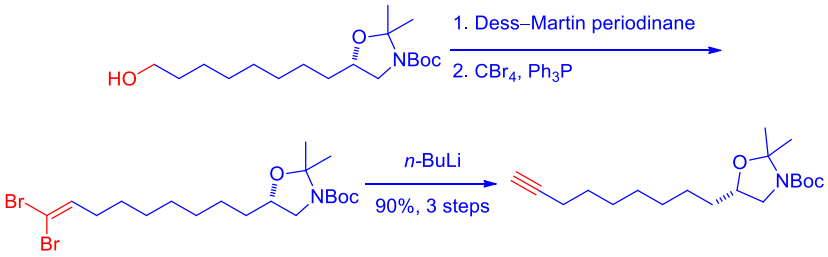
Example 5[12]



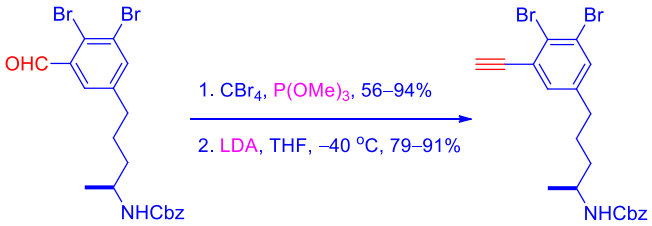
Example 6[12]



Example 7, Prepation of terminal alkyne as a Sonogashira precursor[14]



Example 8, Large-scale process Corey–Fuchs reaction[16]

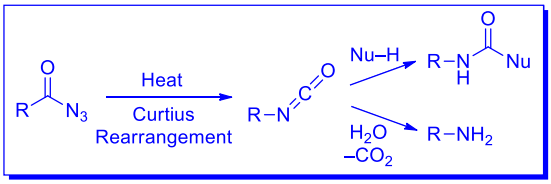


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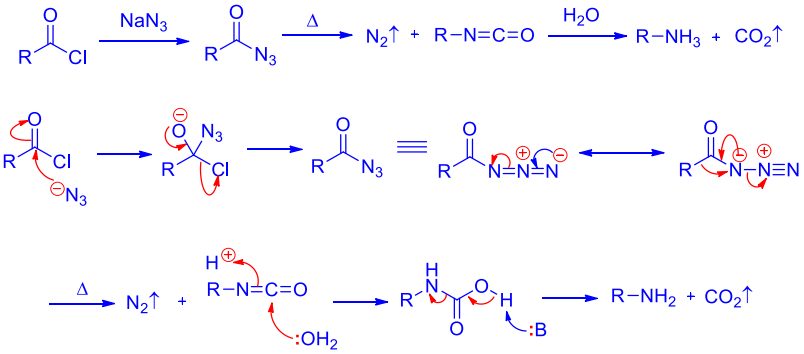
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Curtius Rearrangement

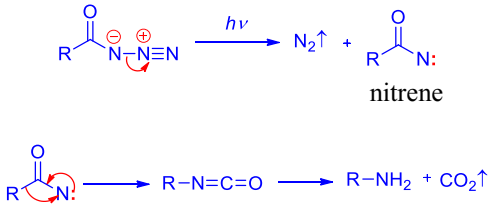
Alkyl-, vinyl-, and aryl-substituted acyl azides undergo thermal 1,2-carbon-to-nitrogen migration with extrusion of dinitrogen — the Curtius rearrangement — producing isocyantes. Reaction of the isocyanate products with nucleophiles, often *in situ*, provides carbamates, ureas, and other *N*-acyl derivatives. Alternatively, hydrolysis of the isocyanates leads to primary amines.



The thermal rearrangement:



The photochemical rearrangement:



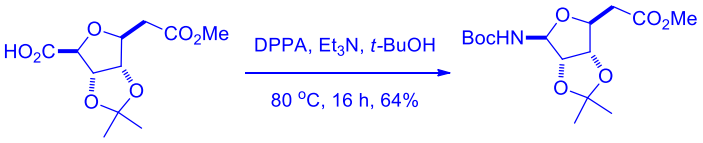
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Example 1, The Shioiri–Ninomiya–Yamada modification[2]

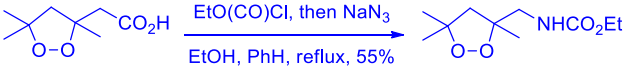


DPPA = diphenylphosphoryl azide

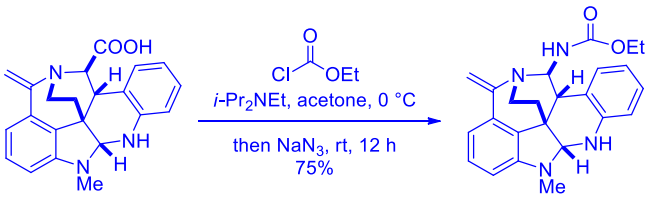
Example 2[3]



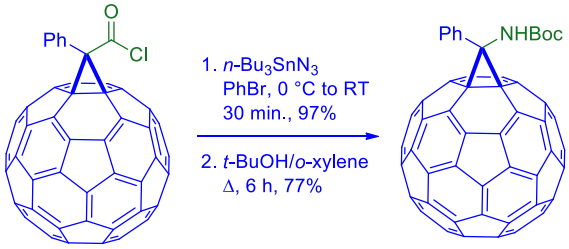
Example 3[4]



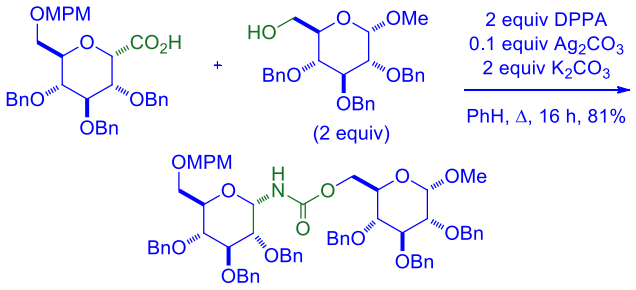
Example 4, The Weinstock variant of the Curtius rearrangement[6]



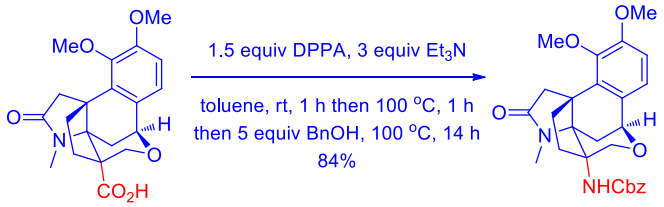
Example 5[7]



Example 6, The Lebel modification[8]



Example 7, Utility in total synthesis[9]

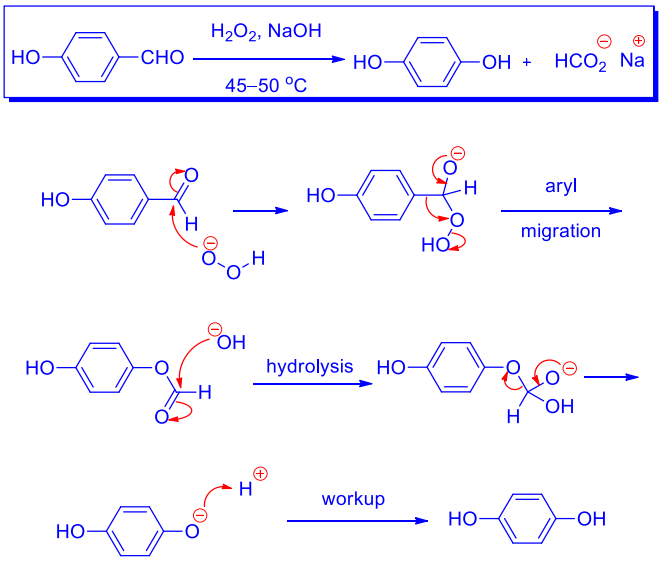


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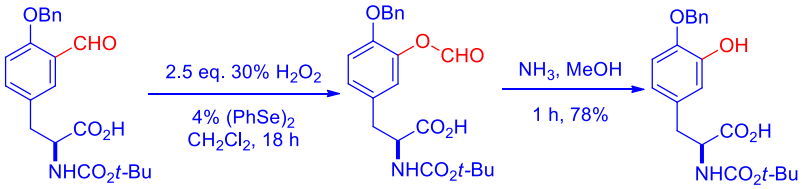
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Dakin Oxidation

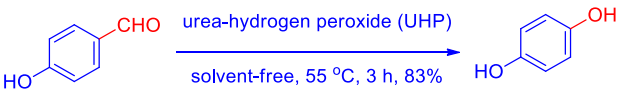
Oxidation of aryl aldehydes or aryl ketones to phenols using basic hydrogen peroxide conditions. *Cf.* A variant of the Baeyer–Villiger oxidation.



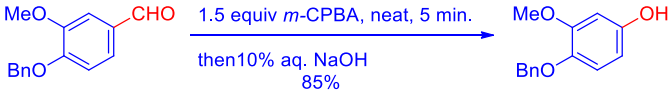
Example 1[6]



Example 2[7]

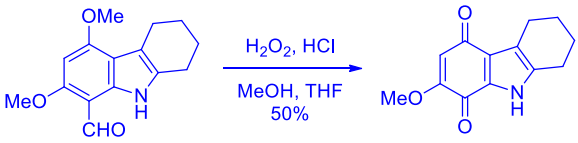


Example 3, Improved solvent-free Dakin oxidation protocol[9]

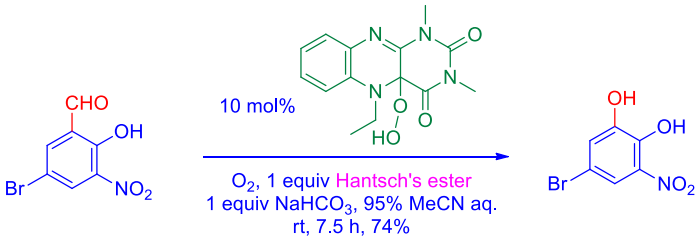


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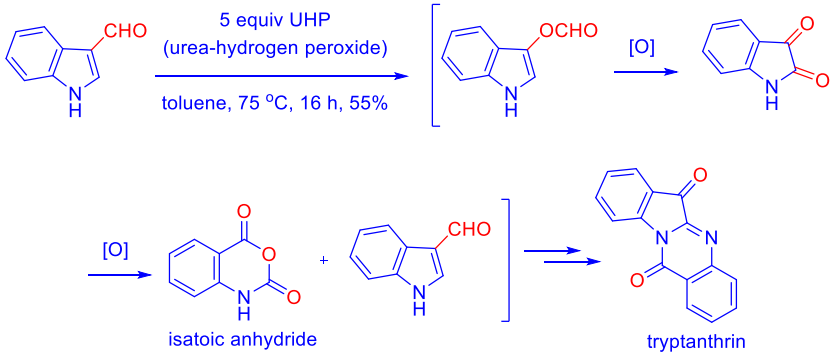
Example 4[10]



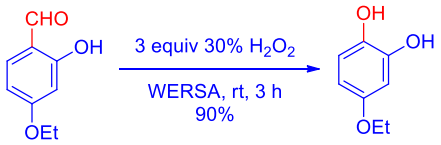
Example 5, Aerobic organocatalytic oxidation: flavin catalyst turnover by Hantsch′s ester[11]



Example 6, One-pot synthesis of tryptanthrin[12]



Example 7, Employing "Water Extract of Rice Straw Ash" (WERSA) as catalysts (for real!)[13]

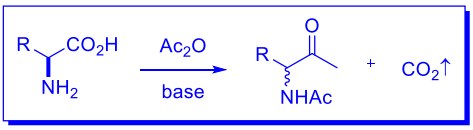


References

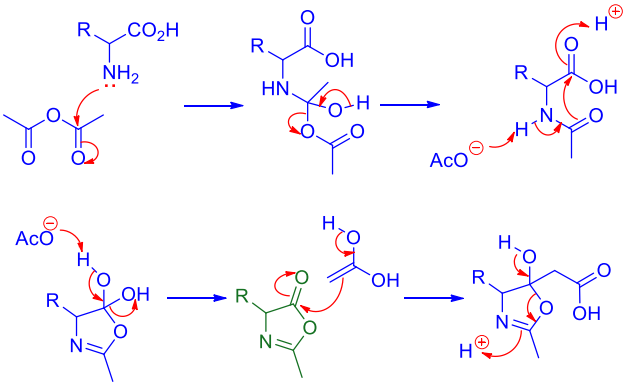
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Dakin–West Reaction

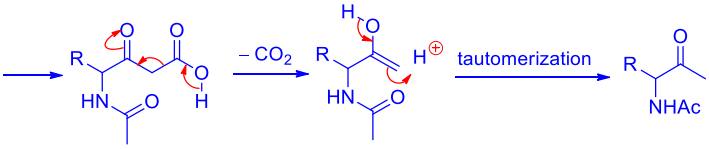
The direct conversion of an α-amino acid into the corresponding α-acetylamino-alkyl methyl ketone, *via* oxazolone (azalactone) intermediates. The reaction proceeds in the presence of acetic anhydride and a base, such as pyridine, with the evolution of CO_2. The reaction racemizes that chiral center as shown.



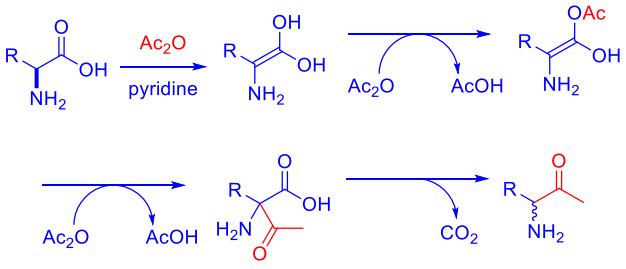
a. Mechanism proposed by Dakin and West[1]



oxazolone (azalactone) intermediate



b. Mechanism proposed by Levene and Steiger[2]

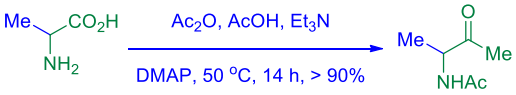


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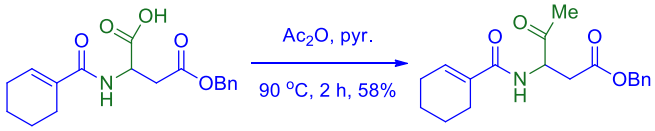
c. Mechanism proposed by Wiley for the reaction of *N*-acetyl sarcosine[3]



Example 1[5]



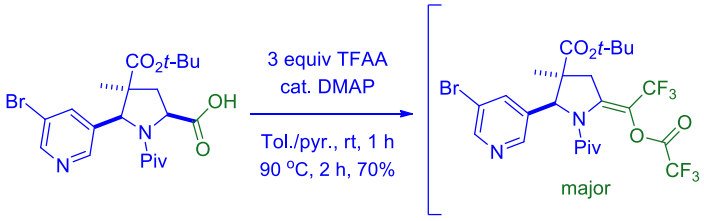
Example 2[7]

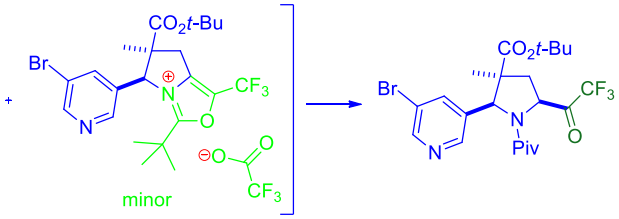


Example 3, A green Dakin–West reaction using the heteropoly acid catalyst, acetonitrile is a reactant[9]

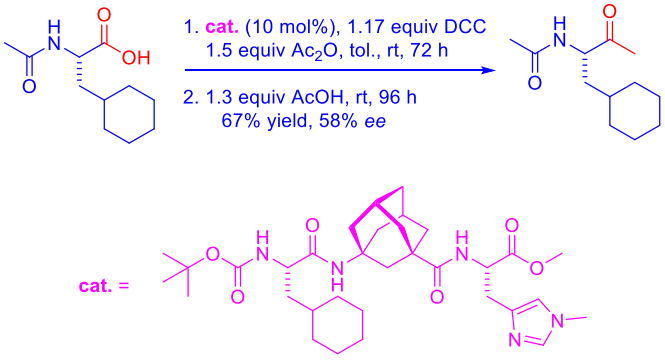


Example 4, A diasteroselective trifluoroacetylation of hghly substituted pyrrolidines[12]

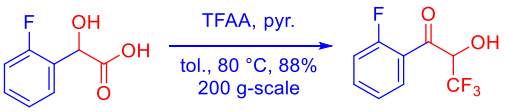




Example 5, Enantioselective Dakin–West reaction[13]



Example 6, Dakin–West reaction to make trifluoromethyl acyloin[14]



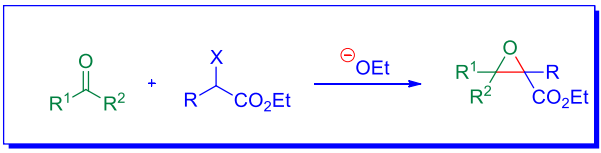
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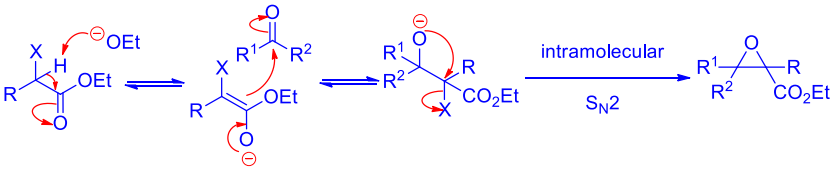
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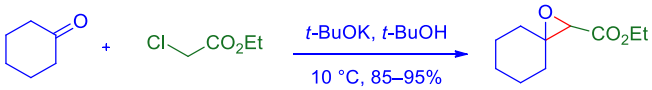
Darzens Condensation

α,β-Epoxy esters (glycidic esters) from base-catalyzed condensation of α-haloesters with carbonyl compounds.

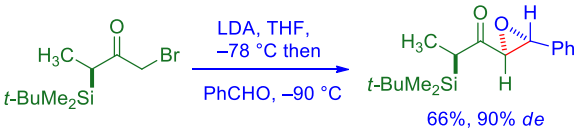




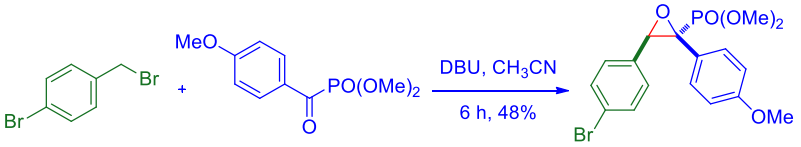
Example 1[4]



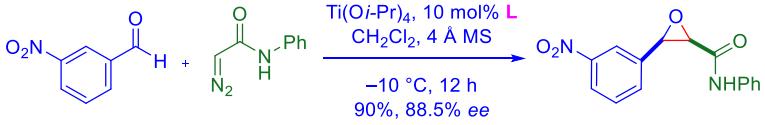
Example 2[6]



Example 3, the phenyl ring substituting for the carbonyl to acidify the protons[10]



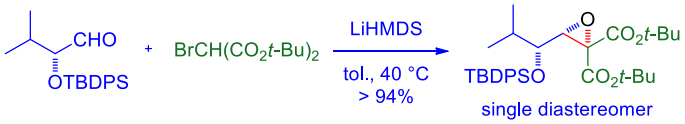
Example 4, A variation[11]



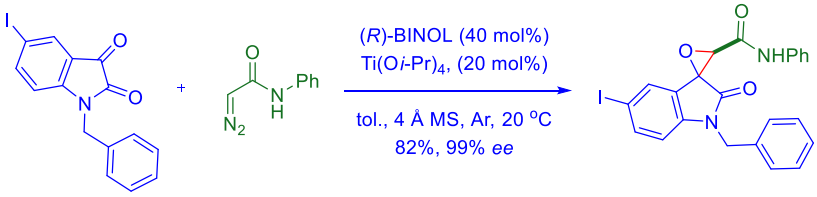
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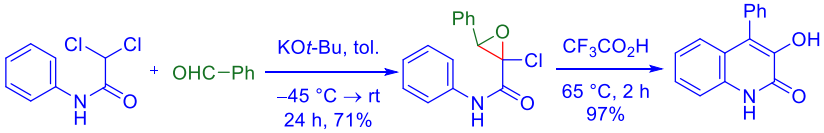
Example 5, Substrate-controlled stereoselective Darzens reaction[12]



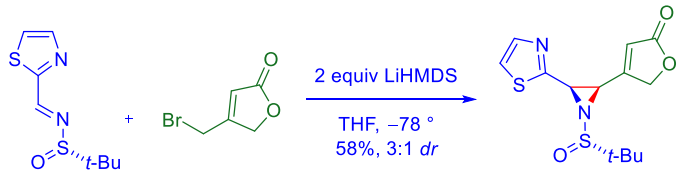
Example 6, Asymmetric Darzens reaction between isatin and diazoacetamide[13]



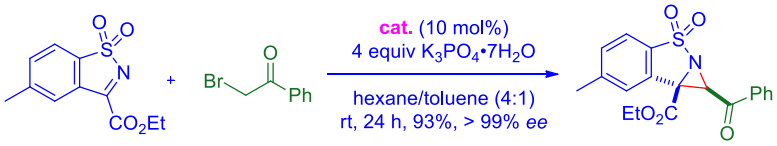
Example 7, Darzens condensation/Friedel–Crafts alkylation cascade[14]

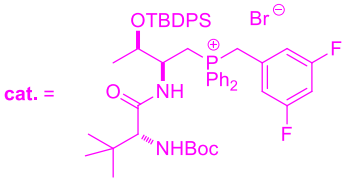


Example 8, Asymmetric vinylogous aza-Darzens approach to vinyl aziridines[15]



Example 9, Enantioselective aza-Darzens reaction[16]



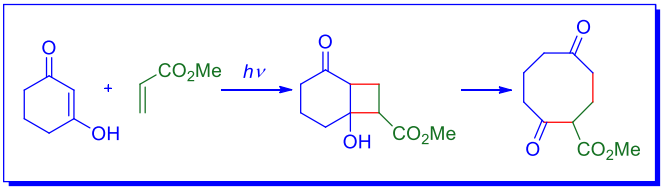


References

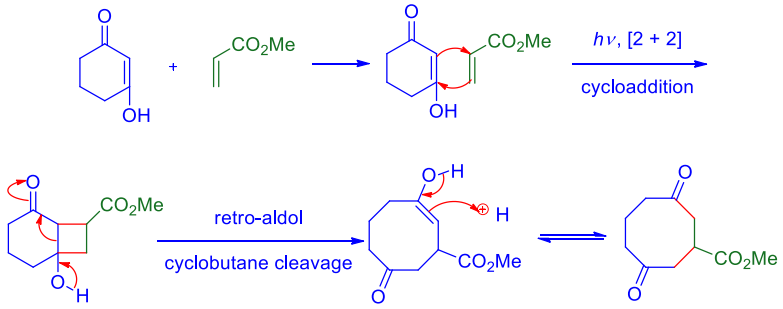
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de Mayo Reaction

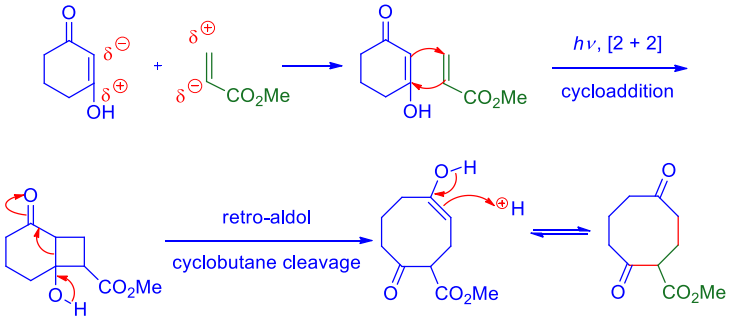
[2 + 2]-Photochemical cyclization of enones with olefins is followed by a retro-aldol reaction to give 1,5-diketones.



Head-to-tail alignment gives the major product:[1b]

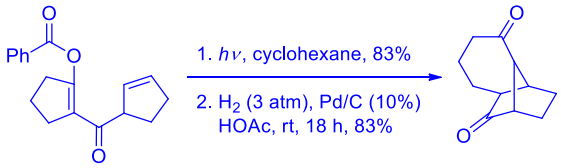


Head-to-head alignment gives the minor regioisomer:

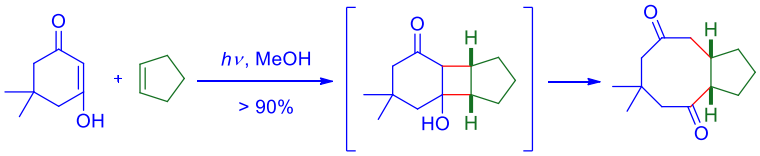


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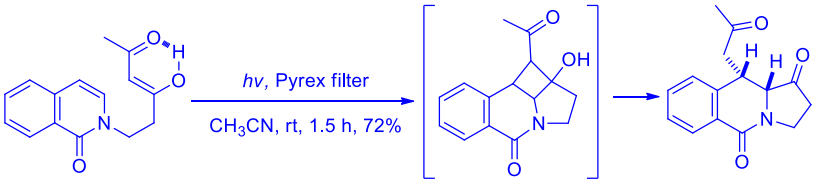
Example 1[3]



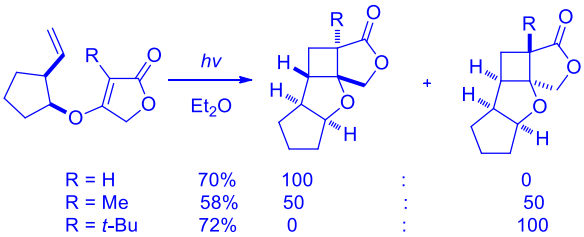
Example 2[6]



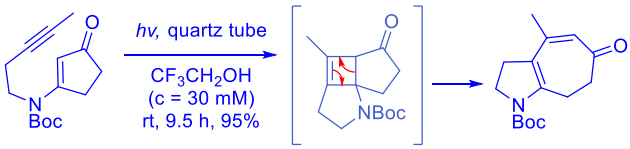
Example 3[9]



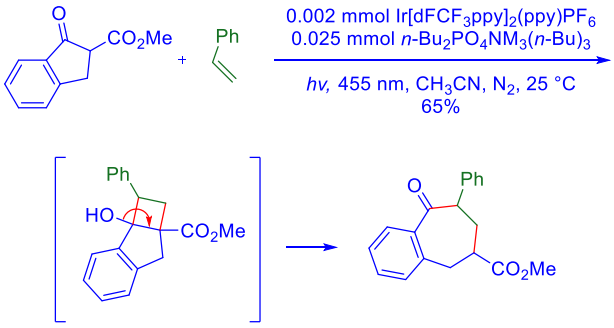
Example 4[10]



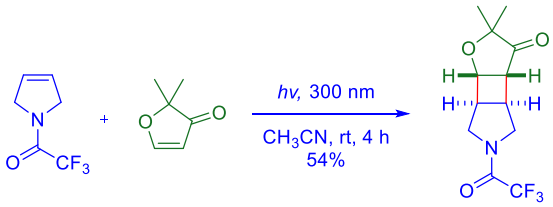
Example 5, Alkyne de Mayo reaction followed by ring expansion[15]



Example 6, via [2 + 2]-cycloaddition[16]



Example 7, Intermolecular [2 + 2]-photocycloaddition[17]



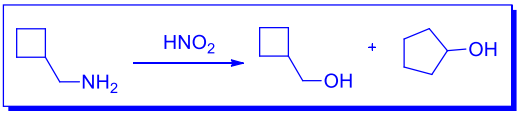
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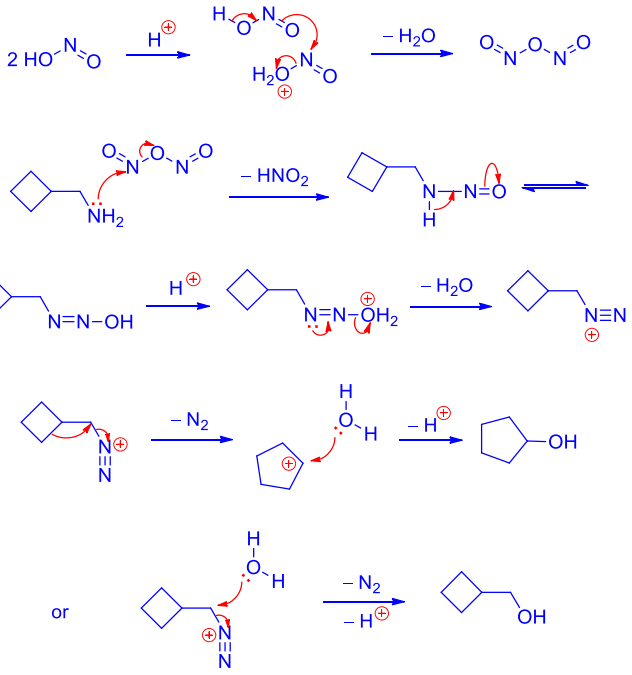
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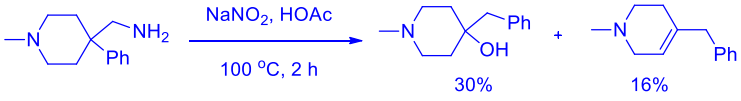
Demjanov Rearrangement

Carbocation rearrangement of primary amines *via* diazotization to give alcohols through C–C bond migration. The Demjanov rearrangement has been largely replaced by the Tiffeneau–Demjanov rearrangement due to the latter's convenience.



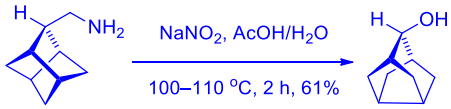


Example 1[3]

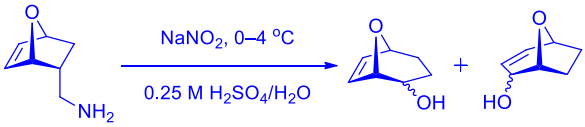


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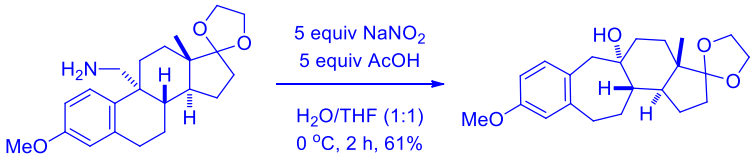
Example 2[6]



Example 3[7]



Example 4[8]

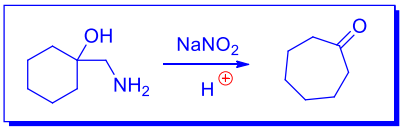


References

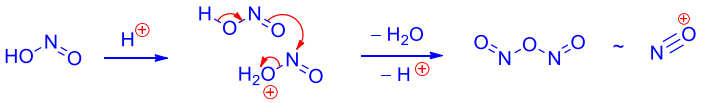
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Tiffeneau–Demjanov Rearrangement

Carbocation rearrangement of β-aminoalcohols *via* diazotization to afford carbonyl compounds through C–C bond migration.

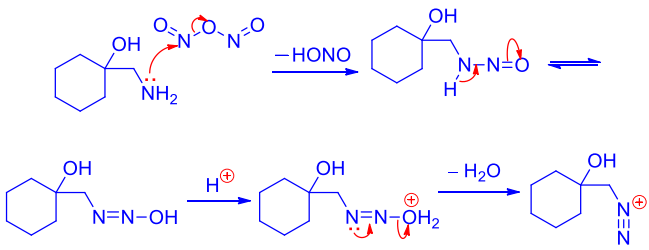


Step 1, Generation of N_2O_3

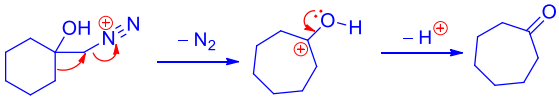


N-nitrosonium ion

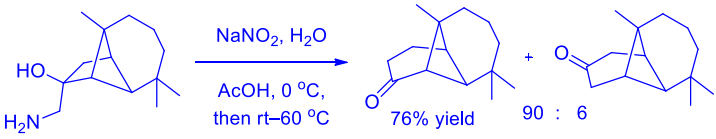
Step 2, Transformation of amine to diazonium salt



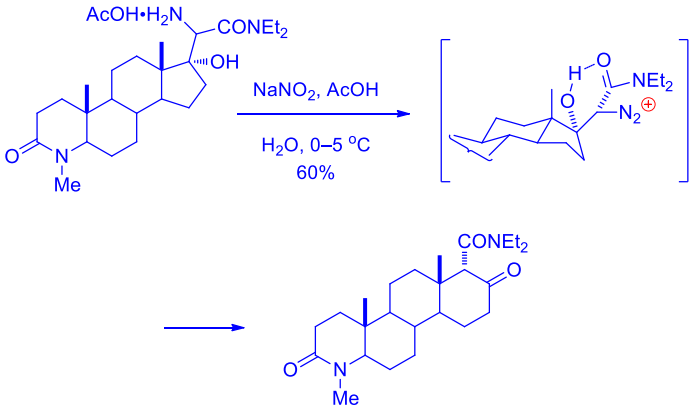
Step 3, Ring-expansion *via* rearrangement



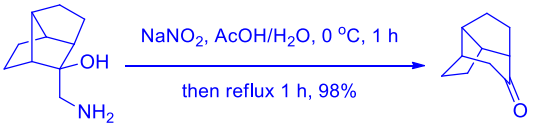
Example 1[5]



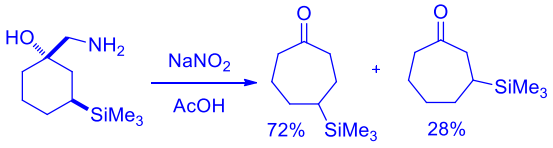
Example 2[6]



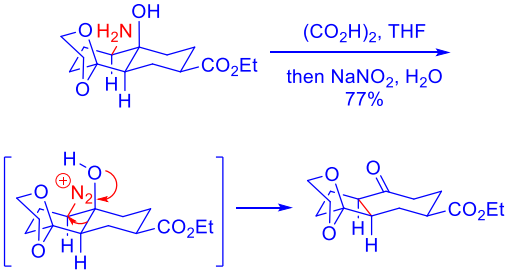
Example 3[7]



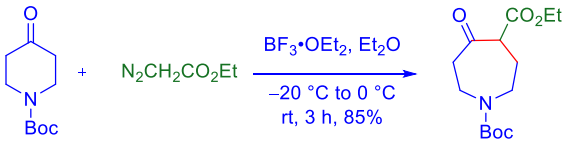
Example 4[9]



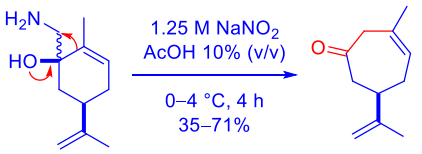
Example 5, In the total synthesis of echinopines[12]



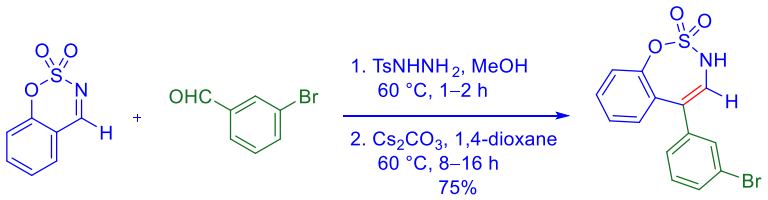
Example 6, Ring expansion of the *N*-Boc-piperidone[13]



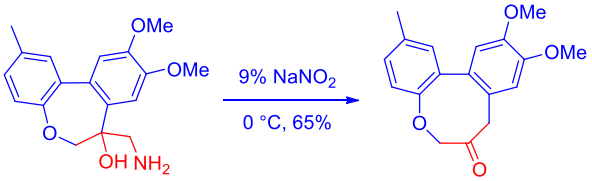
Example 7, Chemo- and region-selective Tiffeneau–Demjanov rearrangement[14]



Example 8, One-pot reaction of cyclic *N*-sulfonylimine with diazo intermediate generated from *N*-tosylhydrazone[15]



Example 9, From seven- to eight-membered ring[16]



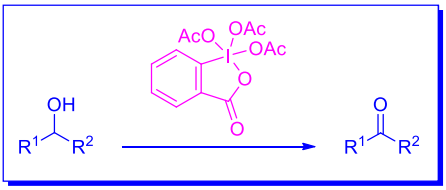
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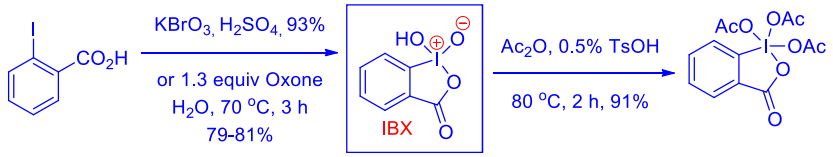
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Dess–Martin Periodinane Oxidation

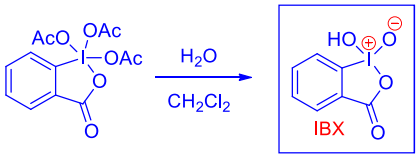
Oxidation of alcohols to the corresponding carbonyl compounds using triacetoxyperiodinane. The Dess–Martin periodinane (DMP), 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one, is one of the most useful oxidant for the conversion of primary and secondary alcohols to their corresponding aldehyde or ketone products, respectively.



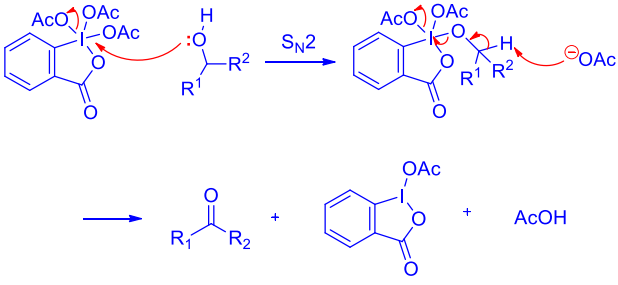
Preparation,[1,2] the oxone preparation is much safer and easier than $KBrO_3$. The IBX intermediate that comes out of it has proven to be far less explosive[12]



However, The Dess–Martin periodinane is hydrolyzed by moisture to *o*-iodoxybenzoic acid (IBX), which is a more powerful oxidizing agent[3]

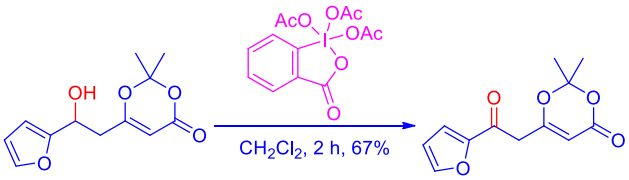


Mechanism[1]

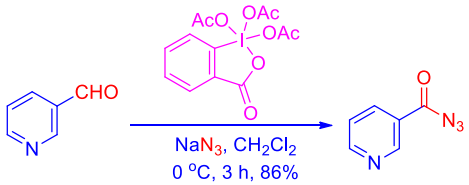


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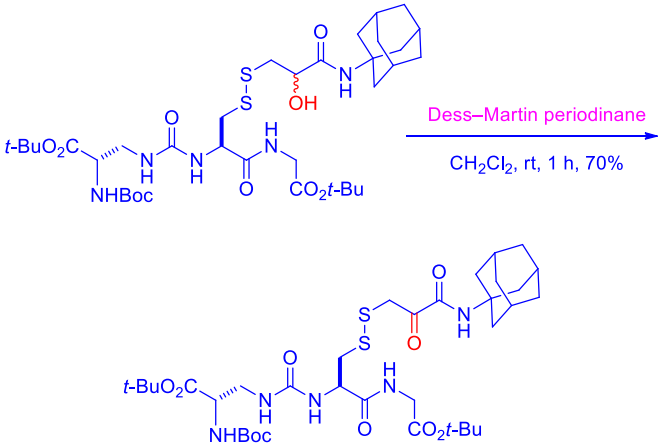
Example 1[6]



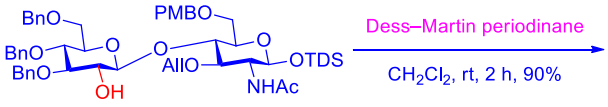
Example 2, An atypical Dess–Martin periodinane (DMP) reactivity[7]

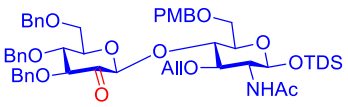


Example 3[10]

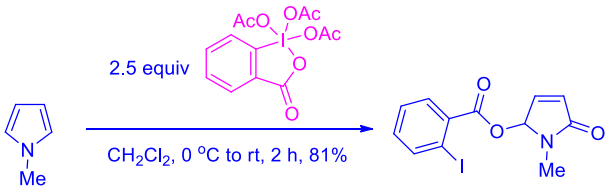


Example 4[11]

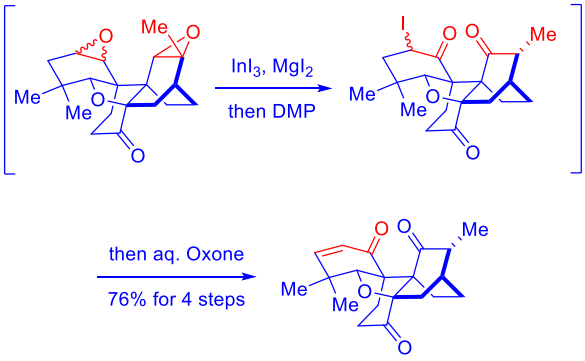




Example 5[12]



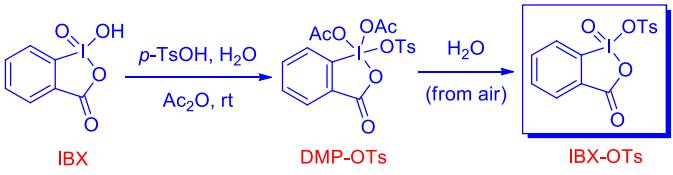
Example 6, In the total synthesis of (−)-maoecrystal[13]

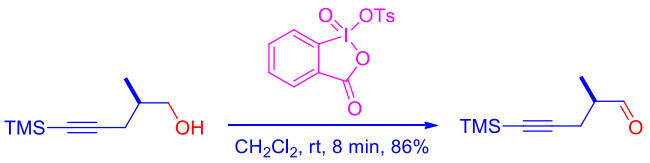


Example 7, As a terminal oxidant in Wacker-type oxidation[14]

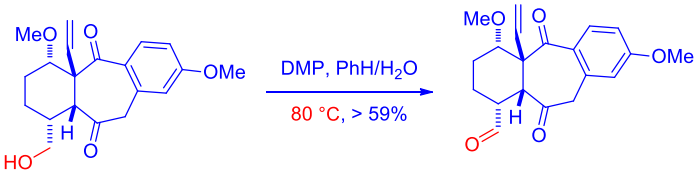


Example 8, Iodoxybenzoic acid tosylate (IBX-OTs) as an alternative to DMP[15]

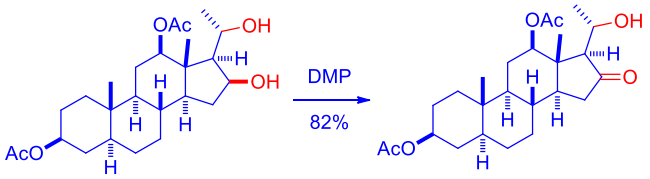




Example 9, In the total synthesis of hestisine-type C_{20}-diterpenoid alkaloids: *The Dess–Martin oxidation was run at 80 °C*![16]



Example 10, In the total synthesis of cephalostatin 1: dilution was key to achieve selectivity against the two secondary alcohols (0.08 M, 86:3)[17]



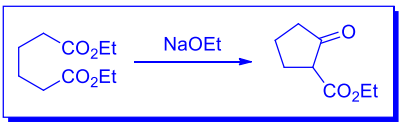
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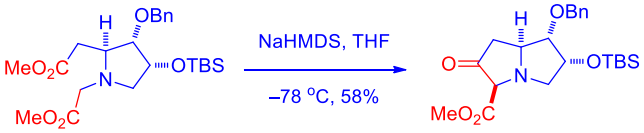
Dieckmann Condensation

The Dieckmann condensation is the intramolecular version of the Claisen condensation.

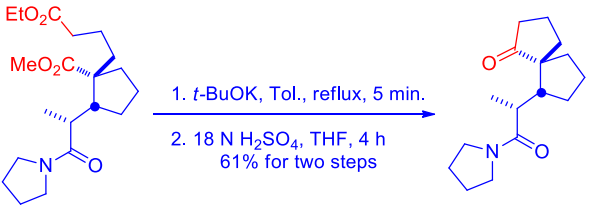




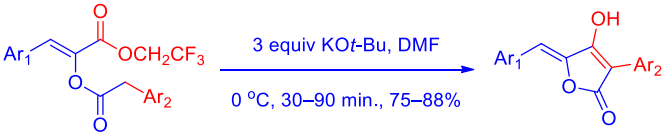
Example 1[4]



Example 2, Followed by decarboxylation[6]

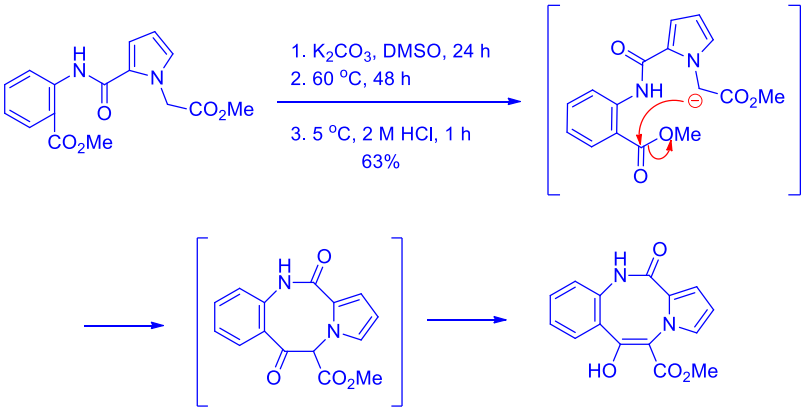


Example 3[7]

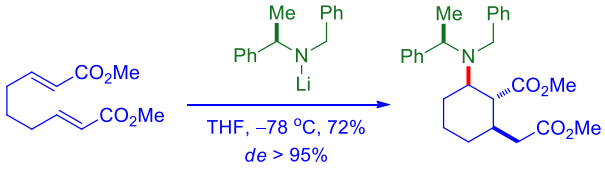


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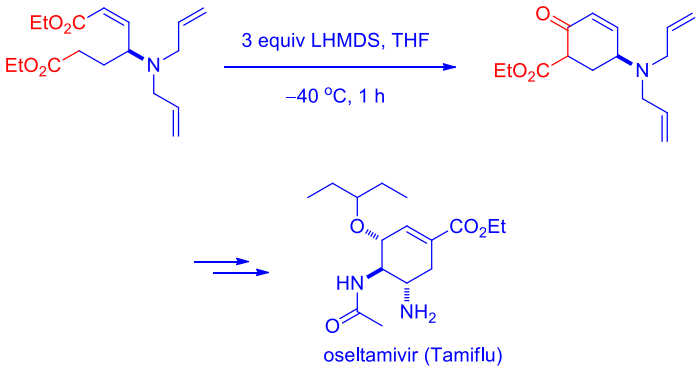
Example 4[8]



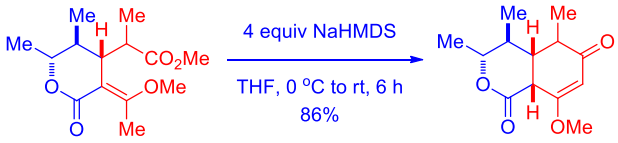
Example 5, Michael–Dieckmann condensation[10]



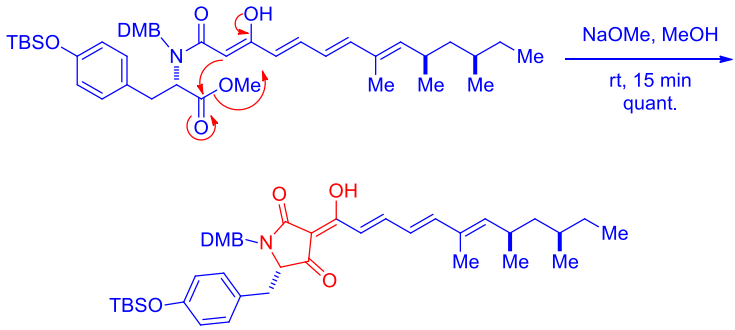
Example 6, Toward preparation of oseltamivir[10]



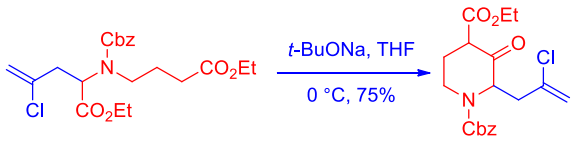
Example 7, On surface, the double bond rotated. But in reality, it rotated as a single bond in one of the resonance structures[11]



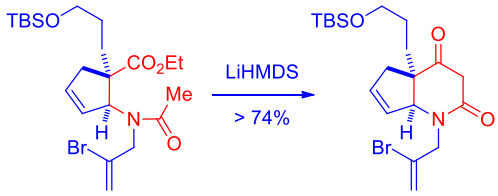
Example 8, From an enol and an ester[12]



Example 8, Large (5.44 Kg)-scale Dieckmann condensation[13]



Example 9, Gram-scale synthesis of a tricycle[14]



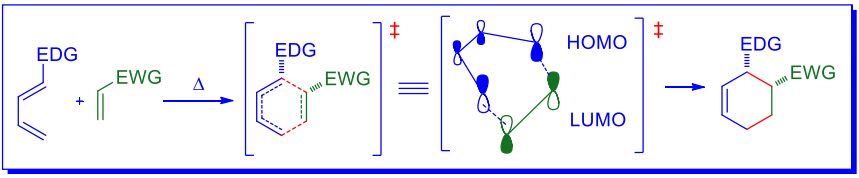
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Diels–Alder Reaction

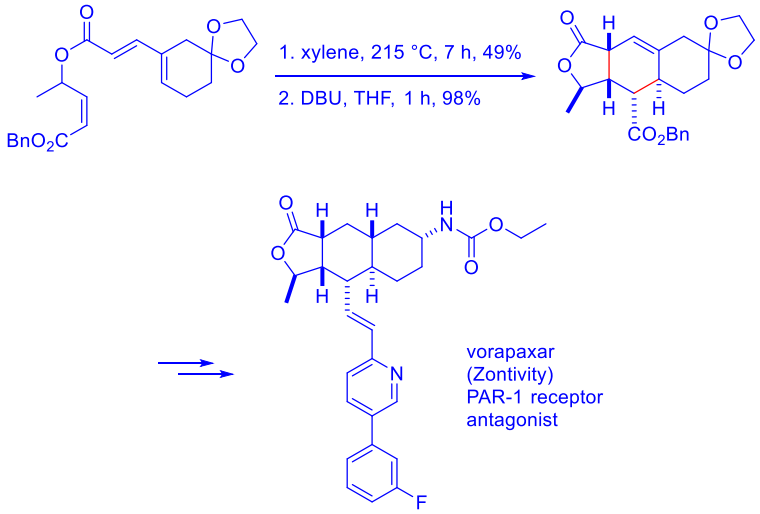
The Diels–Alder reaction, inverse electronic demand Diels–Alder reaction, as well as the hetero-Diels–Alder reaction, belong to the category of *[4+2]-cycloaddition reactions*, which are concerted processes. The arrow pushing here is merely mnemonic.



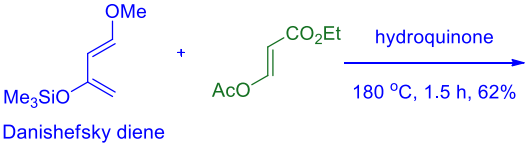
diene dienophile adduct

EDG = electron-donating group; EWG = electron-withdrawing group

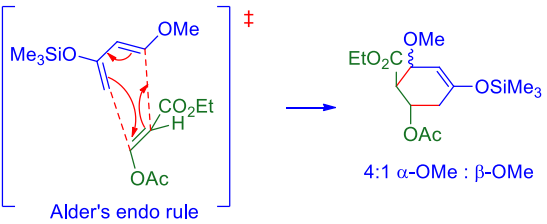
Example 1, Intramolecular Diels–Alder reaction to prepare an intermediate for Scherring–Plough′s thrombin receptor (also known as protease activated receptor-1, PAR-1) antagonist, vorapaxar (Zontivity)[6]



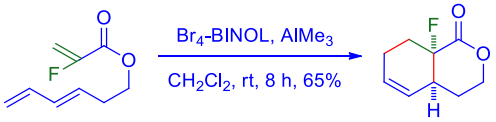
Example 2[7]



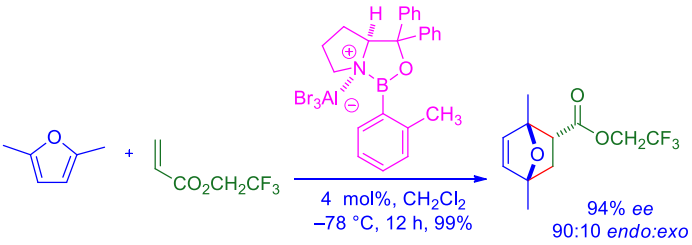
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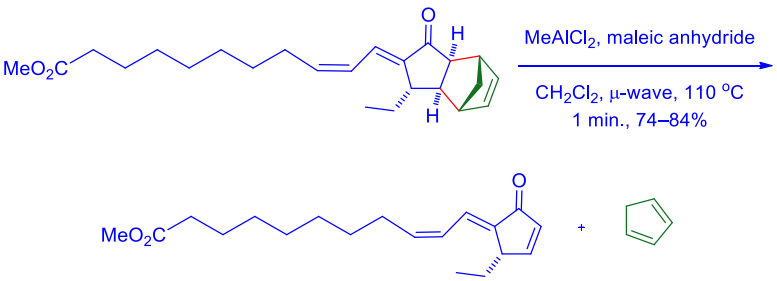
Example 3, Intramolecular Diels–Alder reaction[8]



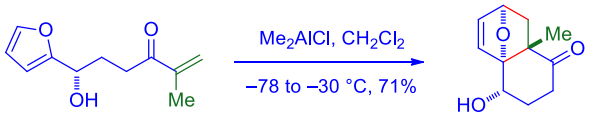
Example 4, Asymmetric Diels–Alder reaction employing a CBS-like catalyst[9]



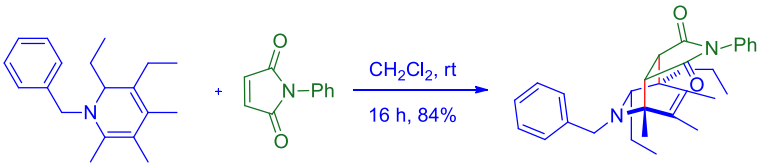
Example 5, Retro-Diels–Alder reaction[10]



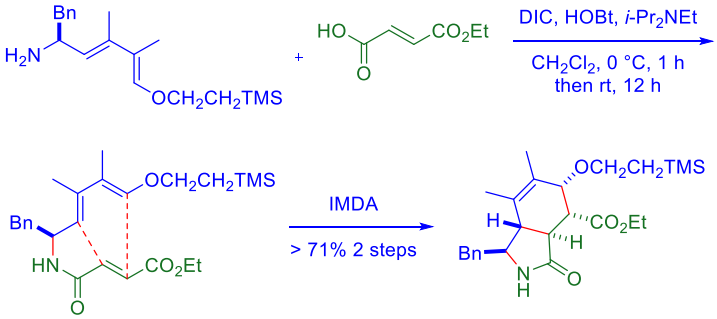
Example 6, Intramolecular Diels–Alder reaction[11]



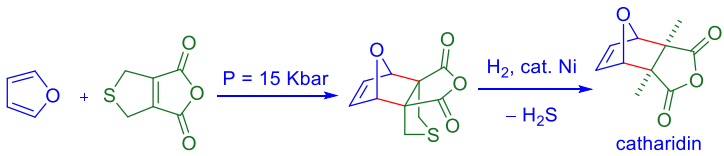
Example 7[12]



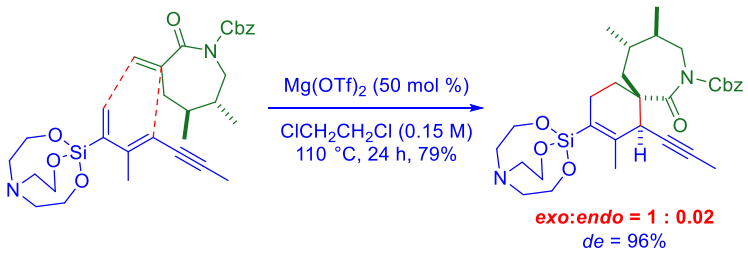
Example 8, Intramolecular Diels–Alder cyclization[13]



Example 9, Toward the total synthesis of catharidin[14]



Example 10, *exo*-Selective (bulky silatrane helped the selectivity) intermolecular Diels–Alder reaction[15]

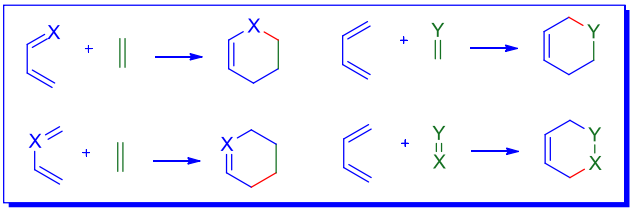


References

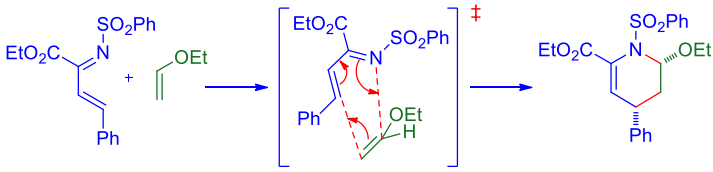
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Hetero-Diels–Alder Reaction

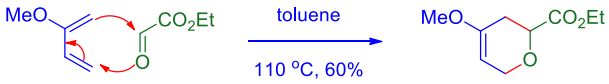
Heterodiene addition to dienophile or heterodienophile addition to diene. Typical hetero-Diels–Alder reactions are aza-Diels–Alder reaction and oxo-Diels–Alder reaction.



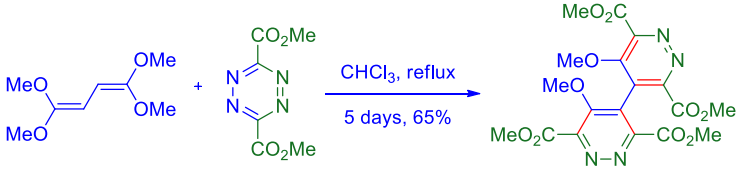
Example 1,



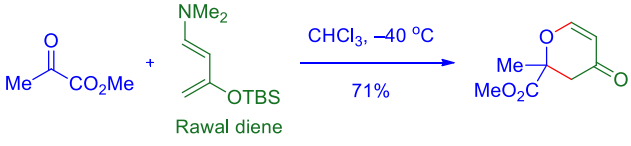
Example 2, Heterodienophile addition to diene[1]



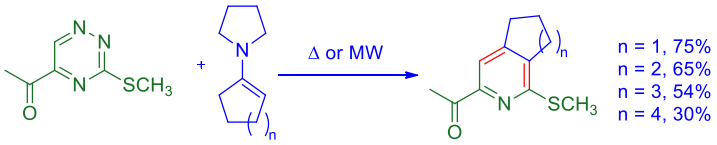
Example 3, Similar to the Boger pyridine synthesis[2]



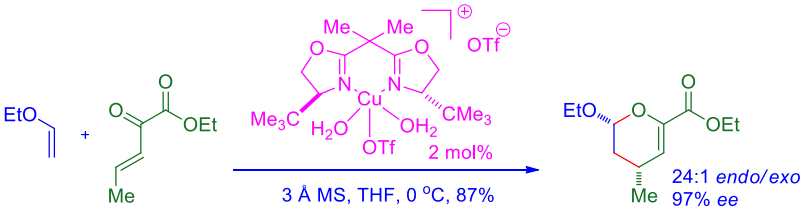
Example 4, Using the Rawal diene[4]



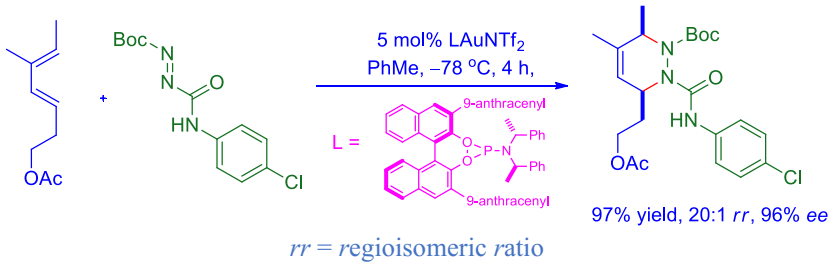
Example 5, Also similar to the Boger pyridine synthesis[6]



Example 6, Asymmetric hetero-Diels–Alder reaction[7]

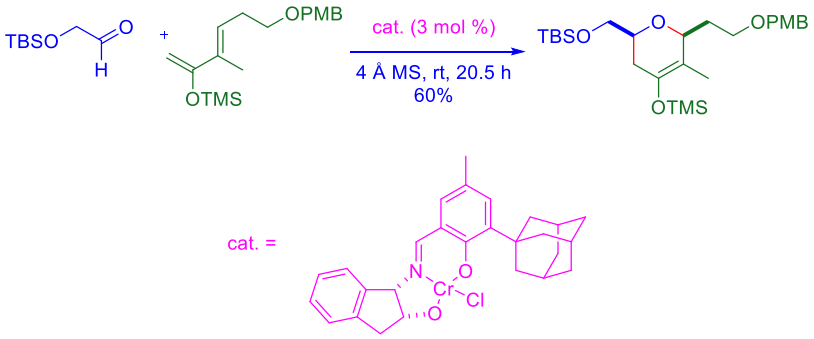


Example 7, Asymmetric hetero-Diels–Alder reaction[8]

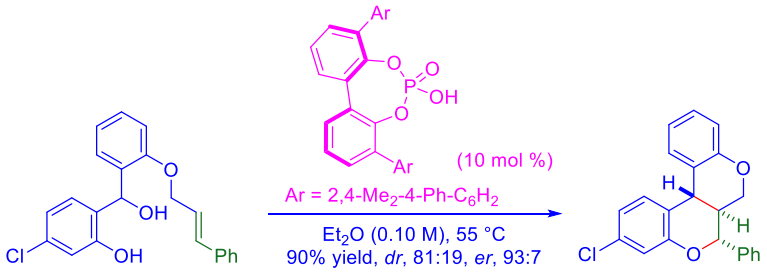


rr = regioisomeric ratio

Example 8, Asymmetric hetero-Diels–Alder reaction[10]



Example 9, Enantioselective intramolecular oxa-Diels–Alder reaction[11]

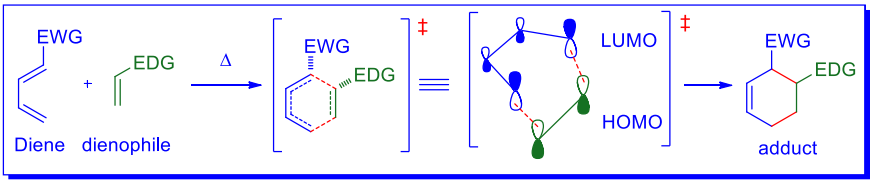


References

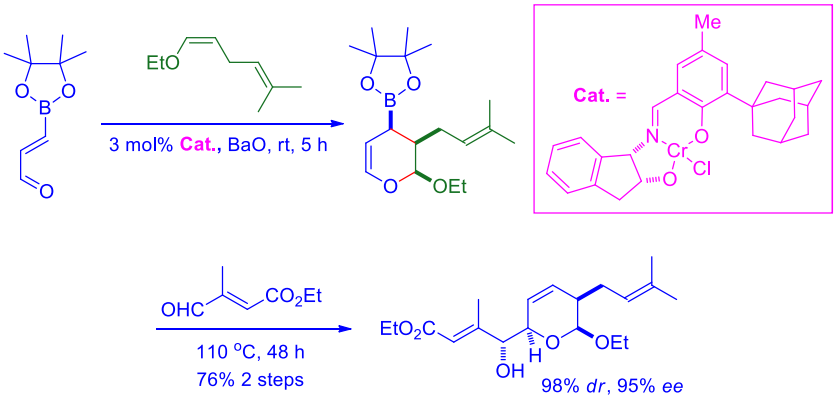
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Inverse-electron-demand Diels–Alder Reaction

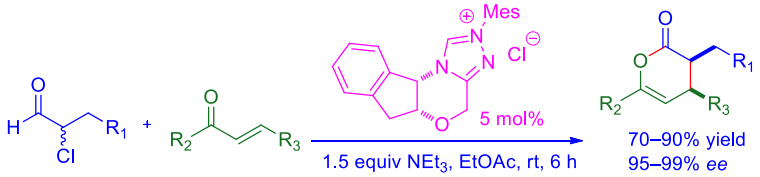
Inverse-electron-demand Diels–Alder reaction (IEDDA) employs dienes with electron-withdrawing groups (EWG) and dienophile with electron-donating groups (EDG).



Example 1, Catalytic asymmetric IEDDA[2]

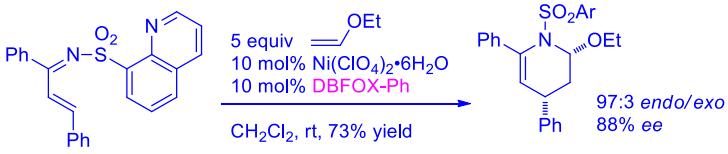


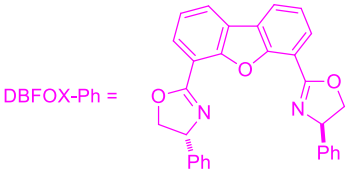
Example 2, Catalytic asymmetric IEDDA[3]



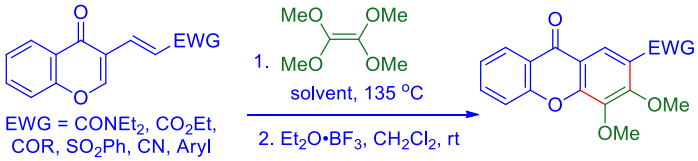
oxodiene

Example 3, Catalytic asymmetric IEDDA[4]

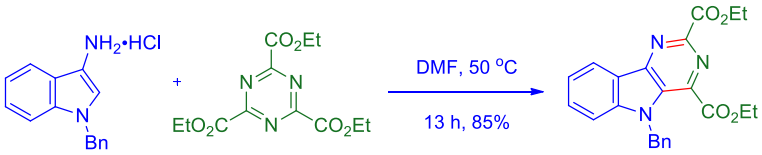




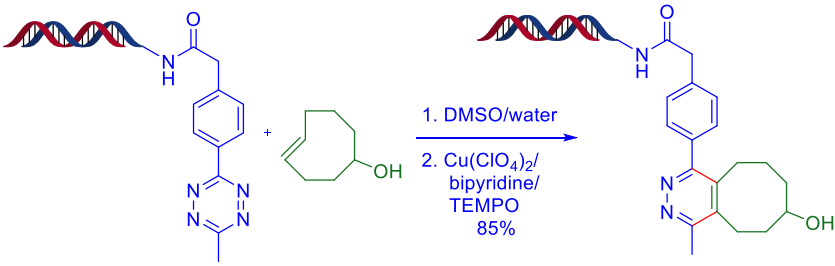
Example 4, IEDDA[5]



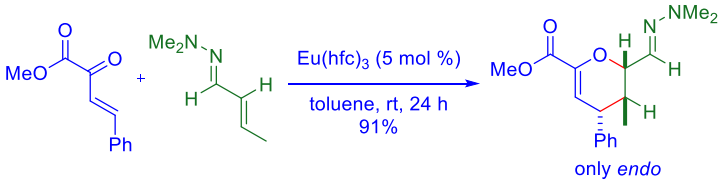
Example 5, IEDDA[6]



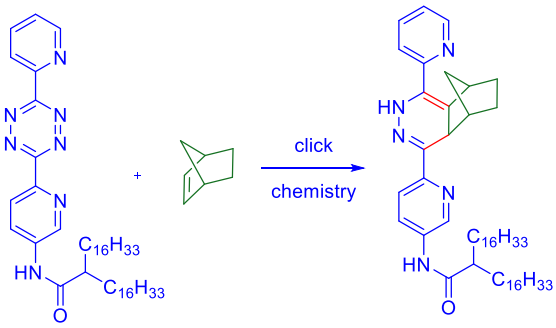
Example 6, Application of IEDDA in DNA-encoded library (DEL) synthesis[7]



Example 7, Inverse electron-demand oxa-Diels–Alder reaction (oxa-IEDDA)[8]



Example 8, IEDDA carried out in liposomes[9]

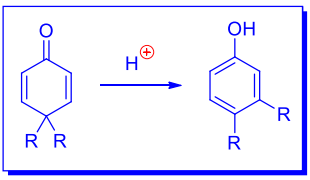


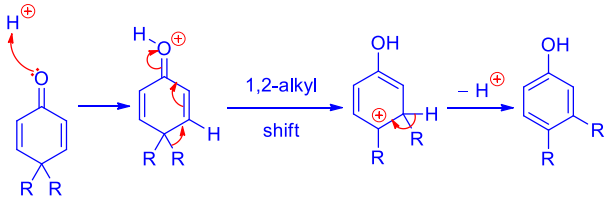
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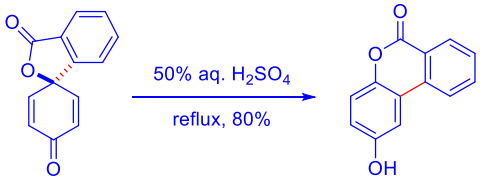
Dienone–Phenol Rearrangement

Acid-promoted rearrangement of 4,4-disubstituted cyclohexadienones to 3,4-disubstituted phenols.

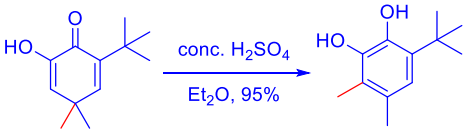




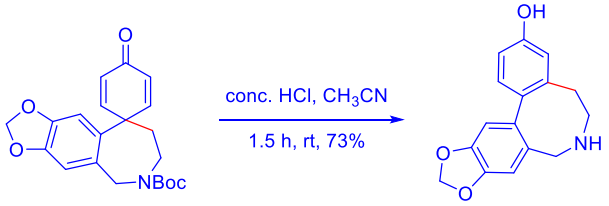
Example 1, Intramolecular dienone–phenol rearrangement[4]



Example 2, Classic dienone–phenol rearrangement[5]

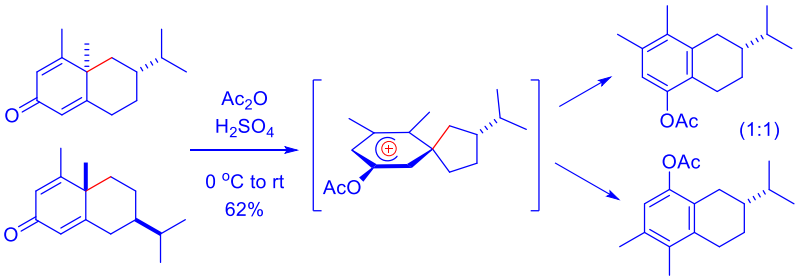


Example 3, Intramolecular dienone–phenol rearrangement[9]

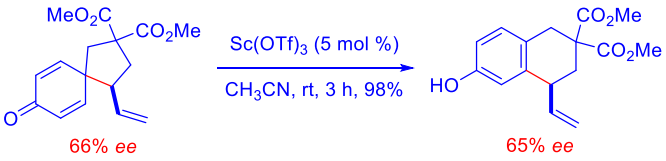


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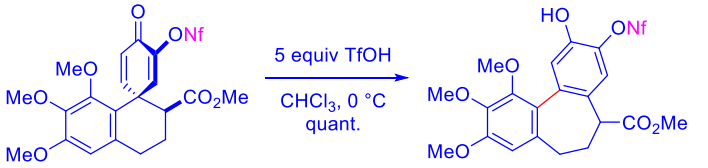
Example 4, Via a common intermediate[10]



Example 5, Dienone–phenol rearrangement using an optically active substrate[11]

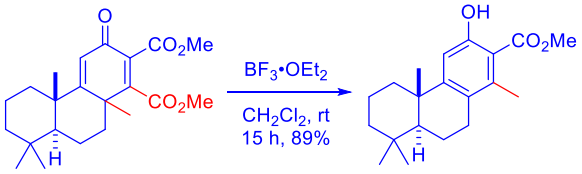


Example 6, Intramolecular dienone–phenol rearrangement[12]



Nf = nonafluorobutanesulfonyl, $-SO_2CF_2CF_2CF_2CF_3$, a protecting group for –OH

Example 7, An unprecedented *decarboxylative* dienone–phenol rearrangement[13]



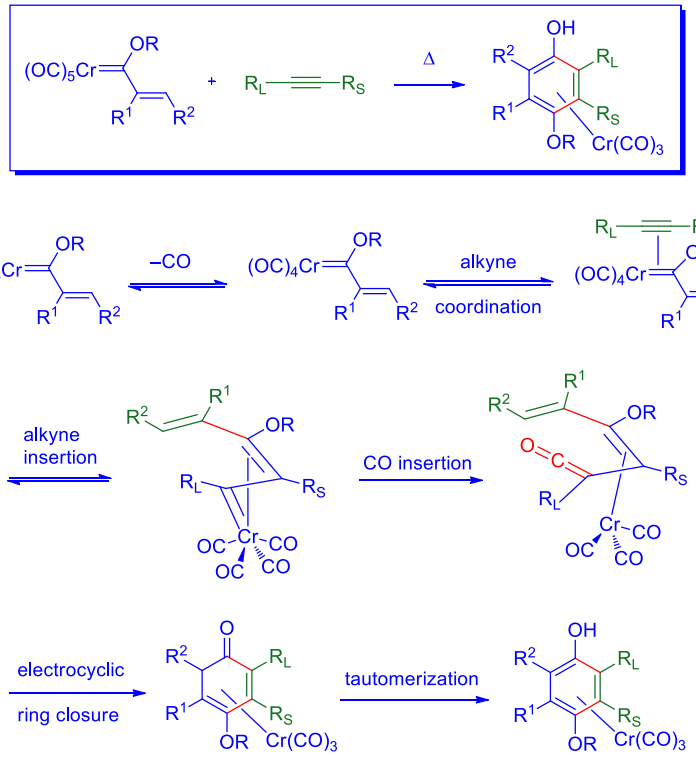
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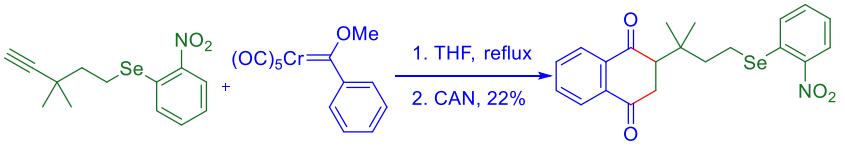
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Dötz Reaction

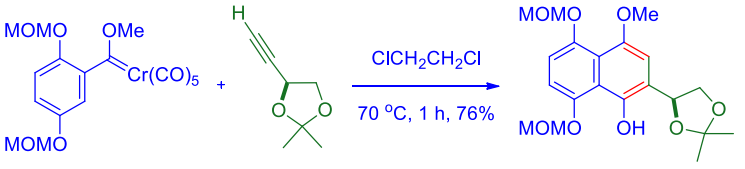
Also known as the Dötz benzannulation, the Dötz reaction is the $Cr(CO)_3$-coordinated hydroquinone from vinylic alkoxy pentacarbonyl chromium carbene (Fischer carbene) complex and alkynes.



Example 1[5]

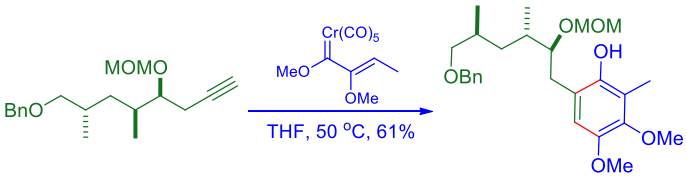


Example 3[8]

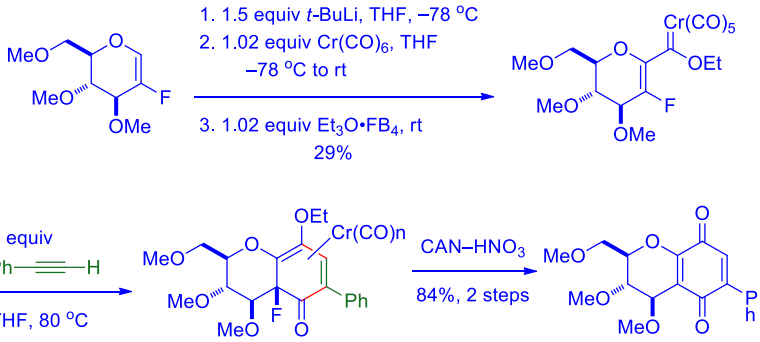


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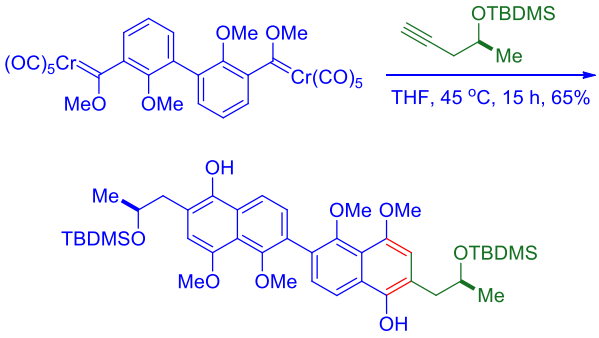
Example 3[8]



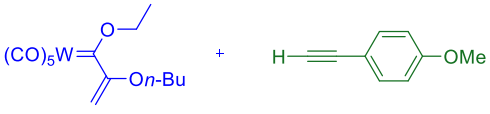
Example 3[9]



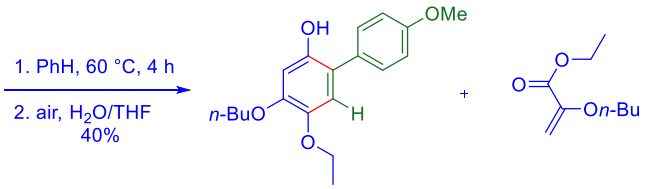
Example 4[10]



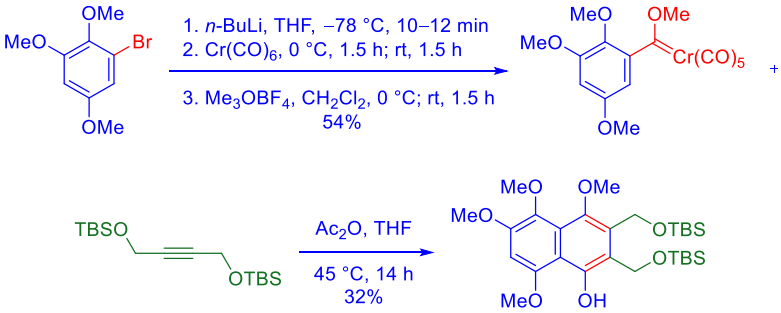
Example 5, Assembly of polysubstituted and highly oxygenated phenols, a tungsten (W) variant[11]



α-alkoxyvinyl(ethoxy) carbene complex



Example 6, Dötz benzannulation[12]



References

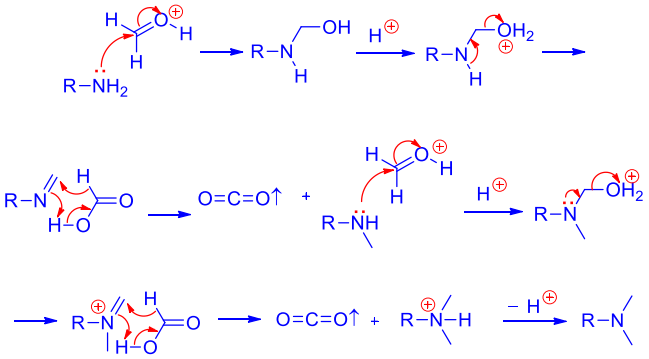
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Eschweiler–Clarke Reductive Amination

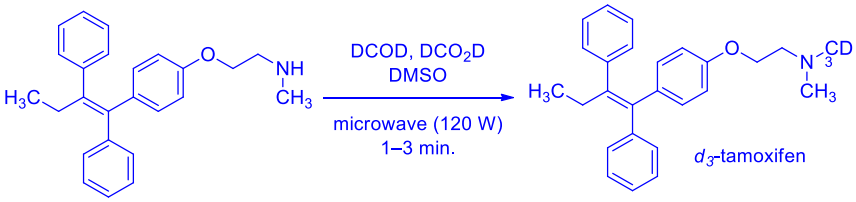
Reductive methylation of primary or secondary amines using formaldehyde and formic acid. *Cf*. Leuckart–Wallach reaction.



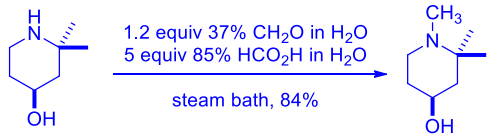
formic acid is the hydride source, serving as a reducing agent



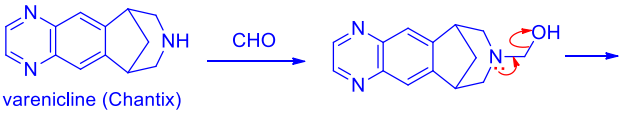
Example 1[7]



Example 2[9]

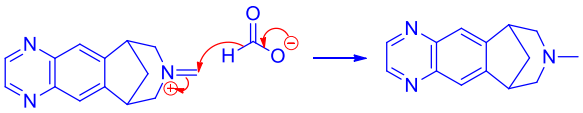


Example 3[10]

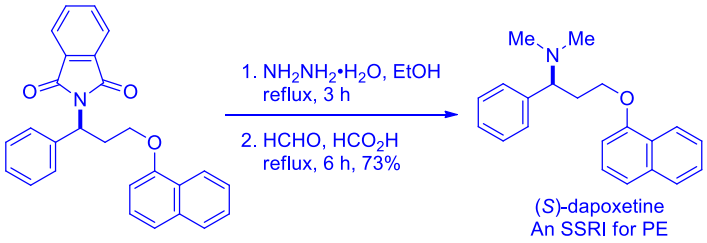


varenicline (Chantix)

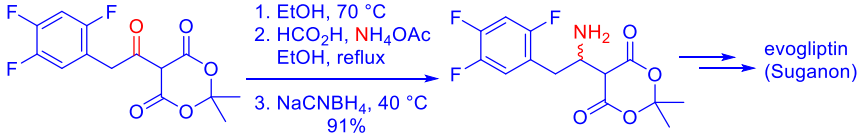
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J. J. Li, *Name Reactions*, https://doi.org/10.1007/978-3-030-50865-4_48



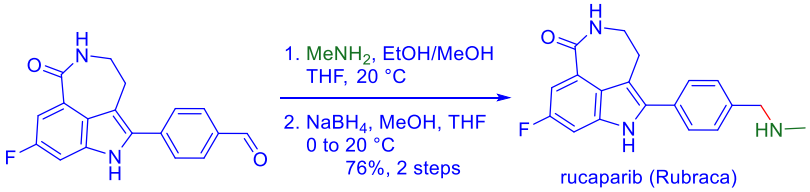
Example 4, Preparation of a selective serotonin reuptake inhibitor (SSRI) for treatment of premature ejaculation (PE)[11]



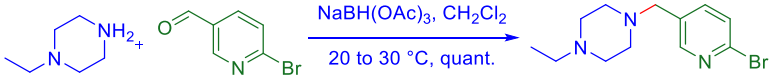
Example 5, Toward synthesis of evogliptin (Suganon), a dipeptidyl peptidase IV (DPP-4) inhibitor[12]

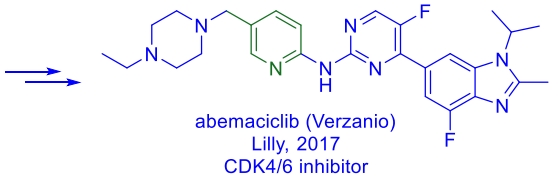


Example 6, Toward synthesis of rucaparib (Rubraca), a poly(ADP-ribosyl) polymerase (PARP) inhibitor[13]

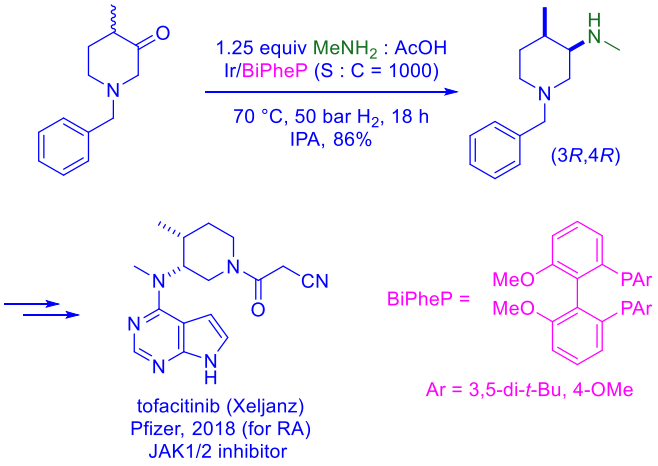


Example 7, Toward the synthesis of abemaciclib (Verzanio), a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor[14]





Example 8, Dynamic kinetic resolution (DKR)–asymmetric reductive amination (ARA) protocol[15]



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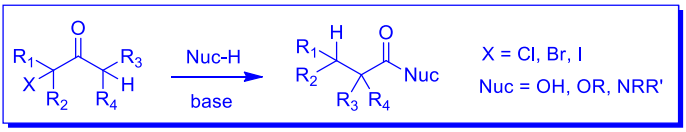
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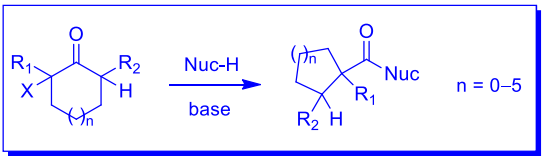
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Favorskii Rearrangement

Transformation of enolizable α-haloketones to esters, carboxylic acids, or amides *via* alkoxide-, hydroxide-, or amine-catalyzed rearrangements, respectively.

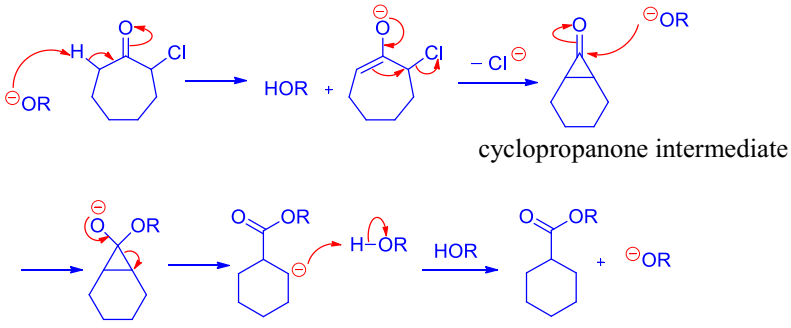


The intramolecular Favorskii Rearrangement:



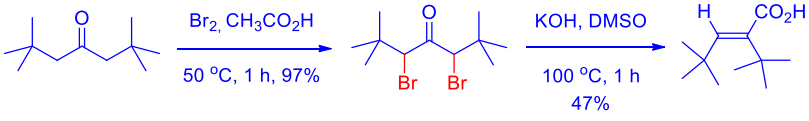


enolizable α-haloketone



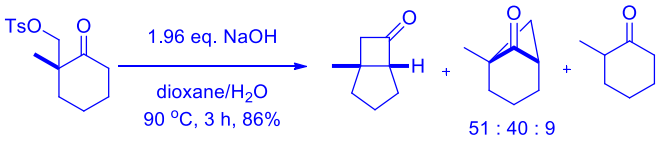
cyclopropanone intermediate

Example 1[2]

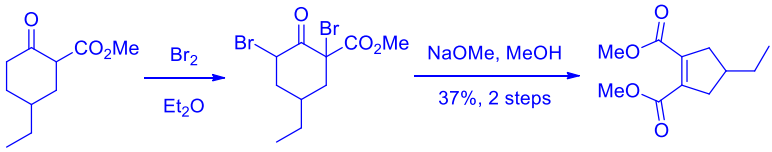


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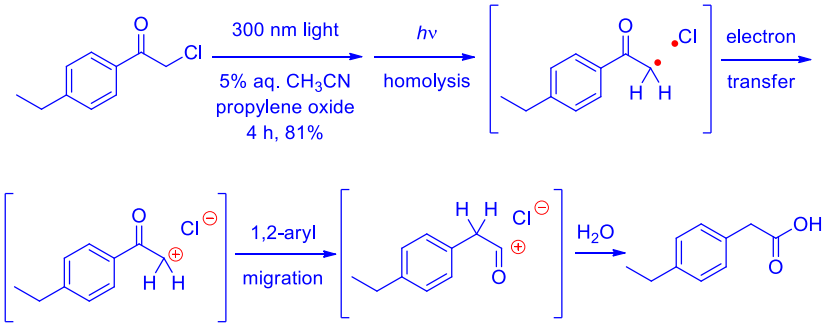
Example 2, Homo-Favorskii rearrangement[3]



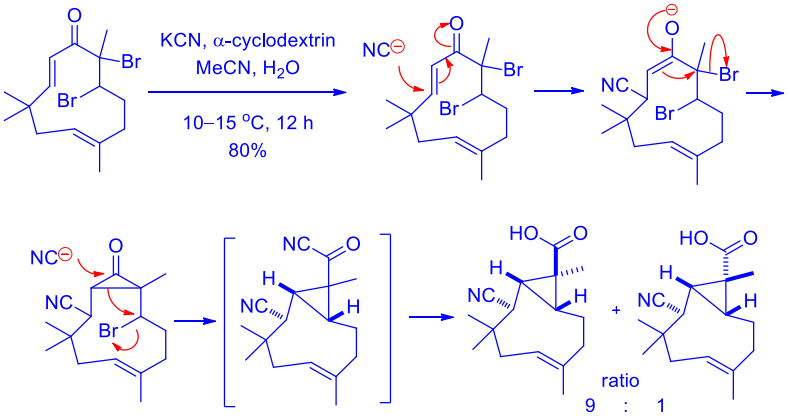
Example 3[6]



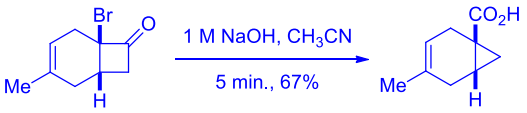
Example 4, Photo-Favorskii Rearrangement[7]



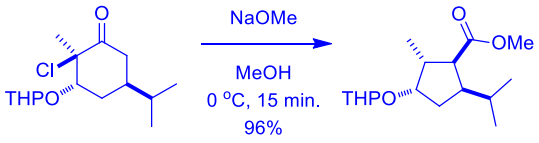
Example 5[8]



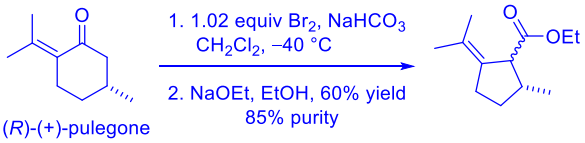
Example 6[10]



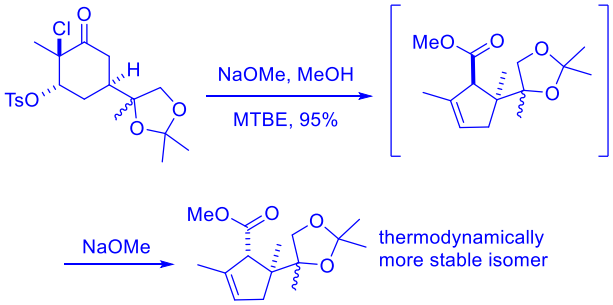
Example 7[11]



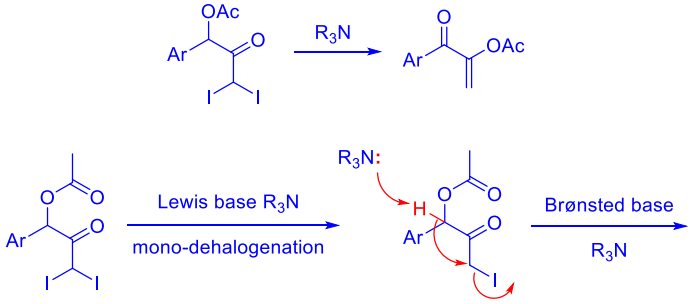
Example 8, Process scale (5 kg)[14]

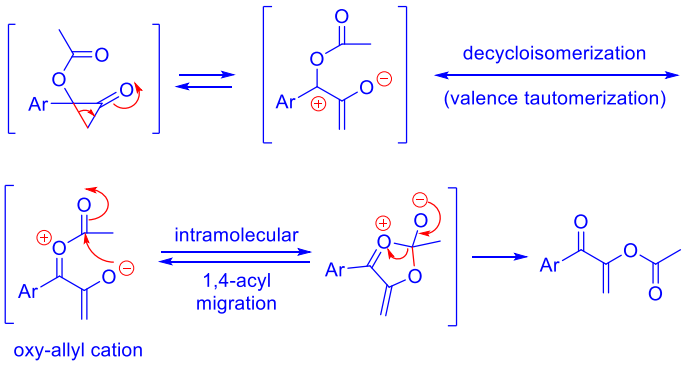


Example 9, Process scale (3.5 kg)[15]



Example 10, A semi-Favorskii Rearrangement[16]



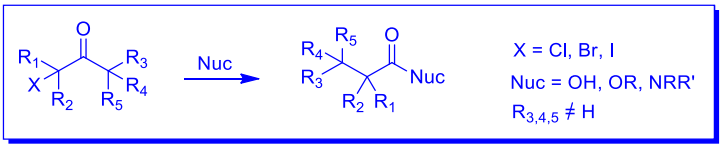


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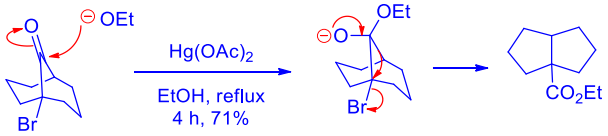
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Quasi-Favorskii Rearrangement

If there are no enolizable hydrogens present, the classical Favorskii rearrangement is not possible. Instead, a semi-benzylic mechanism can lead to a rearrangement referred to as quasi-Favorskii.

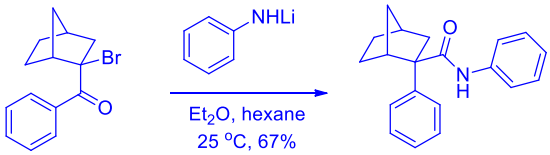


Example 1, Arthur C. Cope′s initial discovery[1]

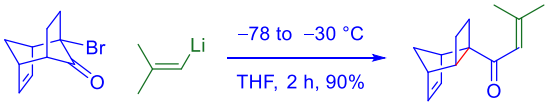


non-enolizable ketone

Example 2[5]



Example 3[6]



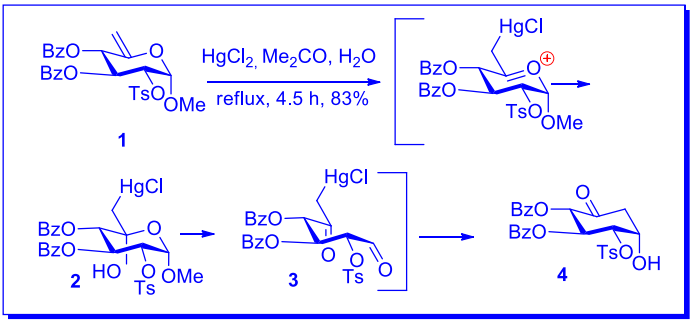
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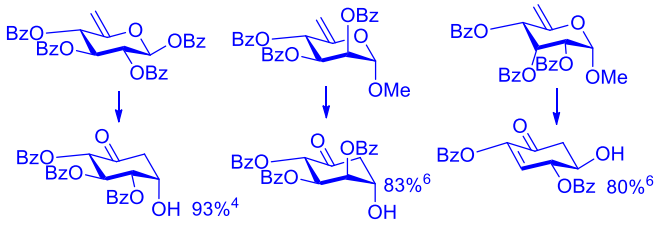
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Ferrier Carbocyclization

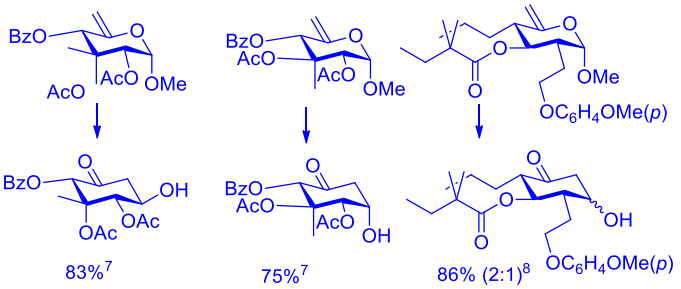
This process has proved to be of considerable value for the efficient, one-step conversion of 5,6-unsaturated hexopyranose derivatives into functionalized cyclohexanones useful for the preparation of such enantiomerically pure compounds as inositols and their amino, deoxy, unsaturated and selectively *O*-substituted derivatives, notably phosphate esters. In addition, the products of the carbocyclization have been incorporated into many complex compounds of interest in biological and medicinal chemistry.[1,2]

General examples:[3]



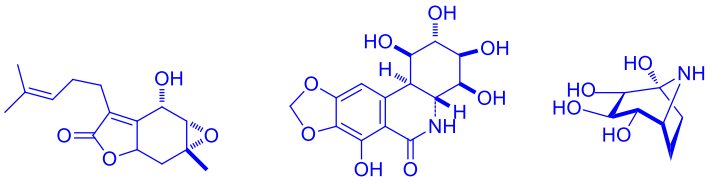


More complex products:

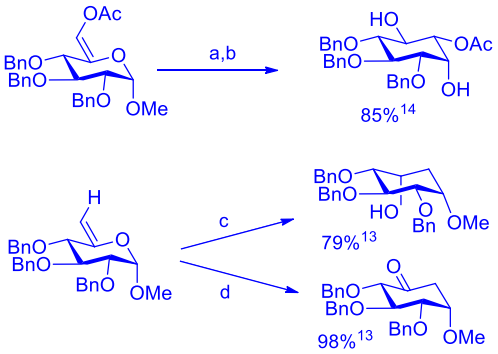


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Complex bioactive compounds made following the application of the reaction:

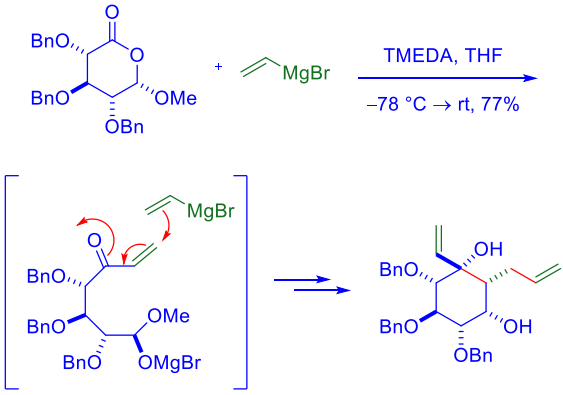


Modified hex-5-enopyranosides and reactions



a, $Hg(OCOCF_3)_2$, Me_2CO, H_2O, 0 °C; b, $NaBH(OAc)_3$, AcOH, MeCN, rt; c, *i*-Bu_3Al, PhMe, 40 °C; d, Ti(O*i*-Pr)Cl_3, CH_2Cl_2, –78 °C, 15 min. (Note: The aglycon is retained in the Al- and Ti-induced reactions).

A recent example of a novel Ferrier-type carbocyclization[19]

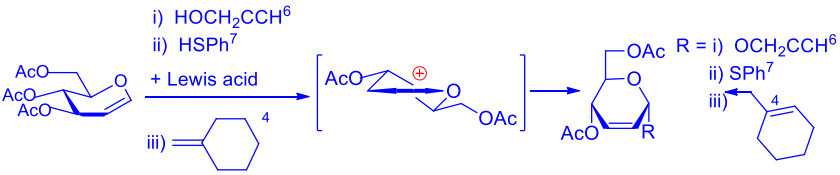


References

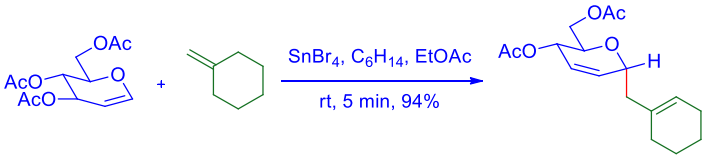
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Ferrier Glycal Allylic Rearrangement

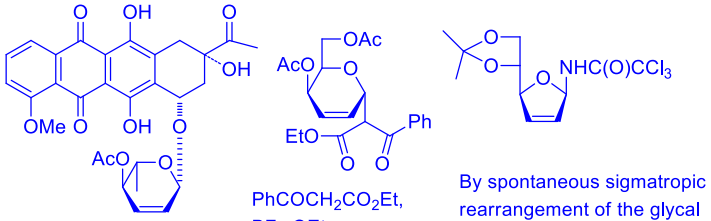
In the presence of Lewis acid catalysts *O*-substituted glycal derivatives can react with *O*-, *S*-, *C*- and, less frequently, *N*-, *P*- and halide nucleophiles to give 2,3-unsaturated glycosyl products.[1,2] This allylic transformation has been "Ferrier Rearrangement". However, the reaction was first noted by Emil Fischer when he heated tri-*O*-acetyl-*D*-glucal in water.[3] When carbon nucleophiles are involved, the term "Carbon Ferrier Reaction" has been used,[4] although the only contribution the Ferrier group made in this area was to find that tri-*O*-acetyl-*D*-glucal dimerizes under acid catalysis to give a *C*-glycosidic product.[5] The general reaction is illustrated by the separate conversions of tri-*O*-acetyl-*D*-glucal with *O*-, *S*- and *C*-nucleophiles to the corresponding 2,3-unsaturated glycosyl derivatives. Normally, Lewis acids are used as catalysts, boron trifluoride etherate being the most common. Allyloxycarbenium ions are involved as intermediates, high yields of products are obtained, and glycosidic compounds with quasi-axial bonds (as illustrated) predominate (commonly in the α,β-ratio of about 7:1). The examples illustrated[4,6,7] are typical of a very large number of literature reports.[1]



General examples[4]



More complex products made directly from the corresponding glycols:



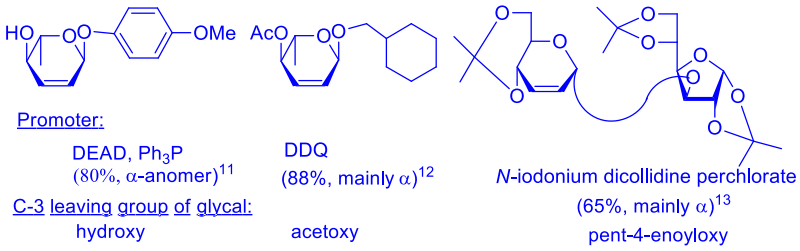
benzene, BF_3•OEt_2, 5 °C, 10 min, (67%, α-anomer).[8]

$PhCOCH_2CO_2Et$, BF_3•OEt_2, rt, 15 min, (81% α-anomer).[9]

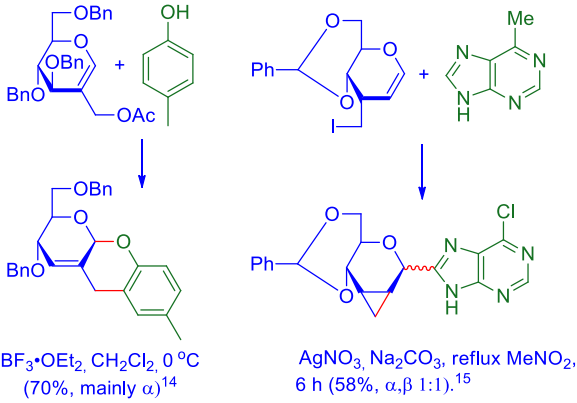
By spontaneous sigmatropic rearrangement of the glycal 3-trichloroacetimidate made with NaH, Cl_3CCN, (78% α-anomer).[10]

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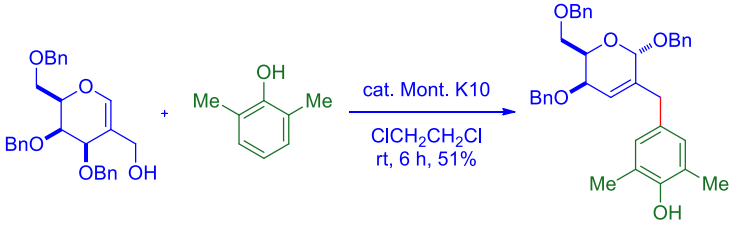
Products formed without acid catalysts:



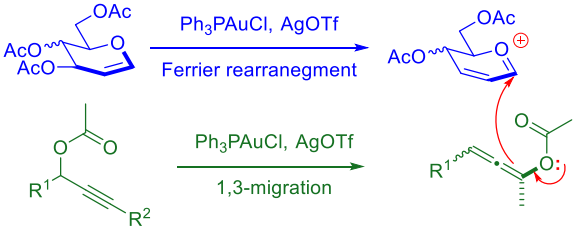
Modified glycols and their reactions:

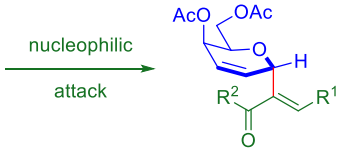


A variant using inexpensive Montmorillonite K-10 clay as the catalyst:



A recent example, A gold(I)-catalyzed tandem 1,3-acyloxy migration/Ferrier rearrangement[21]



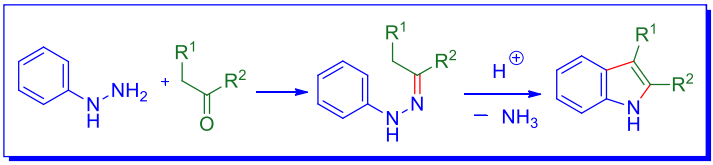


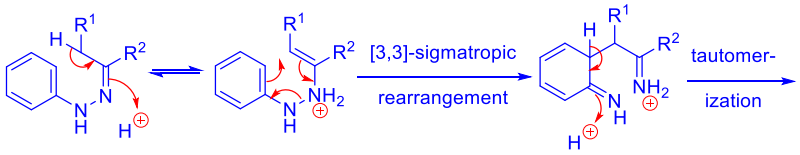
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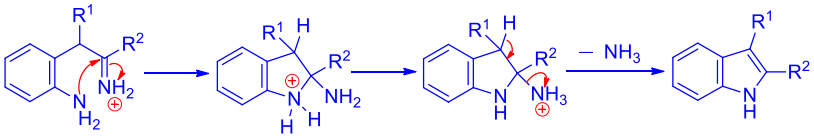
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Fischer Indole Synthesis

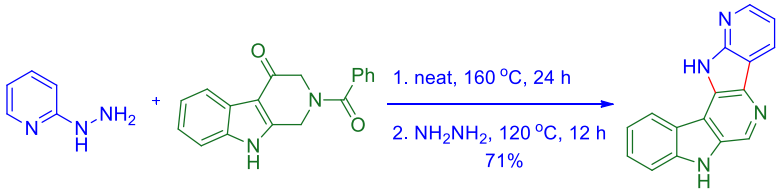
Cyclization of arylhydrazones to indoles.



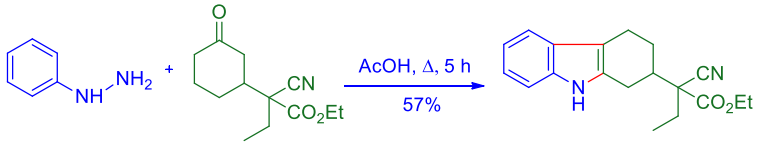




Example 1[3]

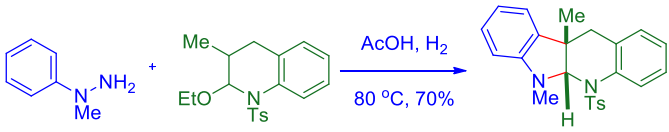


Example 2[3]

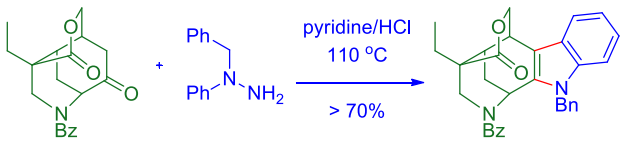


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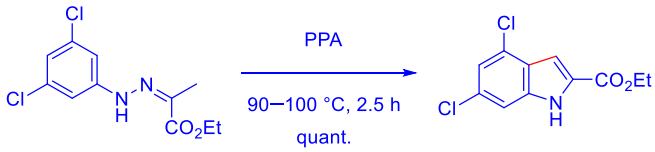
Example 3[10]



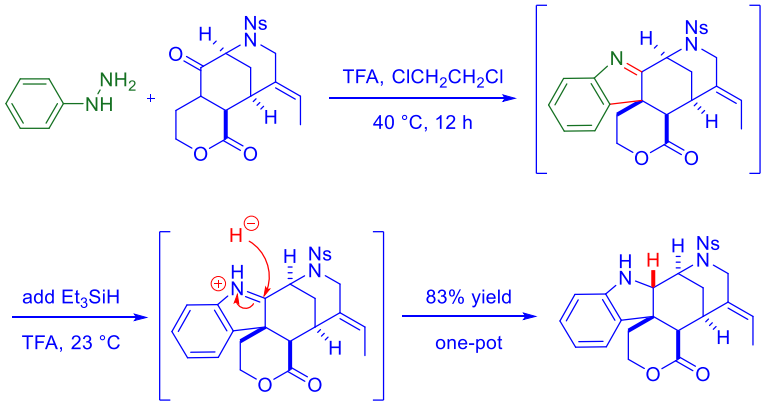
Example 4[12]



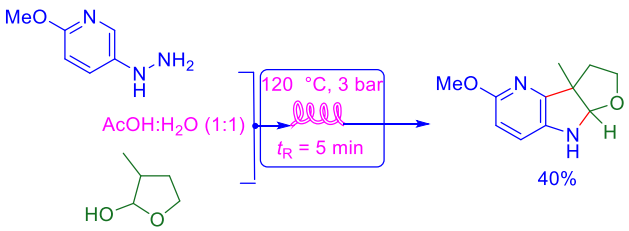
Example 5, An eco-friendly industrial scale Fischer indole cyclization (3 kg scale, PPA = phosphoric acid)[13]



Example 6, Reductive interrupted Fischer indolization[14]



Example 7, Fused-indoline via reductive interrupted indolization in a microfluidic reactor[15]



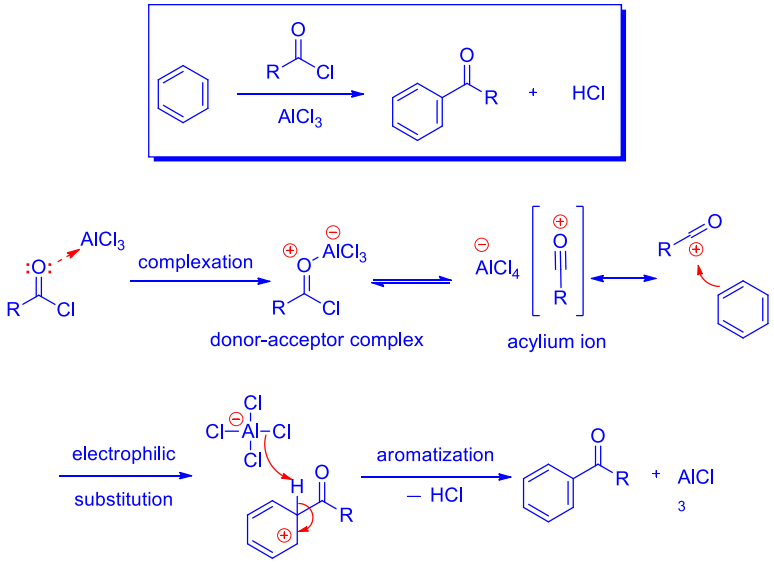
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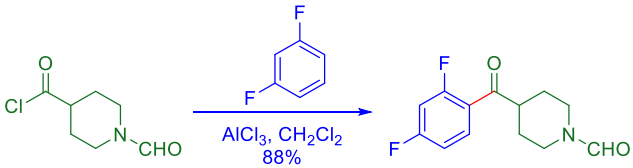
Friedel–Crafts Reaction

Friedel–Crafts Acylation Reaction:

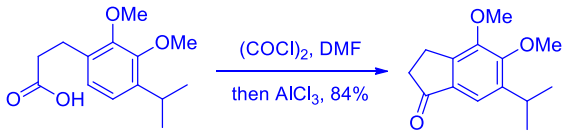
Introduction of an acyl group onto an aromatic substrate by treating the substrate with an acyl halide or anhydride in the presence of a Lewis acid.



Example 1, Intermolecular Friedel–Crafts acylation[6]

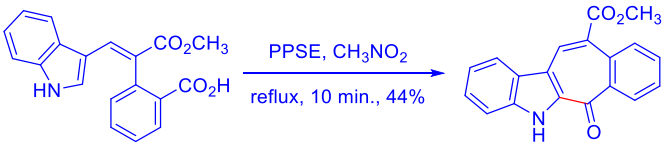


Example 2, Intramolecular Friedel–Crafts acylation[7]



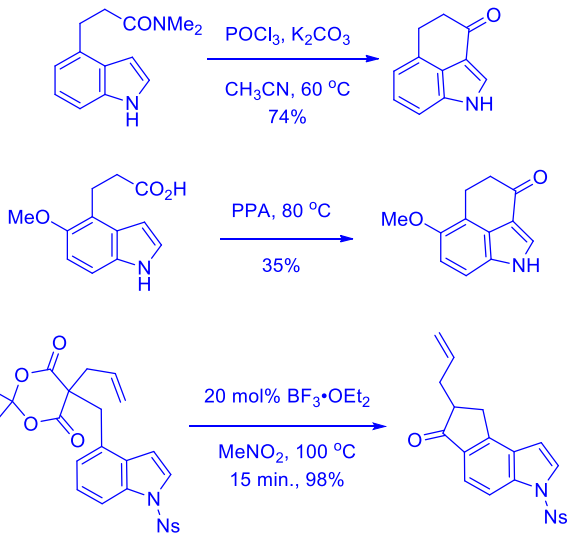
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Example 3, Intramolecular Friedel–Crafts acylation[8]

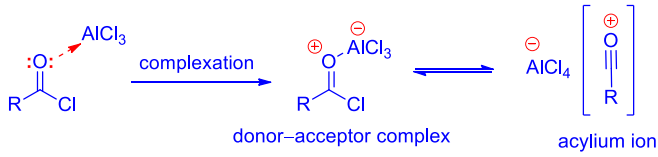


PPSE = Trimethylsilyl polyphosphate

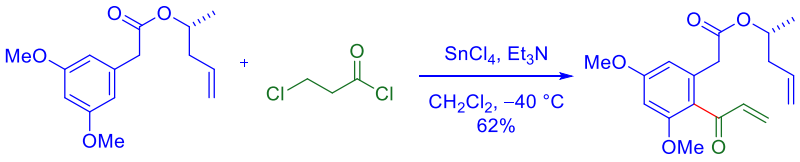
Example 4, Intramolecular Friedel–Crafts acylation[9]



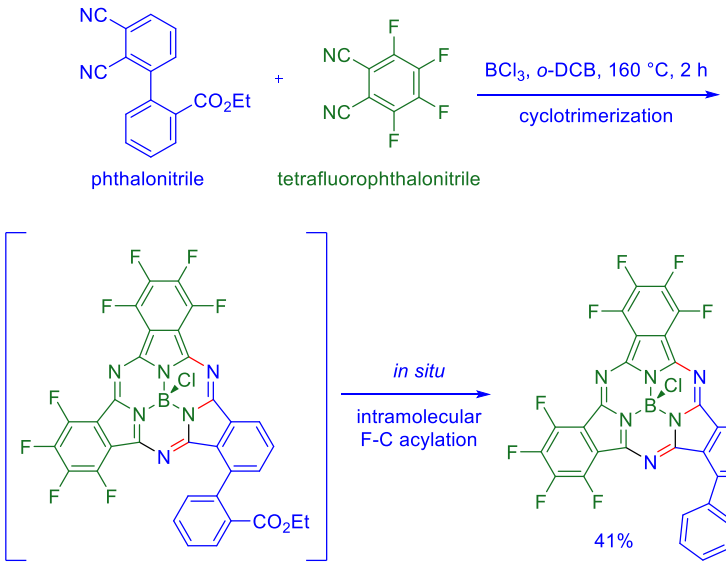
Example 5, "Kinetic capture" of acylium ion[11]



Example 6, Introduction of an acrolyl group by Friedel–Crafts acylation followed by elimination under mild conditions[12]



Example 7, Intramolecular Friedel–Crafts acylation "*in situ*"[13]



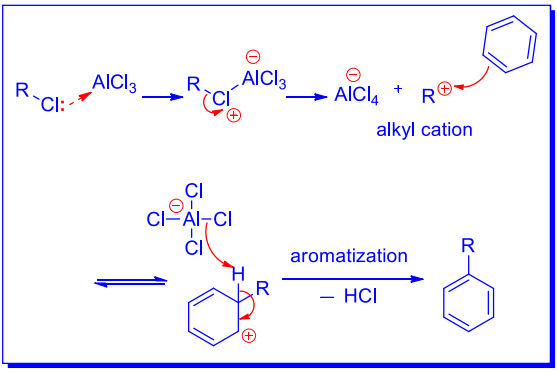
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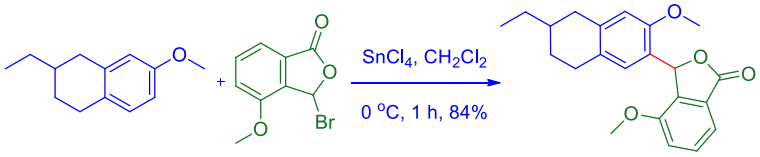
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Friedel–Crafts Alkylation Reaction:

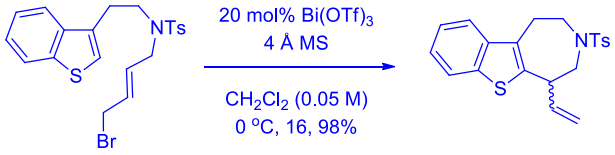
Introduction of an alkyl group onto an aromatic substrate by treating the substrate with an alkylating agent such as alkyl halide, alkene, alkyne and alcohol in the presence of a Lewis acid.



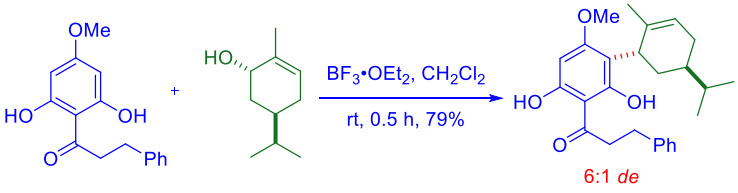
Example 1[1]



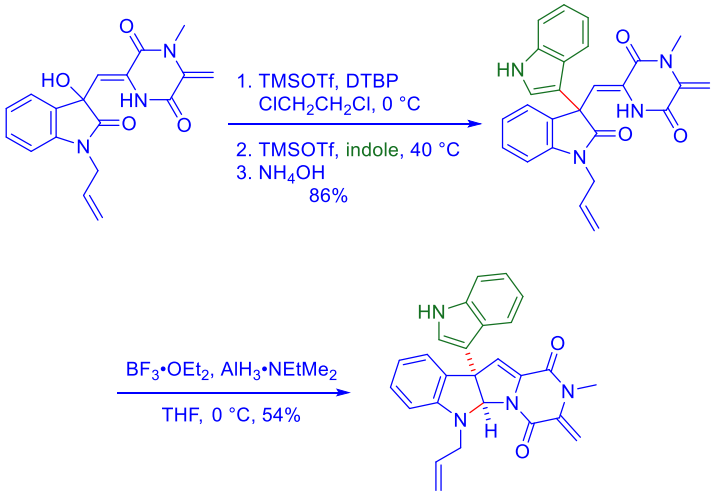
Example 2, An intramolecular Friedel–Crafts alkylation[6]



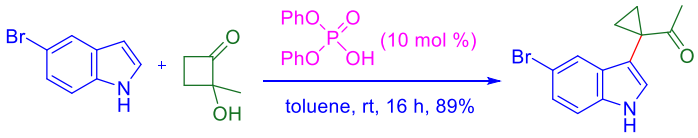
Example 3, Diastereoselctive Friedel–Crafts alkylation[7]



Example 4, Friedel–Crafts alkylation to set up a quaternary carbon center (DTBP = di-*tert*-butyl peroxide)[8]



Example 5, Friedel–Crafts alkylation followed by ring contraction[9]

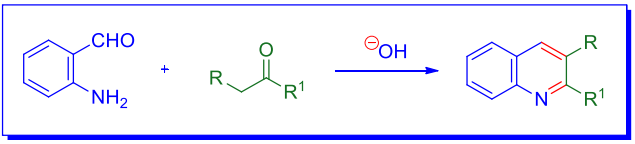


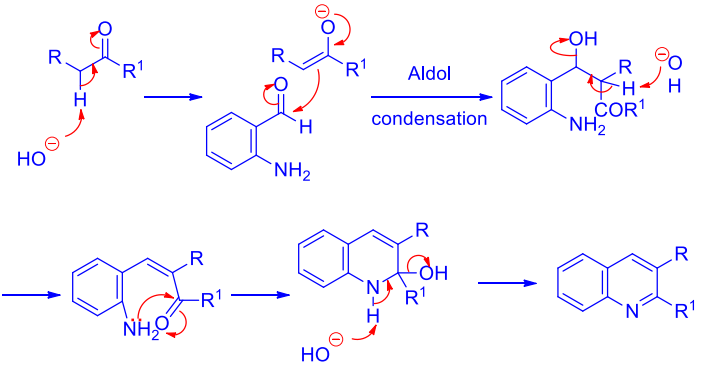
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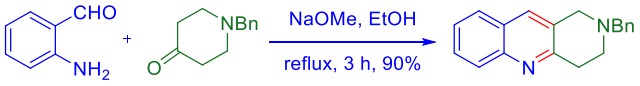
Friedländer Quinoline Synthesis

Also known as the Friedländer condensation, it combines an α-amino aldehyde or ketone with another aldehyde or ketone with at least one methylene α adjacent to the carbonyl to furnish a substituted quinoline. The reaction can be promoted by either acid, base, or heat.

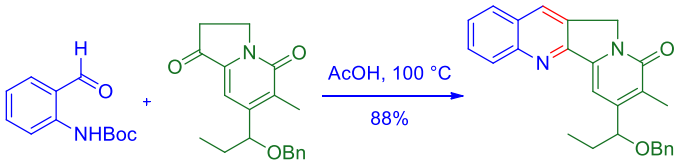




Example 1[5]

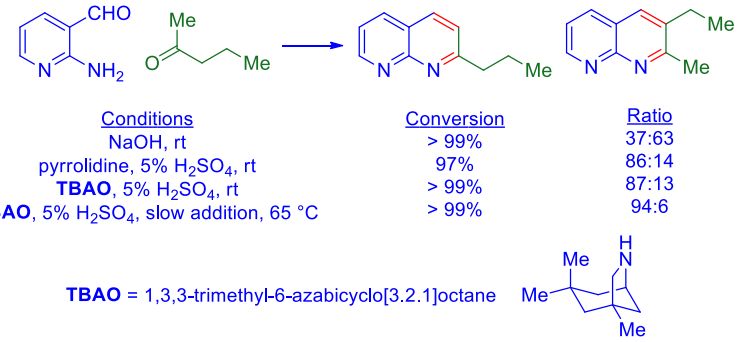


Example 2[7]

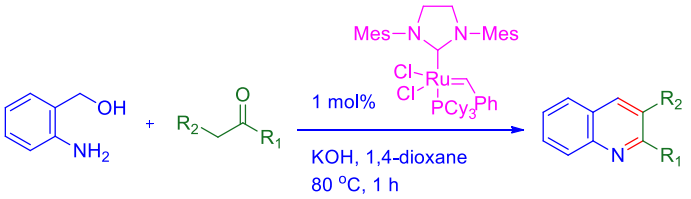


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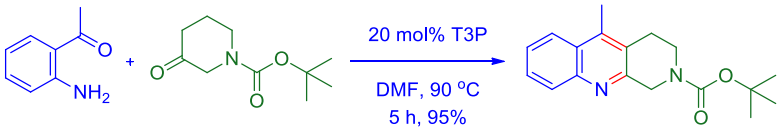
Example 3[8]



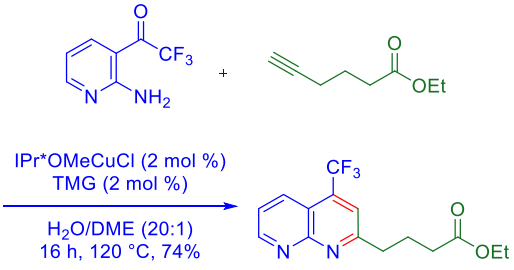
Example 4[10]



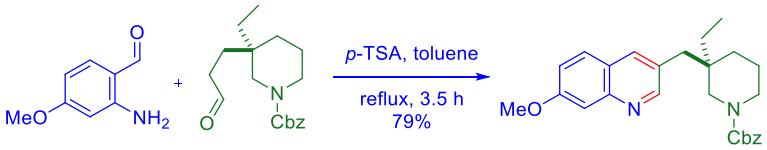
Example 5, Using propylphosphonic anhydride (T3P) as the coupling agent[11]



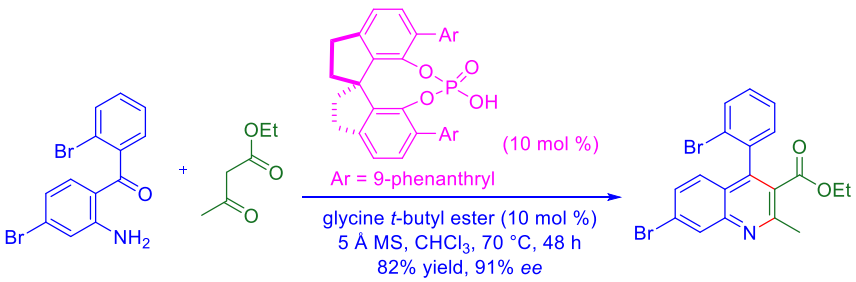
Example 6, NHC-Cu(I)-catalyzed Friedländer-type annulation of fluorinated *o*-aminophenones with alkynes on water[12]



Example 7, Toward total synthesis of (+)-eburnamonine[13]



Example 8, Organocatalytic atroposelective Friedländer quinoline heteroannulation[14]

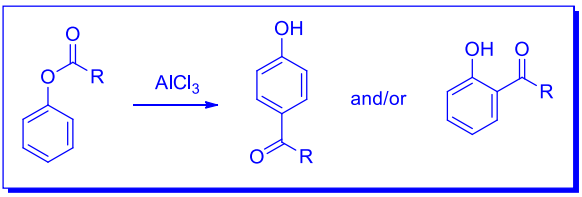


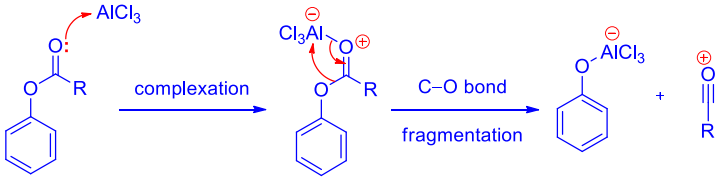
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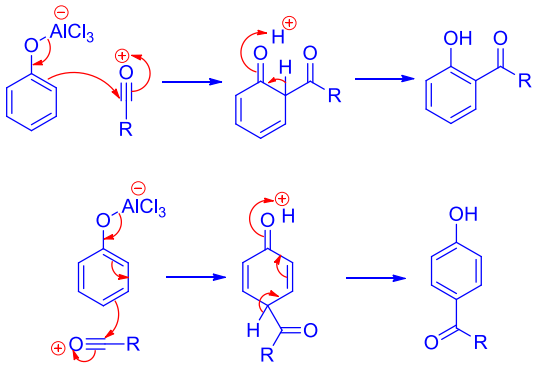
Fries Rearrangement

Lewis acid-catalyzed rearrangement of phenol esters and lactams to 2- or 4-ketophenols. Also known as the Fries–Finck rearrangement.

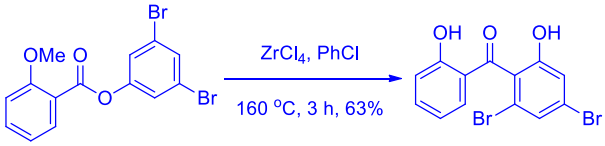




aluminum phenolate, acylium ion

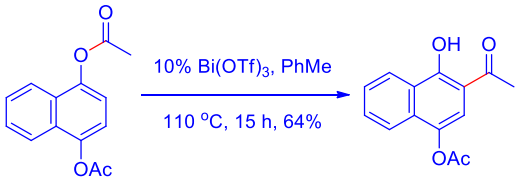


Example 1[5]

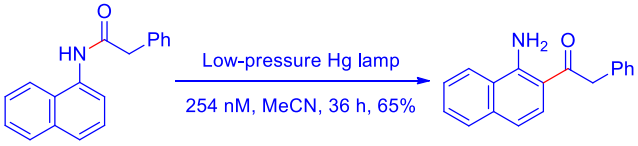


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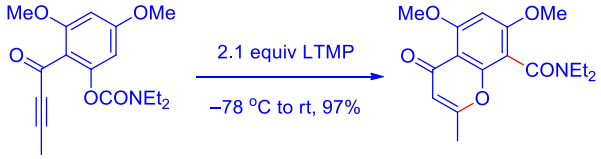
Example 2[6]



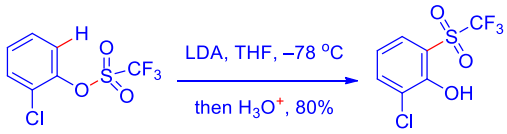
Example 3, Photo-Fries rearrangement[7]



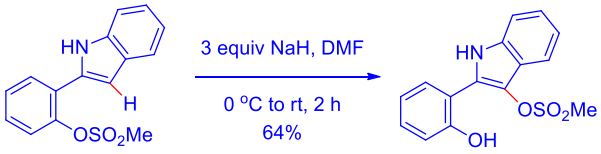
Example 4, *ortho*-Fries rearrangement[8]



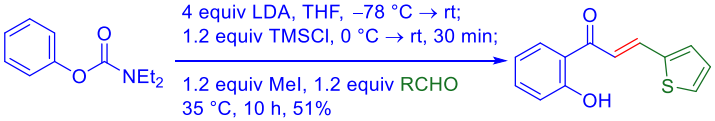
Example 5, Thia-Fries rearrangement[9]



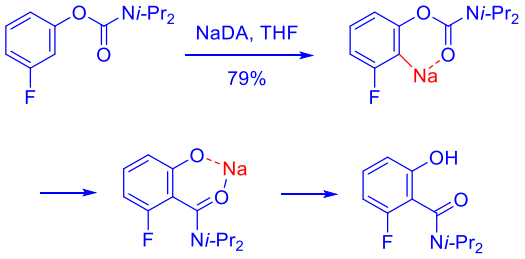
Example 6, Remote anionic thia-Fries rearrangement[10]



Example 7, A consecutive Snieckus–Fries rearrangement, anionic Si→C alkyl rearrangement, and Claisen–Schmidt condensation[11]



Example 8, Orthosodiations employing sodium diisopropylamide (NaDA) and Snieckus–Fries Rearrangement of aryl carbamates[12]

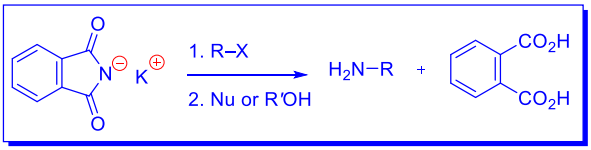


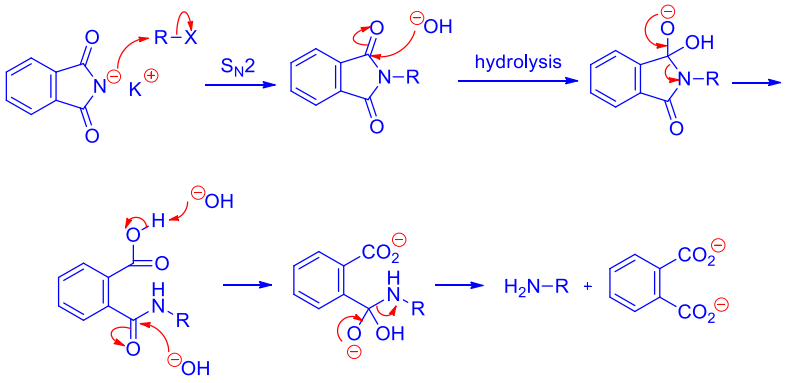
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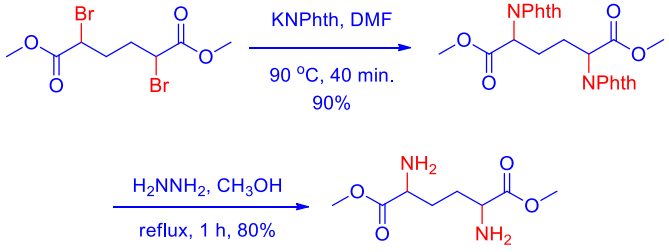
Gabriel Synthesis

Synthesis of primary amines using potassium phthalimide and alkyl halides.

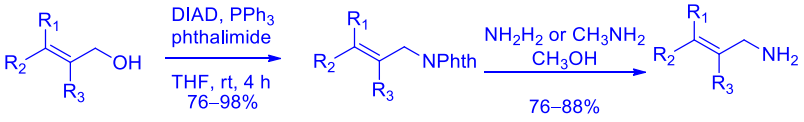




Example 1[2]

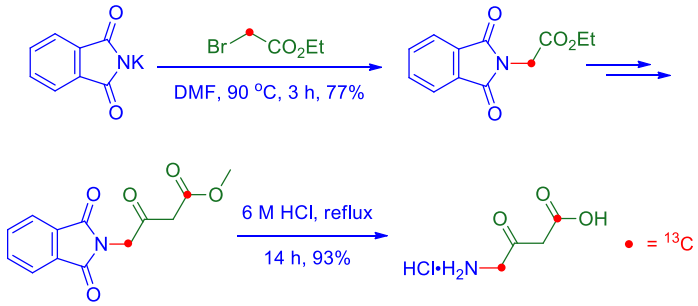


Example 2[6]

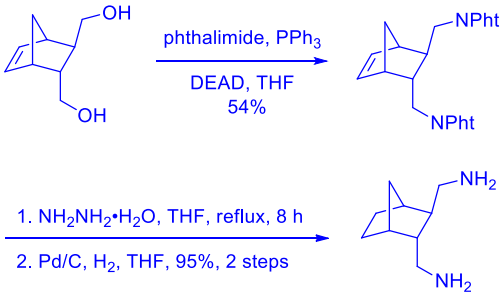


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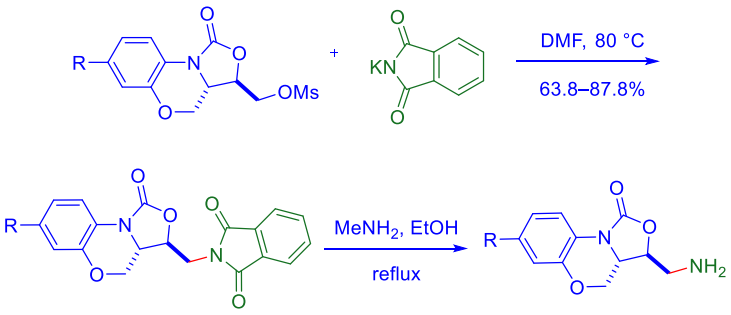
Example 3[8]



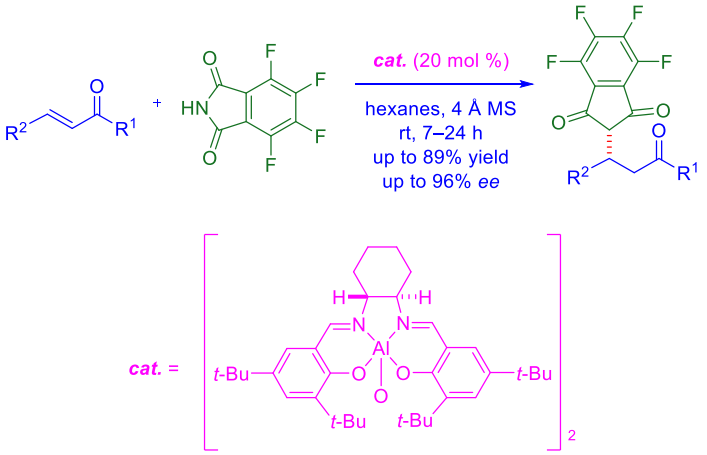
Example 4[9]



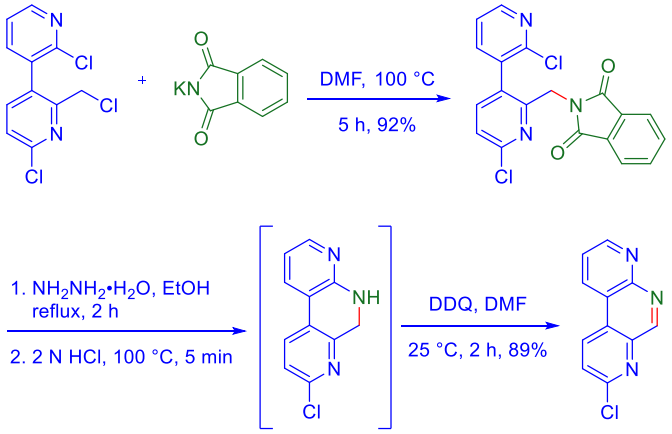
Example 5, Utility in medicinal chemistry[14]



Example 6, Enantioselective Gabriel synthesis[15]



Example 7, Intermolecular cyclization after Gabriel synthesis[16]



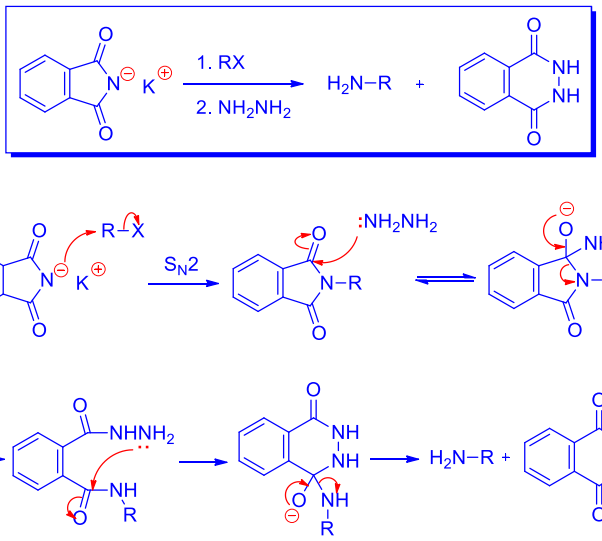
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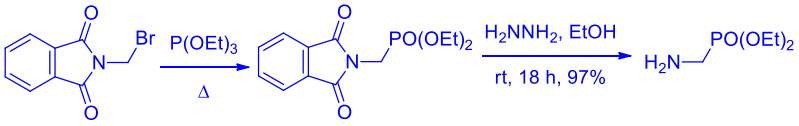
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Ing–Manske Procedure

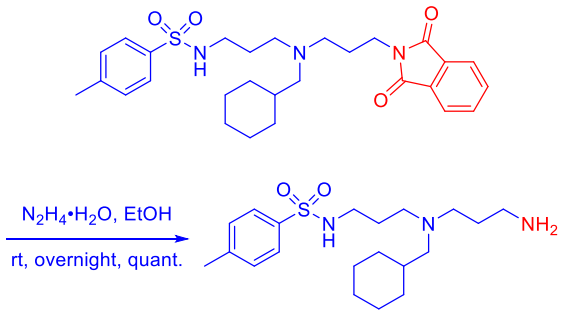
A variant of Gabriel amine synthesis where hydrazine is used to release the amine from the corresponding phthalimide:



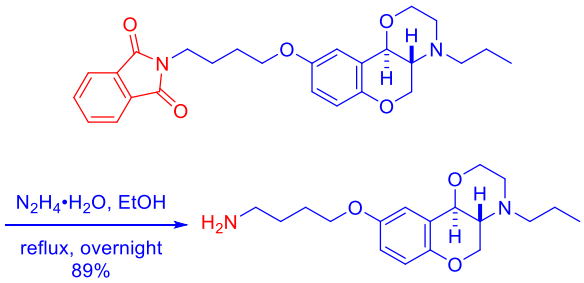
Example 1[6]



Example 2, Toward preparation of human cluster of differentiation 4 (CD4) receptor modulators[10]



Example 3, Toward preparation of D_3 dopamine receptor agonist[11]



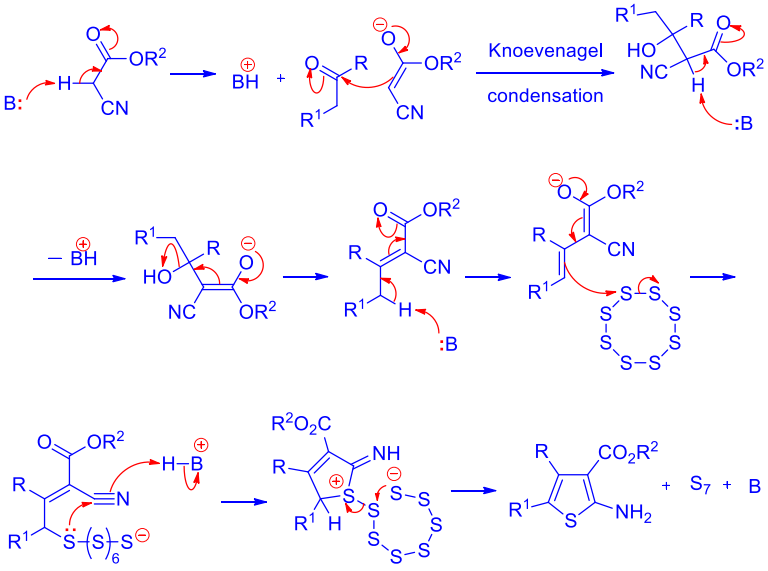
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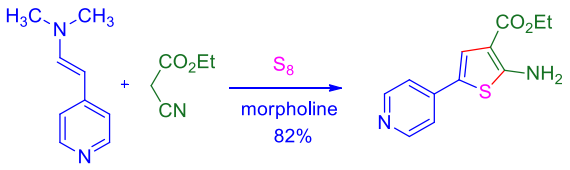
Gewald Aminothiophene Synthesis

Base-promoted aminothiophene formation from ketone, α-active methylene nitrile and elemental sulfur.

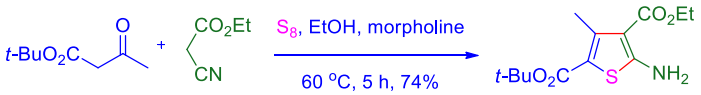




Example 1[4]

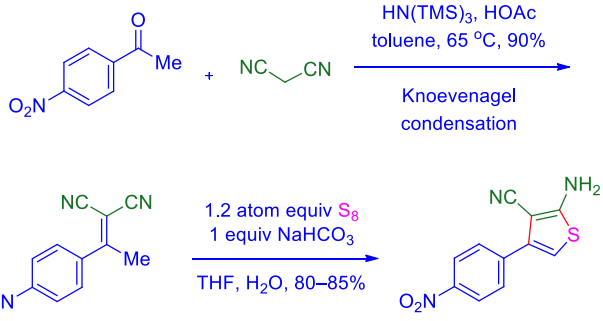


Example 2[7]

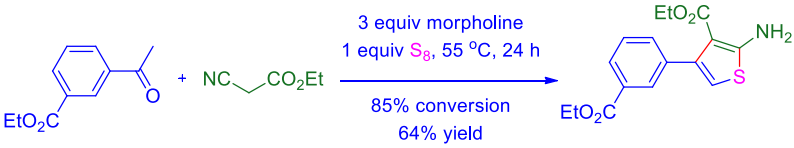


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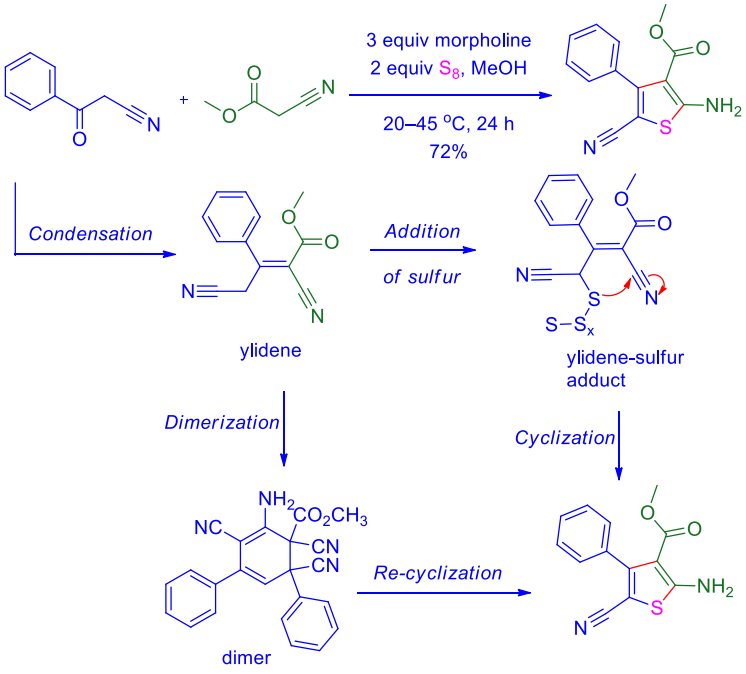
Example 3[9]



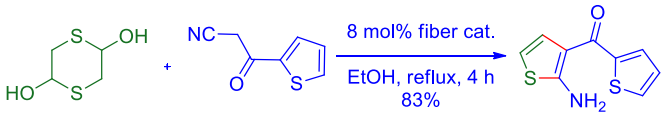
Example 4[10]



Example 5[11]



Example 6, *N*-Methylpiperazine-functionalized polyacrylonitrile fiber catalyst[12]



Example 7, $NaAlO_2$ as an environmentally-friendly and inexpensive catalyst[13]

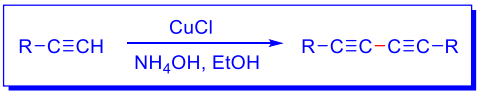


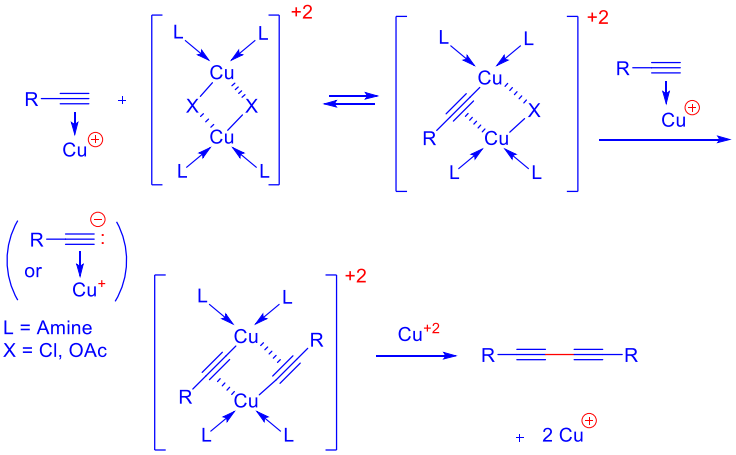
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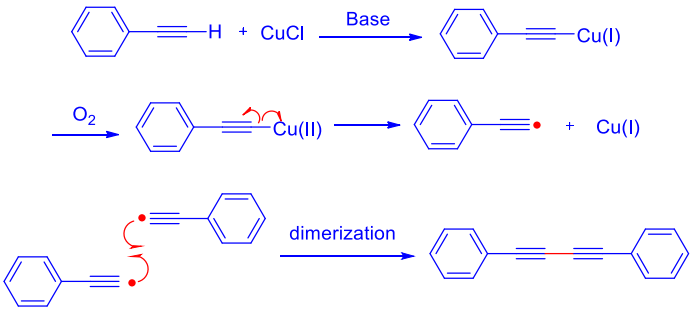
Glaser Coupling

Sometimes known as the Glaser–Hay coupling, it is the oxidative homo-coupling of terminal alkynes using copper catalyst in the presence of oxygen.

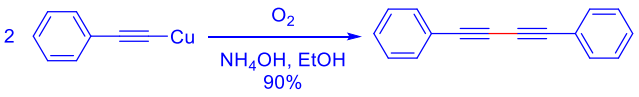




Alternatively, the radical mechanism is also operative:

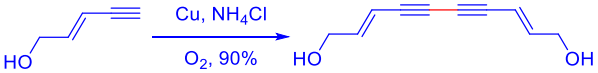


Example 1[1]

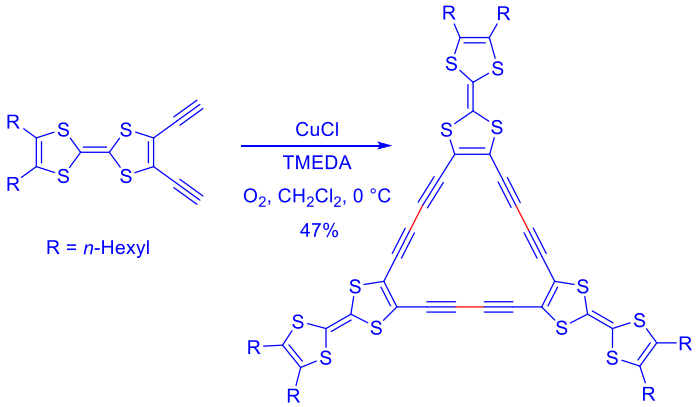


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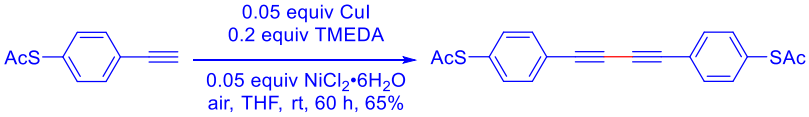
Example 2, Homo-coupling[2]



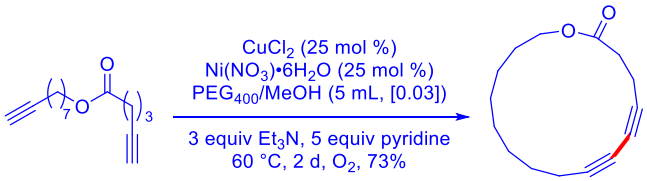
Example 3[7]



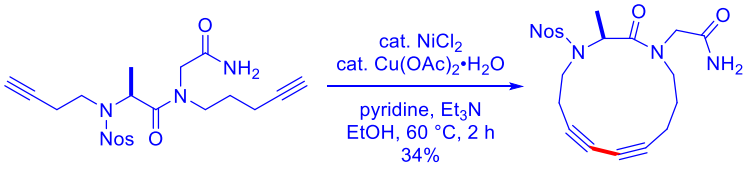
Example 4[9]



Example 5, Macrocyclic Glaser–Hay coupling[10]



Example 6, Macrocyclic Glaser–Hay coupling to prepare amino acids[13]

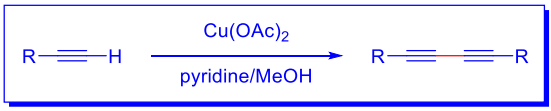


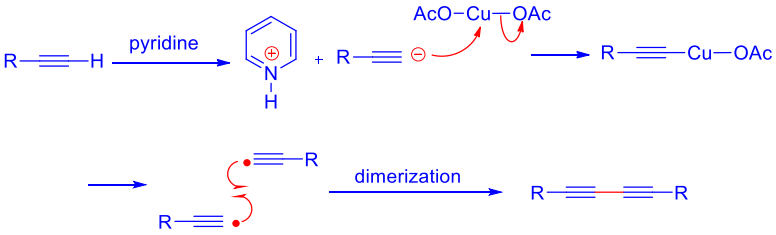
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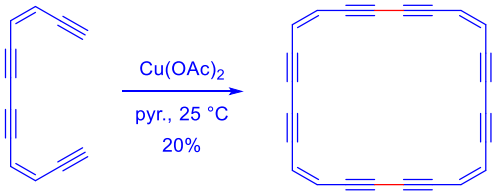
Eglinton Coupling

Oxidative homo-coupling of terminal alkynes mediated by stoichiometric (or often excess) $Cu(OAc)_2$. A variant of the Glaser coupling reaction.

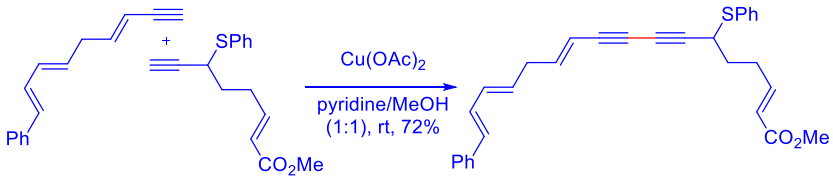




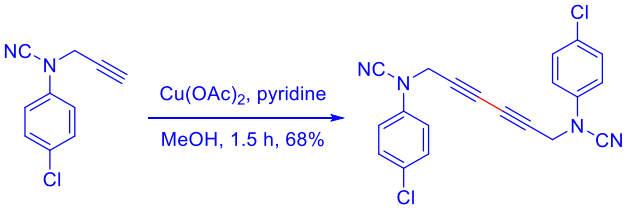
Example 1, Homo-coupling[2]



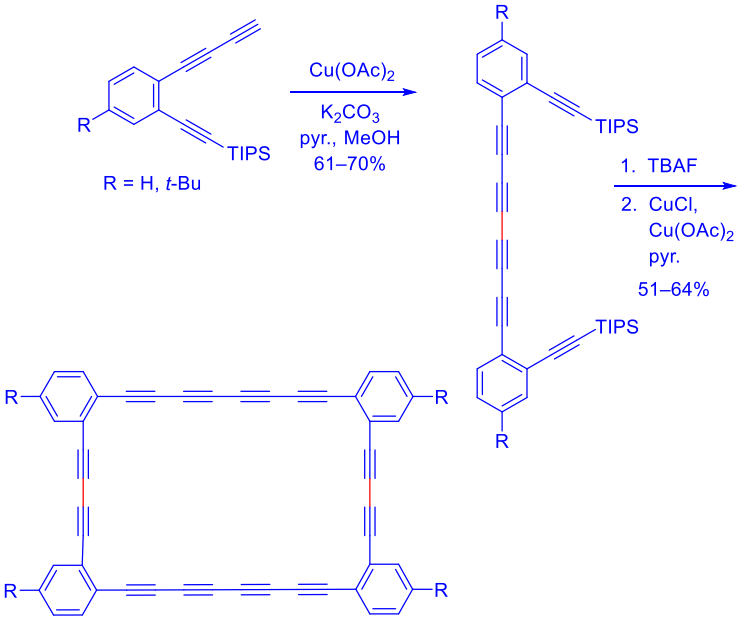
Example 2, Cross-coupling[3]



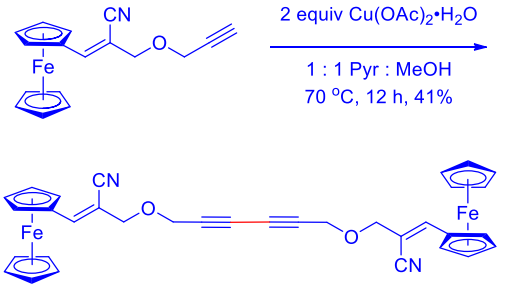
Example 3, Homo-coupling[4]



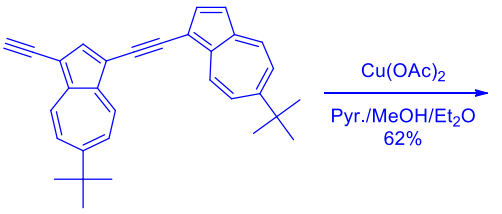
Example 4[5]

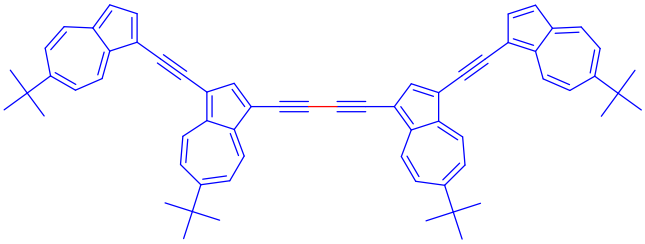


Example 5[11]

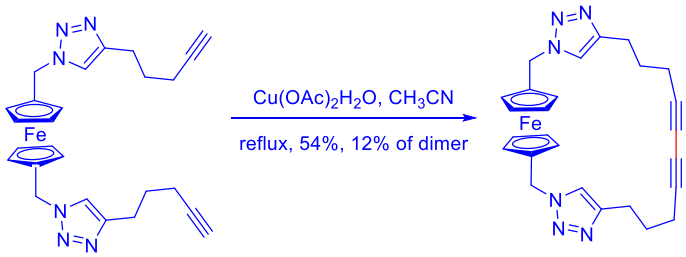


Example 6[12]

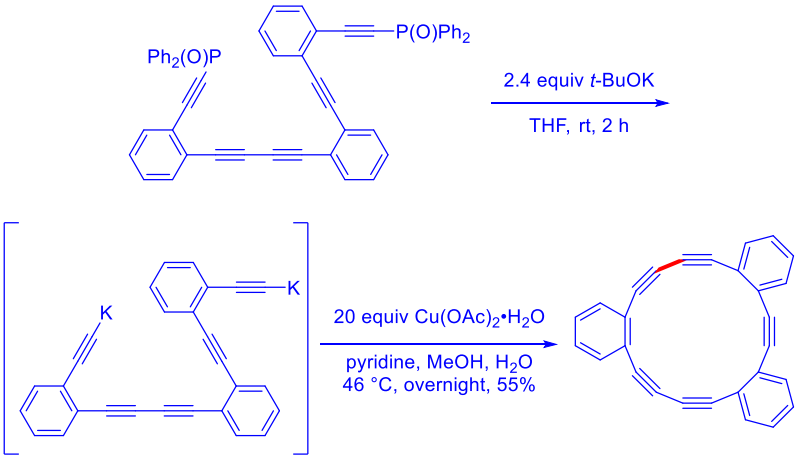




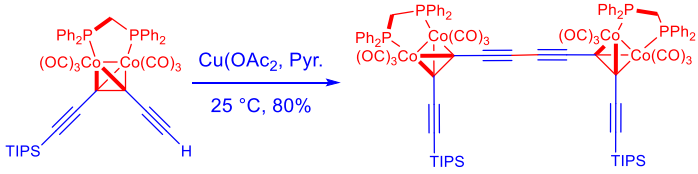
Example 7[13]



Example 8, $Cu(OAc)_2$-catalyzed intramolecular Eglington coupling[14]



Example 9, Employing dicobalt masking group to protect alkynes[15]



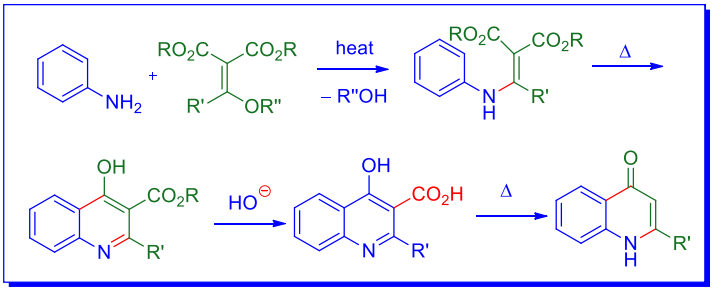
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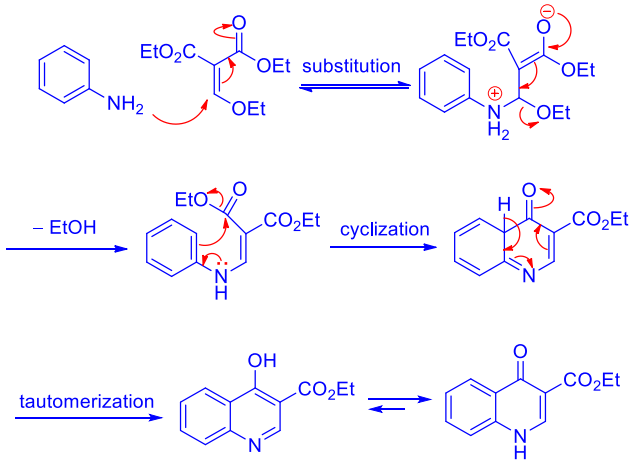
Gould–Jacobs Reaction

The Gould–Jacobs reaction is a sequence of the following reactions:

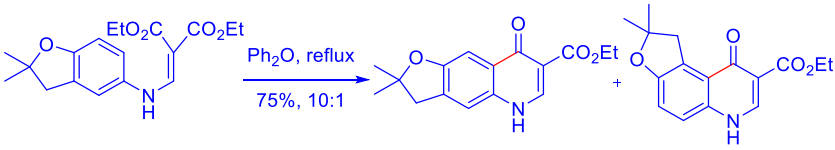
a. Substitution of an aniline with either alkoxy methylenemalonic ester or acyl malonic ester providing the anilinomethylenemalonic ester;
b. Cyclization of to the 4-hydroxy-3-carboalkoxyquinoline (4-hydroxyquinolines exist predominantly in 4-oxoform);
c. Saponification to form acid;
d. Decarboxylation to give the 4-hydroxyquinoline. Extension could lead to unsubstituted parent heterocycles with fused pyridine ring of Skraup type.



R = alkyl; R′ = alkyl, aryl, or H; R″ = alkyl or H

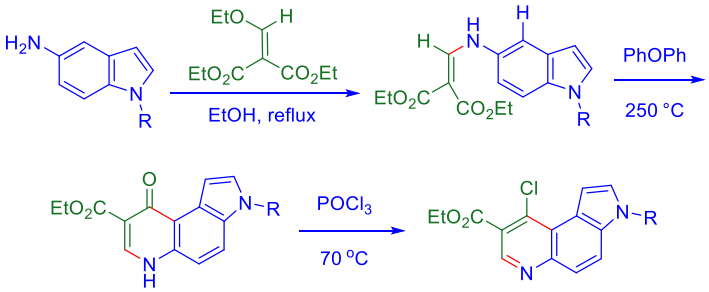


Example 1[3]

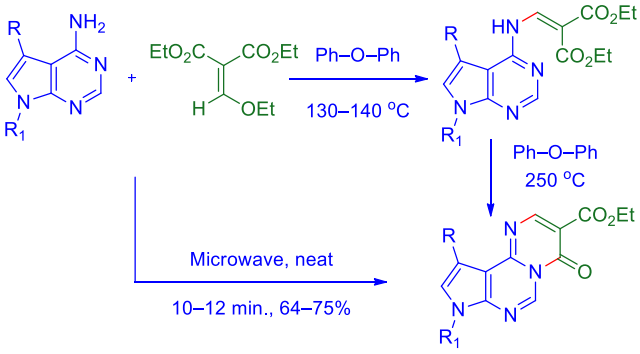


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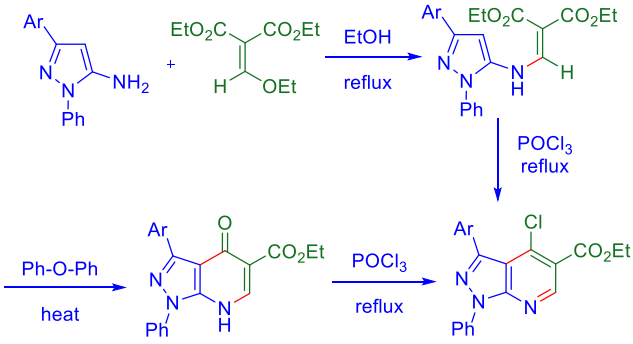
Example 2[7]



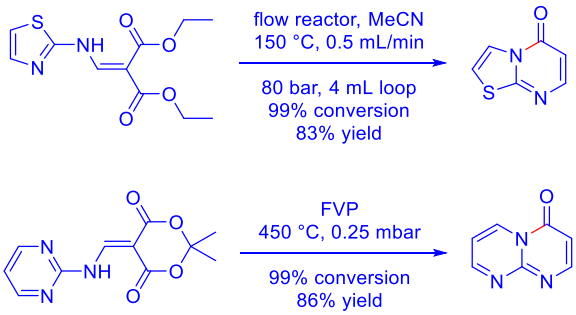
Example 3, Microwave-assisted Gould–Jacobs reaction[8]



Example 4[9]



Example 5, Gould–Jacobs reaction in a novel three-mode pyrolysis reactor[11]

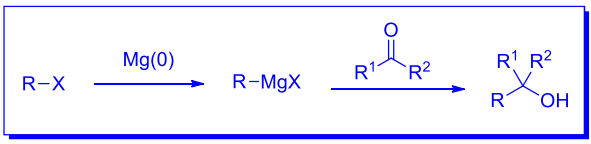


References

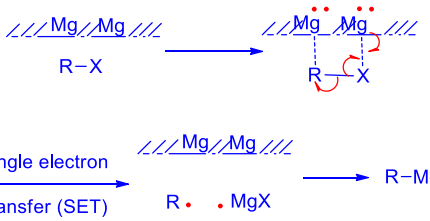
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Grignard Reaction

Addition of organomagnesium compounds (Grignard reagents), generated from organohalides and magnesium metal, to electrophiles.



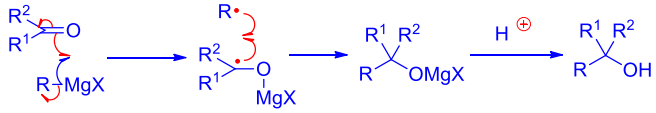
Formation of the Grignard reagent:



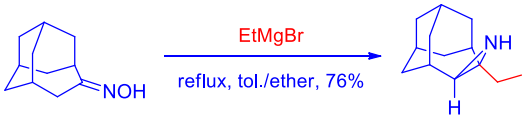
Grignard reaction, ionic mechanism:



Grignard reaction, radical mechanism,



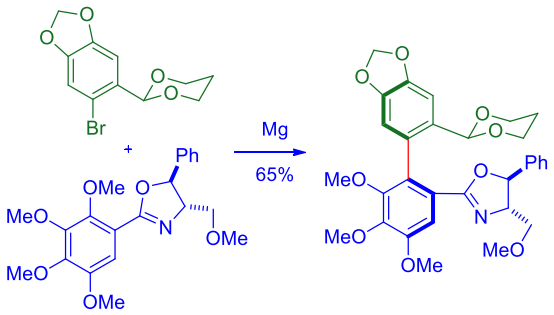
Example 1[4]



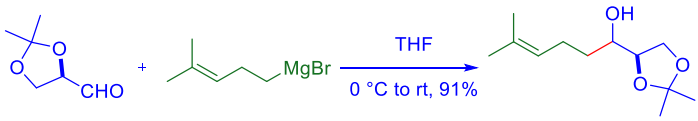
This reaction is known as the *Hoch–Campbell aziridine synthesis*, which entails treatment of ketoximes with excess Grignard reagents and subsequent hydrolysis of the organometallic complex to produce aziridines.

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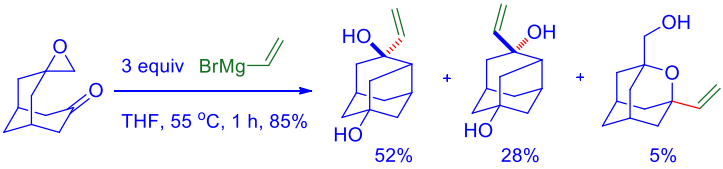
Example 2[5]



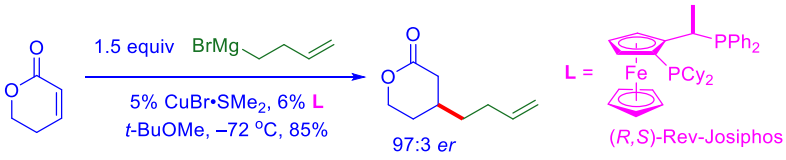
Example 5[10]



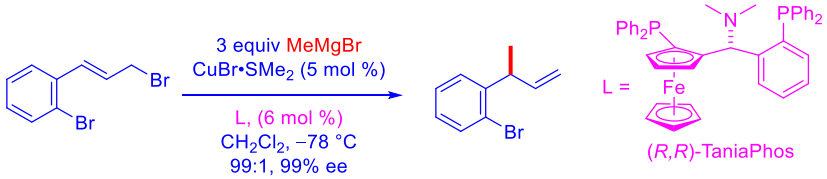
Example 6[11]



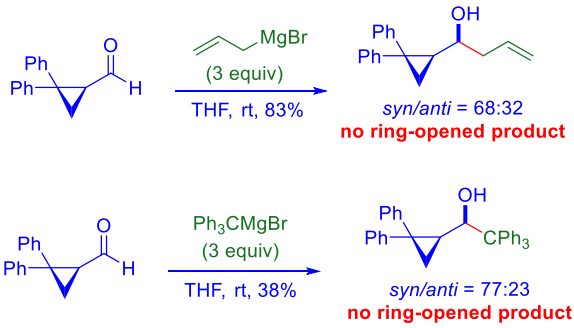
Example 7, Asymmetric conjugate addition[12]



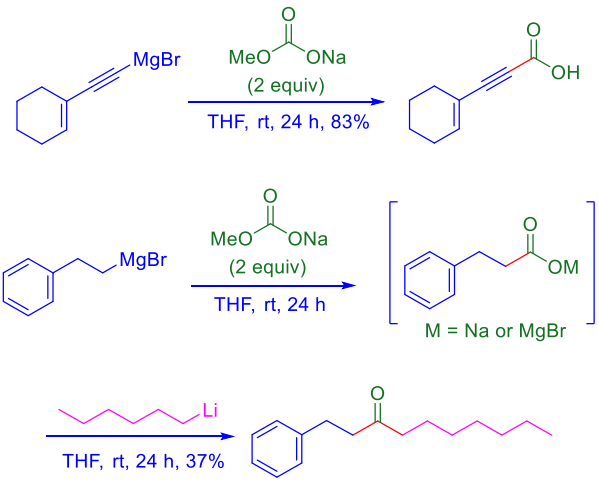
Example 7, Regio- and enantioselective copper-catalyzed allylic alkylation of with Grignard reagents[13]



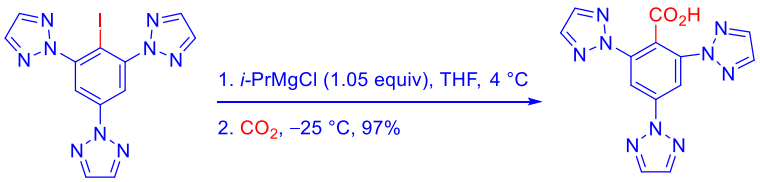
Example 8, Additions of Grignard reagents to aliphatic aldehydes do not involve single-electron-transfer (SET) processes[14]



Example 9, Sodium methyl carbonate (SMC) as an effective C1 synthon[15]



Example 10, Grignard carboxylation[16]

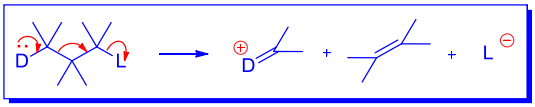


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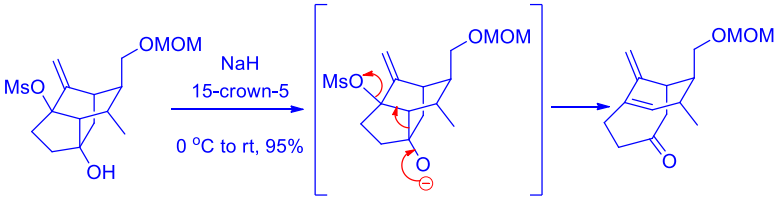
Grob Fragmentation

The C–C bond cleavage primarily via a concerted process involving a five-atom system.
General scheme:

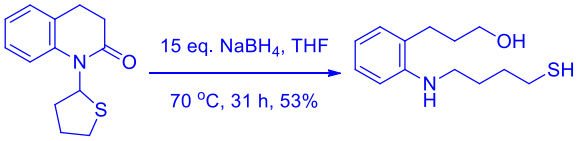


D = O^-, NR_2; L = OH_2^+, OTs, I, Br, Cl

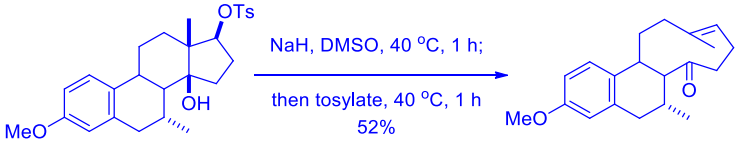
Example 1[2]



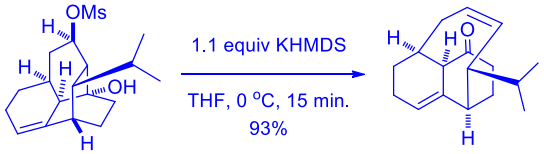
Example 2, Aza-Grob fragmentation[3]



Example 3[7]

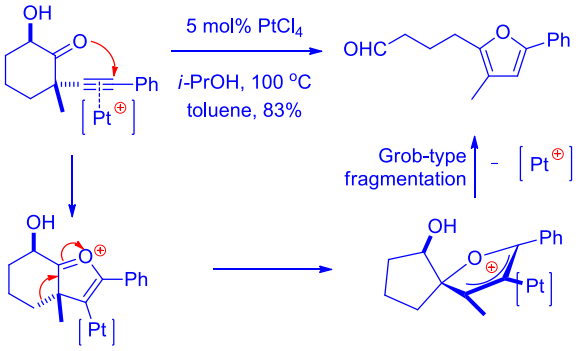


Example 4[8]

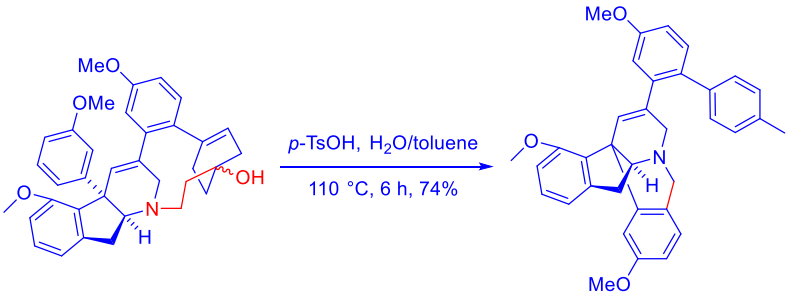


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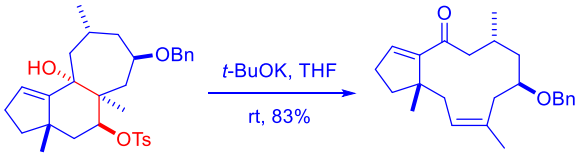
Example 5[8]



Example 6, Grob-type fragmentation releases paracyclophane ring strain in a late-stage precursor of haouamine A[12]



Example 7, Grob-fragmentation-enabled approach to clavulactone analogs[13]



References

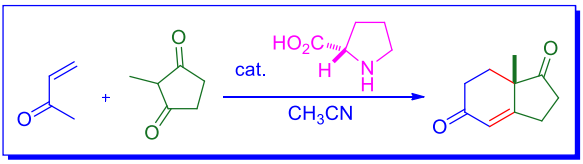
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cessor in 1960. An investigation of the reductive elimination of bromine from 1,4-dibromides in the presence of zinc led in 1955 to the recognition of heterolytic fragmentation as a general reaction principle. The heterolytic fragmentation has now entered textbooks under his name. Experimental evidence for vinyl cations as discrete reactive intermediates was also first provided by Grob. Cyril Grob never acted impulsively, but always calmly and deliberately. He never sought attention in public, but fulfilled his social duties efficiently, reliably, and without a fuss. He died in his home in Basel (Switzerland) on December 15, 2003 at the age of 86. (Schiess, P. *Angew. Chem. Int. Ed.* **2004,** *43,* 4392.) A review[10] revealed that Grob was not even the first to investigate such reactions.

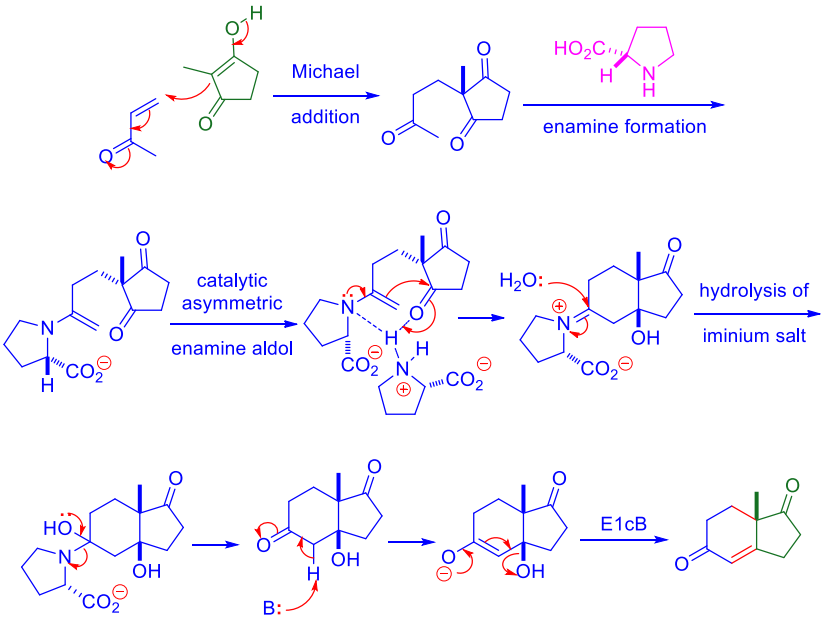
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Hajos–Wiechert Reaction

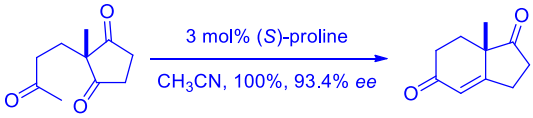
Asymmetric Robinson annulation catalyzed by (*S*)-(−)-proline.



Hajos–Wiechert ketone



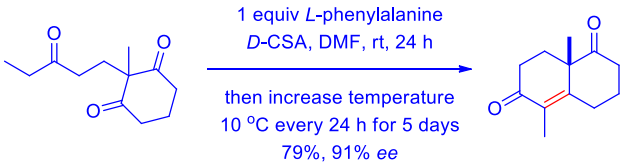
Example 1, Intramolecular Hajos–Wiechert reaction[1a]



Hajos–Wiechert ketone

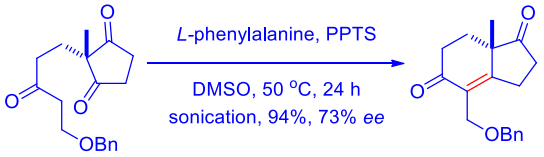
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Example 2[3]



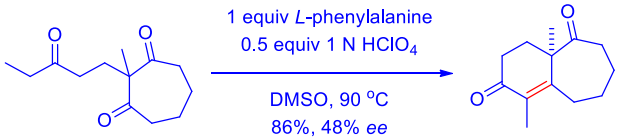
Wieland–Miescher ketone

Example 3[8]

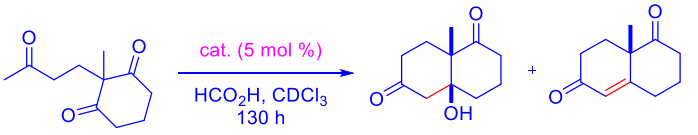


Hajos–Wiechert ketone

Example 4[9]

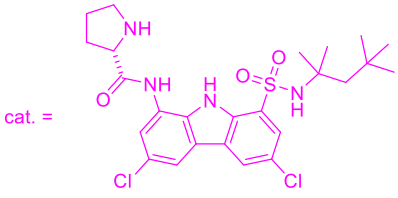


Example 5, Bifunctional organocatalysts based on a carbazole scaffold[14]



15 (99.9% *ee*) : 75 (99.9% *ee*)

Wieland–Miescher ketones



Example 5, Hajos–Parrish–Eder–Sauer–Wiechert-type reaction (a mouthful?!)[15]



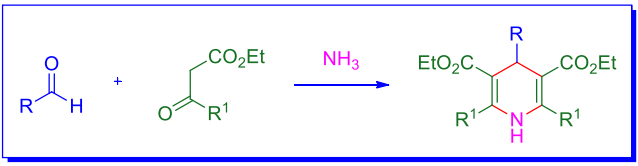
Hajos–Wiechert ketone

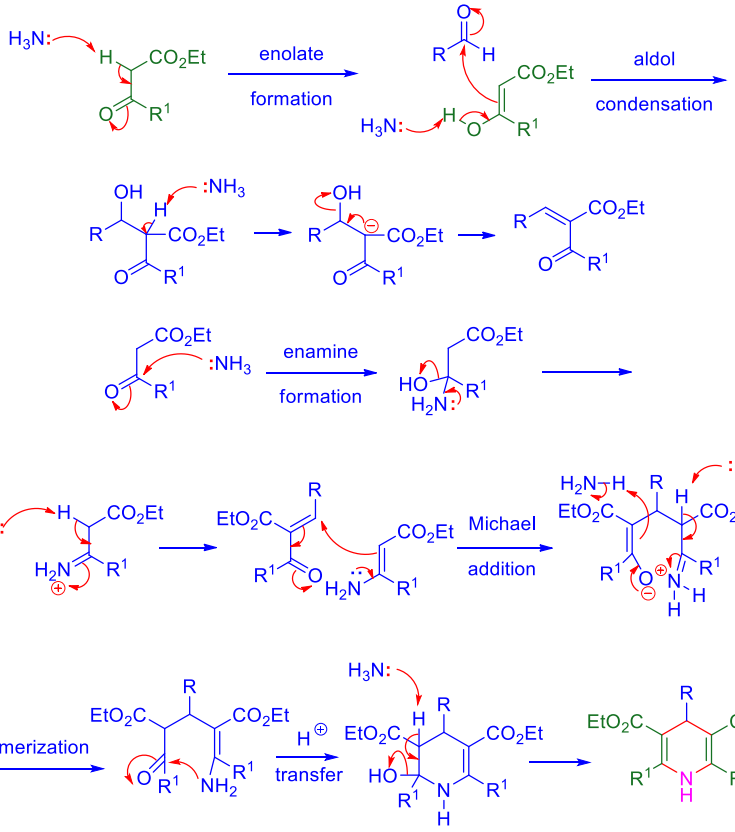
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Hantzsch Dihydropyridine Synthesis

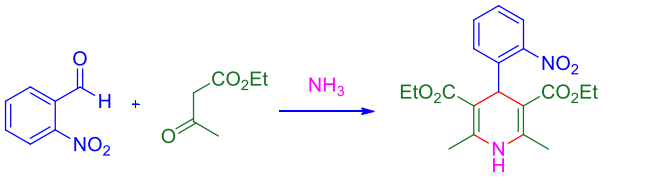
1,4-Dihydropyridine from the condensation of aldehyde, β-ketoester and ammonia. Hantzsch 1,4-dihydropyridines are popular reducing reagents in organocatalysis. Well-known calcium channel blockers (CCBs) nifedipine (Adalat), felodipine (Plendil), and amlodipine (Norvasc) for treating hypertension all have 1,4-dihydropyridine core structures.





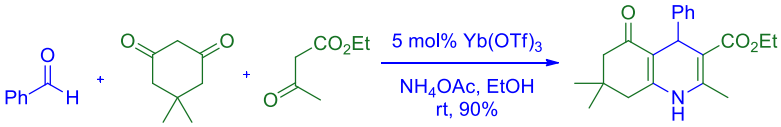
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Example 1[2]

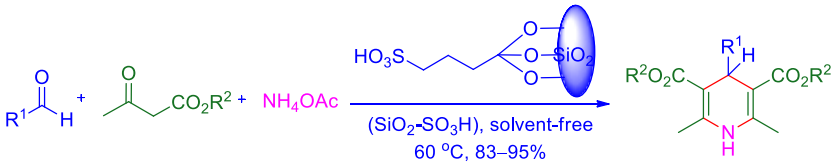


nifedipine, the first calcium channel blocker

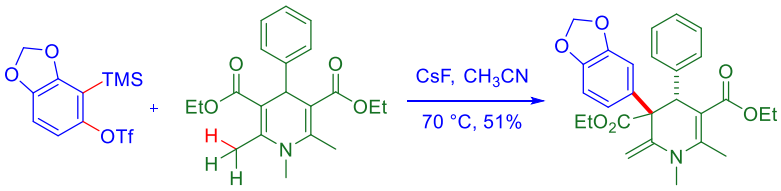
Example 2[10]



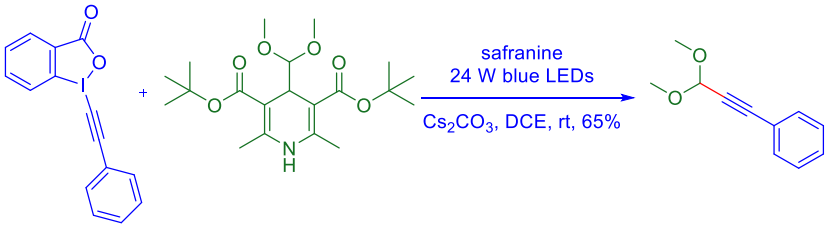
Example 3, Covalently anchored sulfonic acid on silica gel as catalyst[10]



Example 4, Intermolecular aryne *ene reaction*[13]



Example 5, Hantzsch ester for radical alkynylation (photochemistry)[14]

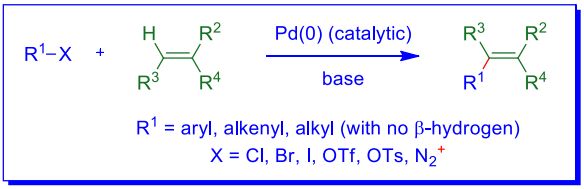


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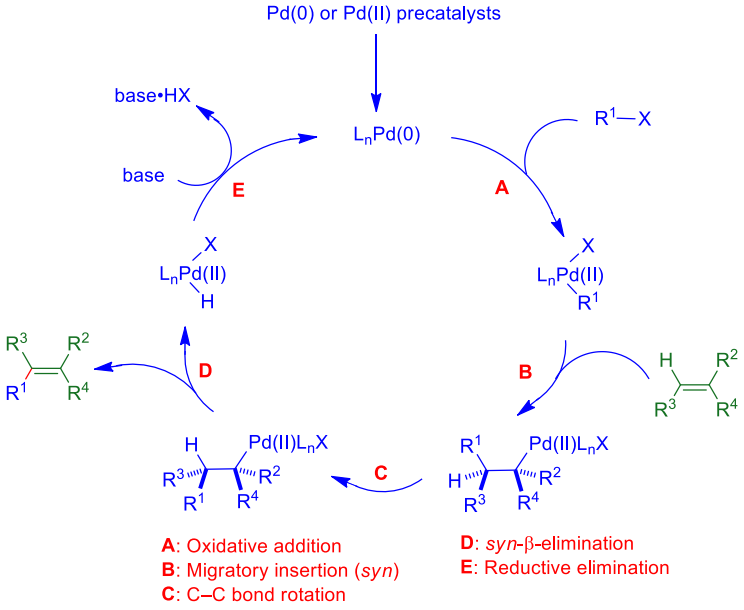
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Heck Reaction

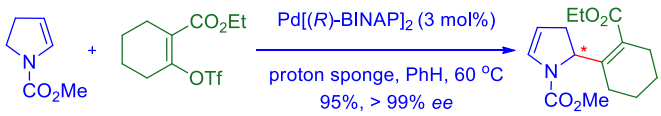
The palladium-catalyzed alkenylation or arylation of olefins.



The catalytic cycle:

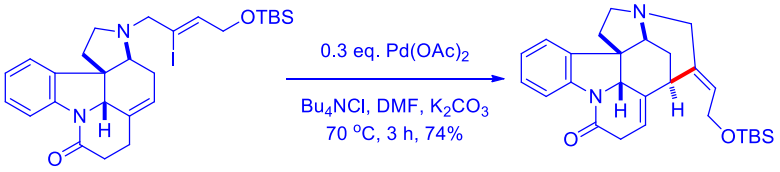


Example 1, Asymmetric intermolecular Heck reaction[6]

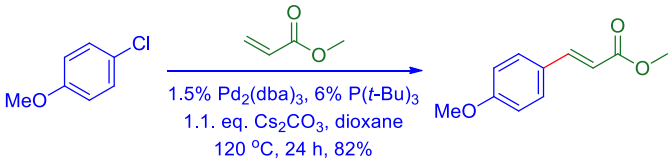


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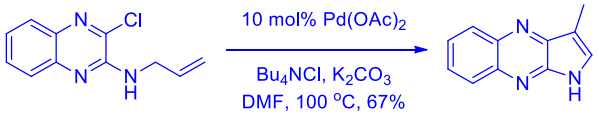
Example 2, Intramolecular Heck[7]



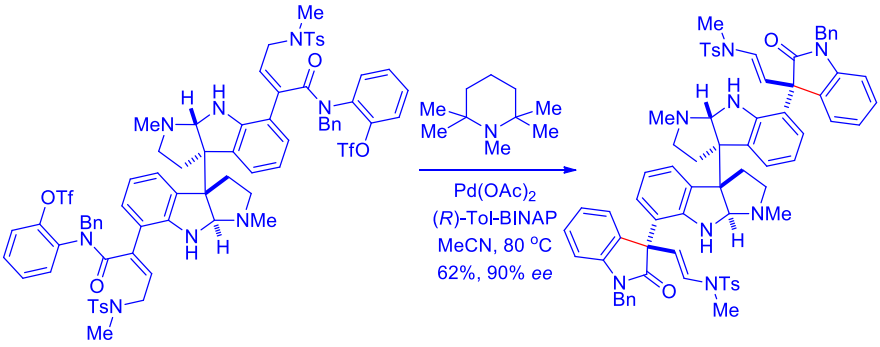
Example 3[8]



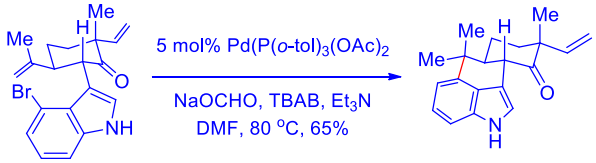
Example 4, Intramolecular Heck[9]



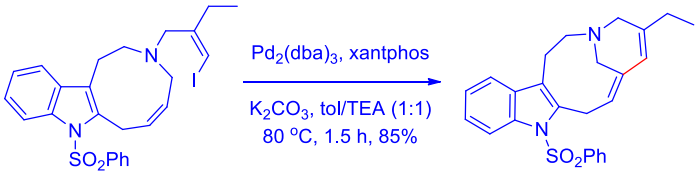
Example 5, Intramolecular Heck[13]



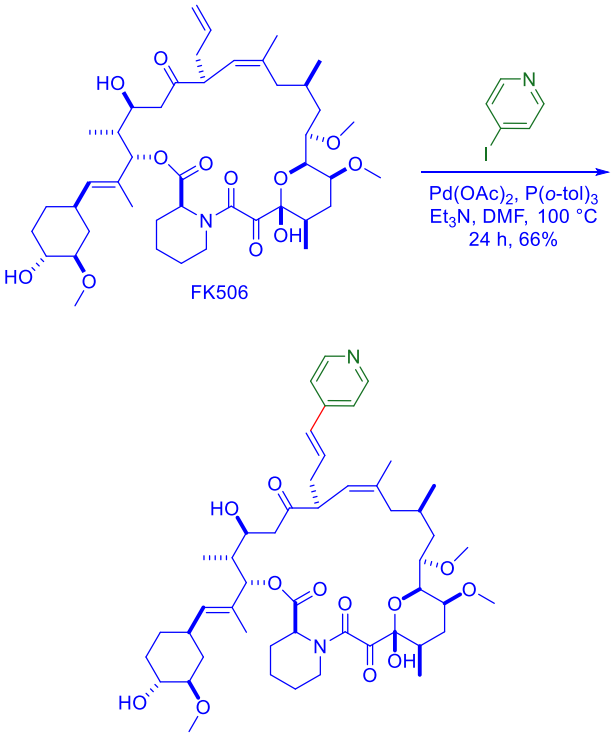
Example 6, Reductive Heck reaction[17]



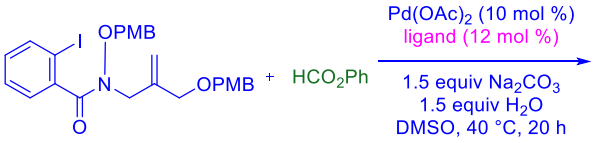
Example 7, Intramolecular Heck[20]

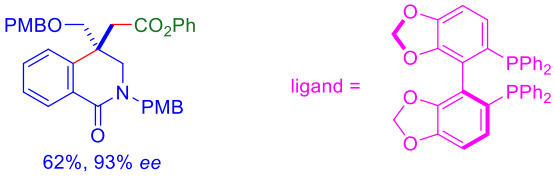


Example 8, Converting FK506 to its non-immunosuppressive analogs[21]



Example 9, Asymmetric Heck carbonylation to prepare quaternary carbon enantiaoselectively[22]



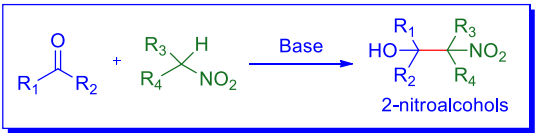


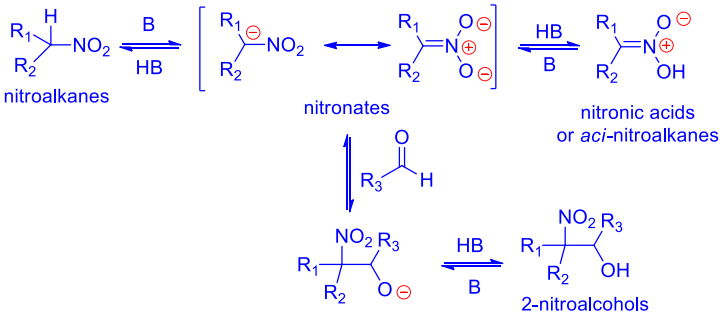
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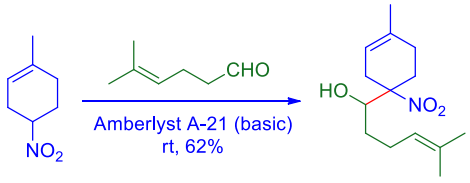
Henry Nitroaldol Reaction

The nitroaldol condensation reaction involving aldehydes and nitronates, derived from deprotonation of nitroalkanes by bases.

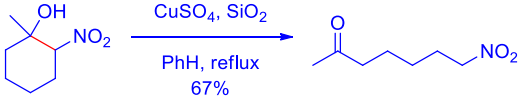




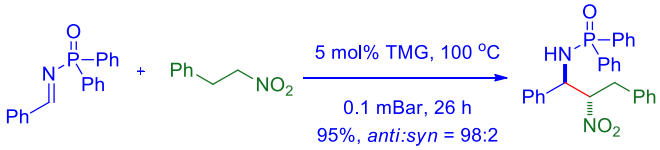
Example 1[4]



Example 2, Retro-Henry reaction[5]

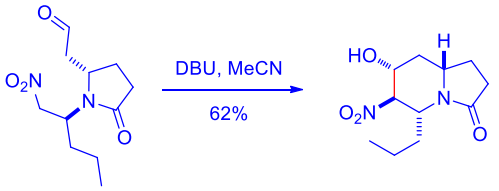


Example 3, Aza-Henry reaction[8]

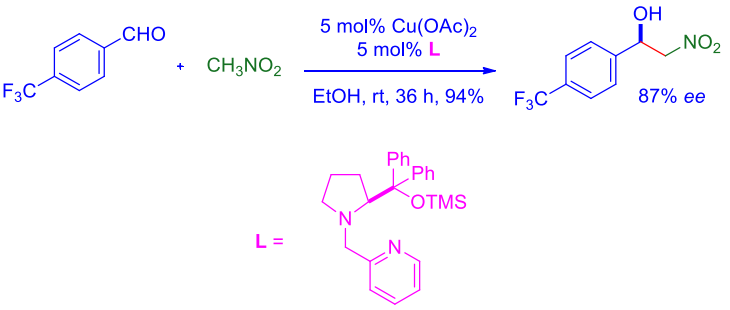


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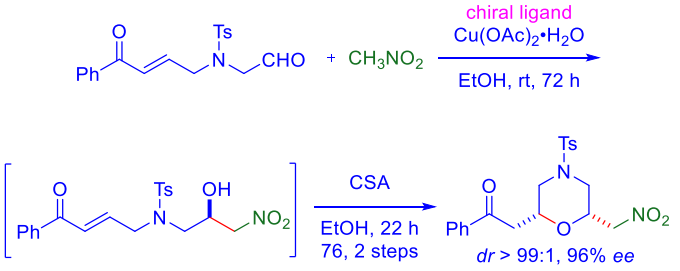
Example 4, Intramolecular Henry reaction[10]



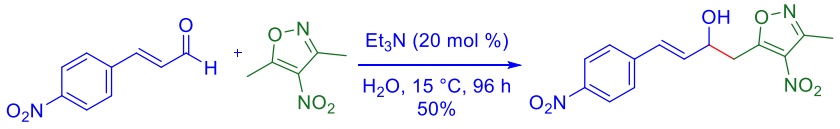
Example 5, A highly asymmetric Henry reaction catalyzed by chiral copper(II) complexes[12]



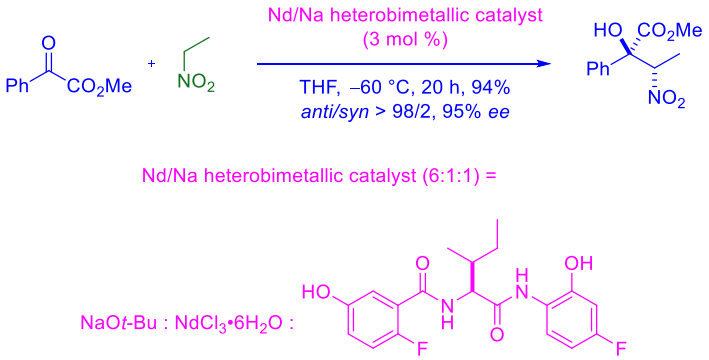
Example 6, 2,6-*cis*-Substituted tetrahydropyrans using a one-pot sequential catalysis[13]



Example 7, Vinylogous Henry reaction, also works for trifluoromethylketone substrates[14]



Example 8, An asymmetric Henry reaction catalyzed by a Nd/Na heterobimetallic catalyst[15]

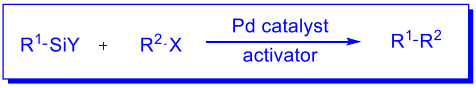


References

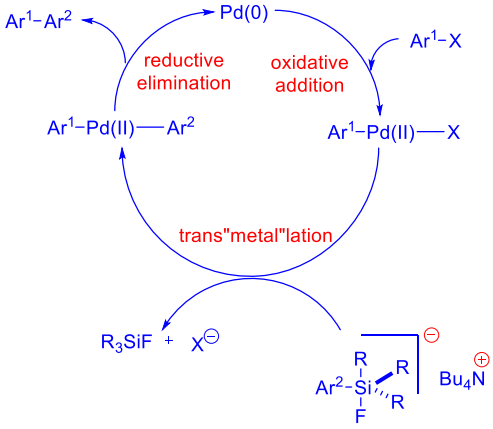
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Hiyama Reaction

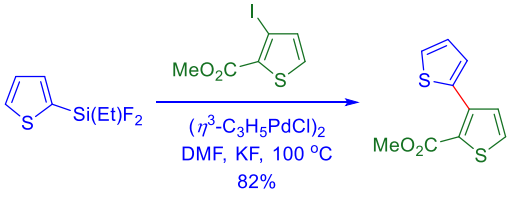
Palladium-catalyzed cross-coupling reaction of organosilicons with organic halides, triflates, *etc*. In the presence of an activating agent such as fluoride or hydroxide (transmetalation is reluctant to occur without the effect of an activating agent). For the catalytic cycle, see the Kumada coupling.



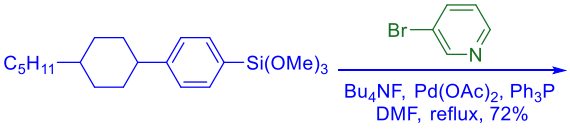
R^1 = alkenyl, aryl, alkynyl, alkyl
R^2 = aryl, alkyl, alkenyl
Y = $(OR)_3$, Me_3, Me_2OH, $Me_{(3-n)}F_{(n+3)}$
X = Cl, Br, I, OTf
activator = TBAF, base



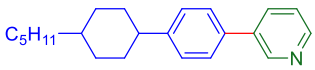
Example 1[1a]



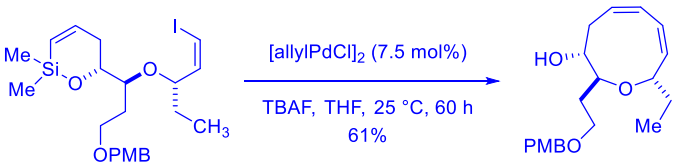
Example 2[2]



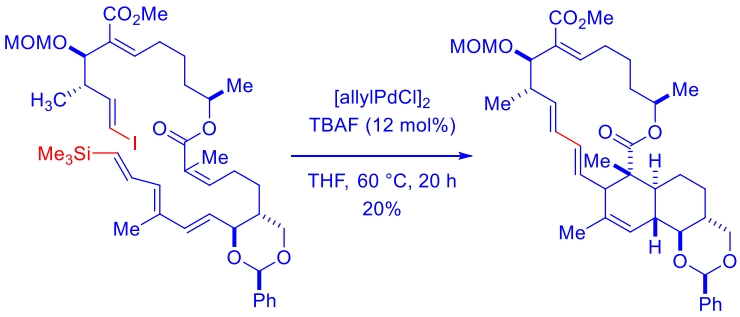
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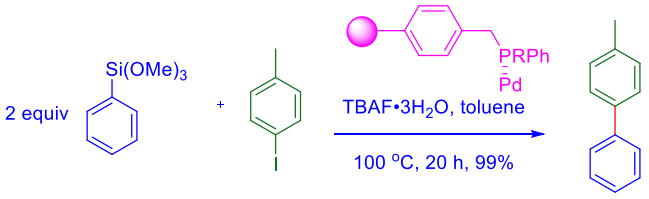
Example 3[7]



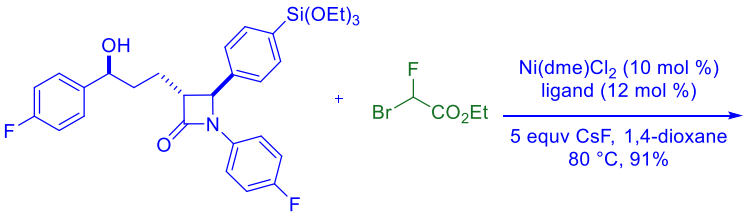
Example 4[9]

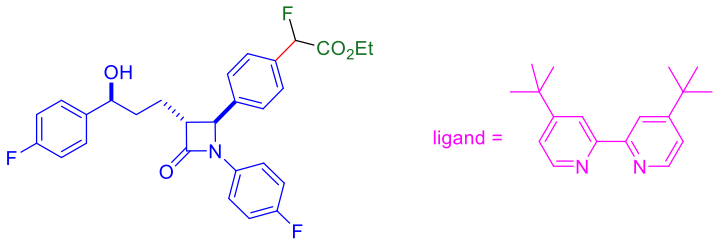


Example 5, Re-usable polystyrene-supported palladium catalyst[11]

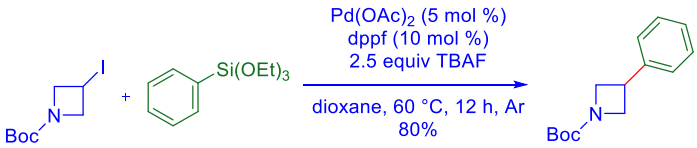


Example 6, Nickel-catalyzed monofluoroalkylation[12]





Example 7, 3-Arylazetidine from 3-iodoazetidine[13]

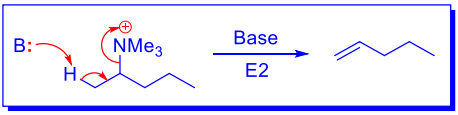


References

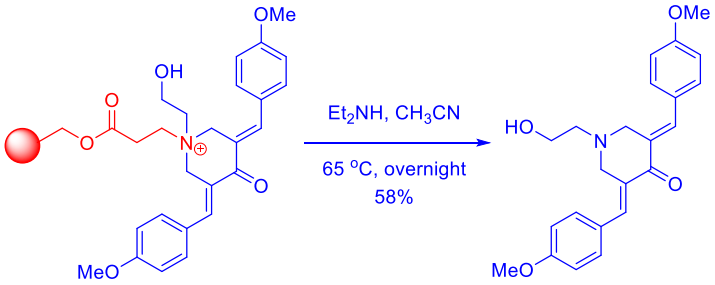
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Hofmann Elimination

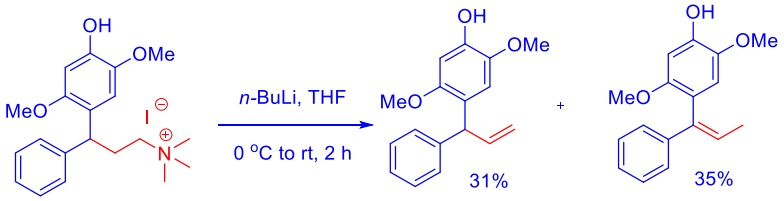
Elimination reaction of alkyl trialkyl amines proceeds with *anti*-stereochemistry, furnishing the least highly substituted olefins.



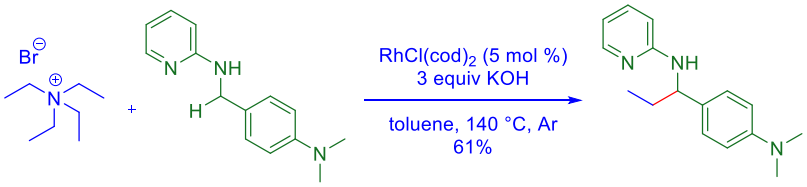
Example 1, Amine released from the resin by Hofmann elimination[10]



Example 2, Isomerization to a thermodynamically more stable olefin also occurred below[11]

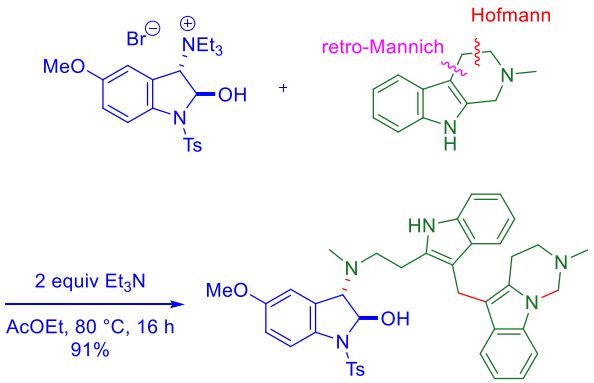


Example 3, Hofmann elimination product, the olefin, is the substrate for C–H activation[12]



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Example 4, Double "open and shut" transformation of γ-carbolines triggered by ammonium salts[13]

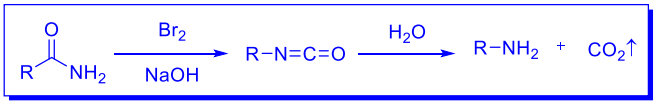


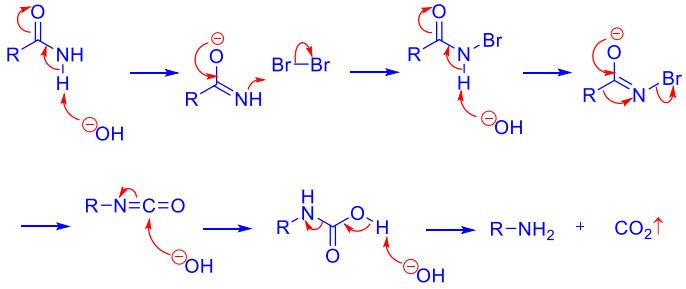
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Hofmann Rearrangement

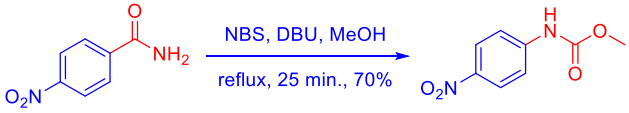
Upon treatment of primary amides with hypohalites, primary amines with one less carbon are obtained *via* the intermediacy of isocyanate. Also known as the Hofmann degradation reaction.



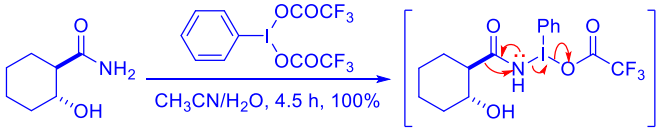


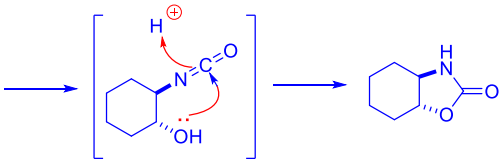
isocyanate intermediate

Example 1, An NBS variant[2]



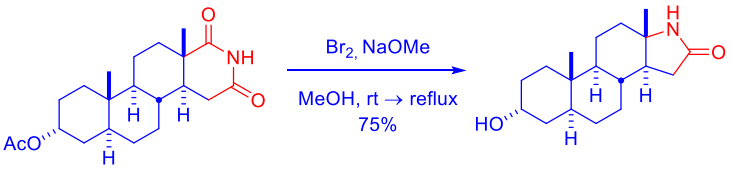
Example 2, Iodosobenzene ditrifluoroacetate[5]



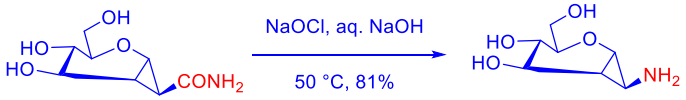


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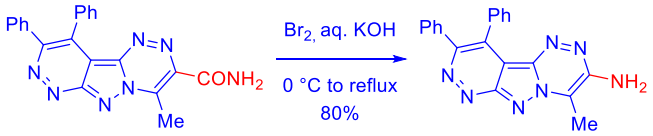
Example 3, Bromine and alkoxide[6]



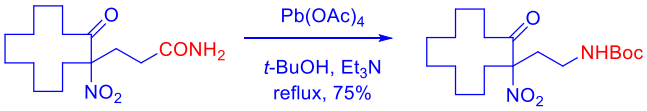
Example 4, Sodium hypochlorite[7]



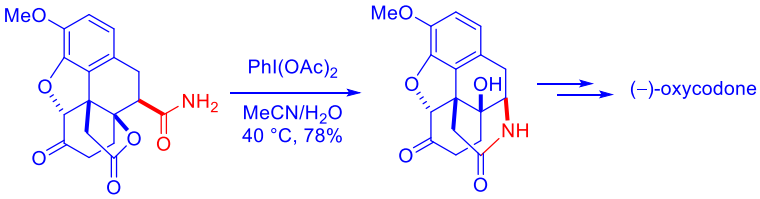
Example 5, The original conditions, bromine and hydroxide[9]



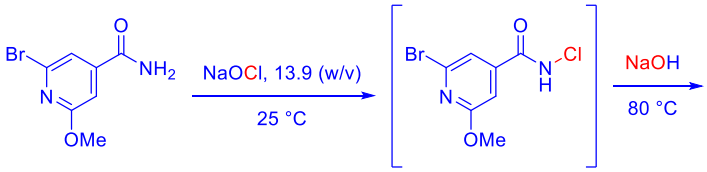
Example 6, Lead tetraacetate[10]



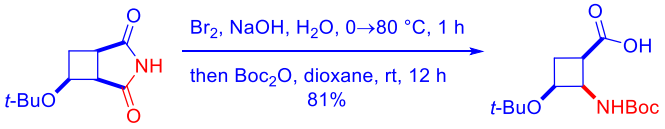
Example 7, Iodosobenzene diacetate (IBDA)[13]



Example 8, A 100 g-scale reaction[14]



Example 9, A 100 g-scale reaction[15]

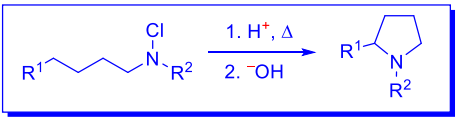


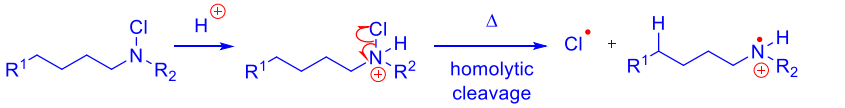
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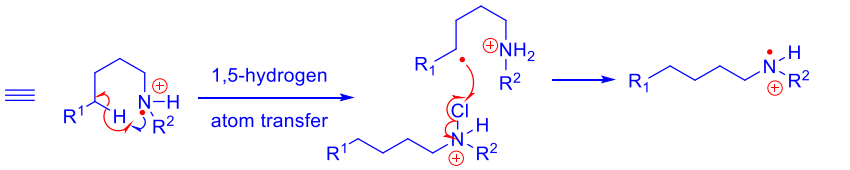
Hofmann–Löffler–Freytag Reaction

Formation of pyrrolidines or piperidines by thermal or photochemical decomposition of protonated *N*-haloamines.

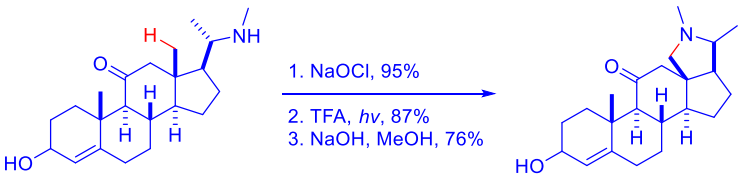




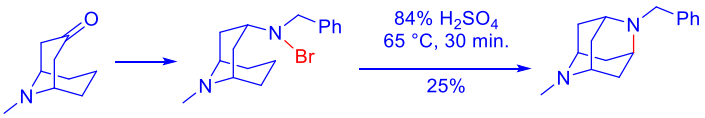
chloroammonium salt nitrogen radical cation



Example 1[2]

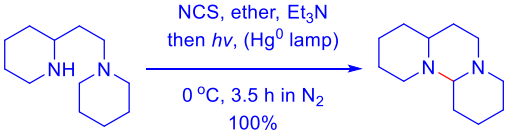


Example 2[4]

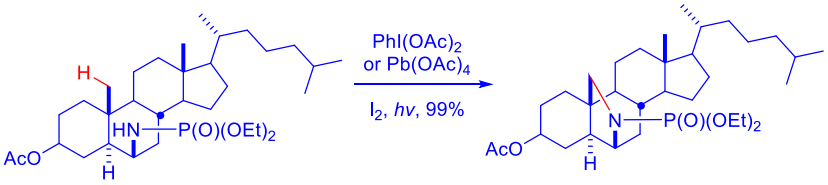


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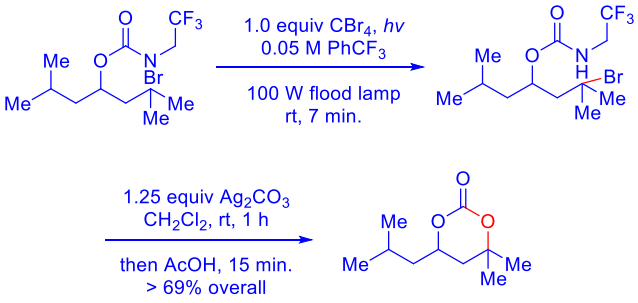
Example 3[5]



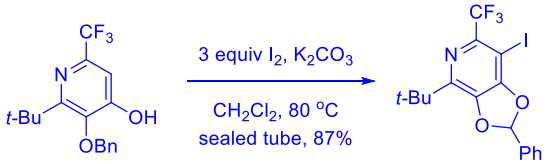
Example 4, Suárez modification of the Hofmann–Löffler–Freytag reaction[7]



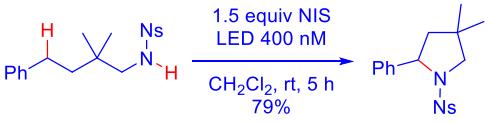
Example 5[12]



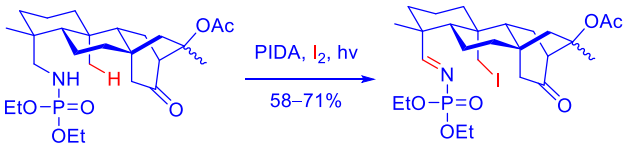
Example 6[13]



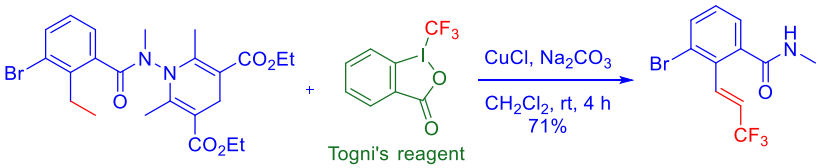
Example 7, NIS-promoted Hofmann–Löffler–Freytag reaction of sulfonimides under visible light (Ns = nosylate)[14]



Example 8, Suárez modification of the Hofmann–Löffler–Freytag reaction (PIDA phenyliodine diacetate = IBDA = iodosobenzene diacetate), similar to Example 4[15]



Example 8, Copper-catalyzed remote C(sp^3)-H oxidative trifluoromethylation[16]

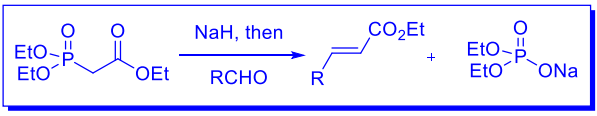


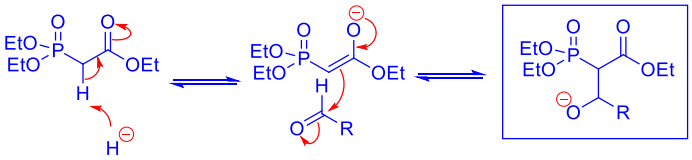
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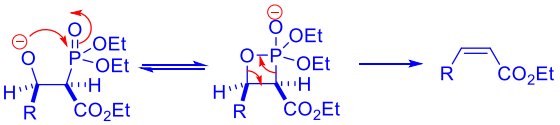
Horner–Wadsworth–Emmons Reaction

Olefin formation from aldehydes and phosphonates. Workup is more advantageous than the corresponding Wittig reaction because the phosphate by-product can be washed away with water. Typically gives the *trans*- rather than the *cis*-olefins.

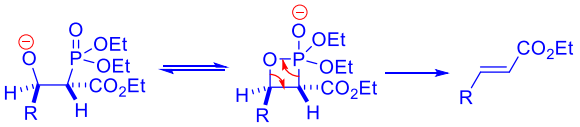




The stereochemical outcome: *erythro* (kinetic) or *threo* (thermodynamic)

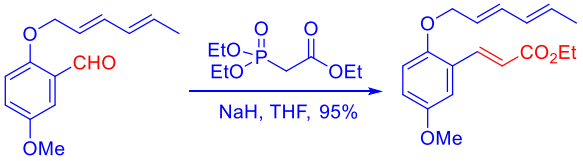


erythro, kinetic adduct



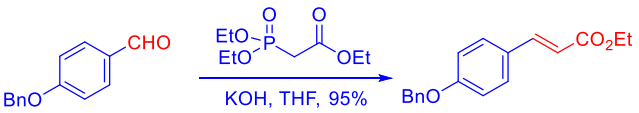
threo, thermodynamic adduct

Example 1[3]

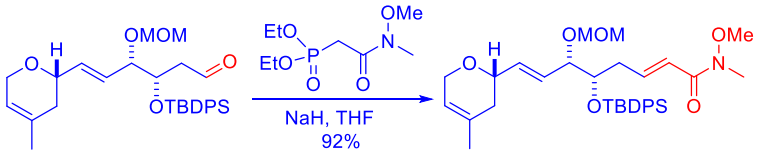


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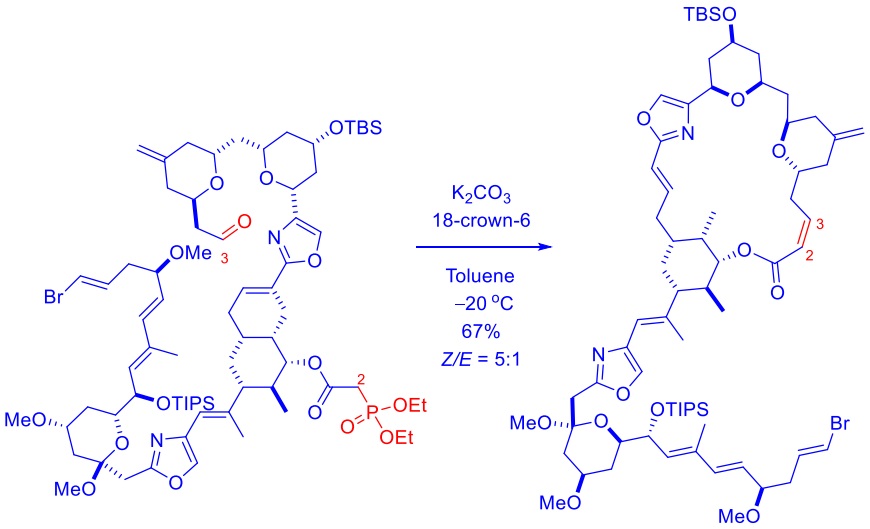
Example 2[4]



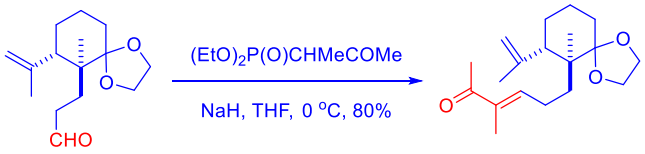
Example 3, Weinreb amide[7]



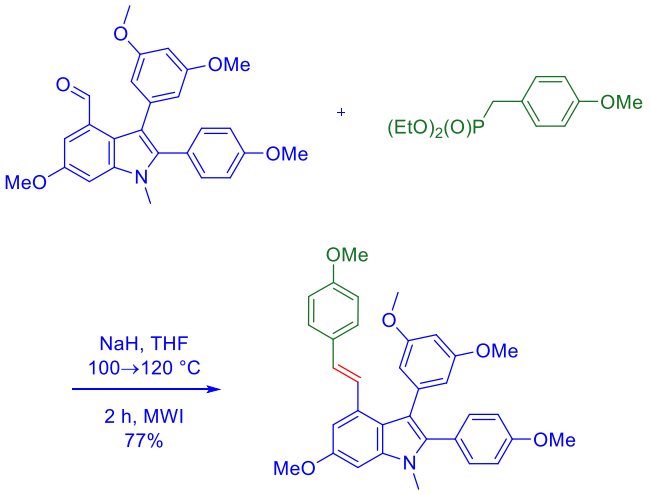
Example 4, Intramolecular Horner–Wadsworth–Emmons[9]



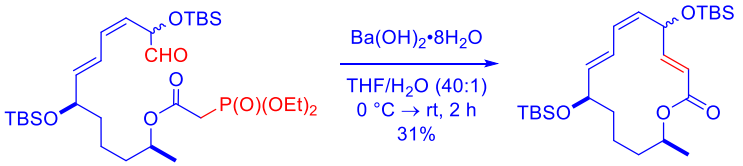
Example 4[11]



Example 5, MWI = Microwave irradiation[12]



Example 6, Intramolecular Horner–Wadsworth–Emmons to form a 14-membered lactone[13]



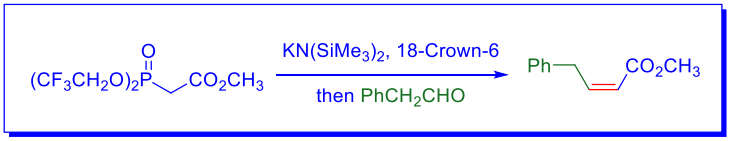
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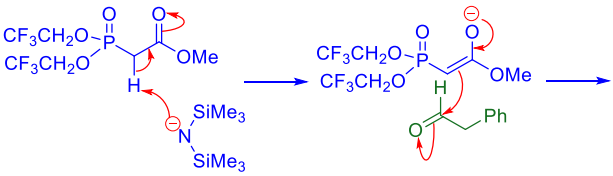
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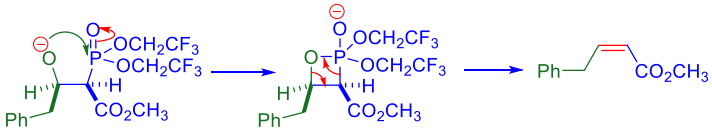
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Still–Gennari Phosphonates

A variant of the Horner–Wadsworth–Emmons reaction using bis(trifluoroethyl)-phosphonates (Still–Gennari phosphonates) to give predominantly *Z*-olefins.

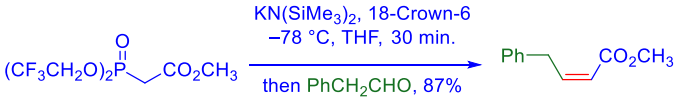




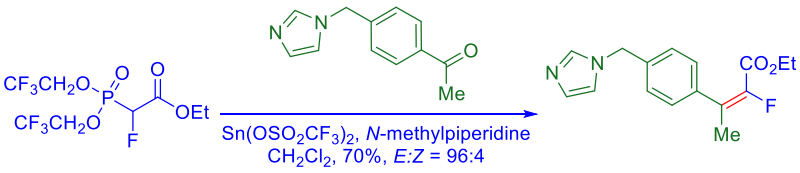


erythro isomer, kinetic adduct

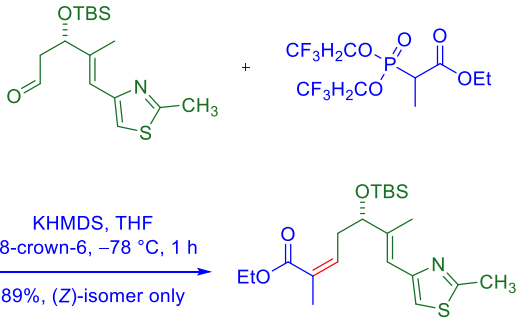
Example 1[2]



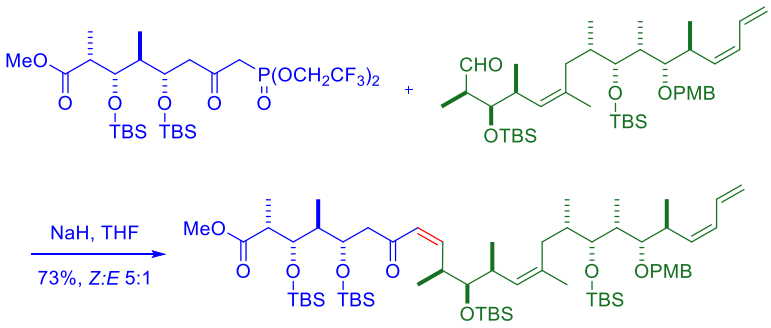
Example 2[3]



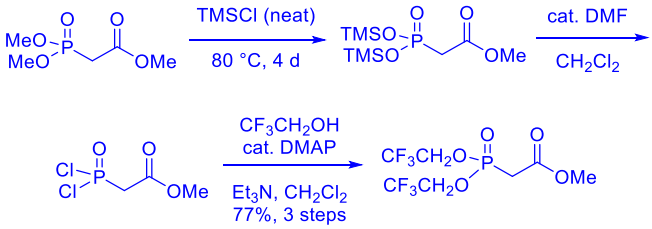
Example 3[4]



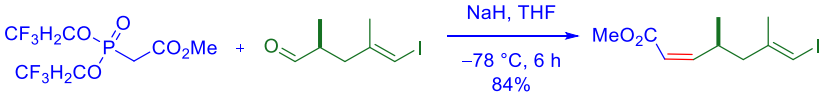
Example 4[9]



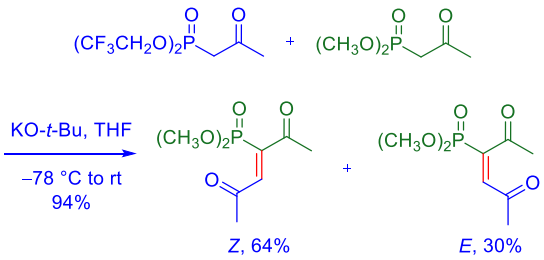
Example 5, An expedient access to Still–Gennari phosphonates[11]



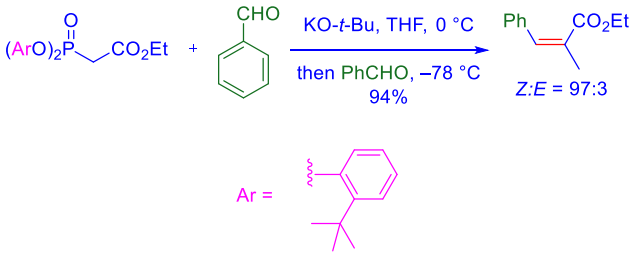
Example 6, Toward synthesis of aglycone of lycoperdinosides[12]



Example 7, For (*Z*)-α,β-unsaturated phosphonates[13]



Example 8, Methylated *Ando-type* Horner–Wadsworth–Emmons reagent is significantly cheaper than the Still–Gennari phosphonates[15]

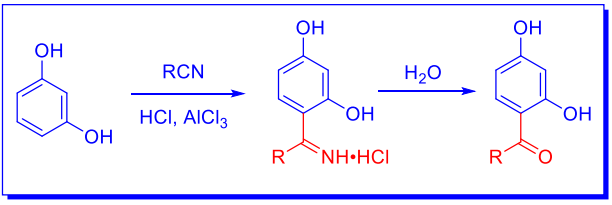


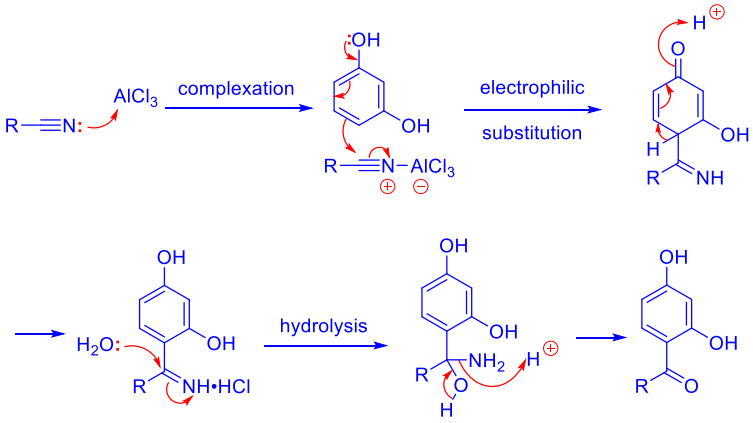
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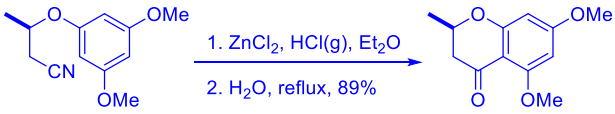
Houben–Hoesch Reaction

Acid-catalyzed acylation of phenols as well as phenolic ethers using nitriles to offer imines, which are hydrolyzed to the corresponding ketones.

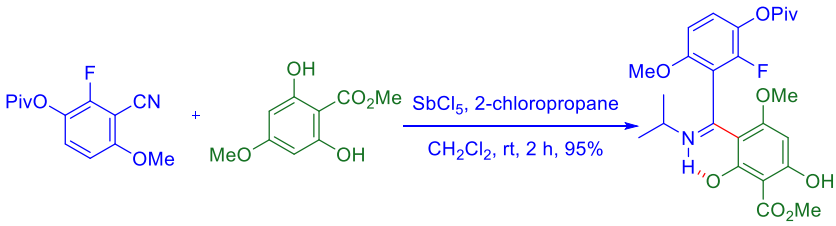




Example 1, Intramolecular Houben–Hoesch reaction[3]

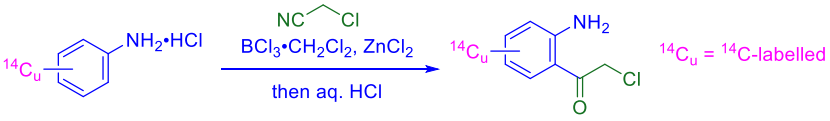


Example 2[6]

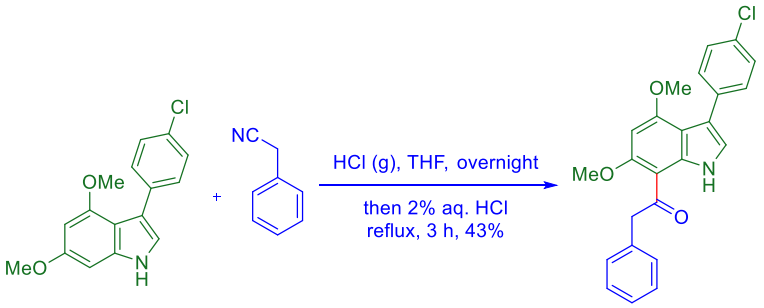


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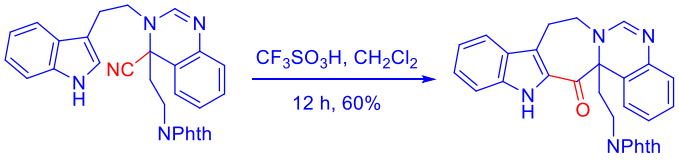
Example 3[8]



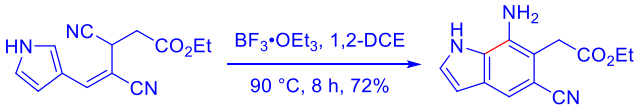
Example 4[9]



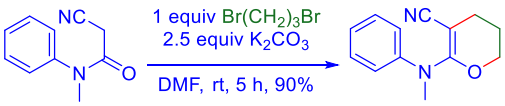
Example 5, Intramolecular Houben–Hoesch reaction[10]

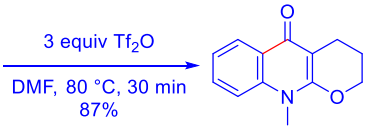


Example 6, Intramolecular Houben–Hoesch reaction, the product was "stuck" as the aniline[11]

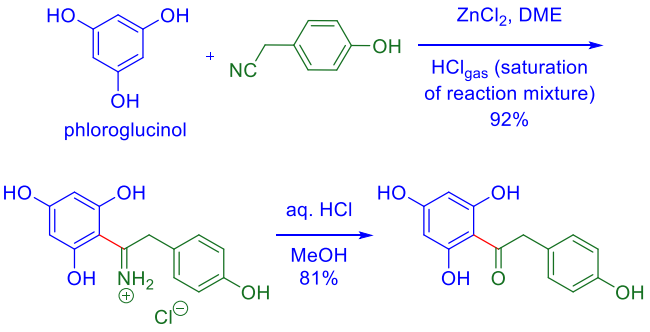


Example 7[12]





Example 8, Toward synthesis of genistein[13]

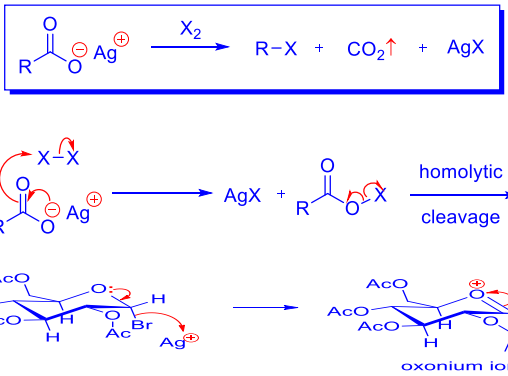


References

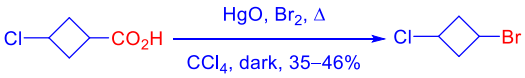
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Hunsdiecker–Borodin Reaction

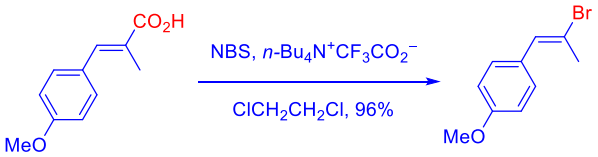
Conversion of silver carboxylate to halide by treatment with halogen.



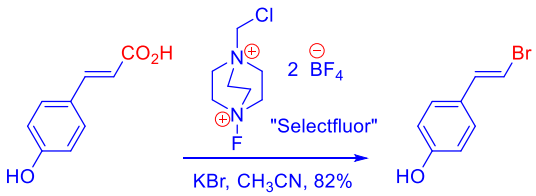
Example 1[5]



Example 2[6]

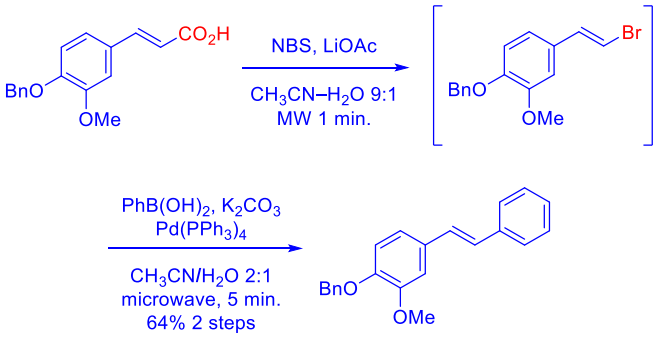


Example 3[8]

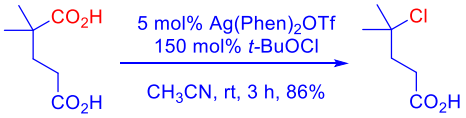


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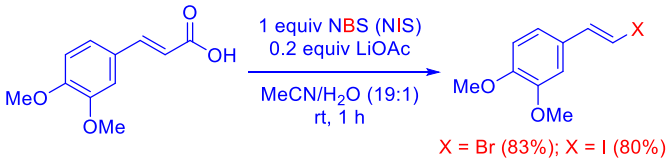
Example 4, One-pot microwave-Hunsdiecker–Borodin followed by Suzuki[10]



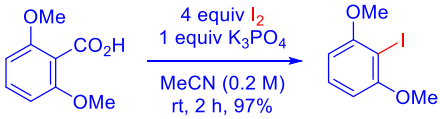
Example 5[11]



Example 6, For cinnamic acid substrates[12]



Example 7, Metal-free decarboxylative iodination, an aromatic Hunsdiecker reaction[13]



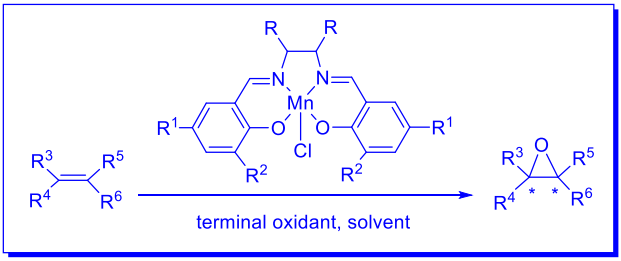
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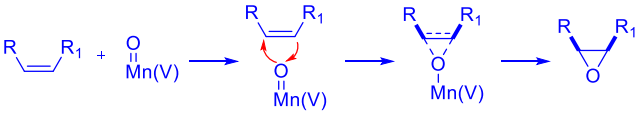
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Jacobsen–Katsuki Epoxidation

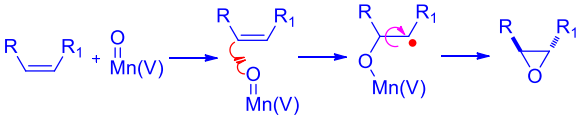
Mn(III)salen-catalyzed asymmetric epoxidation of (*Z*)-olefins.



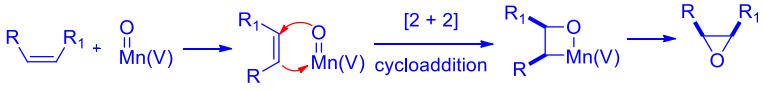
1. Concerted oxygen transfer (*cis*-epoxide):



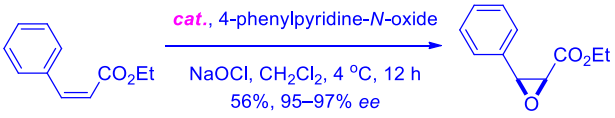
2. Oxygen transfer *via* radical intermediate (*trans*-epoxide):



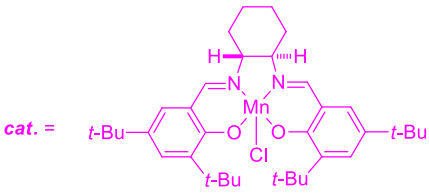
3. Oxygen transfer *via* manganaoxetane intermediate (*cis*-epoxide):



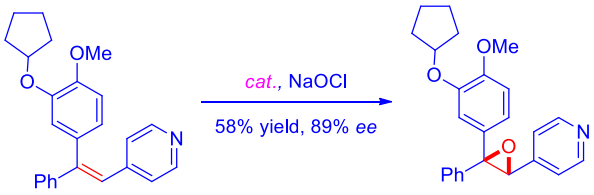
Example 1[2]



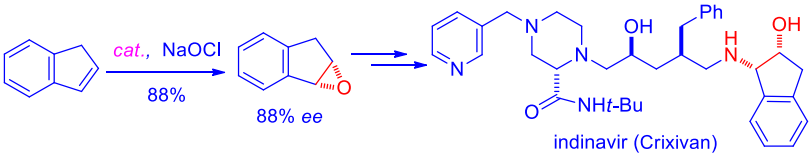
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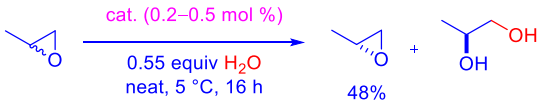
Example 2[5]

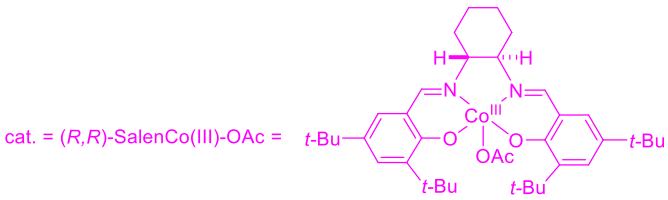


Example 3[6]

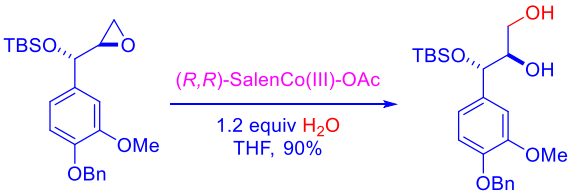


Example 4, Jacobsen hydrolytic kinetic resolution (HKR)[9]

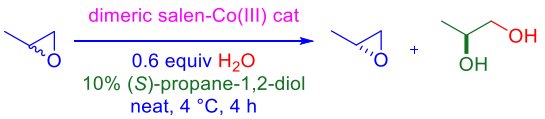


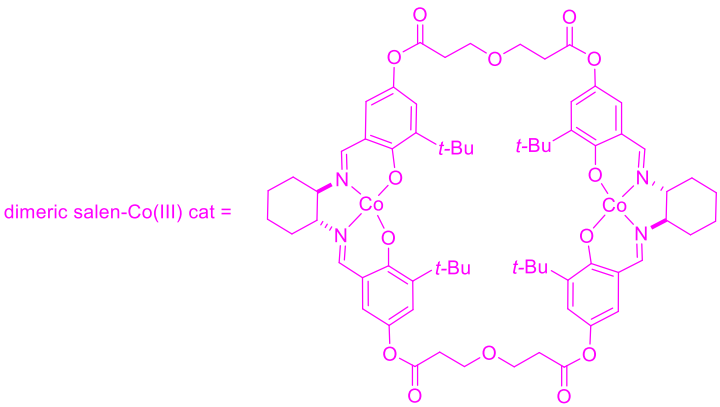


Example 5, Jacobsen hydrolytic kinetic resolution (HKR)[13]



Example 6, Hydrolytic kinetic resolution (HKR) using Jacobsen's dimeric (second generation) salen-Co(III) catalyst[14]





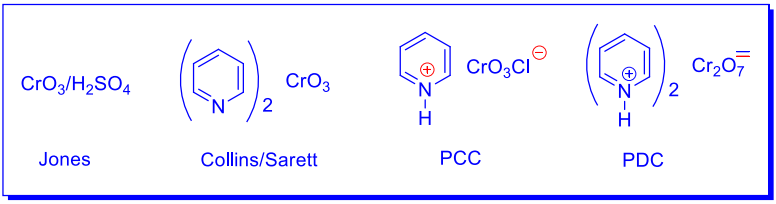
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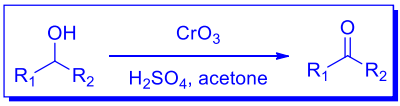
Jones Oxidation

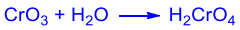
The **Collins/Sarett oxidation** (chromium trioxide-pyridine complex), and **Corey´s PCC** (pyridinium chlorochromate) and **PDC** (pyridinium dichromate) **oxidations** follow a similar pathway as the **Jones oxidation** (chromium trioxide and sulfuric acid in acetone). All these oxidants have a chromium (VI), normally orange or yellow, which is reduced to Cr(III), often green.

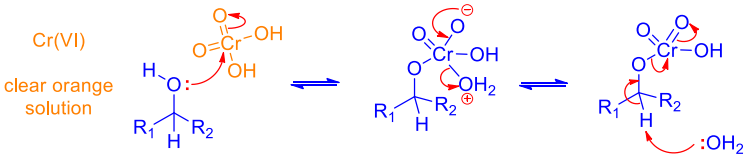


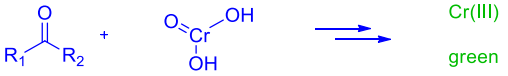
Jones Oxidation

By the Jones oxidation, the primary alcohols are oxidized to the corresponding aldehyde or carboxylic acids, whereas the secondary alcohols are oxidized to the corresponding ketones.

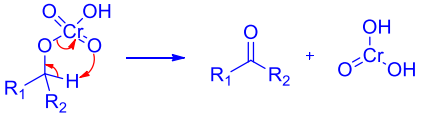






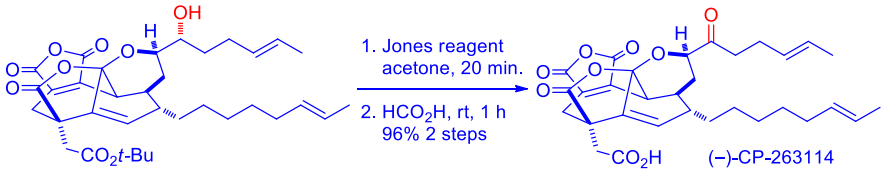


The intramolecular mechanism is also operative:

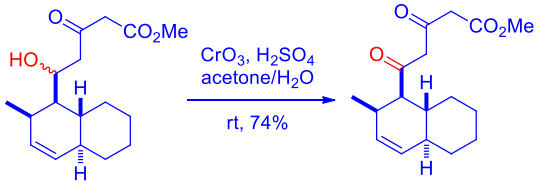


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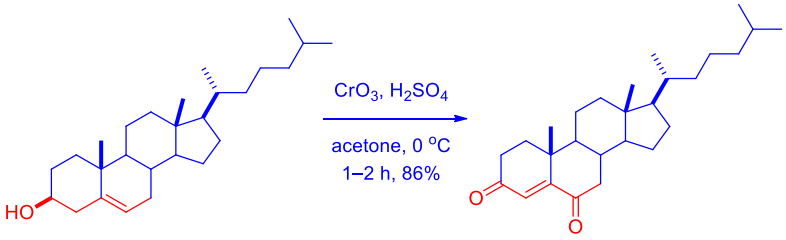
Example 1[6]



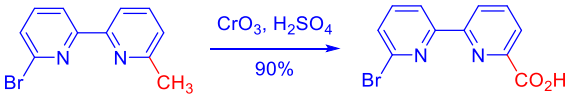
Example 2[7]



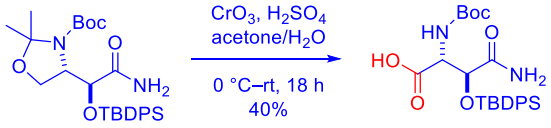
Example 3[9]



Example 4, Working up the reaction mixture with cold ice−water to precipitate out the pure carboxylic acid[12]



Example 5, Boc protection survived the Jones oxidation conditions (at least 40% of it)[13]



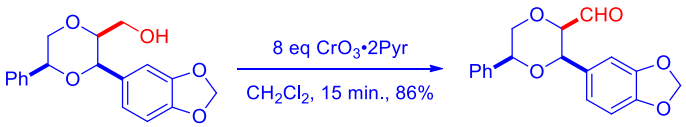
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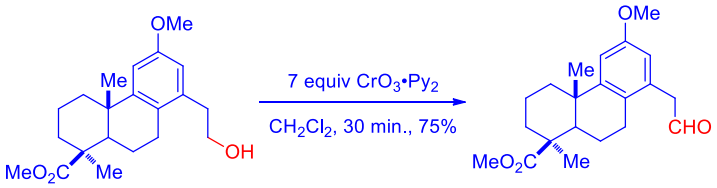
Collins Oxidation

Different from the Jones oxidation, the Collins oxidation, also known as the Collins–Sarett oxidation, converts primary alcohols to the corresponding aldehydes. CrO_3•2Pyr is known as the ***Collins reagent***.

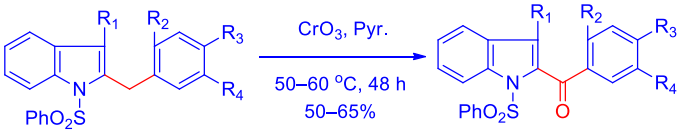
Example 1[5]



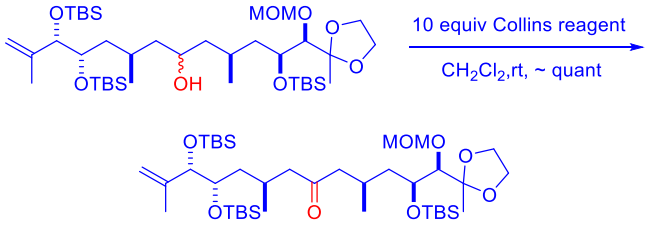
Example 2[7]



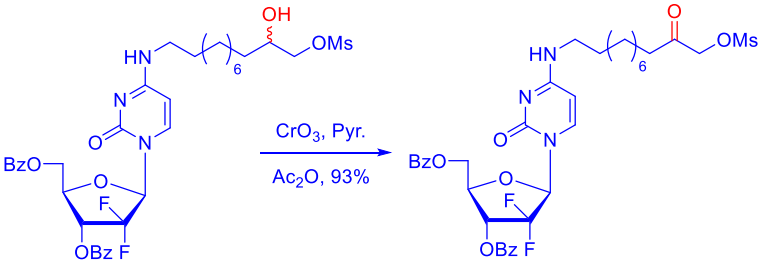
Example 3[9]



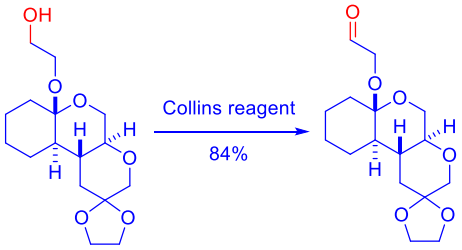
Example 4, TBS and MOM-ether protective groups survived Collins reagent[10]



Example 5, Gemcitabine analog[11]



Example 6[12]



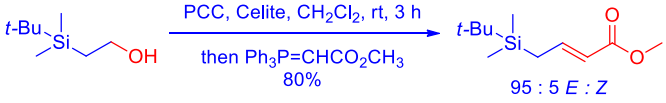
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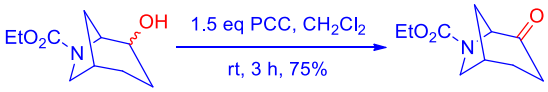
PCC Oxidation

Alcohols are oxidized by pyridinium chlorochromate (PCC) to the corresponding aldehydes or ketones. They are not further oxidized to the corresponding carboxylic acids because the reaction was done in organic solvents, not in water. If water existed, the carbonyls would form *aldehyde hydrates* or *ketone hydrates*, which are then oxidized to acids.

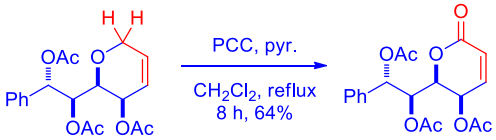
Example 1, One-pot PCC–Wittig reactions[2]



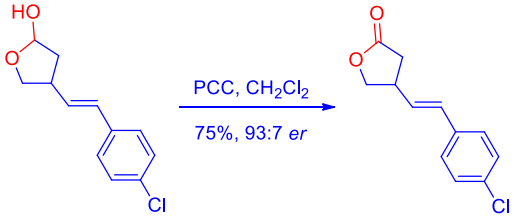
Example 2[3]



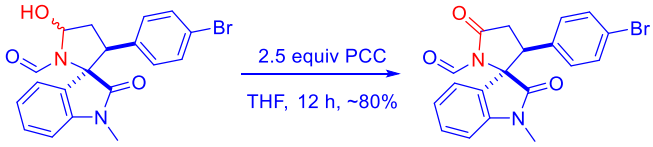
Example 3, Allylic oxidation[4]



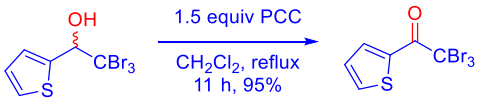
Example 4, Hemiacetal oxidation[5]



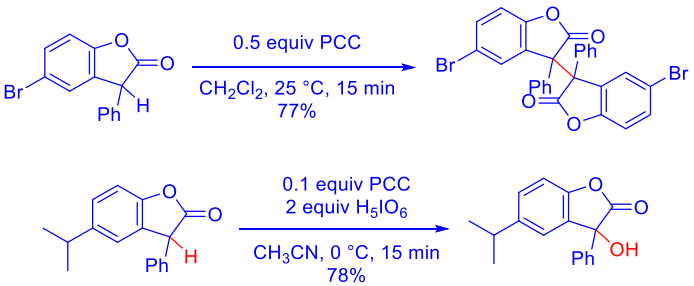
Example 5[8]



Example 6[9]



Example 7[10]



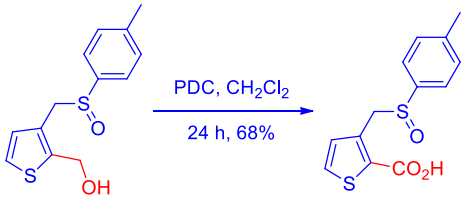
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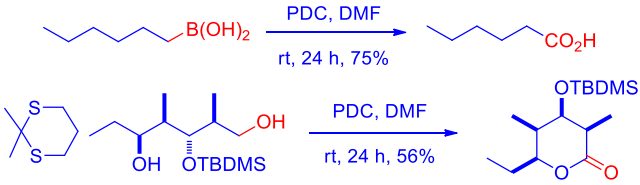
PDC Oxidation

Pyridinium dichromate (PDC) may oxidize alcohols all the way to the corresponding carboxylic acids instead of aldehydes and ketones as PCC does.

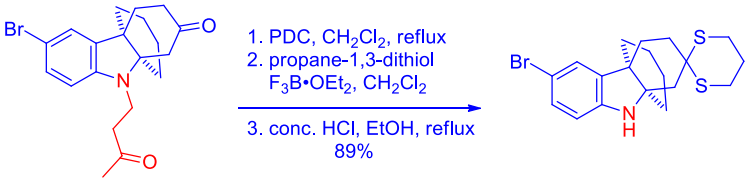
Example 1[2]



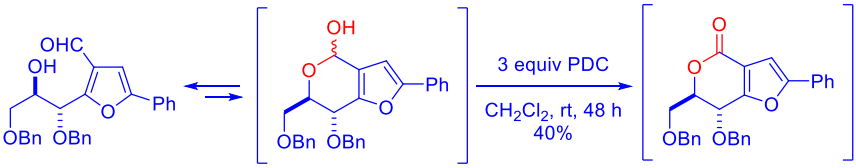
Example 2, Cleavage of primary carbon–boron bond[3]



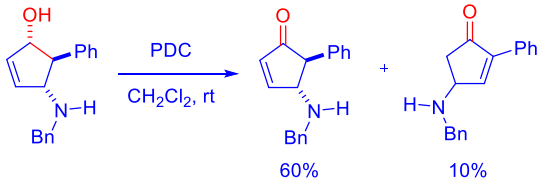
Example 4, PDC oxidation provided the β-keto-amide, which was hydrolyzed off after protection of the ketone as dithiane[9]



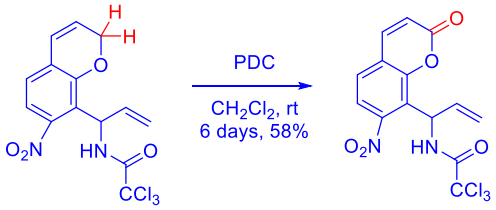
Example 5, Oxidation of lactol to lactone[10]



Example 6, The 10% impurity was the result of the Piancatelli rearrangement with the aid of water after exposure to silica gel[11]



Example 7, Chemoselective oxidation of 2*H*-chromenes to coumarins[12]

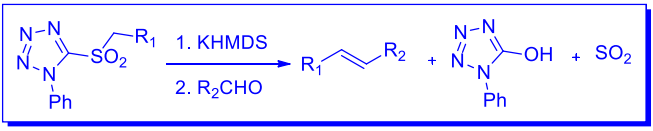


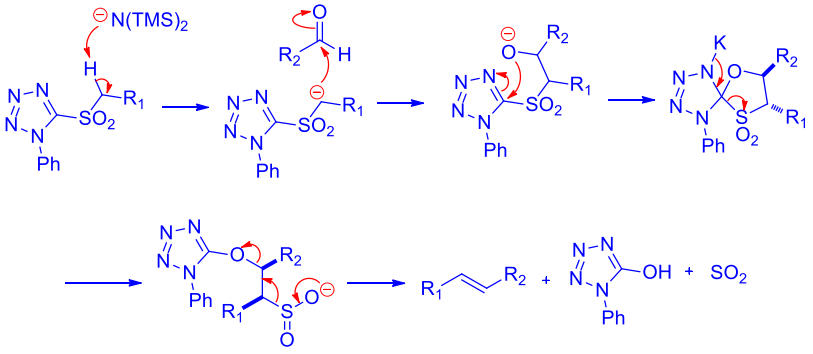
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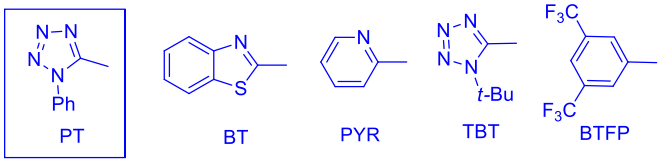
Julia–Kocienski Olefination

Modified one-pot Julia olefination to give predominantly (*E*)-olefins from heteroarylsulfones and aldehydes. A sulfone reduction step is *not* required.

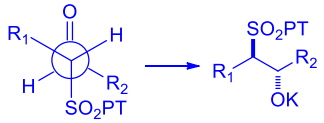




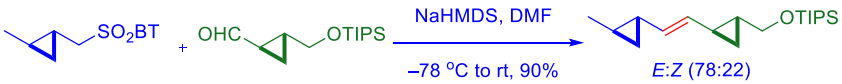
Alternatives to tetrazole:



The use of larger counter-ion (such as K^+) and polar solvents (such as DME) favors an open transition state (PT = *N*-phenyltetrazolyl):

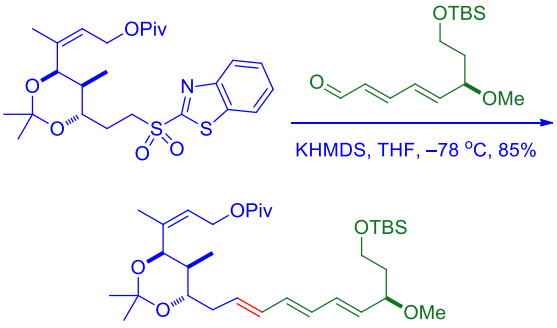


Example 1, (BT = benzothiazole)[2]

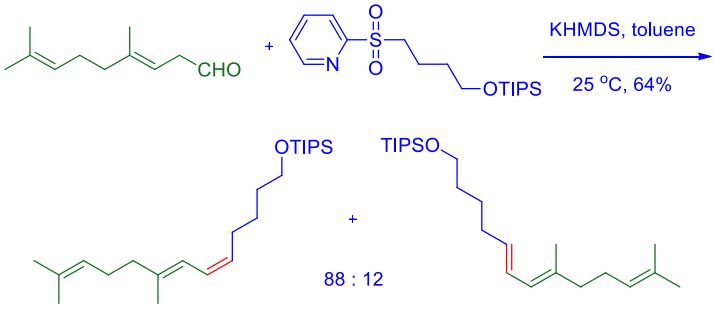


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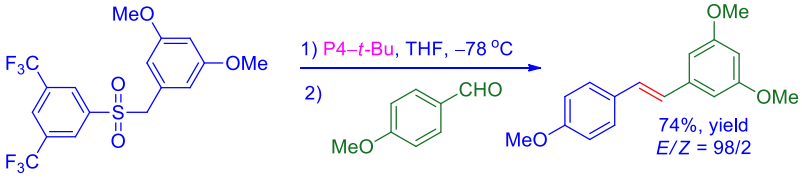
Example 2[3]



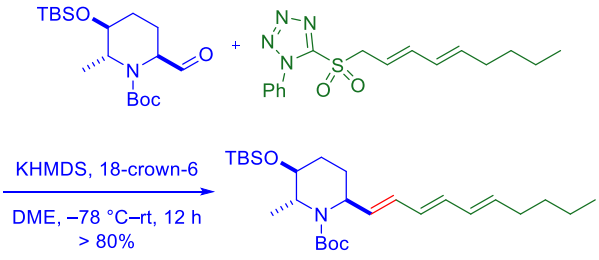
Example 3[7]



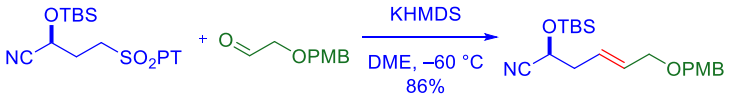
Example 4, P4-*t*-Bu is a strong base, but a weak nucleophile[8]



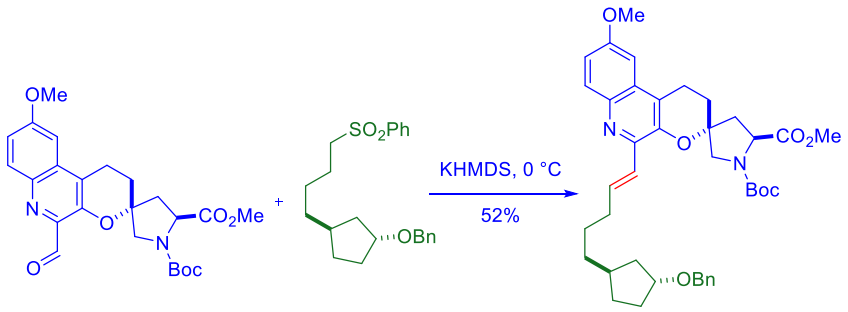
Example 5, (*E*)-Isomer only[12]



Example 6, (*E*)-Isomer only[13]



Example 7, *En route* to preparation of HCV NS3/4A inhibitors[15]

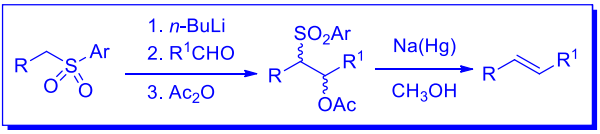


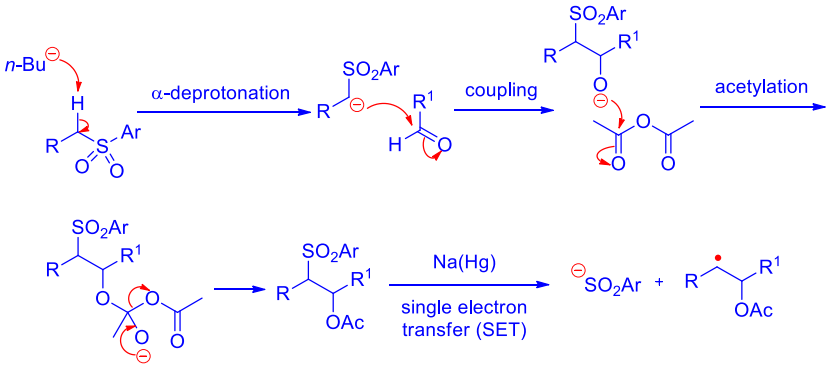
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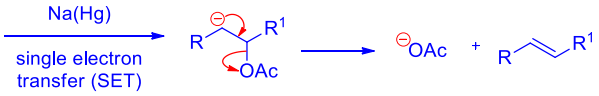
Julia–Lythgoe Olefination

(*E*)-Olefins from sulfones and aldehydes.

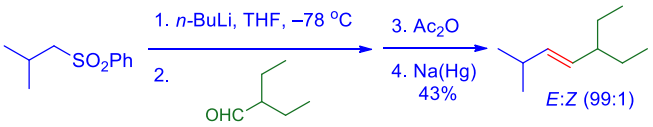




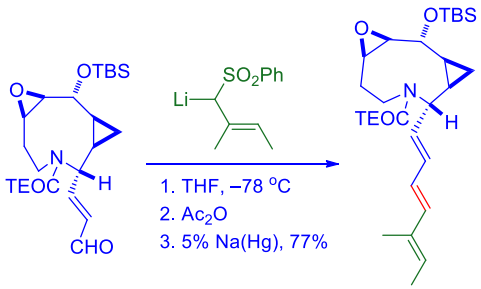
4 possible diastereomers



Example 1[2]

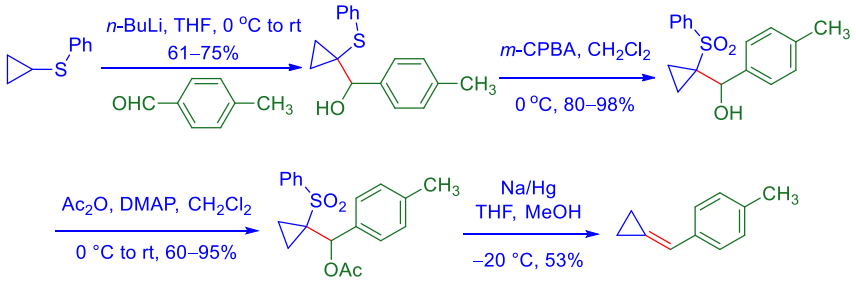


Example 2[3]

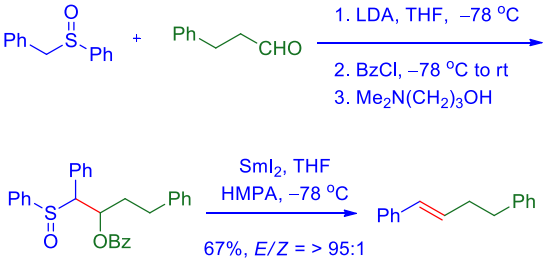


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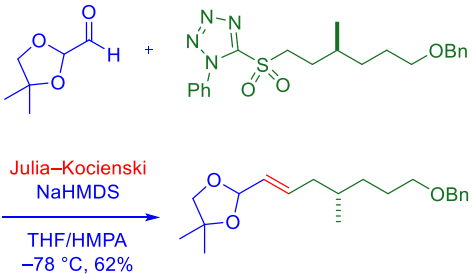
Example 3[7]



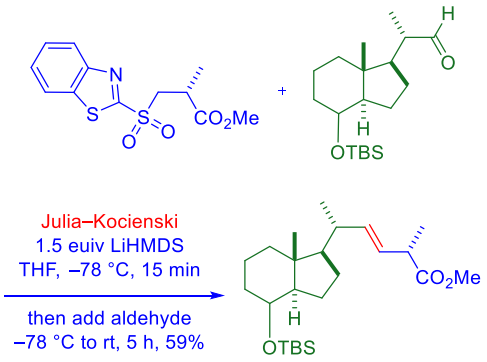
Example 4[8]



Example 5, Sometimes, the difference between Julia–Kocienski olefination and Julia–Lythgoe olefination is blurred, rightfully so as Kocienski and Lythgoe were coauthors for reference 2[12]



Example 6, As above, this is more appropriate to call it Julia–Kocienski olefination[13]

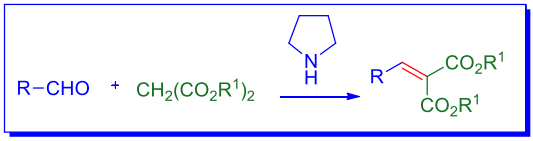


References

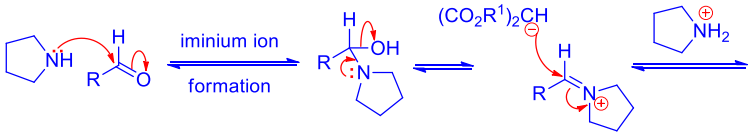
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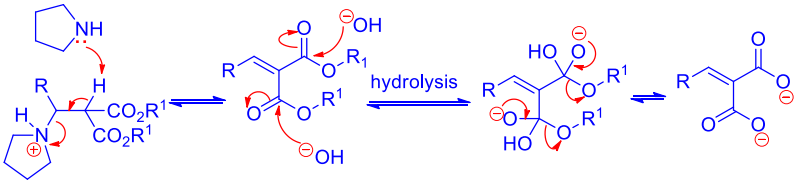
Knoevenagel Condensation

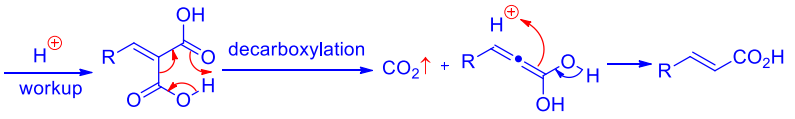
Condensation between carbonyl compounds and activated methylene compounds catalyzed by amines.



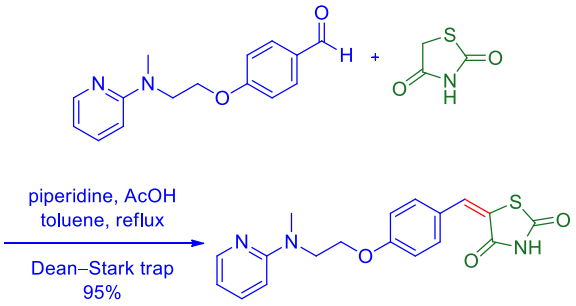






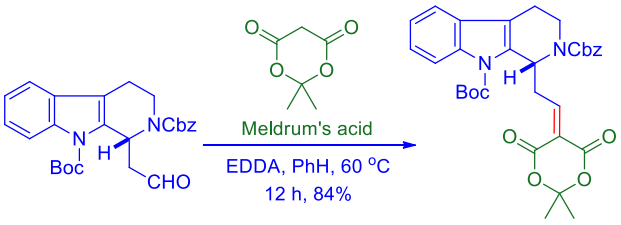


Example 1[3]

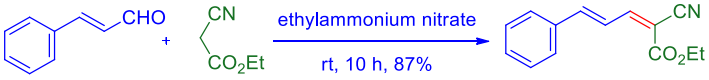


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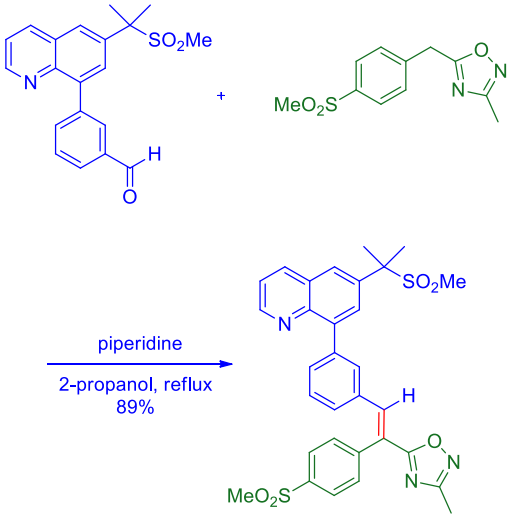
Example 2, EDDA = Ethylenediamine diacetate[5]



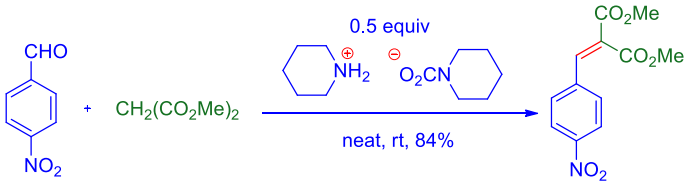
Example 3, Using ionic liquid ethylammonium nitrate (EAN) as solvent[8]



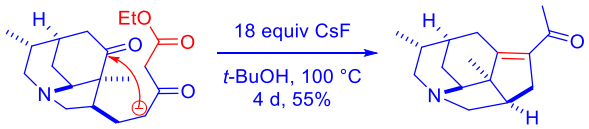
Example 4[9]



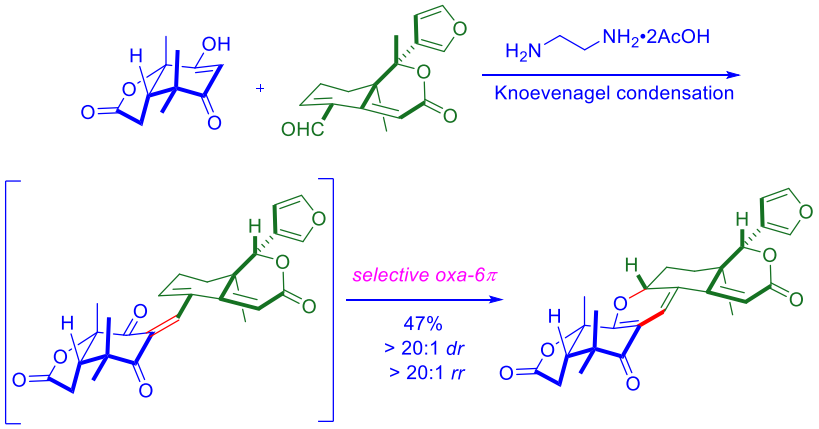
Example 5[11]



Example 6, Fluoride as the base for an intramolecular Knoevenagel condensation and unexpected decarboxylation[12]



Example 7, EDDA = Ethylenediamine diacetate as the base here[13]



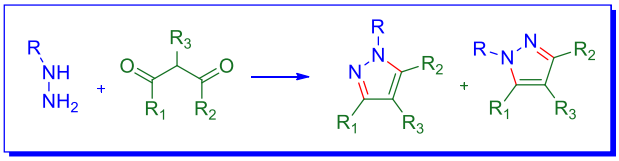
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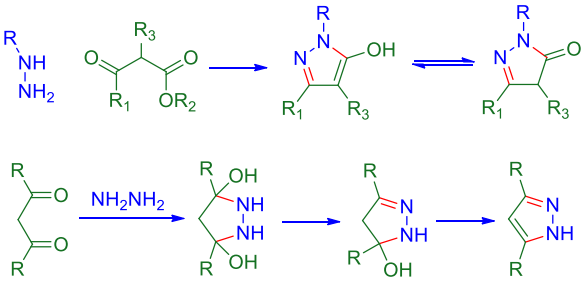
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Knorr Pyrazole Synthesis

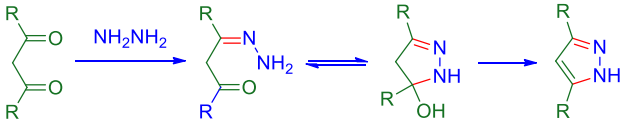
Also known as Knorr reaction. Reaction of hydrazine or substituted hydrazine with 1,3-dicarbonyl compounds to provide the pyrazole or pyrazolone ring system. *Cf.* Paal–Knorr pyrrole synthesis.



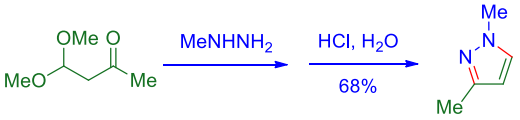
R = H, Alkyl, Aryl, Het-aryl, Acyl, *etc*.



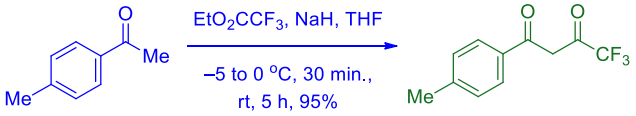
Alternatively,



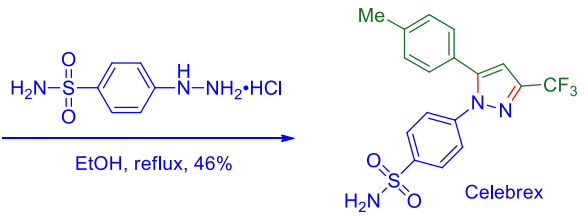
Example 1[2]



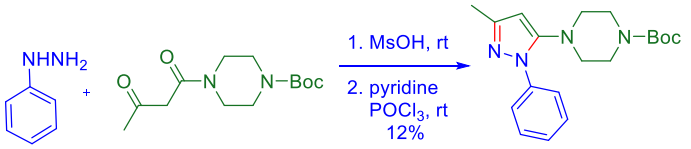
Example 2[8]



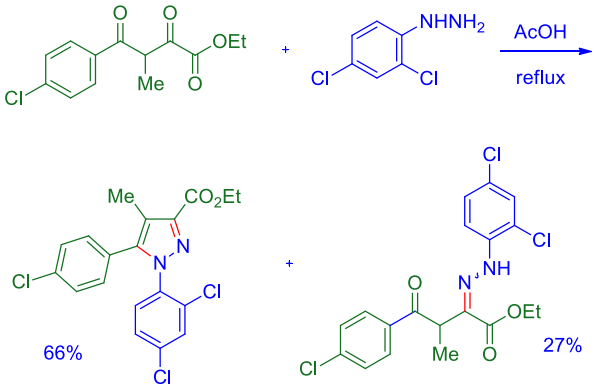
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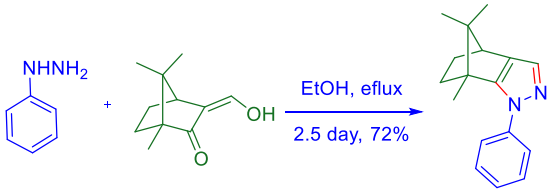
Example 3, Preparation of an intermediate for teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor[9]



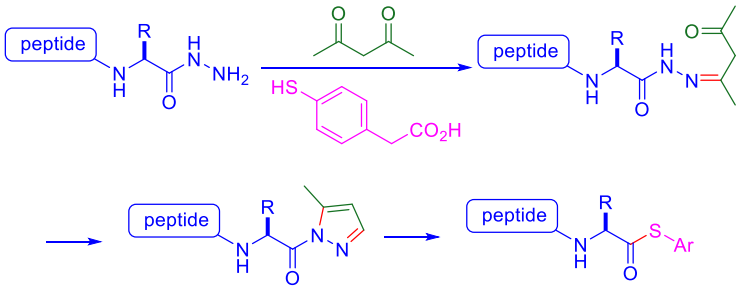
Example 4[10]



Example 5[11]



Example 6, Knorr pyrazole-thioester generation employed in the native chemical ligation (NCL) strategies for chemical protein synthesis[12]



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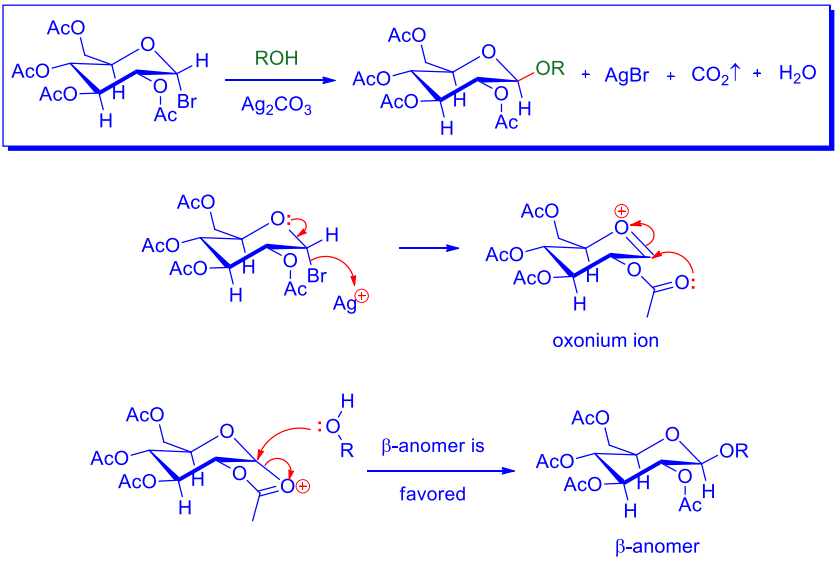
11 Nozari, M.; Addison, A. W.; Reeves, G. T.; Zeller, M.; Jasinski, J. P.; Kaur, M.; Gilbert, J. G.; Hamilton, C. R.; Popovitch, J. M.; Wolf, L. M.; et al. *J. Heterocycl. Chem.* **2018,** *55*, 1291–1307.

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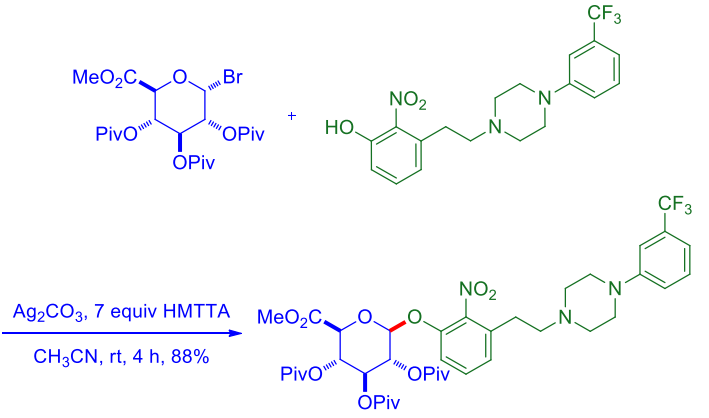
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Koenig–Knorr Glycosidation

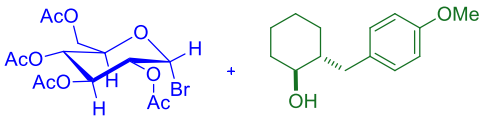
Formation of the β-glycoside from α-halocarbohydrate under the influence of silver salt.



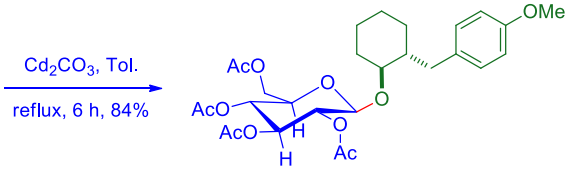
Example 1[7]



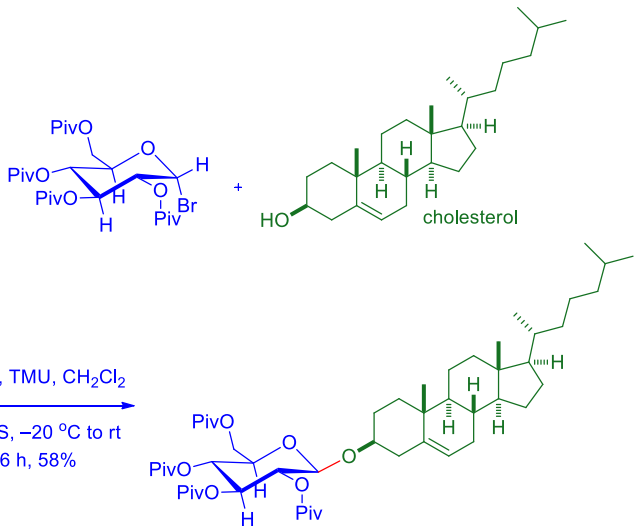
Example 2[8]



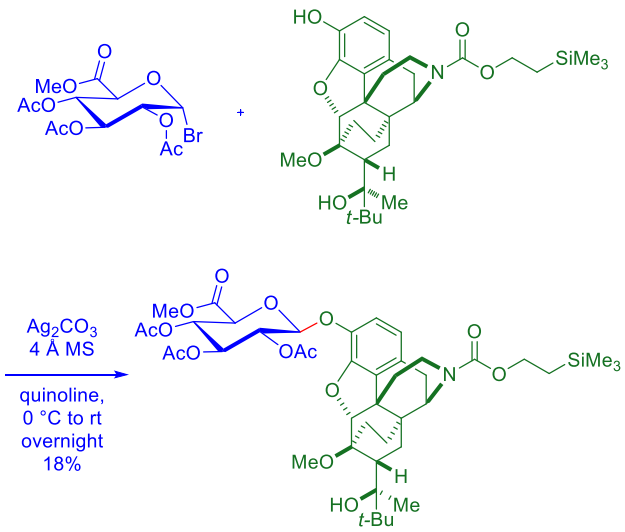
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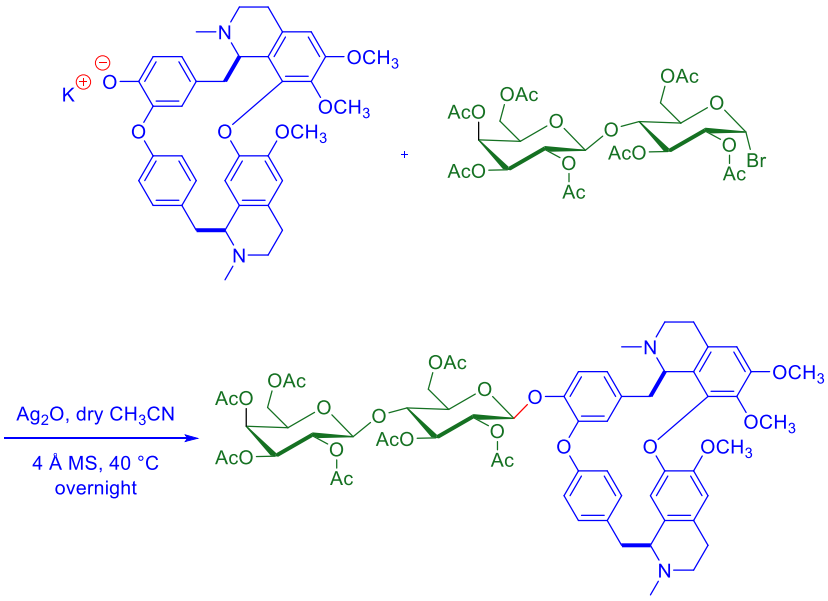
Example 3, TMU = tetramethylurea[9]



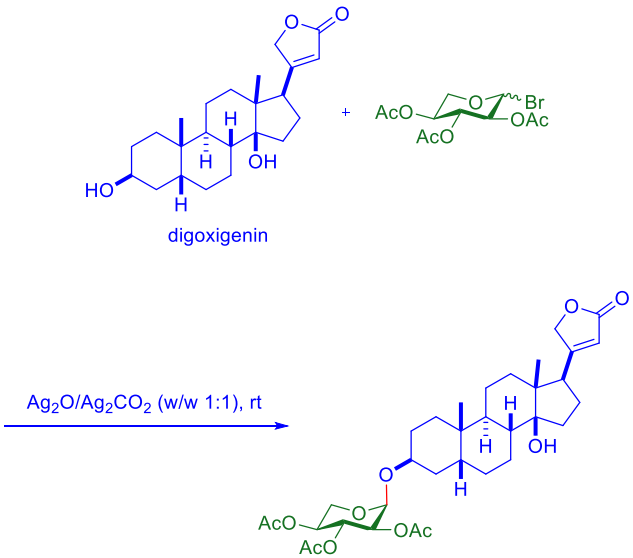
Example 4[11]



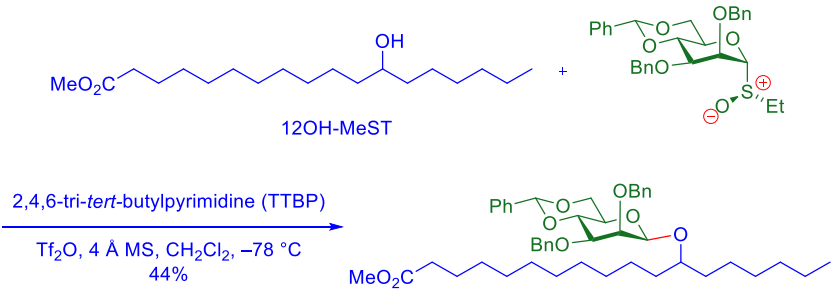
Example 5, Antitumor agents[12]



Example 6, C_3-Neoglycosides of digoxigenin with anticancer activities[13]



Example 7, Macrophage-inducible C-type lectin (Mincle) receptor agonists[14]

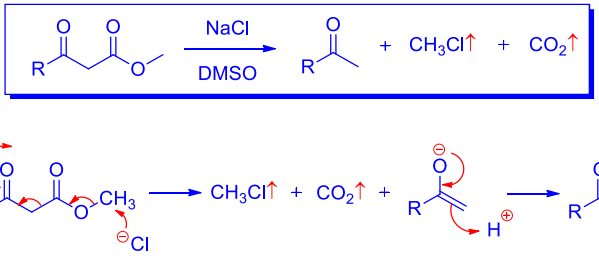


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Krapcho Reaction

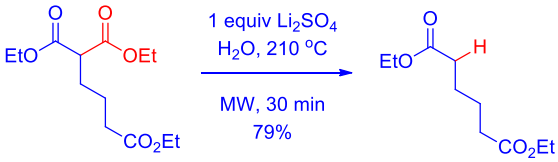
Nucleophilic decarboxylation of β-ketoesters, malonate esters, α-cyanoesters, or α-sulfonylesters.



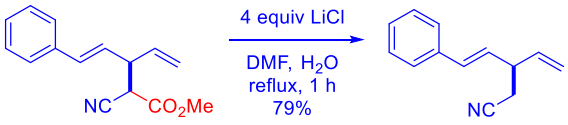
Example 1[5]



Example 2[10]

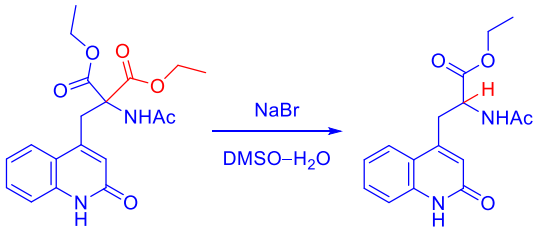


Example 3, Synthesis of homoallylic chiral nitriles[11]

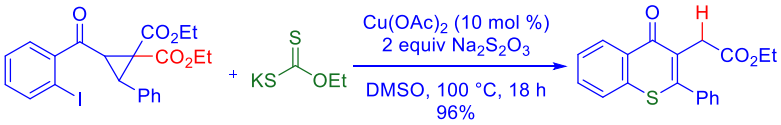


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Example 4, Toward production of rebamipide, an antiulcer drug[12]



Example 5, A reaction cascade with a Krapcho decarboxylation step[13]

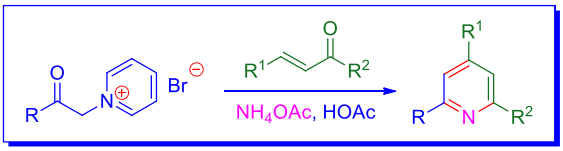


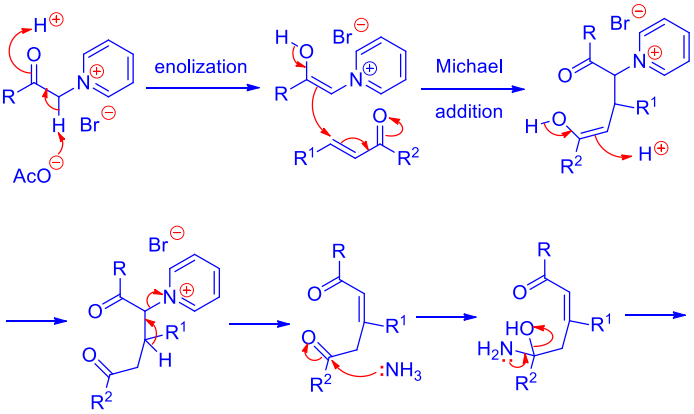
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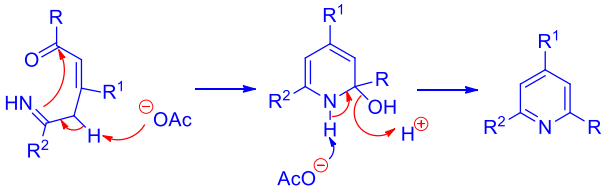
Kröhnke Pyridine Synthesis

Pyridines from α-pyridinium methyl ketone salts and α,β-unsaturated ketones.

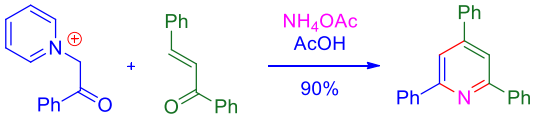




The ketone is more reactive than the enone

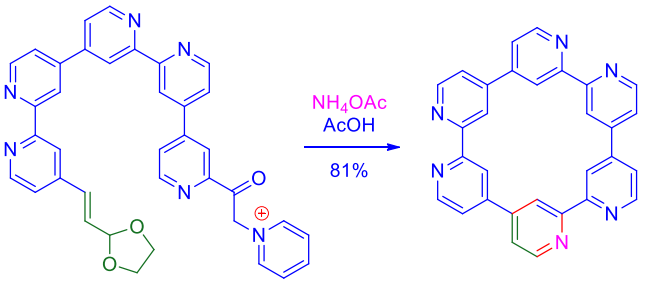


Example 1[1b]

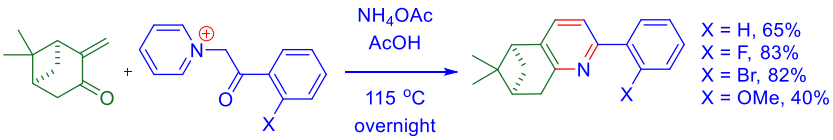


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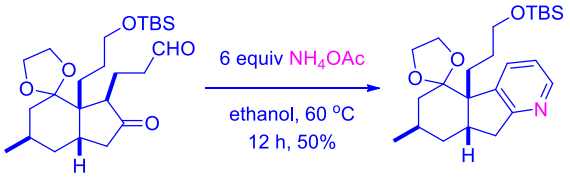
Example 2[4]



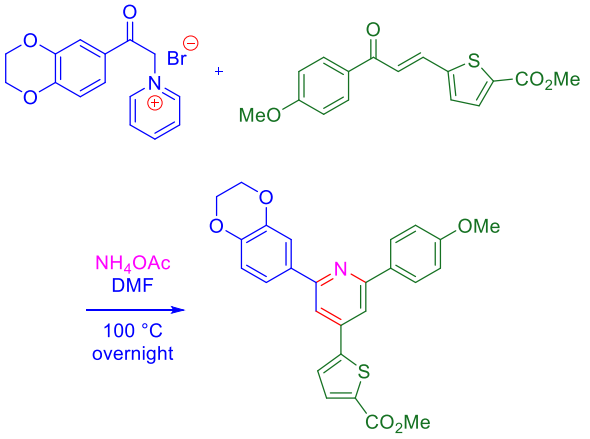
Example 3[6]



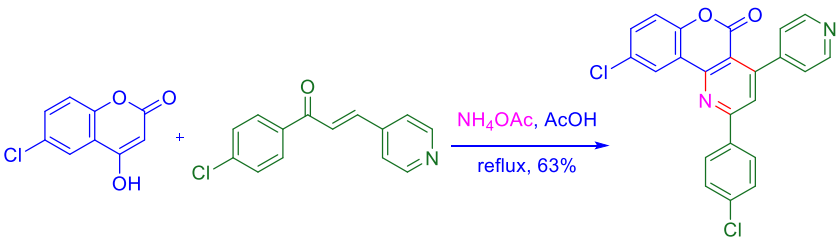
Example 4, For total synthesis of lycopodium alkaloid (+)-lycopladin A[10]



Example 5, Mining a Kröhnke pyridine library for anti-arenavirus activities[12]



Example 6, Bipyrido-fused coumarins with antimicrobial activities[14]

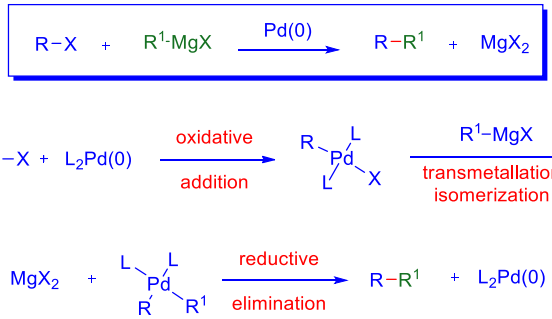


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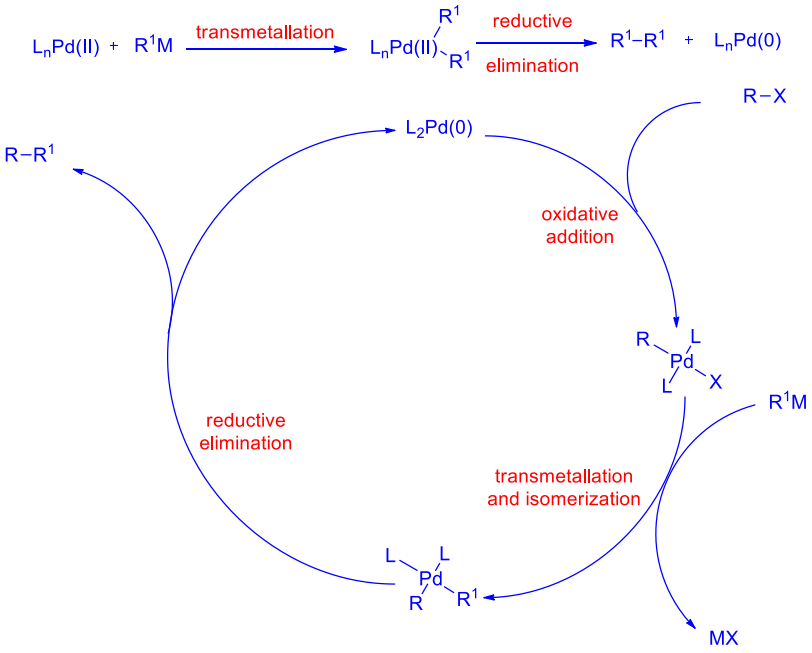
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Kumada Reaction

The Kumada cross-coupling reaction (also known as Kumada–Tamao–Corriu coupling, also occasionally known as the Kharasch cross-coupling reaction) was originally reported as the nickel-catalyzed cross-coupling of Grignard reagents with aryl- or alkenyl halides. It has subsequently been developed to encompass the coupling of organolithium or organomagnesium compounds with aryl-, alkenyl- or alkyl halides, catalyzed by either nickel or palladium. These reactions follow a general mechanistic catalytic cycle as shown below. There are slight variations for the Hiyama and Suzuki reactions, for which an additional activation step is required for the transmetalation to occur.

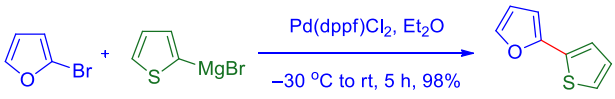


The catalytic cycle:

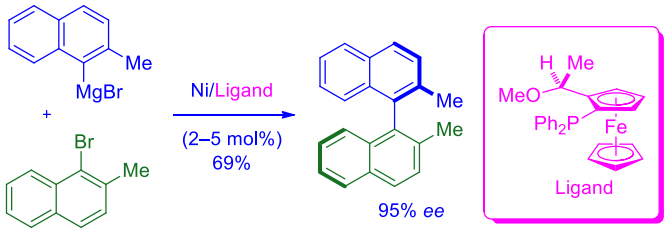


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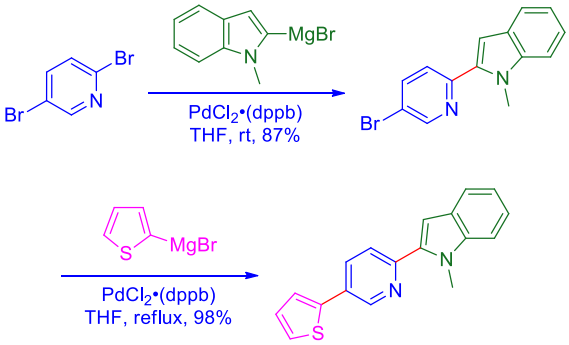
Example 1[2]



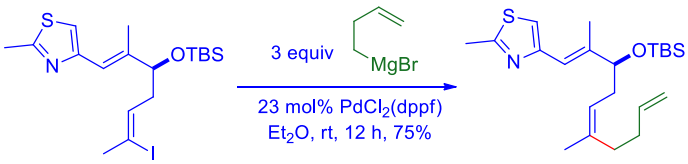
Example 2[3]



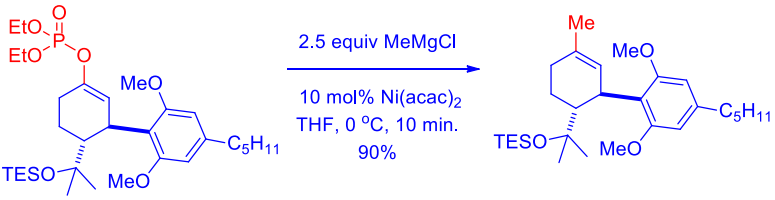
Example 3[5]



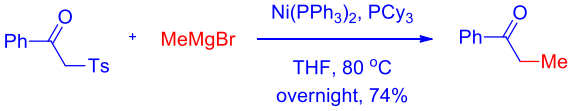
Example 4[8]



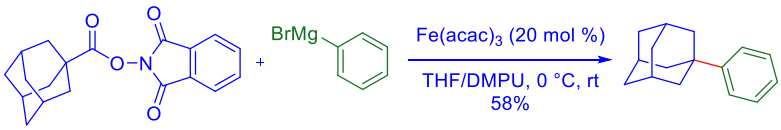
Example 5[9]



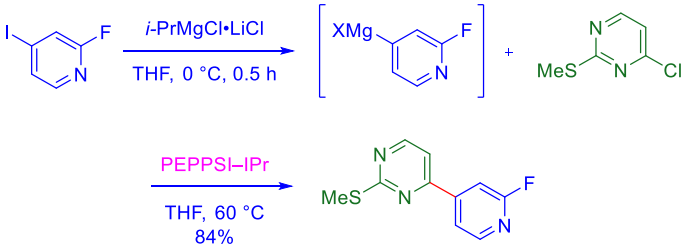
Example 6, Nickel-catalyzed Kumada reaction of tosylalkanes[11]



Example 7, Redox-active esters in Fe-catalyzed C–C coupling (DMPU = N,N′-dimethylpropyleneurea)[13]

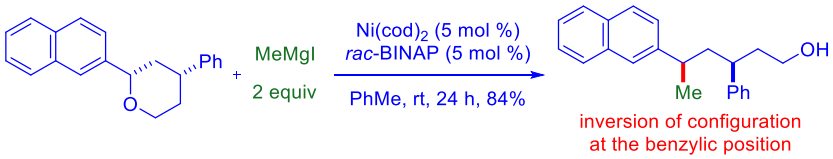


Example 8, Toward the synthesis of GDC-0994, an extracellular signal-regulated kinase (ERK) inhibitor[14]



PEPPSI = pyridine-enhanced pre-catalyst preparation, stabilization, and initiation; IPr = diidopropyl-phenylimidazolium derivative

Example 9, Benzyl ethers as the substrates of the Kumada reaction[15]

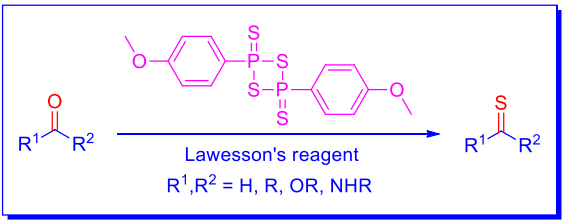


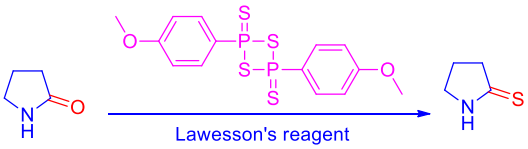
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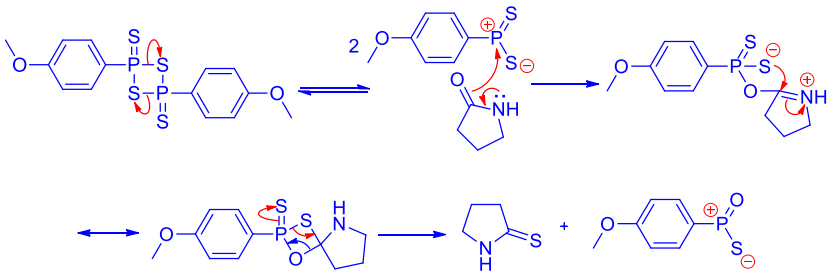
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Lawesson′s Reagent

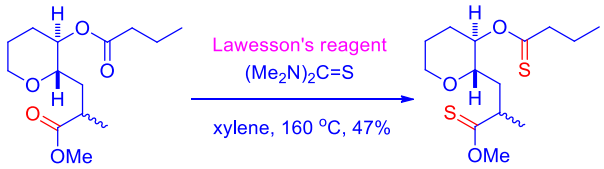
2,4-Bis(4-methoxyphenyl)-1,3-dithiadiphosphetane-2,4-disulfide transforms the carbonyl groups of aldehydes, ketones, amides, lactams, esters and lactones into the corresponding thiocarbonyl compounds. *Cf.* Knorr thiophene synthesis.



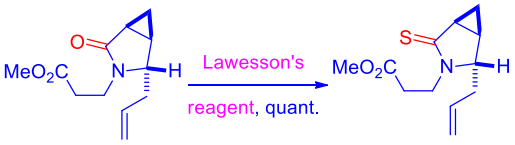




Example 1, Double Lawesson reaction[4]

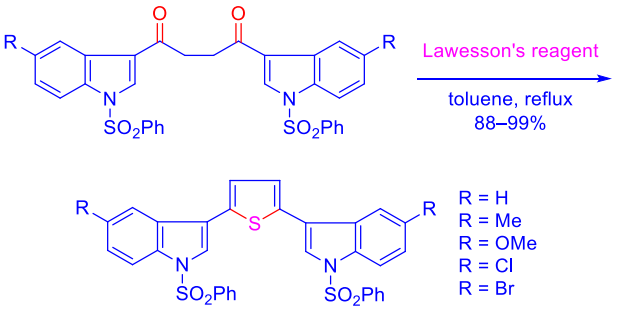


Example 2[5]

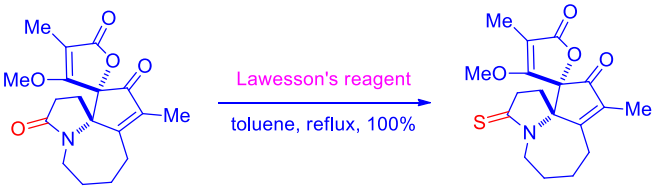


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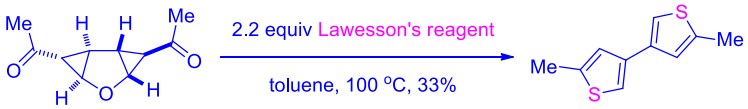
Example 3, Thiophene from dione[8]



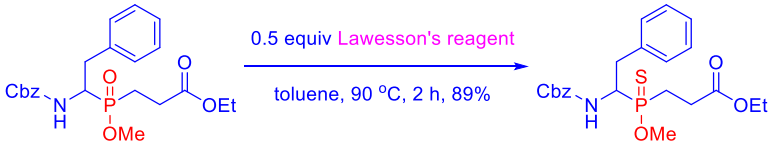
Example 4, Latam is more reactive than lactone and enone[10]



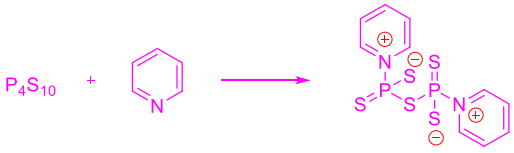
Example 5[11]

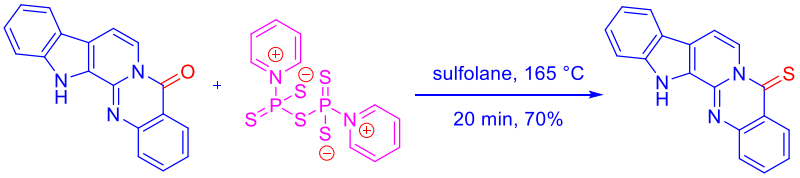


Example 6, Thiophosphinyl dipeptide isosteres (TDIs) to replace phosphinyl dipeptide isosteres (PDIs)[12]

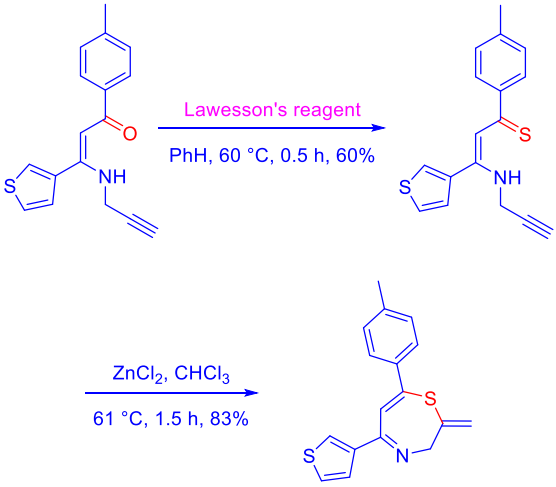


Example 7, A reagent prepared from P_4S_{10} and pyridine as a thionation reagent[13]





Example 8, Synthesis of 1,4-thiazepines[14]

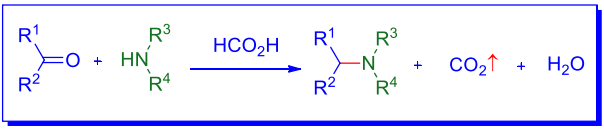


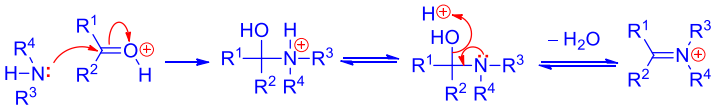
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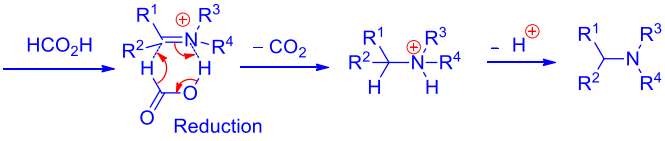
Leuckart–Wallach Reaction

Amine synthesis from reductive amination of a ketone and an amine in the presence of excess formic acid, which serves as the reducing reagent by delivering a hydride. When the ketone is replaced by formaldehyde, it becomes the Eschweiler–Clarke reductive amination.

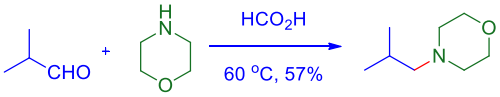




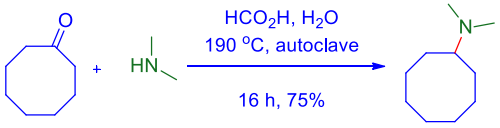
gem-aminoalcohol; iminium ion intermediate



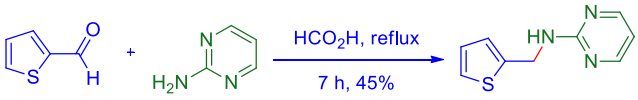
Example 1[4]



Example 2[6]

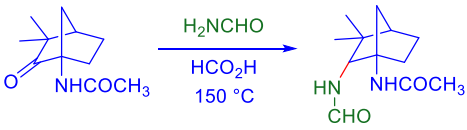


Example 3[7]

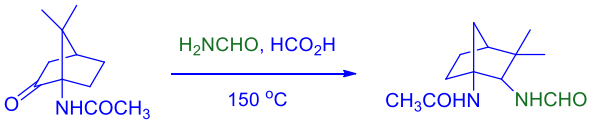


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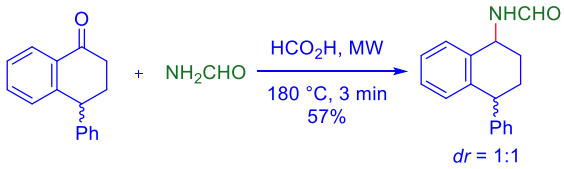
Example 4[8]



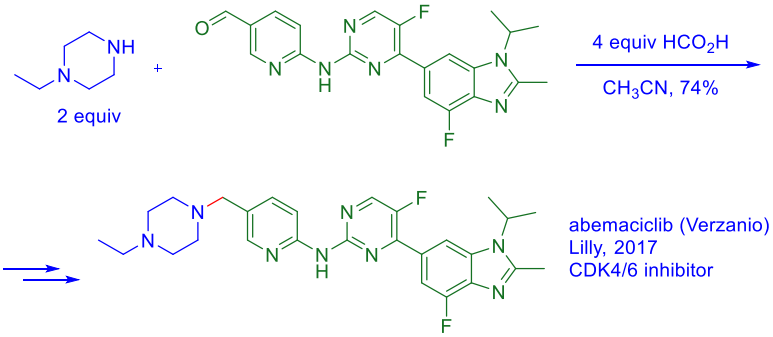
An unexpected intramolecular transamidation *via* a Wagner–Meerwein shift after the Leuckart–Wallach reaction



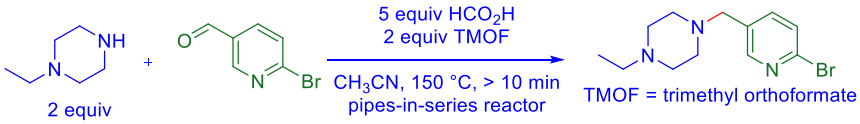
Example 5[12]

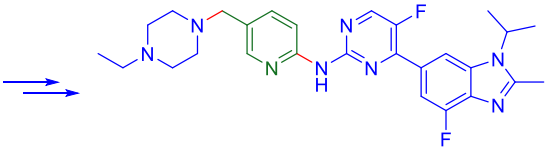


Example 6[13]



Example 7, Flow chemistry[14]





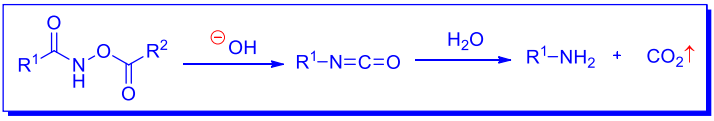
abemaciclib (Verzanio)
Lilly, 2017
CDK4/6 inhibitor

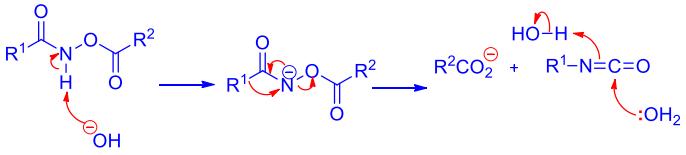
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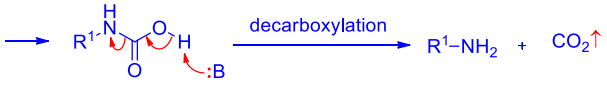
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Lossen Rearrangement

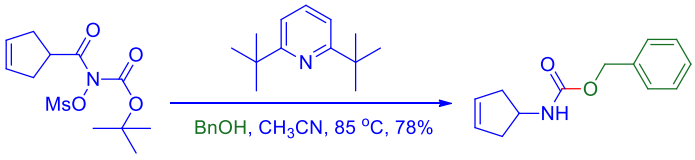
The Lossen rearrangement involves the generation of an isocyanate via thermal or base-mediated rearrangement of an activated hydroxamate which can be generated from the corresponding hydroxamic acid. Activation of the hydroxamic acid can be achieved through *O*-acylation, *O*-arylation, chlorination, or *O*-sulfonylation. Such hydroxamic acids can also be activated using polyphosphoric acid, carbodiimide, Mitsunobu conditions, or silyation. The product of the Lossen rearrangement, an isocyanate can be subsequently converted to a urea or an amine resulting in the net loss of one carbon atom relative to the starting hydroxamic acid.



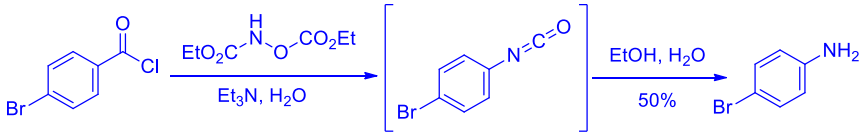




Example 1[6]

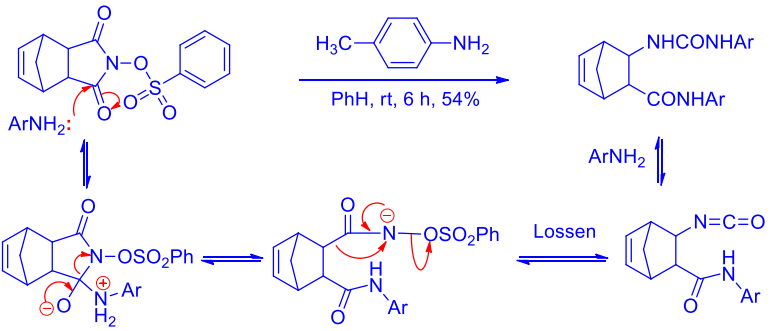


Example 2[7]

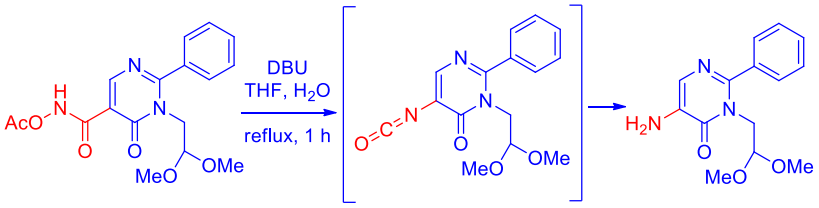


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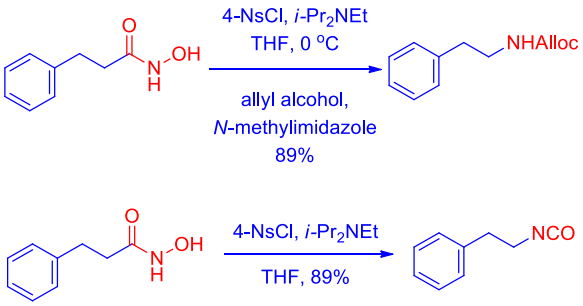
Example 3[8]



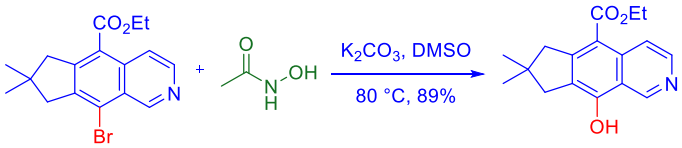
Example 4[9]



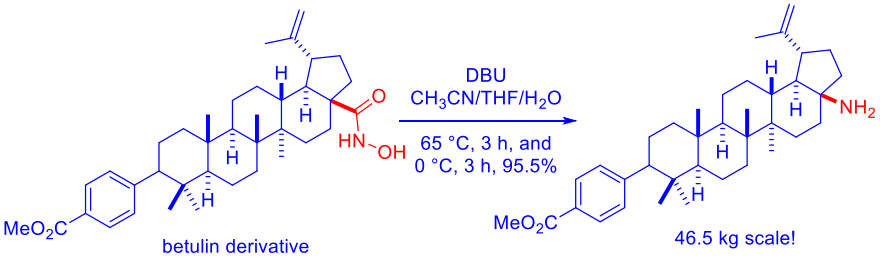
Example 5[11]



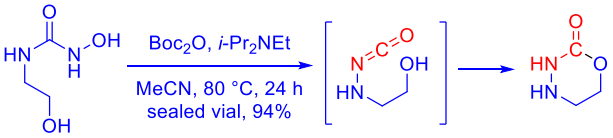
Example 6, Tandem S_NAr/Lossen rearrangement sequence[12]



Example 7[13]



Example 8, Aza-Lossen rearrangement[14]

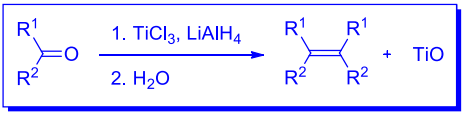


References

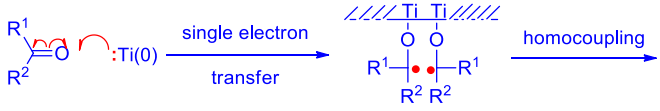
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McMurry Coupling

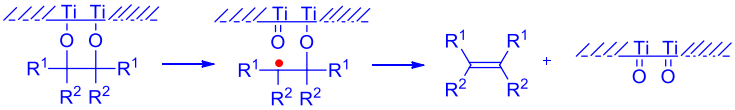
Olefination of carbonyls with low-valent titanium such as Ti(0) derived from $TiCl_3/LiAlH_4$. A single-electron process.





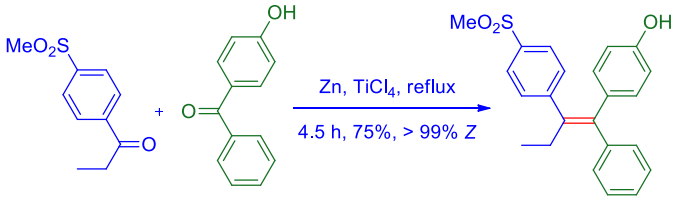


radical anion intermediate

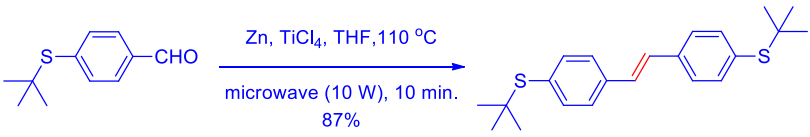


oxide-coated titanium surface

Example 1, Cross-McMurry coupling[7]

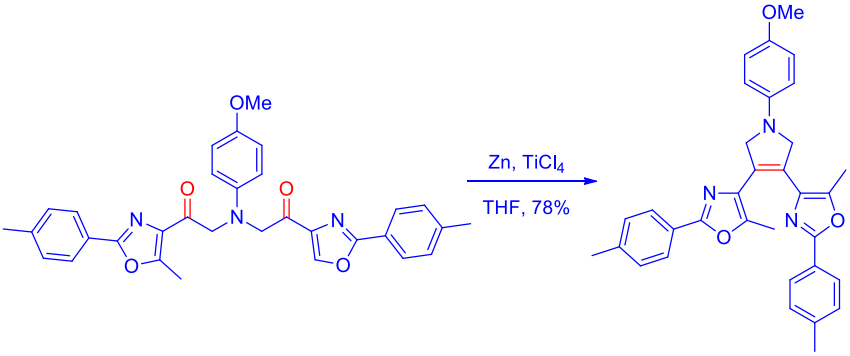


Example 2, Homo-McMurry coupling[8]

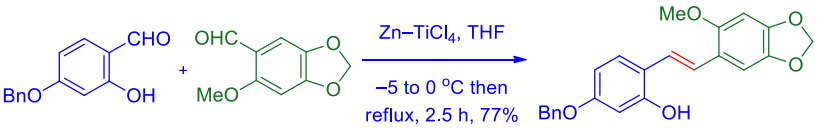


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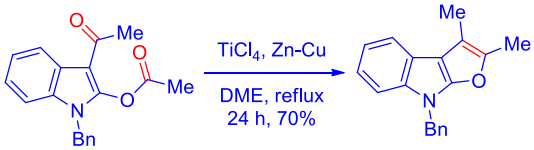
Example 3, Cross-McMurry coupling[9]



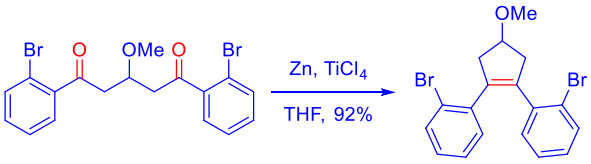
Example 4, Cross-McMurry coupling[10]



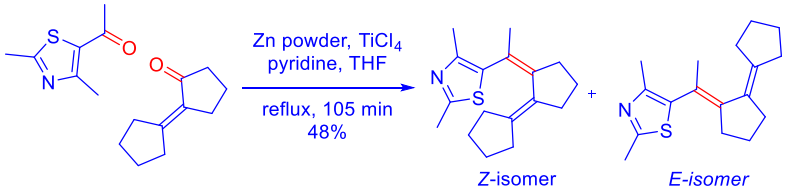
Example 5[12]



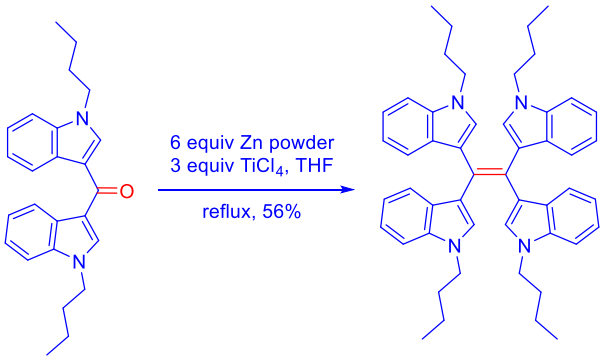
Example 6, Intramolecular McMurry coupling[13]



Example 7[14]



Example 8, Tetra-indole synthesis[15]

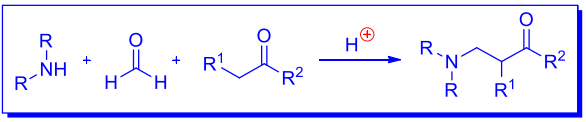


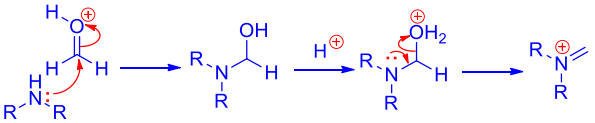
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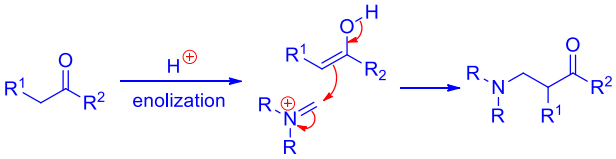
Mannich Reaction

Three-component aminomethylation from amine, aldehyde and a compound with an acidic methylene moiety.

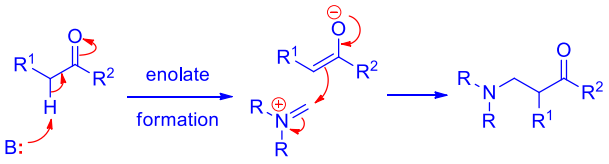




When R = Me, the $^{+}Me_2N{=}CH_2$ salt is known as *Eschenmoser's salt*

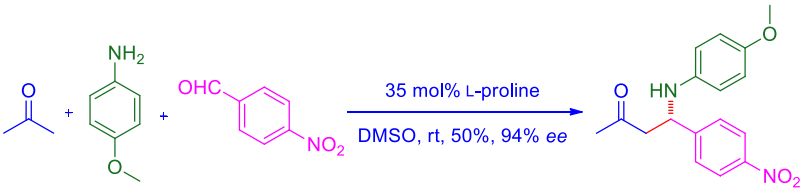


The Mannich reaction can also operate under basic conditions:

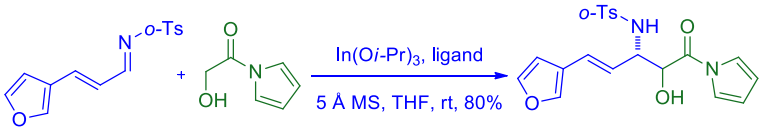


Mannich Base

Example 1, Asymmetric Mannich reaction[2]

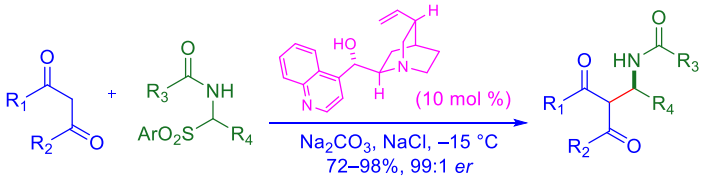


Example 2, Asymmetric Mannich-type reaction[9]

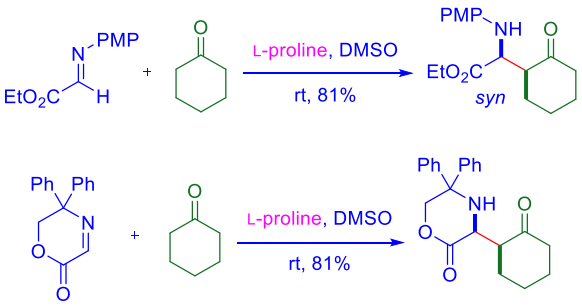


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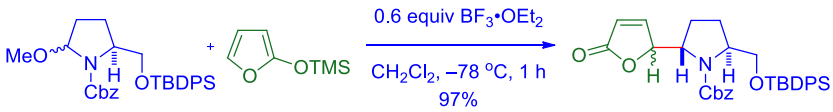
Example 3, Asymmetric Mannich-type reaction[10]



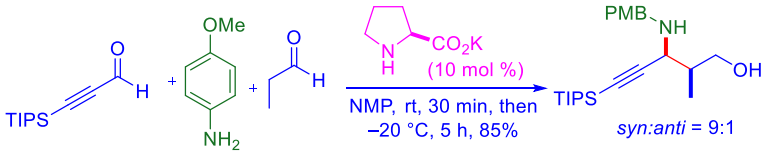
Example 4[11]



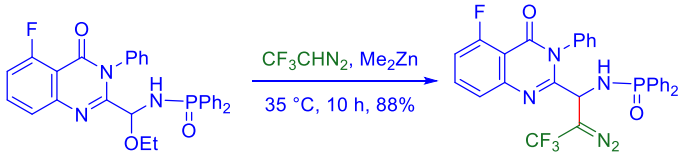
Example 5, Vinylogous Mannich reaction (VMR)[13]



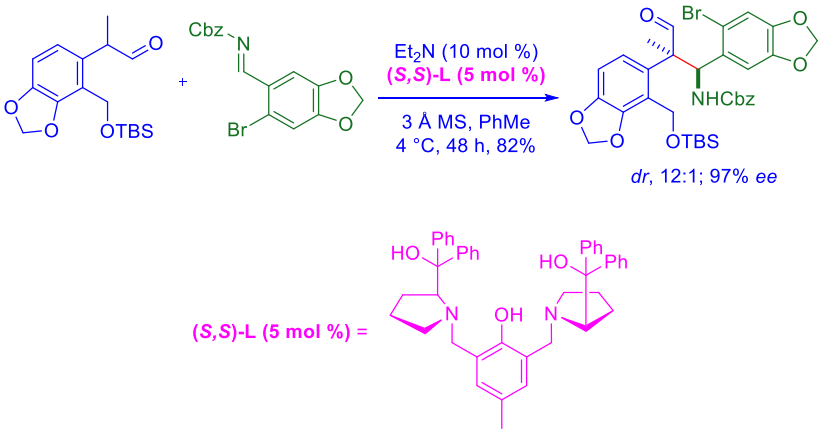
Example 6, Asymmetric Mannich reaction[15]



Example 7, A zinc-mediated Mannich-type transformation of 2,2,2-trifluorodiazoethane[16]



Example 8, Using preformed imine[17]

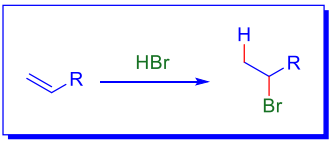


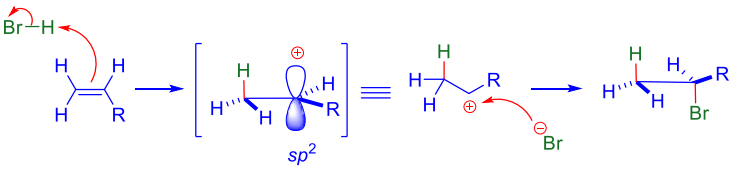
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Markovnikov's Rule

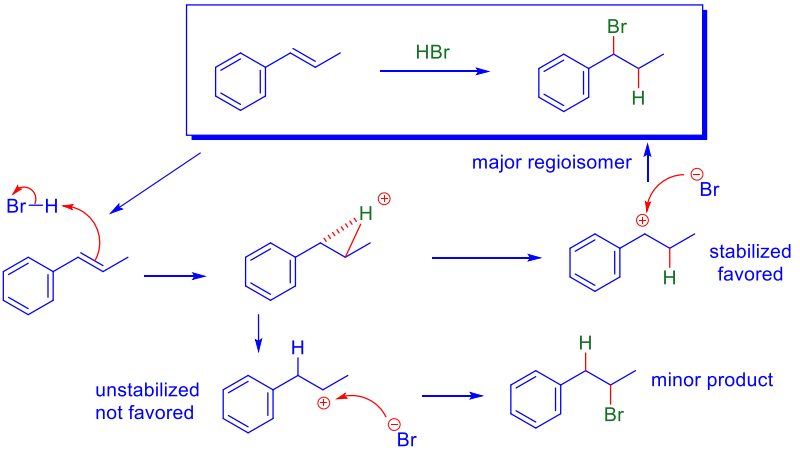
For addition of HX to olefins, Markovnikov's rule predicts the regiochemistry of HX addition to unsymmetrically substituted alkenes: The halide component of HX bonds preferentially at the more highly substituted carbon, whereas the hydrogen prefers the carbon which already contains more hydrogen atoms.



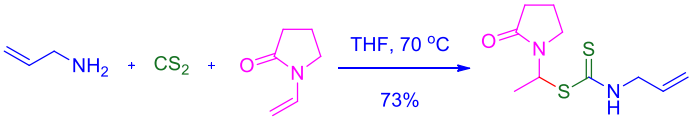


The intermediate is the more stable secondary cation, and the formal charge is on one carbon.

Regiochemistry favors the benzylic position:

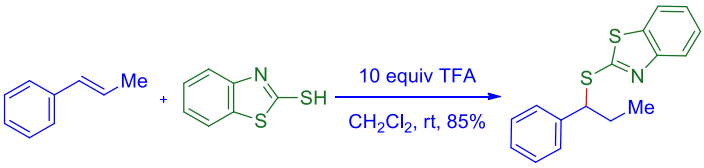


Example 1[3]

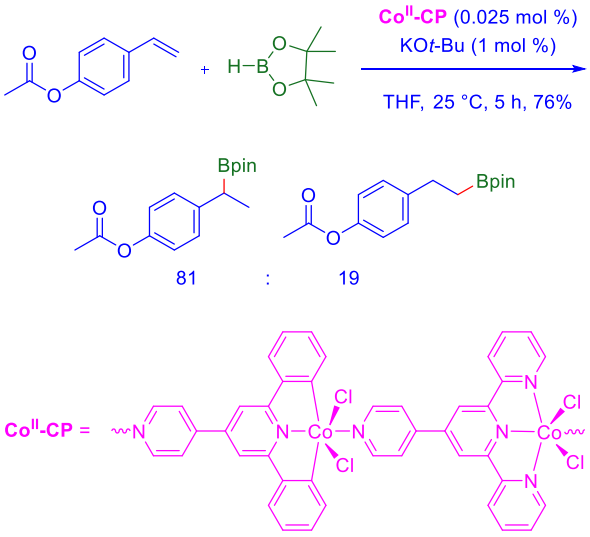


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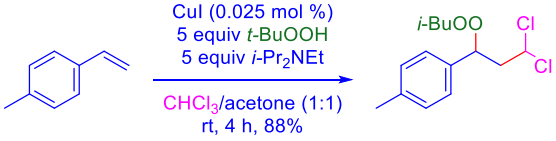
Example 2, Markovnikov-selective hydrothiolation of styrenes[4]



Example 3, Markovnikov-regioselective hydroboration of alkenes[5]



Example 4, Markovnikov-regioselective despite a radical mechanism[6]



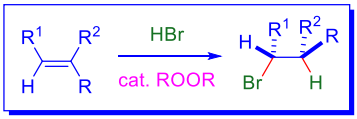
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2 Oparina, L. A.; Artem'ev, A. V.; Vysotskaya, O. V.; Kolyvanov, N. A.; Bagryanskaya, Y. I.; Doronina, E. P.; Gusarova, N. K. *Tetrahedron* **2013,** *69*, 6185–6195.
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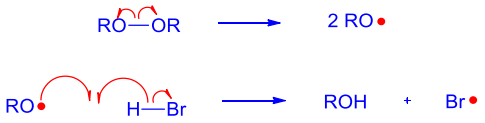
Anti-Markovnikov's Rule

Some reactions do not follow Markovnikov's rule, and *anti*-Markovnikov products are isolated. The outcome of the regioselectivity may be explained by the relative stability of the radical intermediates.

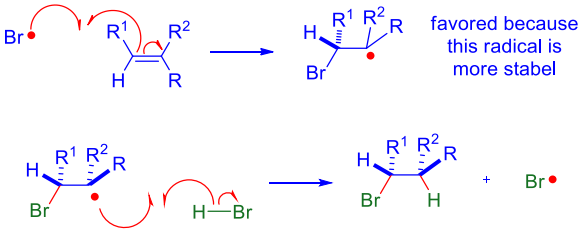


Radical mechanism:

Initiation:



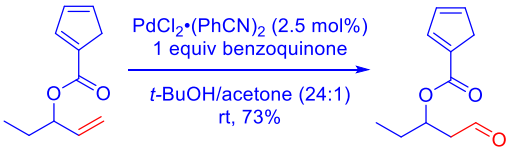
Propagation:



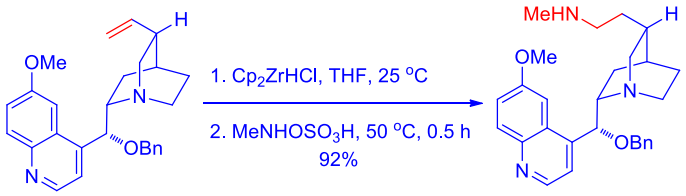
Termination:



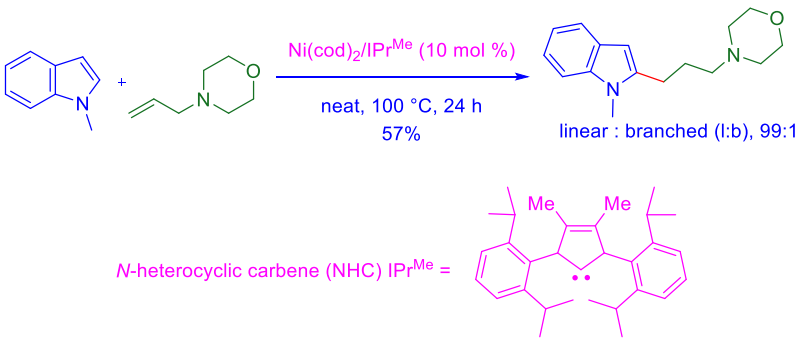
Example 1, Anti-Markovnikov oxidation of allylic esters[1]



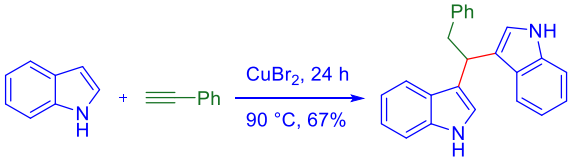
Example 2, Anti-Markovnikov hydroamination[3]



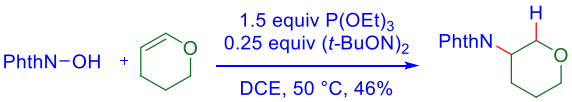
Example 3, Anti-Markovnikov hydroheteroarylation of unactivated alkenes[4]



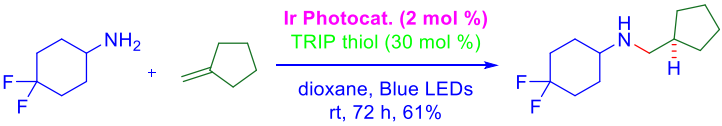
Example 4, Anti-Markovnikov addition to alkynes[5]

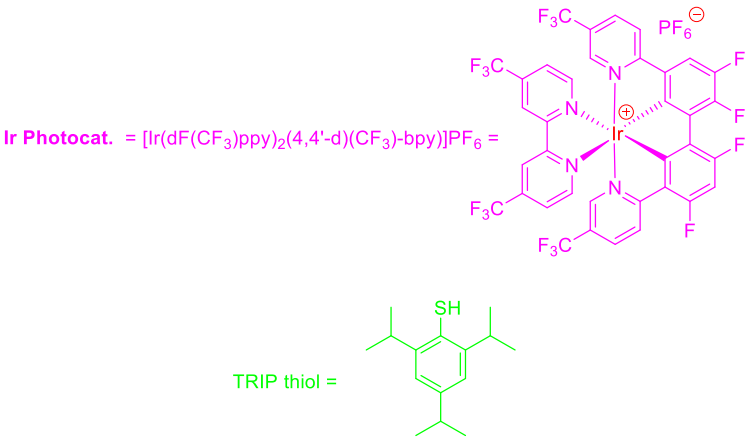


Example 5, Anti-Markovnikov hydroamination using *N*-hydroxyphthalimide[6]



Example 6, Anti-Markovnikov hydroamination of unactivated alkenes with primary amines[7]



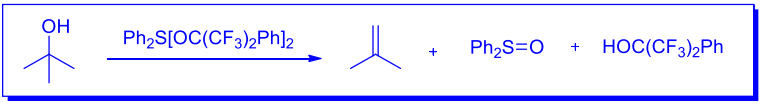


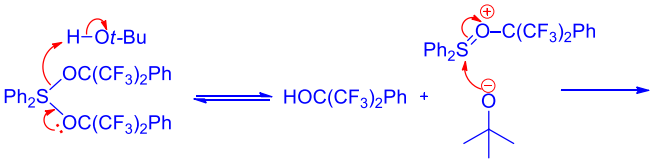
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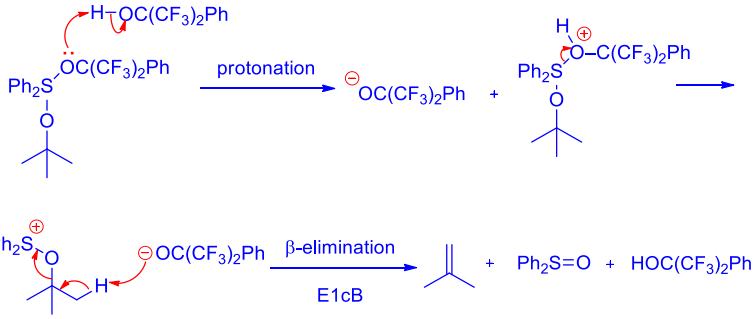
Martin's Sulfurane Dehydrating Reagent

Dehydrates secondary and tertiary alcohols to give olefins, but forms ethers with primary alcohols. *Cf.* Burgess dehydrating reagent.

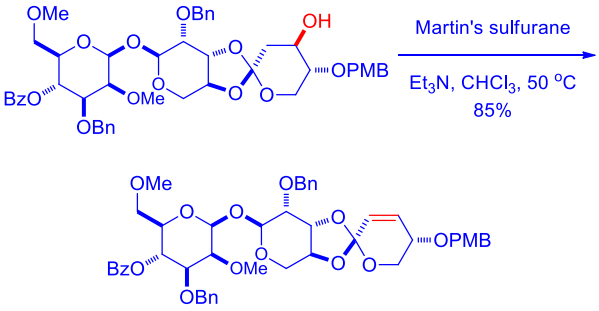




The alcohol is acidic

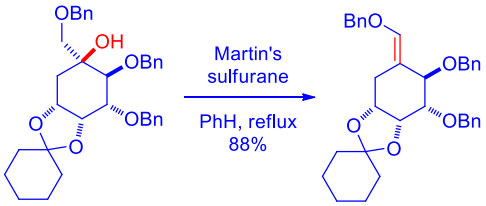


Example 1[5]

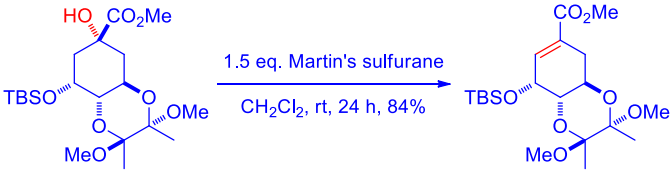


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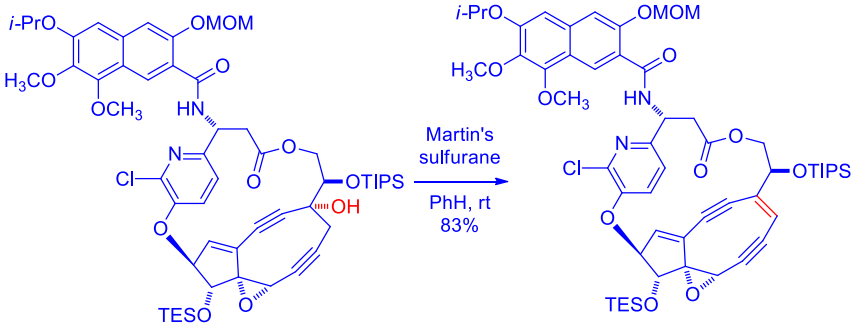
Example 2[6]



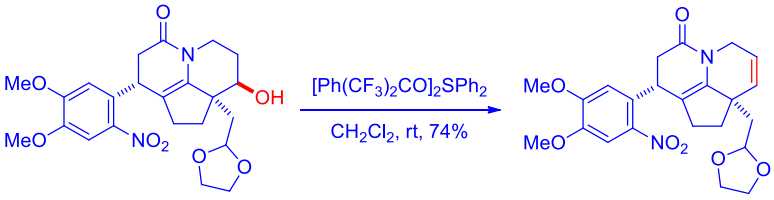
Example 3[7]



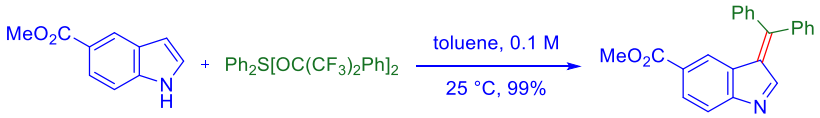
Example 4[9]



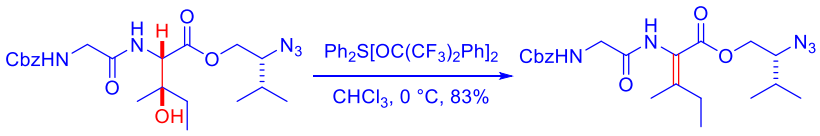
Example 5[12]



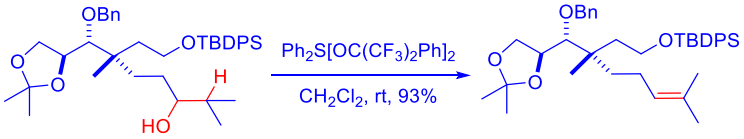
Example 6, Direct ylide transfer in indoles[13]



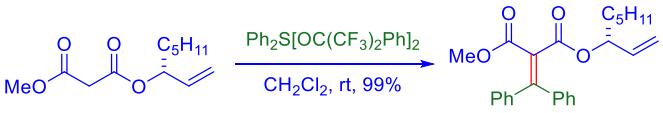
Example 7[14]



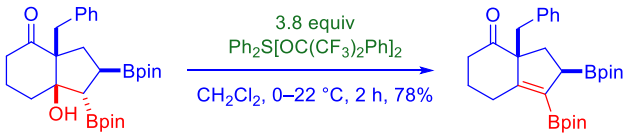
Example 8[15]



Example 9[16]



Example 10[17]



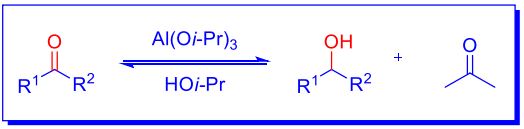
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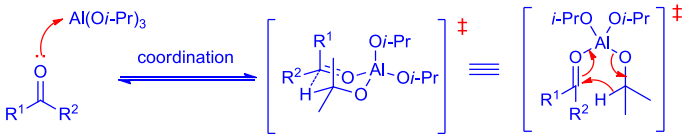
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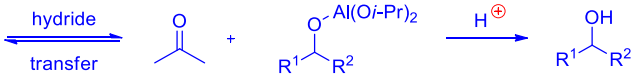
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Meerwein–Ponndorf–Verley Reduction

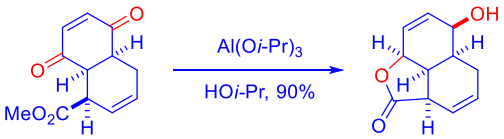
Reduction of ketones to the corresponding alcohols using $Al(O\textit{i}\text{-}Pr)_3$ in isopropanol. Reverse of the Oppernauer oxidation.



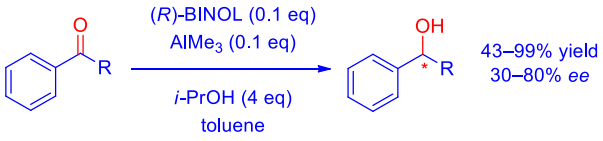




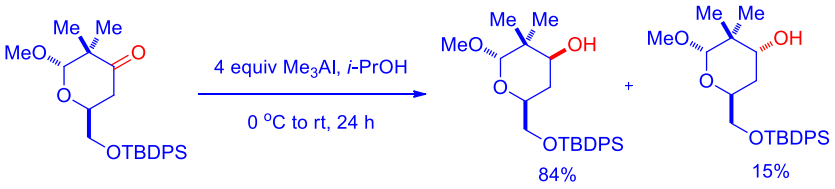
Example 1[2]



Example 2[4]

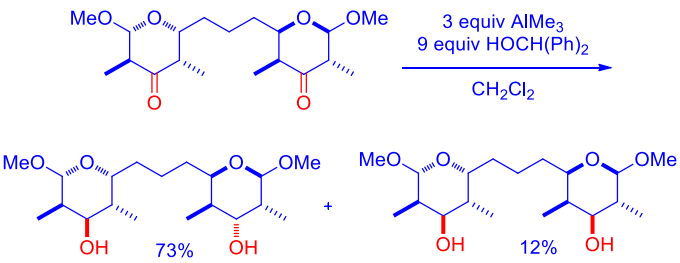


Example 3[7]

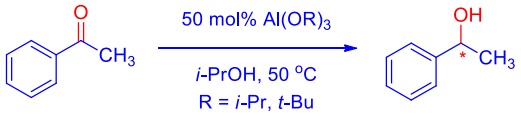


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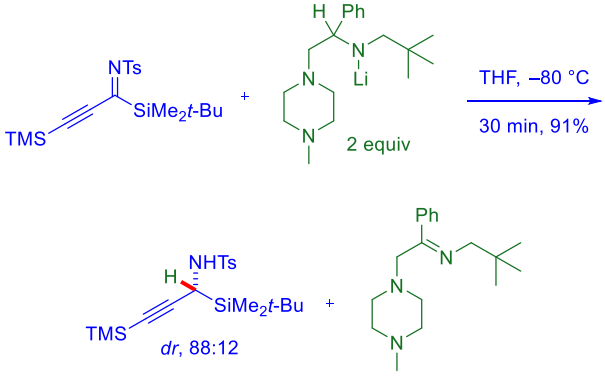
Example 4[9]



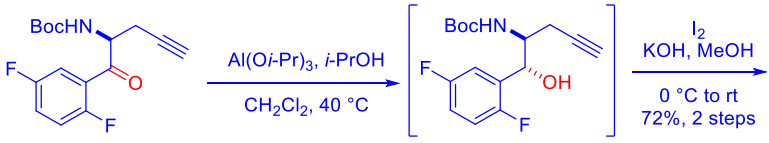
Example 5[10]

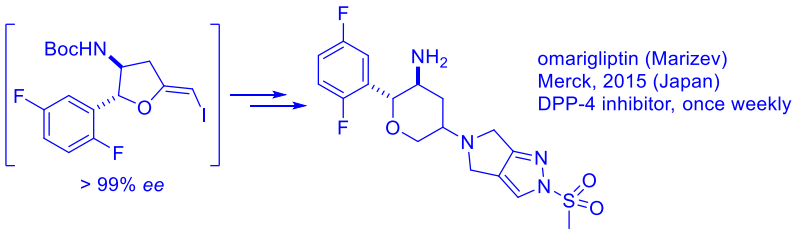


Example 6, Reuction of α-silylimines by a chiral lithium amide (a Meerwein–Ponndorf–Verley-*type* reduction)[11]

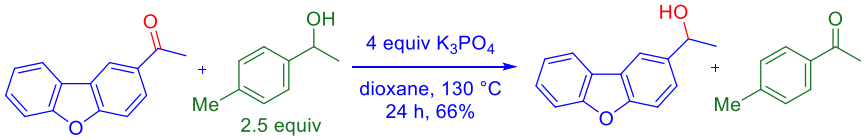


Example 7, A process synthesis of a key intermediate of omarigliptin, a DPP-4 inhibitor[12]





Example 8, A base-mediated Meerwein–Ponndorf–Verley reduction[13]

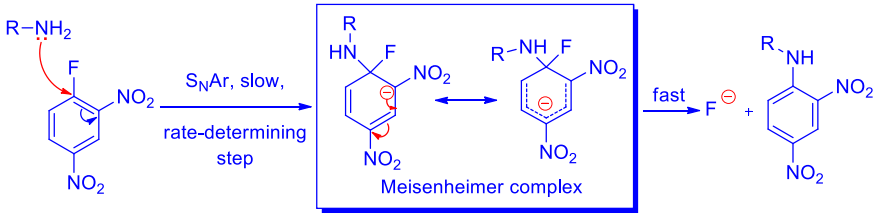


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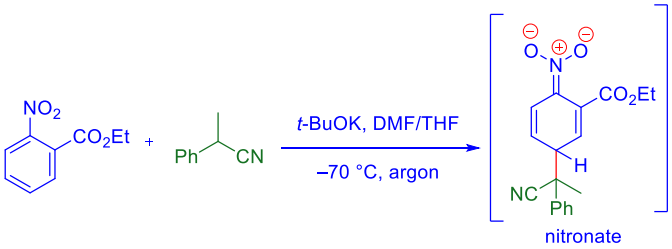
Meisenheimer Complex

Also known as **the Meisenheimer–Jackson salt**, the stable intermediate for certain S_NAr reactions.

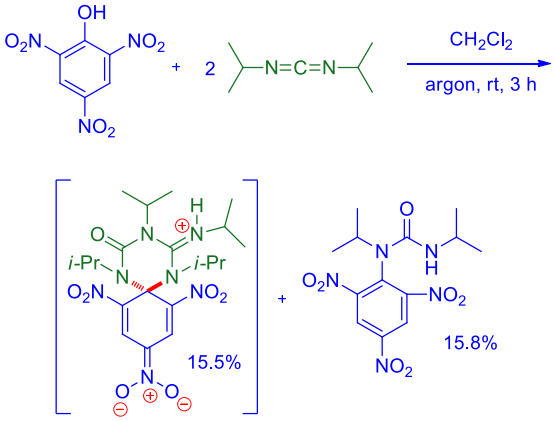


Sanger′s reagent, *ipso* attack *ipso* substitution

Example 1[7]



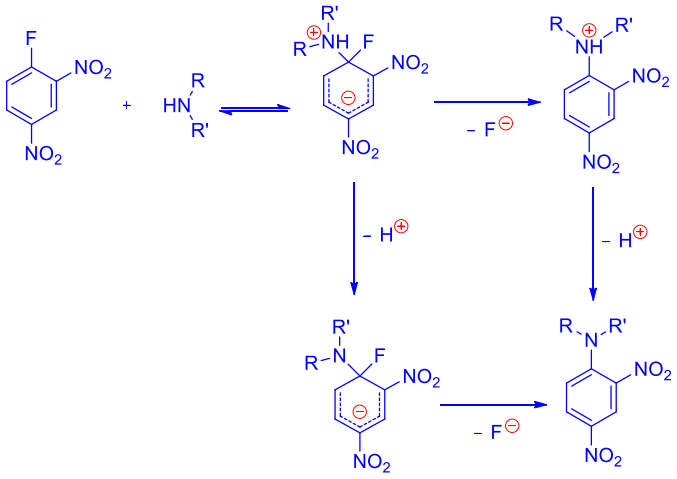
Example 2, A fluorescent zwitterionic spirocyclic Meisenheimer complex[9]



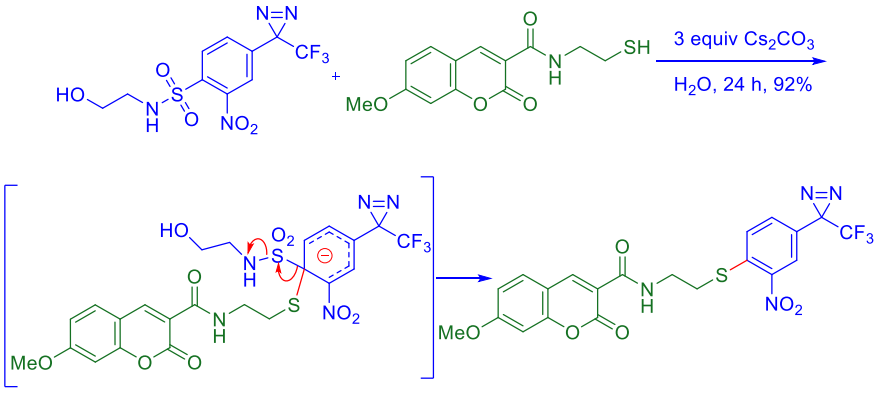
The reaction using Sanger′s reagent is faster than using the corresponding chloro-, bromo-, and iododinitrobenzene—the fluoro-Meisenheimer complex is the most stabilized because F is the most electron-withdrawing. The reaction rate does not depend upon the capacity of the leaving group.

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Example 3[10]



Example 4[14]



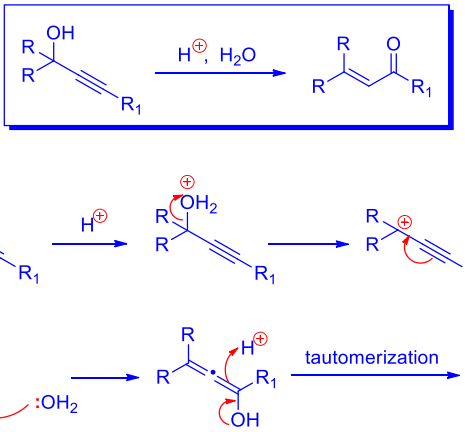
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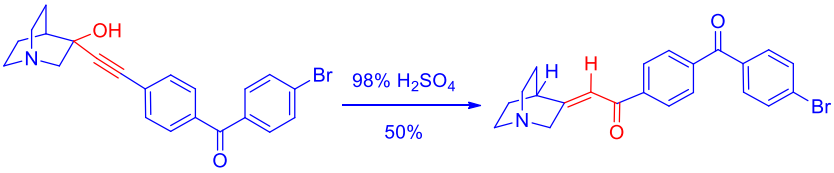
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Meyer–Schuster Rearrangement

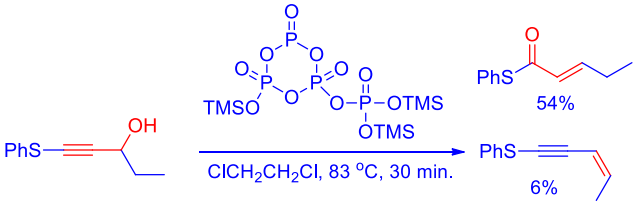
The isomerization of secondary and tertiary α-acetylenic alcohols to α,β-unsaturated carbonyl compounds *via* 1,3-shift. When the acetylenic group is terminal, the products are aldehydes, whereas the internal acetylenes give ketones. *Cf.* Rupe rearrangement.



Example 1[6]

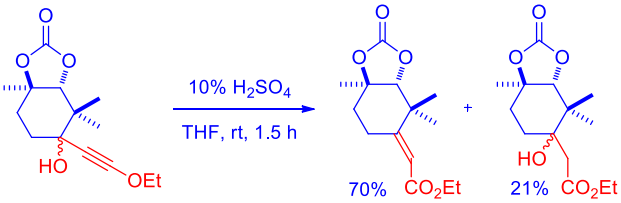


Example 2[7]

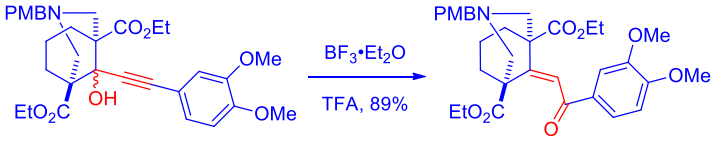


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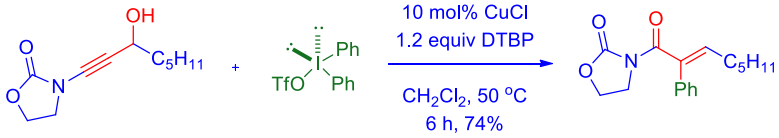
Example 3[8]



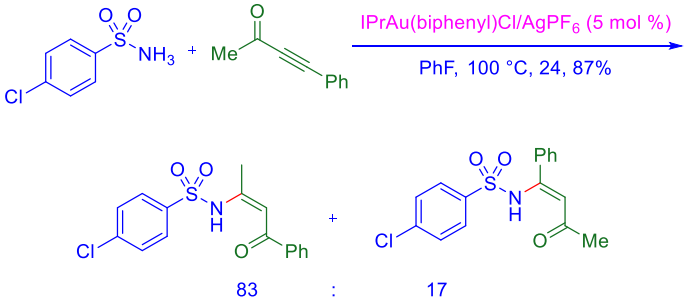
Example 4[9]



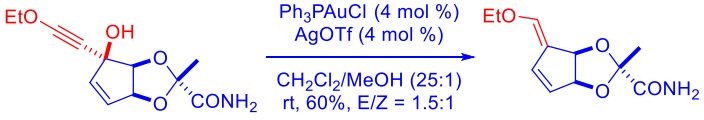
Example 5, DTBP = di-*tert*-butyl peroxide[11]



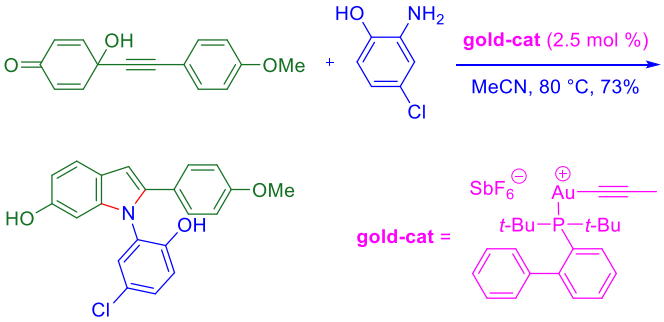
Example 6[12]



Example 7, Gold-catalyzed Meyer–Schuster rearrangement[13]



Example 8[14]

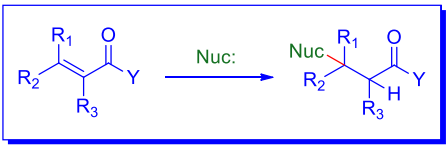


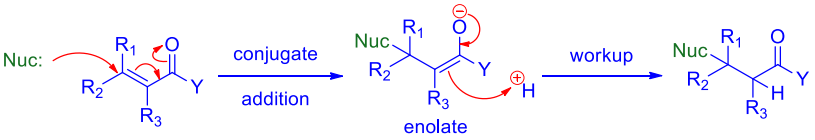
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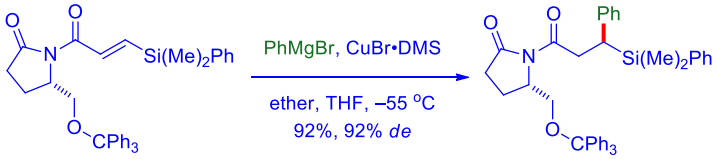
Michael Addition

Also known as conjugate addition, Michael addition is the 1,4-addition of a nucleophile to an α,β-unsaturated system.

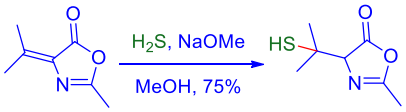




Example 1, Asymmetric Michael addition[2]



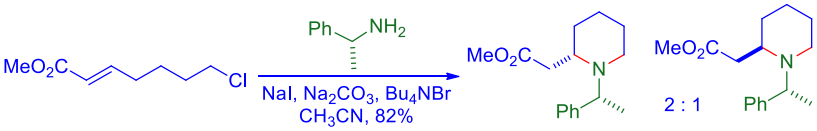
Example 2, Thia-Michael addition[3]



Example 3, Phospha-Michael addition[7]

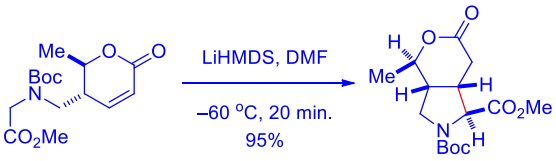


Example 4, Asymmetric aza-Michael addition[9]

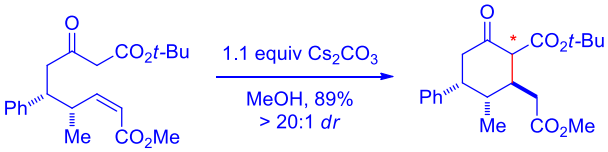


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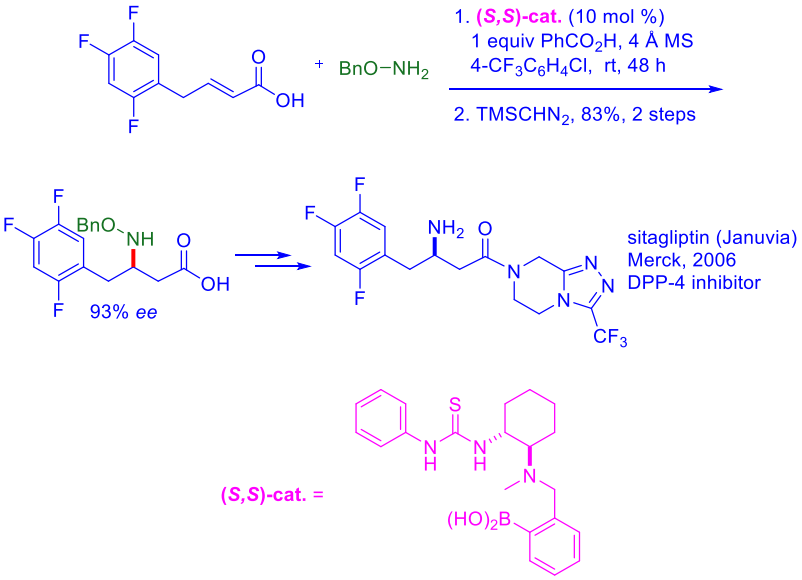
Example 5, Intramolecular Michael addition[10]



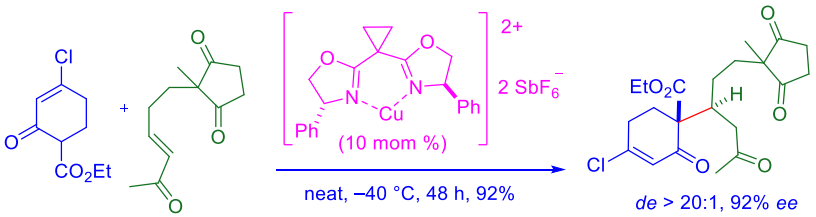
Example 6, Intramolecular Michael addition[11]



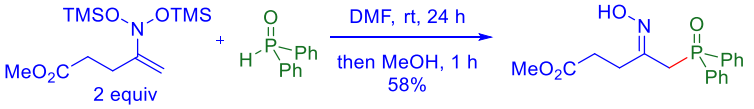
Example 7, Hetero-Michael addition[12]



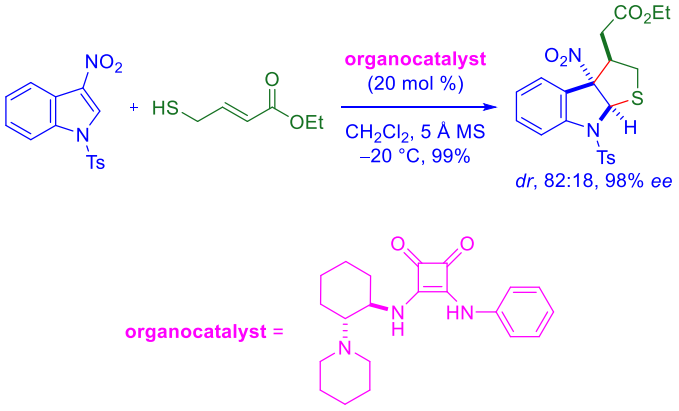
Example 8, Cu(II)-catalyzed asymmetric Michael addition[13]



Example 9, Michael addition of phosphonates to ene-nitrosoacetals[14]



Example 10, Organocatalytic asymmetric double Michael addition[15]



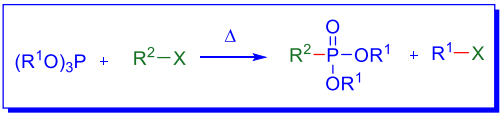
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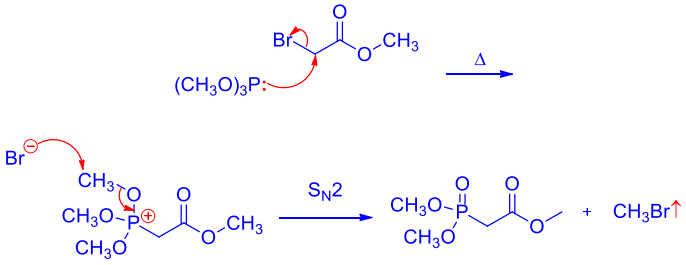
Michaelis–Arbuzov Phosphonate Synthesis

Aliphatic phosphonate synthesis from the reaction of alkyl halides with phosphites.
General scheme:

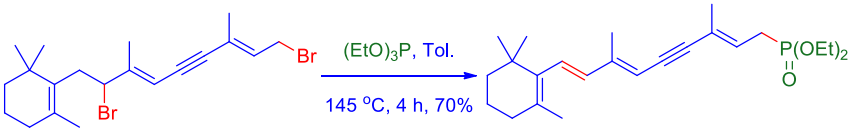


R^1 = alkyl, *etc.*; R^2 = alkyl, acyl, *etc.*; X = Cl, Br, I

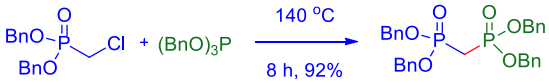
For instance:



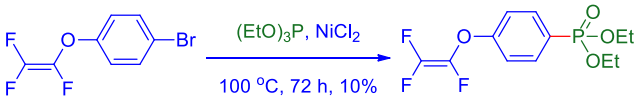
Example 1[2]



Example 2[6]

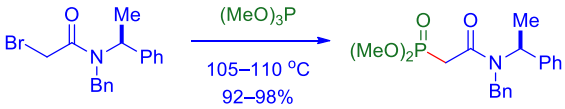


Example 3, Transition metal-catalyzed coupling, not via S_N2[7]

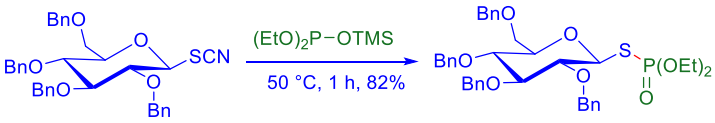


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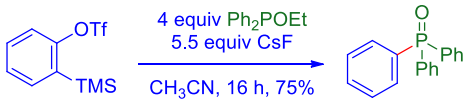
Example 4[9]



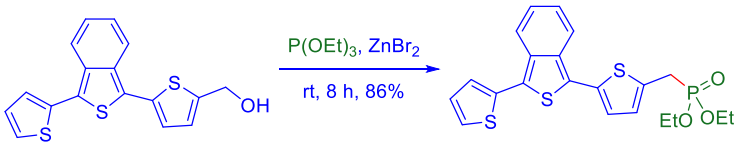
Example 5[10]



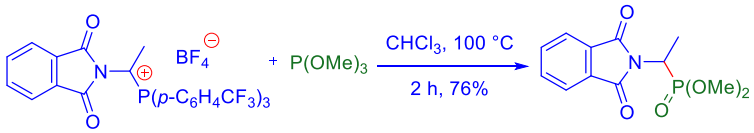
Example 6, An approach to prepare aromatic phosphonates via the intermediacy of benzyne[11]



Example 7, Alcohol-based Michaelis–Arbuzov reaction[12]



Example 8, Michaelis–Arbuzov-type reaction of 1-imidoalkyltriarylphosphonium salts[13]



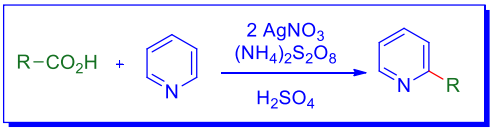
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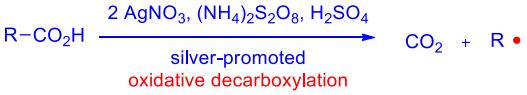
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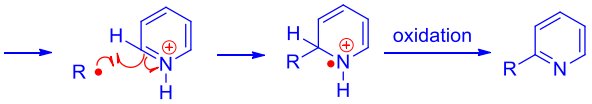
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Minisci Reaction

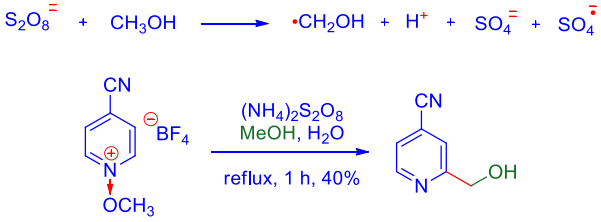
Radical-based carbon–carbon bond formation with electron-deficient heteroaromatics. The reaction entails an intermolecular addition of a nucleophilic *radical* to protonated heteroaromatic nucleus.



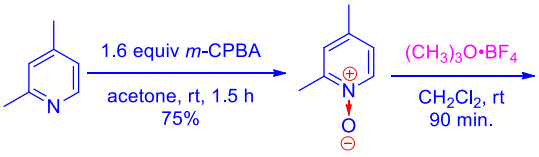


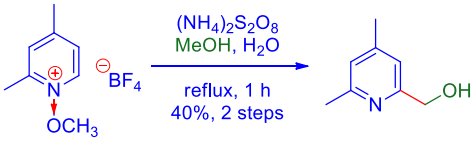


Example 1[4]

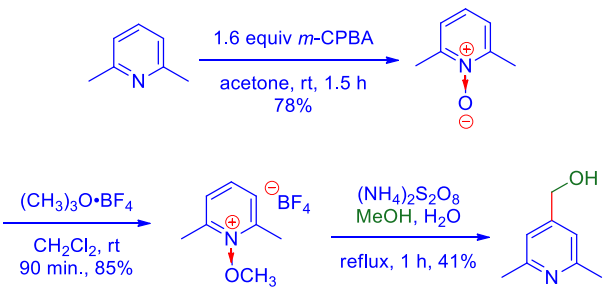


Example 2[5]

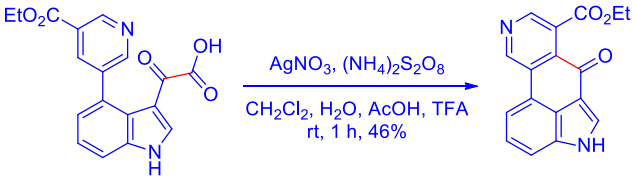




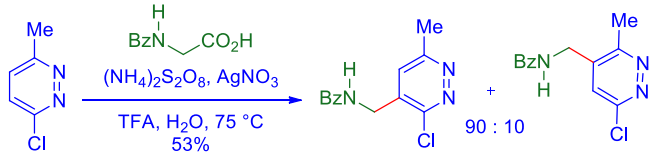
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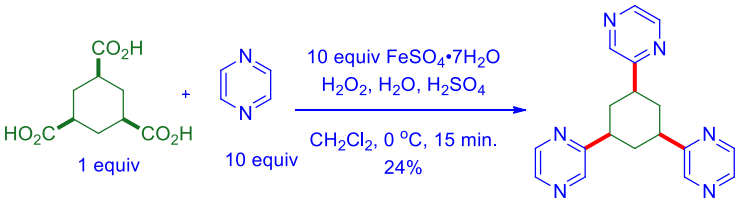
Example 3, Intramolecular Minisci reaction[6]



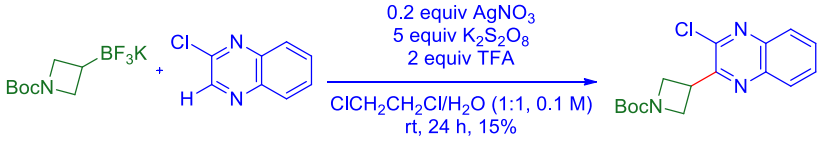
Example 4[7]



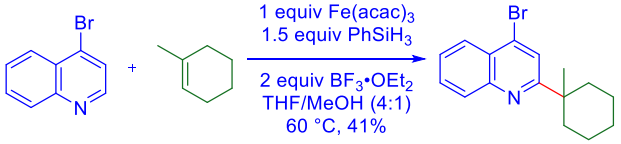
Example 5[10]



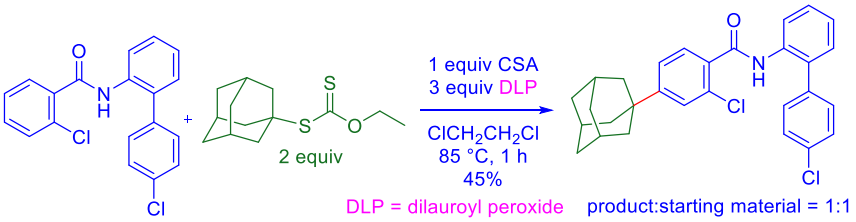
Example 6[12]



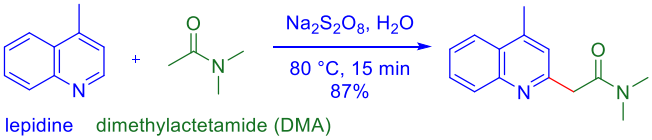
Example 7[13]



Example 8[14]



Example 9[15]

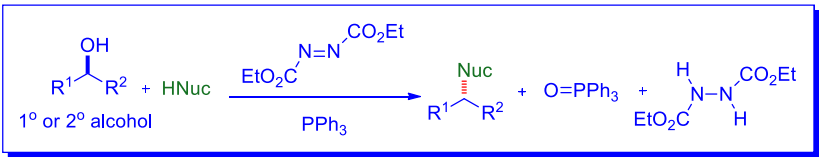


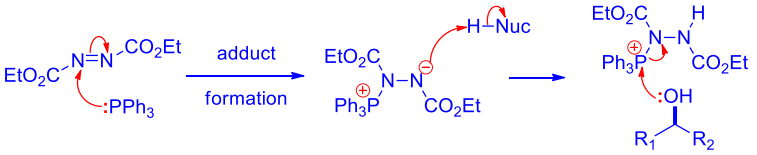
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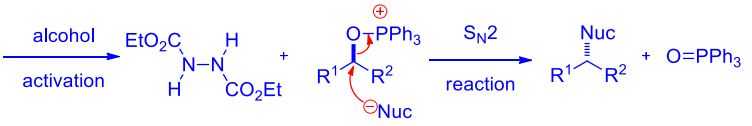
Mitsunobu Reaction

S_N2 inversion of an alcohol by a nucleophile using disubstituted azodicarboxylates (originally, diethyl diazodicarboxylate, or DEAD) and trisubstituted phosphines (originally, triphenylphosphine).

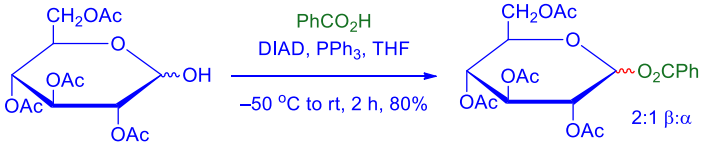




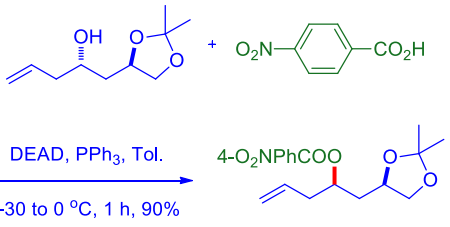
Diethyl azodicarboxylate (DEAD)



Example 1[2]

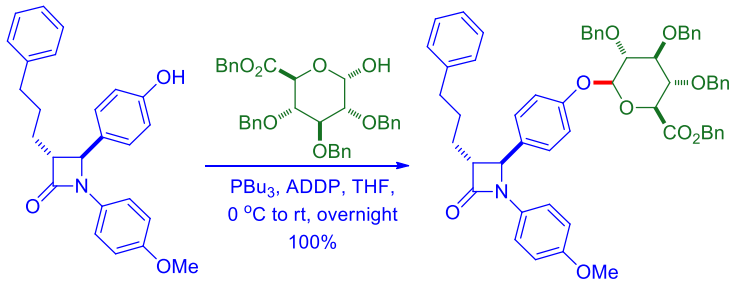


Example 2[3]



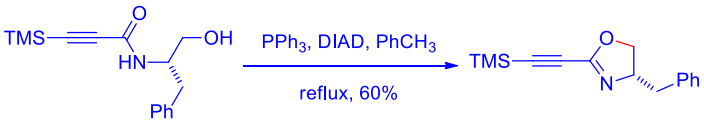
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Example 3, Glucoronidation of the phenol: preparing a secondary drug metabolite[6]

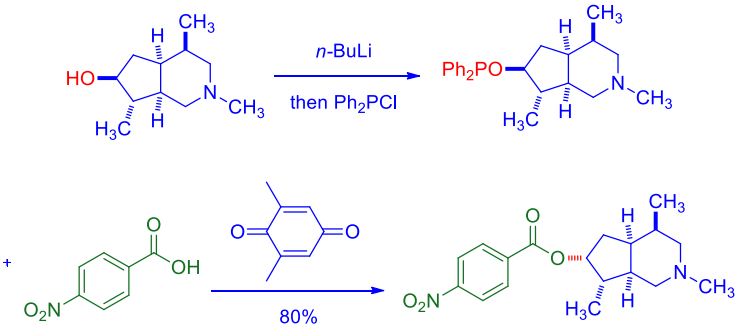


ADDP = 1,1′-(azodicarbonyl)dipiperidine

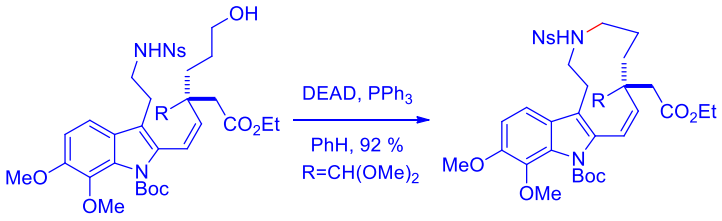
Example 4, Intramolecular Mitsunobu reaction[7]



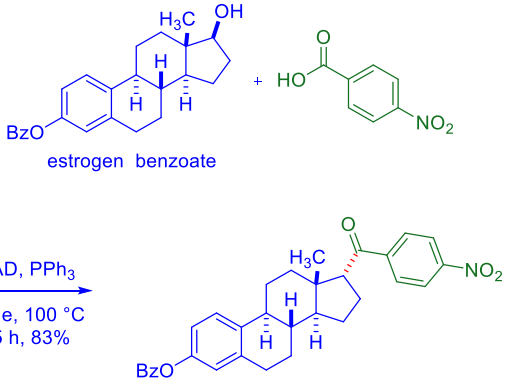
Example 5[8]



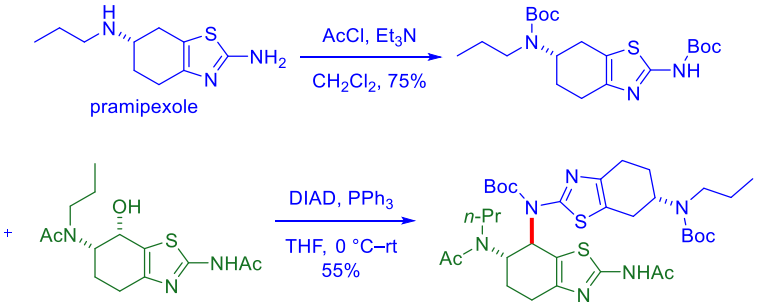
Example 6, Intramolecular Mitsunobu reaction[9]



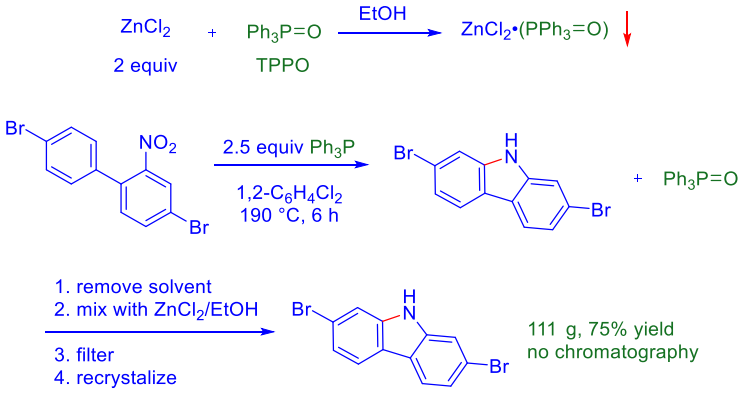
Example 7[13]



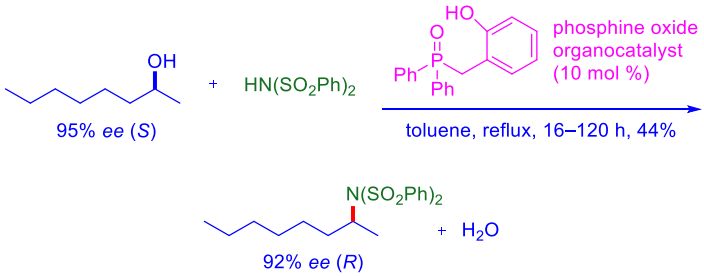
Example 8, Synthesis of an impurity during pramipexole process[14]



Example 8, Removal of triphenylphosphine oxide (TPPO) by precipitation with zinc chloride in polar solvents (compatible with RNHBoc, but not compatible with compounds with basic amines)[15]



Example 10, Redox-neutral organocatalytic Mitsunobu reactions[16]

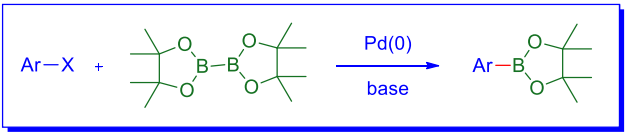


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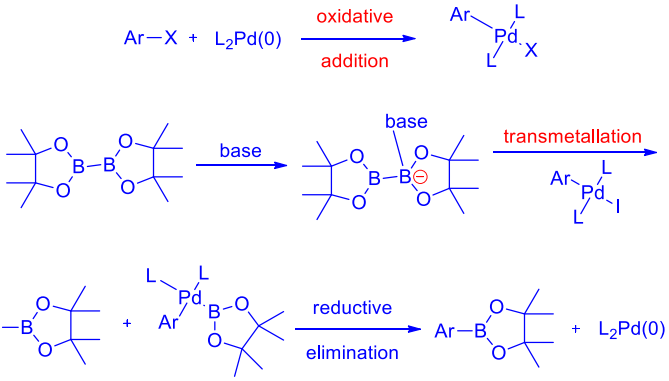
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Miyaura Borylation

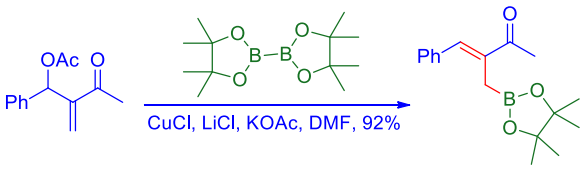
Palladium-catalyzed reaction of aryl halides with diboron reagents to produce arylboronates. Also known as Hosomi–Miyaura borylation.



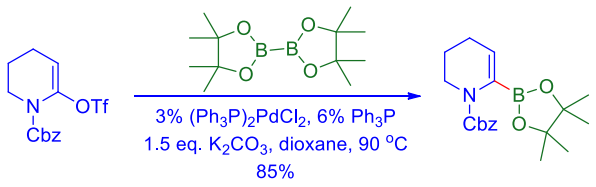
X = I, Br, Cl, OTf.



Example 1[7]

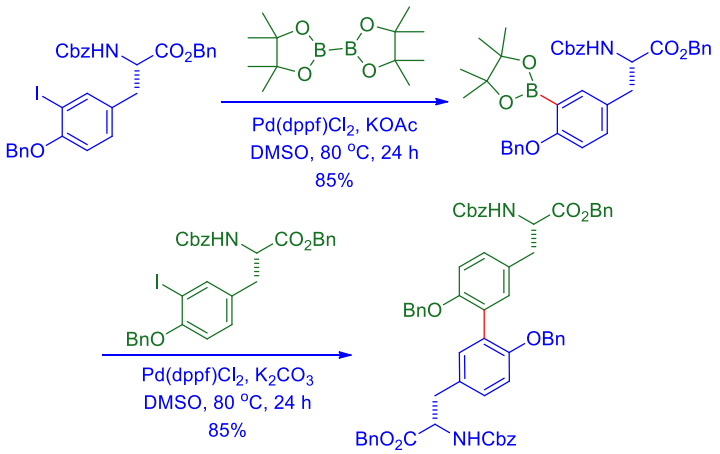


Example 2[8]

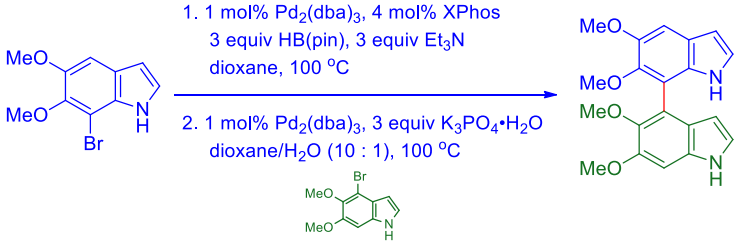


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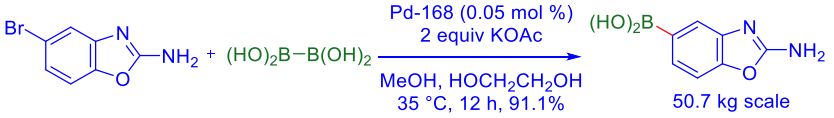
Example 3[9]



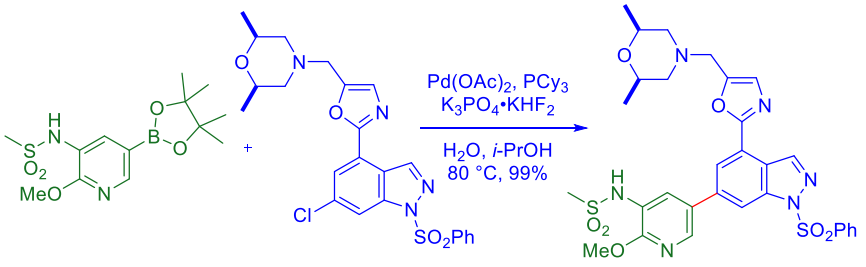
Example 4, One-pot synthesis of biindolyl[10]



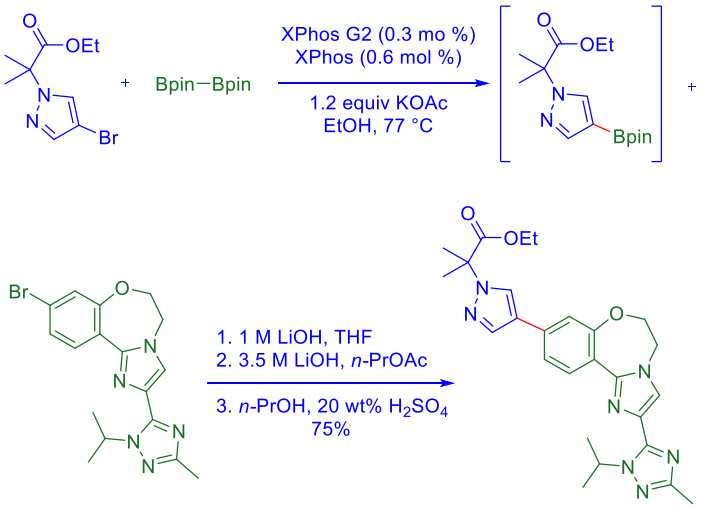
Example 4, An efficient Miyaura borylation process using tetrahydroxydiboron[13]



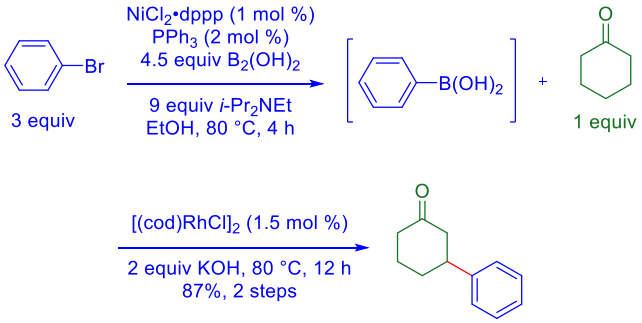
Example 5, Synthesis of PI3K$_\delta$ inhibitors[4]



Example 6[15]



Example 7, Nickel-catalyzed Miyaura borylation using tetrahydroxydiboron[16]



References

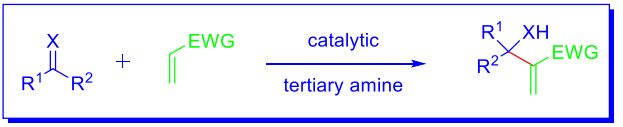
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Morita–Baylis–Hillman Reaction

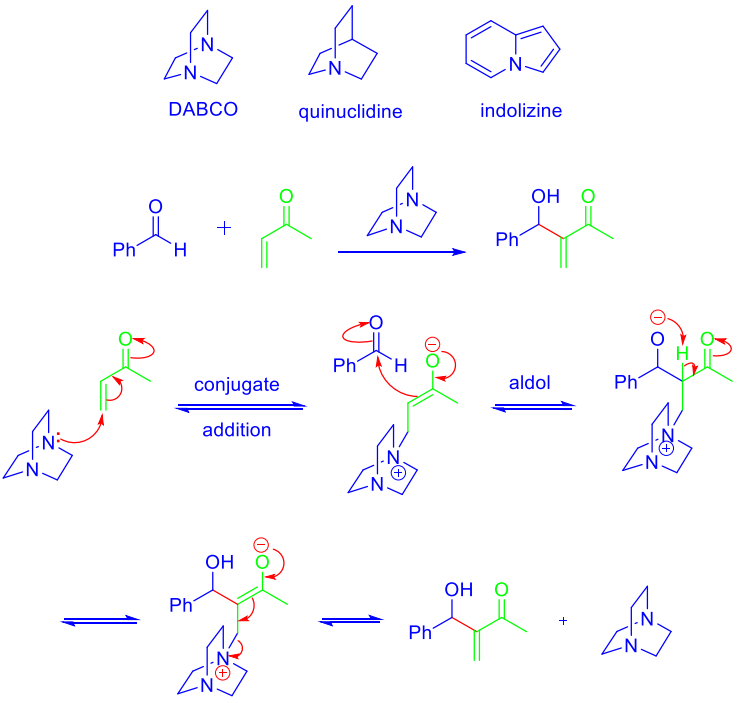
Also known as the Baylis–Hillman reaction. It is a carbon–carbon bond-forming transformation of an electron-poor alkene with a carbon electrophile. Electron-poor alkenes include acrylic esters, acrylonitriles, vinyl ketones, vinyl sulfones, and acroleins. On the other hand, carbon electrophiles may be aldehydes, α-alkoxycarbonyl ketones, aldimines, and Michael acceptors.

General scheme:



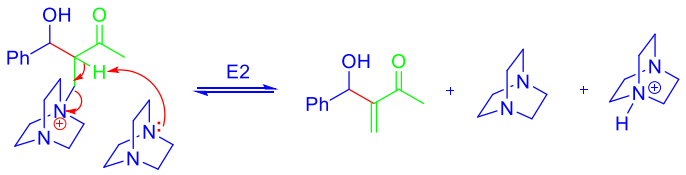
X = O, NR_2, EWG = CO_2R, COR, CHO, CN, SO_2R, SO_3R, $PO(OEt)_2$, $CONR_2$, $CH_2{=}CHCO_2Me$

Catalytic tertiary amines:

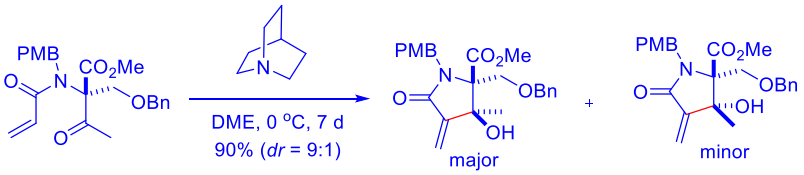


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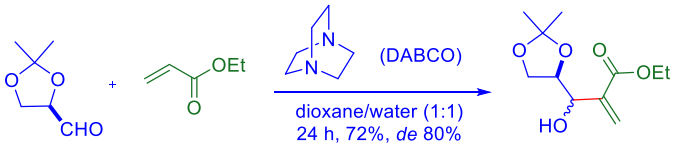
E2 (bimolecular elimination) mechanism is also operative here:



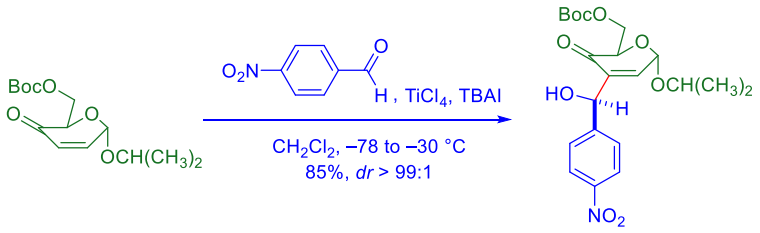
Example 1, Intramolecular Baylis–Hillman reaction[6]



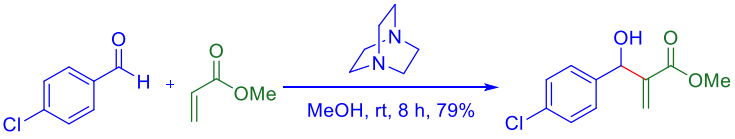
Example 2[7]



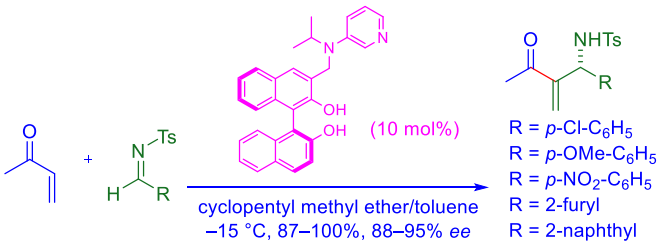
Example 3, TBAI = tetra-*n*-butylammonium iodide[8]



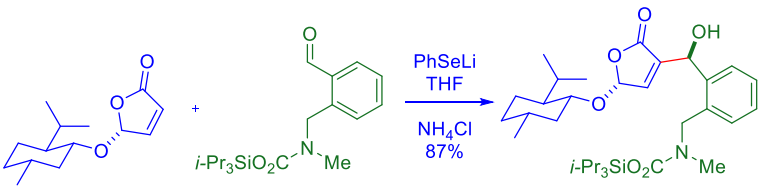
Example 4[9]



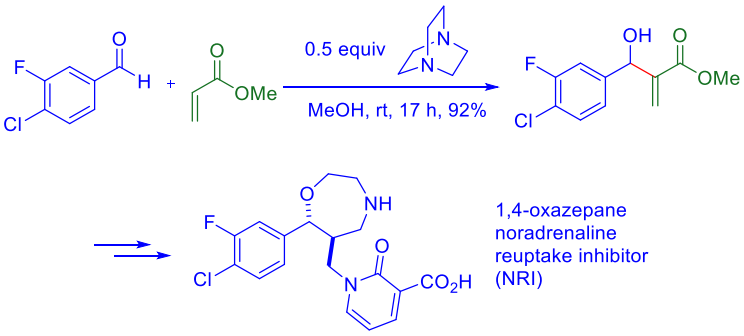
Example 5[10]



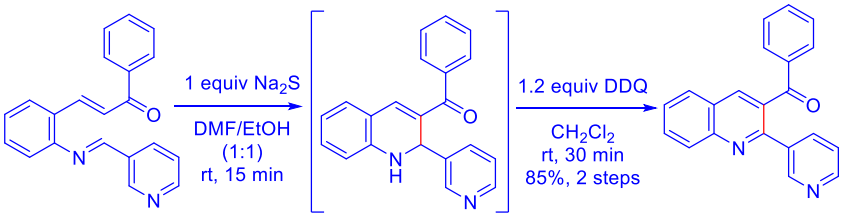
Example 6[13]



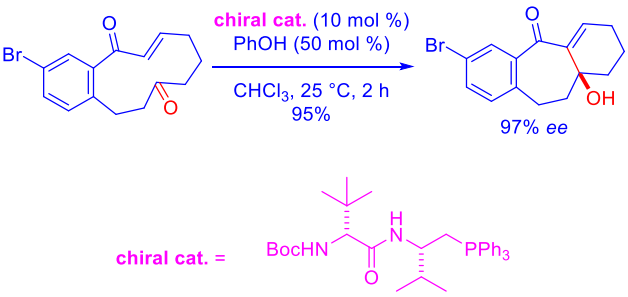
Example 7, Toward the synthesis of a 1,4-oxazepane noradrenaline reuptake inhibitor (NRI)[16]



Example 8, Intramolecular aza-Morita–Baylis–Hillman reaction[17]



Example 9, Catalytic enantioselective transannular Morita–Baylis–Hillman reaction[18]

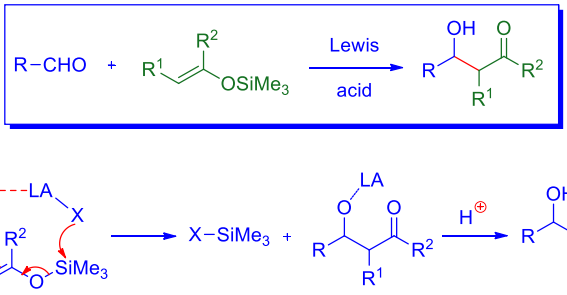


References

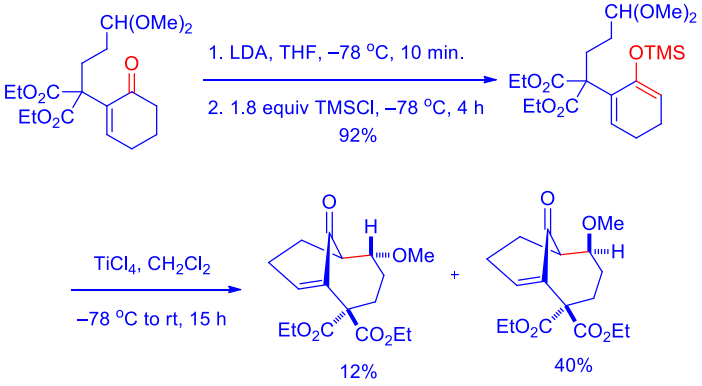
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Mukaiyama Aldol Reaction

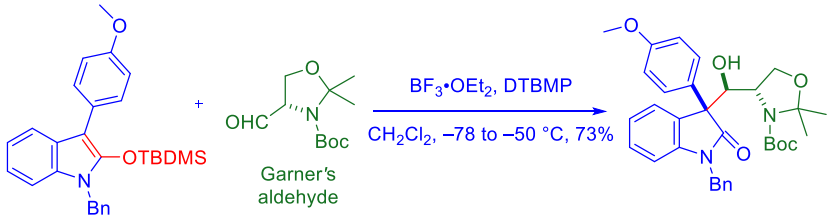
Lewis acid-catalyzed aldol condensation of aldehyde and silyl enol ether.



Example 1, Intramolecular Mukaiyama aldol reaction[3]

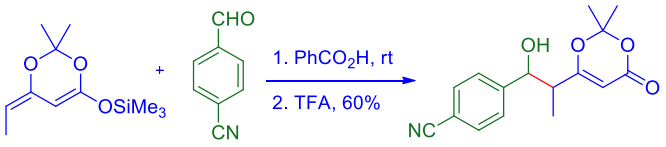


Example 2, Intermolecular Mukaiyama aldol reaction (DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine)[7]

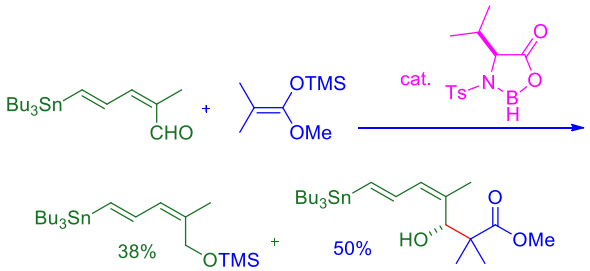


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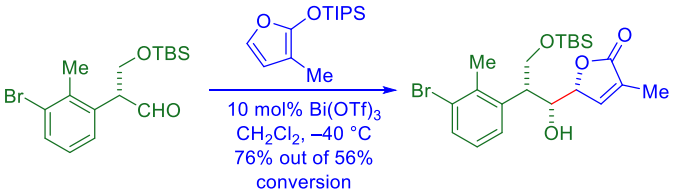
Example 3, Vinylogous Mukaiyama aldol reaction[8]



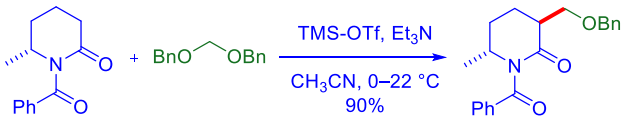
Example 4, Asymmetric Mukaiyama aldol reaction[10]



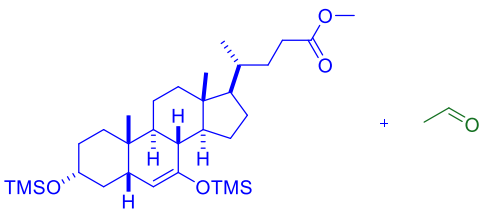
Example 5[12]

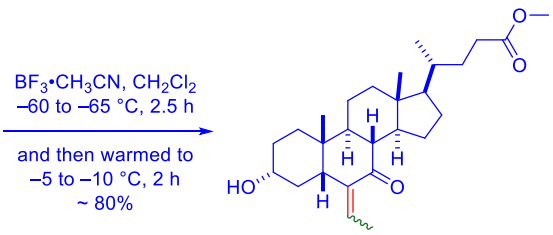


Example 6[13]



Example 7[14]



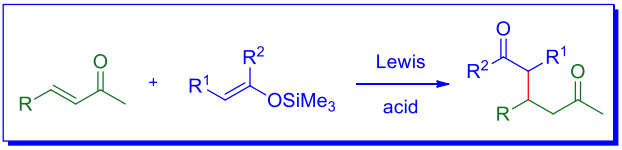


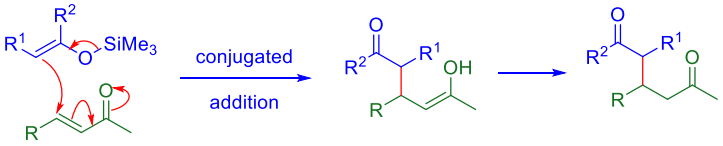
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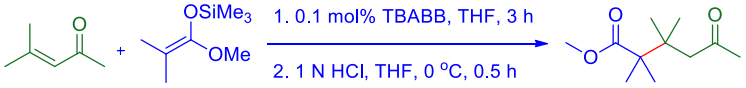
Mukaiyama Michael Addition

Lewis acid-catalyzed Michael addition of silyl enol ether to an α,β-unsaturated system.



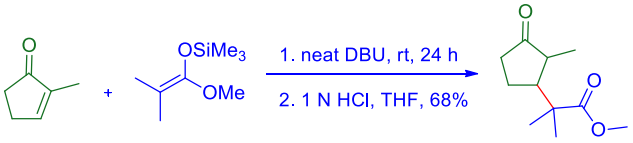


Example 1[2]

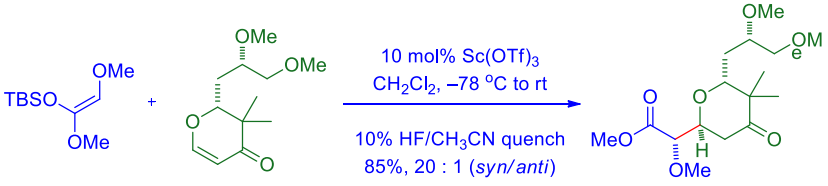


TBABB = tetra-*n*-butylammonium bibenzoate

Example 2[5]

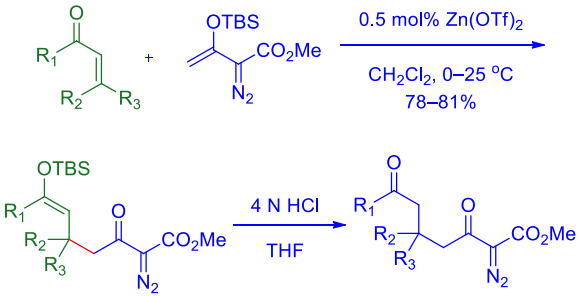


Example 3[8]

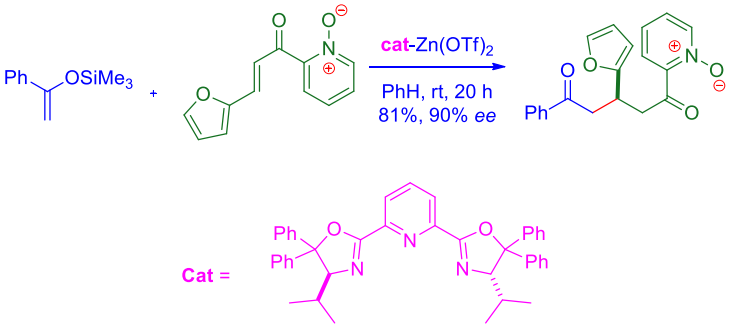


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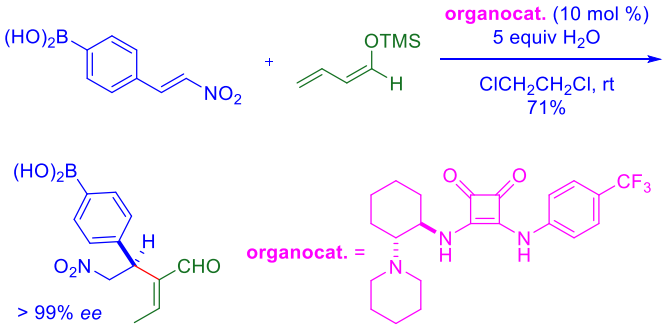
Example 4, Intramolecular Mukaiyama–Michael reaction[9]



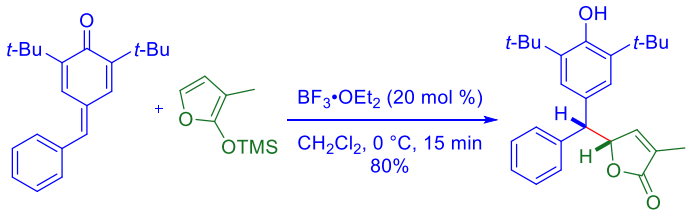
Example 5, Enantioselective Mukaiyama–Michael reaction[11]



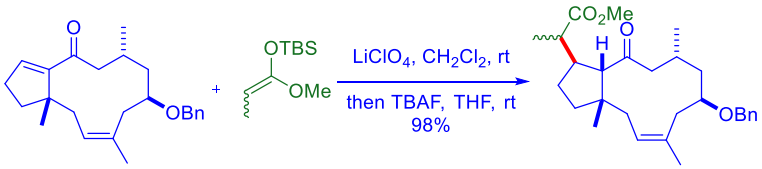
Example 6, Mukaiyama–Michael reaction to prepare Rauhut–Currier-type products[12]



Example 7, A γ-addition[13]



Example 8[14]



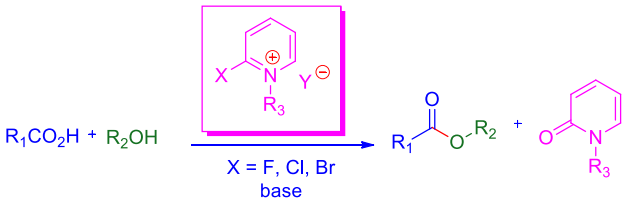
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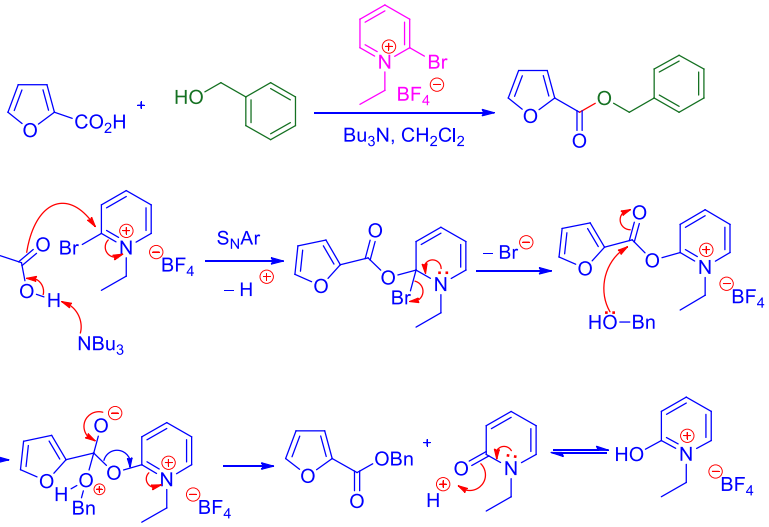
Mukaiyama Reagent

Pyridinium halide reagent for esterification or amide formation.

General scheme:

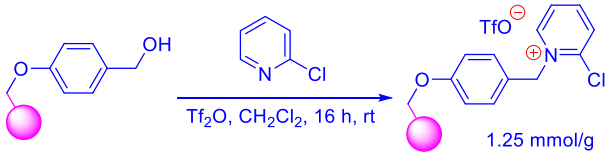


Example 1[1c]

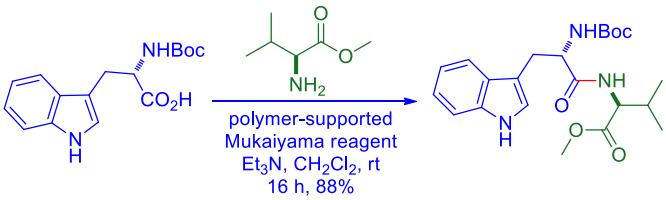


Amide formation using the Mukaiyama reagent follows a similar mechanistic pathway.[1d]

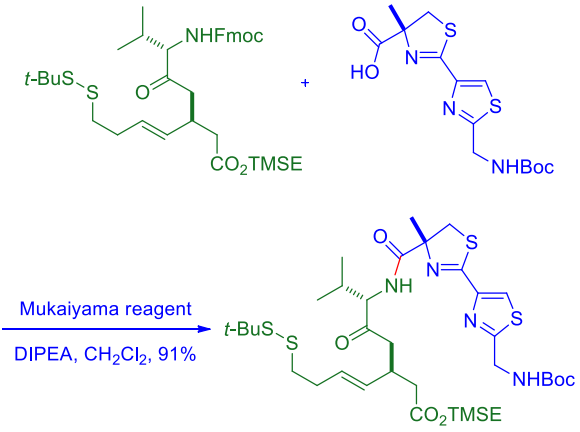
Example 2, Polymer-supported Mukaiyama reagent[5]



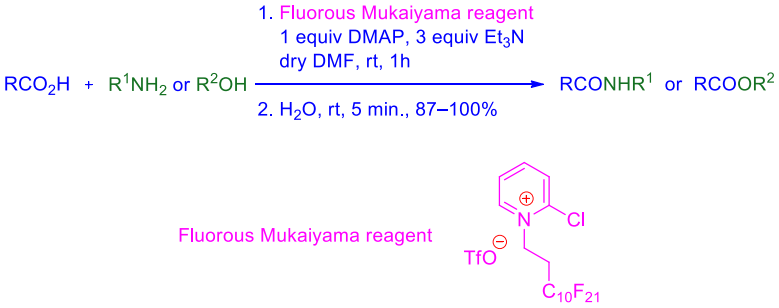
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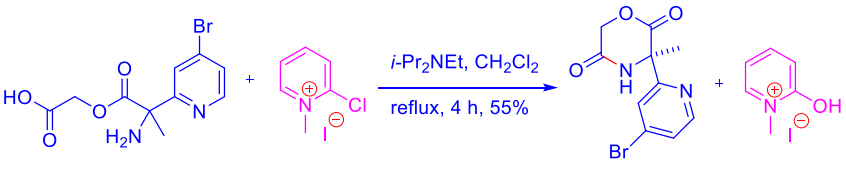
Example 3[9]



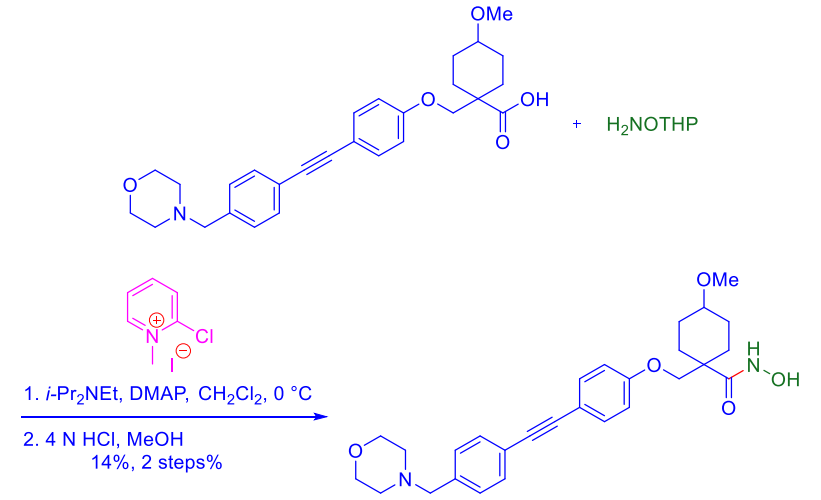
Example 4, Fluorous Mukaiyama reagent[10]



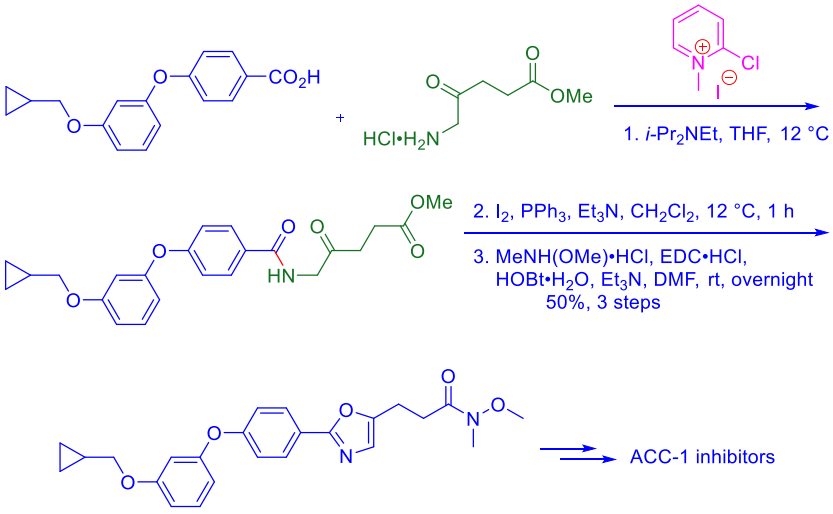
Example 5, Lactamization[12]



Example 6, Preparing an UDP-3-*O*-(acyl)-*N*-acetylglucosamine deacetylase (LpxC) inhibitor[13]



Example 7, Preparing selective acetyl-coa carboxylase (ACC) 1 inhibitors[14]



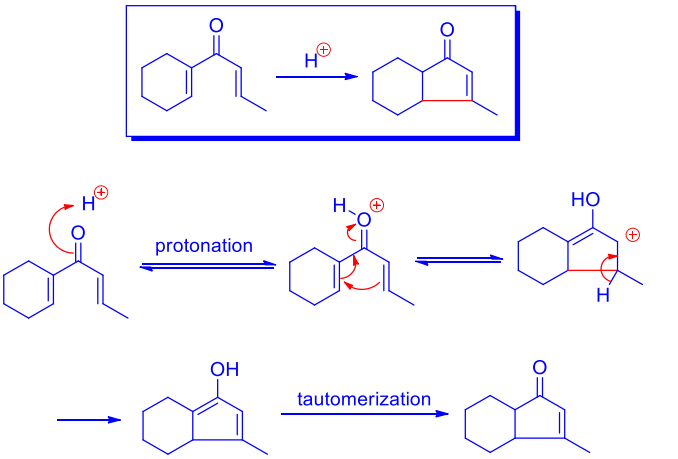
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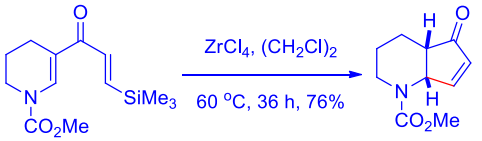
formation, see: Huang, H.; Iwasawa, N.; Mukaiyama, T. *Chem. Lett.* **1984,** 1465–1466.
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Nazarov Cyclization

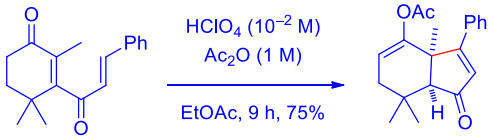
Acid-catalyzed electrocyclic formation of cyclopentenone from di-vinyl ketone.



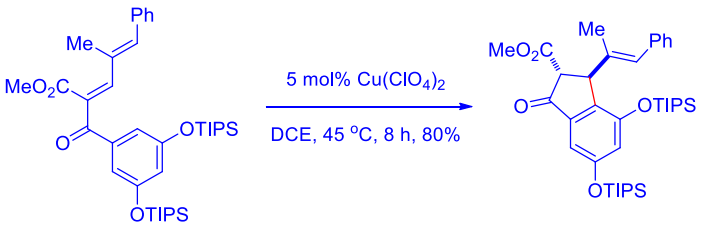
Example 1[2]



Example 2[6]

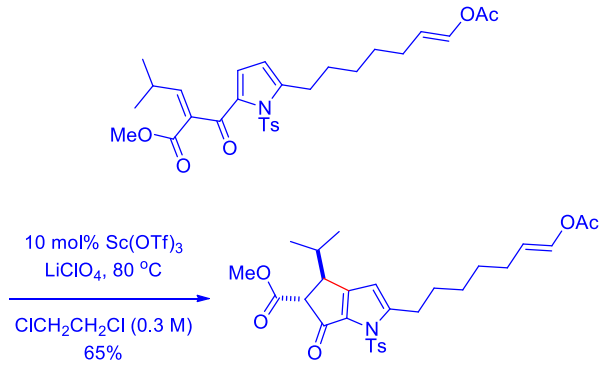


Example 3[9]

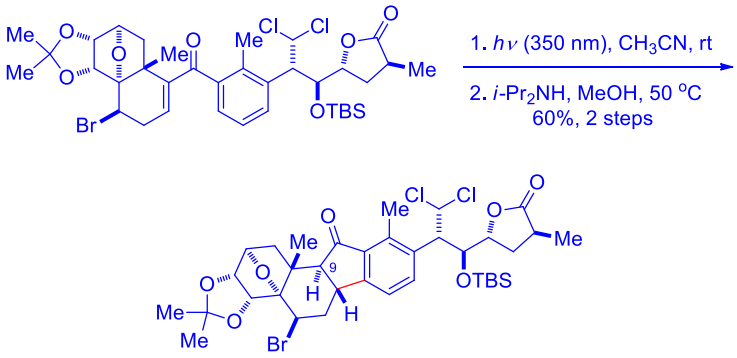


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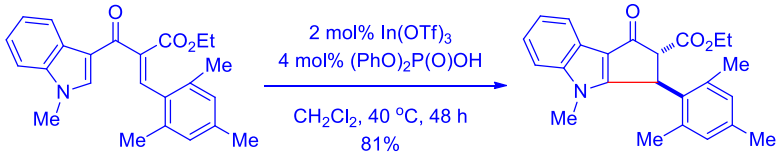
Example 4[10]



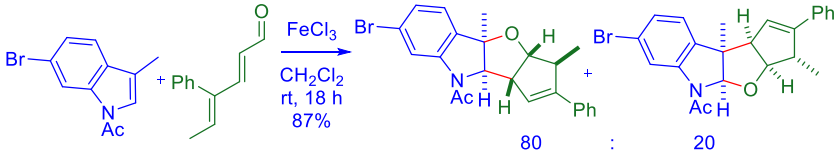
Example 5, An example with a different mechanism[11]



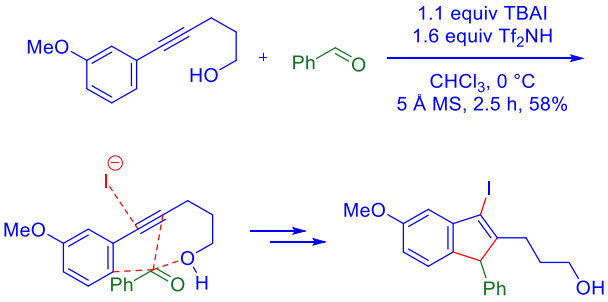
Example 6[12]



Example 7, Iron-mediated domino interrupted iso-Nazarov/dearomative (3 + 2)-cycloaddition of electrophilic indoles[14]



Example 8, One-pot cationic cascade to haloindene involving a halo-Nazarov cyclization[16]

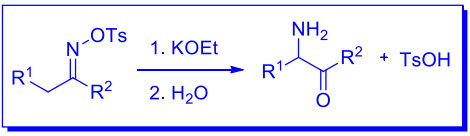


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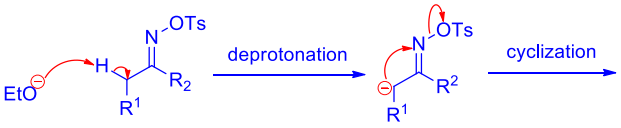
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Neber Rearrangement

α-Aminoketone from tosyl ketoxime and base. The net conversion of a ketone into an α-aminoketone *via* the oxime.



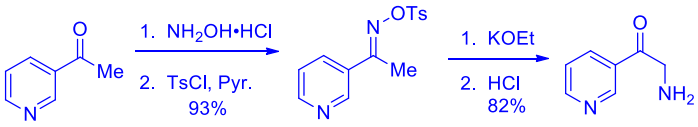
ketoxime α-aminoketone



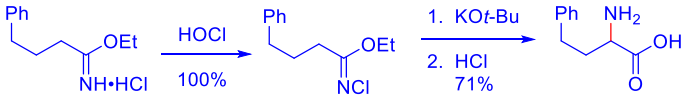


azirine intermediate

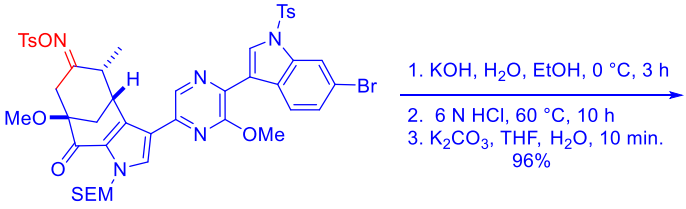
Example 1[3]



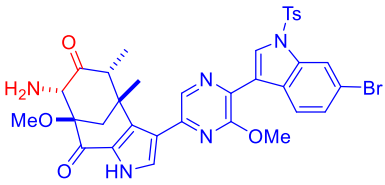
Example 2, A variant using iminochloride[5]



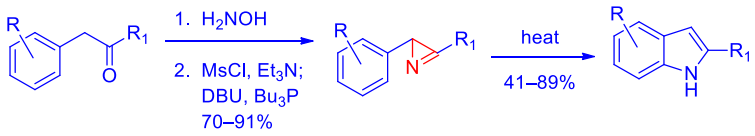
Example 3[8]



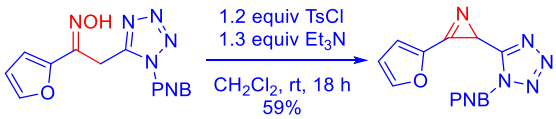
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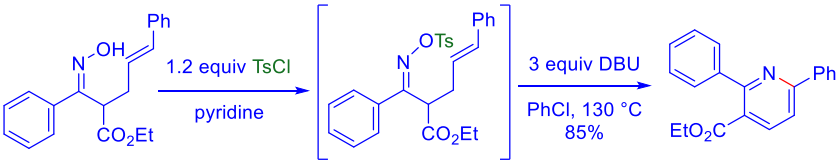
Example 4[9]



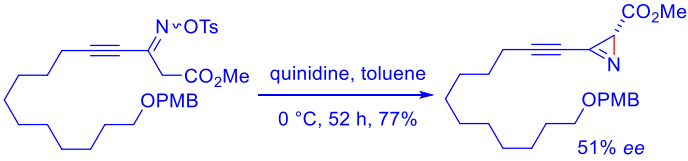
Example 5, PNB = *p*-nitrobenzyl[11]



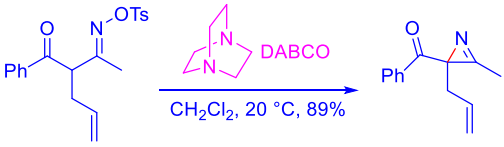
Example 6, One-pot synthesis of pyridine employing the Neber reaction[13]



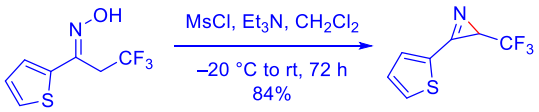
Example 7, Toward total synthesis of (*R*)-(*Z*)-antazirine[14]



Example 8, *C*-Attack prevails (acidic conditions favor *O*-attack)[15]



Example 9, Trifluoromethyl-azirines via metal-free, Et_3N-mediated Neber reaction[16]

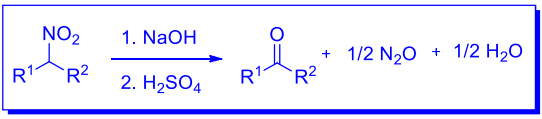


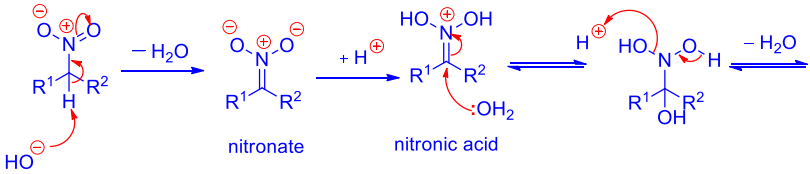
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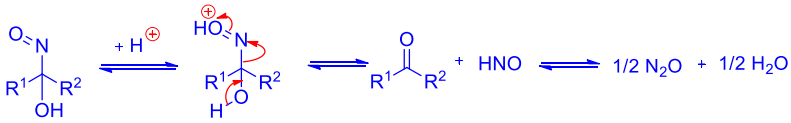
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Nef Reaction

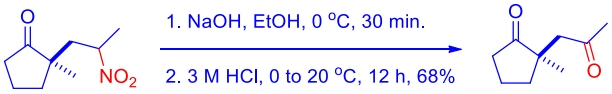
Conversion of a primary or secondary nitroalkane into the corresponding carbonyl compound.



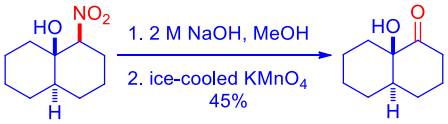




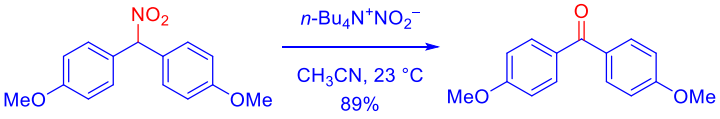
Example 1[4]



Example 2[6]

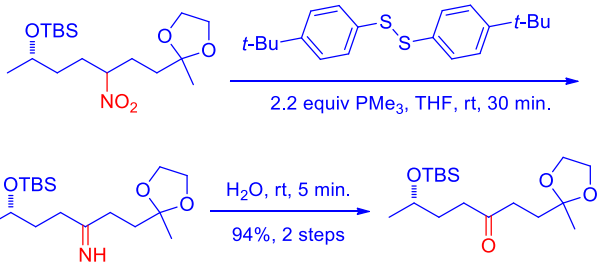


Example 3[7]

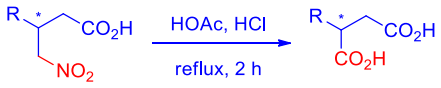


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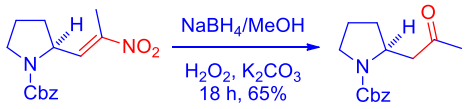
Example 4[9]



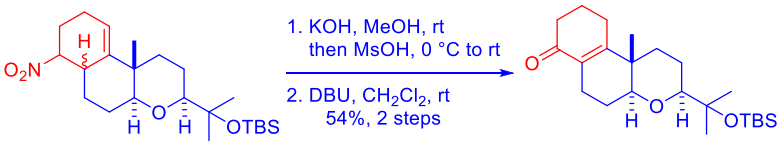
Example 5[10]



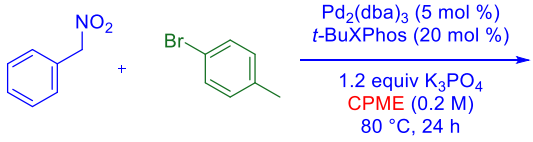
Example 6[11]



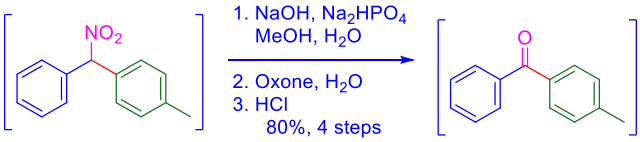
Example 7, Nef reaction was followed by a DBU-mediated alkene isomerization to afford thermodynamically more stable α,β-unsaturated ketone[13]



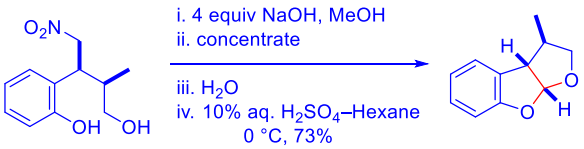
Example 8, The Nef nitro substrates prepared from palladium-catalyzed a-arylation of aryl nitromethanes[14]



CPME = Cyclopentyl methyl ether, a solvent more resistant to auto-oxidation than THF and ethers



Example 9[15]

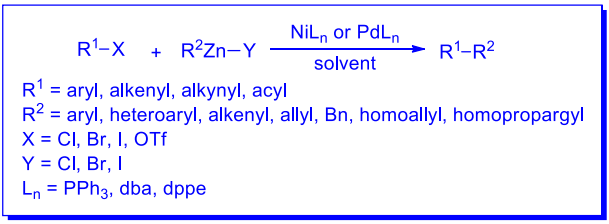


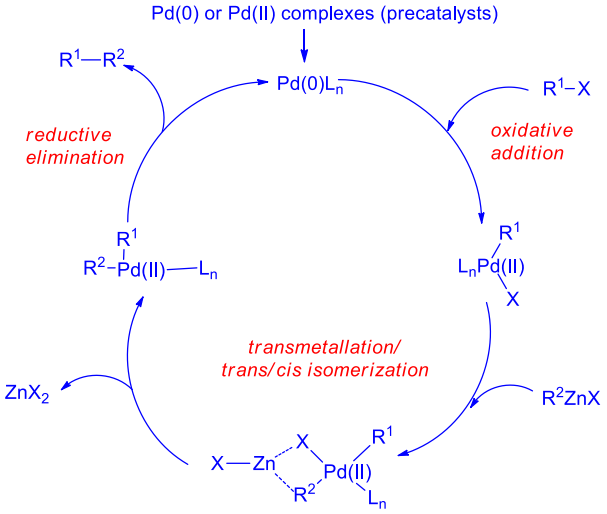
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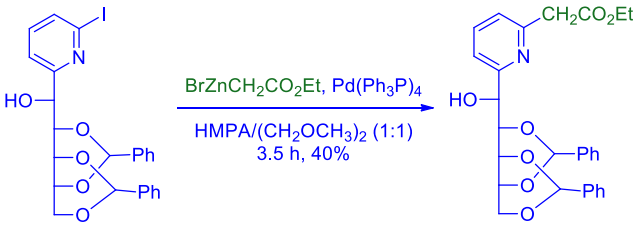
Negishi Cross-Coupling Reaction

The Negishi cross-coupling reaction is the nickel- or palladium-catalyzed coupling of organozinc compounds with various halides or triflates (aryl, alkenyl, alkynyl, and acyl).



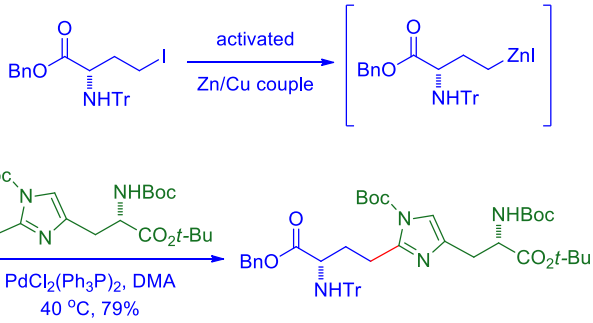


Example 1[3]

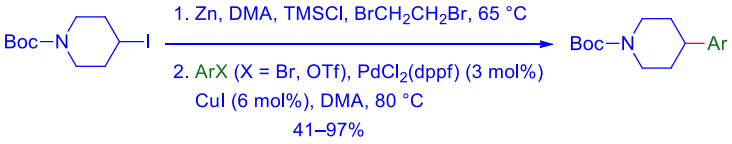


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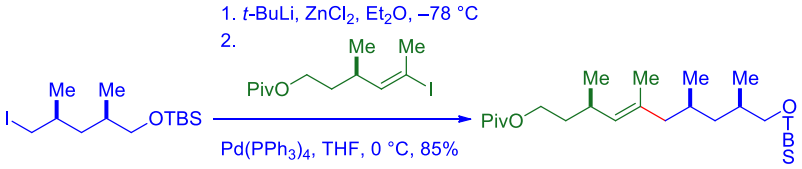
Example 2[4]



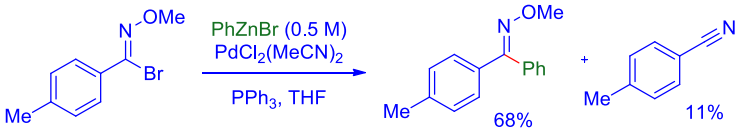
Example 3[8]



Example 4[9]



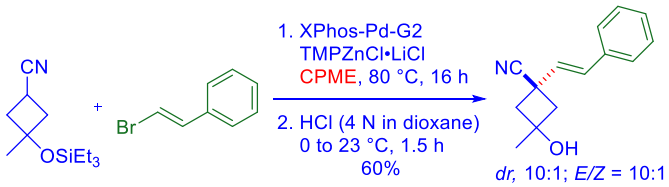
Example 5[11]



Example 6, Site-selective *N,N*-di-Boc activation for N–C cleavage of primary amides[12]

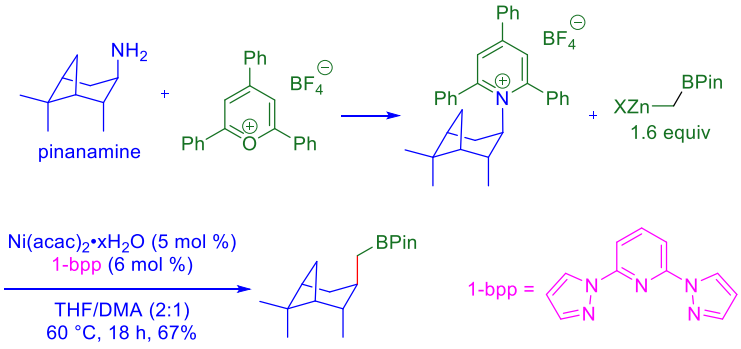


Example 7[13]

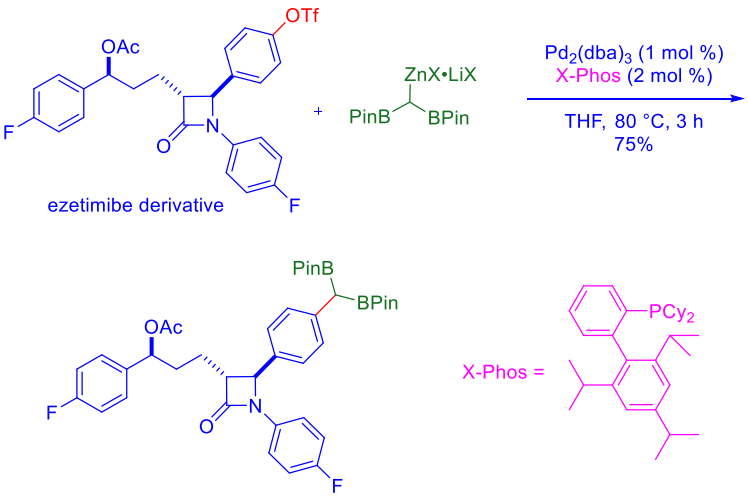


CPME = Cyclopentyl methyl ether, a solvent more resistant to auto-oxidation than THF and ethers

Example 8, Alkylpyridinium salts as electrophiles in deaminative alkyl–alkyl cross-couplings[15]



Example 9[16]

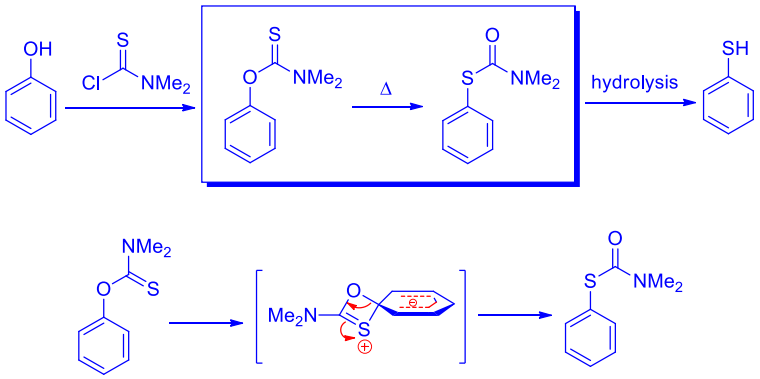


References

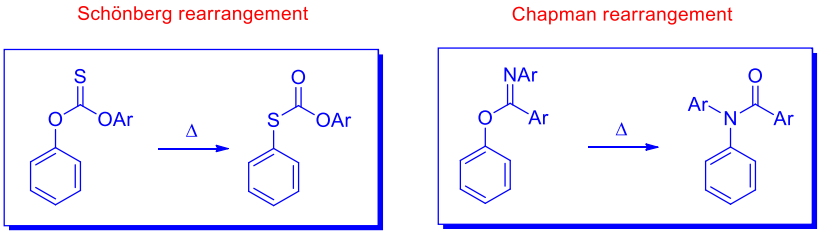
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Newman–Kwart Rearrangement

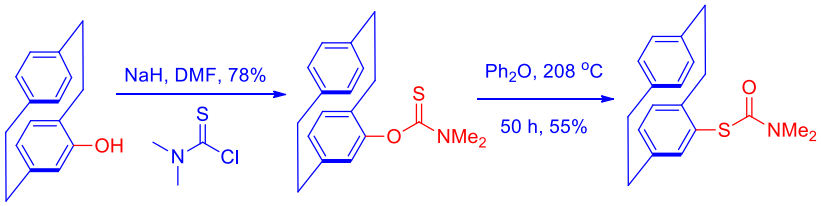
Transformation of phenol to the corresponding thiophenol, a variant of the Smiles reaction.



The Newman–Kwart rearrangement is a member of a series of related rearrangements, such as the **Schönberg rearrangement** and the **Chapman rearrangement**, in which aryl groups migrate intramolecularly between nonadjacent atoms. The Schönberg rearrangement is the most similar and involves the 1,3-migration of an aryl group from oxygen to sulfur in a diarylthiocarbonate. The Chapman rearrangement involves an analogous migration but to nitrogen.

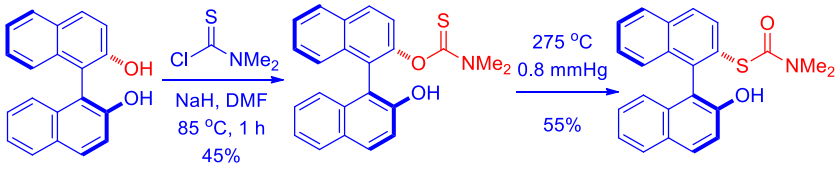


Example 1[5]

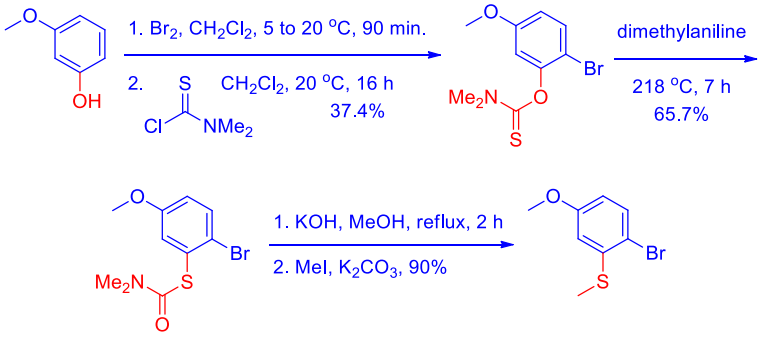


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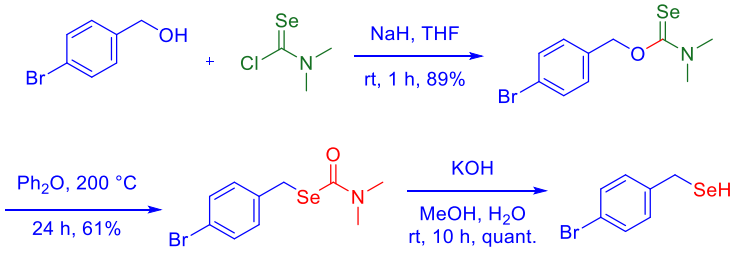
Example 2[6]



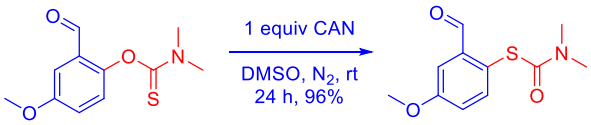
Example 3[7]



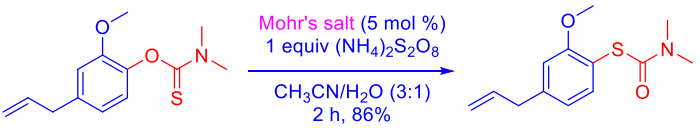
Example 4, Benzylic thio- or seleno-Newman–Kwart rearrangement[13]



Example 5, One-electron oxidation at room temperature[14]



Example 6[15]

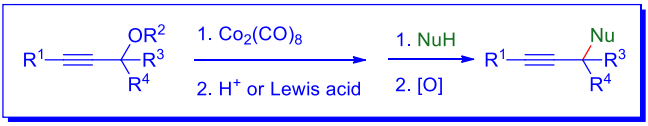


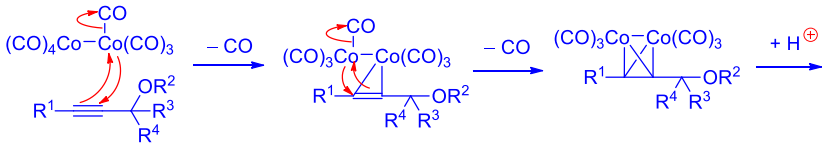
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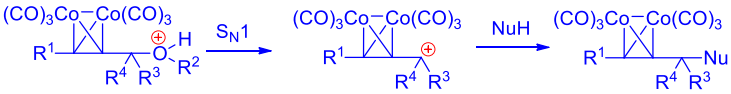
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Nicholas Reaction

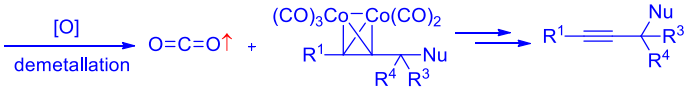
Hexacarbonyldicobalt-stabilized propargyl cation is captured by a nucleophile. Subsequent oxidative demetallation then gives the propargylated product.



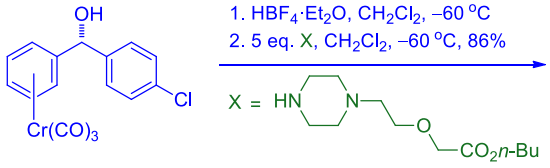


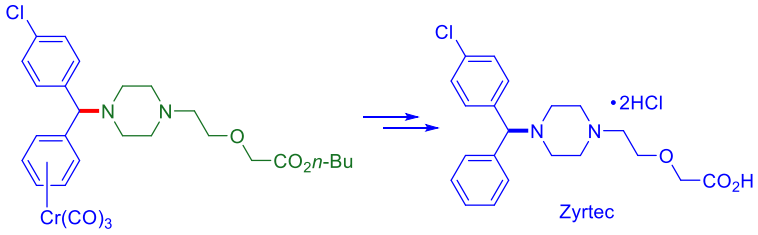


propargyl cation intermediate (stabilized by the hexacarbonyldicobalt complex).



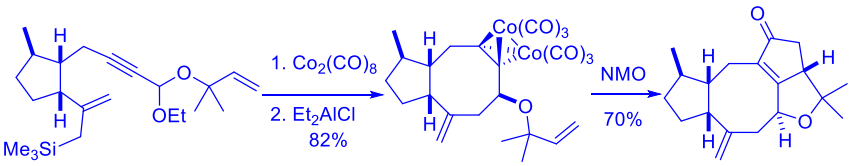
Example 1, A chromium variant of the Nicholas reaction[3]



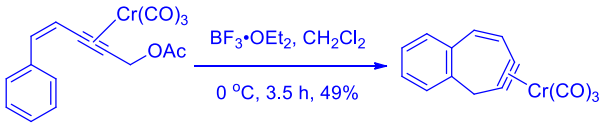


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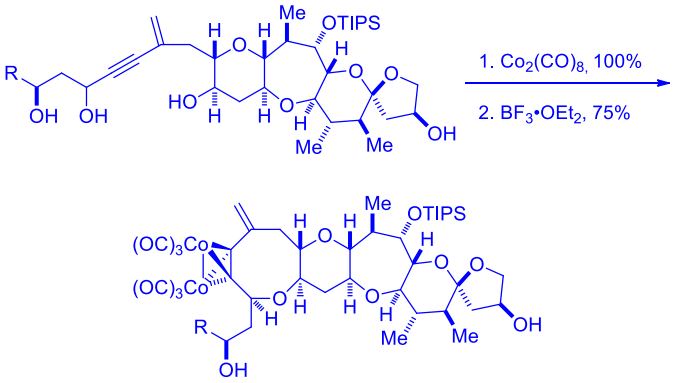
Example 2, A Nicholas–Pauson–Khand sequence[4]



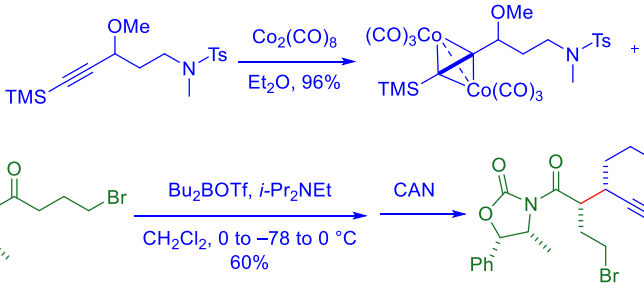
Example 3, Intramolecular Nicholas reaction using chromium[7]



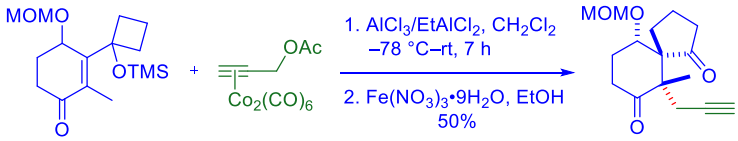
Example 4[9]



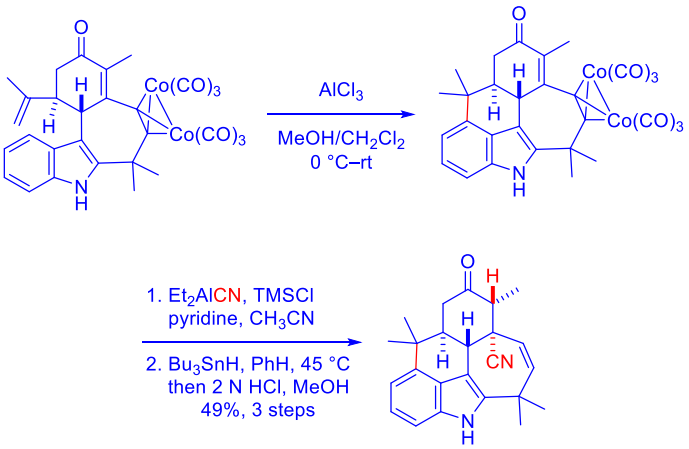
Example 5, Cobalt cokmplex to boost steric hindrance[12]



Example 6[13]



Example 7[14]

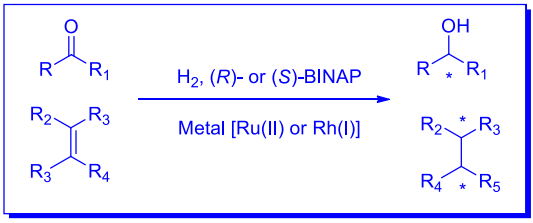


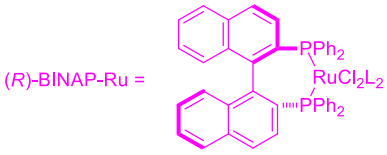
References

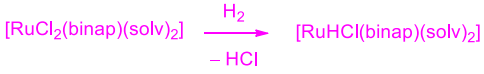
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Noyori Asymmetric Hydrogenation

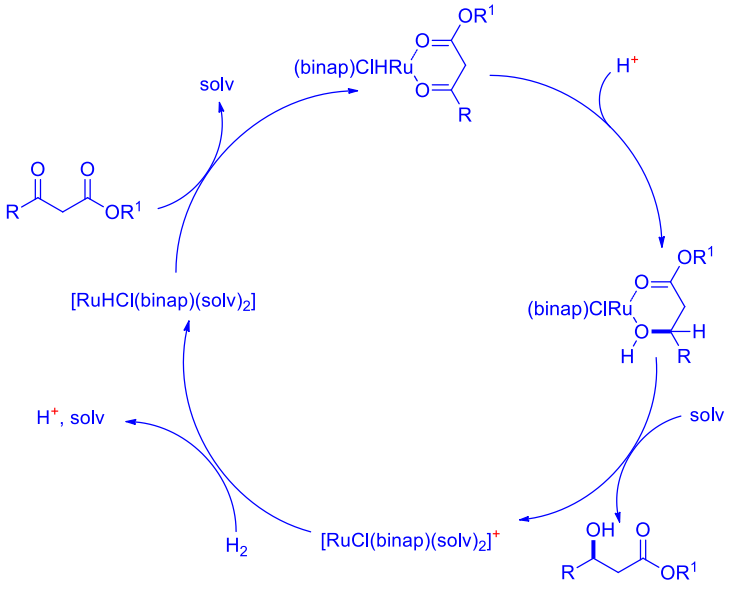
Asymmetric reduction of carbonyls and alkenes *via* hydrogenation, catalyzed by a ruthenium(II) BINAP complex.





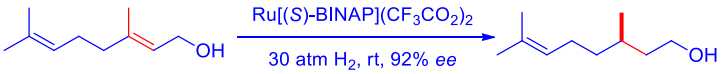


The catalytic cycle:

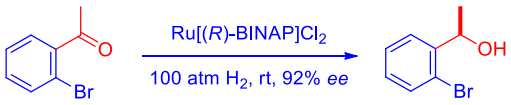


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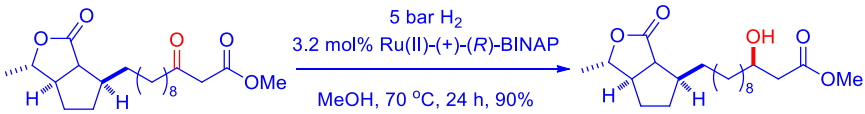
Example 1[1b]



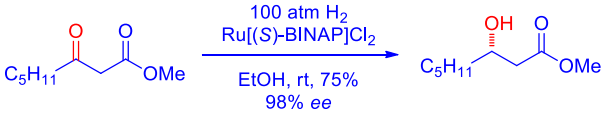
Example 2[1c]



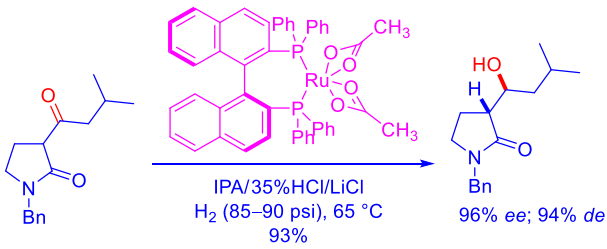
Example 3[9]



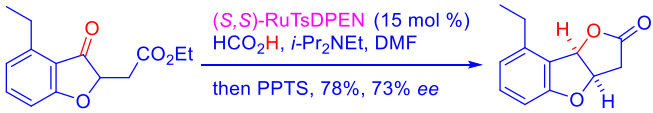
Example 4[10]

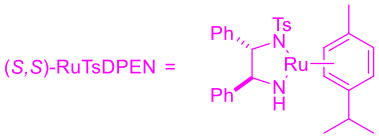


Example 5[11]

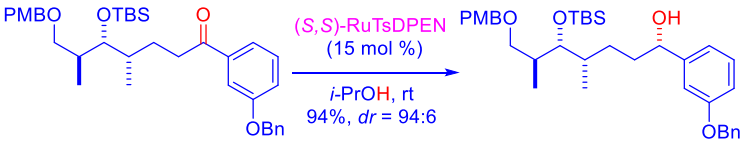


Example 6, Noyori asymmetric transfer hydrogenation (ATH) with resulted in a dynamic kinetic resolution (DKR) with spontaneous lactonization[12]

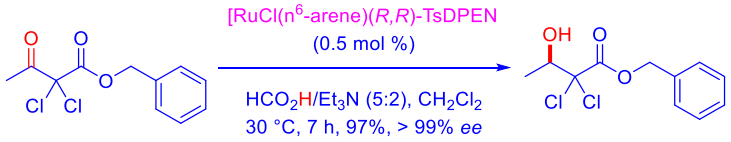




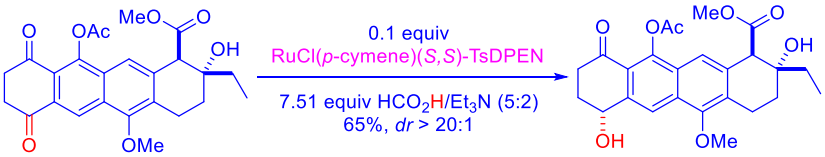
Example 7[13]



Example 8, Ruthenium-catalyzed asymmetric transfer hydrogenation (ATH)[14]



Example 9[15]



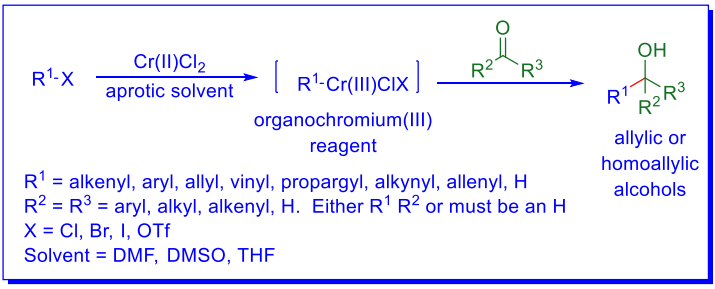
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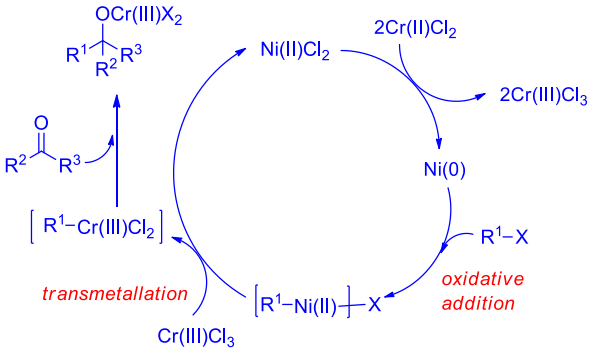
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Nozaki–Hiyama–Kishi Reaction

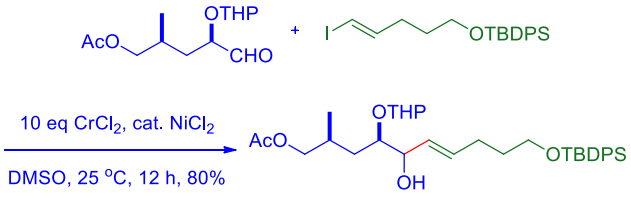
Cr–Ni bimetallic catalyst-promoted redox addition of vinyl- or propargyl-halides to aldehydes.



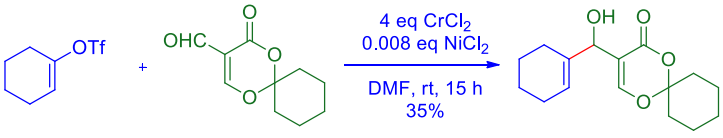
The catalytic cycle:[2]



Example 1[3]

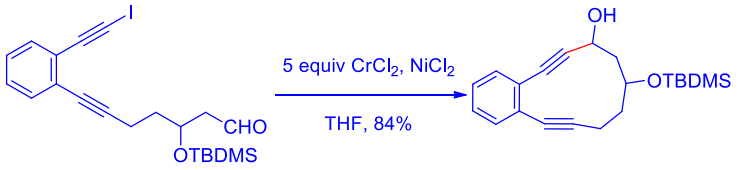


Example 2[5]

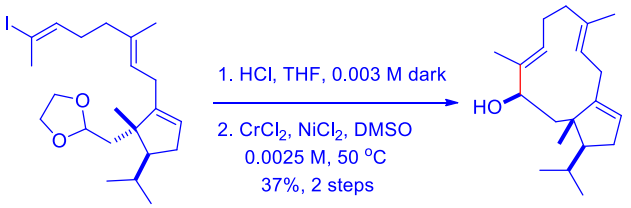


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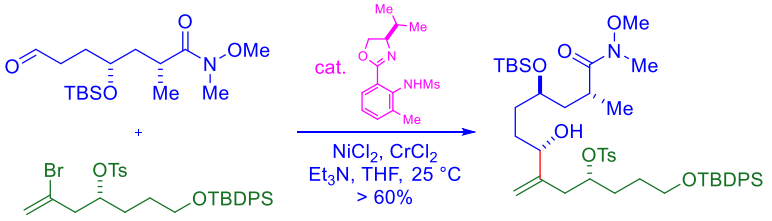
Example 3, Intramolecular Nozaki–Hiyama–Kishi reaction[8]



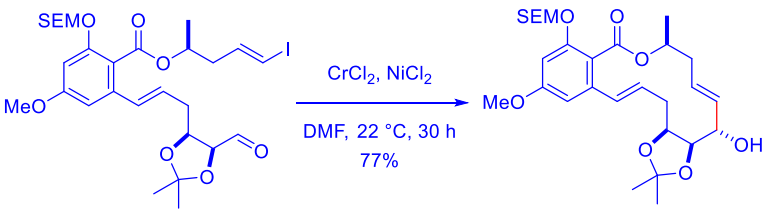
Example 4, Intramolecular Nozaki–Hiyama–Kishi reaction[9]



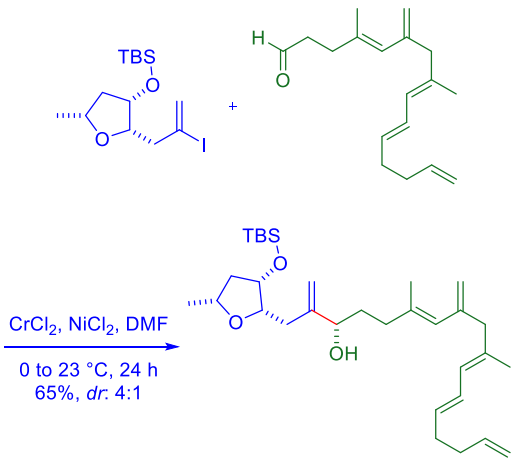
Example 5, Asymmetric Nozaki–Hiyama–Kishi reaction[11]



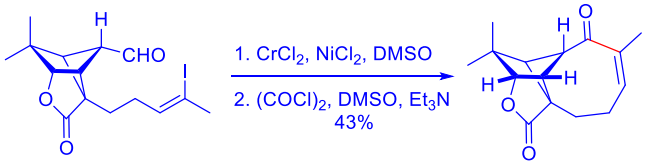
Example 6, Late-stage Nozaki–Hiyama–Kishi macrolactonization[12]



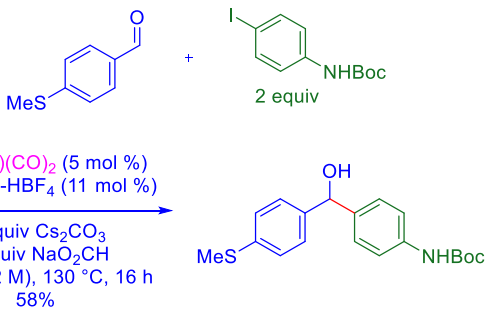
Example 7[14]



Example 8[15]



Example 9[17]



References

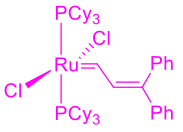
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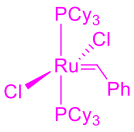
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Olefin Metathesis

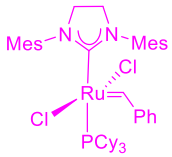
Grubbs, Schrock, Heveyda and many others have made significant contributions to the field of olefin metathesis. Rather than giving one name reaction, it is collectively called olefin metathesis here.



original catalyst

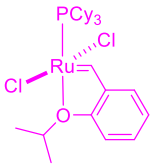


Grubbs I

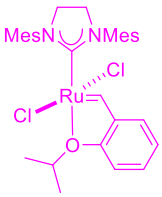


Grubbs II

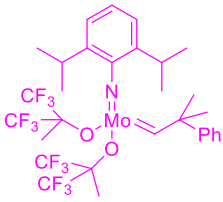
Mes = mesityl



Hoveyda–Grubbs I



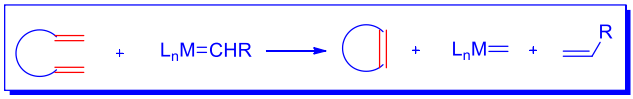
Hoveyda–Grubbs II



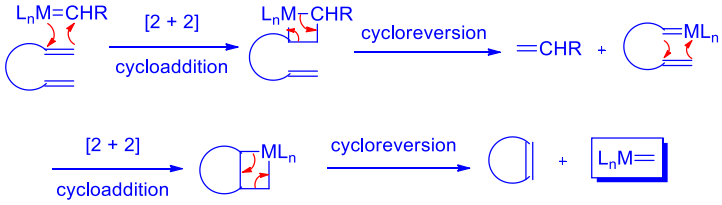
Schrock's catalyst

All three catalysts are illustrated as "L_nM=CHR" in the mechanism below.

Generation of the real catalyst from the precatalysts:



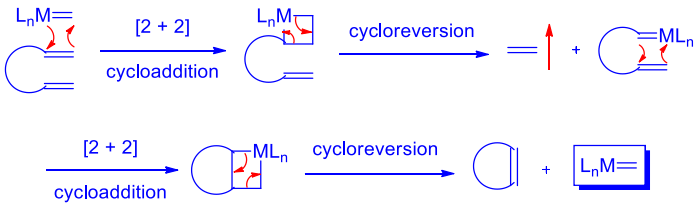
the active catalyst



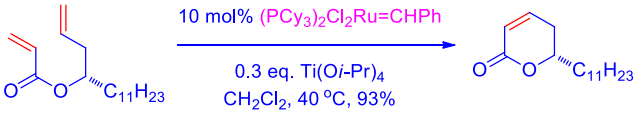
Catalytic cycle:



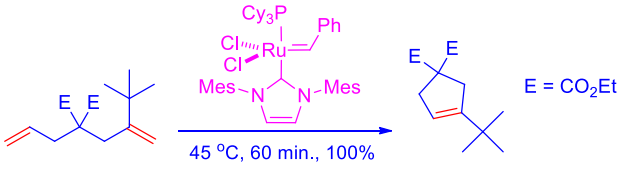
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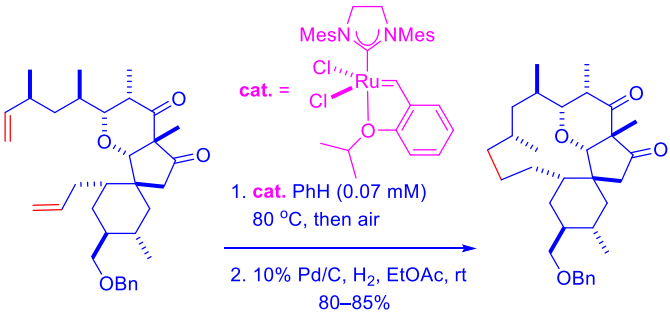
Example 1[3]



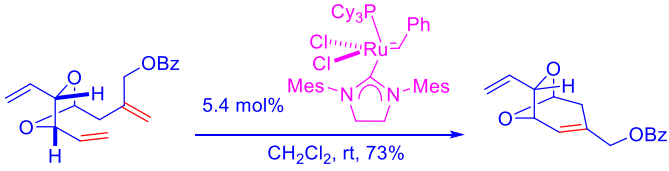
Example 2[4]

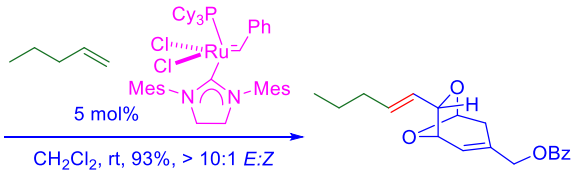


Example 3[7]

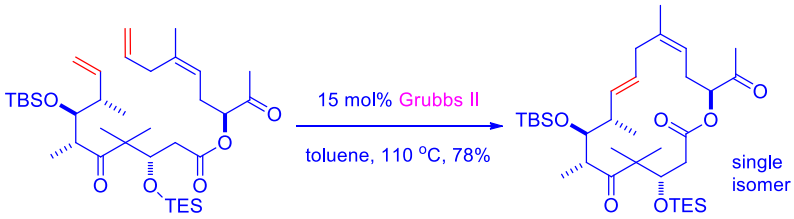


Example 4[9]

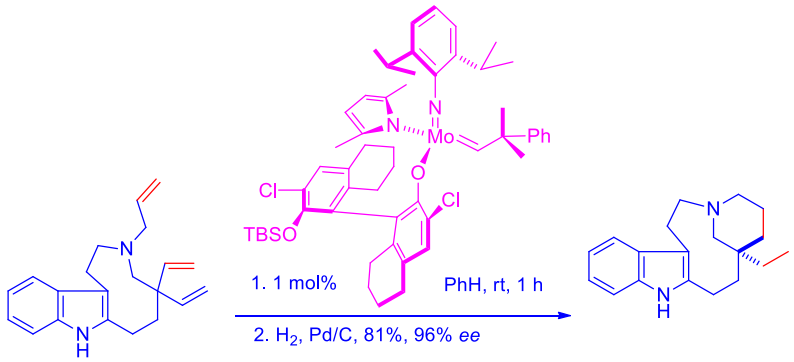




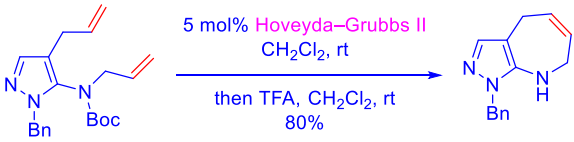
Example 5[10]



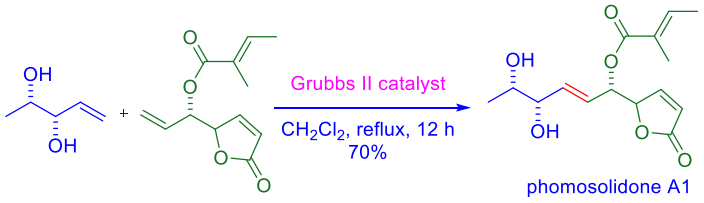
Example 6[12]



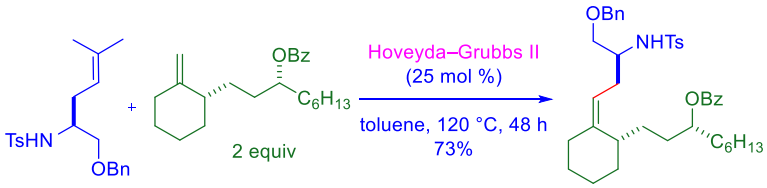
Example 7[13]



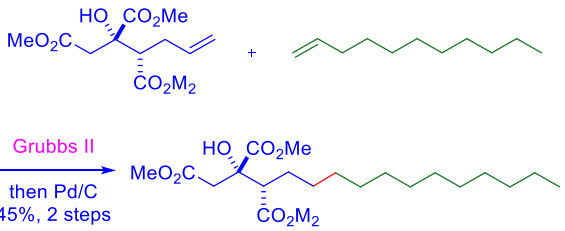
Example 8, Intermolecular olefin metathesis[14]



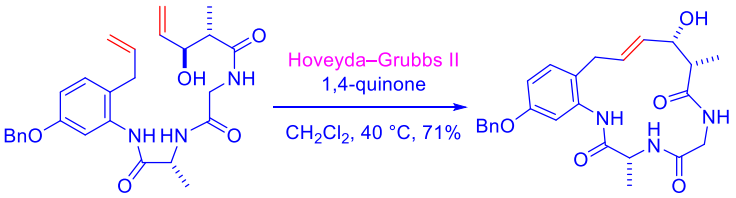
Example 9[15]



Example 10[18]



Example 11[19]



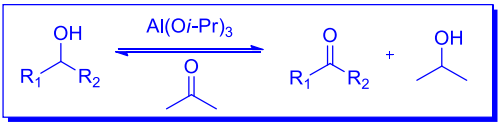
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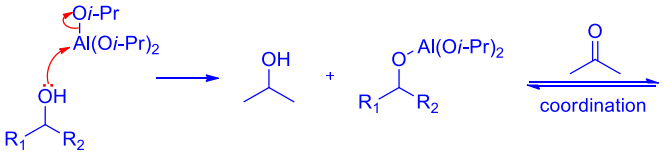
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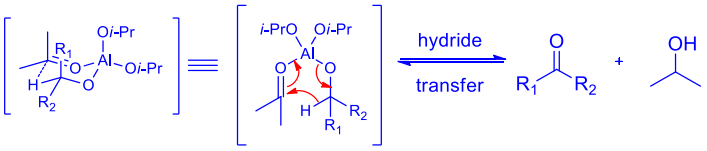
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Oppenauer Oxidation

Alkoxide-catalyzed oxidation of secondary alcohols. Reverse of the Meerwein–Ponndorf–Verley reduction.

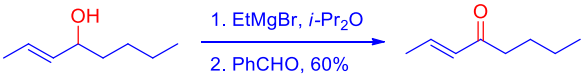




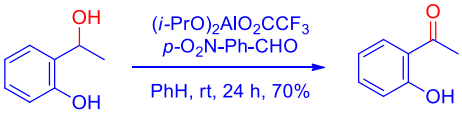


cyclic transition state

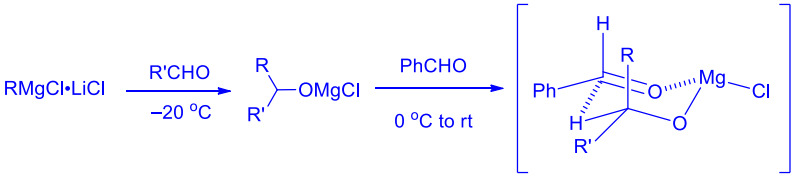
Example 1, Mg-Oppenauer oxidation[3]



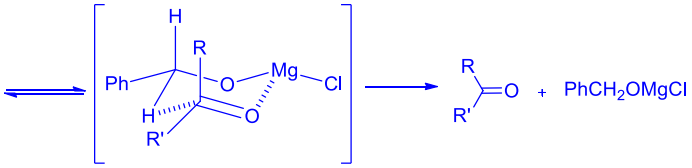
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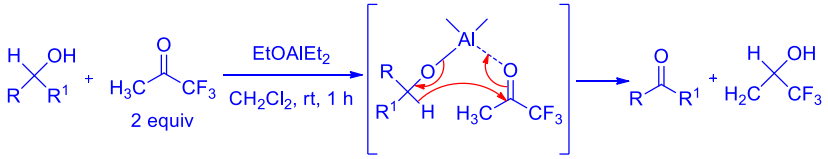
Example 3, Mg-Oppenauer oxidation[8]



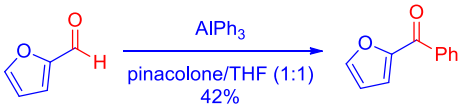
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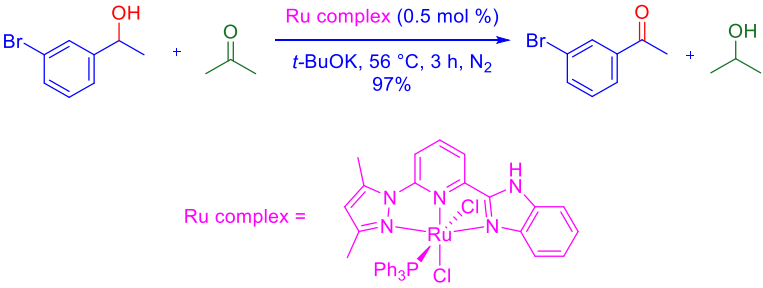
Example 4[10]



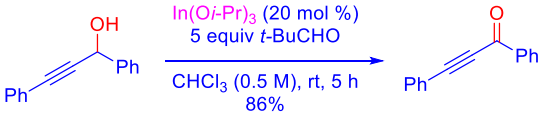
Example 5, Tandem nucleophilic addition–Oppenauer oxidation[12]



Example 6, Ruthenium(II)-NNN complex as the catalyst[13]



Example 7, Indium(III) isopropoxide as a hydrogen transfer catalyst[14]



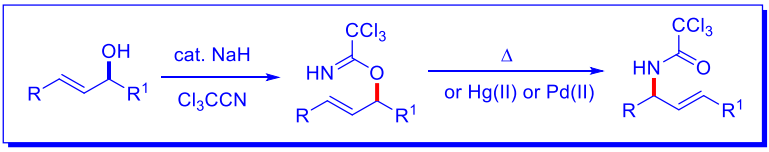
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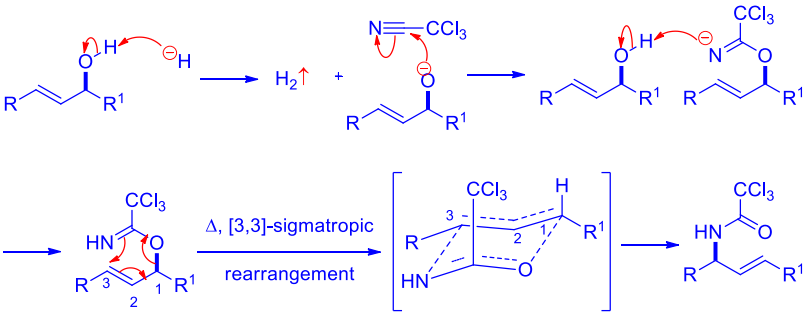
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Overman Rearrangement

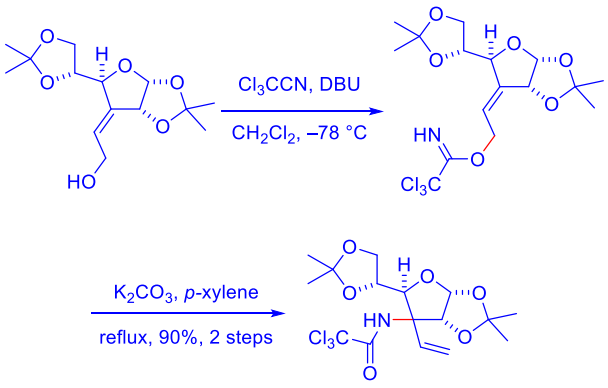
Stereoselective transformation of allylic alcohol to allylic trichloroacetamide *via* trichloroacet*imidate* intermediate.



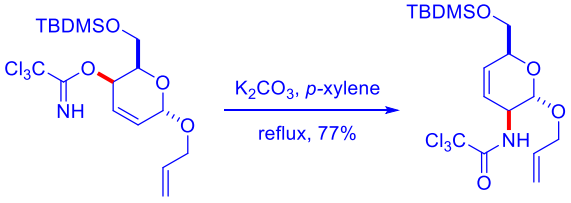
trichloroacetimidate



Example 1[5]

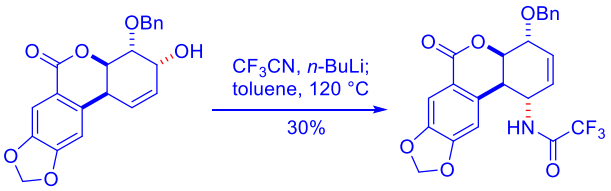


Example 2[6]

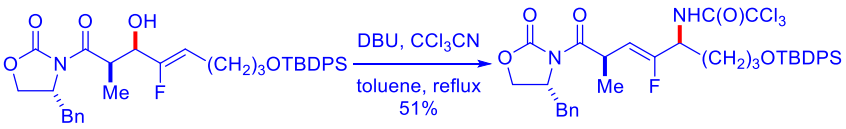


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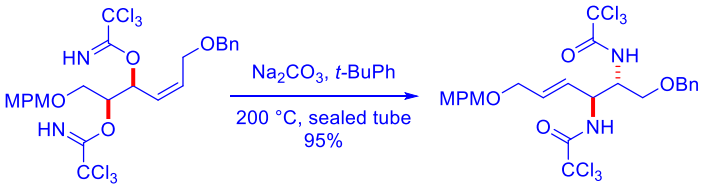
Example 3[7]



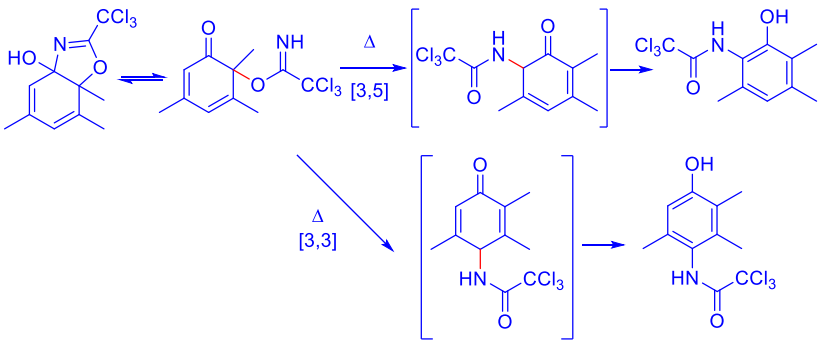
Example 4[9]



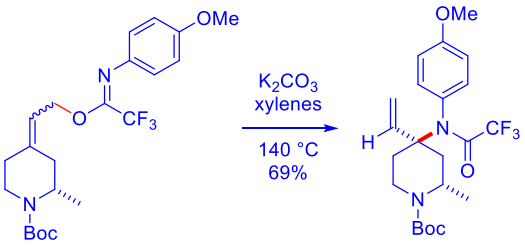
Example 5, Cascade-type Overman rearrangement[11]



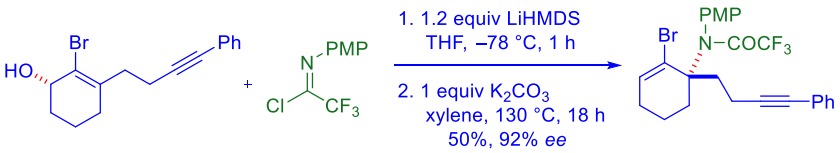
Example 6, Thermal [3,3]- and [3,5]-rearranegment[12]



Example 7[13]



Example 8[14]

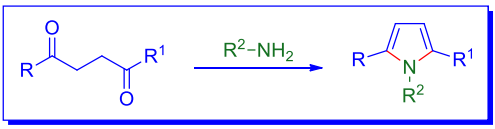


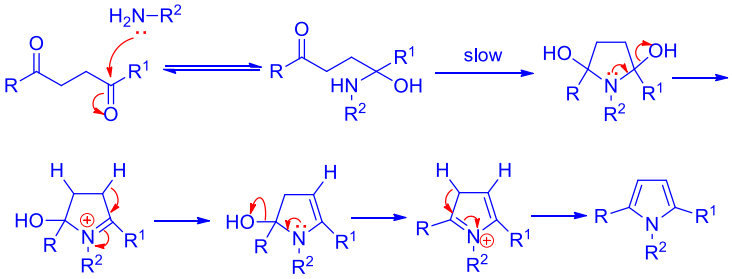
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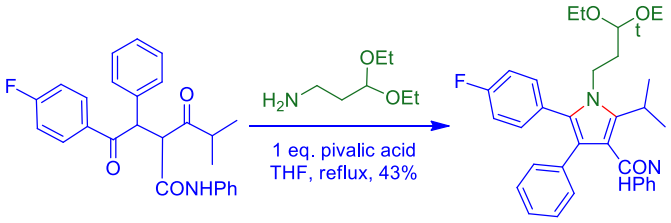
Paal–Knorr Pyrrole Synthesis

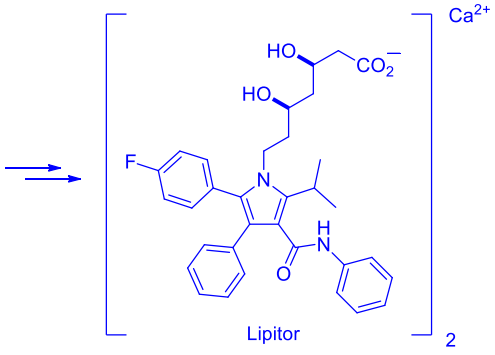
Reaction between 1,4-diketones and primary amines (or ammonia) to give pyrroles. A variation of the Knorr pyrazole synthesis.





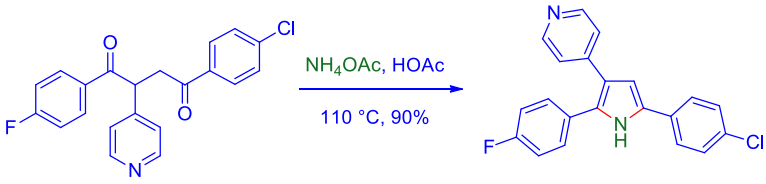
Example 1[4]



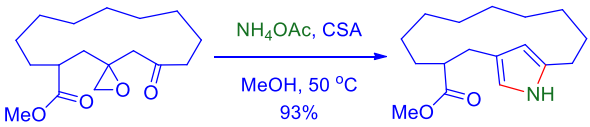


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Example 2[5]



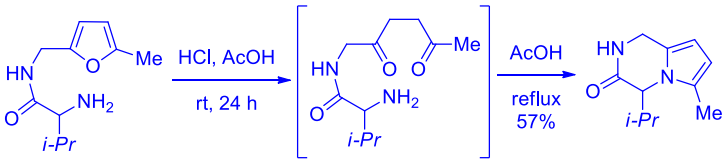
Example 3[9]



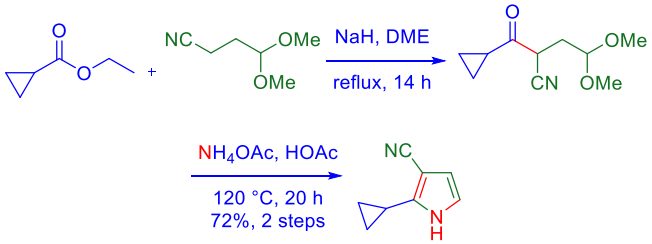
Example 4[10]



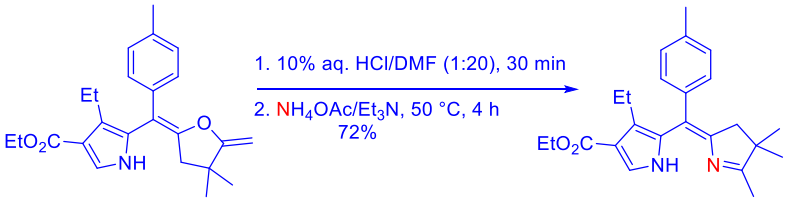
Example 5, Furan ring opening–pyrrole ring closure[10]



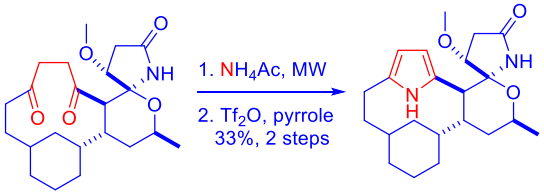
Example, A route to 2-substituted 3-cyanopyrroles[12]



Example 6, Toward the synthesis of dihydropyrrin[13]



Example 7, In total synthesis of marineosin A[14]

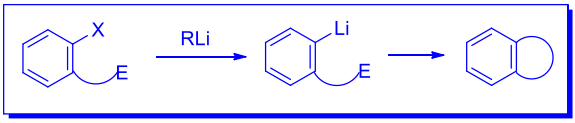


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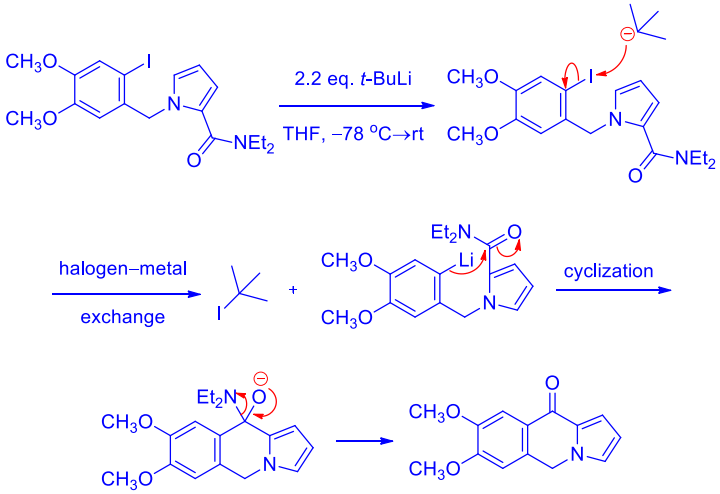
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Parham Cyclization

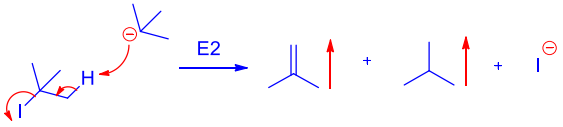
The Parham cyclization is the generation by halogen–lithium exchange of aryllithiums and heteroaryllithiums, and their subsequent intramolecular cyclization onto an electrophilic site.



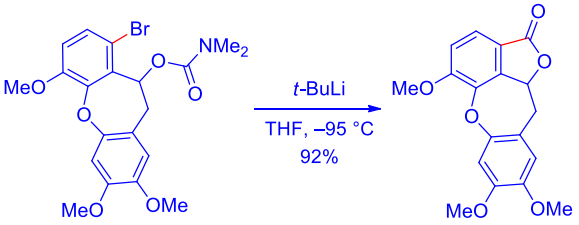
Example 1[1b]



The fate of the second equivalent of *t*-BuLi:

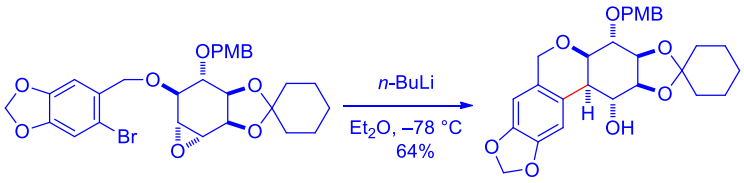


Example 2[2]

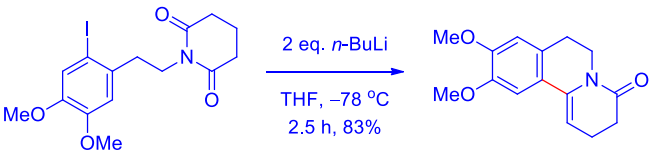


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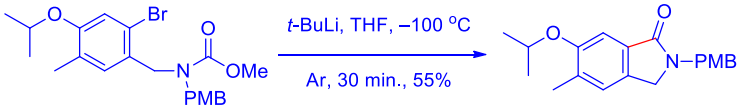
Example 3[4]



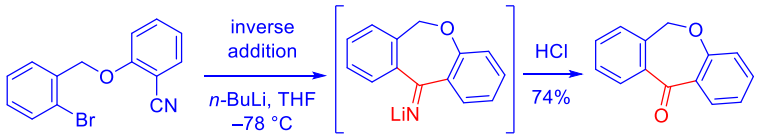
Example 4[5]



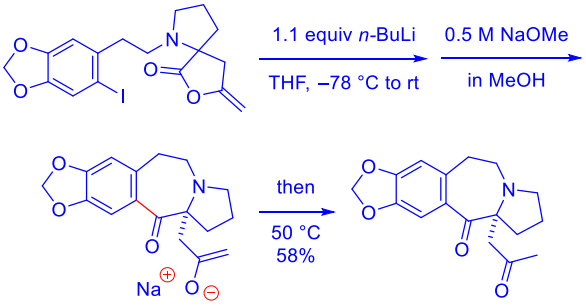
Example 5[9]



Example 6, Diaryl-fused seven-membered ring heterocyclic ketones[12]



Example 7, A one-pot Parham–Aldol sequence[13]

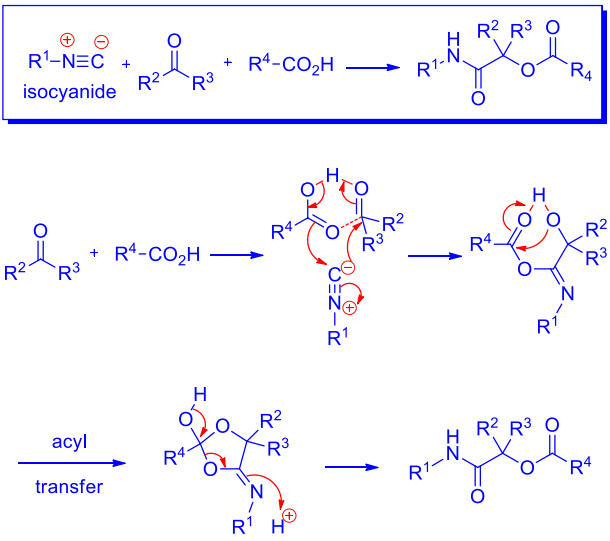


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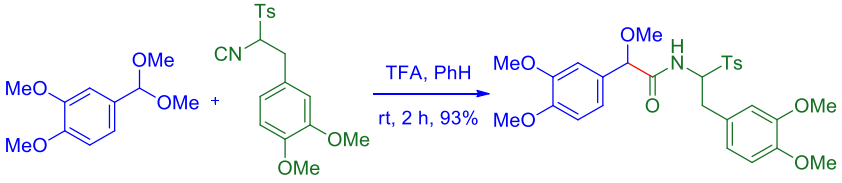
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Passerini Reaction

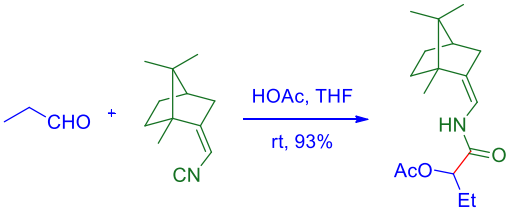
Three-component condensation (3CC), one of the multicomponent reactions (MCRs), of carboxylic acids, *C*-isocyanides, and carbonyl compounds to afford α-acyloxycarboxamides. Also known as three-component reaction (3CR). *Cf.* Ugi reaction.



Example 1[3]

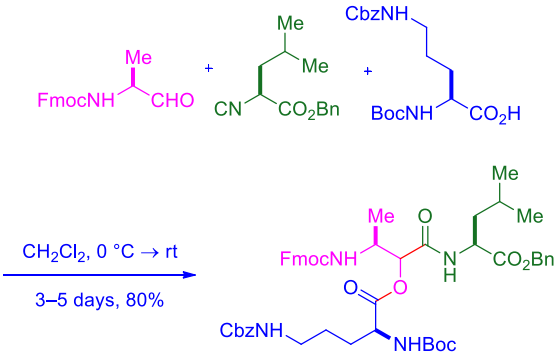


Example 2[5]

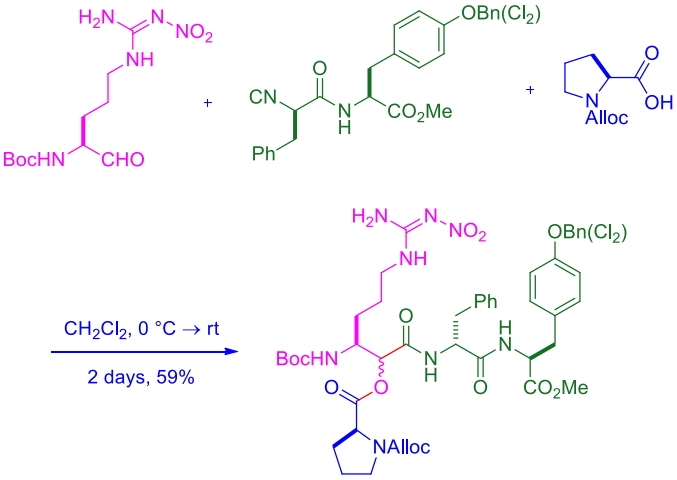


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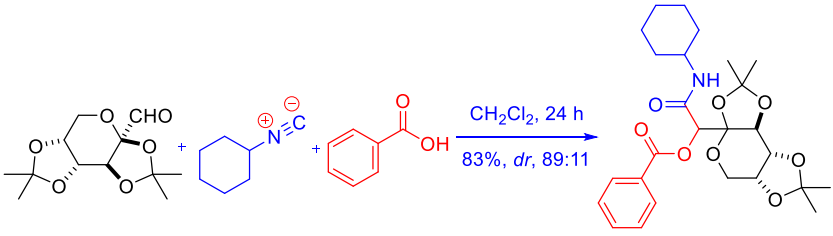
Example 3[6]



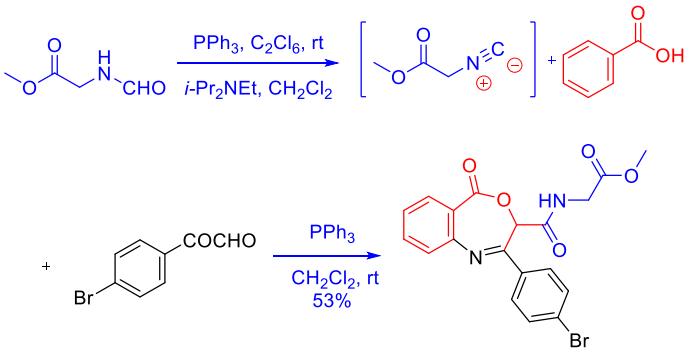
Example 4[7]



Example 5, Glycomimetics[12]



Example 6, Odorless isocyanides and *in situ* capture[13]

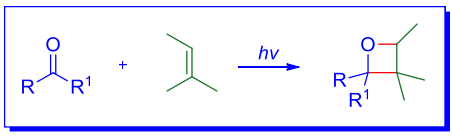


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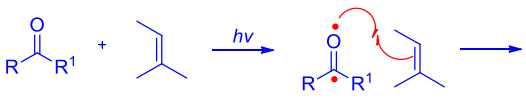
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Paternó–Büchi Reaction

Photoinduced electrocyclization of a carbonyl with an alkene to form polysubstituted oxetane ring systems



oxetane

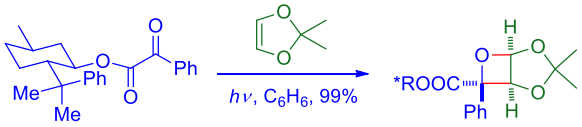


n,π^* triplet

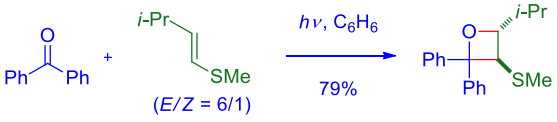


triplet diradical singlet diradical

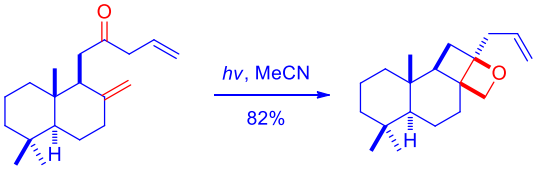
Example 1[2]



Example 2[4]

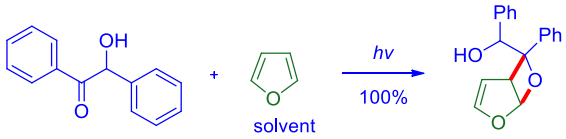


Example 3[6]

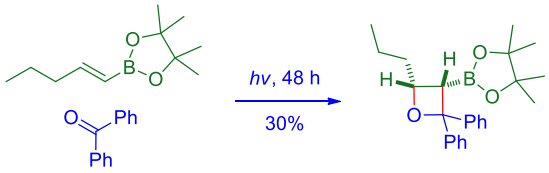


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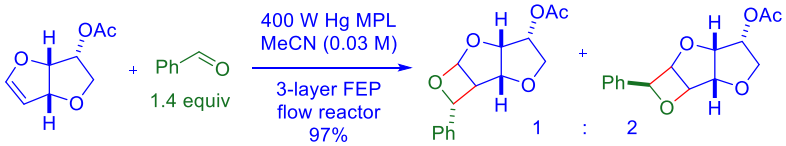
Example 4[8]



Example 5[9]



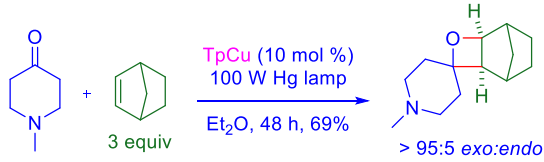
Example 6, Flow chemistry, MPL = medium pressure lamp; FEP = fluorinated ethylene propene[12]

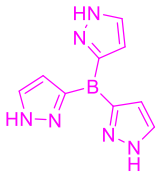


Example 7, Transposed Paternó–Büchi reaction: $\pi\pi^*$ inplace of $n\pi^*$ excited state[13]



Example 8, Metal to ligand charge transfer (MLCT) as an alternative to the Paternó–Büchi reaction: Cu-catalyzed carbonyl–olefin [2 + 2] photocycloaddition (COPC)[14]



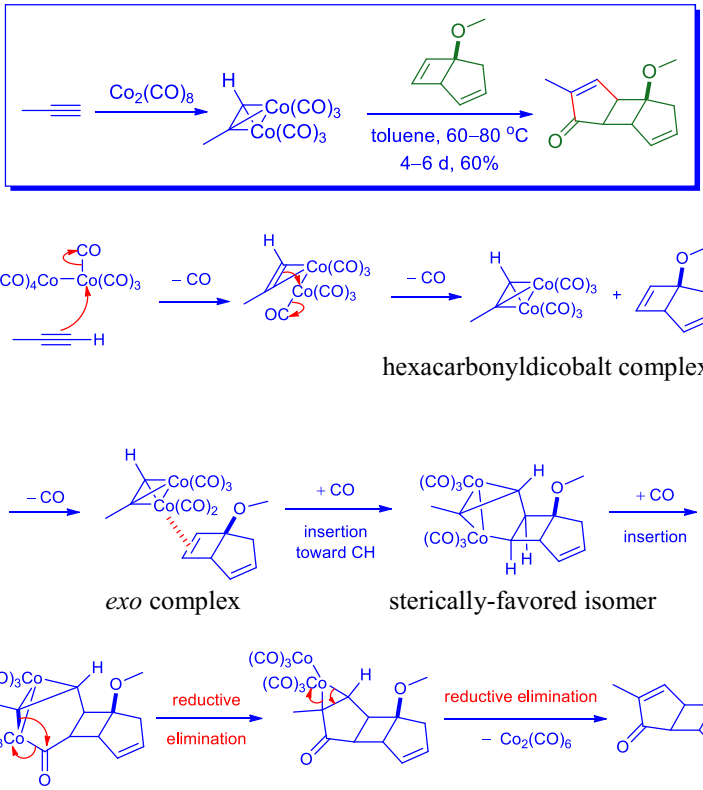
Tp = tris(pyrazolyl)borate = 

References

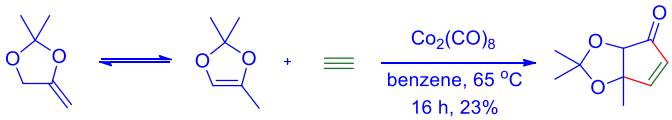
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Pauson–Khand Reaction

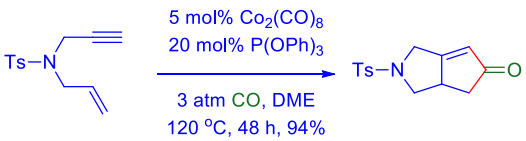
Formal [2 + 2 + 1] cycloaddition of an alkene, alkyne, and carbon monoxide mediated by octacarbonyl dicobalt to form cyclopentenones.



Example 1[3]

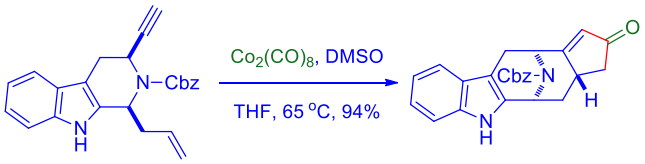


Example 2, A catalytic version[6]

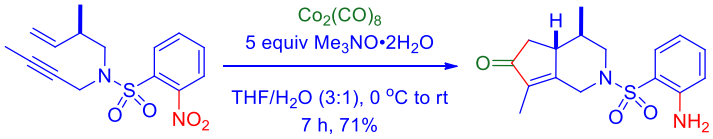


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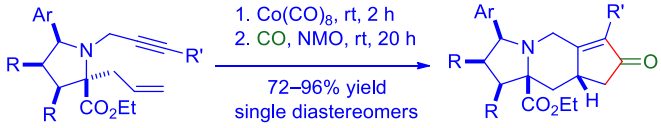
Example 3, Intramolecular Pauson–Khand reaction[9]



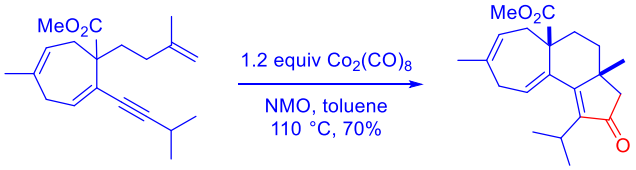
Example 4, Intramolecular Pauson–Khand reaction[10]



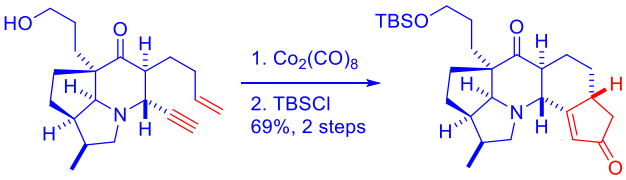
Example 5, Intramolecular Pauson–Khand reaction[12]



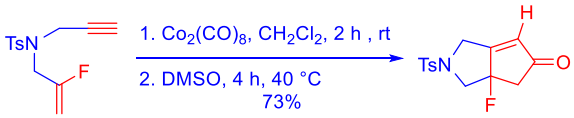
Example 6, Intramolecular Pauson–Khand reaction toward the synthesis of (±)-5-epi-cyanthiwigin I, NMO = N-methylmorpholine N-oxide (NMMO)[13]



Example 7, In total synthesis[14]



Example 8, Vinyl fluorides as substrates[15]

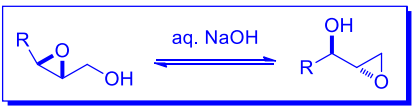


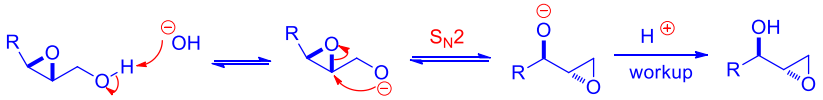
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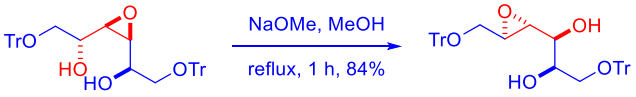
Payne Rearrangement

The isomerization of 2,3-epoxy alcohol under the influence of a base to 1,2-epoxy-3-ol is referred to as the Payne reaction. Also known as epoxide migration.

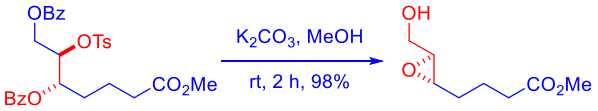




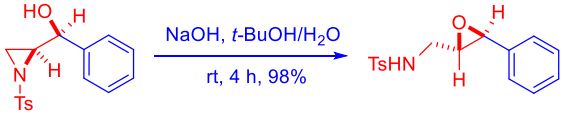
Example 1[2]



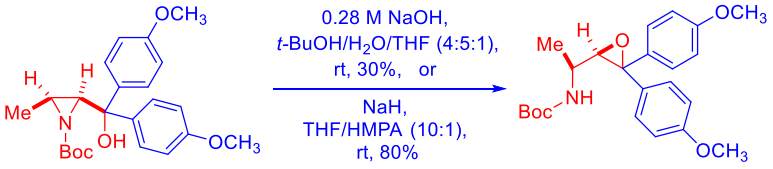
Example 2, Chemo-selective Payne rearrangement[3]



Example 3, Aza-Payne rearrangement[8]

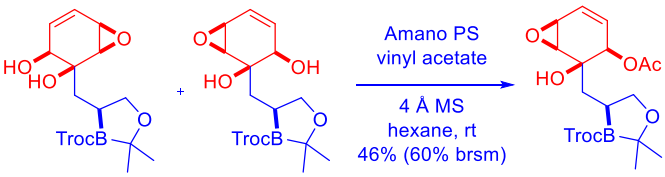


Example 4, Aza-Payne rearrangement[9]

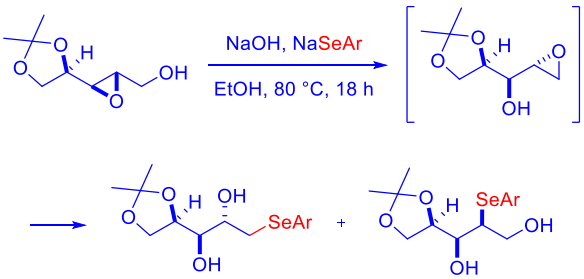


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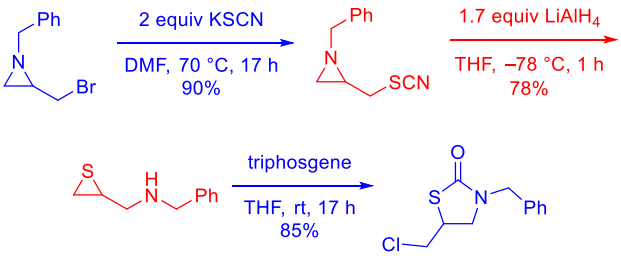
Example 5, Lipase-mediated dynamic kinetic resolution via a *vinylogous* Payne rearrangement[11]



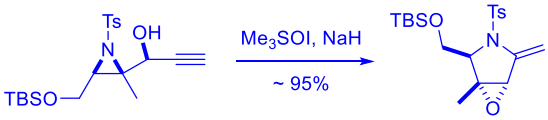
Example 6, Trapping the intermediates[13]



Example 7, $LiAlH_4$-induced thia-aza-Payne rearrangement[14]



Example 8, Aza-Payne/hydroamination sequence[15]



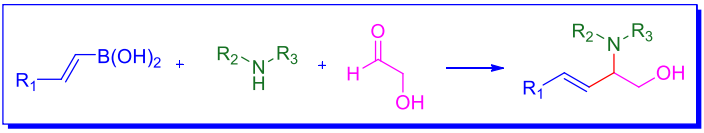
References

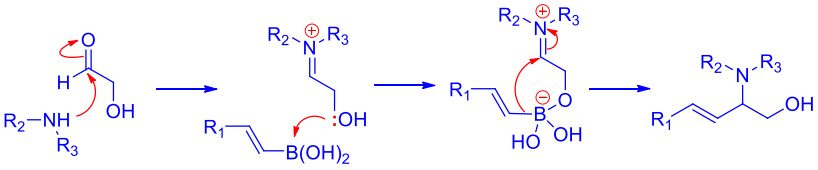
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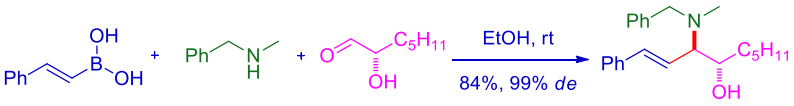
Petasis Reaction

Benzylic or allylic amine from the three-component reaction of an aryl- or a vinylboronic acid, a carbonyl and an amine. Also known as boron-Mannich or Petasis boronic acid-Mannich reaction. *Cf.* Mannich reaction.

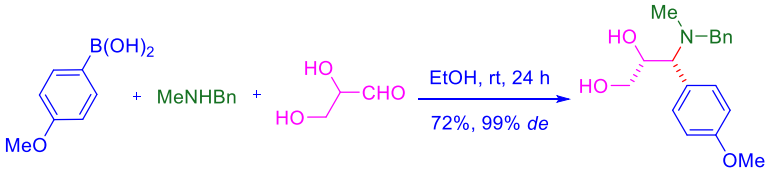




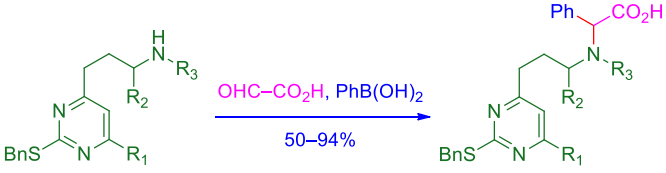
Example 1[2]



Example 2[4]

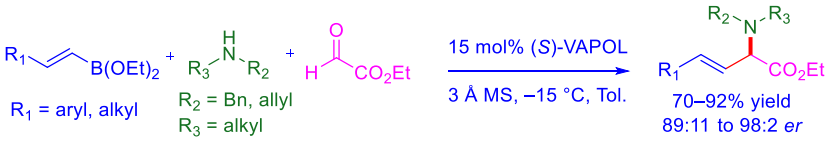


Example 3[9]

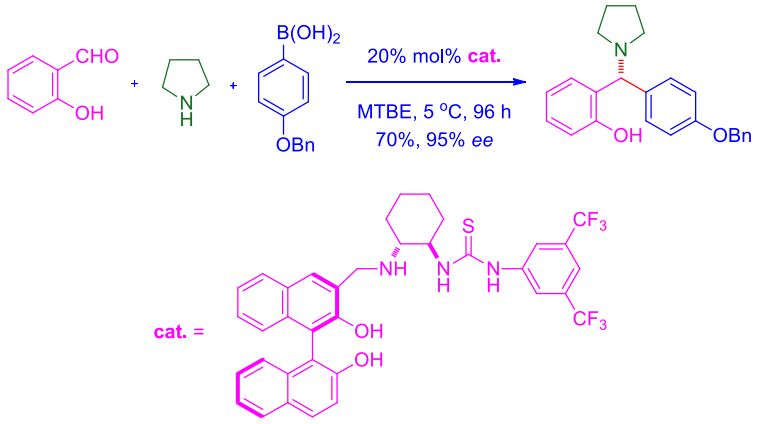


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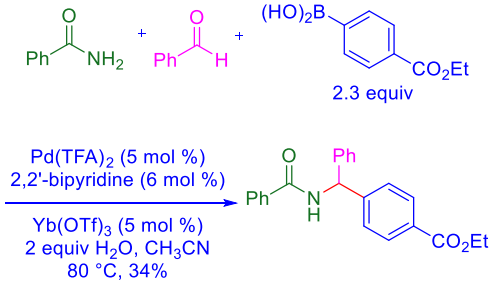
Example 4, Asymmetric Petasis reaction, and VAPOL = 2,2′-diphenyl-(4-biphenanthrol)[10]



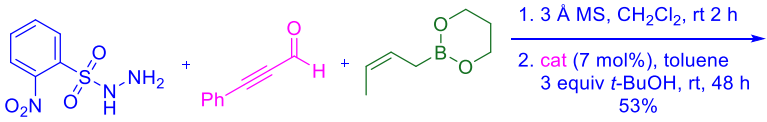
Example 5, Asymmetric Petasis reaction[11]

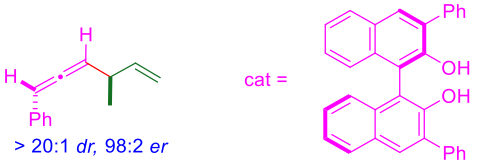


Example 6, Amide in place of amine also works under right conditions[13]

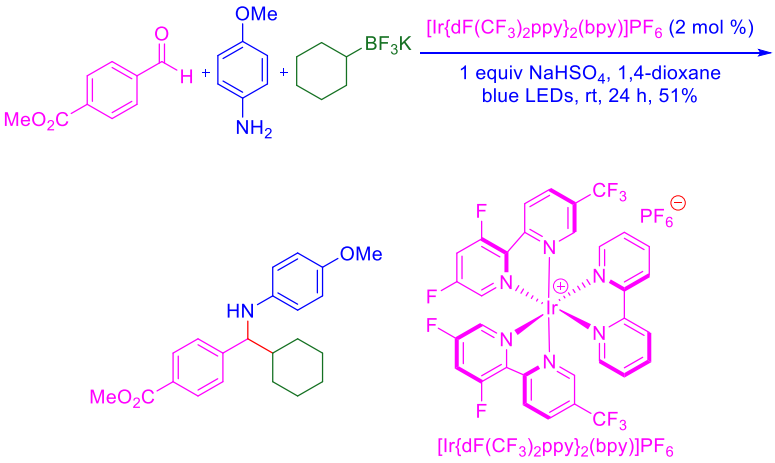


Example 7, Enantioselective synthesis of allenes by catatlytic traceless Petasis reaction[14]





Example 8[15]



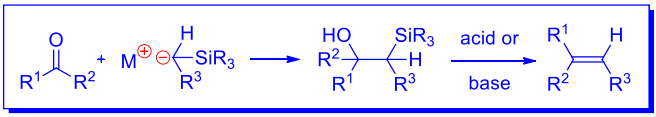
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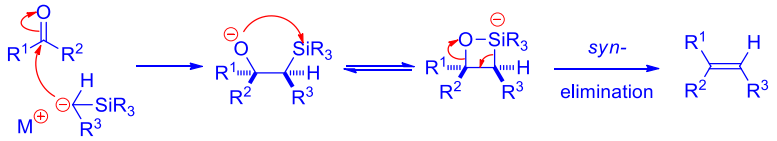
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Peterson Olefination

Alkenes from α-silyl carbanions and carbonyl compounds. Also known as the sila-Wittig reaction.

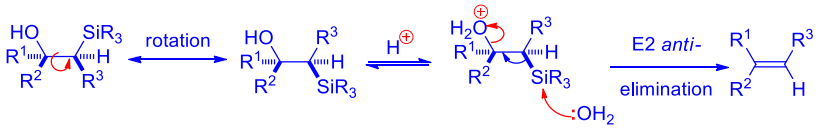


Basic conditions:



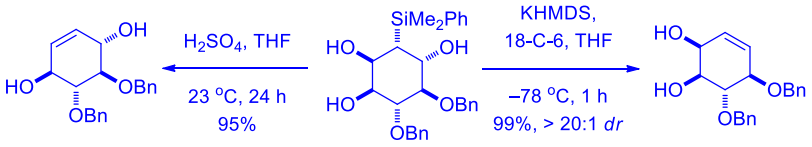
β-silylalkoxide intermediate

Acidic conditions:

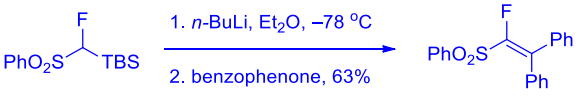


β-hydroxysilane

Example 1[6]



Example 2[7]

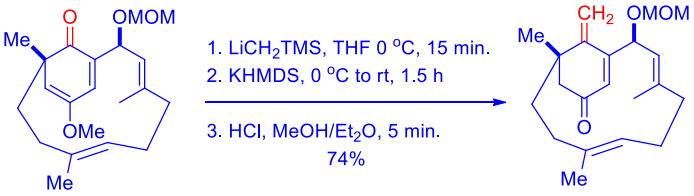


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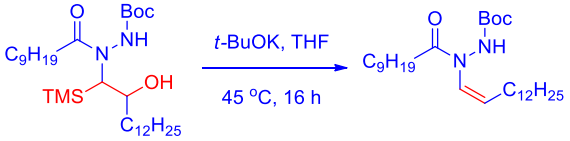
Example 3[8]



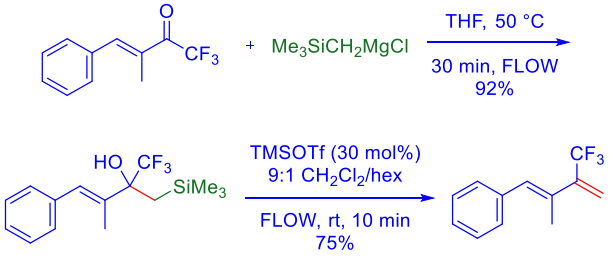
Example 4[10]



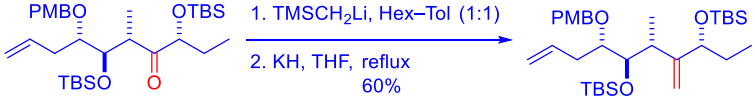
Example 5[12]



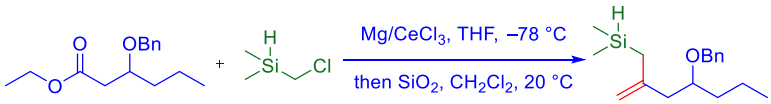
Example 6, Flow chemistry[13]



Example 7, In total synthesis[14]



Example 8, Grignard addition followed by elimination of dimethylsilanol to prepare terminal olefin[15]

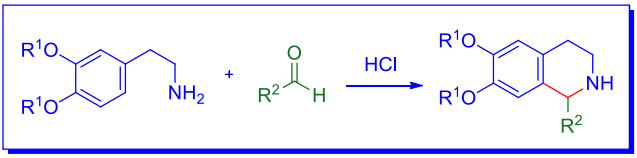


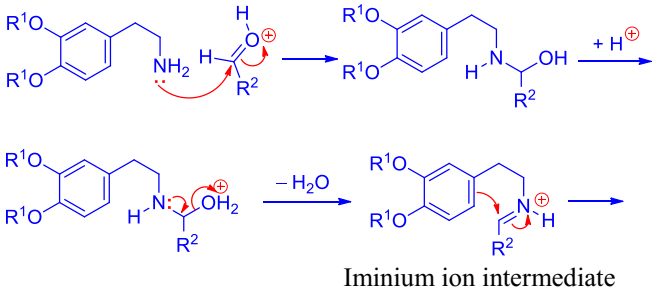
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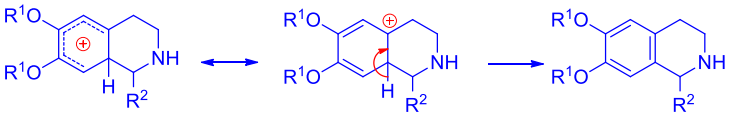
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Pictet–Spengler Tetrahydroisoquinoline Synthesis

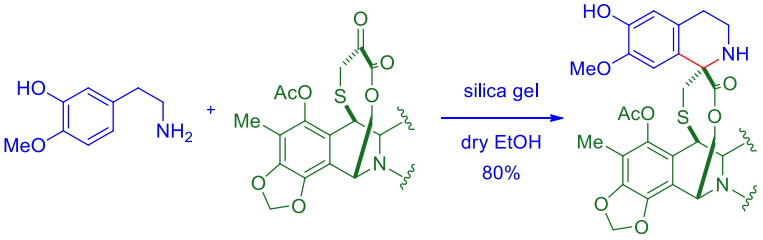
Tetrahydroisoquinolines from condensation of β-arylethylamines and carbonyl compounds followed by cyclization.



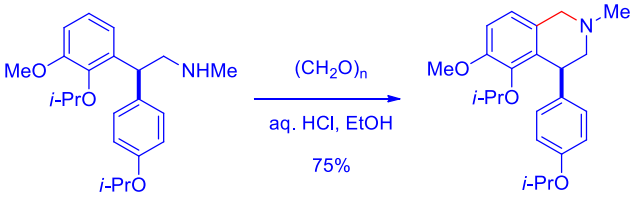




Example 1[4]

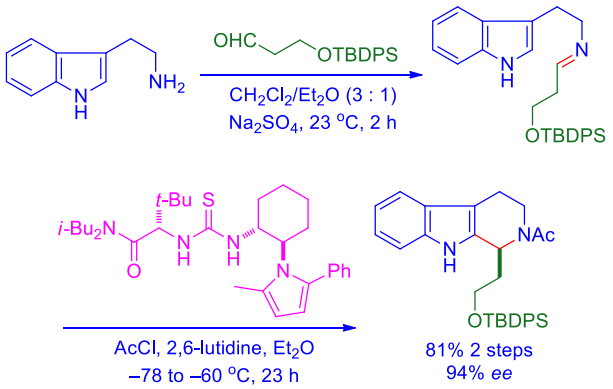


Example 2[7]

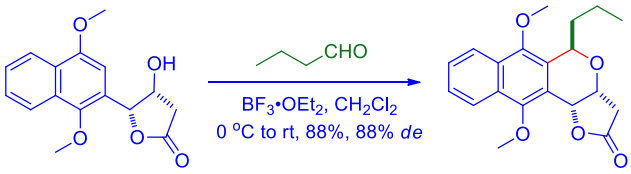


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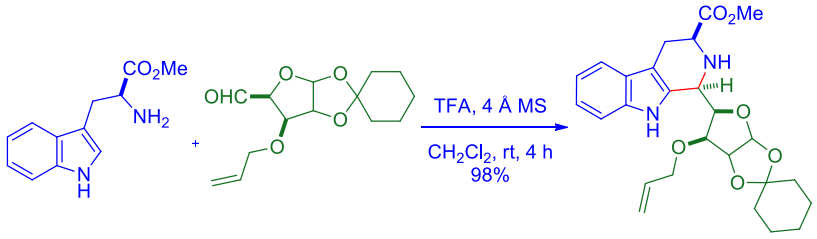
Example 3, Asymmetric acyl Pictet–Spengler[9]



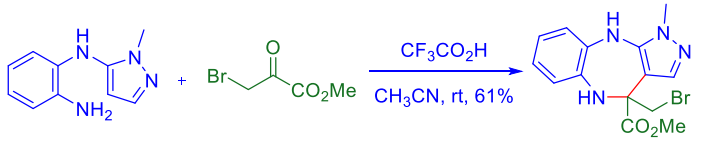
Example 4, Oxa-Pictet–Spengler[10]



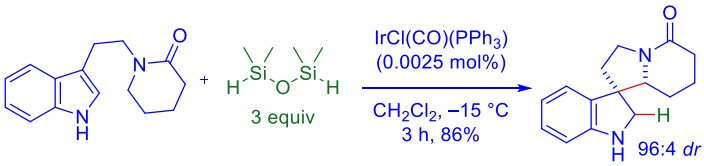
Example 5, A diastereoselective Pictet–Spengler reaction to make tetrahydro-β-carboline glycosides[11]



Example 6, Formation of 7-membered heterocycles[12]



Example 7, An interrupted Pictet–Spengler reaction[13]



Example 8, *En route* to the synthesis of monoterpene indole alkaloid (–)-alstoscholarine[14]

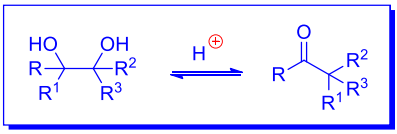


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Pinacol Rearrangement

Acid-catalyzed rearrangement of vicinal diols (pinacols) to carbonyl compounds.

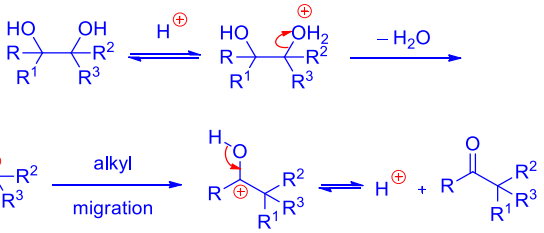


The most electron-rich alkyl group (more substituted carbon) migrates first. The general migration order:

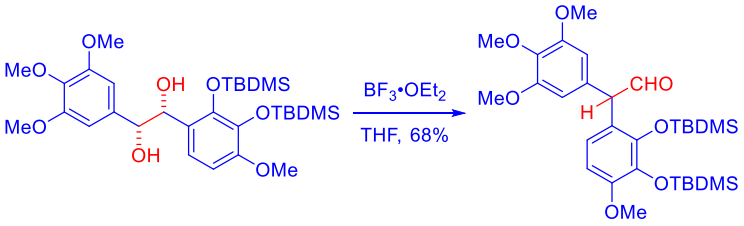
tertiary alkyl > cyclohexyl > secondary alkyl > benzyl > phenyl > primary alkyl > methyl >> H.

For substituted aryls:

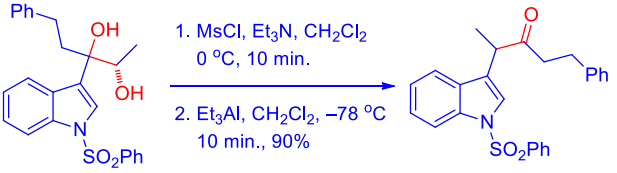
p-MeO-Ar > *p*-Me-Ar > *p*-Cl-Ar > *p*-Br-Ar > *p*-O_2N-Ar



Example 1[4]

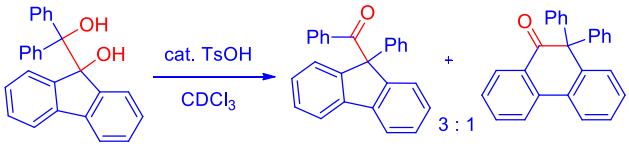


Example 2[5]

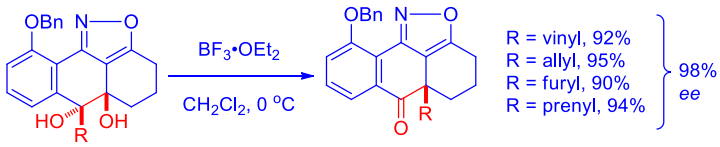


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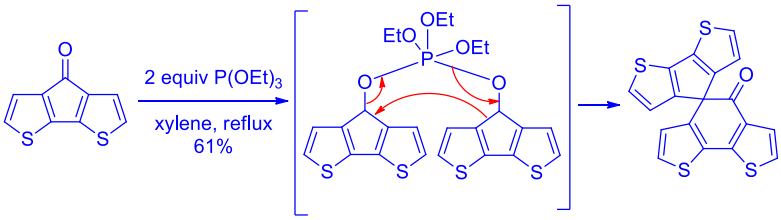
Example 3[7]



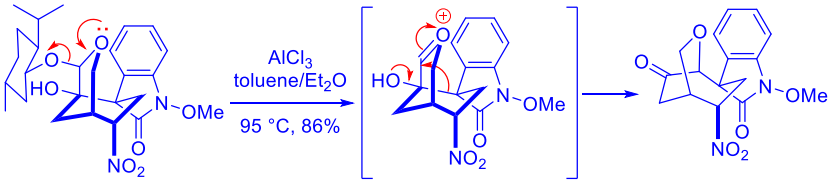
Example 4[9]



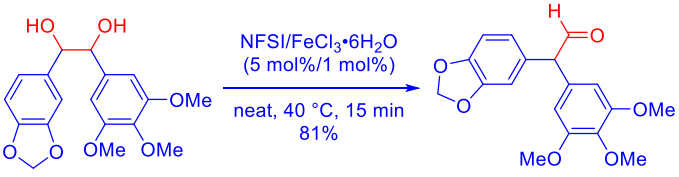
Example 5, A trivalent organophosphorus reagent induced pinacol rearrangement[11]



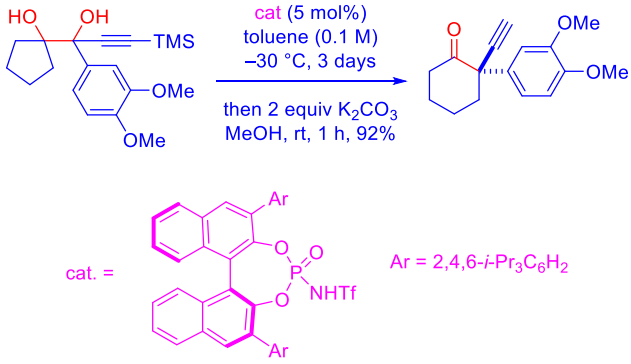
Example 6, Oxonium ion-induced pinacol rearrangement[13]



Example 7, Lewis acid-assisted electrophilic fluorine-catalyzed pinacol rearrangement of hydrobenzoin substrates (NFSI = *N*-fluorobenzenesulfonimide)[14]



Example 8, Catalytic enantioselective pinacol rearrangement[15]

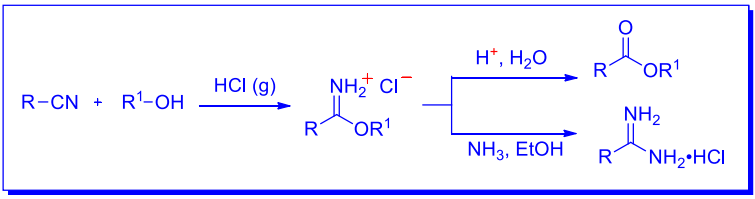


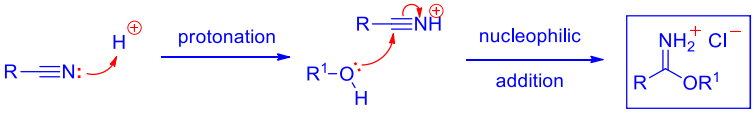
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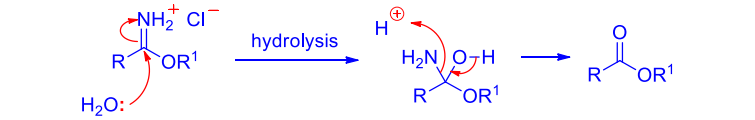
Pinner Reaction

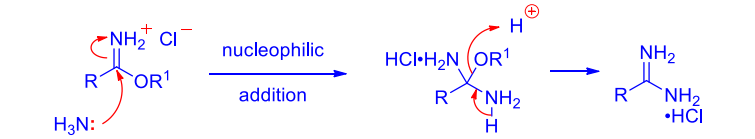
Transformation of a nitrile into an imino ether, which can be converted to either an ester or an amidine.





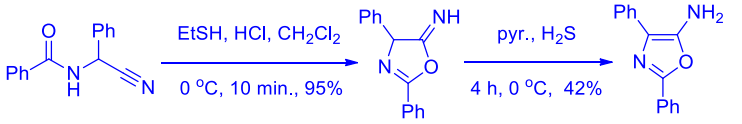
common intermediate



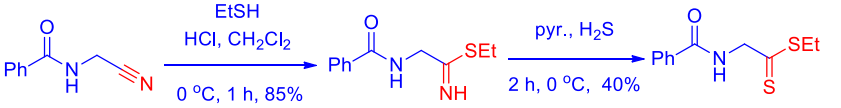


imidate hydrochloride

Example 1[2]

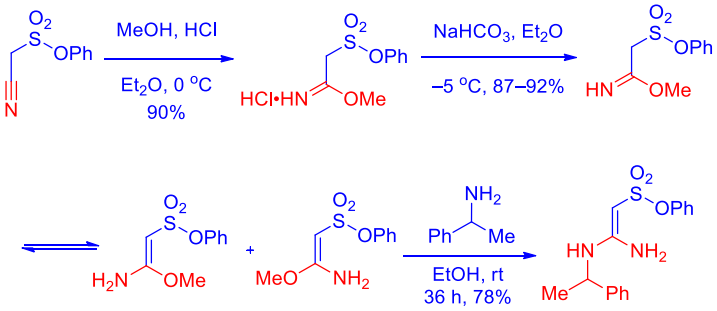


Example 2[2]

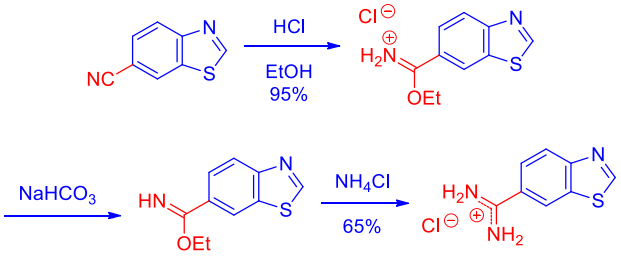


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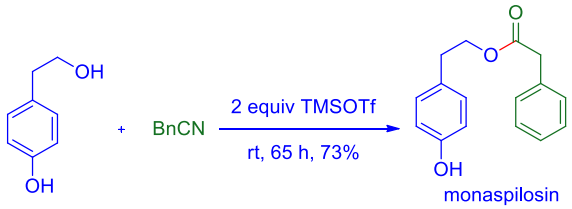
Example 3[6]



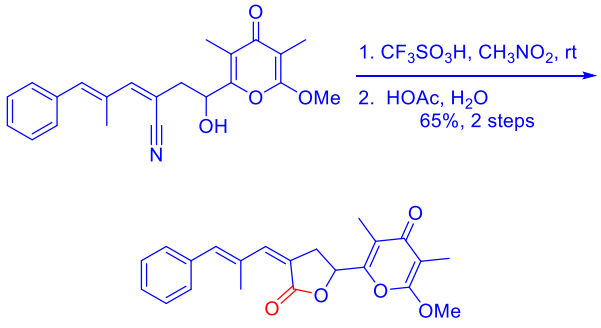
Example 4[10]



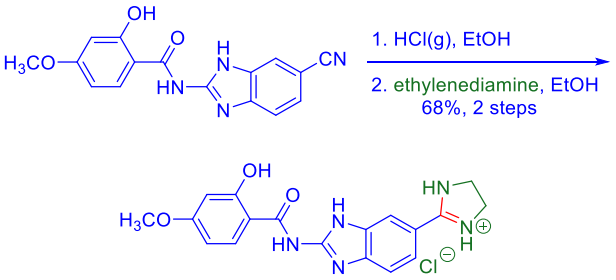
Example 5[11]



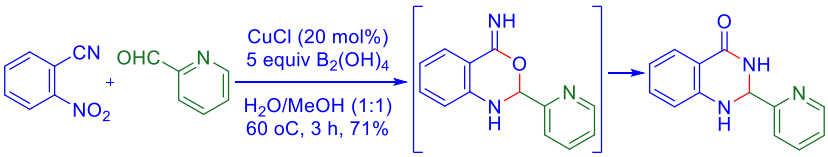
Example 6, Intramolecular 5-*oxo*-*dig* cyclization[12]



Example 7, Utility in drug discovery[13]



Example 8, Pinner reaction followed by a Dimroth rearrangement[14]

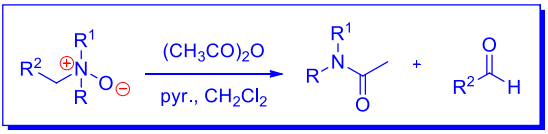


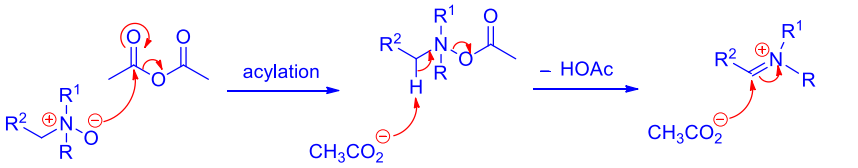
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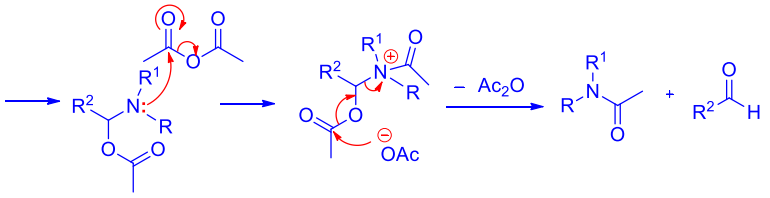
Polonovski Reaction

Treatment of a tertiary *N*-oxide with an activating agent such as acetic anhydride, resulting in rearrangement where an *N,N*-disubstituted acetamide and an aldehyde are generated.

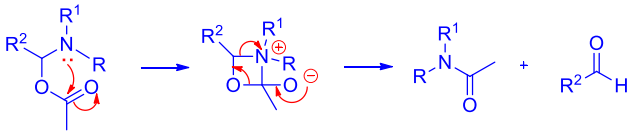




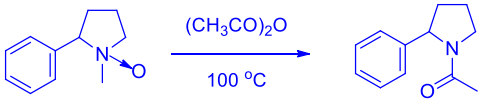
iminium ion



The intramolecular pathway is also operative:

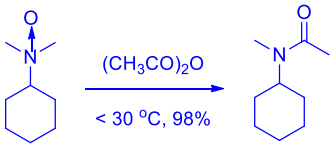


Example 1[1]

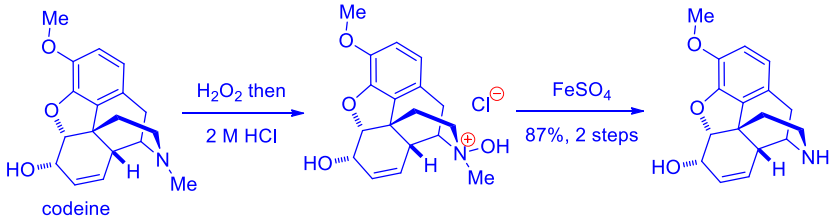


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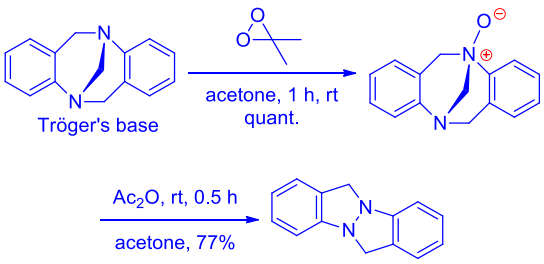
Example 2[2]



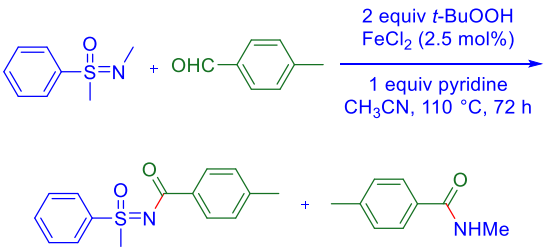
Example 3, Iron salt-mediated Polonovski reaction[9]



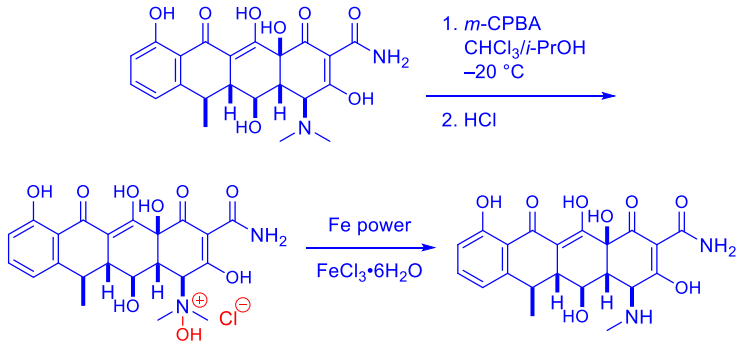
Example 4[11]



Example 5, Iron-catalyzed acylative dealkylation of *N*-alkylsulfoximines[12]



Example 6, A non-classical Polonovski reaction[13]

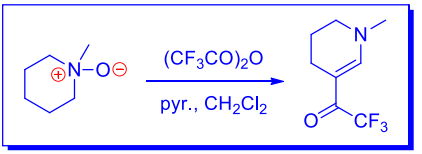


References

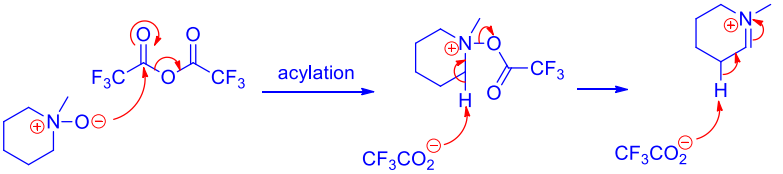
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Polonovski–Potier Reaction

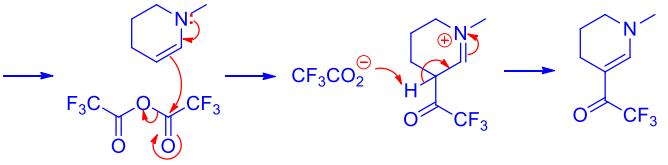
A modification of the Polonovski reaction where trifluoroacetic anhydride is used in place of acetic anhydride. Because the reaction conditions for the Polonovski–Potier reaction are mild, it has largely replaced the Polonovski reaction.



tertiary *N*-oxide

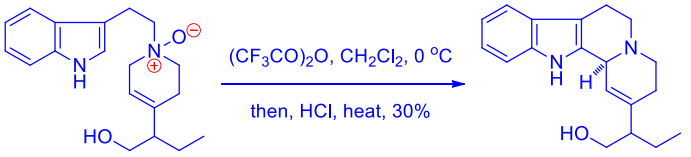


iminium ion

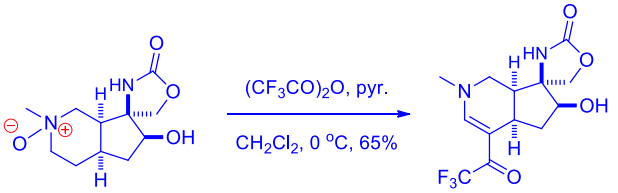


enamine

Example 1[2]

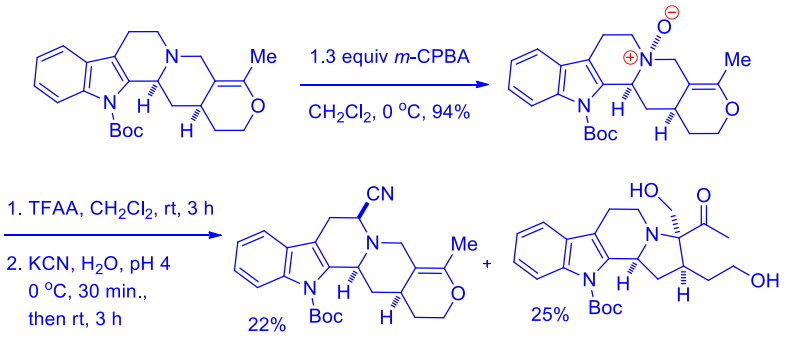


Example 2[5]

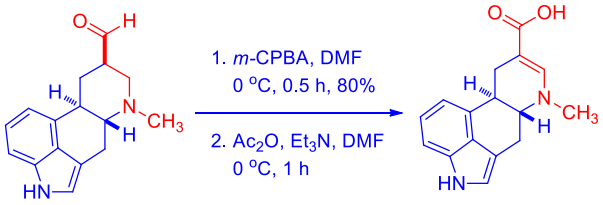


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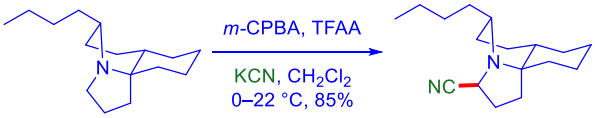
Example 3[8]



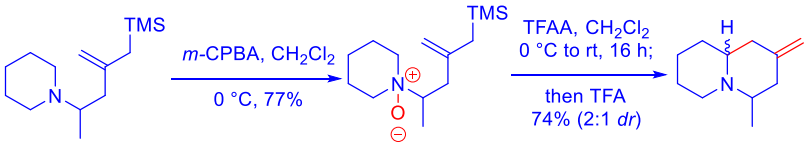
Example 4, Here, *m*-CPBA also concurrently oxidized the aldehyde[10]



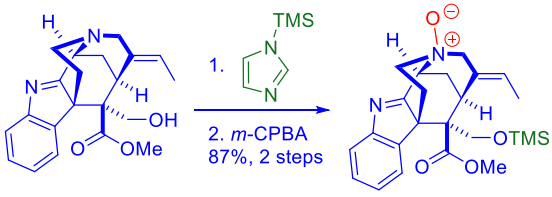
Example 5, Oxidative α-Cyanation[13]

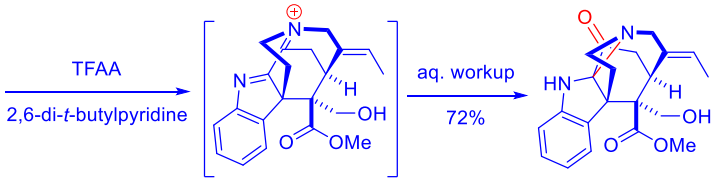


Example 6, Cyclization onto the iminium intermediate[14]



Example 7, Here, *m*-CPBA also concurrently oxidized the aldehyde[15]



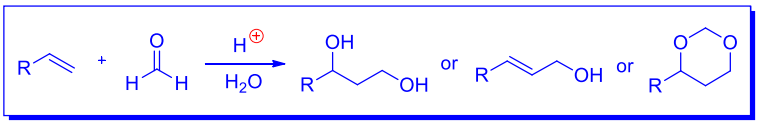


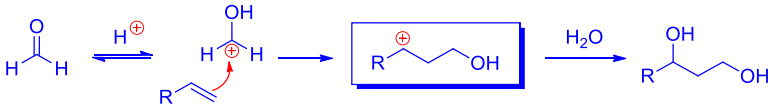
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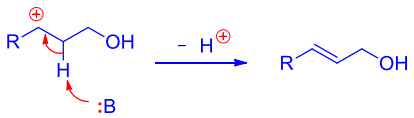
Prins Reaction

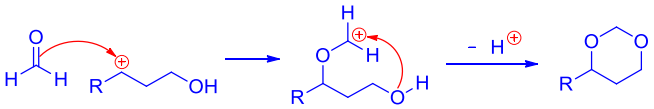
The Prins reaction is the acid-catalyzed addition of aldehydes to alkenes and gives different products depending on the reaction conditions.



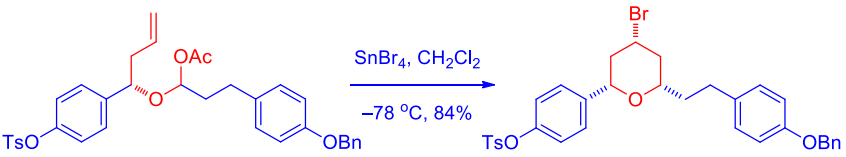


the common intermediate

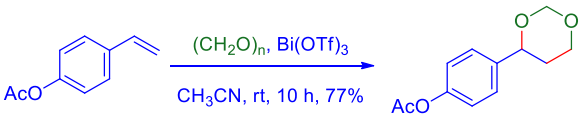




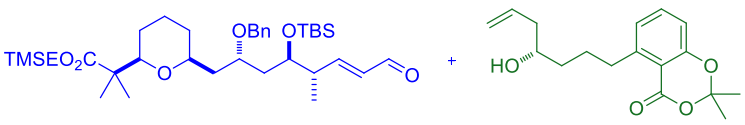
Example 1[5]



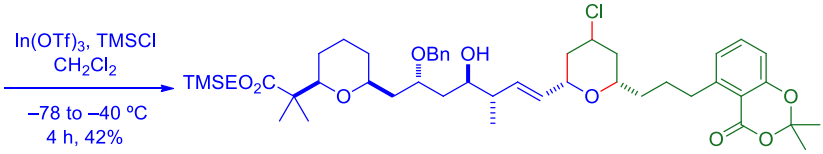
Example 2[7]



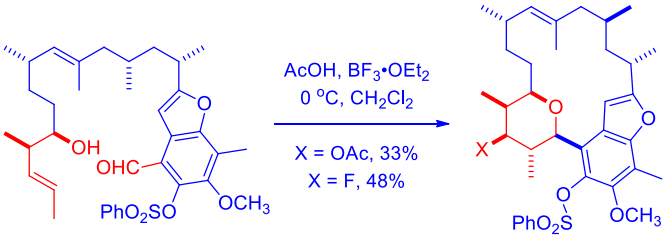
Example 3[9]



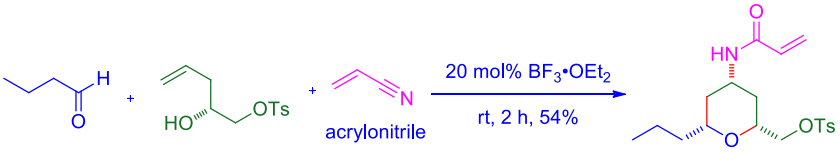
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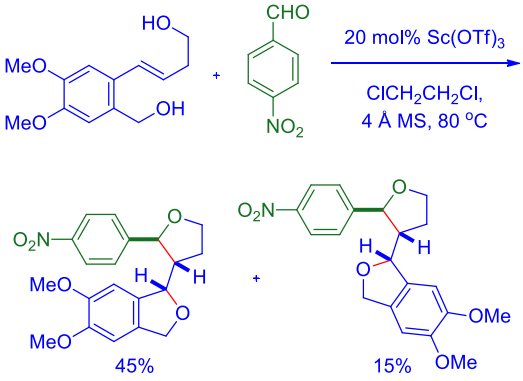
Example 4[10]



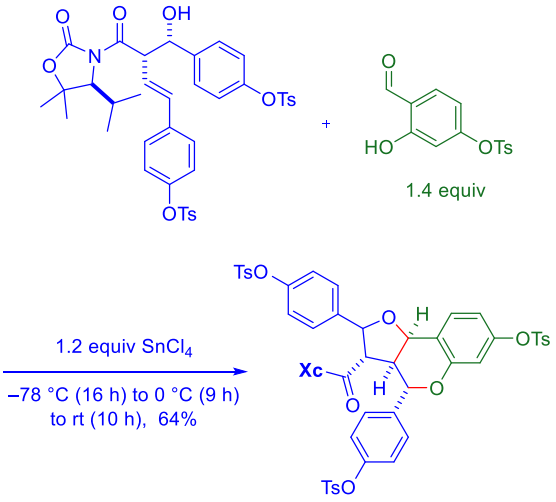
Example 5, A cascade of the Prins/Ritter amidation reaction[11]



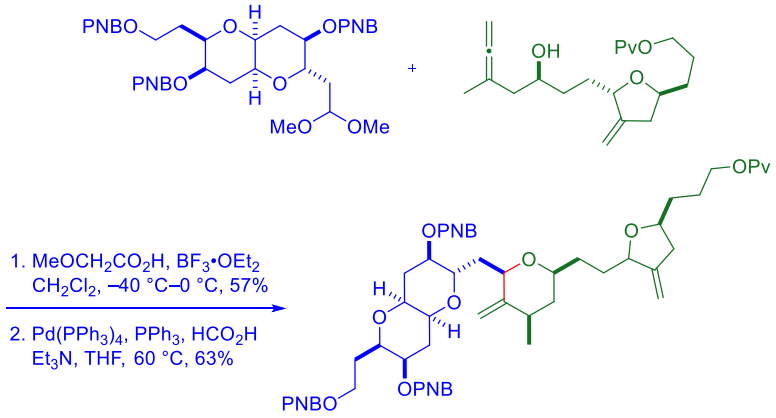
Example 6[12]



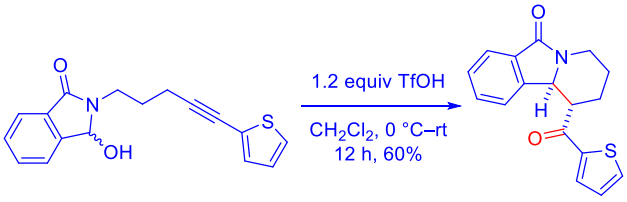
Example 7, $SnCl_4$-promoted oxonium-Prins cyclization[13]



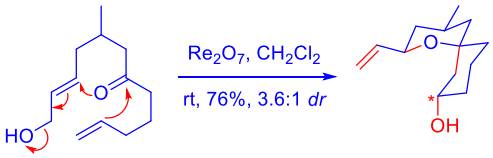
Example 8, Prins reaction of homoallenyl alcohols: access to substituted pyrans in the halichondrin series[14]



Example 9, Aza-Prins cyclization of endocyclic *N*-acyliminium ions[17]



Example 10, Re_2O_7-catalyzed approach to spirocyclic ether formation from acyclic precursors[19]

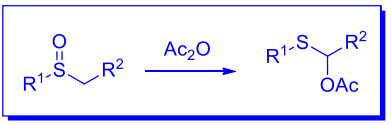


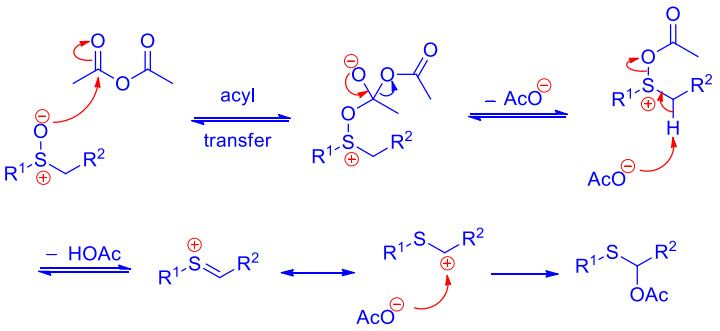
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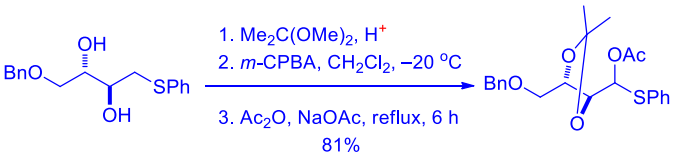
Pummerer Rearrangement

The transformation of sulfoxides into α-acyloxythioethers using acetic anhydride.

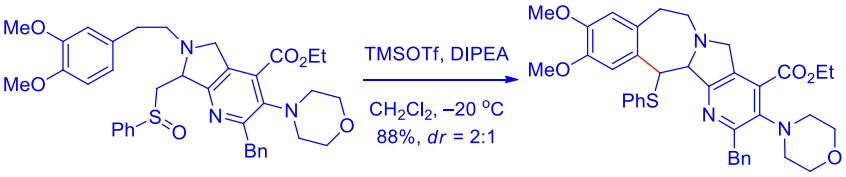




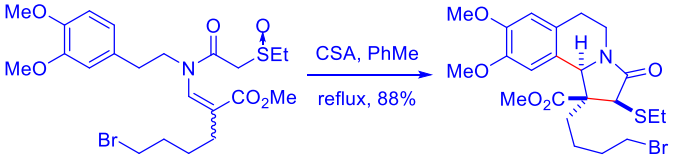
Example 1[2]



Example 2[7]

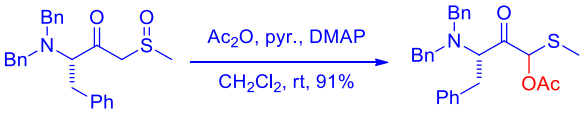


Example 3, A tandem Pummerer/Mannich cyclization sequence[8]

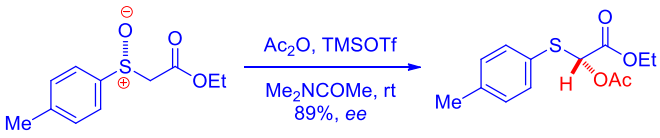


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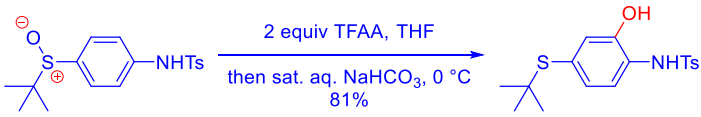
Example 4[9]



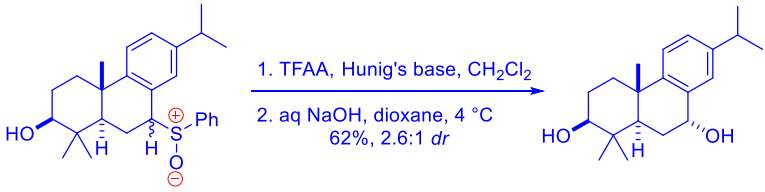
Example 5, Stereoselective Pummerer rearrangement[10,12]



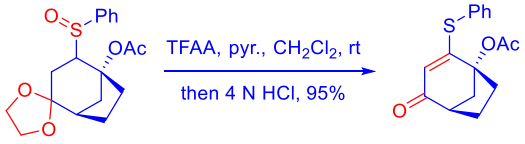
Example 6, An aromatic Pummerer rearrangement[13]



Example 7, Stereoselective Pummerer rearrangement[14]



Example 8, Pummerer rearrangement to afford vinyl sulfide by α-hydrogen elimination[15]



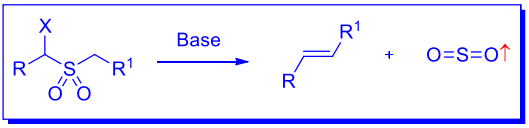
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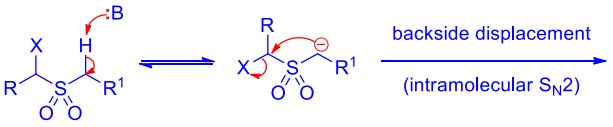
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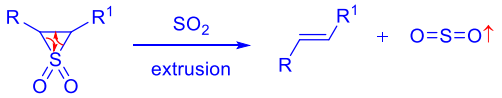
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Ramberg–Bäcklund Reaction

Olefin synthesis *via* α-halosulfone extrusion.

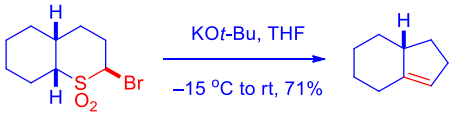




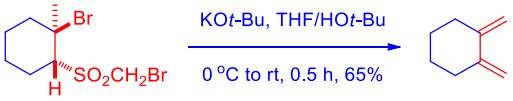


episulfone intermediate

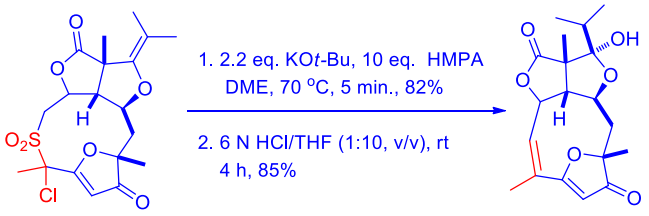
Example 1[4]



Example 2[5]

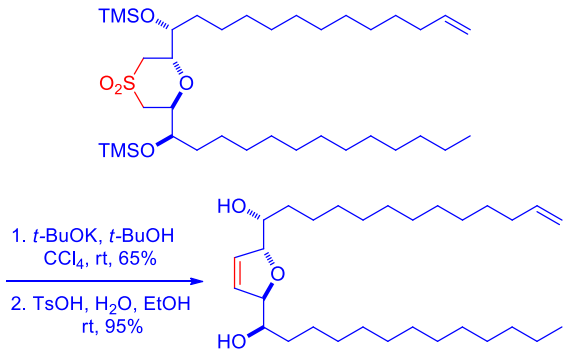


Example 3[6]

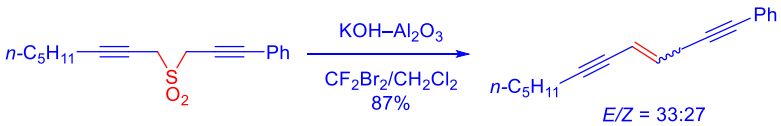


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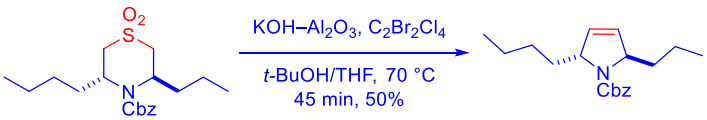
Example 4, *in situ* chlorination[7]



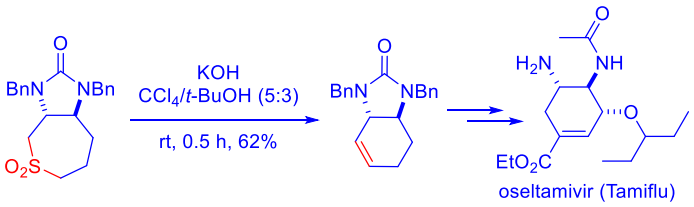
Example 5, Direct conversion of dipropargylic sulfones into ene-diynes by a modified one-flask Ramberg–Bäcklund reaction[8]



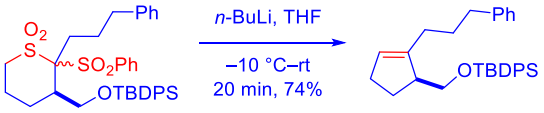
Example 6, Pyrroline synthesis[14]



Example 7, Towards oseltamivir (Tamiflu)[15]



Example 8, Cyclic olefin from optically pure alcohols (sulfone is th leaving group)[17]

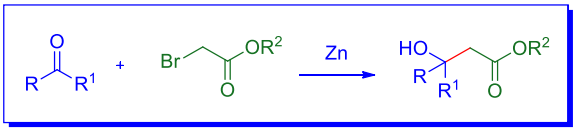


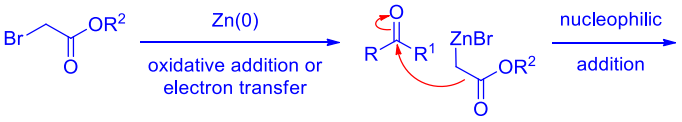
References

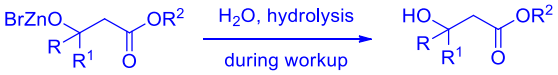
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Reformatsky Reaction

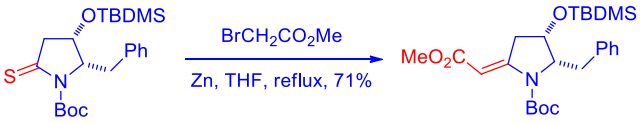
Nucleophilic addition of organozinc reagents generated from α-haloesters to carbonyls.



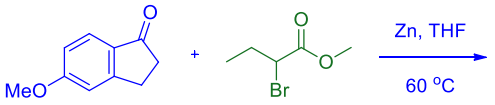


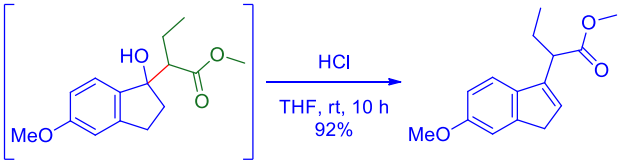


Example 1[4]



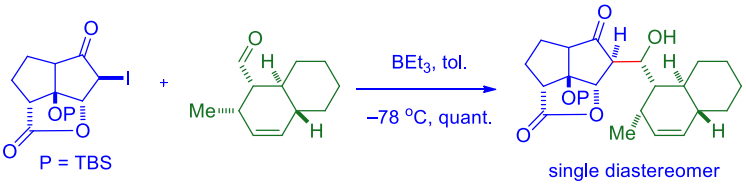
Example 2[6]



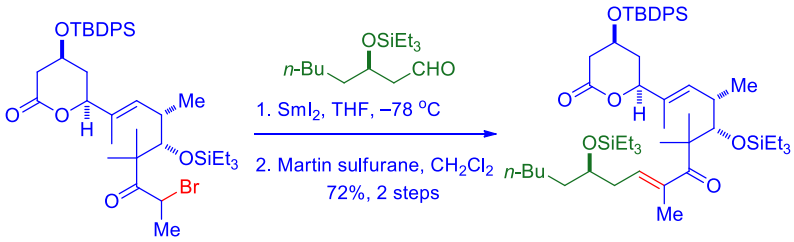


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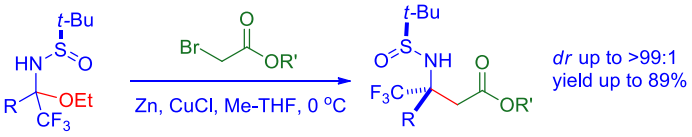
Example 3, Boron-mediated Reformatsky reaction[8]



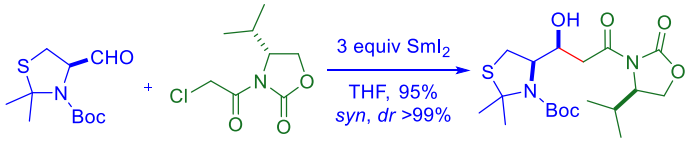
Example 4, SmI_2-mediated Reformatsky reaction[9]



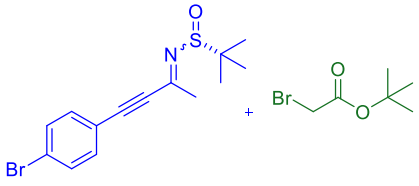
Example 5[6]

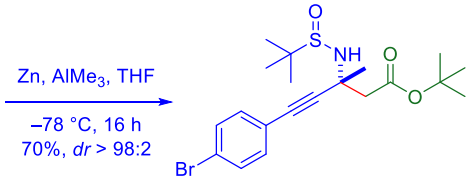


Example 6, SmI_2-mediated Reformatsky reaction[13]



Example 7, Diastereoselective Reformatsky reaction[14]



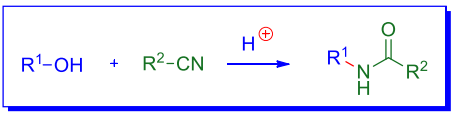


References

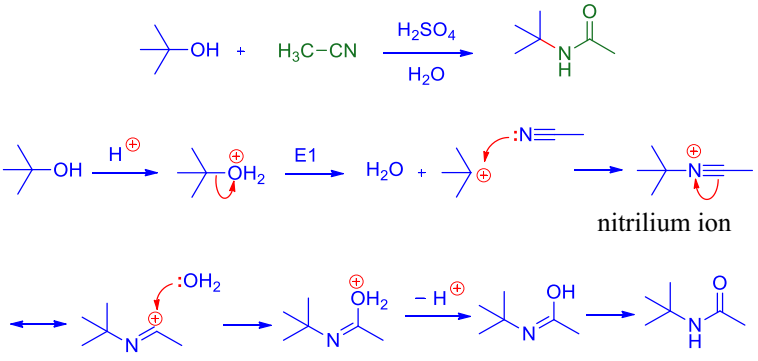
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Ritter Reaction

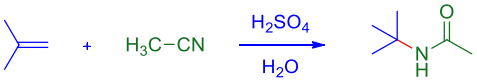
Amides from nitriles and alcohols in strong acids.
General scheme:



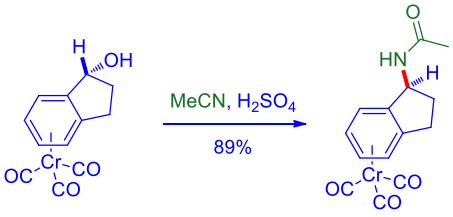
Example 1



Similarly:

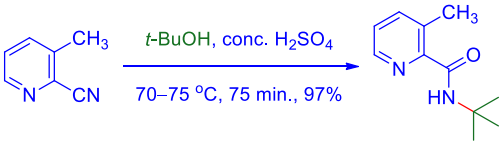


Example 2[3]

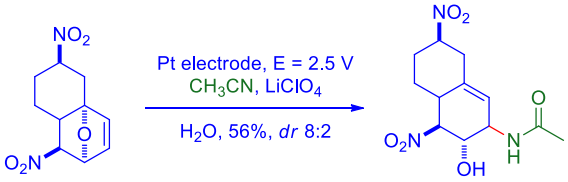


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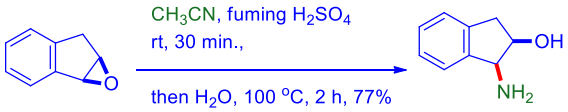
Example 3[4]



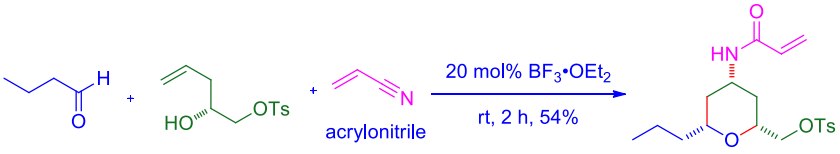
Example 4[5]



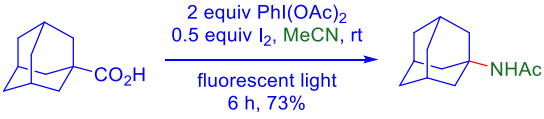
Example 5[6]



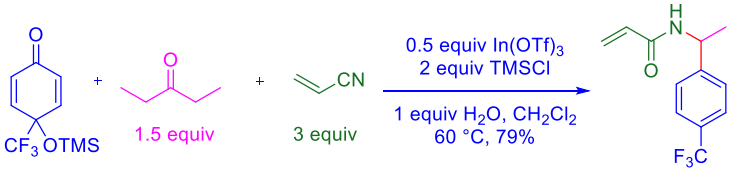
Example 6, A cascade of the Prins/Ritter amidation reaction[12]



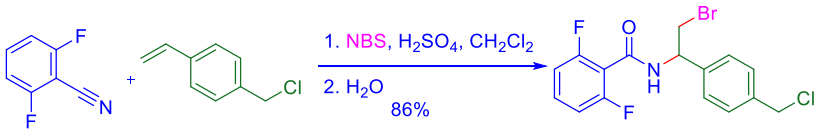
Example 7, Hypervalent iodine(III)-mediated decarboxylative Ritter-type amination[13]



Example 8, A multicomponent reaction involving a Ritter-type route[14]



Example 9, Process-scale Ritter reaction[15]

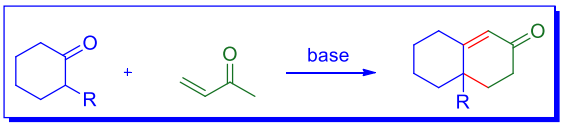


References

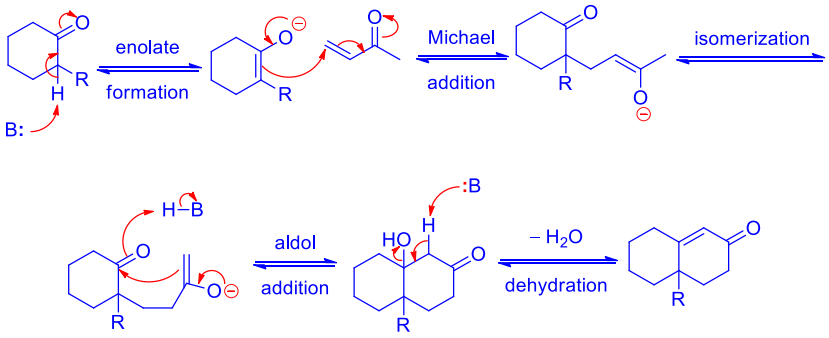
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Robinson Annulation

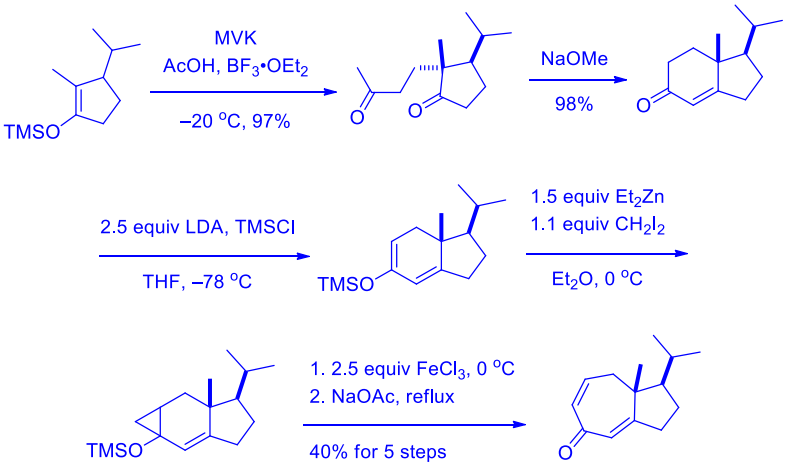
Michael addition of cyclohexanones to methyl vinyl ketone followed by intramolecular aldol condensation to afford six-membered α,β-unsaturated ketones.



methyl vinyl ketone (MVK)

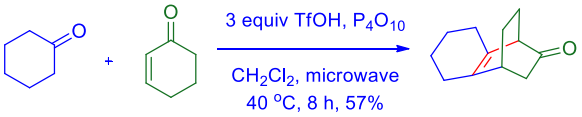


Example 1, Homo-Robinson[7]

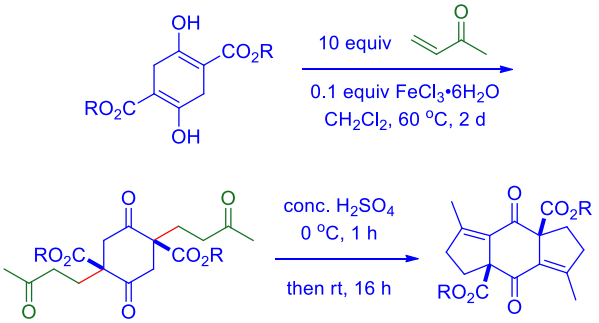


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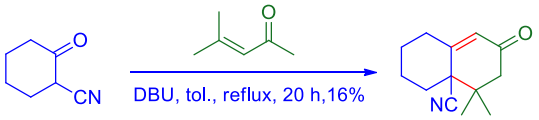
Example 2[8]



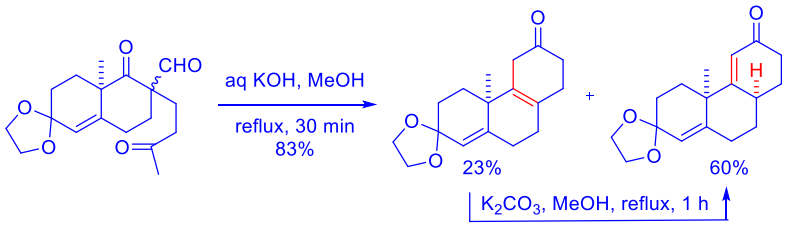
Example 3, Double Robinson-type cyclopentene annulation[9]



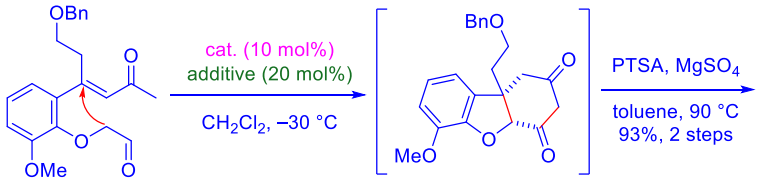
Example 4[10]



Example 5, The thermodynamically less stable Robinson annulation product was converted to the thermaodynamically more stable product under mild basic conditions[13]



Example 6, Enantioselective Robinson annulation, PTSA = *p*-toluenesulfonic acid[14]

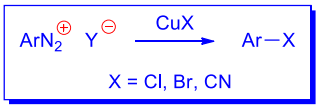


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Sandmeyer Reaction

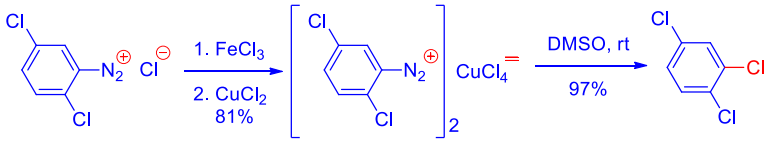
Haloarenes from the reaction of a diazonium salt with CuX.



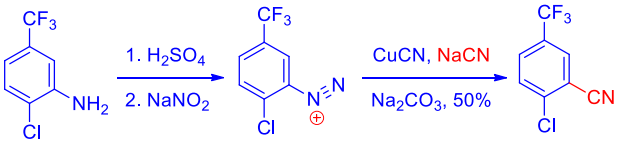
Mechanism:



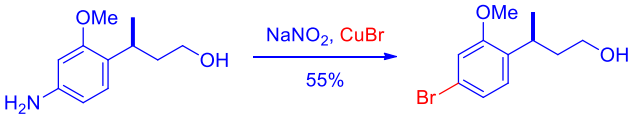
Example 1[4]



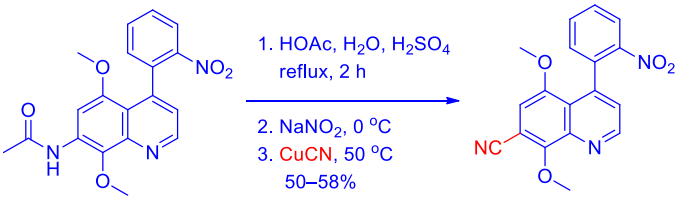
Example 2[7]



Example 3[8]

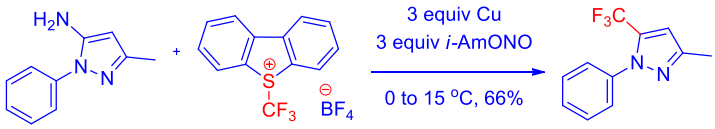


Example 4[9]



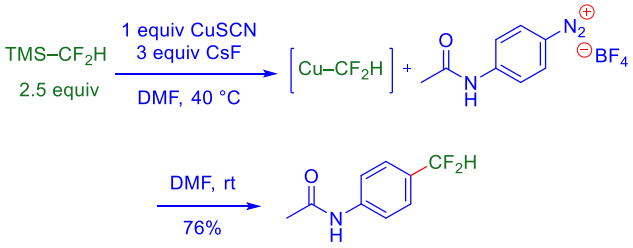
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Example 5, Trifluoromethylation[11]

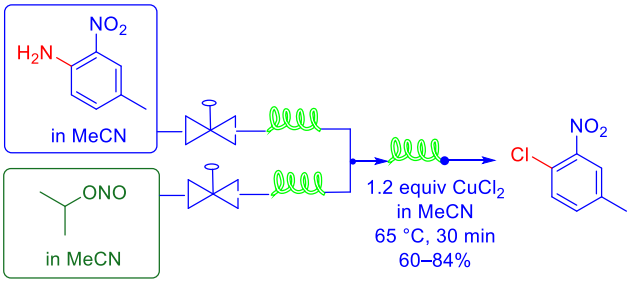


Umemoto′s reagent

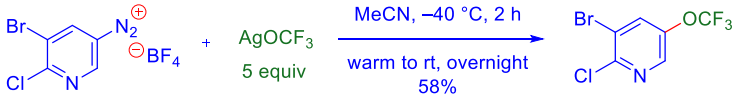
Example 6, Difluoromethylation of (hetero-)arenediazonium salts[13]



Example 7, Safe continuous-flow process[14]



Example 8, Silver-mediated trifluoromethylation of (hetero-)arenediazonium tetrafluoroborates[16]



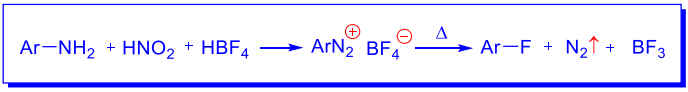
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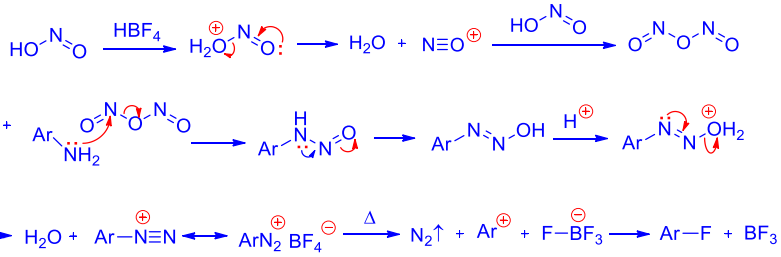
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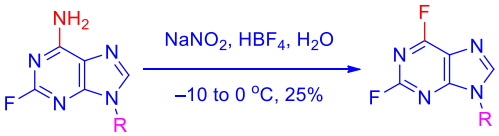
Schiemann Reaction

Fluoroarene formation from anilines. Also known as the Balz–Schiemann reaction.

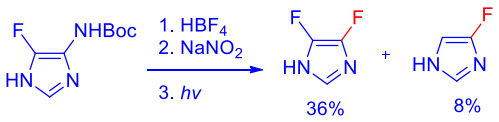




Example 1[4]



Example 2, Photo-Schiemann reaction[6]

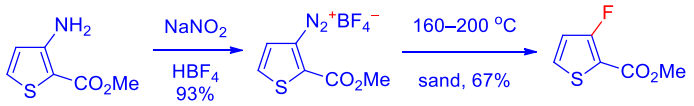


Example 3, Photo-Schiemann reaction, bmim = 1-Butyl-3-methylimidazolium[8]

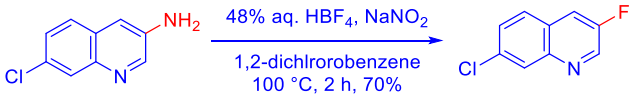


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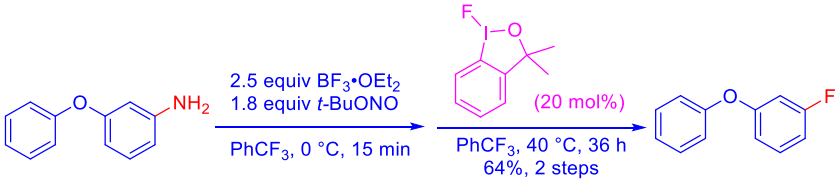
Example 4, Synthesis of 3-fluorothiophene[10]



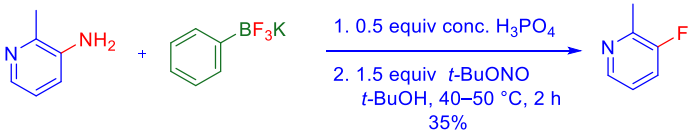
Example 5, From aminoquinoline substrate[12]



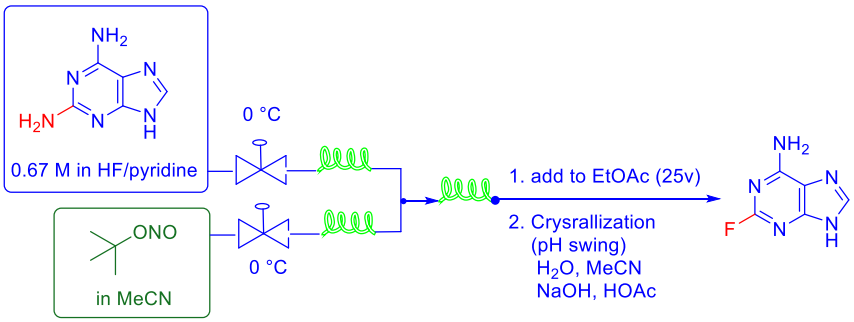
Example 6, Hypervalent iodine (III)-catalyzed fluorination under mild conditions[13]



Example 7, Organotrifluoroborates as competent sources of fluoride ion for fluorodediazoniation[14]



Example 8, One-step synthesis of 2-fluoroadenine using hydrogen fluoride pyridine in continuous flow operation[15]

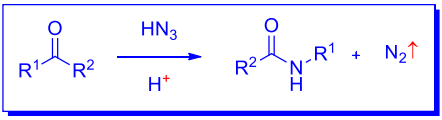


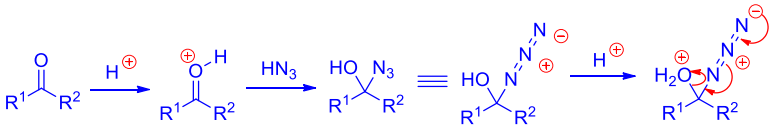
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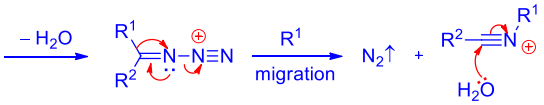
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Schmidt Rearrangement

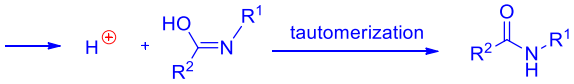
The Schmidt reactions refer to the acid-catalyzed reactions of hydrazoic acid with electrophiles, such as carbonyl compounds, tertiary alcohols and alkenes. These substrates undergo rearrangement and extrusion of nitrogen to furnish amines, nitriles, amides or imines.



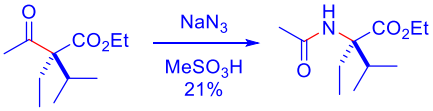




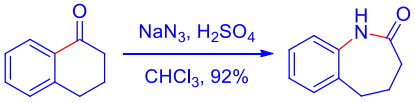
nitrilium ion intermediate (*Cf.* Ritter intermediate)



Example 1, A classic example[3]

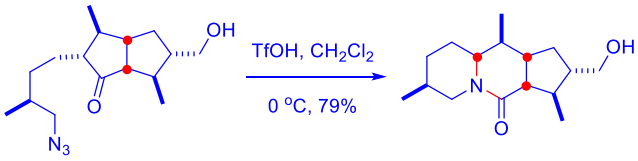


Example 2[5]

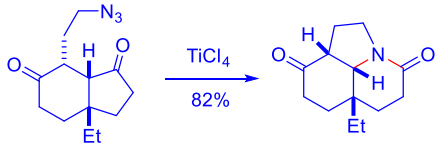


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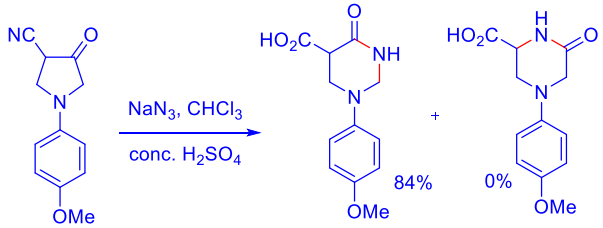
Example 3, Intramolecular Schmidt rearrangement[6]



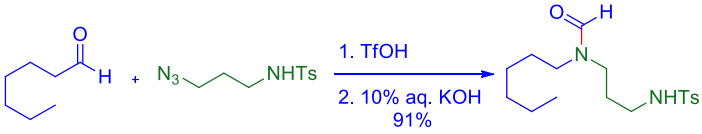
Example 4, Intramolecular Schmidt rearrangement[8]



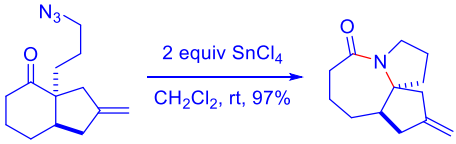
Example 5, Intermolecular Schmidt rearrangement[9]



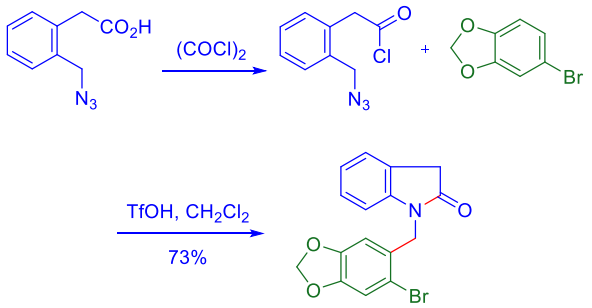
Example 6[11]



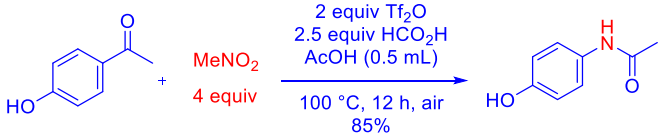
Example 7, Intramolecular Schmidt rearrangement[12]



Example 8, Making 2-oxoindoles[13]



Example 9, Nitromethane as a nitrogen donor in Schmidt-type formation of amides and nitriles[14]

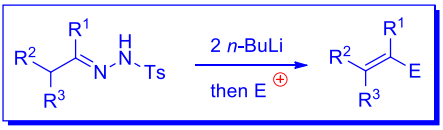


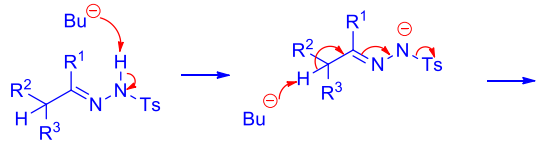
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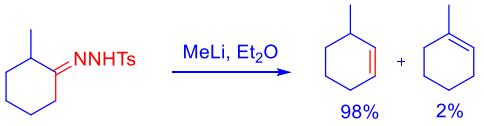
Shapiro Reaction

The Shapiro reaction is a variant of the Bamford–Stevens reaction. The former uses bases such as alkyl lithium and Grignard reagents whereas the latter employs bases such as Na, NaOMe, LiH, NaH, $NaNH_2$, *etc*. Consequently, *the Shapiro reaction generally affords the less-substituted olefins (the kinetic products), while the Bamford–Stevens reaction delivers the more-substituted olefins (the thermodynamic products).*

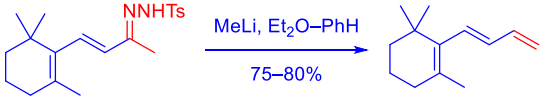




Example 1, Kinetic product is the major product[2]

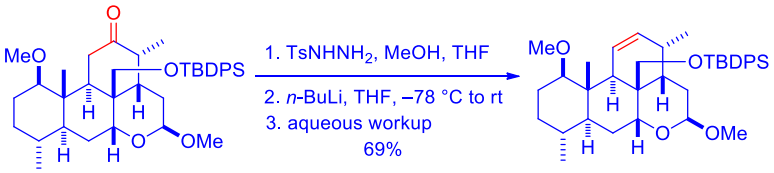


Example 2[3]

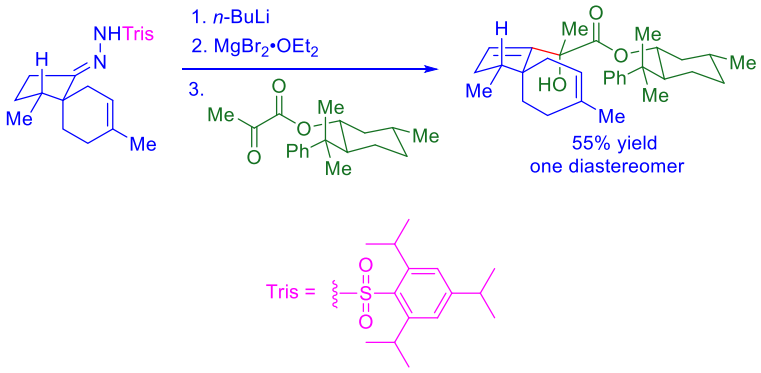


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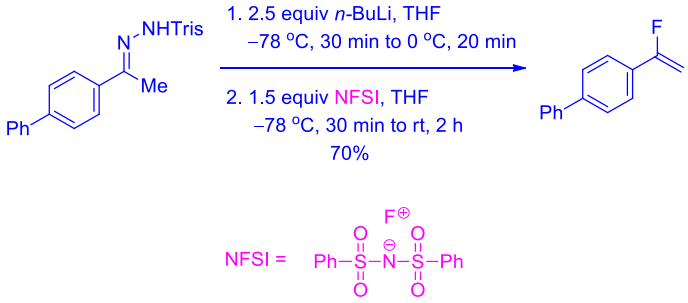
Example 3[7]



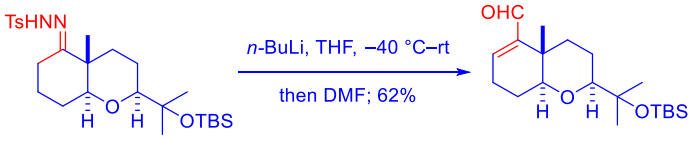
Example 4[8]



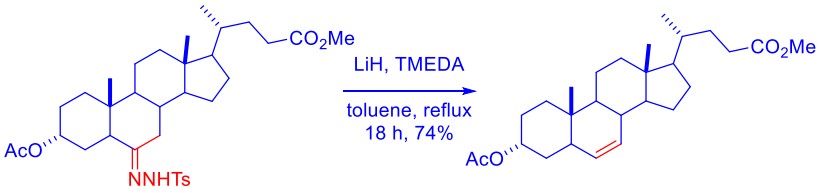
Example 5, NFSI = *N*-fluorobenzenesulfonimide[11]



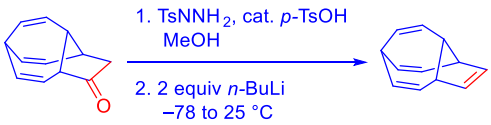
Example 6, Toward total synthesis of paspaline[12]



Example 7, To make ursodeoxycholic acid[13]



Example 8[14]

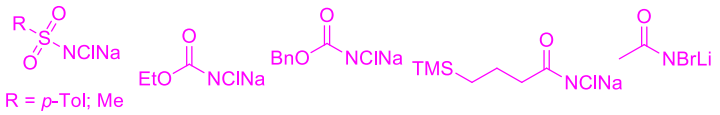


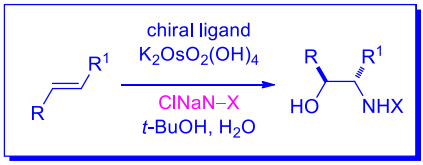
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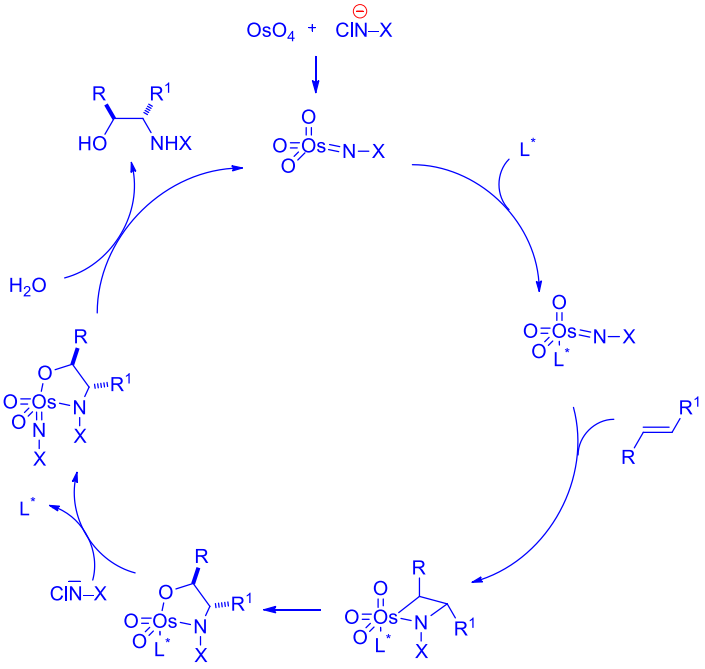
Sharpless Asymmetric Amino-hydroxylation

Osmium-mediated *cis*-addition of nitrogen and oxygen to olefins. Regio-selectivity may be controlled by ligand. Nitrogen sources (X–NClNa) include:

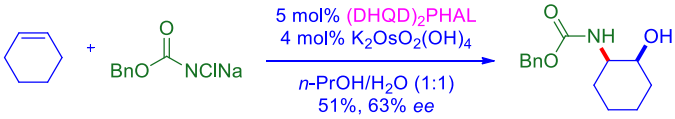




The catalytic cycle:

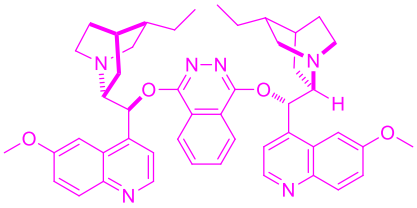


Example 1[1b]

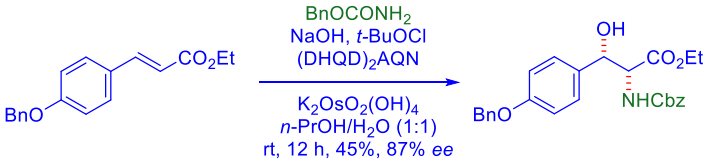


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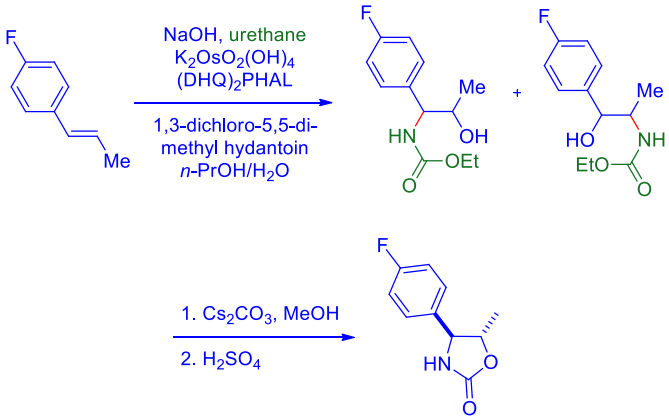
$(DHQD)_2$-PHAL = 1,4-bis(9-*O*-dihydroquinidine)phthalazine:



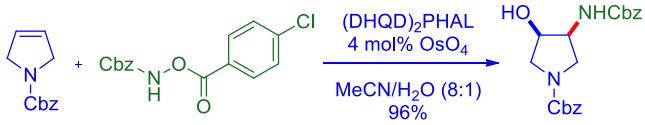
Example 2[2]



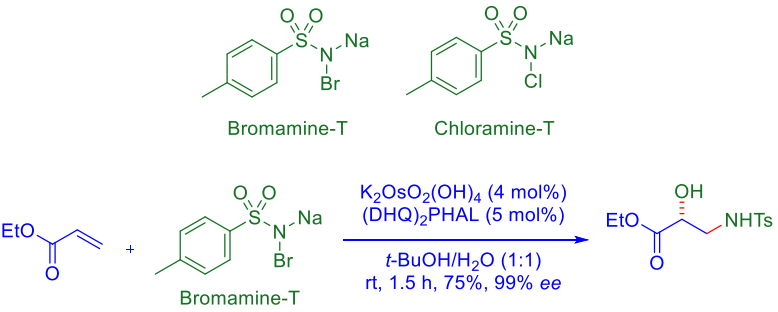
Example 3[6]



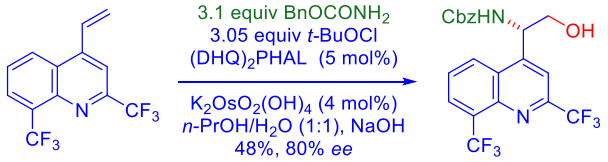
Example 4[13]



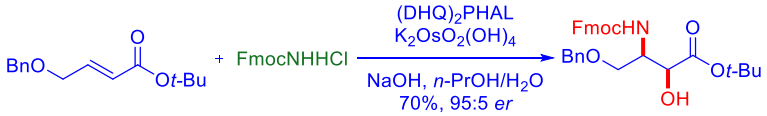
Example 5, Bromamine-T as an efficient amine source[14]



Example 6, Anti-malarial drug[15]



Example 7, Using FmocNH•HCl as the amine source[16]



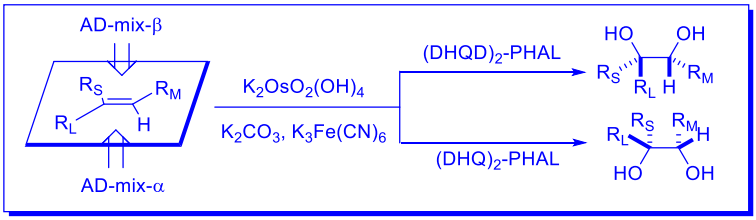
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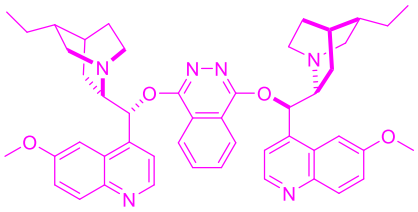
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Sharpless Asymmetric Dihydroxylation

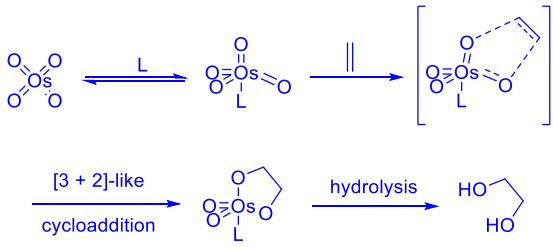
Enantioselective *cis*-dihydroxylation of olefins using osmium catalyst in the presence of cinchona alkaloid ligands.



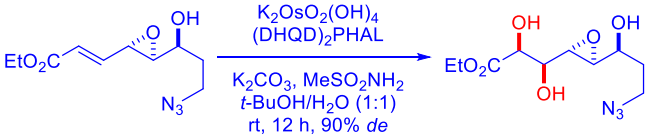
$(DHQ)_2$-PHAL = 1,4-bis(9-*O*-dihydroquinine)phthalazine:



The concerted [3 + 2] cycloaddition mechanism:[5]

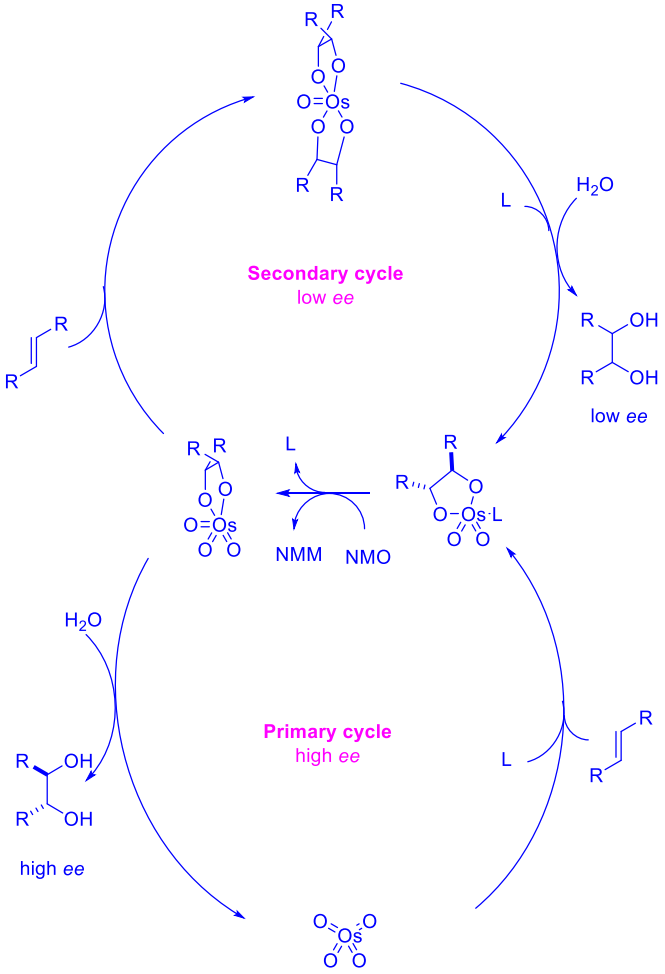


Example 1[2]



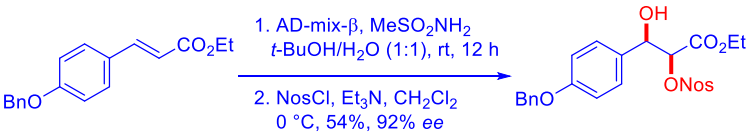
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The catalytic cycle: (the secondary cycle is shut off by maintaining a low concentration of olefin):



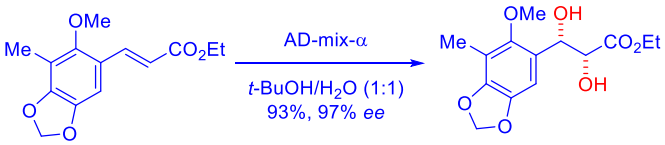
NMO = N-methyl morpholine N-oxide
NMM = N-methyl morpholine

Example 2[4]

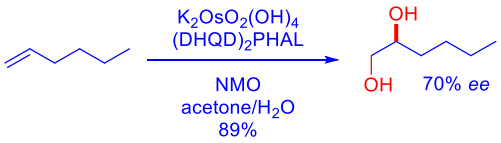


Nos = nosylate = 4-nitrobenzenesulfonyl

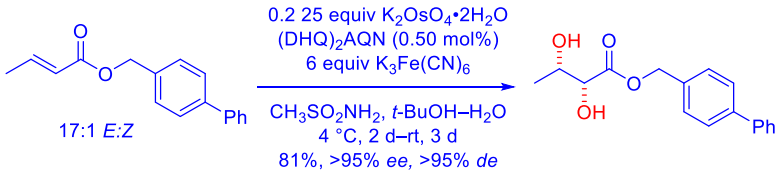
Example 3[9]



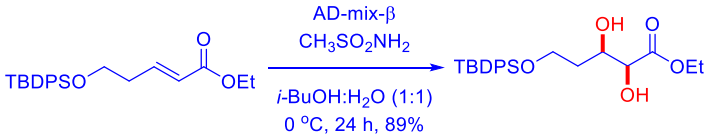
Example 4[10]



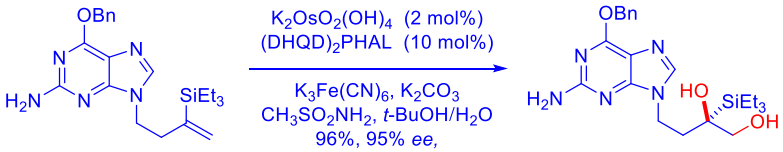
Example 5, A scalable synthesis[13]



Example 5[14]



Example 7[15]



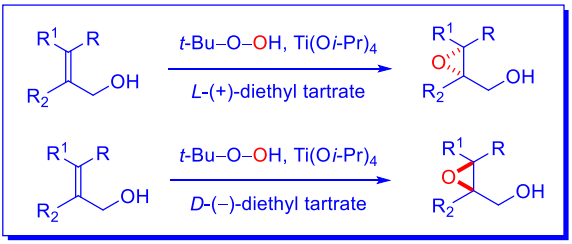
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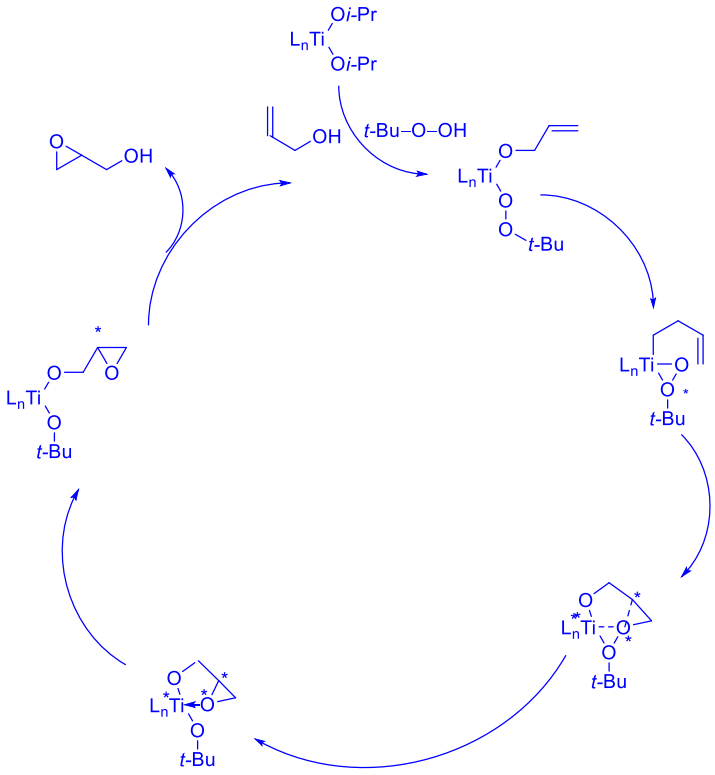
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Sharpless Asymmetric Epoxidation

Enantioselective epoxidation of allylic alcohols using *t*-butyl hydroperoxide (TBHP), titanium tetra-*iso*-propoxide, and optically pure diethyl tartrate (DET).

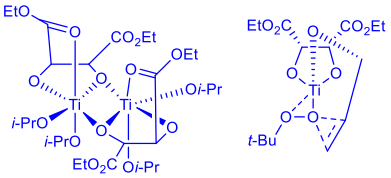


The catalytic cycle:

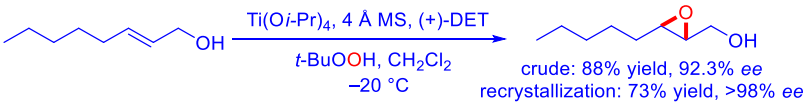


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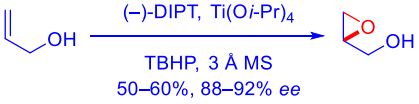
The putative active catalyst:



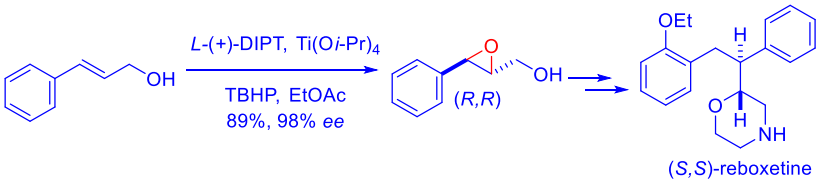
Example 1[3]



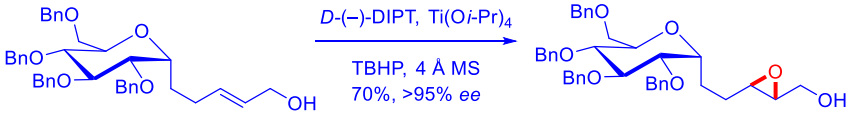
Example 2, DIPT = diisopropyl tartrate[3]



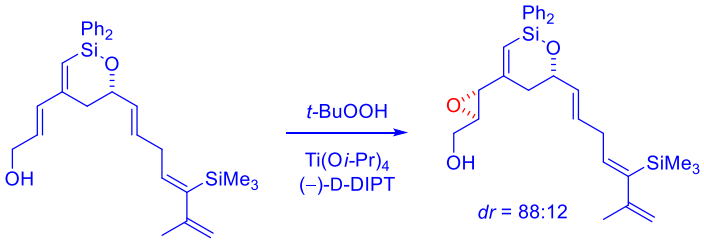
Example 3[11]



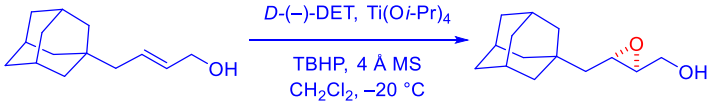
Example 4[12]



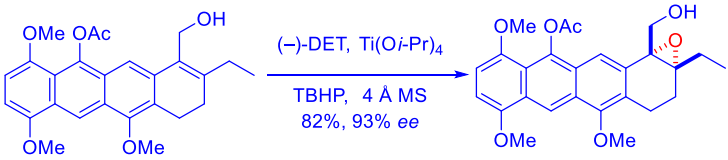
Example 5[14]



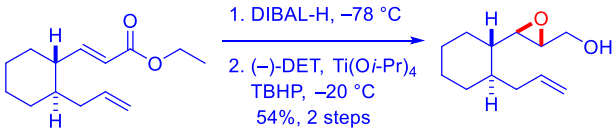
Example 6, Application in medicinal chemistry[16]



Example 7, Total synthesis of (+)-nivetetracyclate A[17]



Example 8, Application in medicinal chemistry[18]



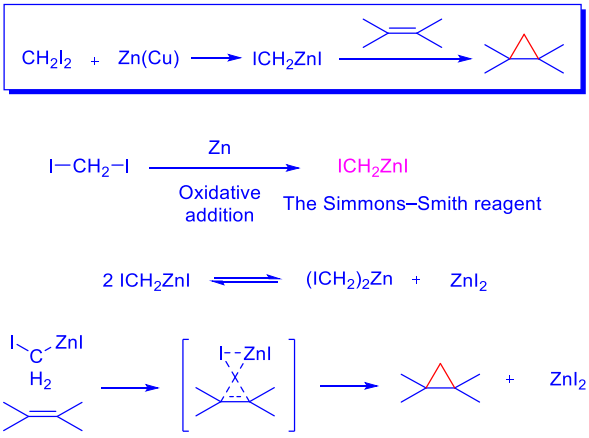
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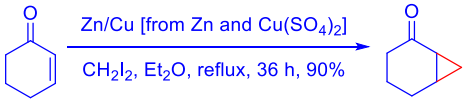
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Simmons–Smith Reaction

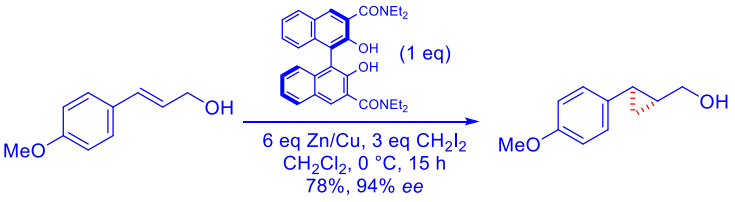
Cyclopropanation of olefins using CH_2I_2 and Zn(Cu).



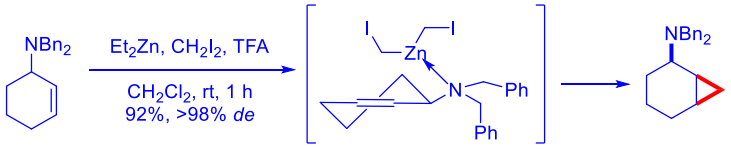
Example 1[2]



Example 2, An asymmetric version[3]

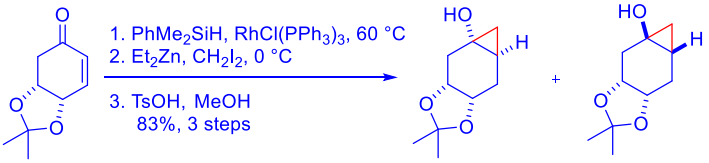


Example 3, Diastereoselective Simmons–Smith cyclopropanations of allylic amines and carbamates[9]

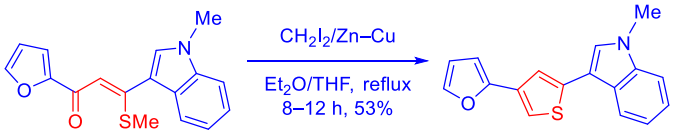


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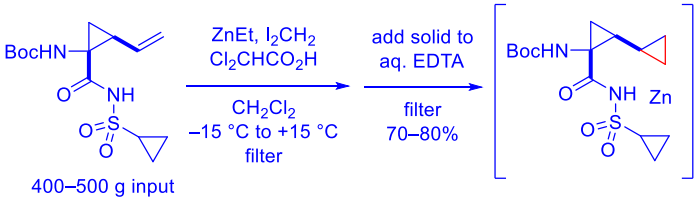
Example 4[10]



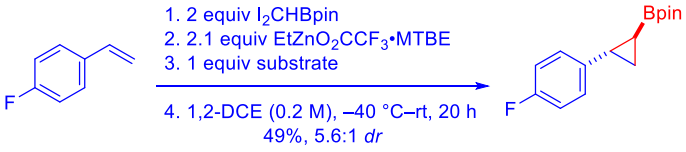
Example 5, Rearrangement after the Simmons–Smith cyclopropanation[12]



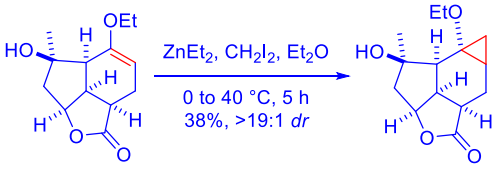
Example 6, EDTA = ethylenediaminetetraacetic acid[13]



Example 7, Diastereoselective borocyclopropanation of allylic ethers using a boromethylzinc carbenoid[14]



Example 8[15]

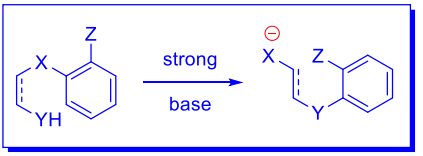


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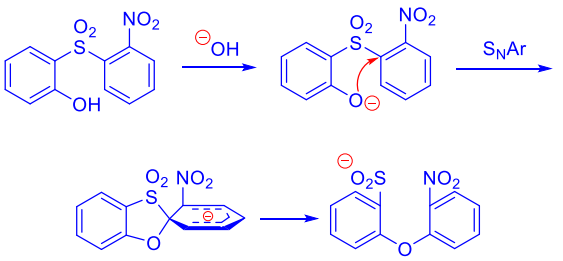
Smiles Rearrangement

Intramolecular nucleophilic aromatic rearrangement. General scheme:



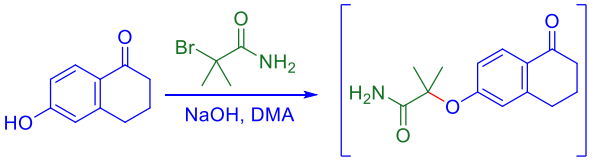
X = S, SO, SO_2, O, CO_2
YH = OH, NHR, SH, CH_2R, CONHR
Z = NO_2, SO_2R

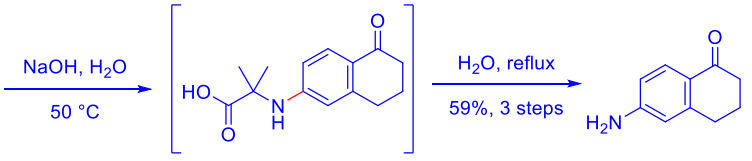
Mechanism:



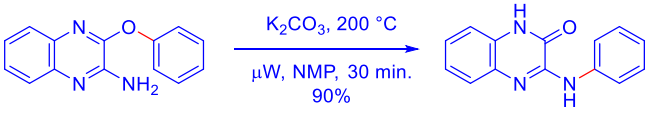
spirocyclic anion intermediate (Meisenheimer complex)

Example 1[7]



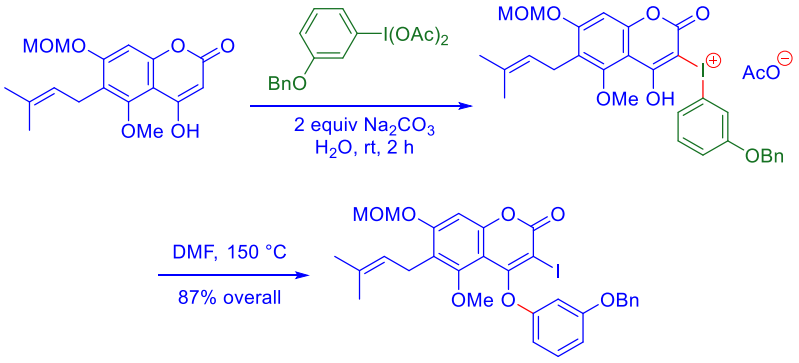


Example 2, Microwave Smiles rearrangement[9]

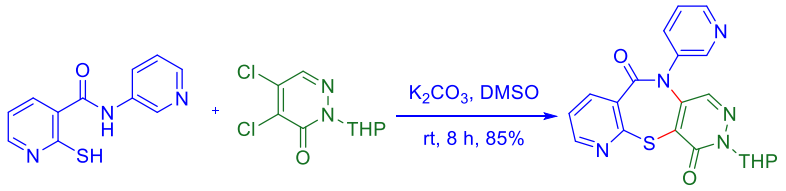


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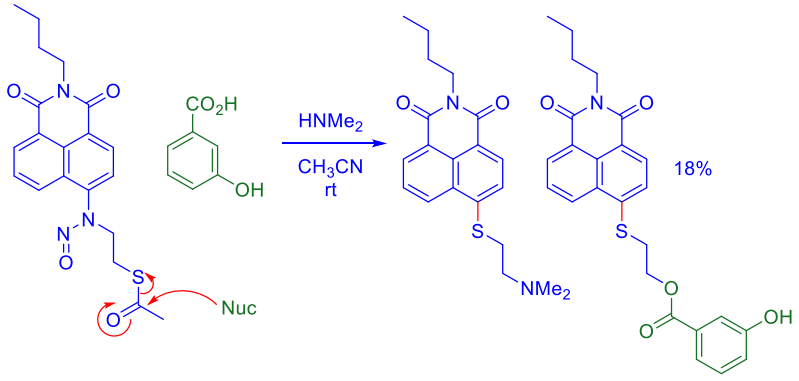
Example 3[10]



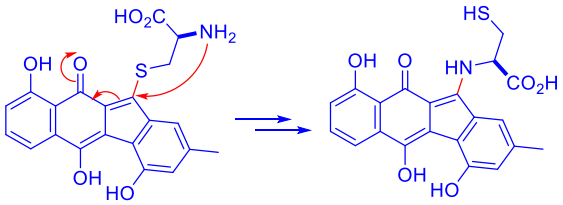
Example 4, The thiol group attacks the chlorine on top first, then Smiles rearrangement ensues[11]



Example 5, Mild chemotriggered generation of a fluorophore-tethered diazoalkane species via Smiles rerrangement[12]



Example 6, S–N-type Smiles rerrangement[14]



Example 7, Phenol to aniline[15]

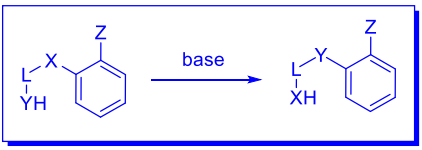


References

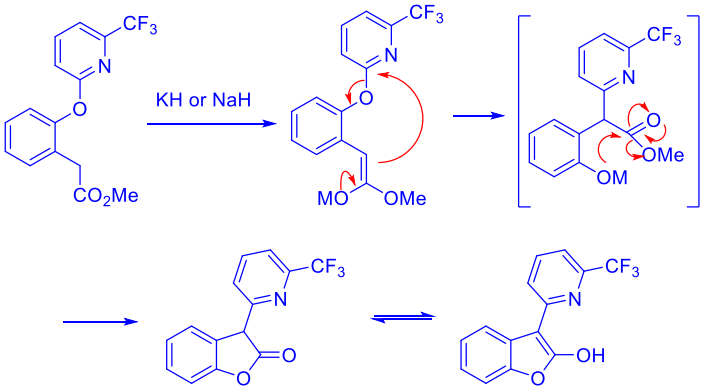
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Truce–Smile Rearrangement

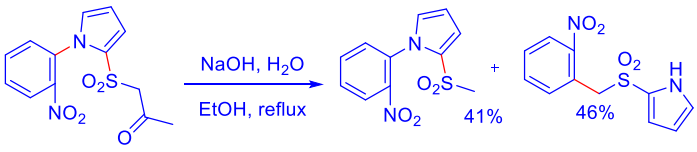
A variant of the Smiles rearrangement where Y is carbon:



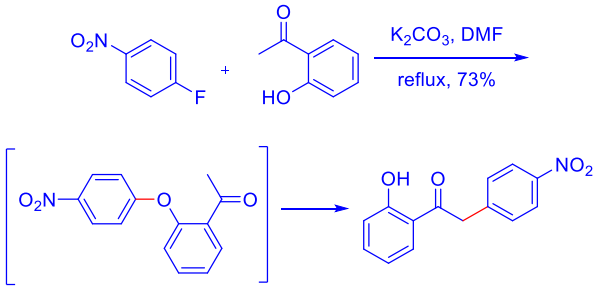
Example 1[6]



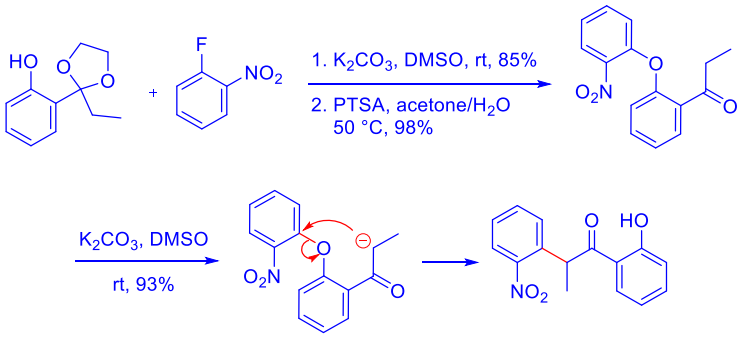
Example 2[7]



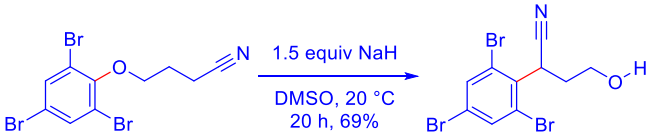
Example 3[8]



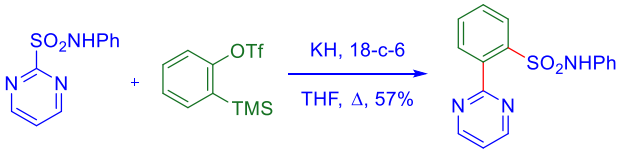
Example 4[10]



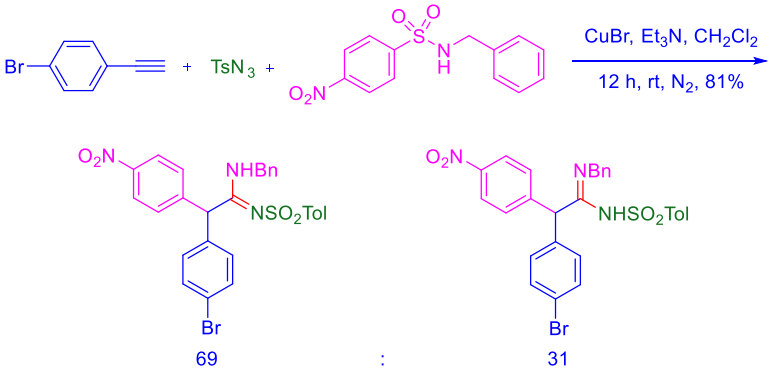
Example 4, Truce–Smile rearrangement of substituted phenylethers[11]



Example 5, A benzyne Truce–Smile rearrangement[12]



Example 6, Copper-catalyzed one-pot approach to α-aryl amidines via Truce–Smile rearrangement[13]

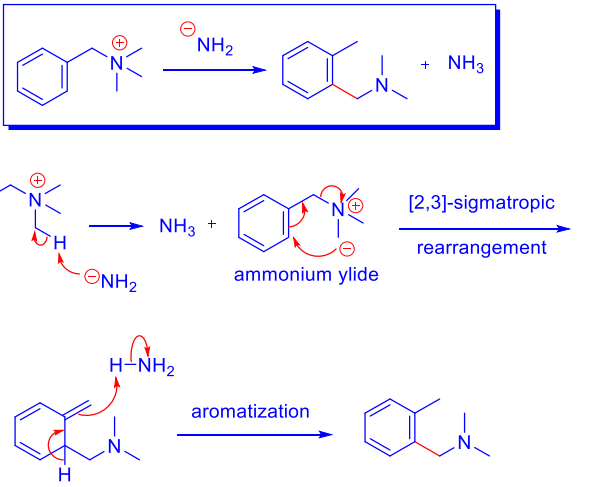


References

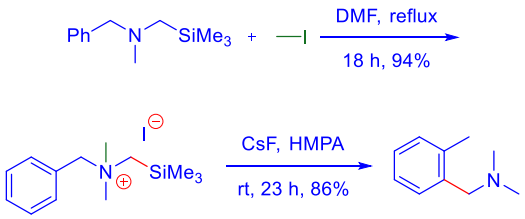
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Sommelet–Hauser Rearrangement

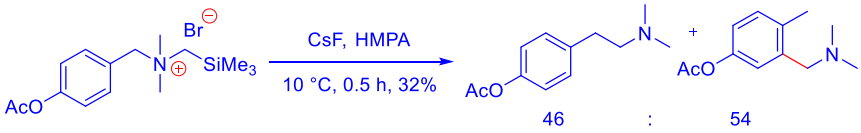
[2,3]-Wittig rearrangement of benzylic quaternary ammonium salts upon treatment with alkali metal amides *via* the ammonium ylide intermediates. *Cf.* Stevens rearrangement.



Example 1, Intermediate investigations[3]

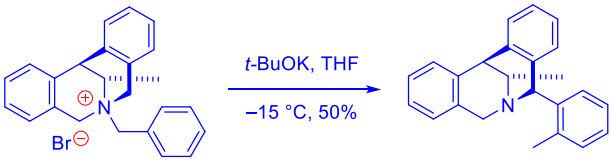


Example 2, Competition between Stevens and Sommelet–Hauser rearrangement[4]

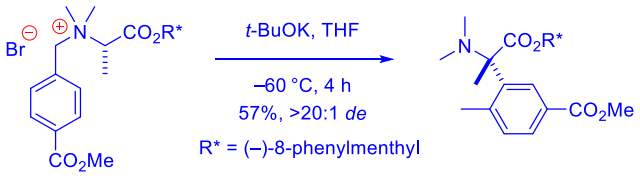


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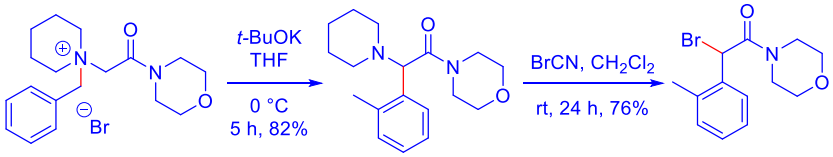
Example 3, Diastereoselective Sommelet–Hauser rearrangement[8]



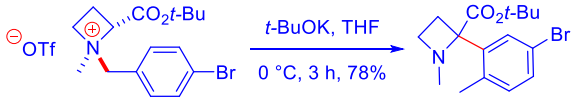
Example 4, Quaternary carbon from a diastereoselective Sommelet–Hauser rearrangement[10]



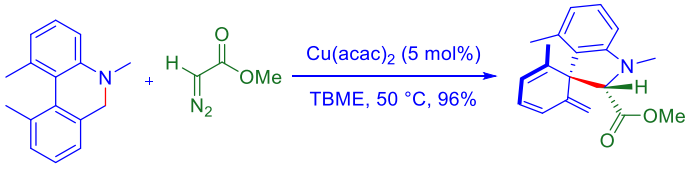
Example 5, Potential method to make amino acids[12]



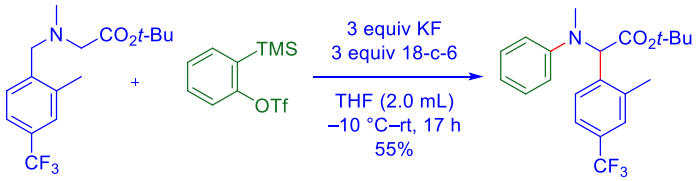
Example 6, Ring-strain effects[13]



Example 7, Cu-catalyzed Sommelet–Hauser rearrangement, resulting in de-aromatization[14]



Example 8, The aryne Sommelet–Hauser rearrangement[15]

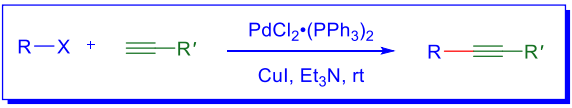


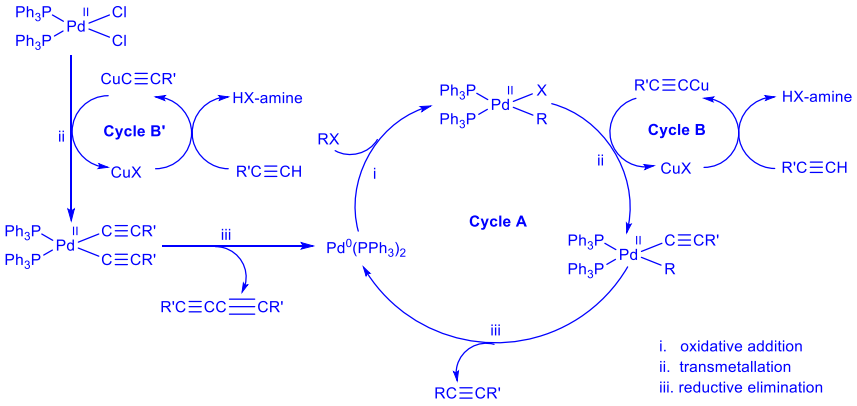
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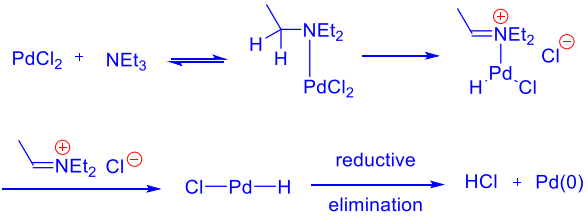
Sonogashira Reaction

Pd/Cu-catalyzed cross-coupling of organohalides with terminal alkynes. *Cf.* Cadiot–Chodkiewicz coupling and Castro–Stephens reaction. The Castro–Stephens coupling uses stoichiometric copper, whereas the Sonogashira variant uses catalytic palladium and copper.

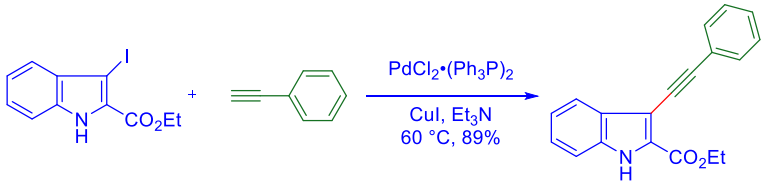




Note that Et_3N may reduce Pd(II) to Pd(0) as well, where Et_3N is oxidized to the iminium ion at the same time:

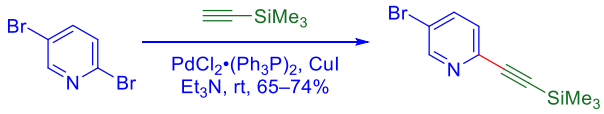


Example 1[2]

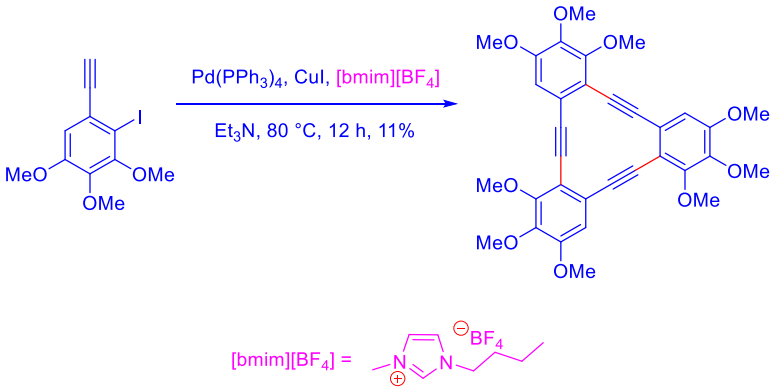


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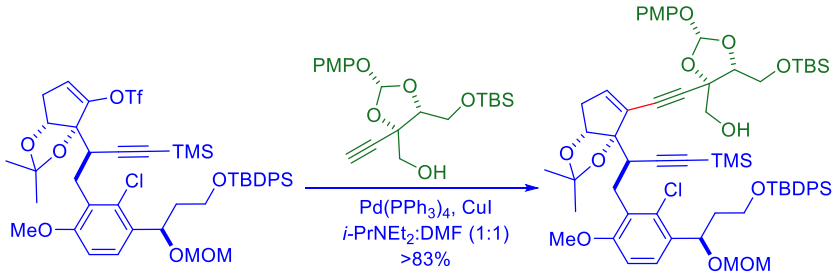
Example 2, Chemoselectivity for 2,5-dibromopyridine[3]



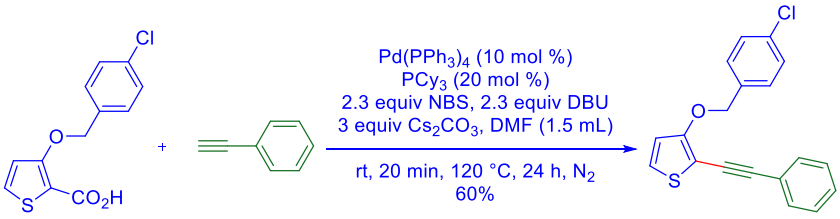
Example 3, Homocoupling in the ionic liquid[8]



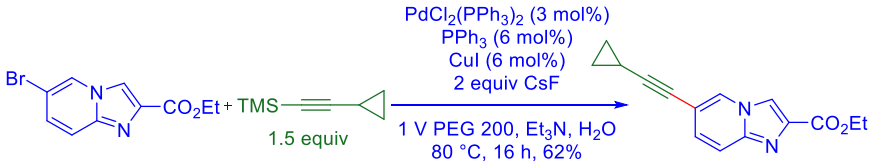
Example 4, Total synthesis of the maduropeptin chromophore aglycon[9]



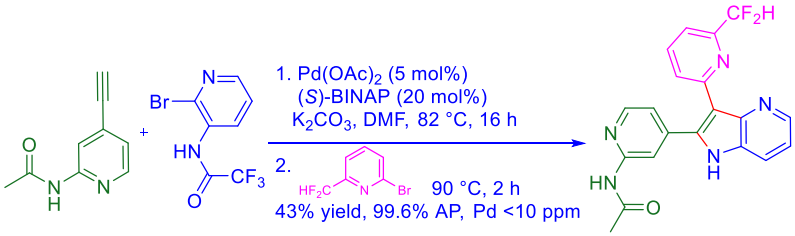
Example 5, Pd-catalyzed decarboxylative Sonogashira reaction via a decarboxylative bromination[14]



Example 6, Sila-Sonogashira reaction[15]



Example 7, One-pot sequential Sonogashira and Cacchi reactions[16]

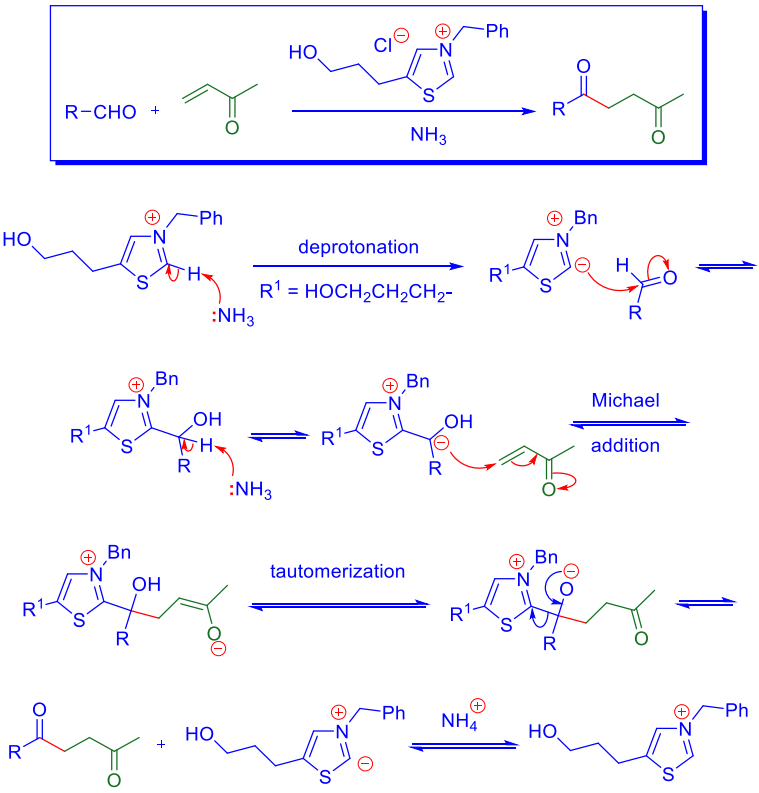


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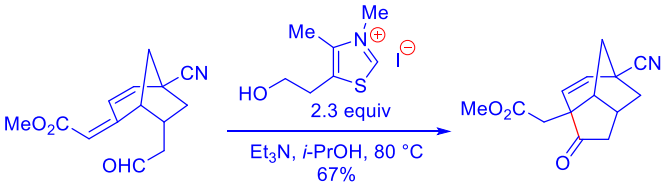
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Stetter Reaction

1,4-Dicarbonyl derivatives from aldehydes and α,β-unsaturated ketones and esters. The thiazolium catalyst serves as a safe surrogate for $^{-}$CN. Also known as the Michael–Stetter reaction. *Cf*. Benzoin condensation.

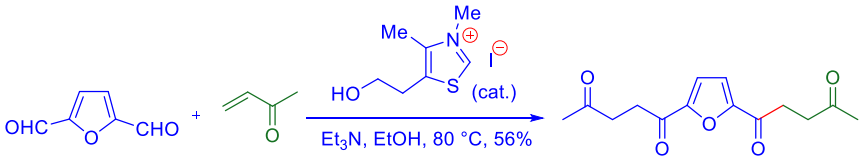


Example 1, Intramolecular Stetter reaction[2]

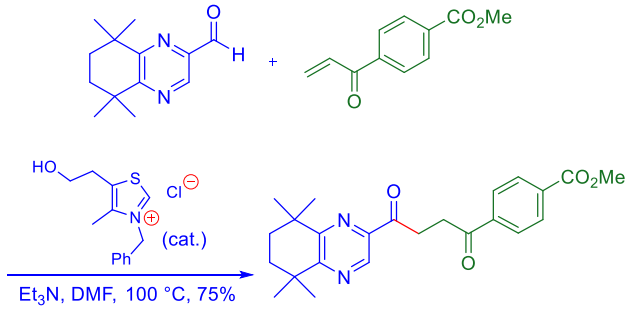


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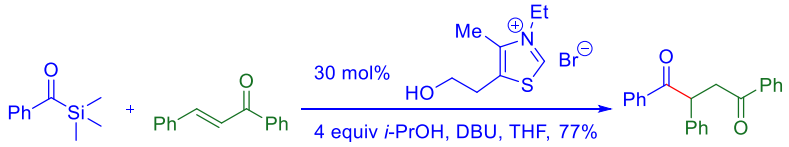
Example 2[3]



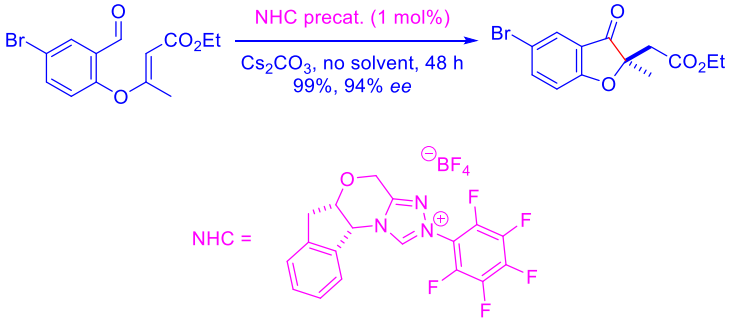
Example 3[5]



Example 4, Sila-Stetter reaction[9]

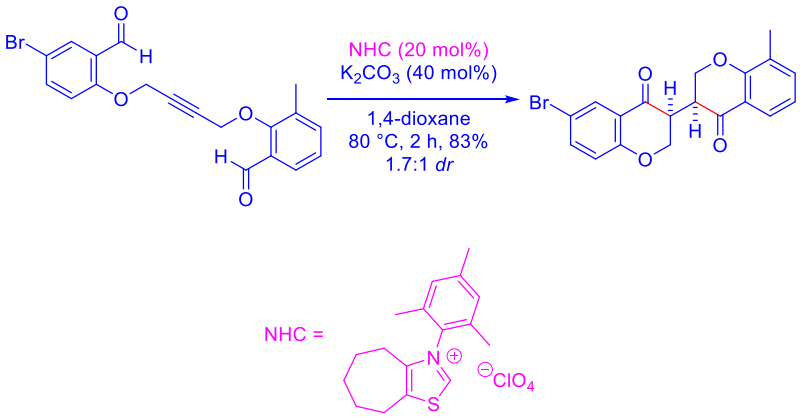


Example 5, NHC-catalyzed intramolecular asymmetric Stetter reaction under solvent-free conditions[13]

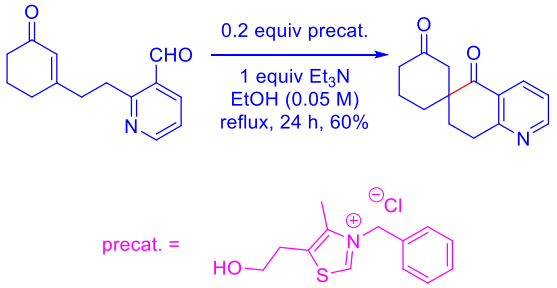


NHC = N-Heterocyclic carbene

Example 6, Construction of bisbenzopyrone via N-heterocyclic carbene-catalyzed intramolecular hydroacylation-Stetter reaction cascade[14]



Example 7, Intramolecular Stetter reaction[15]



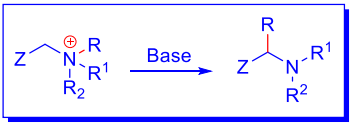
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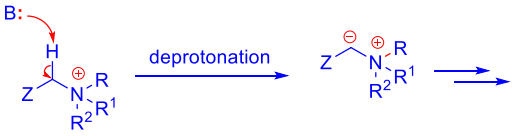
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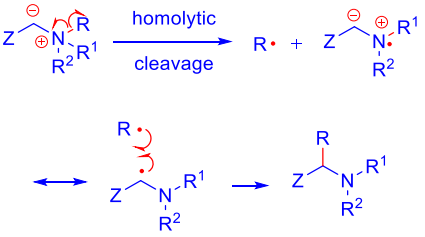
Stevens Rearrangement

A quaternary ammonium salt containing an electron-withdrawing group Z on one of the carbons attached to the nitrogen is treated with a strong base to give a rearranged tertiary amine. *Cf.* Sommelet–Hauser rearrangement.

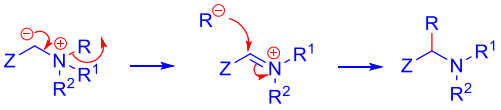




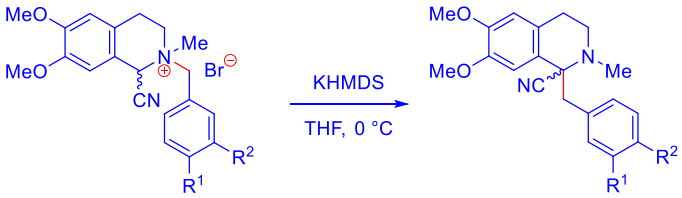
The contemporary radical mechanism:



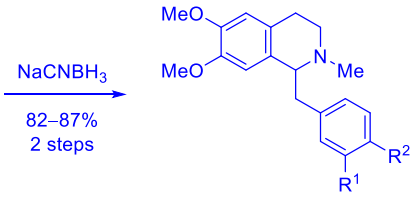
The original ionic mechanism:



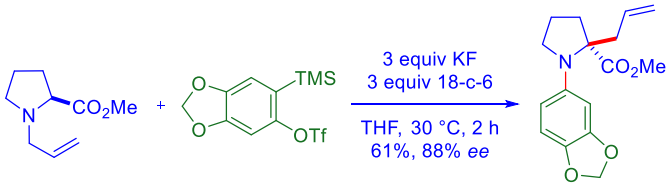
Example 1, Stevens Rearrangement/Reduction Sequence[10]



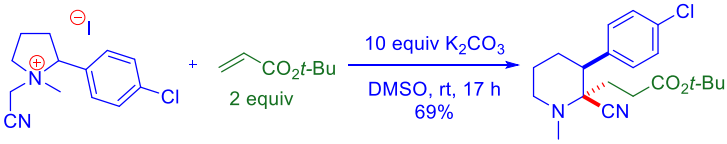
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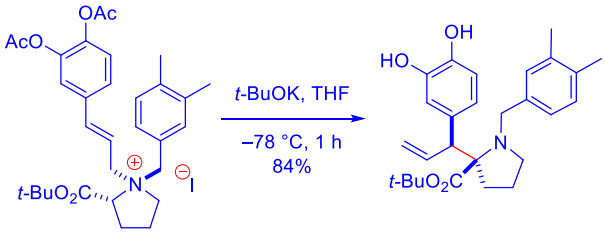
Example 2, The aryne-induced enantiospecific [2,3]-Stevens rearrangement[11]



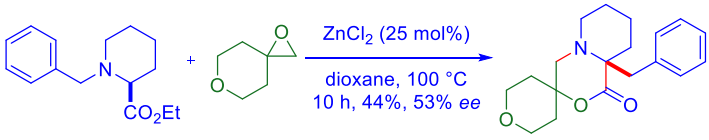
Example 3, Michael addition/[1,2]-Stevens rearrangement[12]



Example 4, Construction of Cα-substituted prolinate via [2,3]-Stevens rearrangement[13]



Example 5, Epoxide-mediated Stevens rearrangement of L-pipecolinic acid derivatives[14]

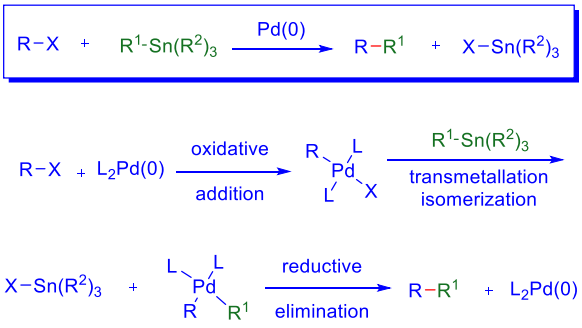


References

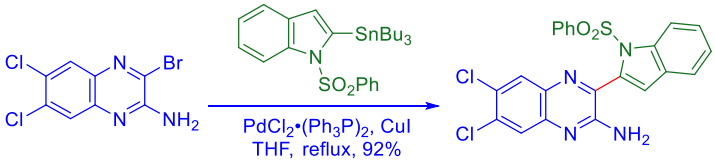
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Stille Coupling

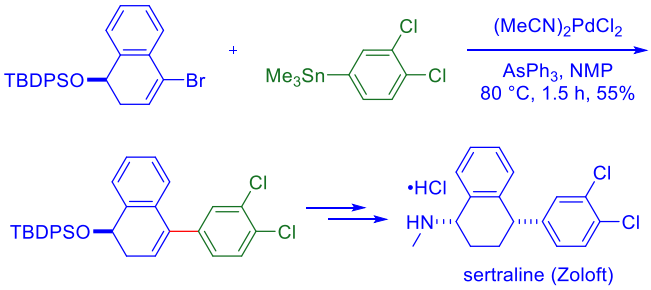
Palladium-catalyzed cross-coupling reaction of organostannanes with organic halides, triflates, *etc*. For the catalytic cycle, see Kumada coupling.



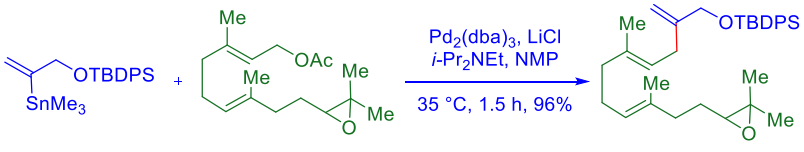
Example 1[4]



Example 2[5]

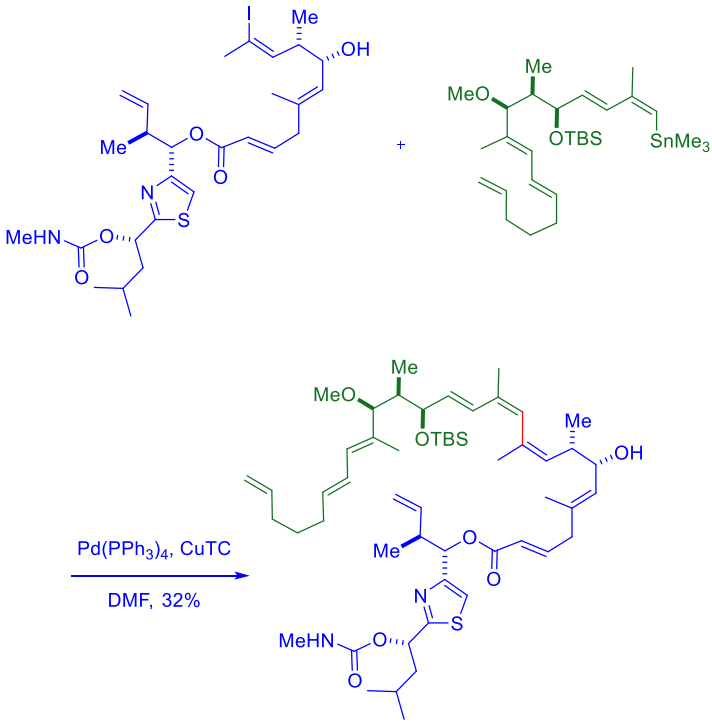


Example 3, π-Allyl Stille coupling[8]

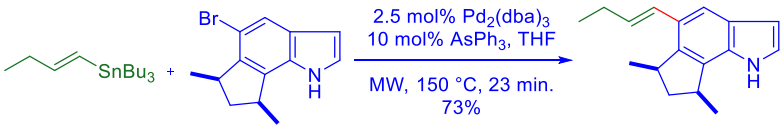


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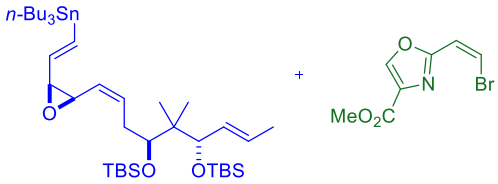
Example 4, In total synthesis[9]

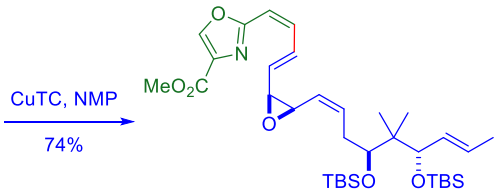


Example 5, In total synthesis[11]

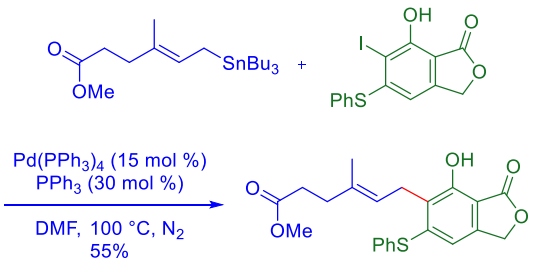


Example 6, In total synthesis[13]

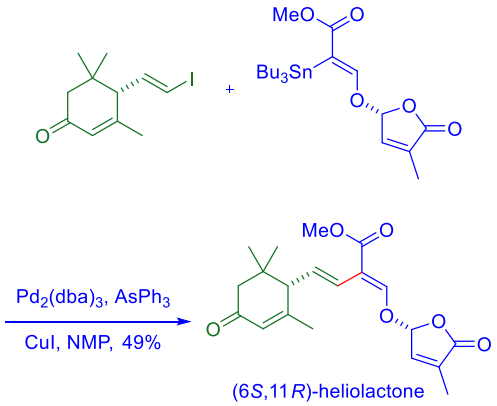




Example 7, Allylic sp^3 stannane[14]



Example 8[15]



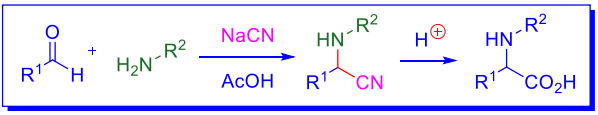
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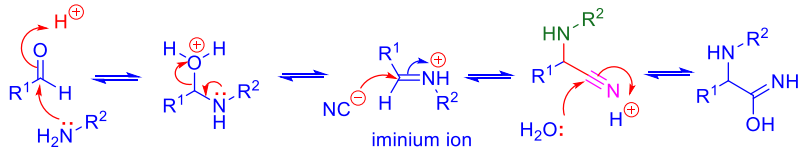
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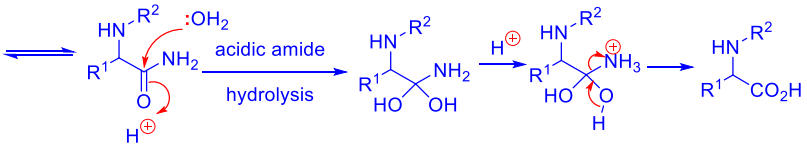
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Strecker Amino Acid Synthesis

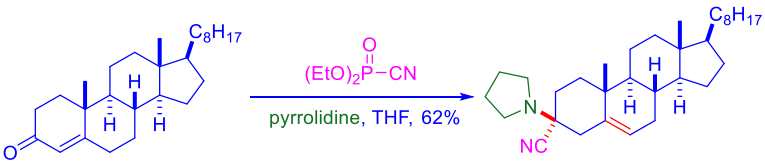
Sodium cyanide-promoted condensation of aldehyde, or ketone, with an amine to afford α-amino nitrile, which may be hydrolyzed to an α-amino acid.



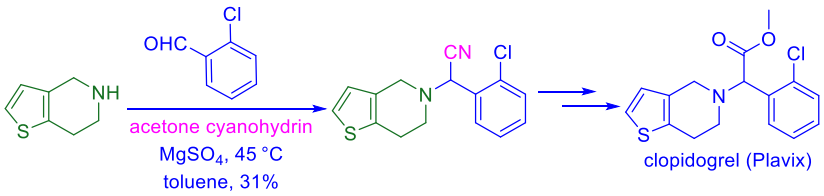




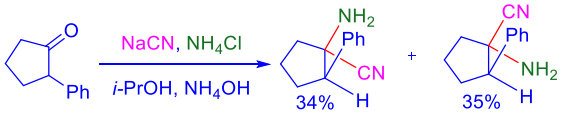
Example 1, Soluble cyanide source[2]



Example 2[3]

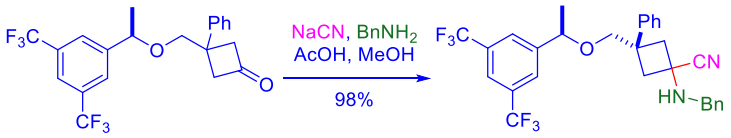


Example 3[8]

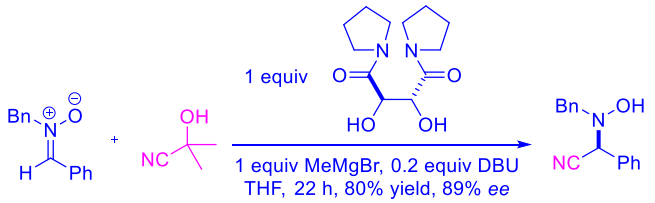


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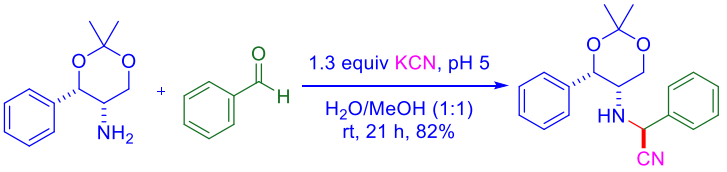
Example 4[9]



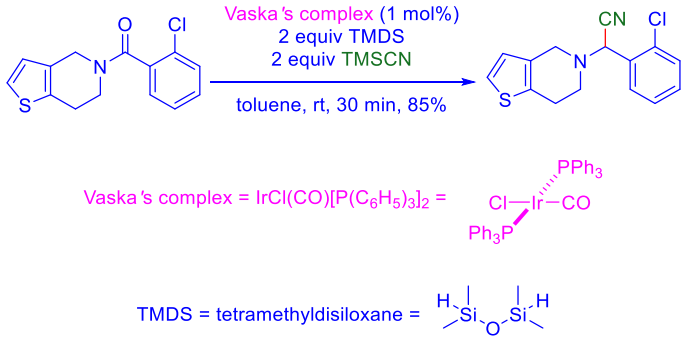
Example 5, Asymmetric Strecker-type reaction of nitrones[11]



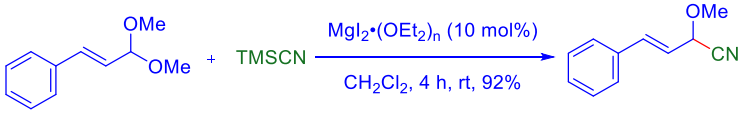
Example 6[13]



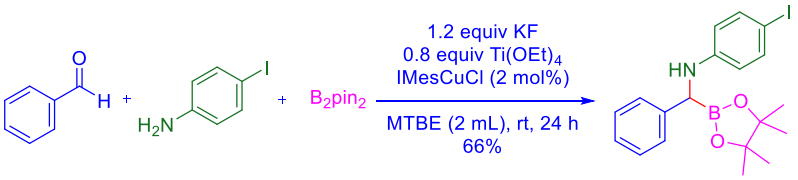
Example 7, Iridium-catalyzed reductive Strecker reaction of amides[14]



Example 8, Chemoselective Strecker reaction of acetals catalyzed by MgI_2-etherate[15]



Example 9, Borono-Strecker reaction[16]

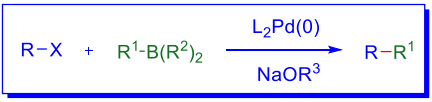


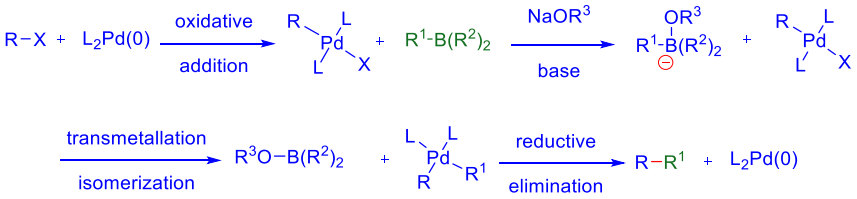
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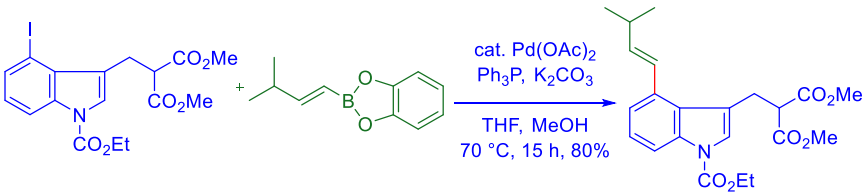
Suzuki–Miyaura Coupling

Palladium-catalyzed cross-coupling reaction of organoboranes with organic halides, triflates, *etc*. In the presence of a base (transmetalation is reluctant to occur without the activating effect of a base). For the catalytic cycle, see Kumada coupling.

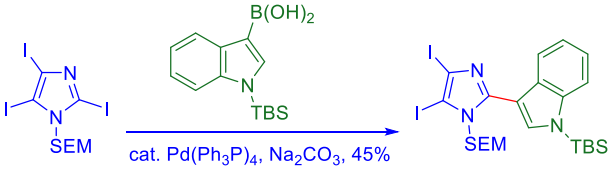




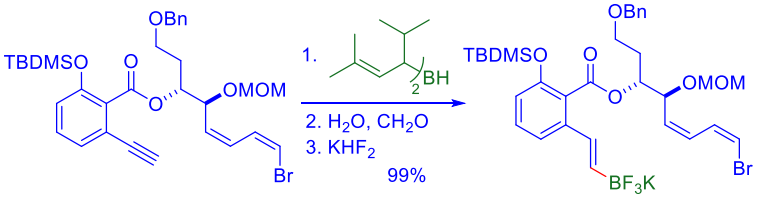
Example 1[2]



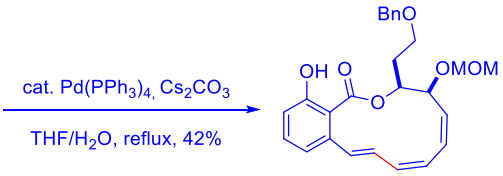
Example 2[4]



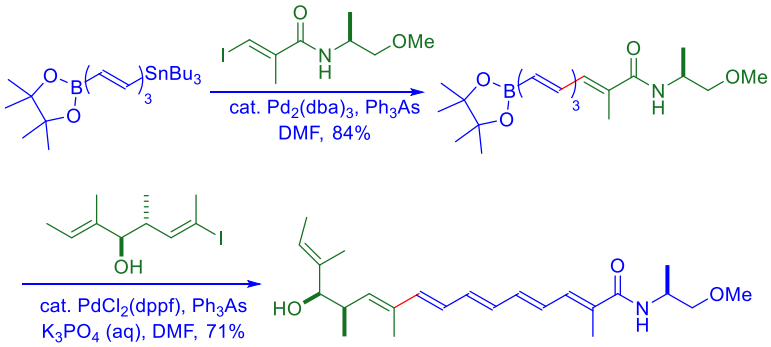
Example 3, Intramolecular Suzuki–Miyaura coupling[8]



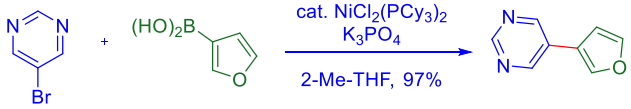
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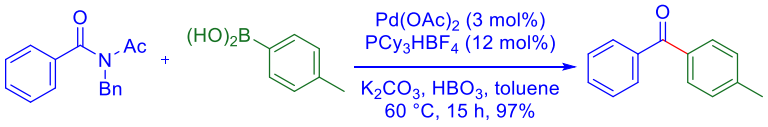
Example 4, Stille coupling followed by Suzuki coupling[9]



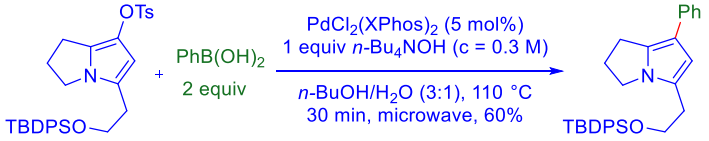
Example 5, Nickel-catalyzed Suzuki–Miyaura coupling[12]



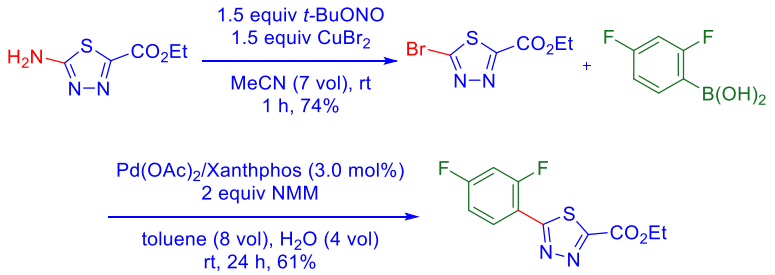
Example 6, Suzuki–Miyaura coupling of acyclic amides in catalytic carbon-nitrogen bond cleavage[15]



Example 7, Palladium-catalyzed Suzuki–Miyaura coupling of pyrrolyl sulfonates[16]



Example 8, Sequential Sandmeyer bromination and room-temperature Suzuki–Miyaura coupling (1 kg scale)[17]

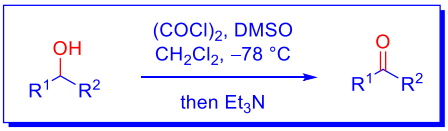


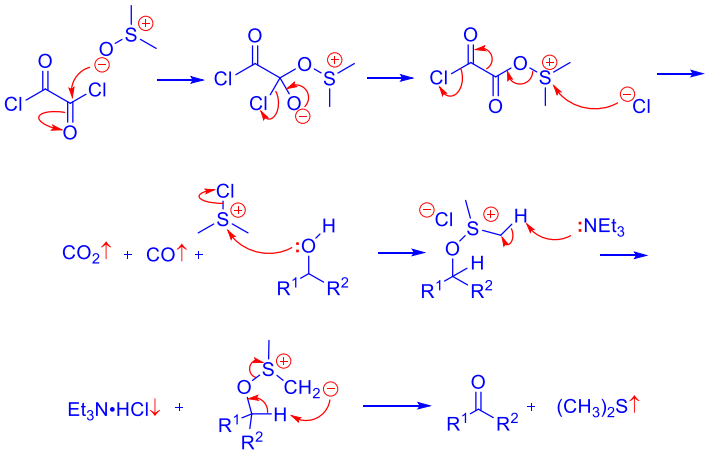
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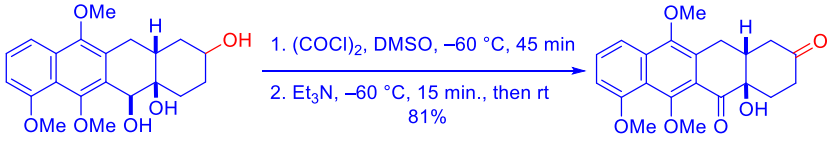
Swern Oxidation

Oxidation of alcohols to the corresponding carbonyl compounds using $(COCl)_2$, DMSO, and quenching with Et_3N.

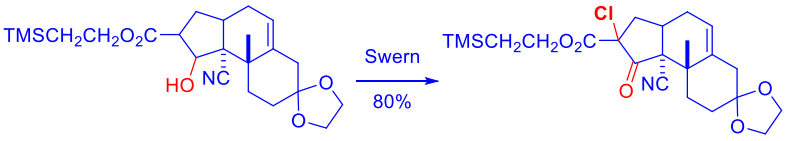




Example 1[2]

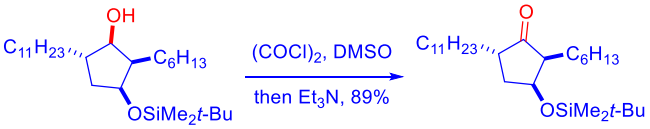


Example 2[3]

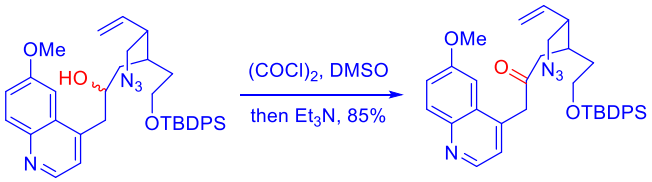


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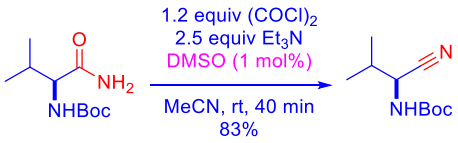
Example 3[5]



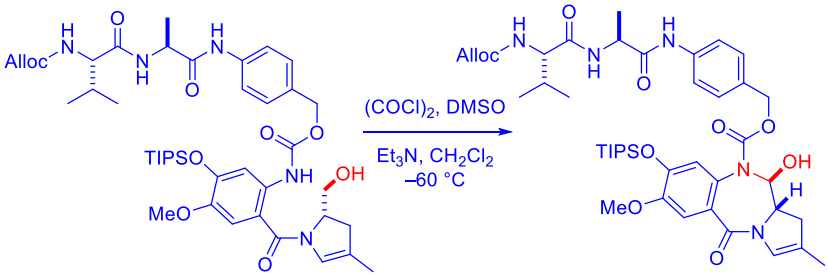
Example 4[7]



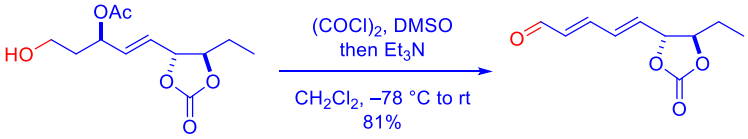
Example 5, Nitriles from primary amides under a catalytic Swern oxidation conditions[12]



Example 6, Scale-up synthesis of tesirine[13]



Example 7, Synthesis of resolvin E3[14]

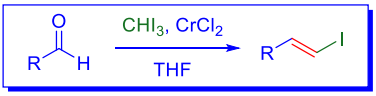


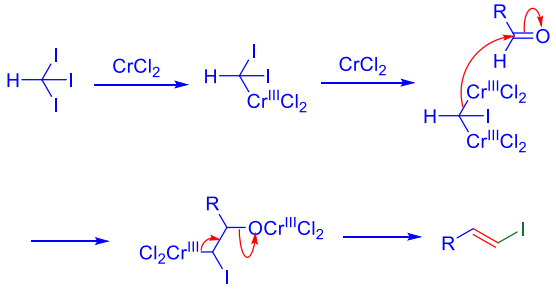
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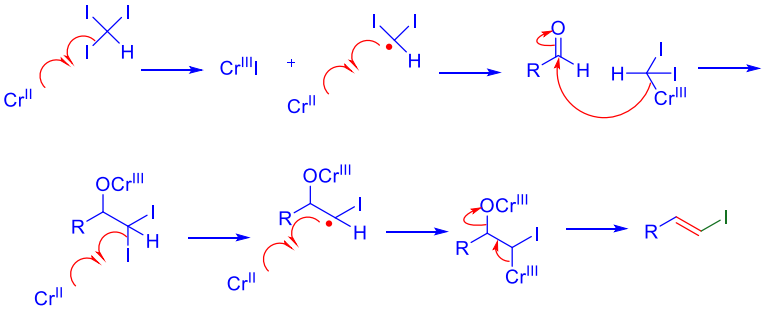
Takai Reaction

Stereoselective conversion of an aldehyde to the corresponding *E*-vinyl iodide using CHI_3 and $CrCl_2$.

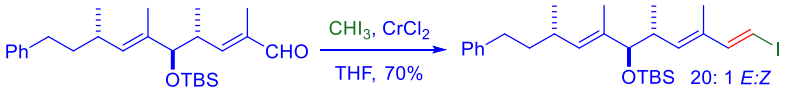




A radical mechanism was proposed[10]

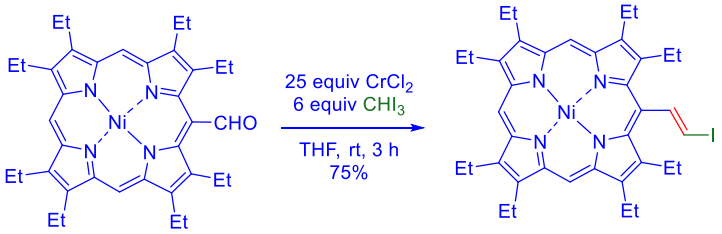


Example 1[2]

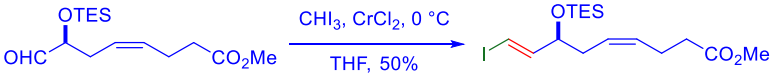


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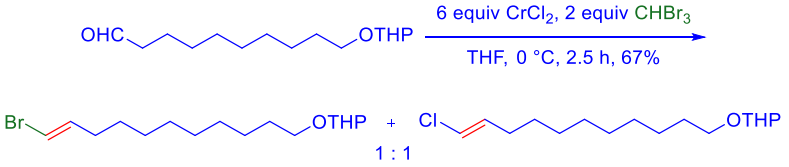
Example 2[3]



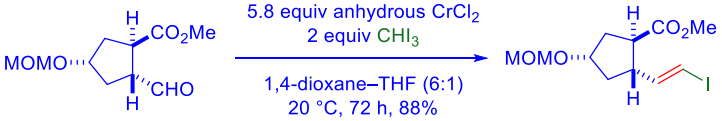
Example 3[4]



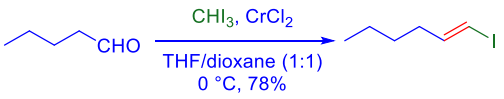
Example 4, A Br/Cl variant[9]



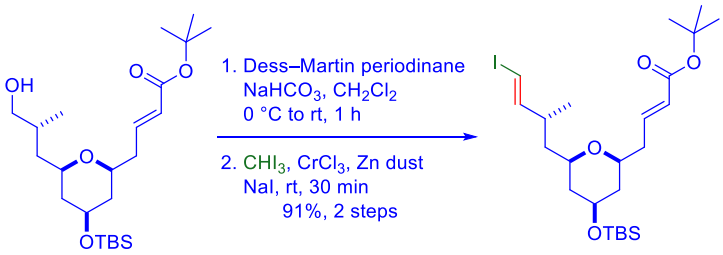
Example 5[10]



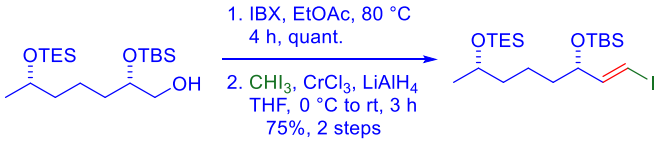
Example 5[10]



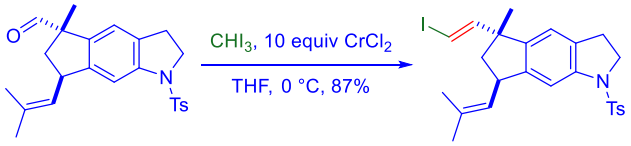
Example 6, Synthesis toward mandelalide A[12]



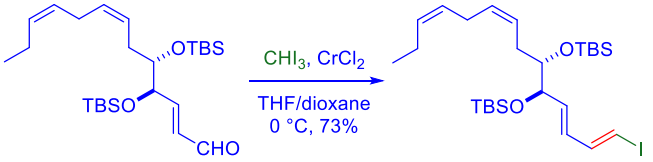
Example 7, Synthesis toward pestalotioprolide E[13]



Example 8, Synthesis toward raputindole A[14]



Example 9, Synthesis toward MaR2$_{n\text{-}3\ DPA}$[15]



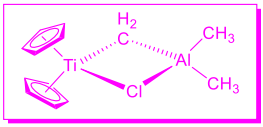
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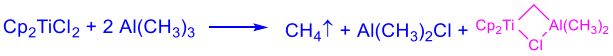
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Tebbe Reagent

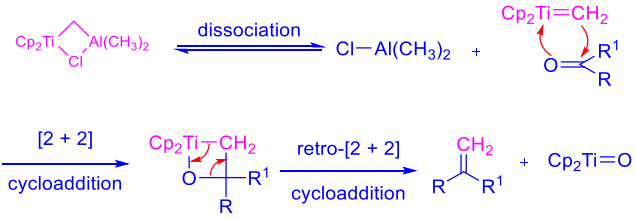
The Tebbe reagent, μ-chlorobis(cyclopentadienyl)(dimethylaluminium)-μ-methylenetitanium, transforms a carbonyl compound to the corresponding *exo*-olefin.



Preparation:[2,6]



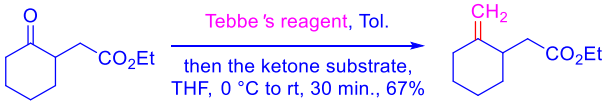
Mechanism:[3]



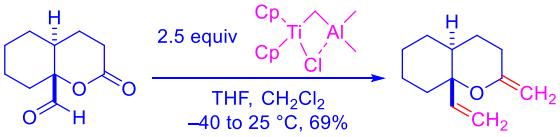
oxatitanacyclobutane

formation of the strong Ti=O bond is the driving force.

Example 1, Chemoselective for ketone in the presence of an ester[2]

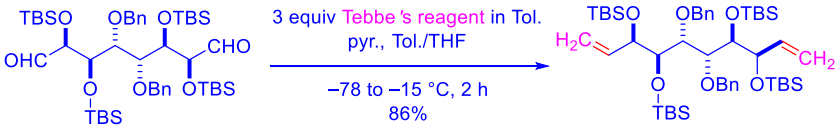


Example 2, Double Tebbe[4]

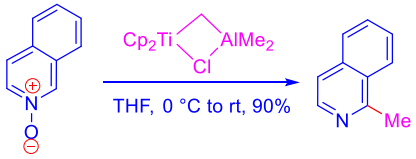


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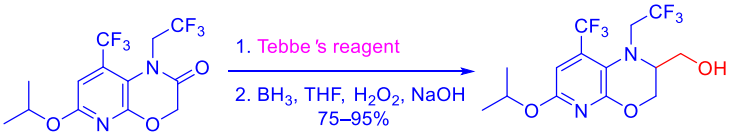
Example 3, Double Tebbe[5]



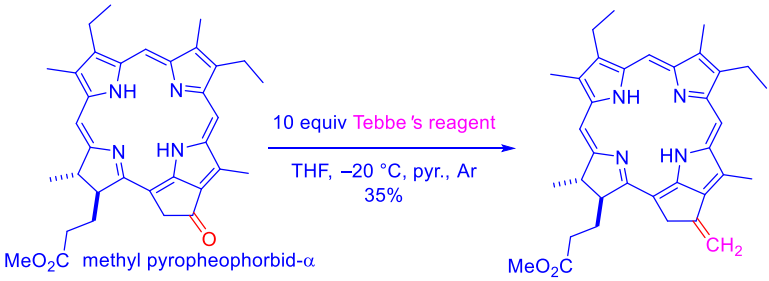
Example 4, *N*-Oxide[6]



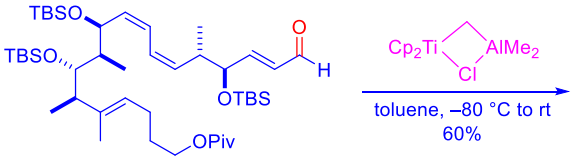
Example 5, Amide[11]

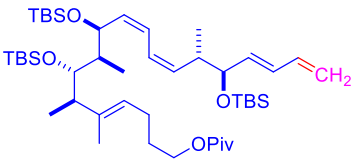


Example 6, Olefination of methyl pyropheophorbid-α (chlorophyll derivative)[14]

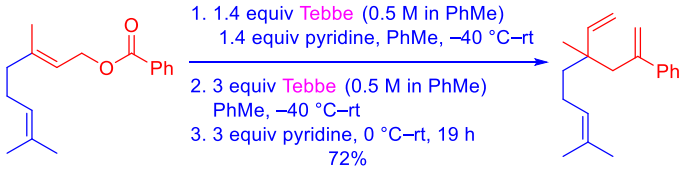


Example 7, Synthesis toward a leiodermatolide analog[15]





Example 8, A methylenation–Claisen–methylenation cascade[16]

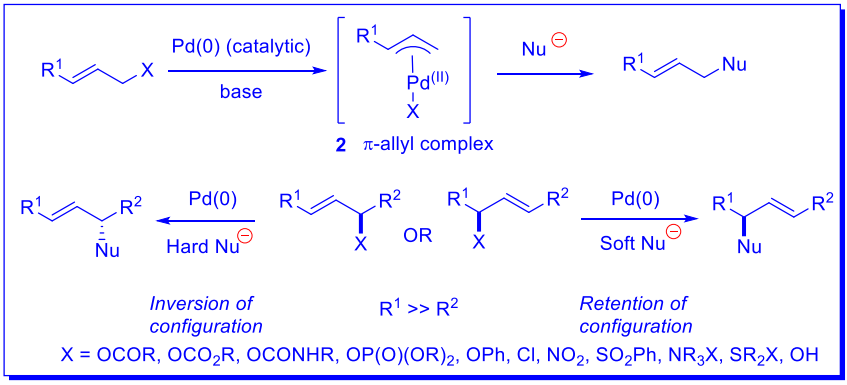


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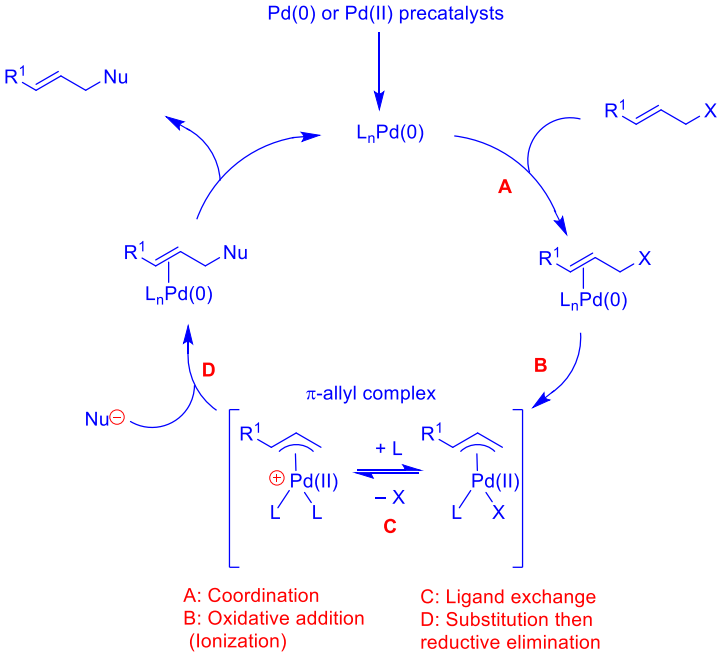
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Tsuji–Trost Reaction

The Tsuji–Trost reaction is the palladium-catalyzed substitution of allylic leaving groups by carbon nucleophiles. These reactions proceed via π-allylpalladium intermediates.

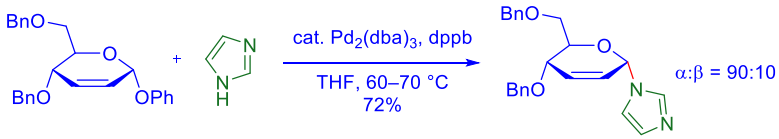


The catalytic cycle:

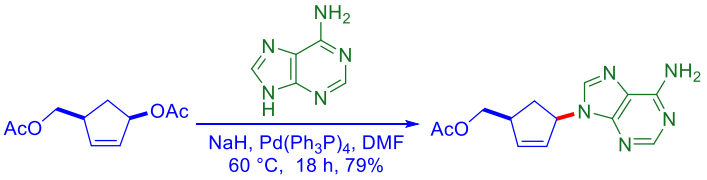


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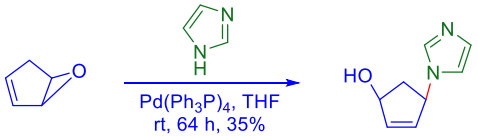
Example 1, Allylic ether[3]



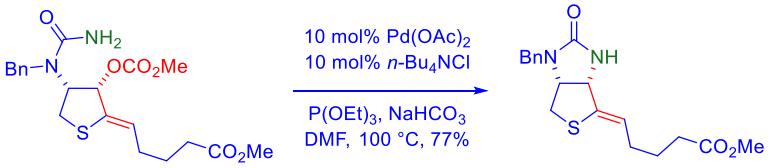
Example 2, Allylic acetate[3]



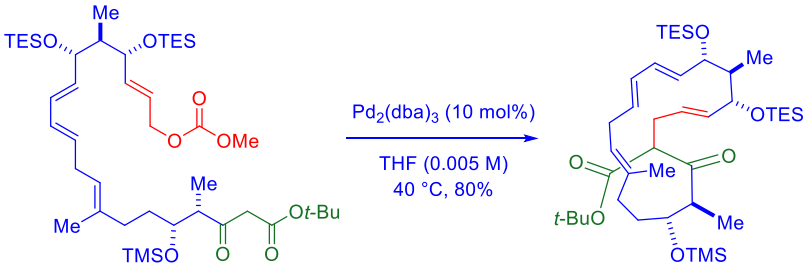
Example 3, Allylic epoxide[5]



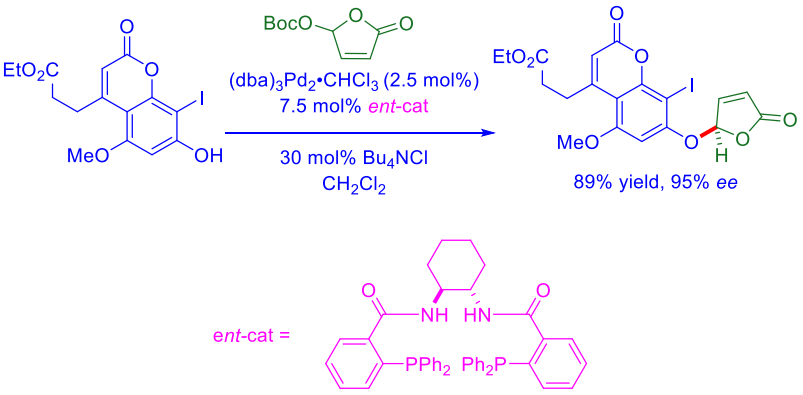
Example 4, Intramolecular Tsuji–Trost reaction[6]



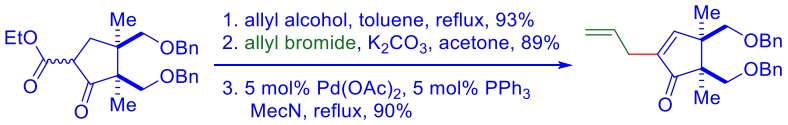
Example 5, Intramolecular Tsuji–Trost reaction[7]



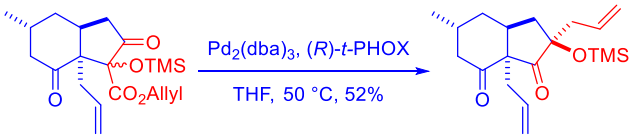
Example 6, Asymmetric Tsuji–Trost reaction[8]



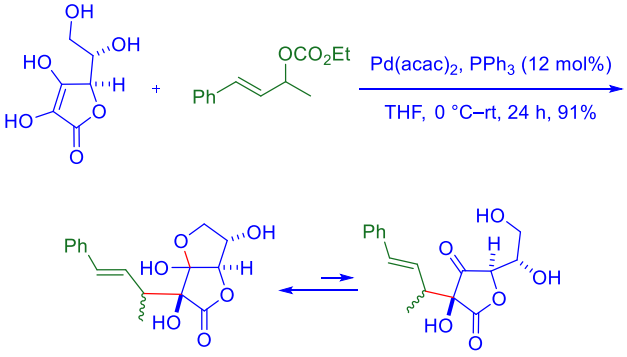
Example 7, Tsuji–Trost decarboxylation–dehydrogenation sequence[12]

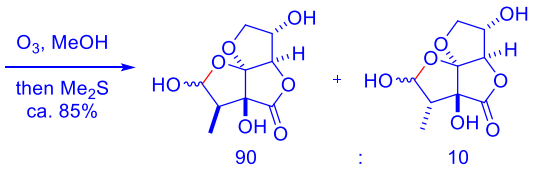


Example 8, Intramolecular Tsuji–Trost reaction[13]

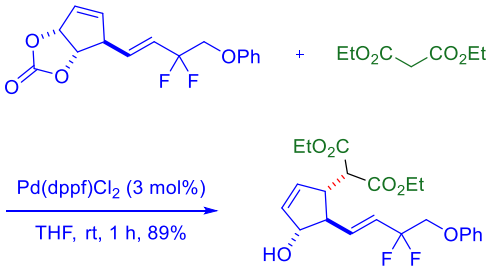


Example 9, Stereoselective Tsuji–Trost alkylation[14]





Example 10, Diethyl malonate as the nucleophile[15]

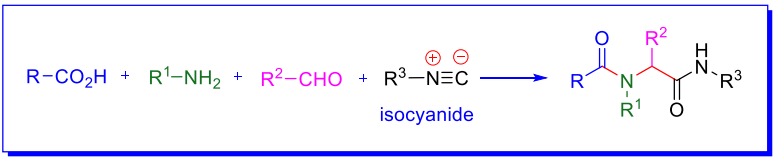


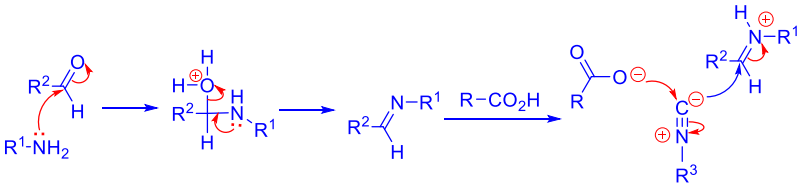
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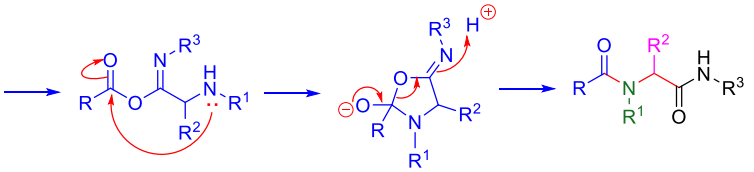
Ugi Reaction

Four-component condensation (4CC) of carboxylic acids, *C*-isocyanides, amines, and carbonyl compounds to afford diamides. Also known as four-component reaction (4CR). *Cf.* Passerini reaction.

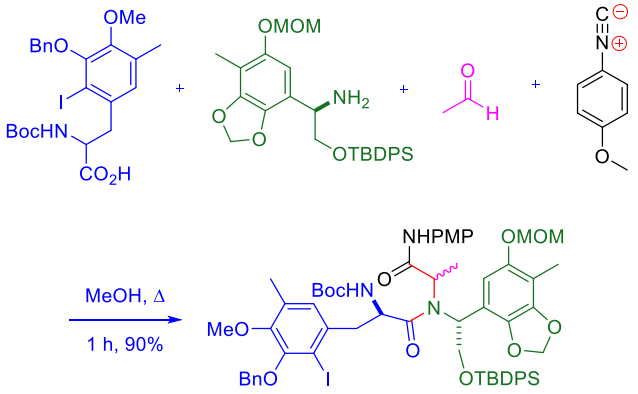




imine

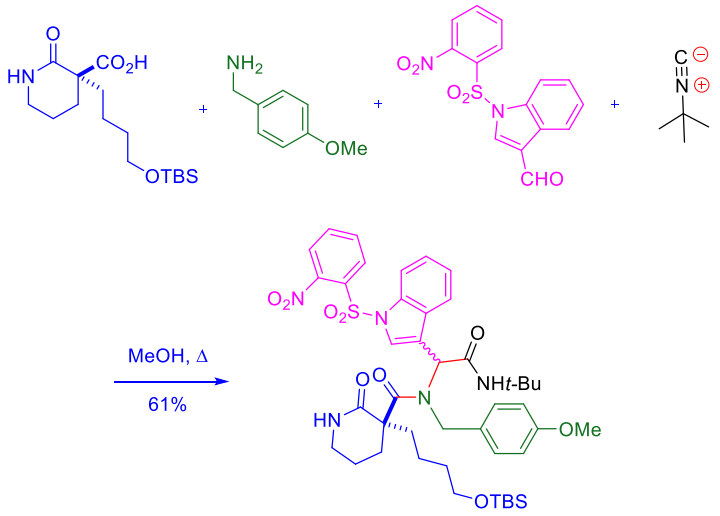


Example 1[2]

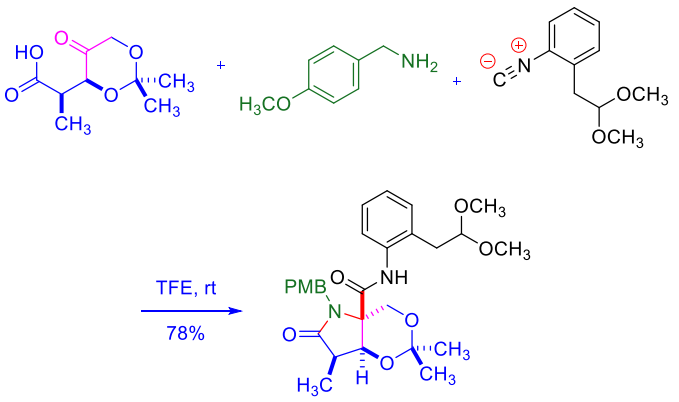


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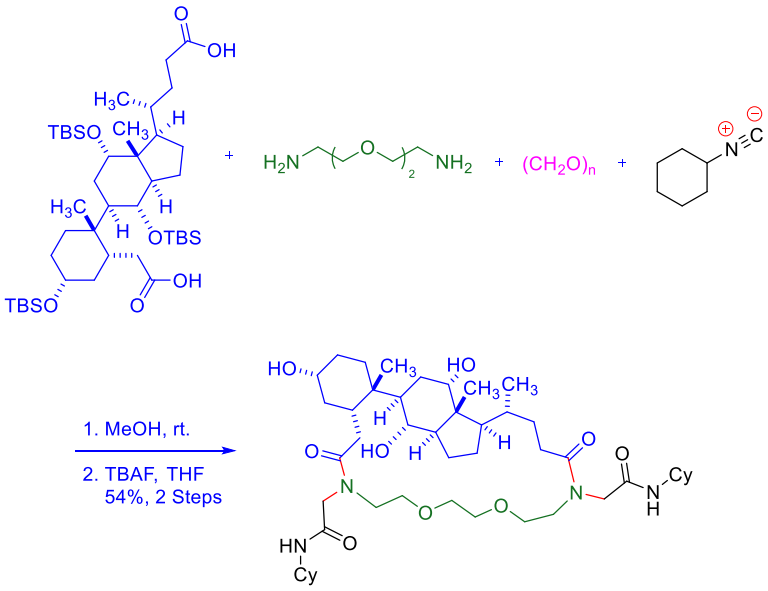
Example 2[5]



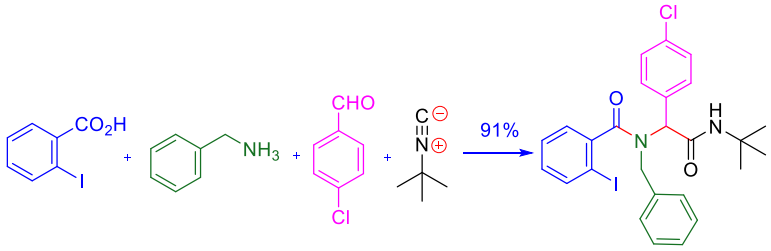
Example 3[7]



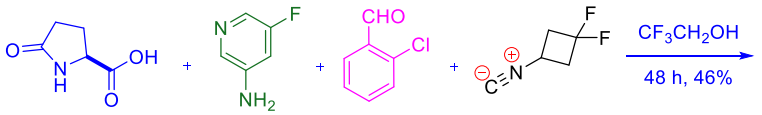
Example 4, “Double whammy” Ugi reaction[8]

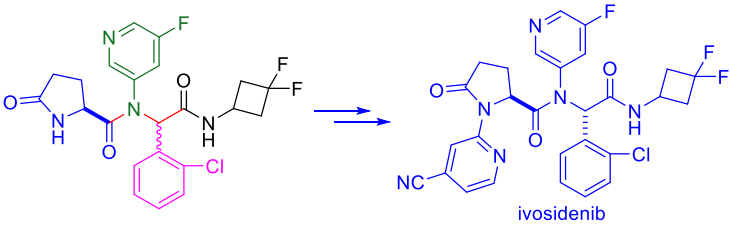


Example 5[11]

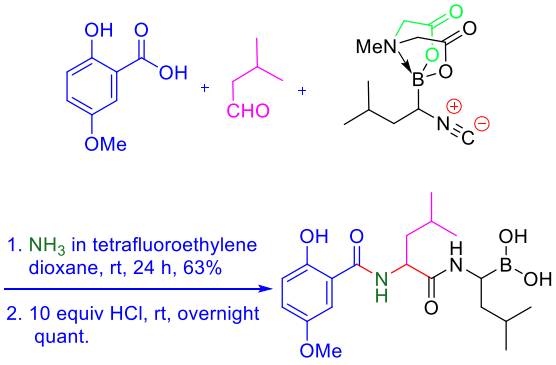


Example 6, Synthesis of ivosidenib (Tibsovo), an isocitrate dehydrogenase 1 (IDH1) inhibitor[12]

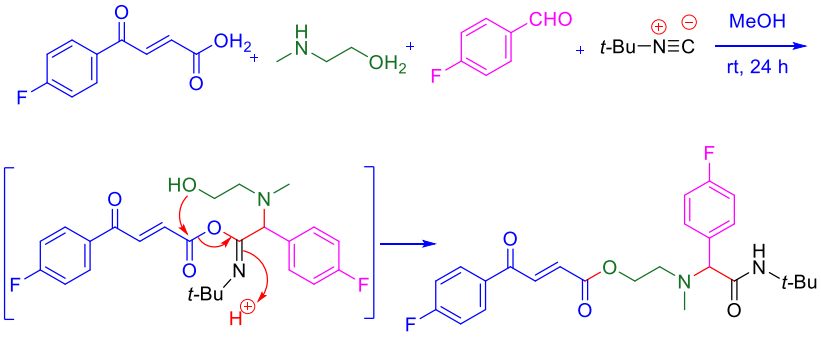




Example 7, Boron-based peptidomimetics as potent inhibitors of human caseinolytic protease P(ClpP)[13]



Example 8, A lead thioredoxin reductase (TrxR) inhibitor[14]



References

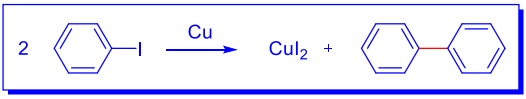
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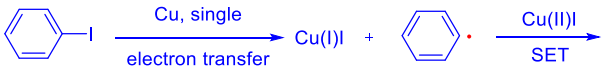
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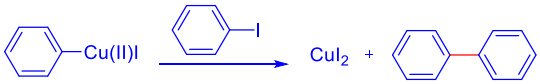
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Ullmann Coupling

Homocoupling of aryl iodides in the presence of Cu or Ni or Pd to afford biaryls.

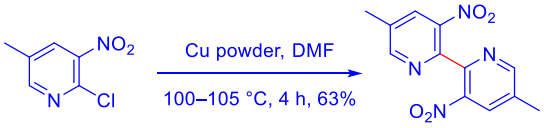




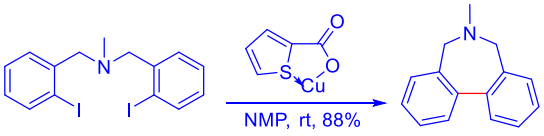


The overall transformation of PhI to PhCuI is an oxidative addition process.

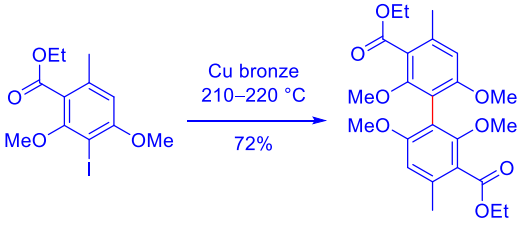
Example 1[3]



Example 2, CuTC-catalyzed Ullmann coupling, CuTC = Copper(I)-thiophene-2-carboxylate[4]

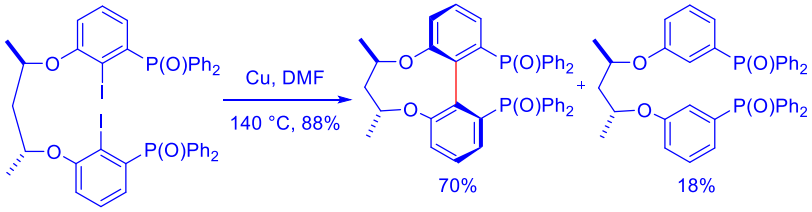


Example 3[5]

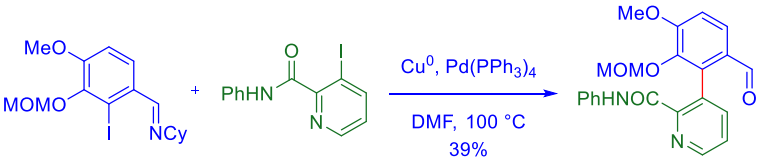


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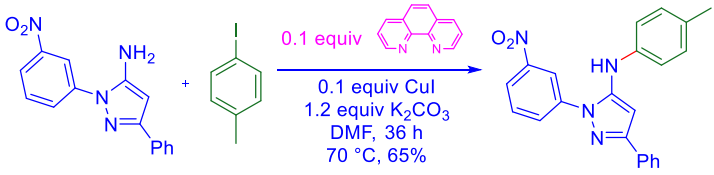
Example 4[8]



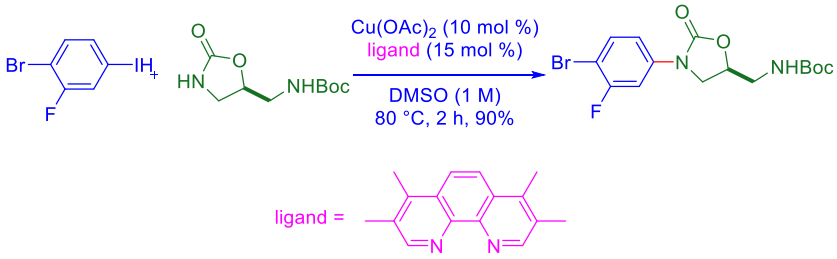
Example 5[9]



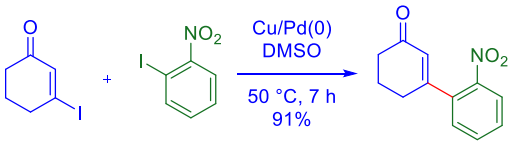
Example 6, Ullman-type C–N coupling[11]



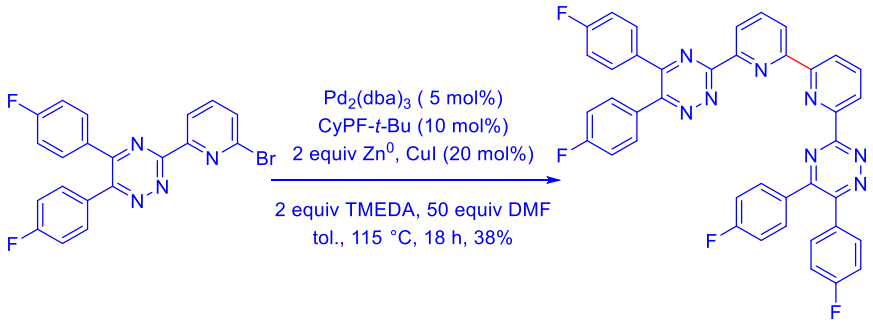
Example 7, Ullman-type C–N coupling[12]



Example 8, Palladium-catalyzed Ullman coupling[13]



Example 8, Palladium-catalyzed Ullman-type coupling[13]

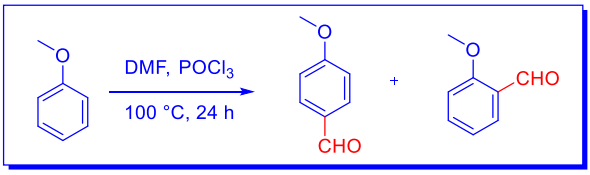


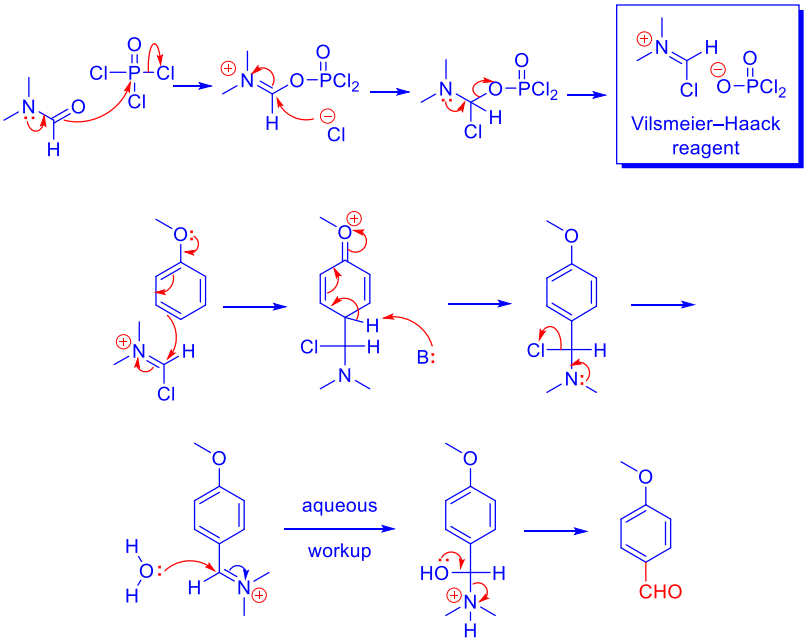
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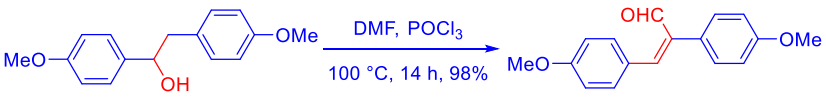
Vilsmeier–Haack Reaction

The Vilsmeier–Haack reagent, a chloroiminium salt, is a weak electrophile. Therefore, the Vilsmeier–Haack reaction works better with electron-rich carbocycles and heterocycles.



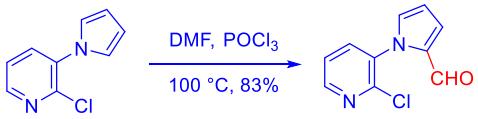


Example 1[2]

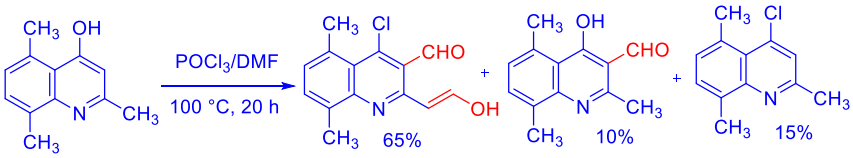


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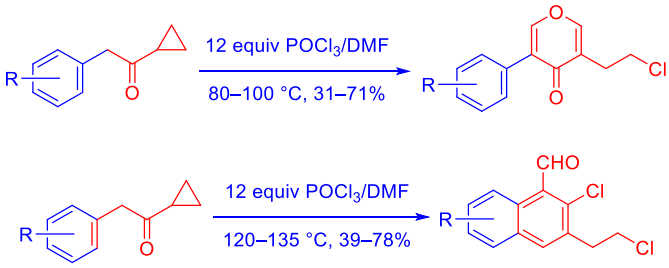
Example 2[3]



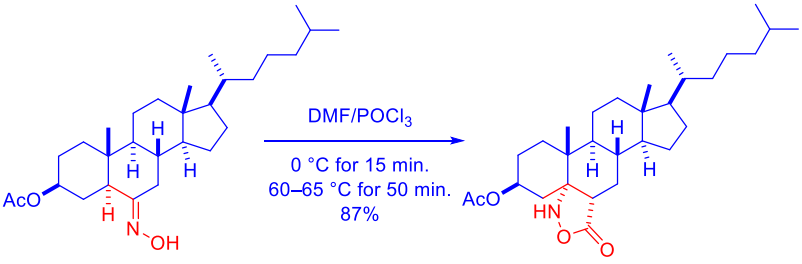
Example 3[9]



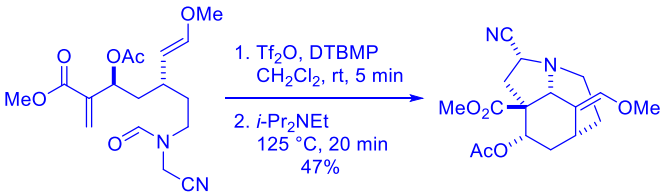
Example 4, Reaction outcomes differ as temperature differs[10]



Example 5, An interesting mechanism[11]

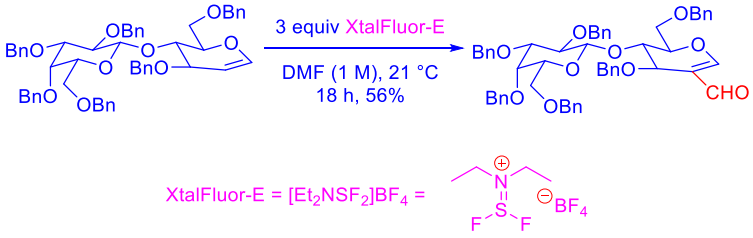


Example 6, One-pot Vilsmeier–Haack cyclization and azomethine ylide cycloaddition[12]

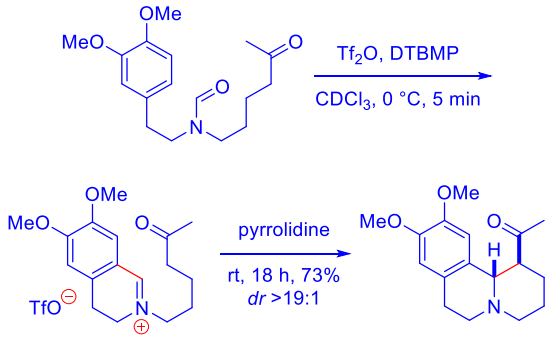


DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine

Example 7, XtalFluor-E as an alternative to $POCl_3$ in the formylation of C2-glycal[13]



Example 8, Sequential one-pot Vilsmeier–Haack and organocatalyzed Mannich cyclization[14]



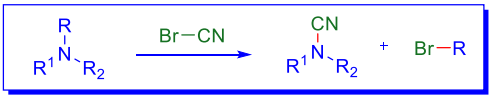
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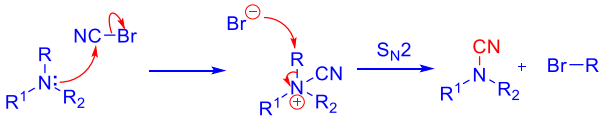
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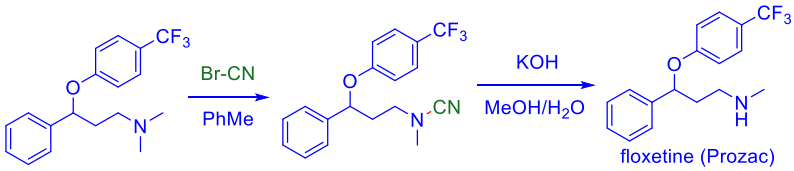
von Braun Reaction

Different from the von Braun degradation reaction (amide to nitrile), the von Braun reaction refers to the treatment of tertiary amines with cyanogen bromide, resulting in a substituted cyanamide.

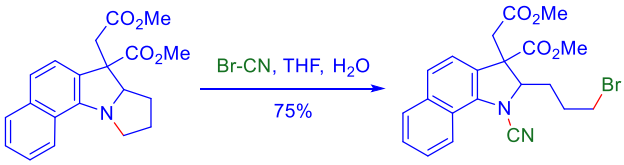




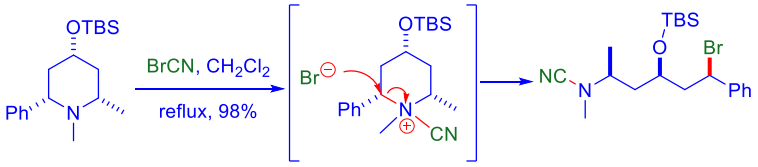
Example 1[4]



Example 2[5]

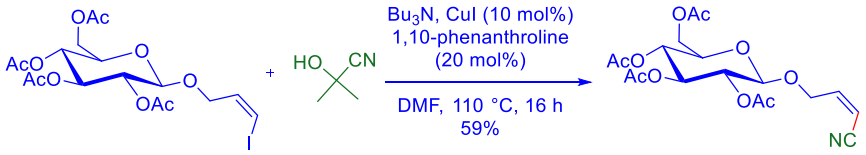


Example 3[9]

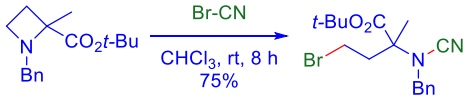


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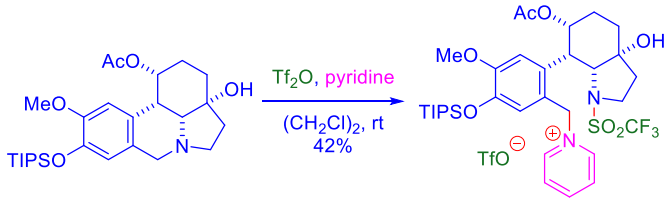
Example 4, A vinylic Rosenmund–von Braun reaction[11]



Example 5, Ring-opening of azetidine by the von Braun reaction[12]



Example 6, Cleavage of C–N bond via ring opening[13]

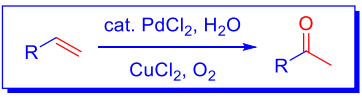


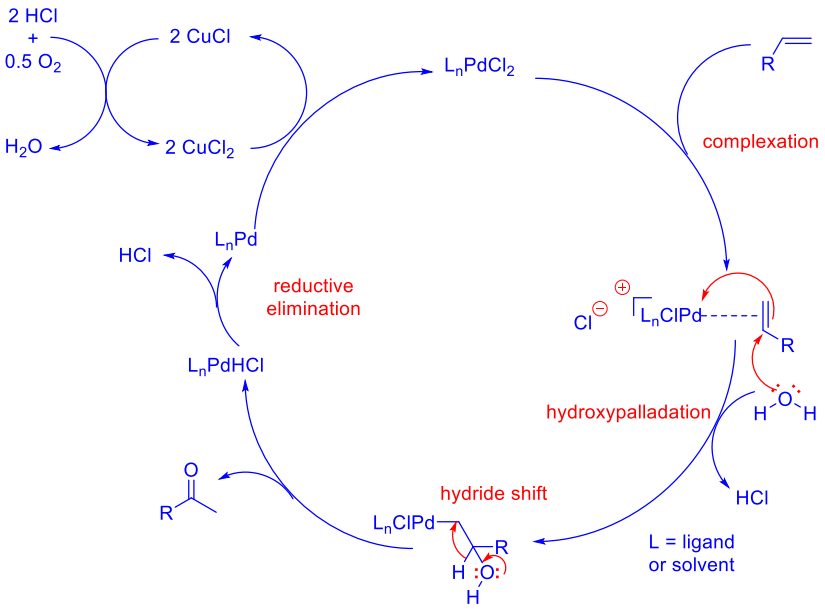
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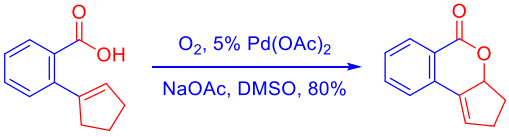
Wacker Oxidation

Palladium-catalyzed oxidation of olefins to ketones, and aldehydes in certain cases.

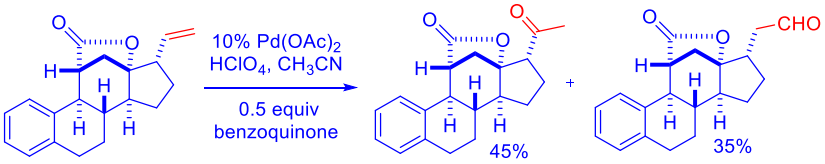




Example 1[5]

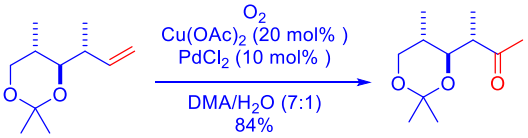


Example 2[7]

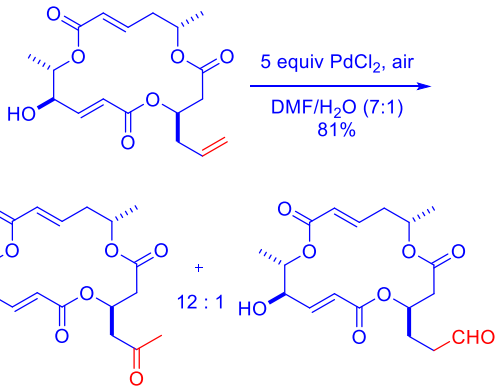


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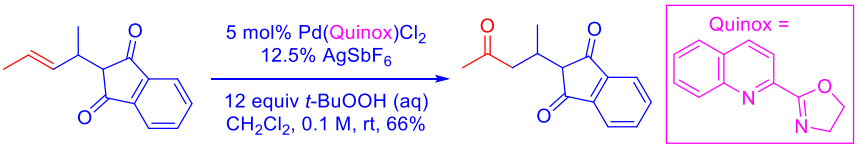
Example 3[9]



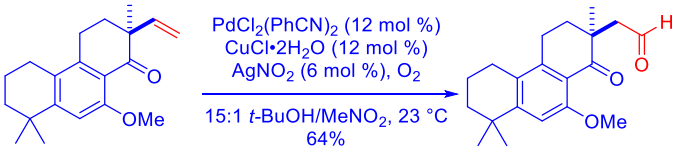
Example 4[10]



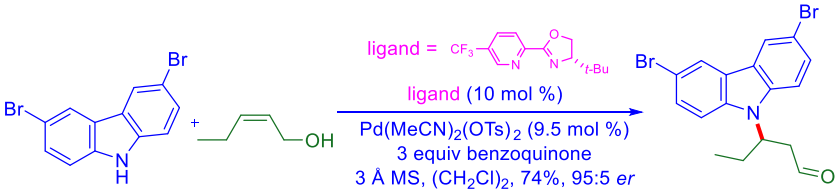
Example 5[10]



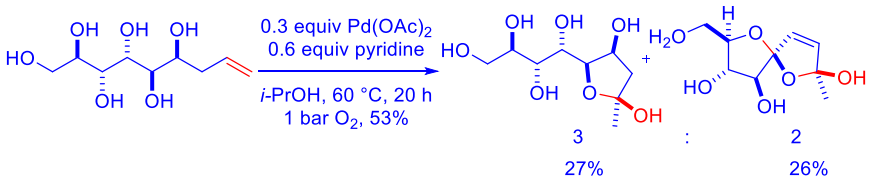
Example 6, Aldehyde-selective Wacker oxidation[16]



Example 7, Asymmetric intermolecular aza-Wacker-type reaction[17]



Example 8, Reacting unprotected carbohydrate-based terminal olefins through the "Uemura system" to hemiketals and α,β-unsaturated diketones[18]

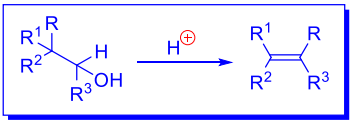


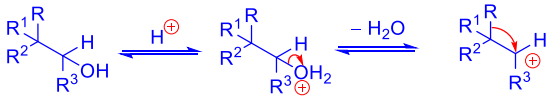
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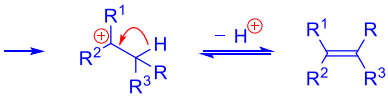
Wagner–Meerwein Rearrangement

Acid-catalyzed alkyl group migration of alcohols to give more substituted olefins.

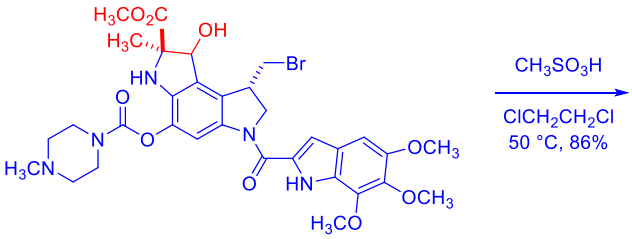


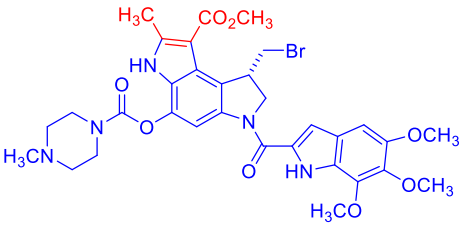


1,2-alkyl shift

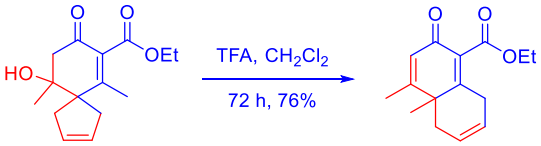


Example 1[3]



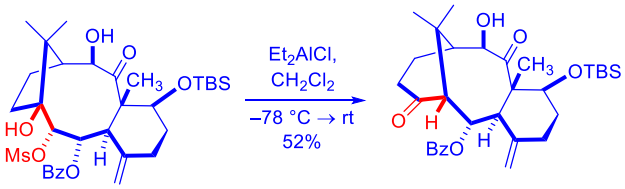


Example 2[6]

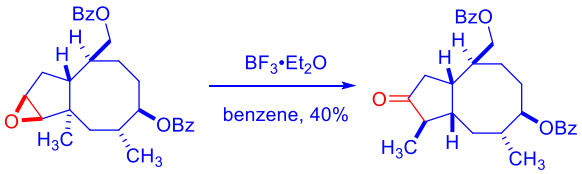


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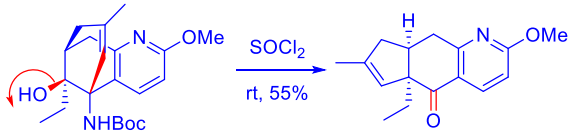
Example 3[7]



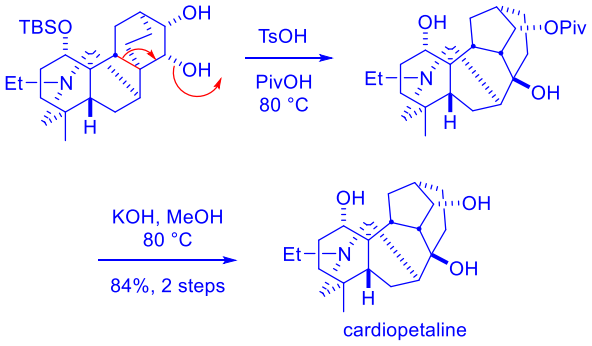
Example 4[9]



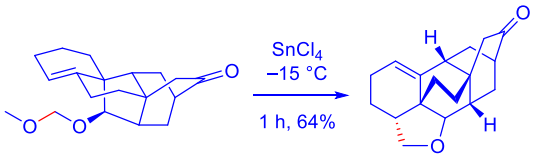
Example 5, Vinyl migration in preference to aryl migration[12]



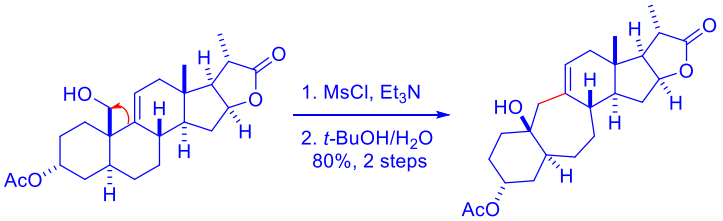
Example 6, Synthesis of cardiopetaline, Wagner–Meerwein rearrangement without preactivation of the pivotal hydroxy group[13]



Example 7, Prins/Wagner–Meerwein rearrangement cascade[14]



Example 8, Synthesis of nortriterpenoid propindilactone G[15]

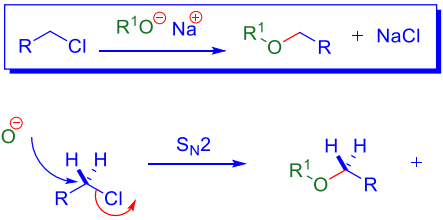


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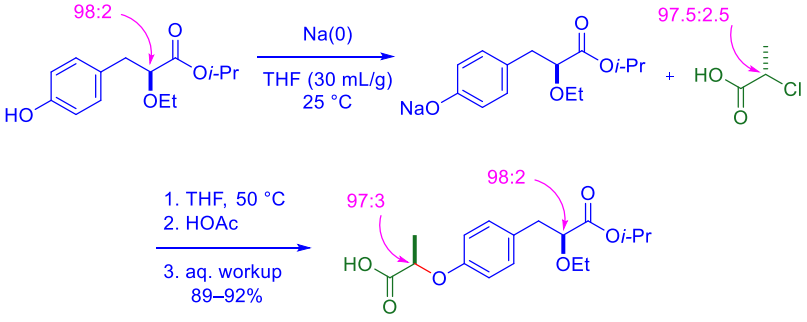
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Williamson Ether Synthesis

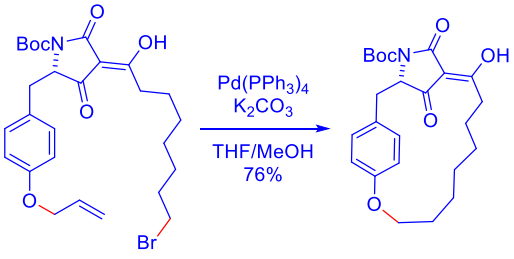
Ether from the alkylation of alkoxides by alkyl halides. In order for reaction to go smoothly, the alkyl halides are preferred to be primary. Secondary halides work as well sometimes, but tertiary halides do not work at all because E_2 elimination will be the predominant reaction pathway.



Example 1, Diastereoselective intermolecular S_N2 reaction[9]

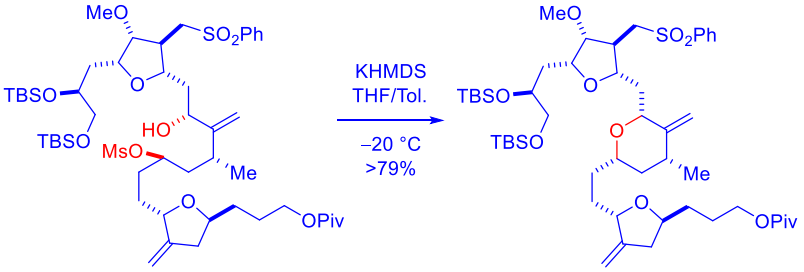


Example 2, Phenolate revealed by $Pd(PPh_3)_4$ and K_2CO_3[10]

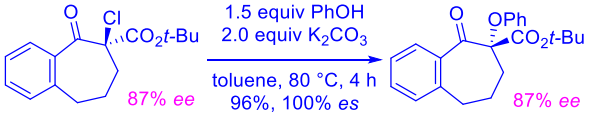


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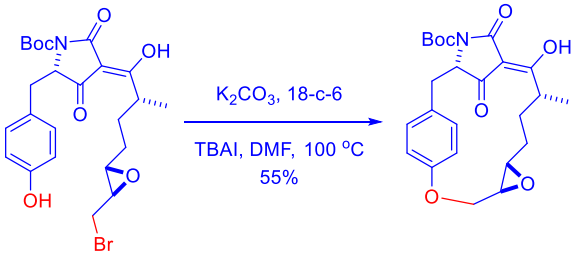
Example 3, Cyclic intramolecular etherification[11]



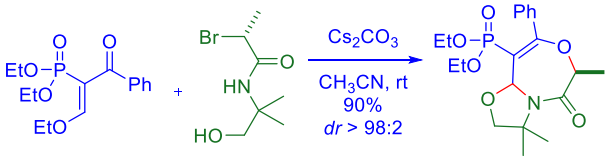
Example 4, Williamson ether synthesis with phenols at a pertiary stereogenic carbon: formal enantioselective phenoxylation of β-keto esters[12]



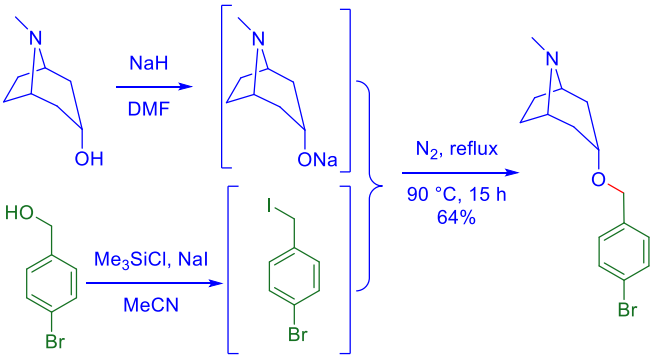
Example 5, Intramolecular S_N2 displacement[13]



Example 6, A domino oxa-Michael/aza-Michael/Williamson cycloetherification sequence[15]



Example 7, One-pot synthesis of benzyl ethers bearing a nitrogen-containing bicycles[16]

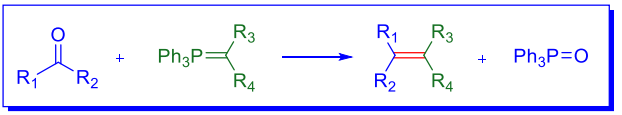


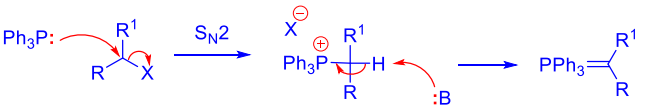
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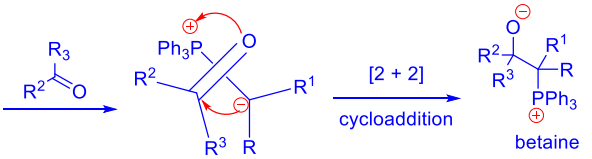
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Wittig Reaction

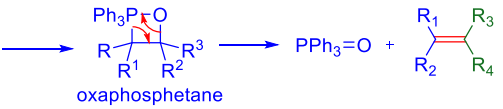
Olefination of carbonyls using phosphorus ylides, typically the *Z*-olefin is the major isomer obtained.



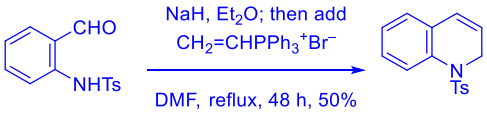




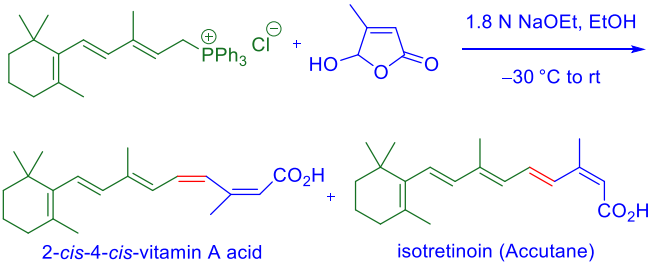
The "puckered" transition state, irreversible and concerted



Example 1[3]

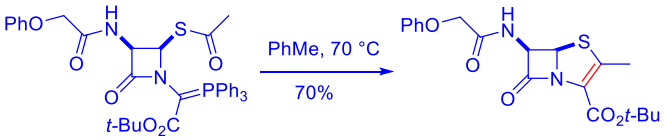


Example 2[4]

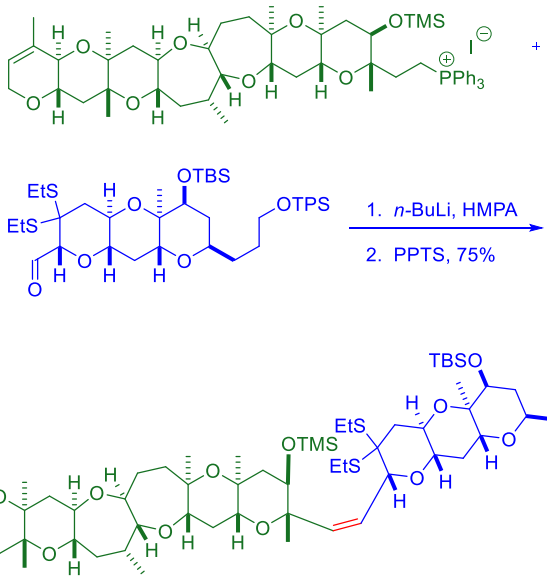


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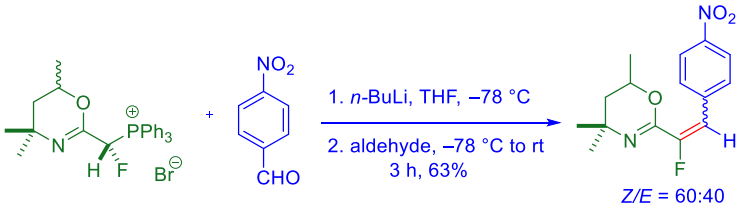
Example 3, Intramolecular Wittig reaction[5]



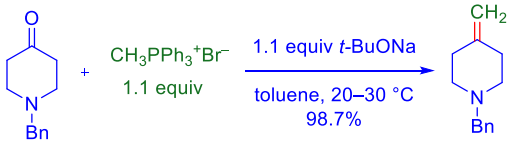
Example 4[9]



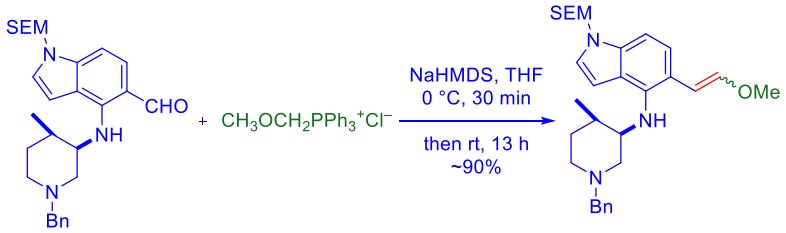
Example 5[11]



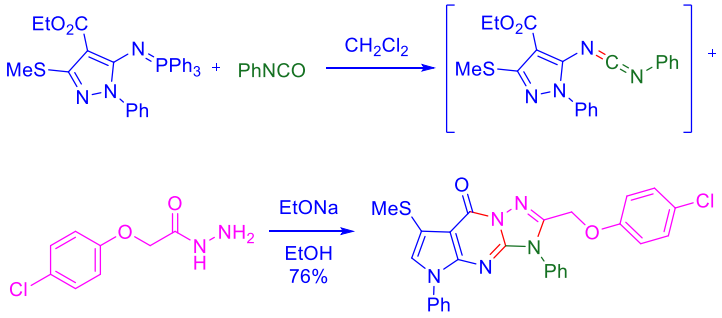
Example 6, Process-scale[14]



Example 7, Manufacturing route for Janus kinase (JAK) inhibitor ASP3627[16]



Example 8, Aza-Wittig reaction[17]



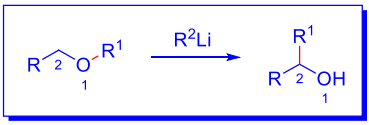
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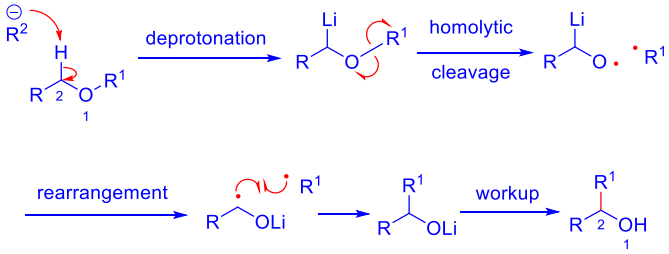
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[1,2]-Wittig Rearrangement

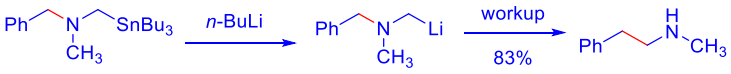
Treatment of ethers with bases such as alkyl lithium results in alcohols.



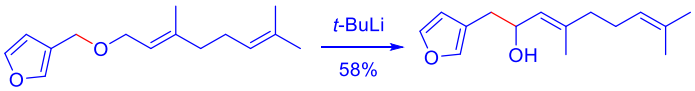
The [1,2]-Wittig rearrangement is believed to proceed via a radical mechanism:



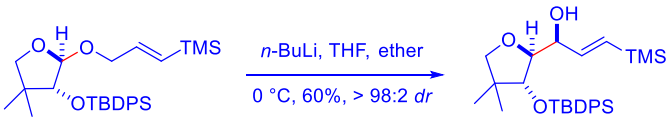
Example 1, Aza [1,2]-Wittig rearrangement[2]



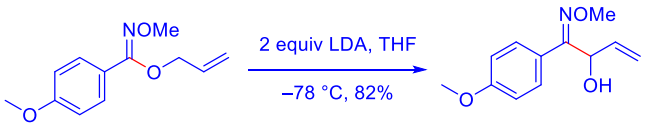
Example 2[3]



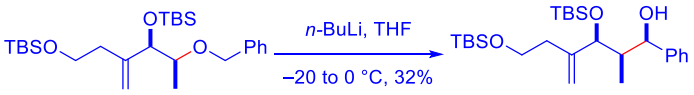
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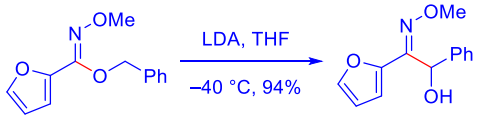
Example 4[6]



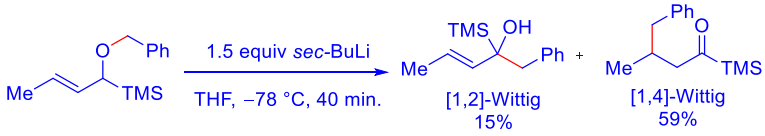
Example 5[8]



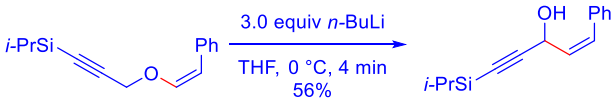
Example 6[9]



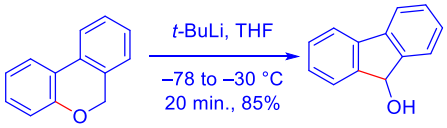
Example 7[11]



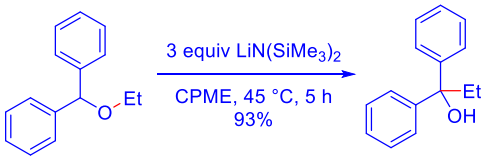
Example 8, Synthesis of (*Z*)-allylic alcohol[12]



Example 9, [1,2]-Wittig rearrangement of 6*H*-benzo[*c*]chromene[13]



Example 10, CPME = cyclopentyl methyl ether[14]

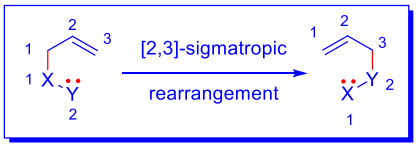


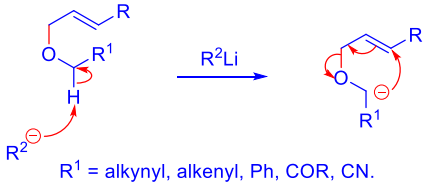
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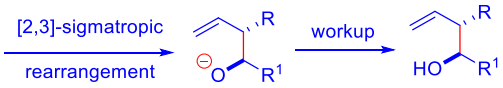
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[2,3]-Wittig Rearrangement

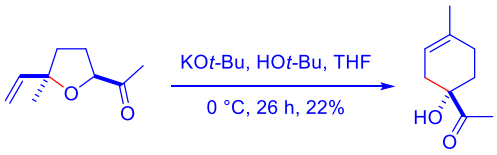
Transformation of allyl ethers into homoallylic alcohols by treatment with base. Also known as the Wittig–Still rearrangement, or Still [2,3]-Wittig rearrangement. *Cf.* Sommelet–Hauser rearrangement.



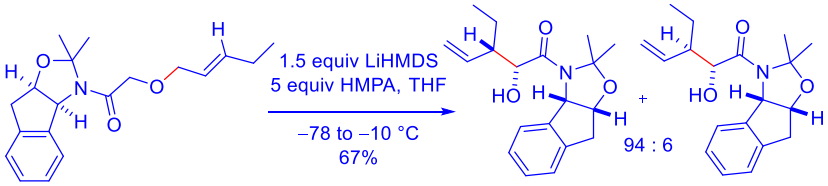




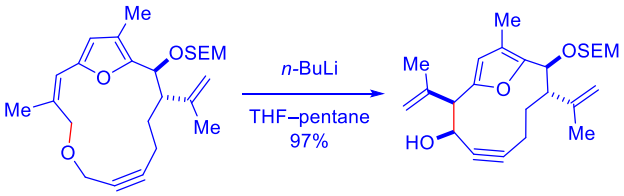
Example 1[4]



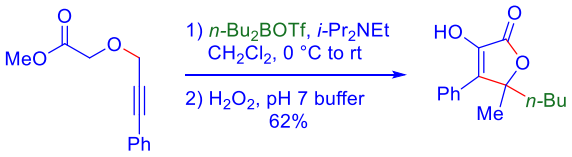
Example 2[5]



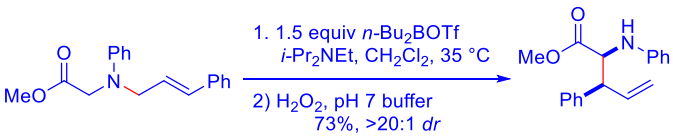
Example 3, Total synthesis of the pseudopterolide kalllolide A[6]



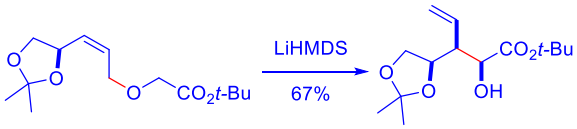
Example 4, Tandem Wittig rearrangement/alkylative cyclization reactions[11]



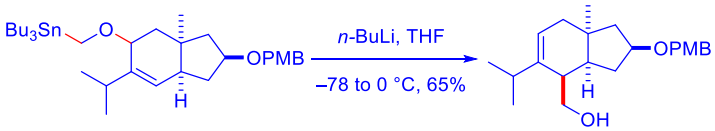
Example 5, Aza-[2,3]-Wittig rearrangement[12]



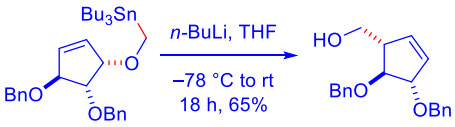
Example 6, Fidelity of the chirality conserved[14]



Example 7, The homoallylic alcohol was obtained as a single stereoisomer[15]



Example 8, Making mechanism-based inhibitors (MBIs) of a-L-arabino-furanosidases[16]

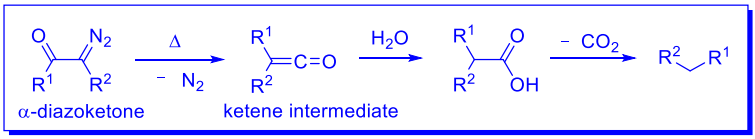


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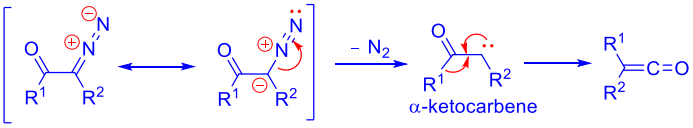
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Wolff Rearrangement

Conversion of an α-diazoketone into a ketene. Often employed to conduct ring constraction.

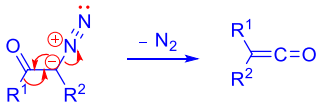


Step-wise mechanism:

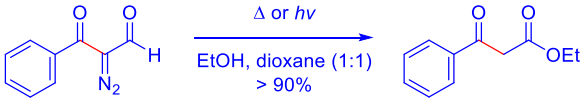


Treatment of the ketene with water would give the corresponding homologated carboxylic acid.

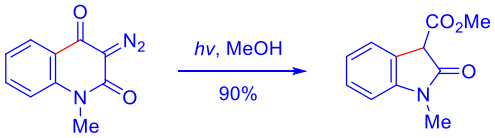
Concerted mechanism:



Example 1, Hydride migrates with higher migratory priority[2]

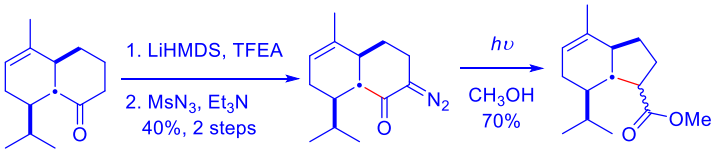


Example 2, Oxindoles[3]

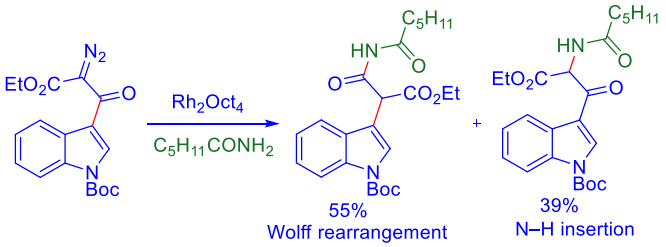


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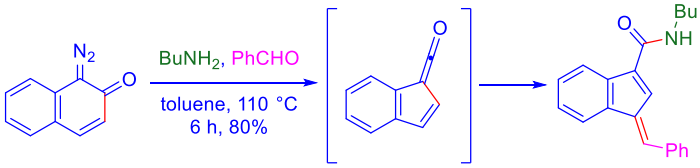
Example 3, TFEA = trifluoroethyl trifluoroacetate[4]



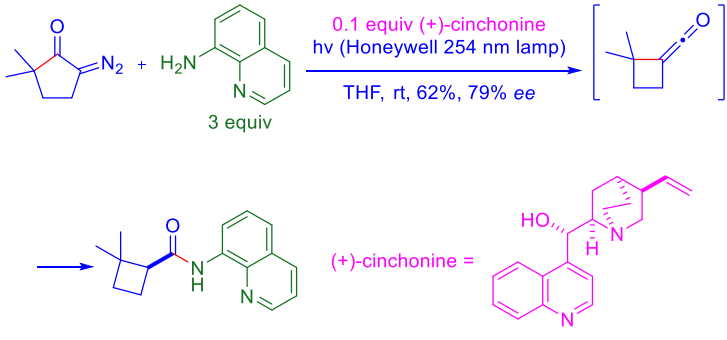
Example 4, Indole ring migrates[9]



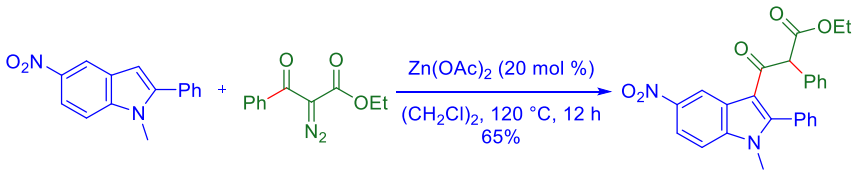
Example 5[11]



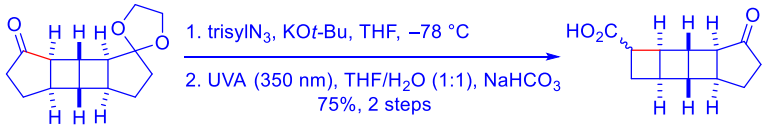
Example 6, The first example of a tandem Wolff rearrangement/catalytic ketene addition[12]



Example 7, Indoles as nucleophiles adding to the ketene intermediates of the Wolff rearrangement[13]



Example 8, Ring contraction[14]

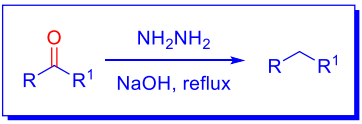


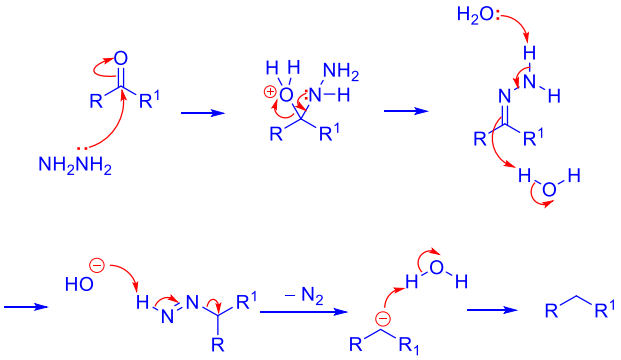
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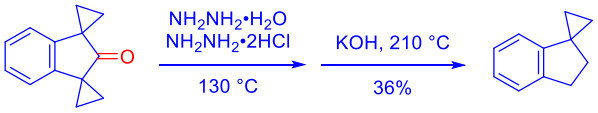
Wolff–Kishner Reaction

Carbonyl reduction to methylene using basic hydrazine.

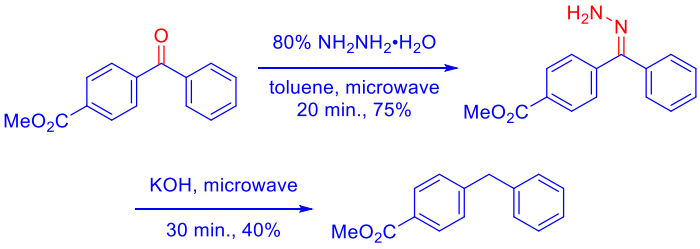




Example 1, The Huang Minlon modification, with loss of ethylene[5]

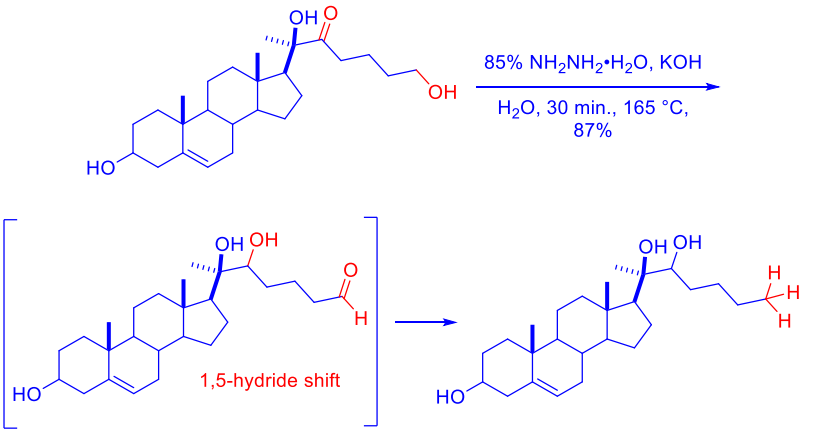


Example 2[7]

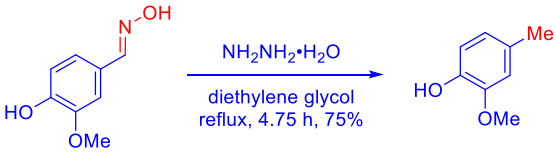


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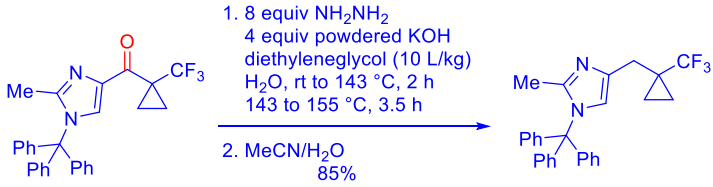
Example 3[8]



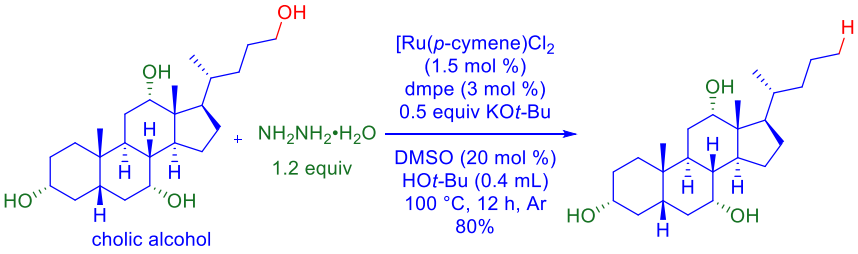
Example 4, Huang Minlon modification[10]



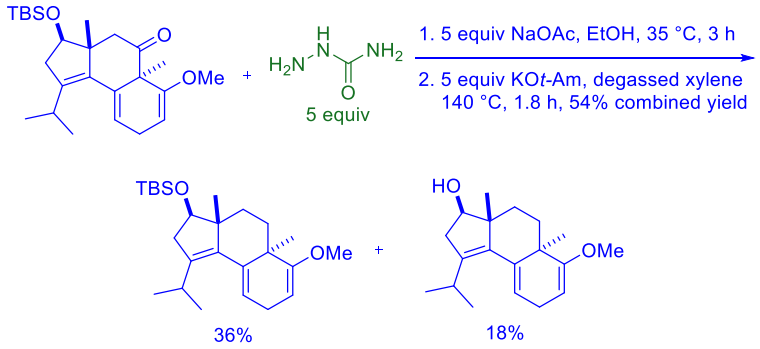
Example 3, Large-scale Wolff–Kishner reaction[13]



Example 4, Oxydative deoxygenation is followed by Wolff–Kishner reaction[14]



Example 5, Wolff–Kishner reaction works better than the Baron–McCombie reaction for deoxygenation here:[15,16]



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