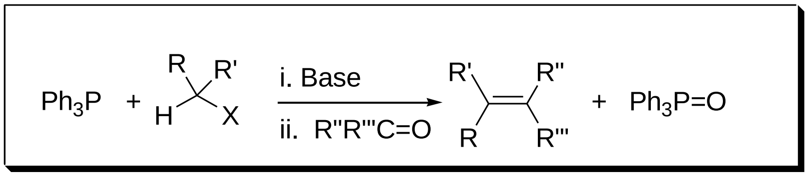
Lecture 23

10.1 Phosphorus-Containing Compounds

The phosphorus reagents have three characteristics: the ease with which phosphorus (III) is converted into phosphorus (V); the relatively strong bonds formed between phosphorus and oxygen; and the availability of vacant 3d orbitals for bonding.

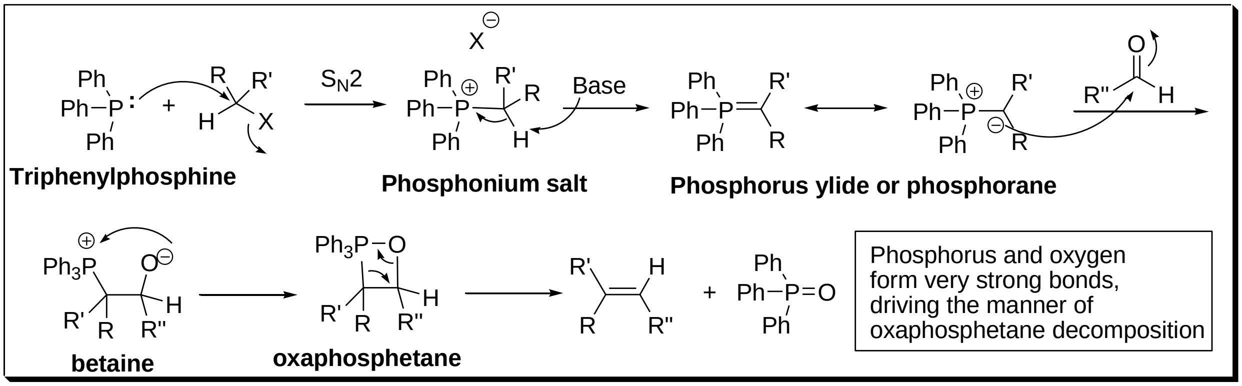
10.1.1 Wittig Olefination

The Wittig reaction for the synthesis of alkenes stems from two properties: First, it is specific for the conversion of aldehydes or ketone to alkenes. Second, the carbonyl compounds can contain a variety of other functional groups (Scheme 1).



Mechanism

The phosphorus ylides are prepared by quaternizing a tervalent phosphorus compounds with an alkyl halide and treating the salt with base. The phosphorane adds as a carbon nucleophile to the carbonyl group and the resulting intermediate reacts via a cyclic intermediate to form the alkene (Scheme 2-3).

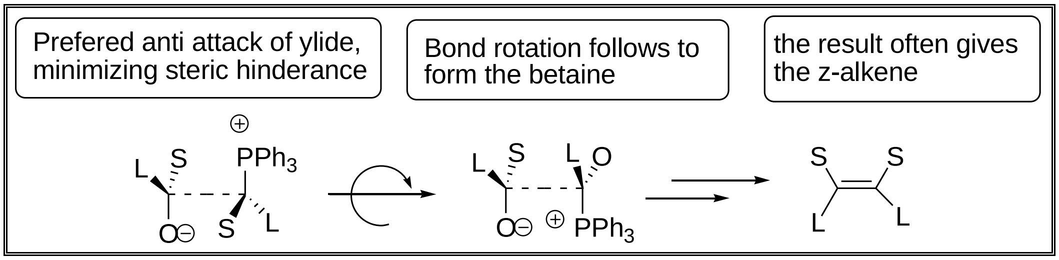


Scheme 2

Notes:

Other phosphines may be used for this reaction, but the choice should not contain a proton that could be abstracted by base, because a mixture of desired and undesired ylides would be formed.

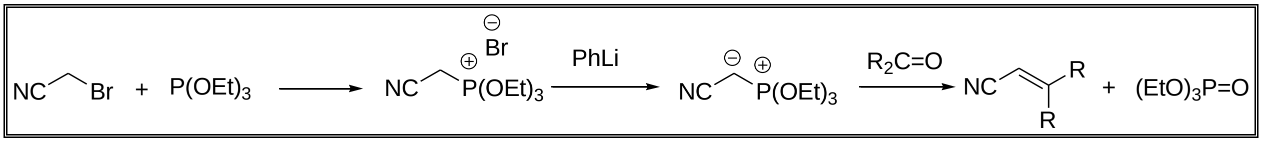
Usually strong bases such as BuLi, NaH and $NaNH_2$ are used.



Scheme 3

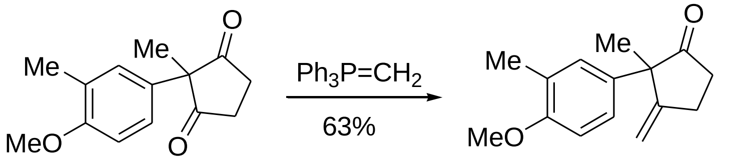
Simple phosphoranes are very reactive and are unstable in the presence of air or moisture. They are therefore prepared in a scrupulously dry solvent under nitrogen and the carbonyl compound is added as soon as the phosphorane has been formed.

More stable phosphoranes are obtained when a –M substituent is adjacent to the anionic carbon (Scheme 4). However, although they react with aldehydes, they do not do so effectively with ketones and for this purpose modification has been introduced in which triphenylphosphine is replaced by triethyl phosphate (Wadsworth-Emmons Reaction).

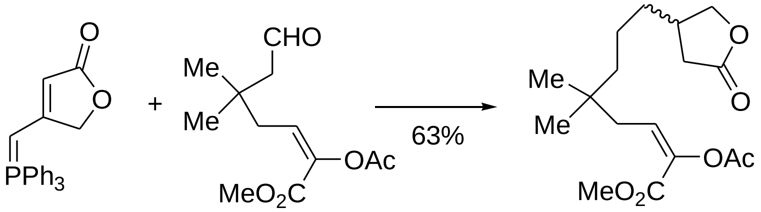


Scheme 4

Examples:



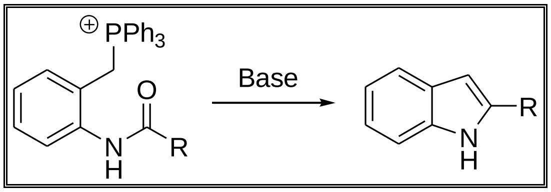
S. P. Chavan, R. K. Kharul, R. R. Kale, D. A. Khobragade, *Tetrahedron* **2003**, 59, 2737.



R. K. Boeckman, Jr., T. R. Aless, *J. Am. Chem. Soc.* **1982**, *104*, 3214.

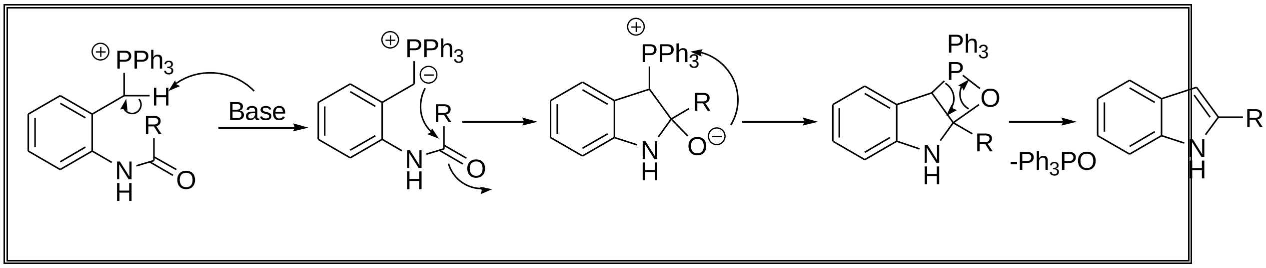
10.1.2 Wittig Indole Synthesis

Indole is an important structural unit present in many natural products and biologically active compounds. The reaction of (2-amidobenzyl)triphenylphosphonium salt with base allows the synthesis of 2-substituted indoles (Scheme 5-6).



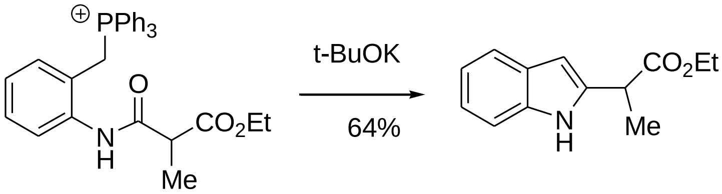
Scheme 5

Mechanism

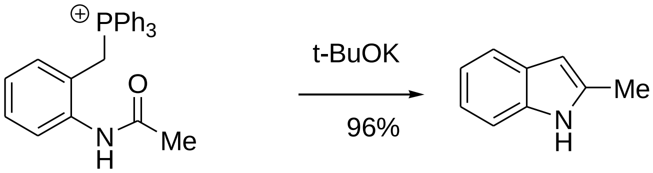


Scheme 6

Examples



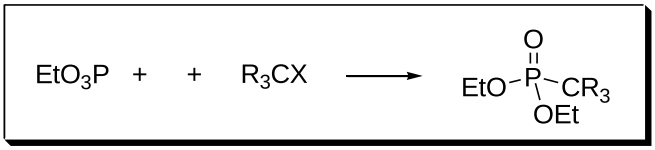
B. Danieli, G. Lesma, G. Palmisano, D. Passarella, s. Silvani, *Tetrahedron* **1994**, *50*, 6941.



M. Le Corre, Y. Le Stane, A. Hercouet, H. Le Brown, *Tetrahedron* **1985**, *41*, 5313.

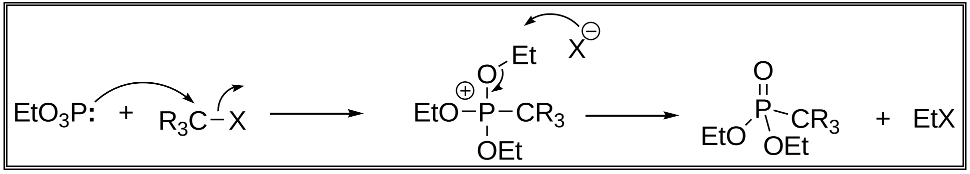
10.1.3 Arbuzov Reaction (Michaelis-Arbuzov Reaction)

It is an effective method for the synthesis of an alkyl phosphonate from a trialkyl phosphate and an alkyl halide (Scheme 7-8). The reaction finds wide applications in the synthesis of phosphonate esters which are used in the Horner-Emmons Reaction.



Scheme 7

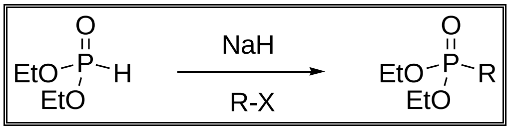
Mechanism



Scheme 8

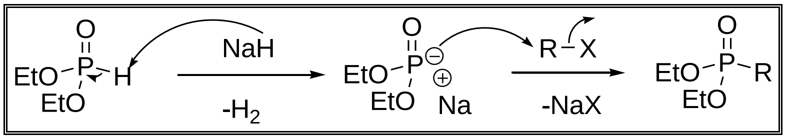
10.1.4 Michaelis Reaction (Michaelis-Becker Reaction)

It is an alternative method for the synthesis of alkyl phosphonate esters (Scheme 9-10). The yield of the process is usually less compared to the above mentioned Michaelis-Arbuzov reaction.



Scheme 9

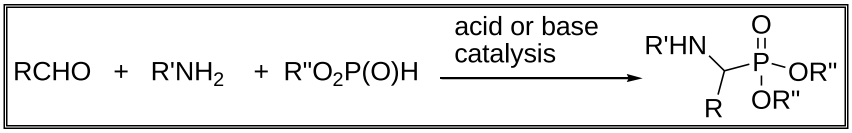
Mechanism



Scheme 10

10.1.5 Kabachnik-Fields Reaction

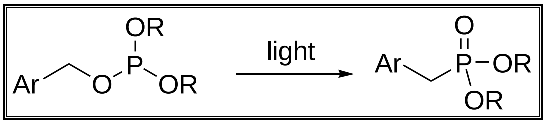
The three-component reaction of a carbonyl, an amine and a hydrophosphoryl compound leads to the formation of α-aminophosphonates which is very important in drug discovery research for generating peptidomimetic compounds (Scheme 11).



Scheme 11

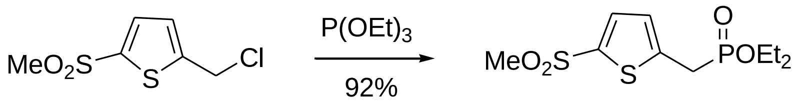
10.1.6 The Photo-Arbuzov Reaction

The direct UV irradiation of phosphite can give phosphonate in moderate to good yield (Scheme 12). The reactions of both acyclic and cyclic phosphites have been explored.

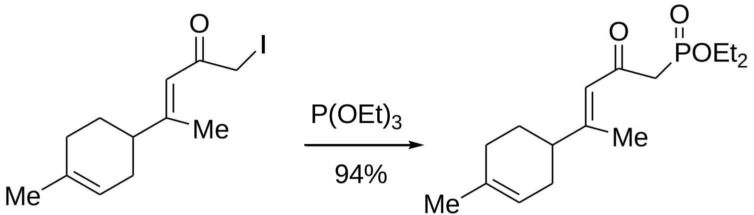


Scheme 12

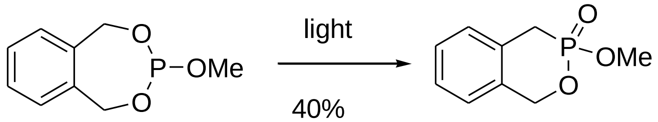
Examples



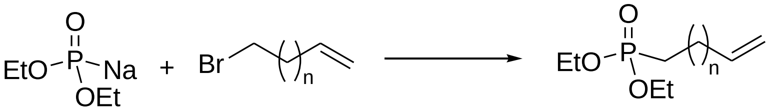
S. S. Chou, D.-J. Sun, J.-Y. Huang, P. K. Yang, K.-C. Lin, *Tetrehedron Lett.* **1996**, *32*, 7279.



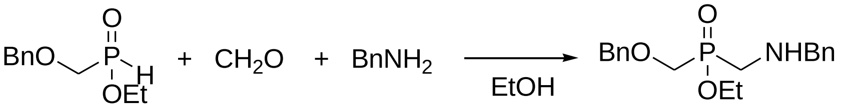
R. W. Driessen, M. Blouin, *J. Org. Chem.* **1996**, *61*, 7202.



M. S. Landis, N. J. Turro, W. Bhanthumnavin, W. G. Bentrude, *J. Organometallic Chem.* **2002**, *646*, 239.



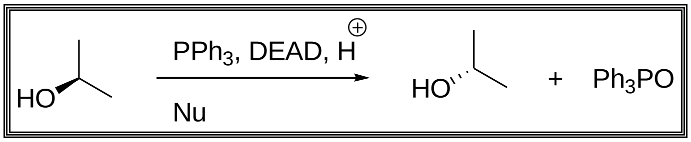
I Pergament, M. Srebnik, *Org. Lett.* **2001**, *3*, 217.



H.-J. Cristan, a. Herve, D. Virieux, Tetrahedron **2004**, *60*, 877.

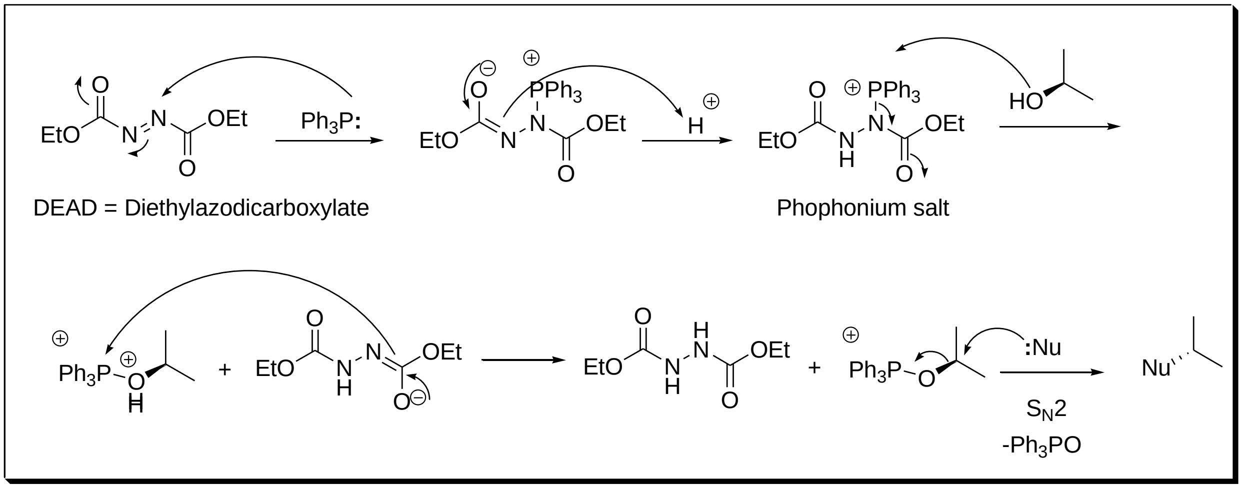
10.1.7 Mitsunobu Reaction

The alkoxyphosphonium ion generated from diethyl azodicarboxyliate (DEAD), triphenyl phosphine and alcohol undergoes reaction with nucleophile (usually carboxylic acid) by S_N2 character (Scheme 13-14). The reaction exploits, first, the reactivity of the azo compound as an electrophile in the formation of the first phosphonium ion and, second, the good leaving group property of the reduced azo compound.



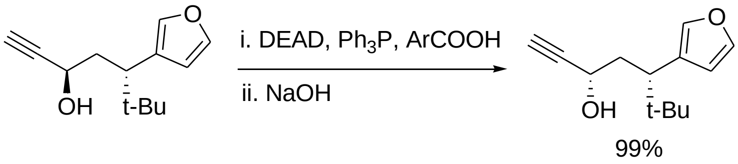
Scheme 13

Mechanism

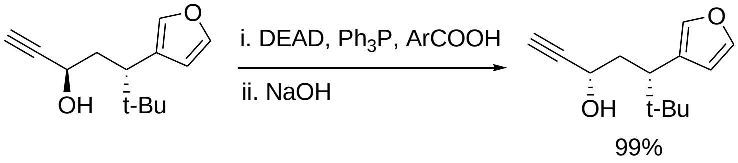


Scheme 14

Examples



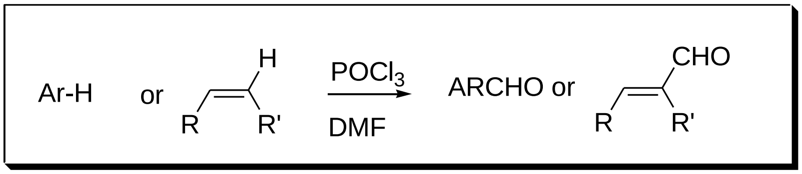
M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *J. Am. Chem. Soc*. **1999**, *121*, 10249.



M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *J. Am. Chem. Soc*. **1999**, *121*, 10249.

10.1.8 Vilsmeier-Haack Reaction

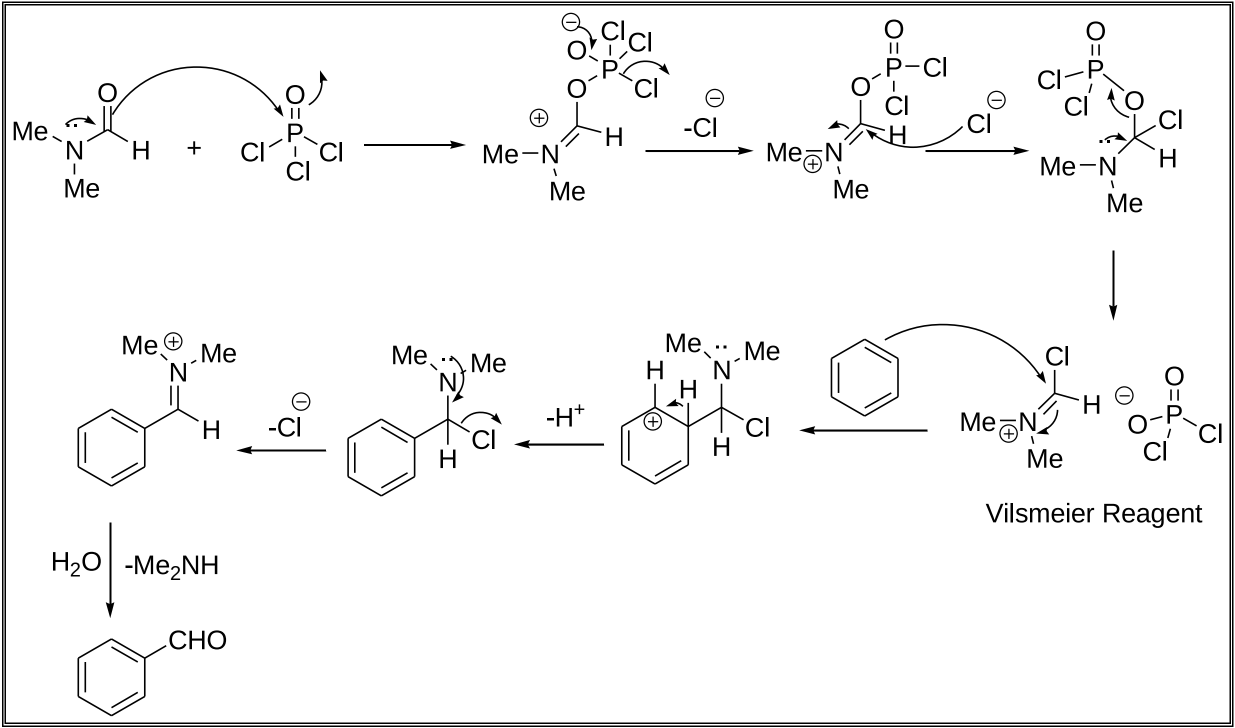
This reaction allows formylation of the reaction of activated alkenes as well as arenes (Scheme 15).



Scheme 15

Mechanism

The formylating agent is generated in situ from DMF and $POCl_3$ (Scheme 16).

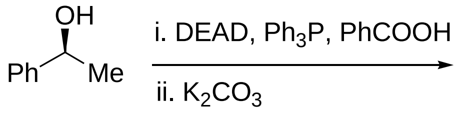


Scheme 16

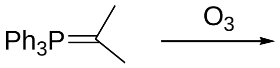
Problems

Write the major product for the following reactions.

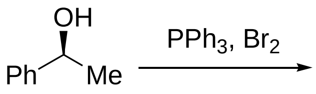
1.



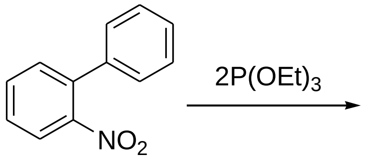
2.



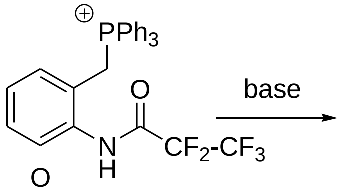
3.



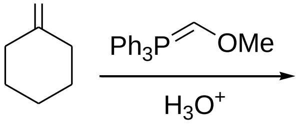
4.



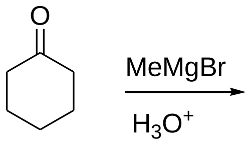
5.



6.



7.



Text Books

B. P. Mundy, M. G. Ellerd, F. G. Favaloro Jr., *Name Reactions and Reagents in Organic Synthesis*, 2nd ed, Wiley-Interscience, Hobken, 2005.

R. O. C. Norman, J. M. Coxon, *Principles of Organic Synthesis*, 3rd ed, CRC Press, New York, 2009.

Lecture 24

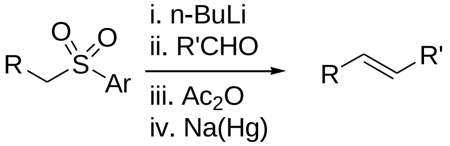
10.2 Sulfur-Containing Compounds

Sulfur-containing compounds find wide applications in organic synthesis. This lecture covers some of the importance processes.

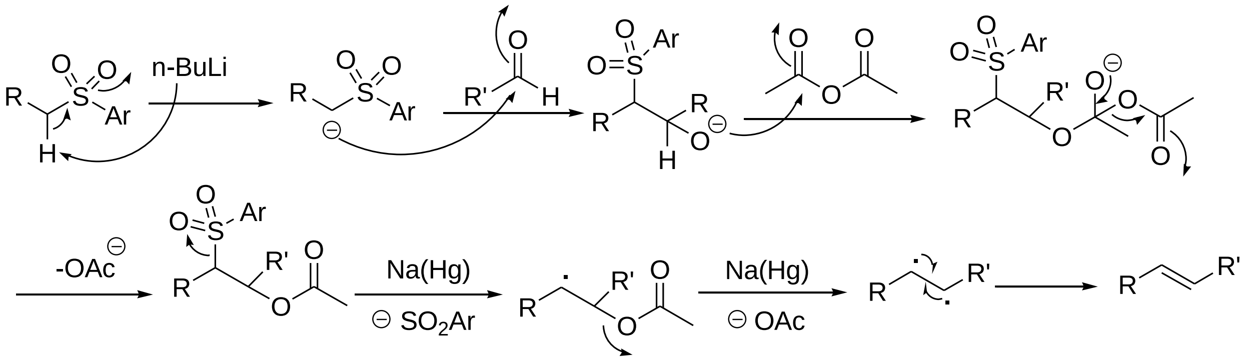
10.2.1 Reactions with Carbonyl Compounds

10.2.1.1 Julia Olefination (Julia-Lythgoe Olefination)

Aldehydes as well as ketones undergo reaction with sulfone having □-H in the presence of base to give an adduct which could be treated with acetic anhydride to afford acetyl derivative that could proceed reductive elimination in the presence of sodium amalgam to form alkene (Scheme 1). One of the important characteristics of this reaction is its high stereoselectivity for (*E*)-disubstituted alkenes.



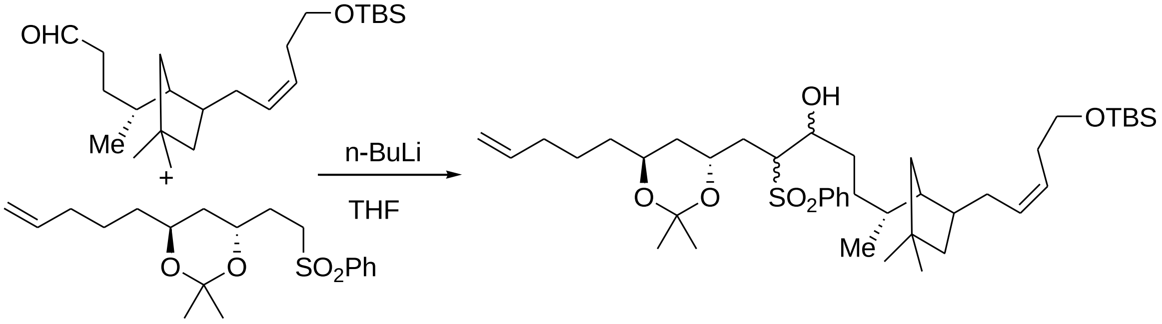
Mechanism



Scheme 1

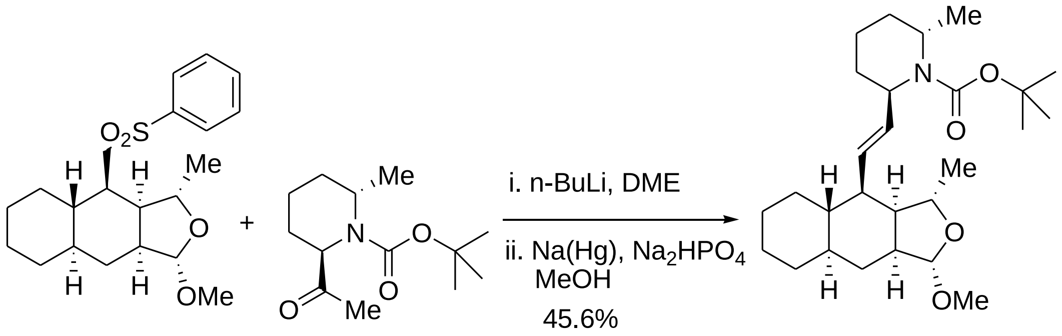
10.2.1.2 Julia Coupling

Sulfones having α-hydrogen can be coupled with aldehydes using base (Scheme 2).

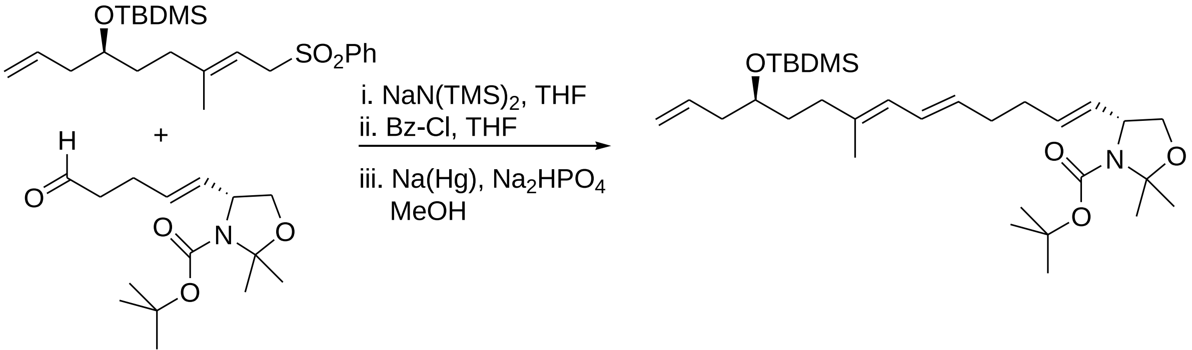


Scheme 2

Examples



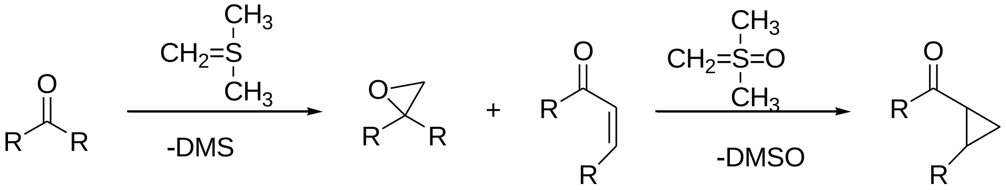
D. J. Hart, J. Li, W.-L. Wu, A. P. Kozikowski, *J. Org. Chem.* **1997**, *62*, 5023.



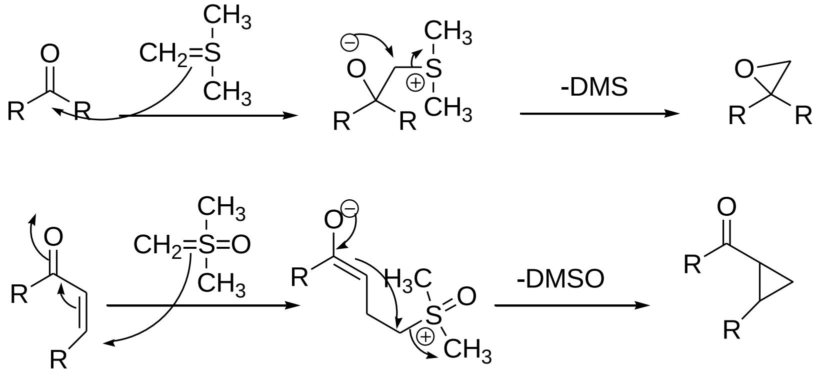
M. Z. Hoemann, K. A. Agriosw, J. Aube, *Tetrahedron Lett.* **1996**, *37*, 953.

10.2.1.3 Corey-Chaykovsky Reaction

The first stage of the reaction of a sulfur ylide with an aldehydes or ketone compound consists of nucleophilic addition, the resultant adduct then proceeds intramolecular nucleophilic substitution to give an epoxide (Scheme 3). In case of □ □ □-unsaturated compounds, based on the nucleoephilicity of the ylide either epoxide or cyclopropanation could be formed.

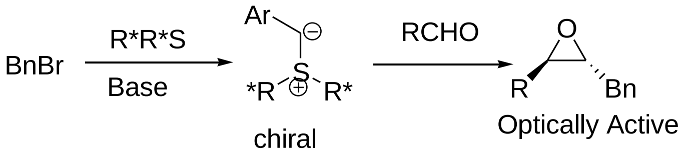


Mechanism



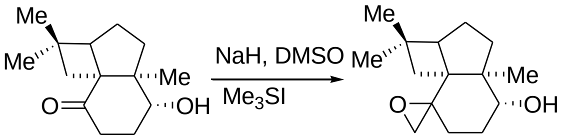
Scheme 3

Recently, chiral version of the reaction has been extensively studied for the synthesis of optically active epoxides as the principle shown in Scheme 4. The products are usually obtained with high enantioselectivity.

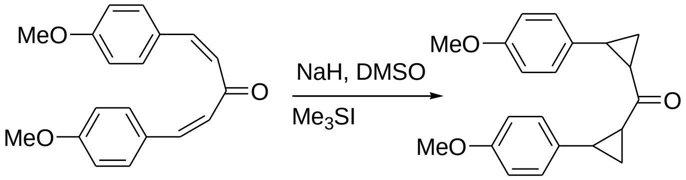


Scheme 4

Examples



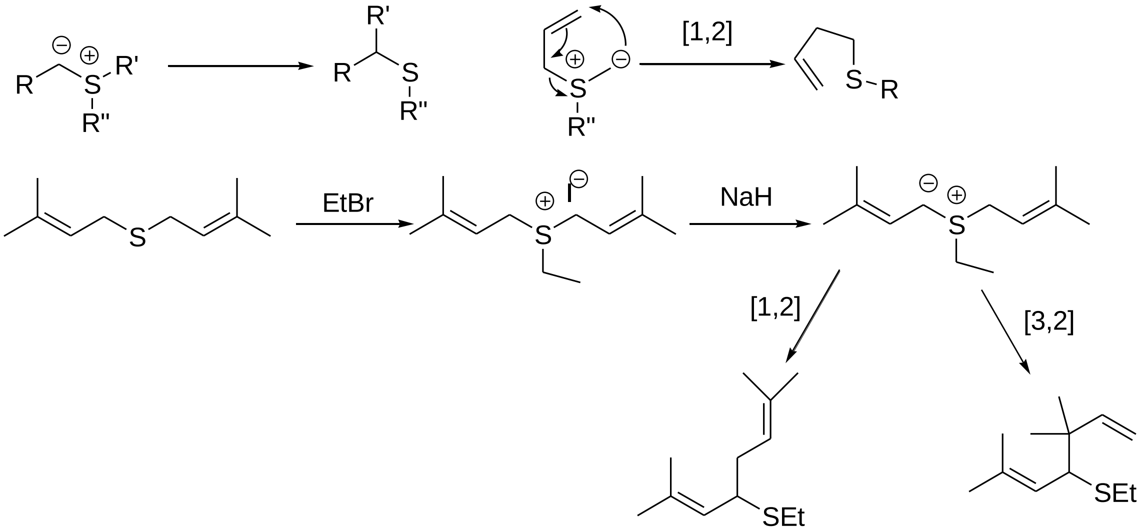
C. F. D. Amigo, I. G. Collado, J. R. Hanson, R. Hernandez-Galam, P. B. Hitchcock, A. J. Macias-Sanchez, D. J. Mobbs, M. *J. Org. Chem.* **2001**, *66*, 4327.



K. Hantawong, W. S. Murphy, N. Russell, D. R. Boyd, *Tetrahedron Lett.* **1984**, *25*, 999.

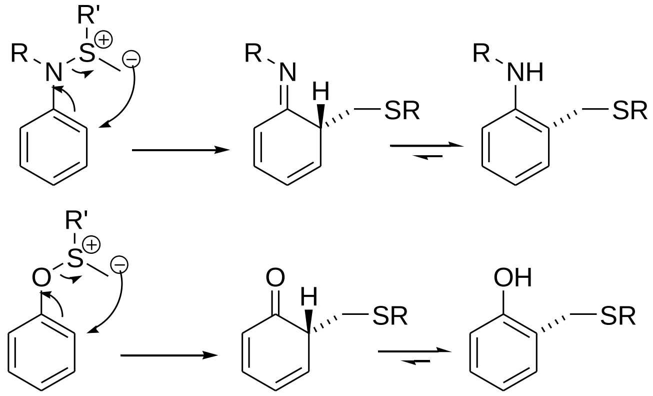
10.2.2 Rearrangement of Sulfur Ylides

Sulfur ylides rearrange as shown in Scheme 4. In case of allylic sulfur ylide, [3,2]-sigmatropic rearrangement is observed.



Scheme 4

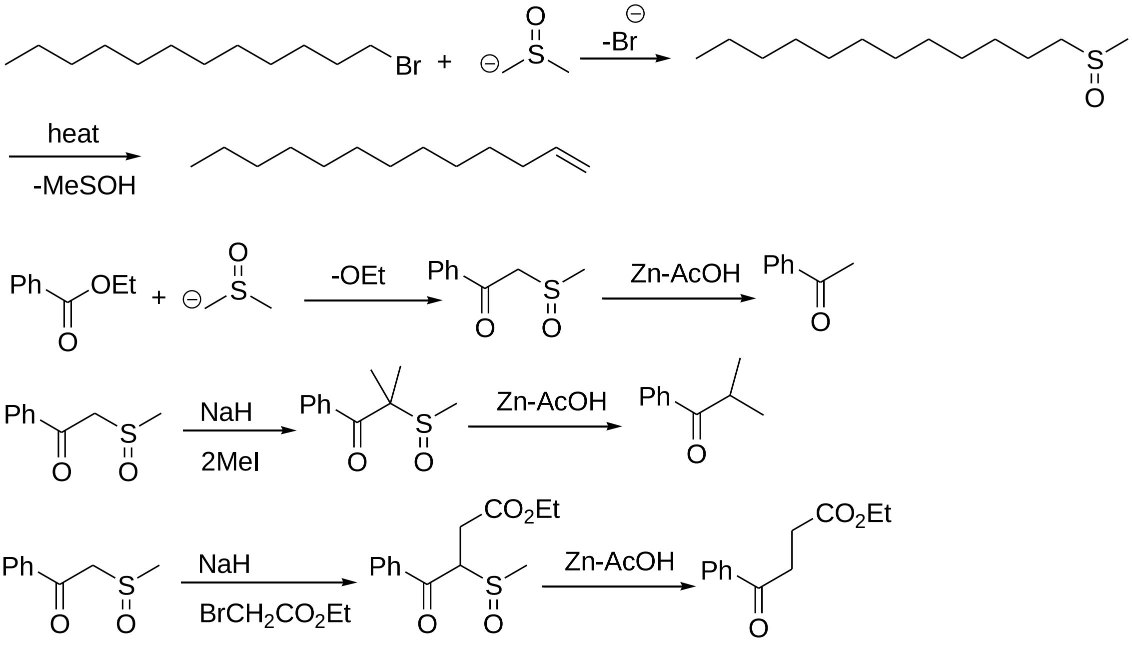
Aza- and oxa-sulfonium salts give ylides that can rearrange to give useful aromatic compounds (Scheme 5).



Scheme 5

10.2.2 Reactions of the Dimsyl Anion

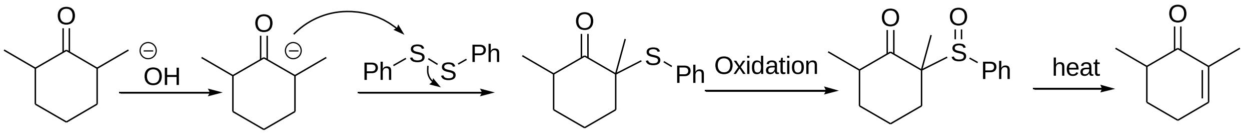
Dimsyl anion is very reactive nucleophile and can be used for various synthetic applications. The sulfur substituent can be easily removed by reduction or thermally (Scheme 6).



Scheme 6

10.2.3 Sulfoxide Elimination

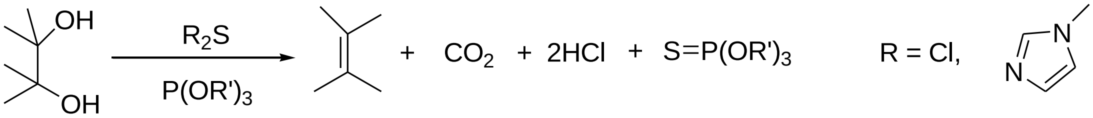
The compound containing an activated C-H bond can underogo reaction with diphenyl or dimethyl disulfide in the presence of base to give substituted sulfide that could be readily oxidized to sulfoxide (Scheme 7). The latter readily undergoes elimination on heating to give α,β-unsaturated carbonyl compound.



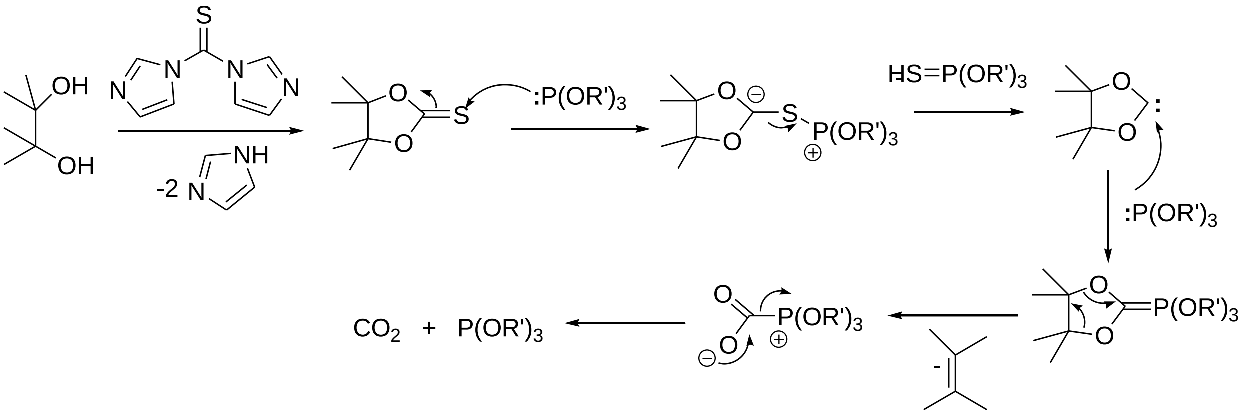
Scheme 7

10.2.4 Corey-Winter Olefination

This method gives an effective route for the transformation of 1,2-diol to alkenes. The cyclic thiocarbonate formed from 1,2-diol and thiocarbonyldiimidaole undergoes reaction with phosphorus reagent via a syn elimination to afford alkene (Scheme 8).

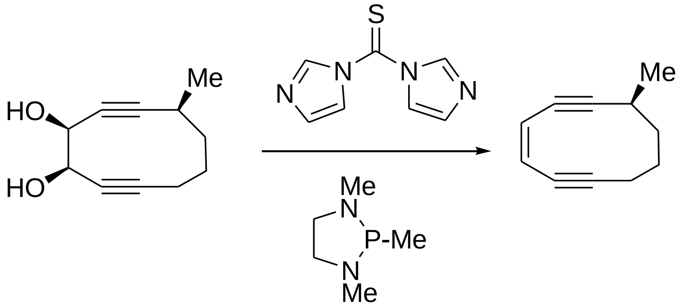


Mechanism

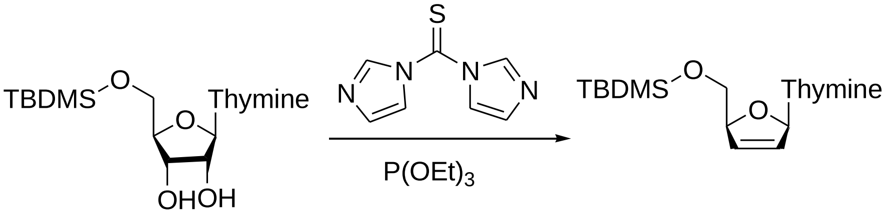


Scheme 8

Examples



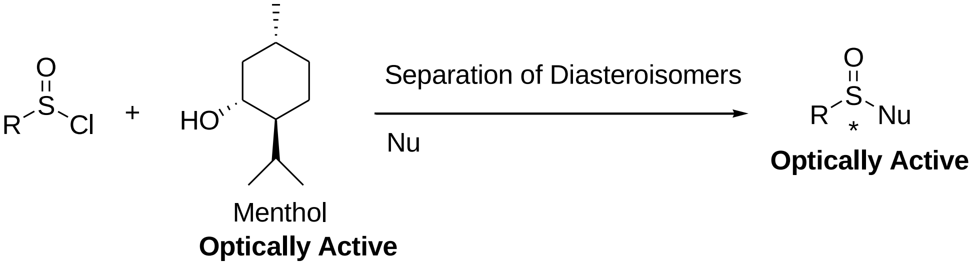
M. F. Semmelhack, J. Gallagher, Tetrahdron Lett. **1993**, *34*, 4121.



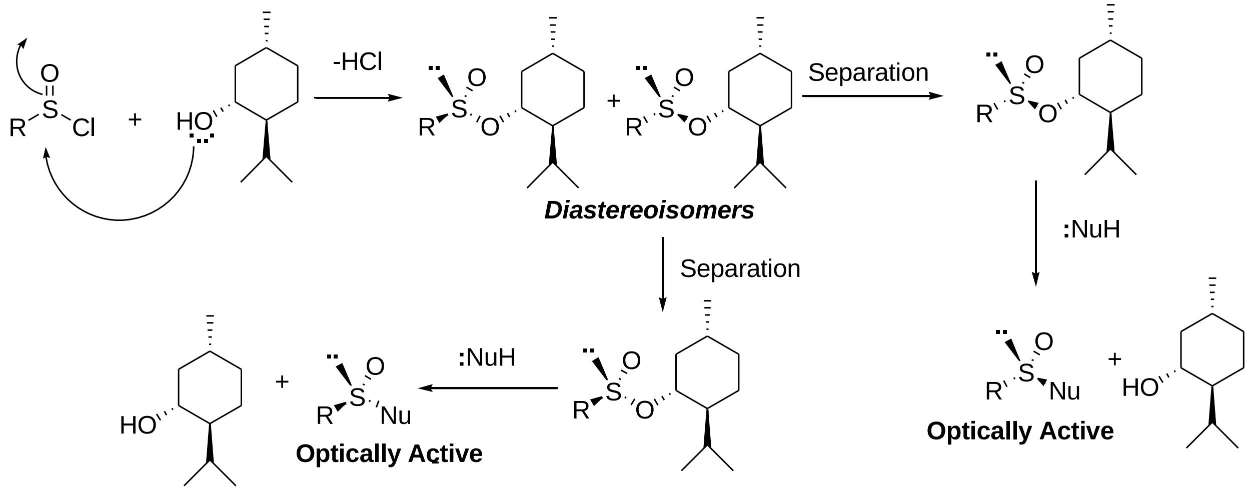
Y. Saito, T. A.. Zevaco, L. A. Agrofoglio, *Tetrahdron* **2002**, *58*, 9593.

10.2.5 Andersen Sulfoxide Synthesis

Synthesis of chiral sulfoxide can be accomplished from sulfinyl chloride by reaction with chiral auxiliaries followed by substitution of the separated diastereomers with nucleophiles (K. K. Andersen, *Tetrahedron Lett.* **1962**. 3, 93).

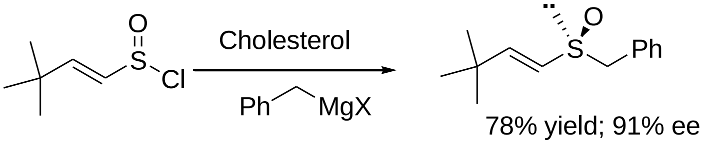


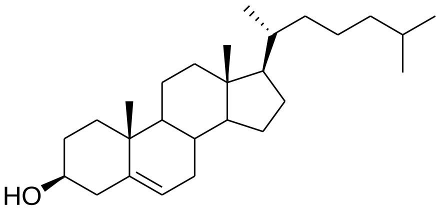
Mechanism



Scheme 9

Example



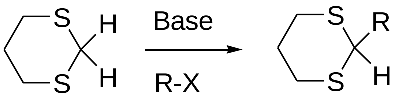


Cholesterol

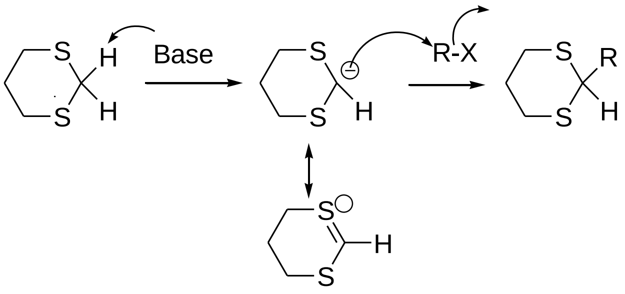
R. R. Strickler, A. L. Schwan, *Tetrahedron: Asymmetry* **1999,** *10*, 4065.

10.2.6 Corey-Seebach Reaction

Corey-Seebach reaction provides an effective route for the transformation of aldehydes to ketones (Scheme 10). The aldehydes can be readily reacted with thiol using acid catalysis to afford dithioacetal. The acidic hydrogen of the acetal can then be removed by base such n-BuLi and the carbonanion, stabilized by vacant d orbital of sulfur atom, can be alkylated in high yield. The resultant thioketal can be hydrolytically cleaved in the presence of mercury(II) salt.

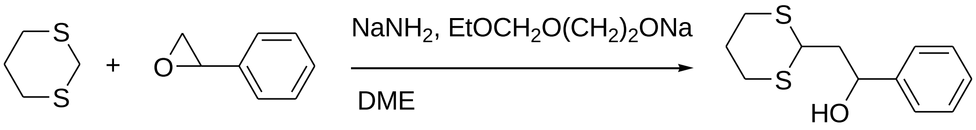


Mechanism

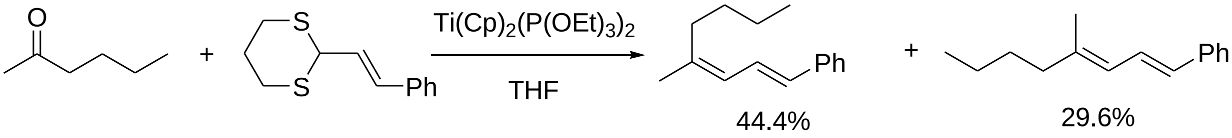


Scheme 10

Examples



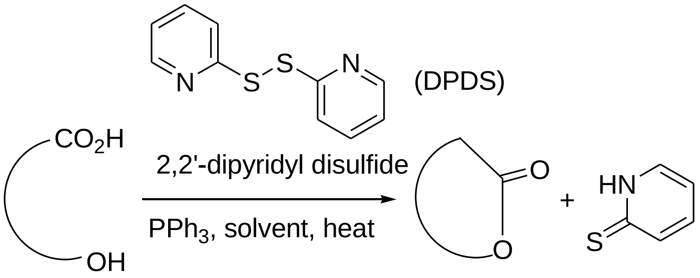
P. Gros, P. Hansen, P. Caubere, *Tetrahedron* **1996**, *52*, 15147.



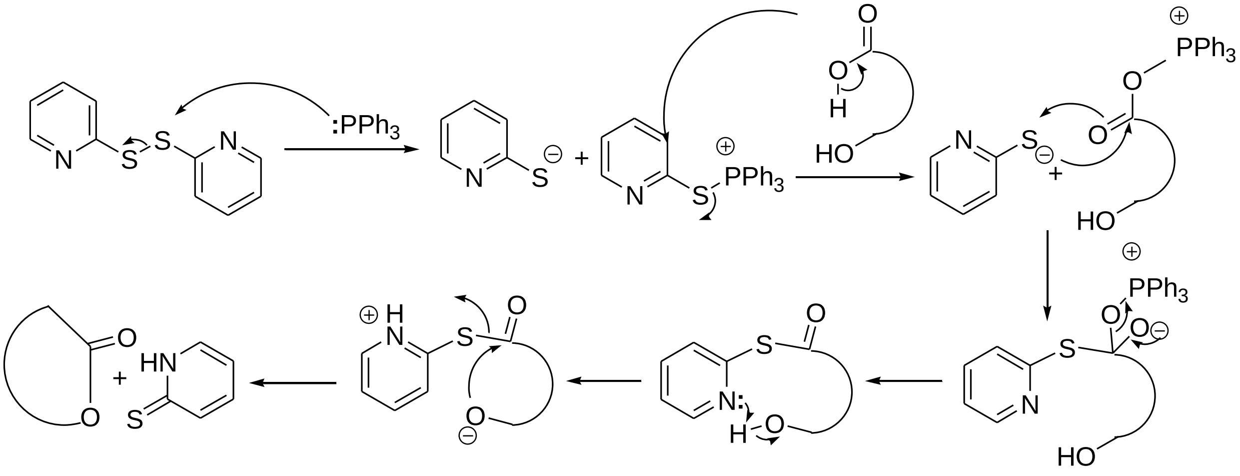
Y. Horikawa, M. Watanabe, T. Fujiwara, T. Takeda, *J. Am. Chem. Soc.* **1997**, *119*, 1127.

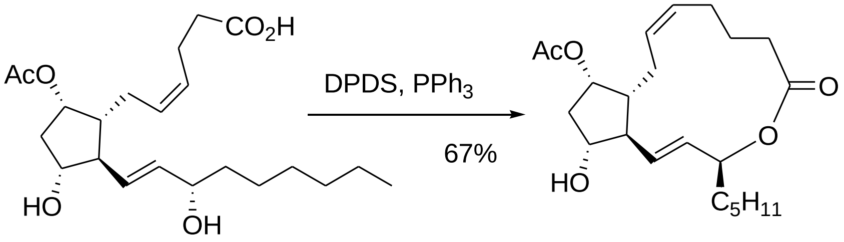
10.2.7 Corey-Nicolaou Macrocyclization

It is one of the popular macrolactonizations in organic synthesis. First, the thioester is formed from the carboxylic group and 2,2’-dipyridyl disulfide at room temperature which on reflux undergoes lactonization (Scheme 11).



Mechanism



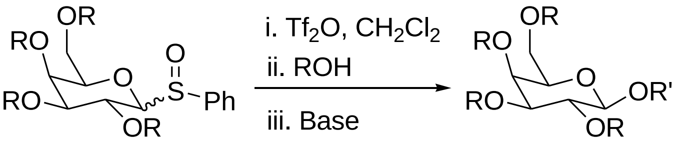


E. J. Corey, K. C. Nicoloau, L. S. Melvin, Jr., J*. Am. Chem. Soc.* **1975**, *97*, 653.

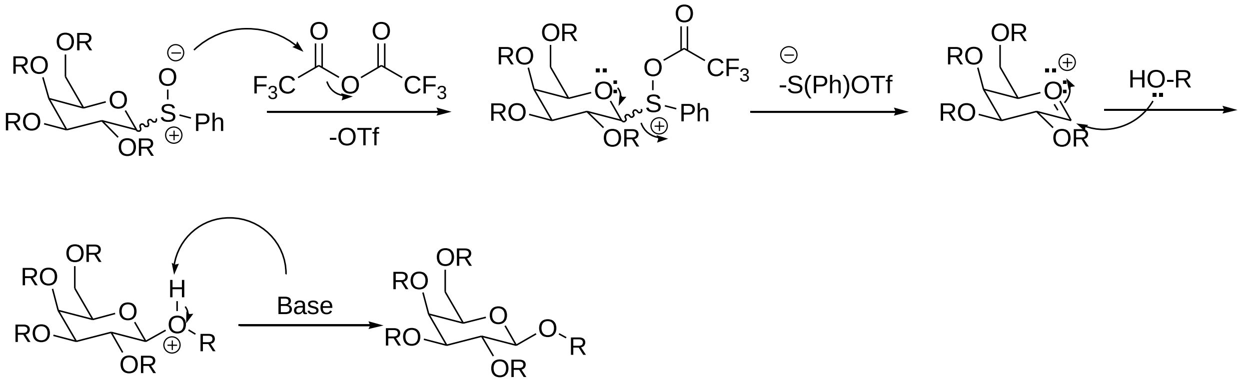
Scheme 11

10.2.8 Kahne Glycosylation

It is a convenient synthesis of glycosides and disaccharides or oligosaccharides between glycosyl phenyl sulfoxide and an acceptor in the presence of a glycosylation promoter such as triflic anhydride (Tf_2O) (Scheme 12).

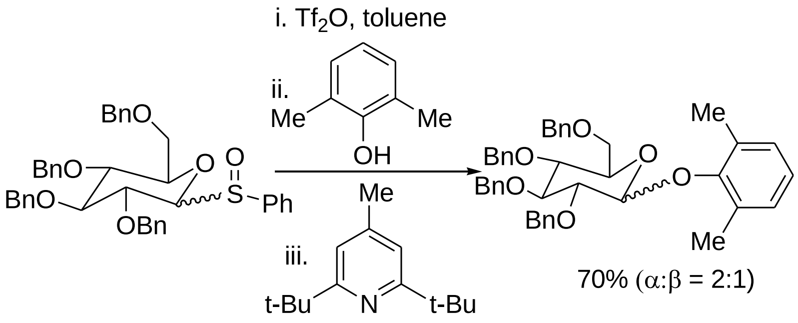


Mechanism

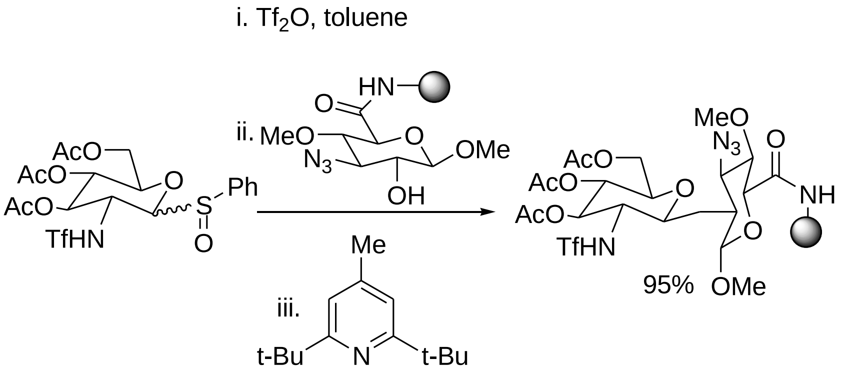


Scheme 12

Examples



D. Kahne, S. Walker, Y. Cheng, D. Van Engen, *J. Am. Chem. Soc.* **1989**, *111*, 6881.

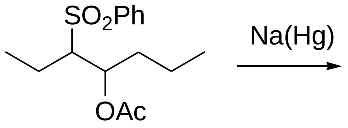


D. J. Silva, H. Wang, N. M. Allanson, R. K. Jain, M. J. Sofia, *J.Org. Chem.* **1999**, *64*, 5926.

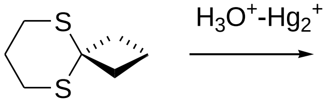
Problems

A. Complete the following reactions.

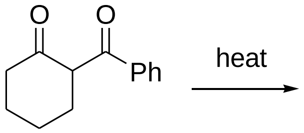
1.



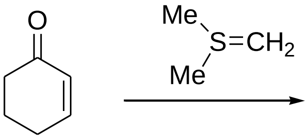
2.



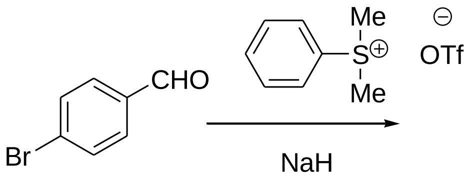
3.



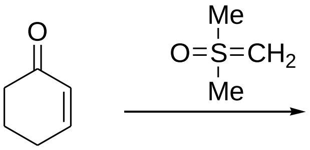
4.



5.

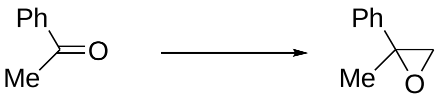


6.



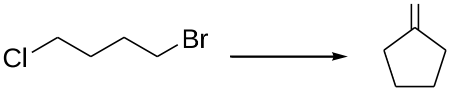
B. How would you use sulfur containing reagents for the following conversions?

1.



2

3.



Text Books

M. B. Smith, *Organic Synthesis*, 2nd Ed., McGraw Hill, Singapore, 2004.

R. O. C. Norman and J. M. Coxon, Principles of Organic Synthesis, CRC Press, London, 2009.

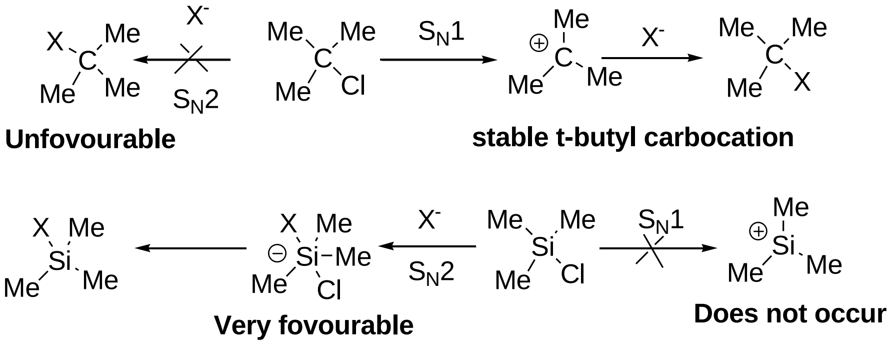
Lecture 25

10.3 Silicon-Containing Compounds

Both silicon and carbon have similarity in having valency of four and formation of tetrahedral compounds. Regarding the differences, carbon forms many stable trigonal and linear compounds having π bonds, while silicon forms few. This is because of the strength of the silicon-oxygen σ bond (368 KJ mol^{-1}) as well as the relative weakness of the silicon-silicon (230 KJ mol^{-1}) bond.

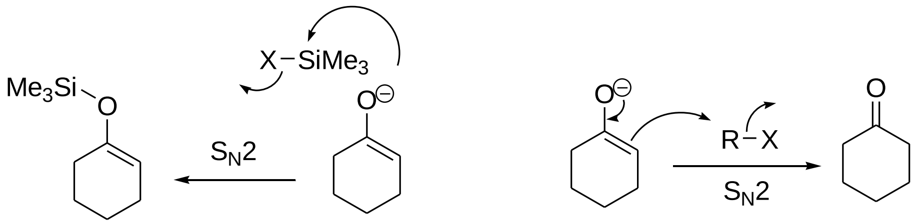
10.3.1 Nucleophilic Substitution Reactions

Nucleophilic substitution at silicon differs in comparison to carbon compounds. For example, trimethylsilyl chloride does not react via S_N1 pathway which is familiar with the analogous carbon compound t-butyl chloride. This is because the S_N2 reaction at silicon is too good.



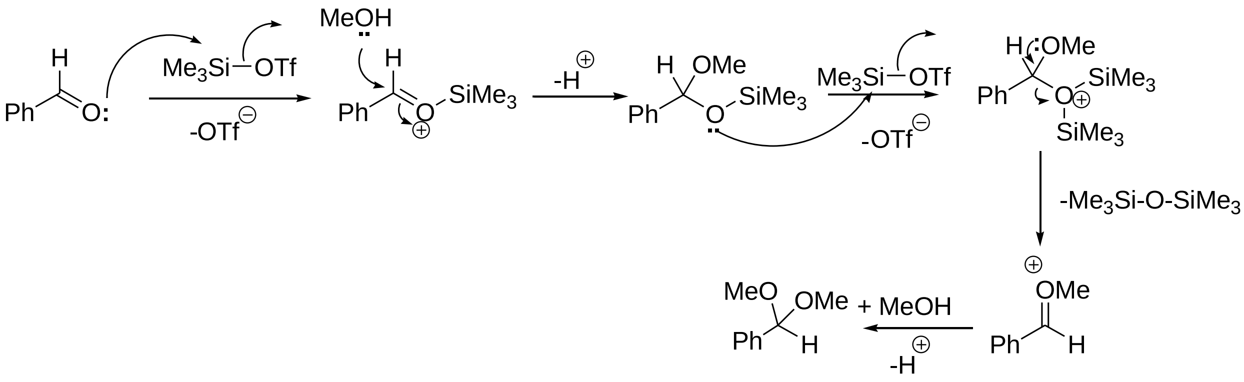
Scheme 1

Let us compare the S_N2 reaction at silicon with the S_N2 reaction at carbon. Alkyl halides are soft electrophiles but silyl halides are hard electrophiles. The best nucleophiles for saturated carbon are neutral or based on elements down the periodic table, whereas the best nucleophiles to silicon are charged or based on highly electronegative atoms. A familiar example is the reaction of enolates at carbon with alkyl halides but at oxygen with silyl chlorides (Scheme 2).



Scheme 2

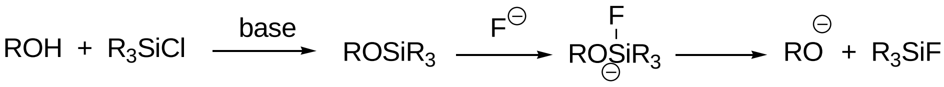
Furthermore, the S_N2 reaction at carbon is not much affected by partial positive charge (□+) on the carbon atom. However, the S_N2 reaction at silicon is affected by the charge on silicon. For example, the most electrophilic silyl triflates react 10^9 times fast with oxygen nucleophiles than silyl chlorides do (Scheme 3).



Scheme 3

10.3.2 Application as Protecting Groups for Alcohols

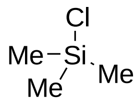
Silicon based protecting groups are the versatile for alcohols. They can be easily introduced and removed in high yield without affecting the rest of the molecule in a wide range of conditions. The rate of the introduction as well as the removel depends on the steric nature of the alcohols as well as the silyl group (Scheme 4).

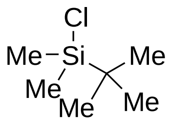


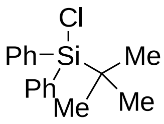
$$ROH + R_3SiCl \xrightarrow{\text{base}} ROSiR_3 \xrightarrow{F^{\ominus}} RO\underset{\ominus}{\overset{F}{Si}}R_3 \longrightarrow \overset{\ominus}{RO} + R_3SiF$$

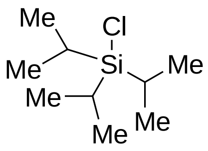
Scheme 4

Some the commonly used protecting for alcohols follows:



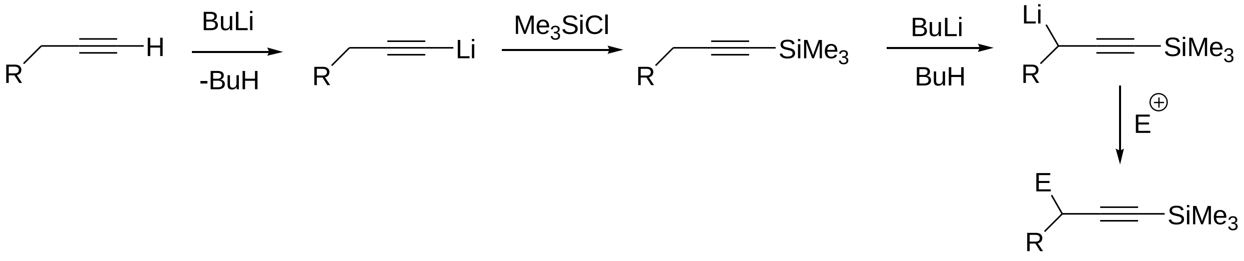






10.3.3 Application as Protecting Groups for Alkynes

The silyl group can be used to protect the terminus of the alkyne during the reaction and can also be easily removed with fluoride or sodium hydroxide (Scheme 5).

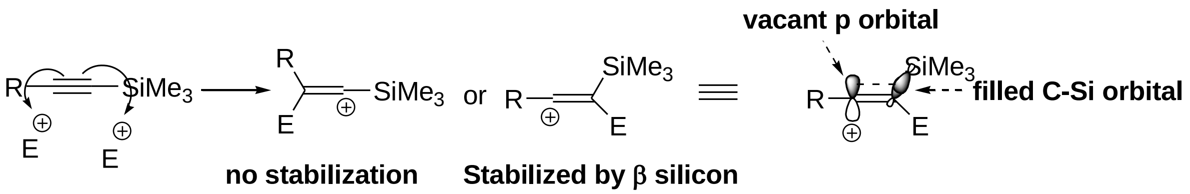


Scheme 5

10.3.3 Directive Influence of SiR_3 in Electrophilic Reactions

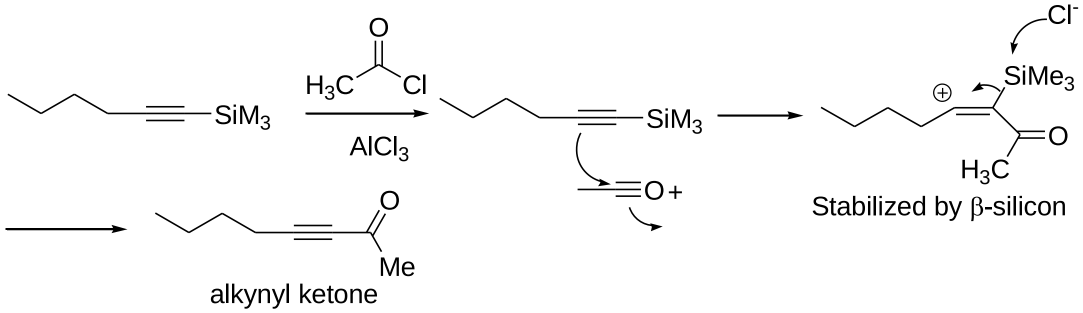
10.3.3.1 Alkynylsilanes

Similar to alkynes, silylated alkynes are too nucleophilic towards electrophiles. However, the presence of silicon has a dramatic effect on the regioselectivity of the reaction: the attack occurs only at the atom directly bonded to silicon (Scheme 6). This is due to the stabilization of the intermediate vacant π orbital by the filled C-Si sigma orbital.



Scheme 6

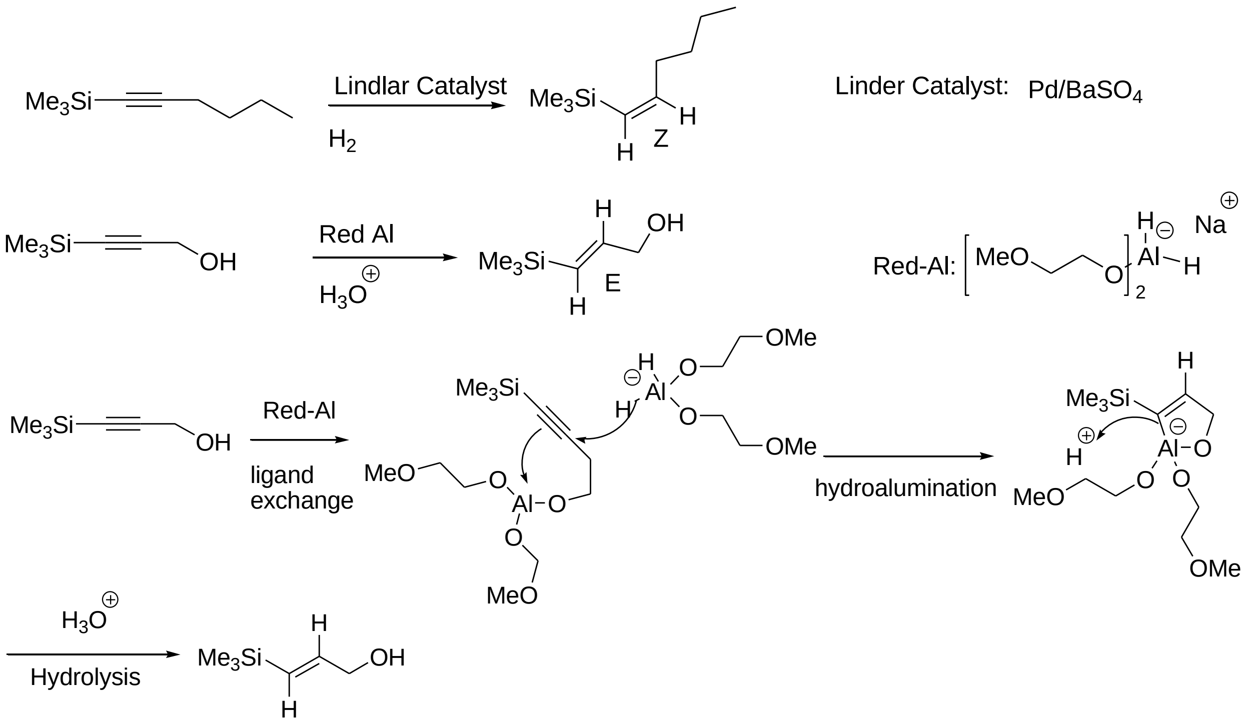
The stabilization of the cation weakens the C-Si bond by the delocalization of the electron density. The attack of a nucleophile on silicon readily removes it from the organic fragment and the net result is the electrophilic substitution in that the silicon is replaced by the electrophile (Scheme 7).



Scheme 7

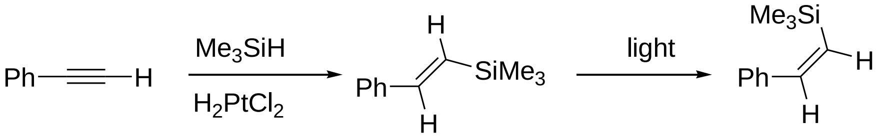
10.3.3.2 Vinyl Silanes

The controlled reduction of alkynyl silanes can produce vinayl silanes. The stereochemistry depends on the methods used. Lindlar hydrogenation takes place via *cis* fashion, while red Al reduction of propargylic alcohol gives *E*-isomer (Scheme 8).



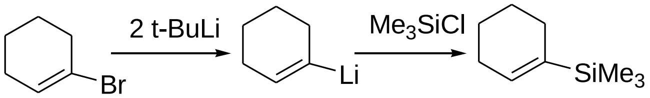
Scheme 8

Alternatively, hydrosilylation of simple alkyne can give E-vinyl silane that could be irradiated to afford Z-isomer (Scheme 9).



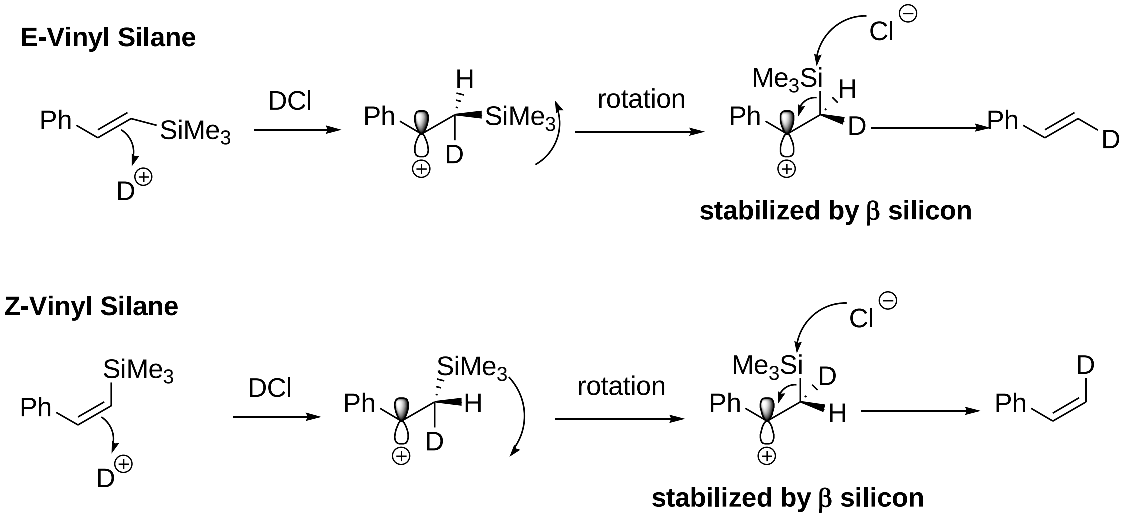
Scheme 9

In addition, metal-halogen exchange of vinyl halide can give vinylic organometallic compound that could be cross-coupled with silyl chloride. These reactions can take place with retention of configuration (Scheme 10).



Scheme 10

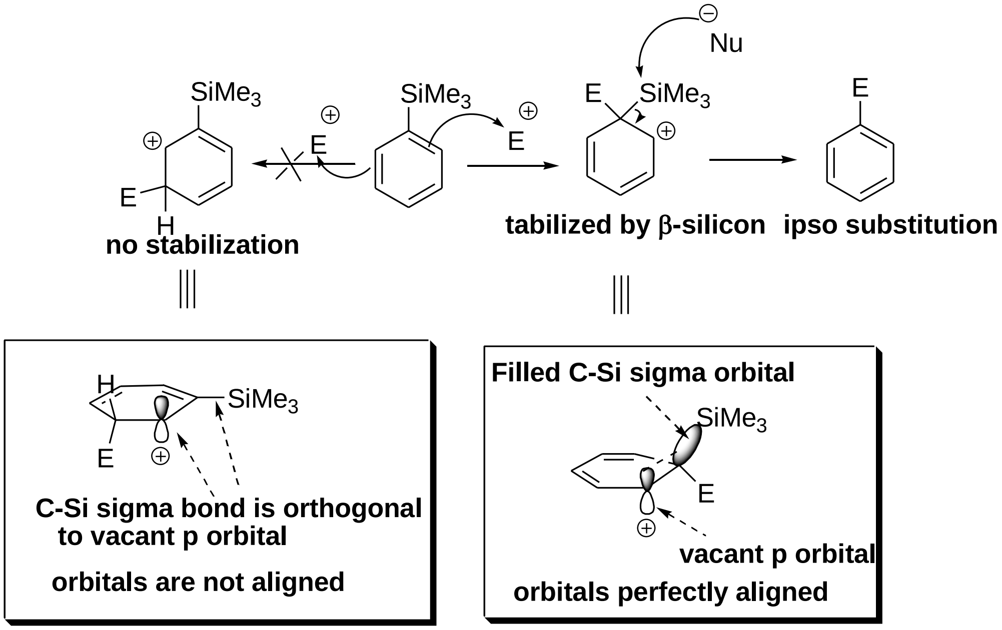
The reactions of vinyl silanes with electrophiles afford an effective route for the synthesis of alkenes with high stereoselectivity. The stereochemistry is important because the exchange usually occurs with retention of geometry (Scheme 11).



Scheme 11

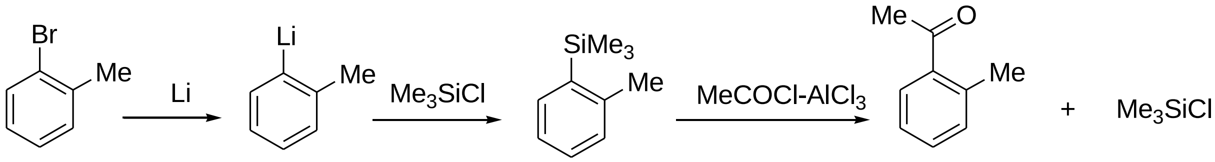
10.3.3.2 Aryl Silanes

The same sort of mechanism involves for reactions of aryl silanes with electrophiles. In these reactions the silyl group is replaced by the electrophiles at the same atom on the ring. This is called as *ipso* substitution (Scheme 12).



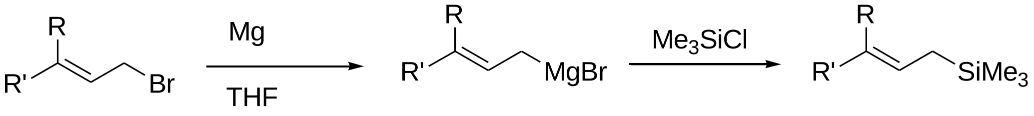
Scheme 12

An example for *ipso* substitution follows:



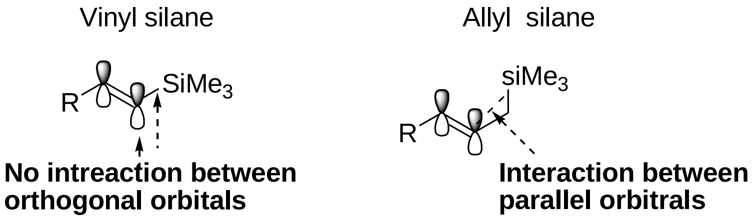
10.3.3.2 Allyl Silanes

Allylsilanes can be readily prepared from allyl halide via Grignard reaction (Scheme 13).

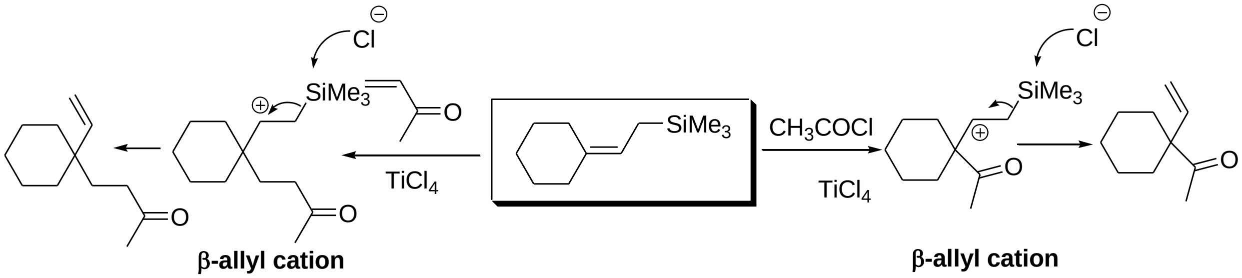


Scheme 13

Allyl silanes are more reactive compared to vinyl silanes (Scheme 14). This is because vinyl silanes have C-Si bonds orthogonal to the p orbitals of the alkene, in contrast, allyl silanes have C-Si bonds that can be parallel to the p orbitals of the double bond so that interaction can be possible. However, both react with electrophiles at the *ipso* atom occupied by silicon. In both cases a□ □-silylcation is an intermediate.

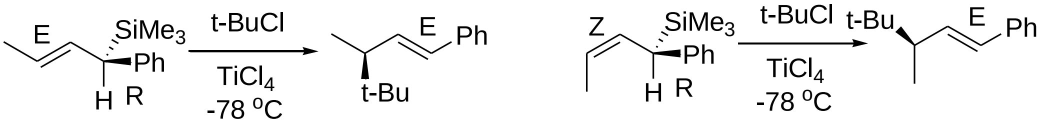


For example,



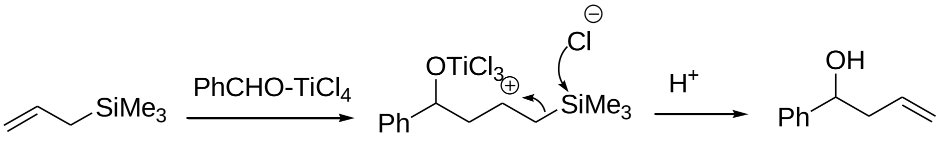
Scheme 14

In optically active compounds, one enantiomer of the allyl silane gives one enantiomer of the product (Scheme 15). The stereogenic centre next to silicon disappears and new one appears.



Scheme 15

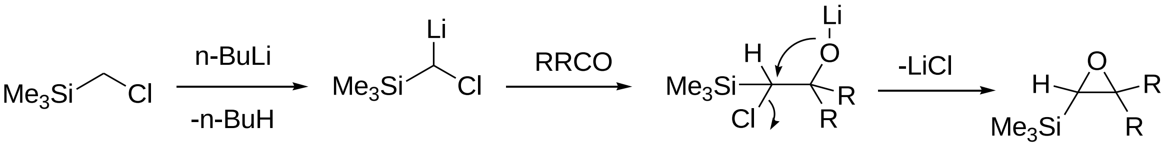
Allyl silanes also attack carbonyl compounds in the presence of Lewis acid which activates the carbonyl group **(Scheme 16)**.



Scheme 16

10.3.3.2 Silyl Epoxides

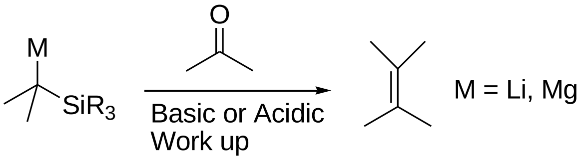
Silyl epoxides can be prepared from vinyl silanes with peroxy acids or from ketones (Scheme 17).



Scheme 17

10.3.5 Peterson Olefination Reaction

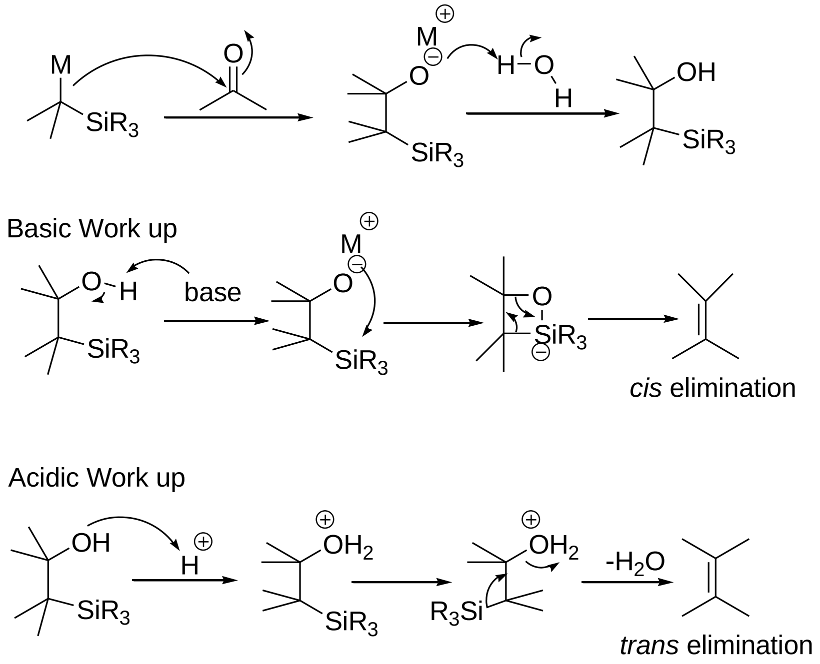
Peterson olefination, which is closely related to the Wittig reaction, can be carried out in two ways using either acid or base and the geometry of the alkenes can be controlled accordingly (Scheme 18).



Scheme 18

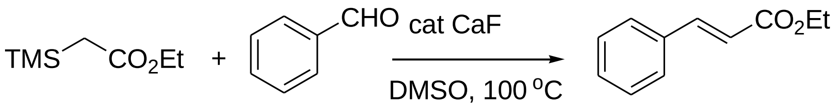
Mechanism

The reactions are *anti* under acidic conditions and *syn* under basic conditions (Scheme 19). The stereoselectivity is due to involvement of a cyclic transition state under basic conditions, whereas under acidic conditions an acylic mechanism involves.

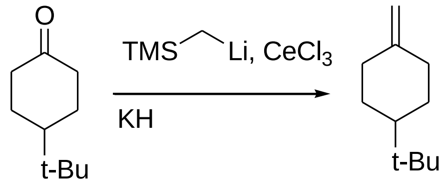


Scheme 19

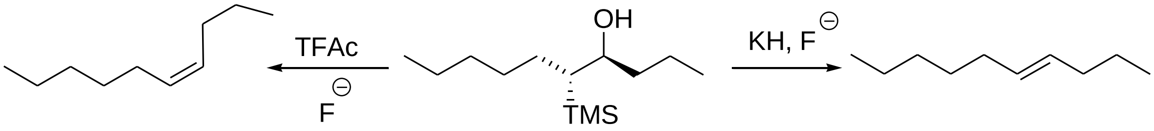
Examples



M. Bellassoued, N. Ozanne, *J Org. Chem.* **1995**, *60*, 6582.



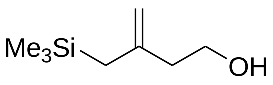
B. Henkel, B. Beck, Westner, B. Mejat, A. Domling, *Tetrahedron Lett.* **2003**, *44*, 89.

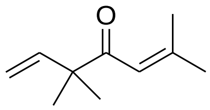


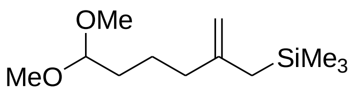
A. G. M. Barrett, J. A. Flygare, *J. Org. Chem*. **1991**, *56*, 638.

Problems

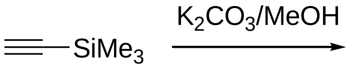
A. How would you utilize silicon-containing reagents in the synthesis of the following compounds?

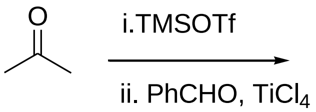


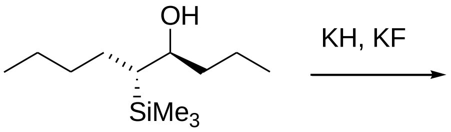


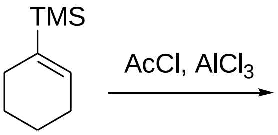


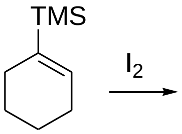
B. Complete the following reactions.

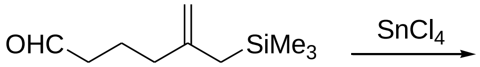
1. 

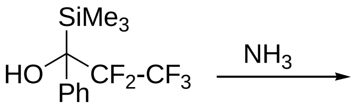
2. 

3. 

4. 

5. 

6. 

7. 

Text Books

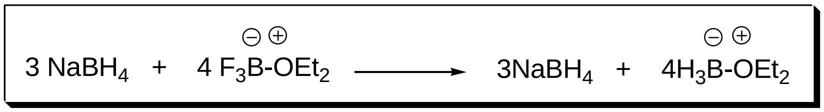
J. Clayden, N. Greeves, S. Warren, P. Wothers, *Organic Chemistry*, Oxford University Press, 2001.

R. O. C. Norman, J. M. Coxon, *Principles Organic Synthesis*, CRC Press, 2009.

Lecture 26

10.4 Boron Containing Compounds

Boron containing compounds find wide applications in organic synthesis. Borane (BH_3) is commercially available in the form of complexes generally with THF, Et_2O and Me_2S. It can also be prepared *in situ* by the reaction of $NaBH_4$ with $BF_3{\cdot}OEt_2$ complex (Scheme 1):



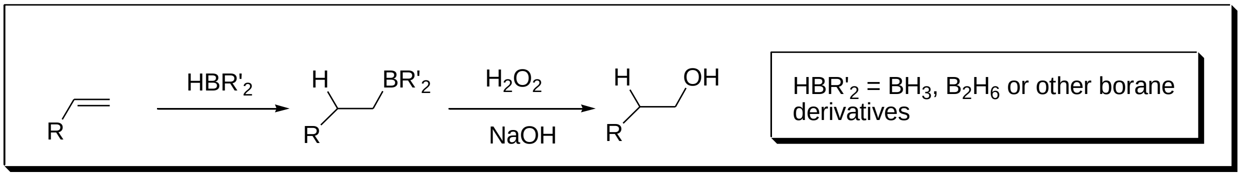
$$3\ NaBH_4 + 4\ F_3\overset{\ominus}{B}\text{-}\overset{\oplus}{O}Et_2 \longrightarrow 3NaBH_4 + 4H_3\overset{\ominus}{B}\text{-}\overset{\oplus}{O}Et_2$$

Scheme 1

Organoboranes are synthesized by the addition reaction of borane to alkenes and alkynes.

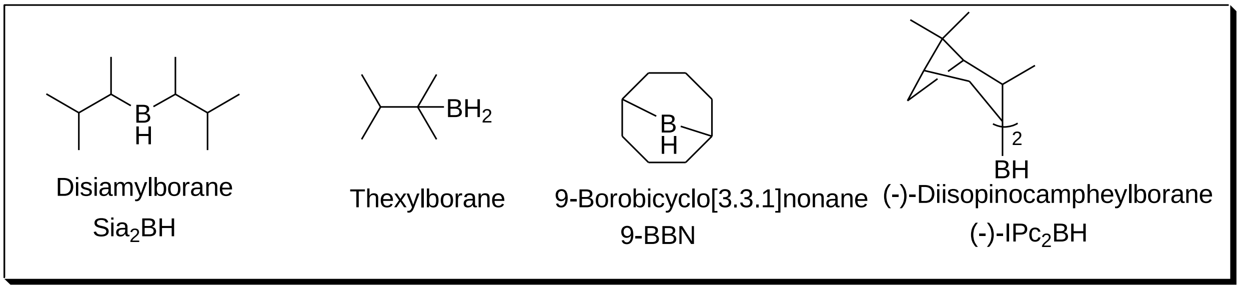
10.4.1 Hydroboration of Alkenes

The reaction of borane with alkenes gives alkylboranes that readily proceed oxidation in the presence of alkaline hydrogen peroxide to yield alcohols (Scheme 2). The conversion of C-B bond into a C-OH takes place with retention of stereochemistry.



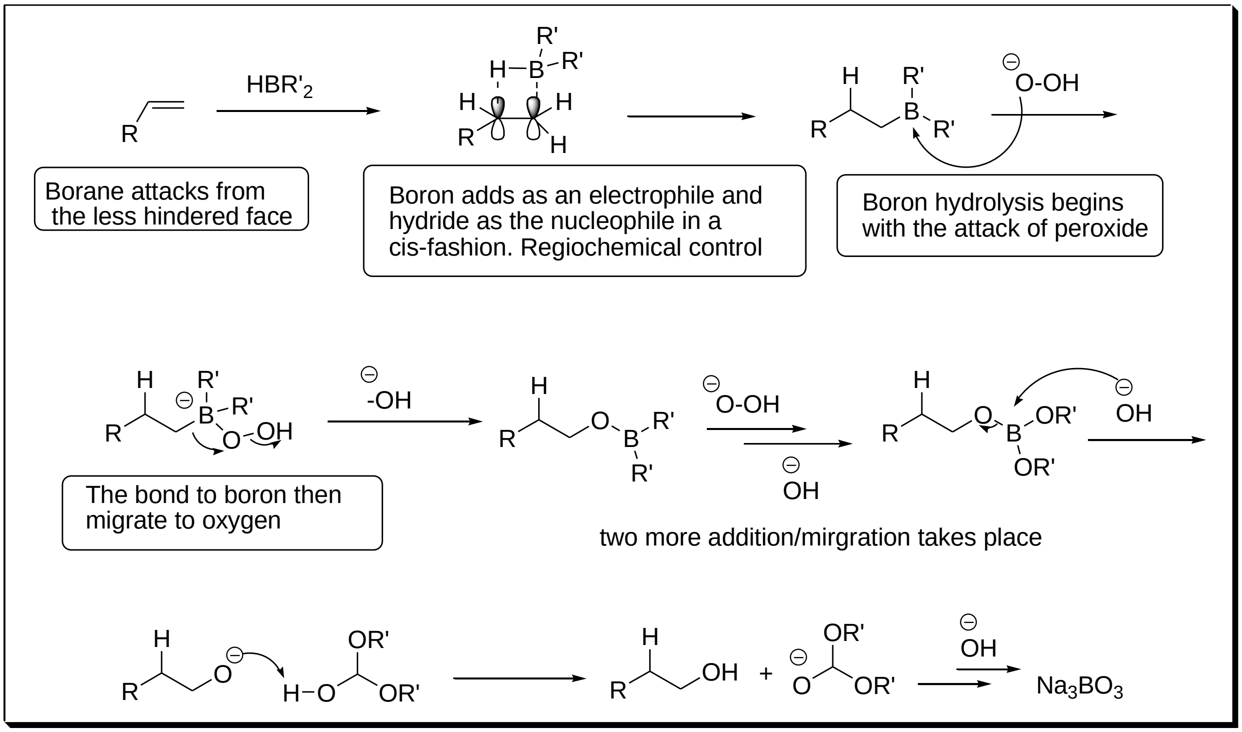
Scheme 2

In case of sterically hindered alkenes such as trisubstituted ones, it is more difficult to add three alkenes to borane. This becomes the basis for the development of a variety of borane derivatives. For some examples, see:



Mechanism

The hydroboration reactions proceed by *cis* addition of hydrogen and boron to alkenes, probably *via* a four-centred cyclic transition state (Scheme 3).



Borane attacks from the less hindered face

Boron adds as an electrophile and hydride as the nucleophile in a cis-fashion. Regiochemical control

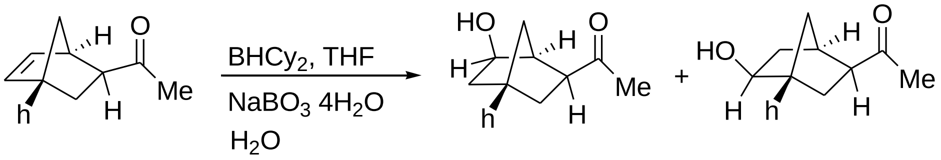
Boron hydrolysis begins with the attack of peroxide

The bond to boron then migrate to oxygen

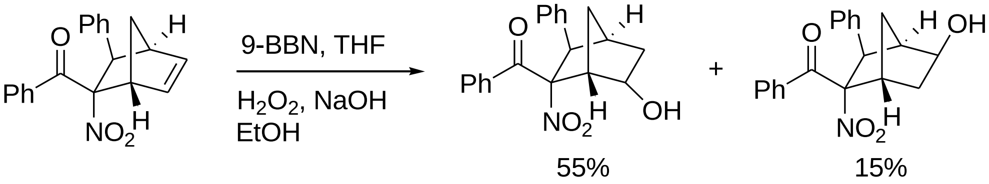
two more addition/mirgration takes place

Scheme 3

Examples:



G. W. Kabalka, S. Yu, N.-S. Li, *Tetrahedron Lett.* **1997**, *38*, 5455.

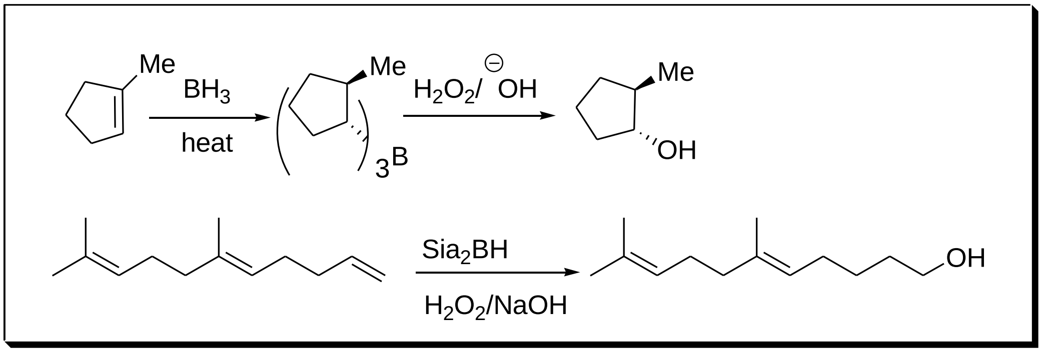


D.L. Gober, R. A. Lerner, B. F. Cravatt, *J. Org. Chem.* **1994**, *59*, 5078.

10.4.2 Reactions of Alkylboranes

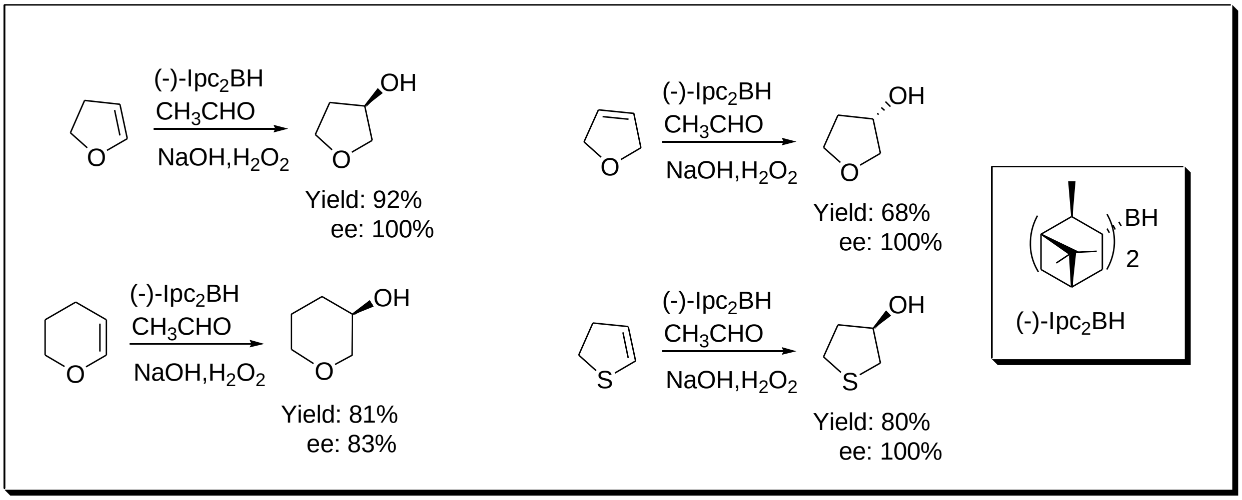
10.4.2.1 Oxidation to Alcohols

Hydroboration and oxidative strategy provides an effective route for the transformation of alkenes to alcohols with retention of configuration at the boron-bearing carbon (Scheme 4).



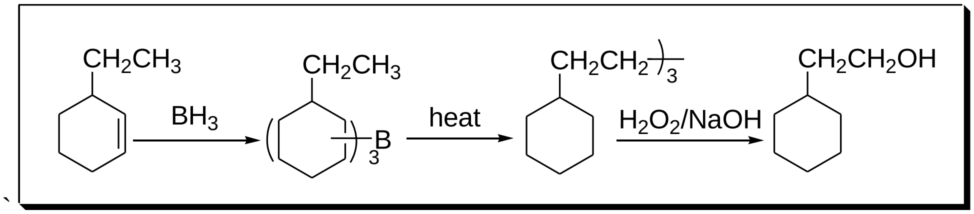
Scheme 4

Asymmetric version of this process has made a remarkable progress using chiral boranes with excellent enantioselectivity (Scheme 5).



Scheme 5

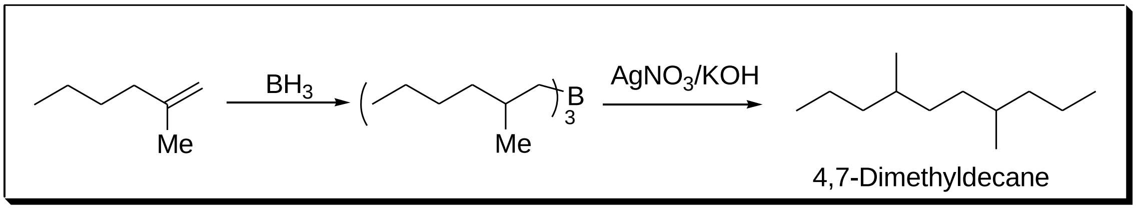
Alkylboranes also undergo isomerization on heating to give products that contain the boron atom at the least hindered position of the alkyl chain (Scheme 6).



Scheme 6

10.4.2.2 Coupling Reaction

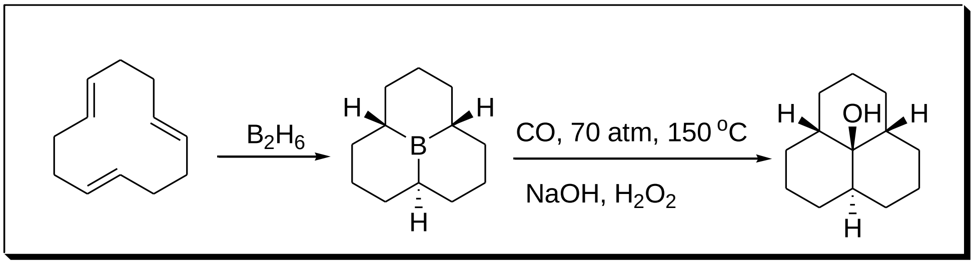
Alkylboranes can be coupled using basic silver nitrate via an alkyl silver intermediate that affords a useful tool for the carbon-carbon bond formation (Scheme 7).



Scheme 7

10.4.2.3 Carbonylation: Formation of Alcohols, Aldehydes and Ketones

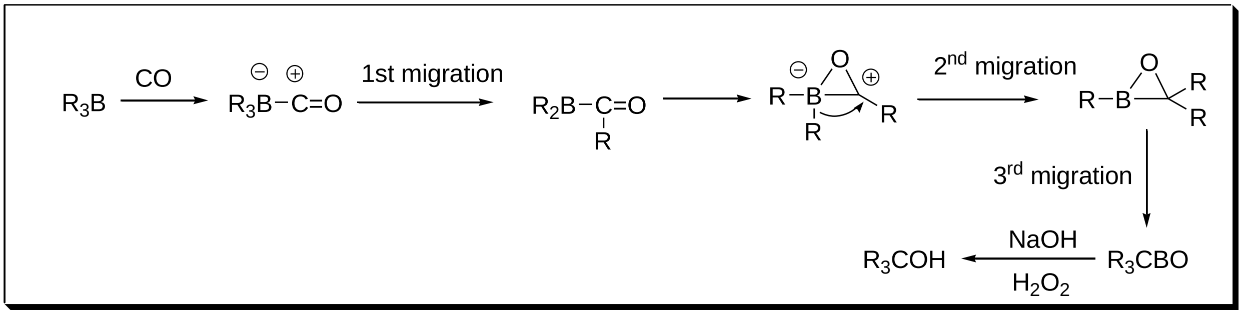
The reactions of organoboranes with carbon monoxide open up a variety of synthetic pathways for the preparation of alcohols, aldehydes and ketones. For example, 1,5,9-cyclododecatriene with B_2H_6 provides tricyclic borane that can be converted into tricylic alcohol via carbonylation and oxidation (Scheme 8).



Scheme 8

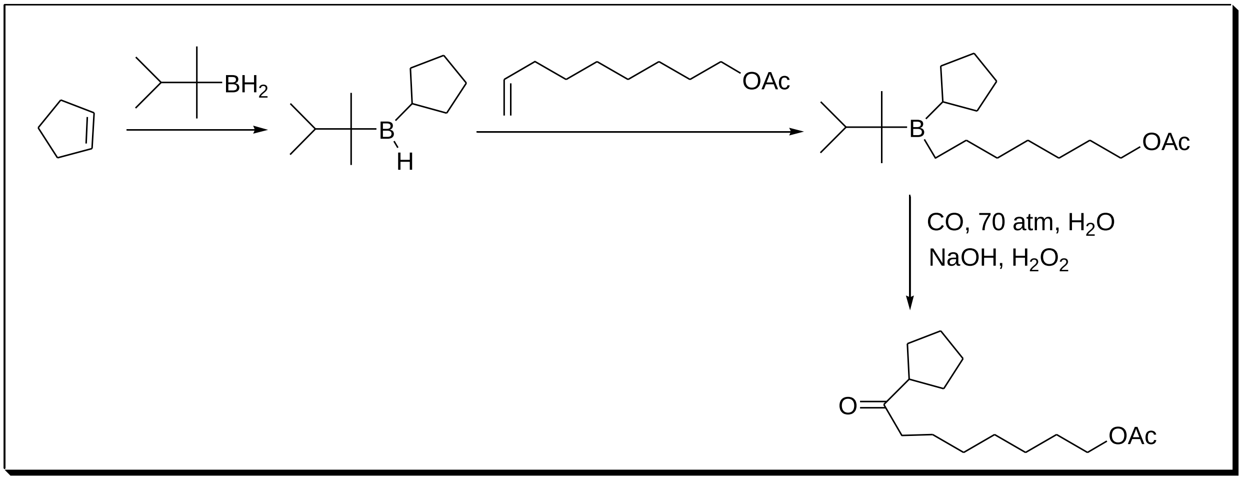
Mechanism

The reaction involves migration of alkyl groups from boron to the carbon atom of CO (Scheme 9).



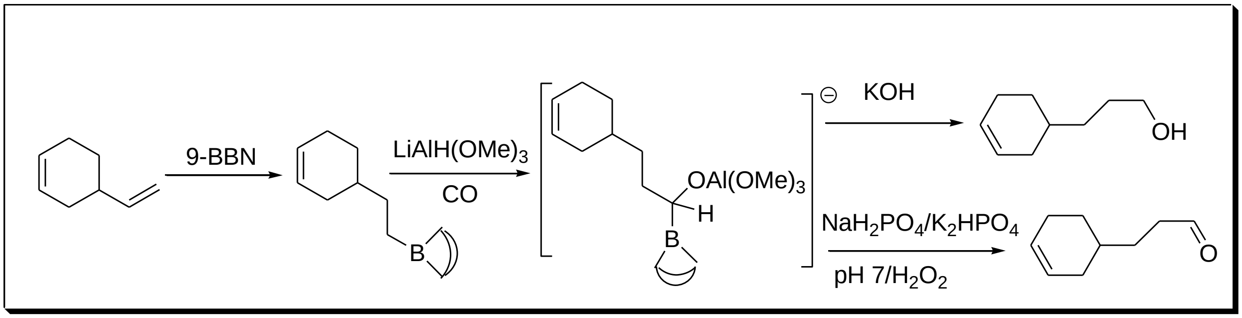
Scheme 9

In presence of a small amount of water, migration of third alkyl group from boron to carbon can be inhibited to give dialkylketone (Scheme 10).



Scheme 10

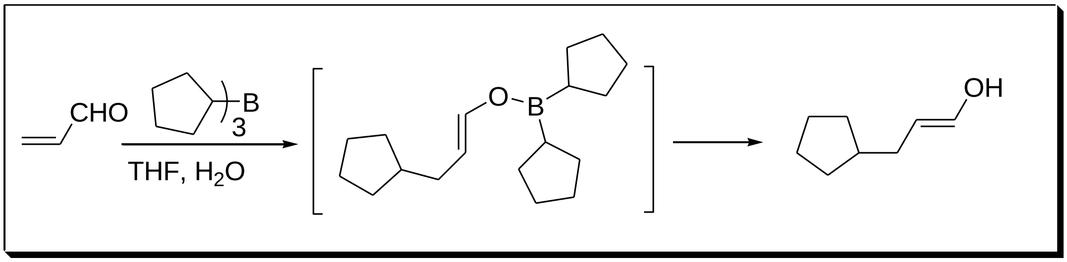
The carbonylation sequence can be modified to give aldehydes and primary alcohols (Scheme 11).



Scheme 11

10.4.2.4 Conjugate Addition

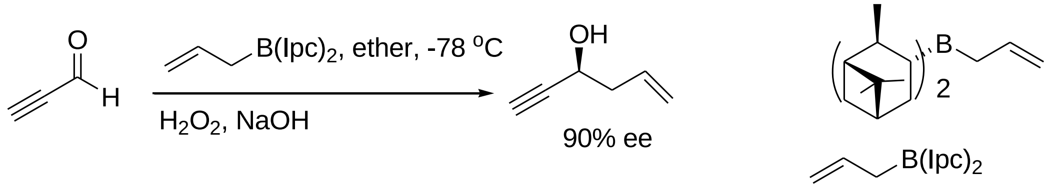
Alkylboranes proceed conjugate addition with α,β-unsaturated aldehydes and ketones (Scheme 12). The alkyl group of the borane undergoes 1,4-addition and boron is transferred to the oxygen, providing a boron enolate that on hydrolysis yields the product.



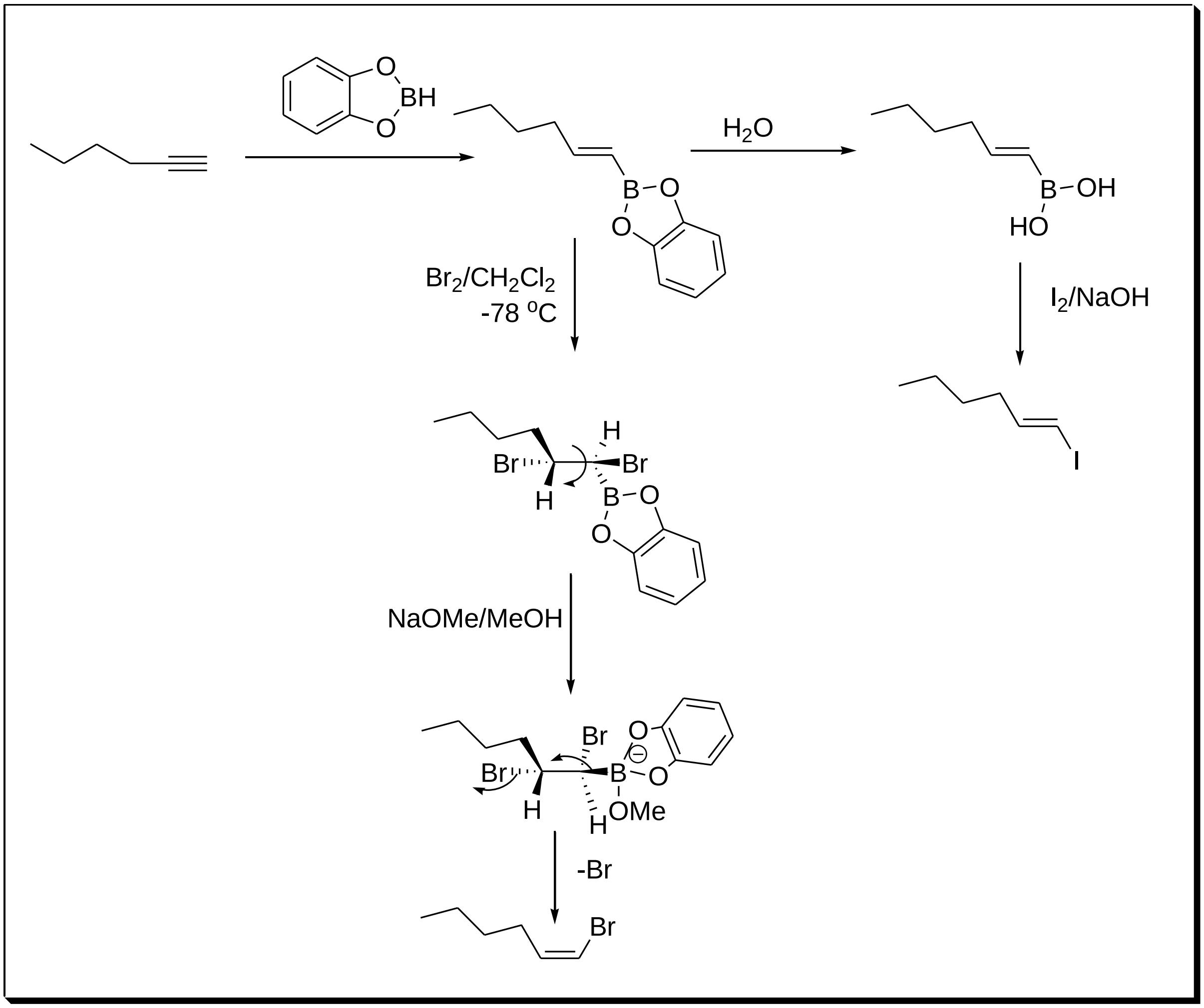
Scheme 12

10.4.2.5 Allylation to Carbonyl Compounds

The reaction of allylboranes with carbonyl compounds has been well explored. Several studies have focused on asymmetric version of the process with excellent enantioselectivity. For example, the reaction of (-)-β-allyl(diisopinocampheyl)borane with propiolaldehyde gives hex-5-ene-1-yn-3-ol with 90% ee after the oxidation (Scheme 13).



Scheme 13

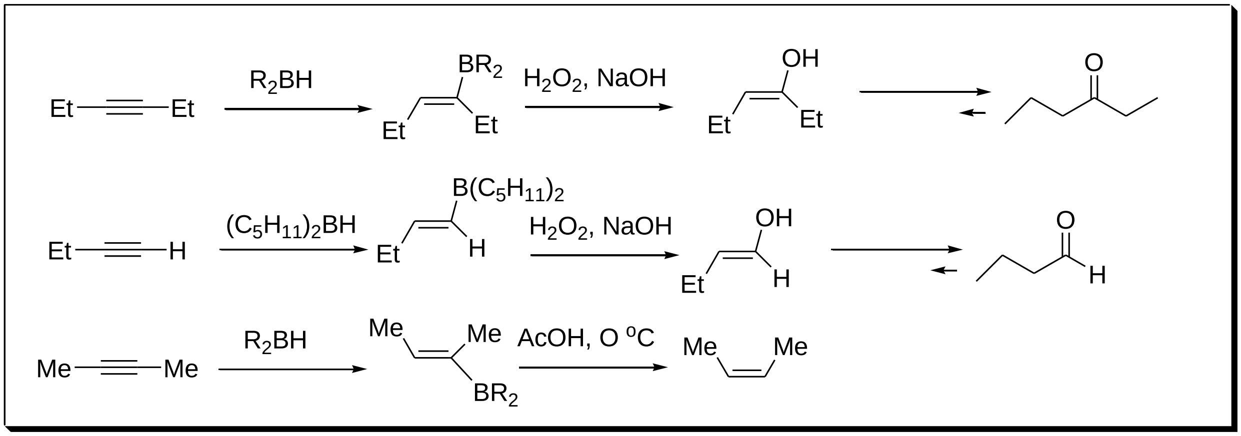


O
BH
O
H$_2$O
B
O
O
B
OH
HO
Br$_2$/CH$_2$Cl$_2$
-78 °C
I$_2$/NaOH
I
H
Br
Br
H
B
O
O
NaOMe/MeOH
Br
O
Br
B
O
H
H
OMe
-Br
Br

Scheme 14

10.4.3 Vinylboranes

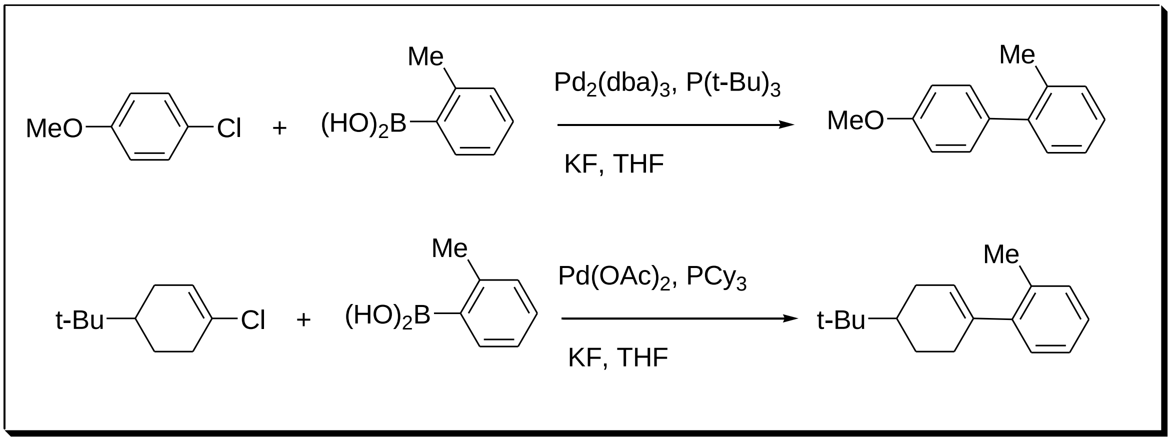
Borane with alkynes gives vinylboranes that serve as useful intermediates in organic synthesis. For example, 1-hexyne with catcholborane yields *trans*-1-alkenylborone that can be converted into *trans*-vinyl iodide and *cis*-vinyl bromide that are substrate precursors for the C-C coupling reactions using palladium catalysis (Scheme 14). Vinylboranes can also be converted into aldehydes, ketones or alkenes and the reactivity and selectivity depend on the nature of organoboranes used (Scheme 15).



Scheme 15

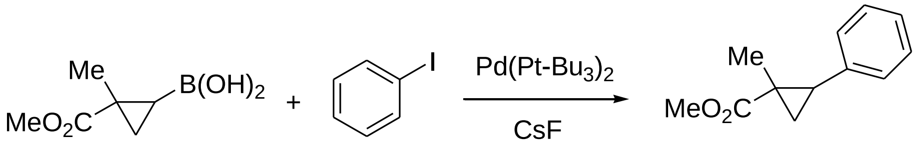
10.4.4 Suzuki Coupling

The coupling of organic boronic acid with halides or triflates using palladium-catalysis leads to a powerful protocol for the carbon-carbon bond formation (Scheme 17). The mechanism has been discussed in lecture 34.

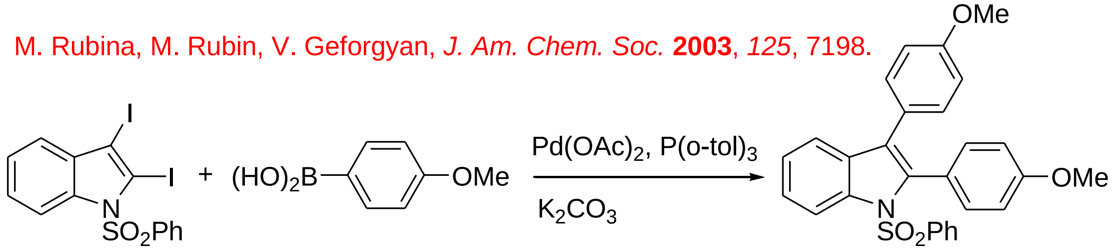


Scheme 16

Examples:



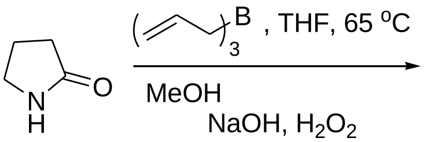
M. Rubina, M. Rubin, V. Geforgyan, *J. Am. Chem. Soc.* **2003**, *125*, 7198.

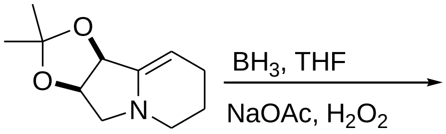


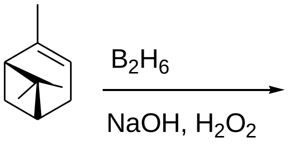
Y. Liu, G. W. Gribble, *Tetrahedron Lett.* **2000**, *41*, 8717.

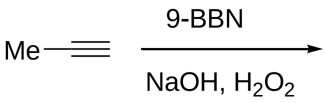
Problems

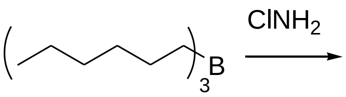
A. What products would you expect from the following reactions?

1. 

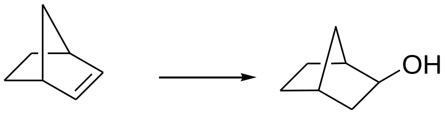
2. 

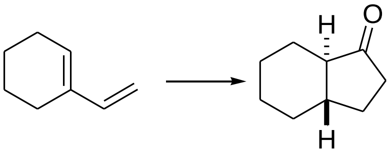
3. 

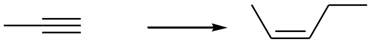
4. 

5. 

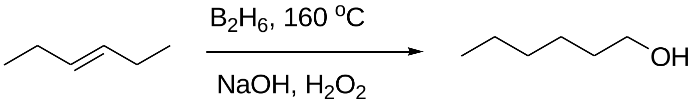
B. How would you utilize boron-containing reagents for the following conversions?

1. 

2. 

3. 

C. Rationalize the following reaction:



Text Books

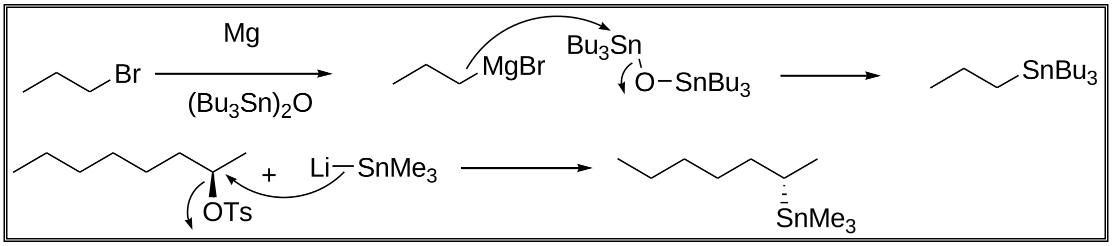
J. Clayden, N. Greeves, S. Warren, P. Wothers, *Organic Chemistry*, Oxford University Press, 2001.

R. O. C. Norman, J. M. Coxon, *Principles Organic Synthesis*, CRC Press, 2009.

Lecture 27

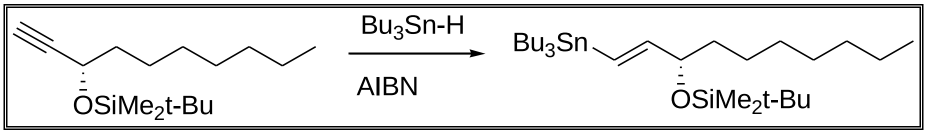
10.5 Tin-Containing Compounds

The synthesis of organotin compounds is similar to that of organosilicones. The reaction of Grignard reagent with bis(tributyltin)oxide gives alkyl tributyltin. The polarity can be reversed and stannyl lithium can add to organic electrophiles (Scheme 1).



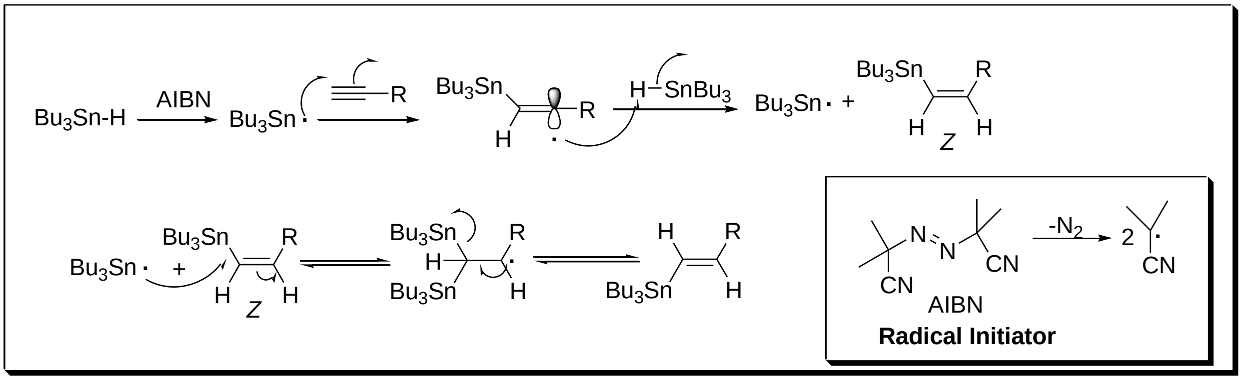
Scheme 1

The hydrostannylation of an alkyne with tin hydride affords kinetically controlled Z-vinyl stannane. If there is an excess of tin hydride or sufficient radicals are present, isomerization may take place to afford the more stable *E*-isomer (Scheme 2-3).



Scheme 2

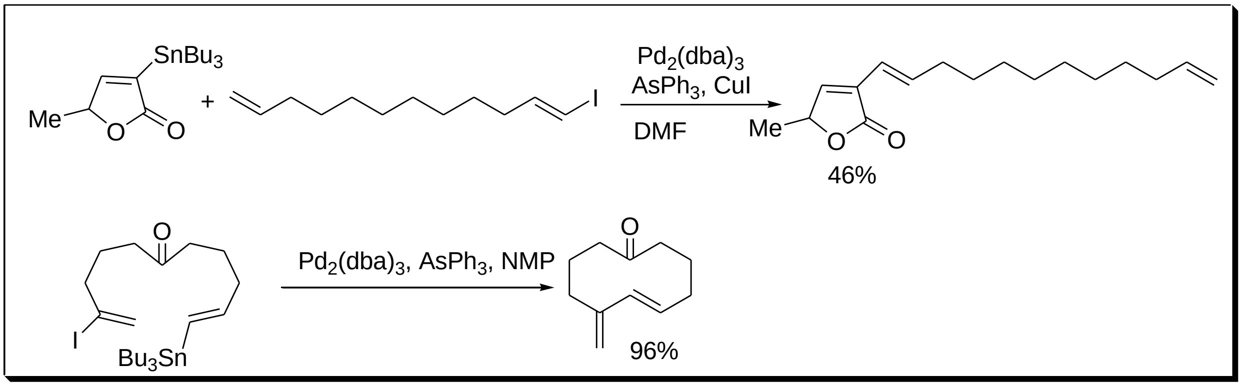
Mechanism



Scheme 3

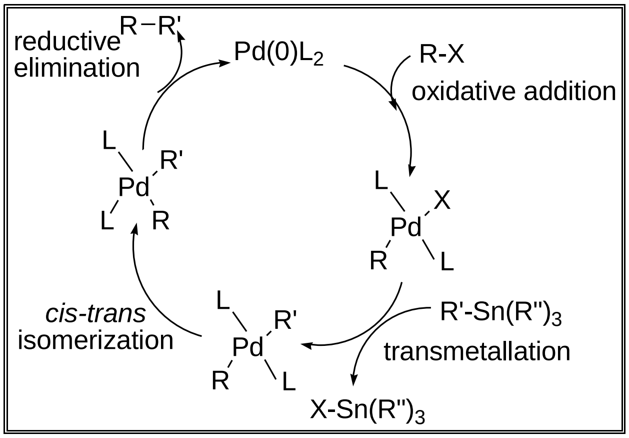
10.5.1 Stille Coupling

Palladium-catalyzed cross-coupling of vinyl stannanes with vinyl halides or triflates give dienes (Scheme 4-5). The reaction functions under relatively neutral conditions and compatible with many functional groups. Both inter- and intramolecular versions of the reactions have been explored and find extensive applications in natural product synthesis.



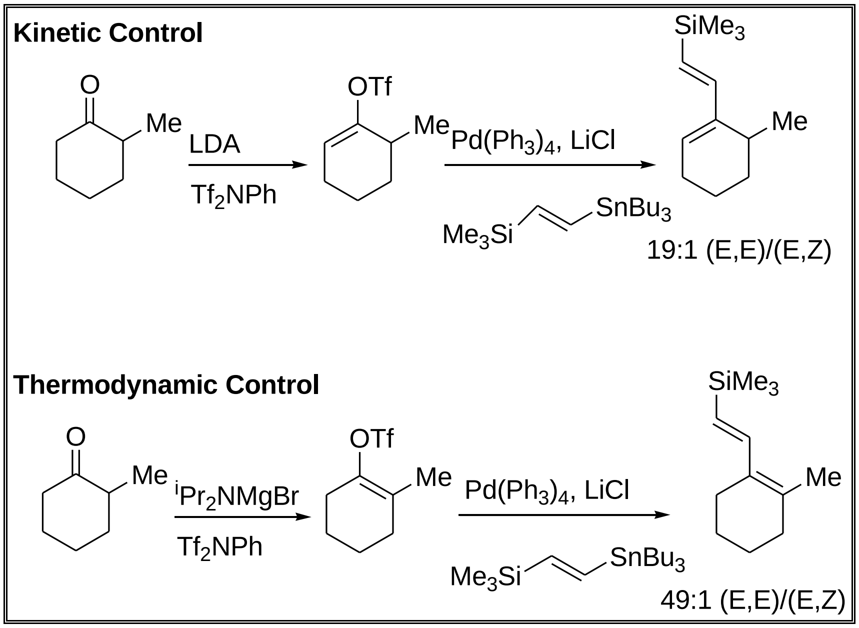
Scheme 4

Mechanism



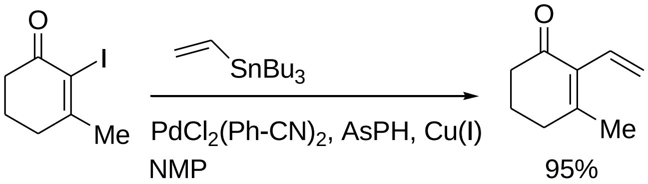
Scheme 5

If the electrophile is a vinyl triflate, the addition of LiCl to the reaction is essential because the chloride may displace triflate form the palladium σ-complex. The transmetallation takes place with chloride on palladium and not with triflate (Scheme 6).

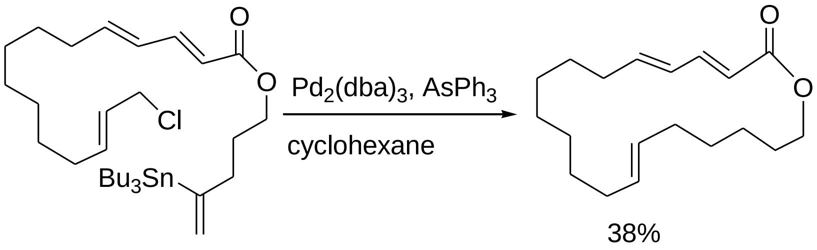


Scheme 6

Examples:



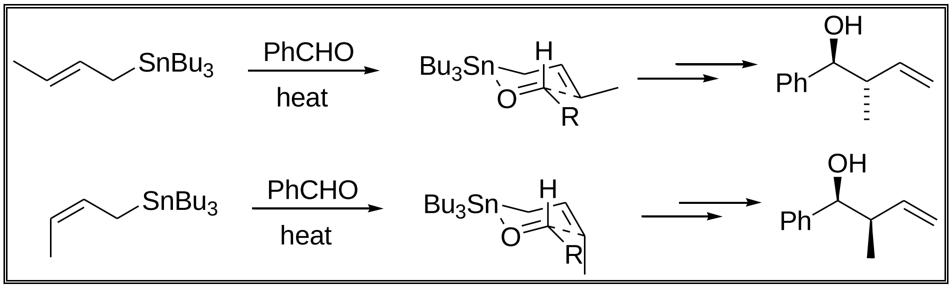
S. T. Handy, X. Zhang, *Org. Lett.* **2001**, *3*, 233.



C. Boden, G. Pattenden, *Synlett* **1994**, 181.

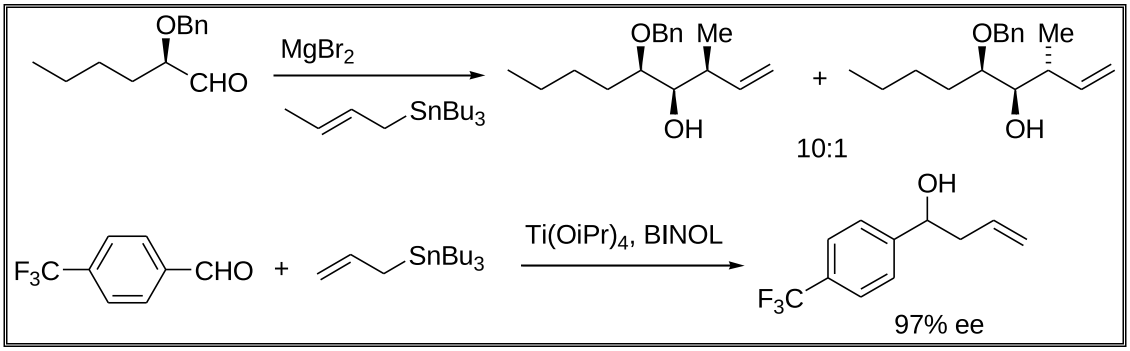
10.5.2 Reactions of Allyl Stannanes

Allyl stannanes are important reagents because they can be used for allylation to aldehydes with excellent stereocontrol (Scheme 7).



Scheme 7

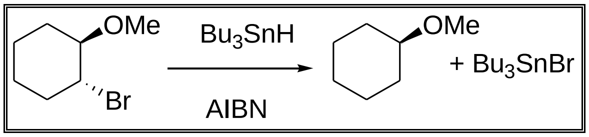
The asymmetric allyllation of aldehydes with ally stannanes has also been explored (Scheme 8).



Scheme 8

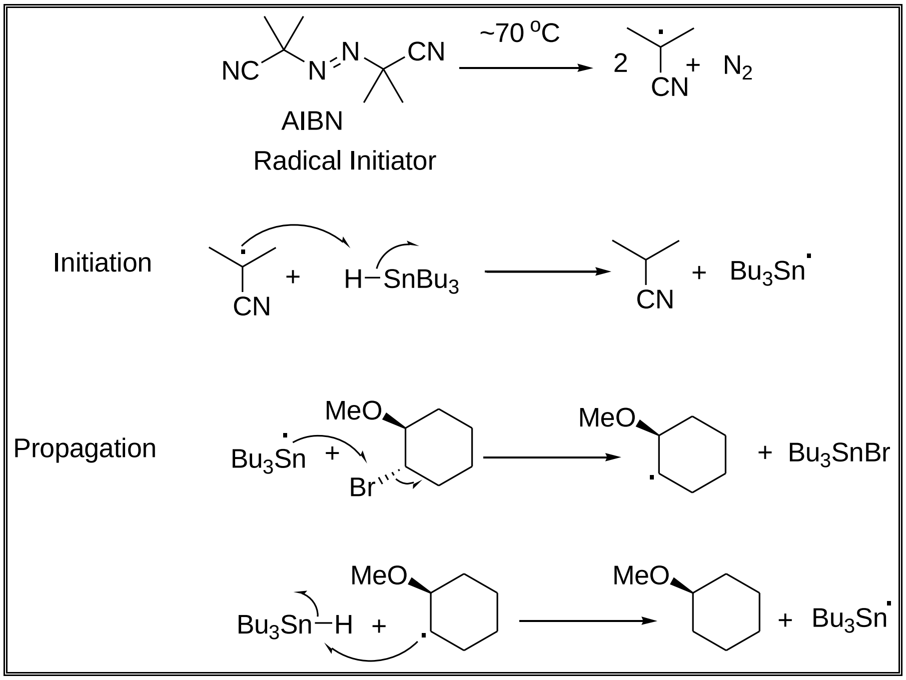
10.5.3 Reactions of Tributyltinhydride

Tributyltinhydride (Bu_4SnH) is a versatile reagent for the removal of halogen (I and Br) from alkyl halides (Scheme 9-10). The reaction is carried out either in the presence of light or AIBN which is a radical initiator.



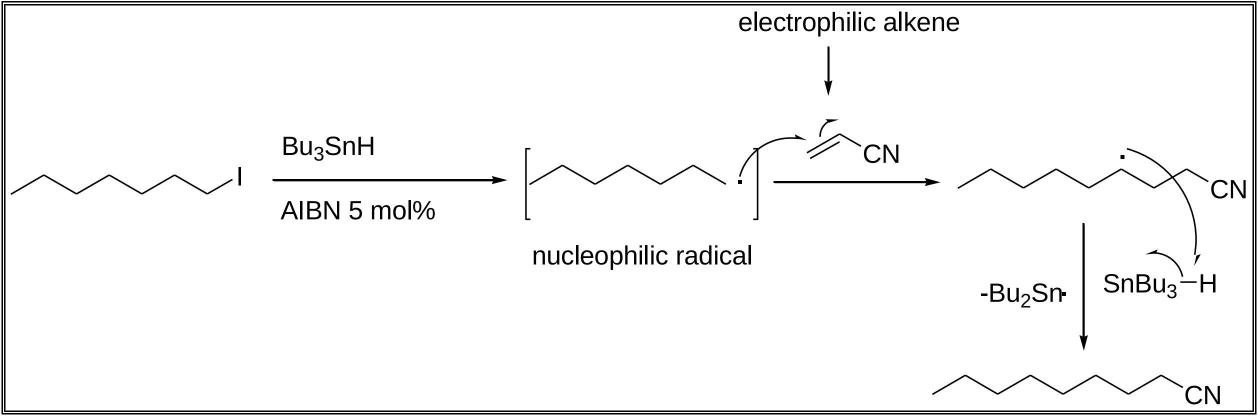
Scheme 9

Mechanism



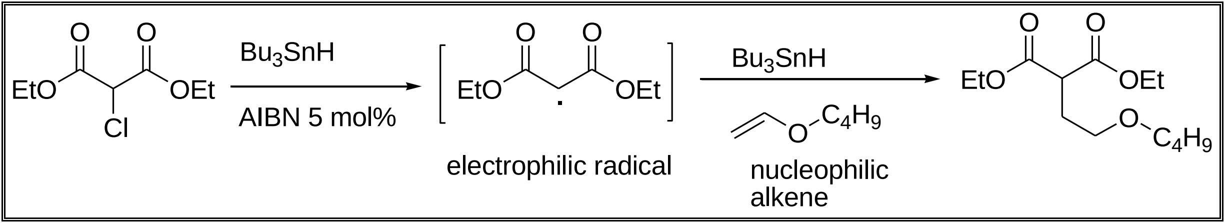
Scheme 10

The alkyl radical can also undergo addition to alkenes to give alkane via the formation new carbon-carbon bond. Both inter- and intramolecular versions of this process have been explored. For example, Bu_3SnH mediated addition of nucleophilic radical to electrophilic alkene can be accomplished in good yield (Scheme 11).



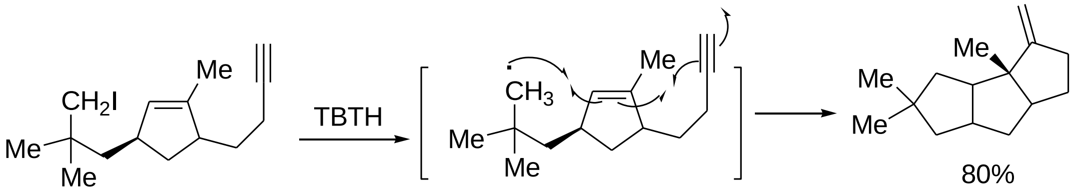
Scheme 11

Similarly, the Bu_3SnH mediated addition of electrophilic radical to nucleophilic alkene can also be accomplished (Scheme 12).

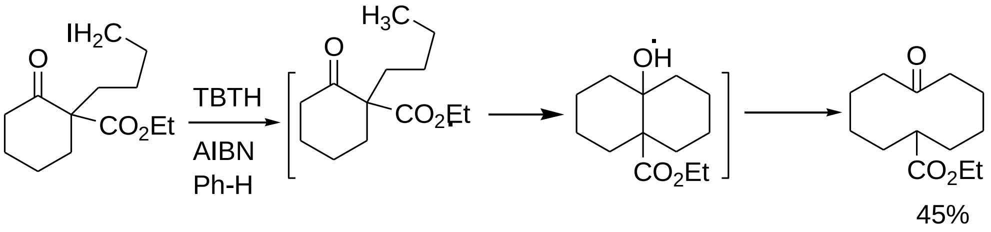


Scheme 12

Examples:



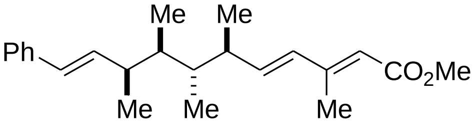
D. P. Curran, D. M. Rakiewicz, *Tetrahedron* **1985**, *41*, 3943.

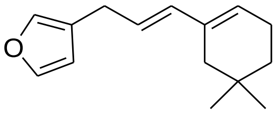


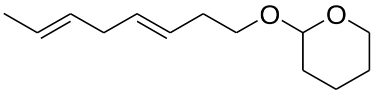
P. Dowd, S. C. Choi, *J. Am. Chem. Soc.* **1987**, *109*, 6548.

Problems

A. How would you utilize tin-containing reagents in the synthesis of the following compounds?

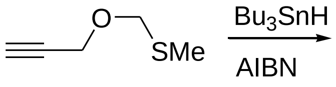


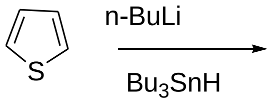


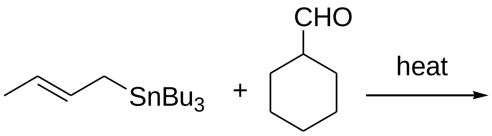


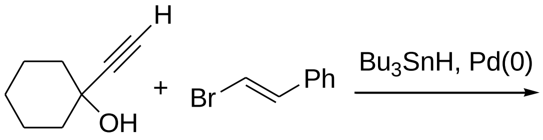
B. Organostannanes are more reactive than organosilanes. Why?

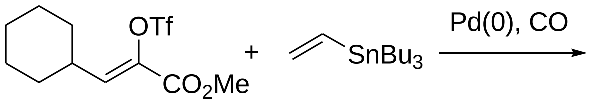
C. Predict the major products of the following reactions.

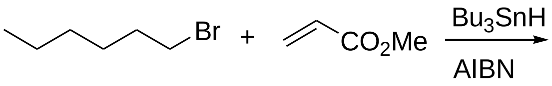
1. 

2. 

3. 

4. 

5. 

6. 

Text Books

J. Clayden, N. Greeves, S. Warren, P. Wothers, *Organic Chemistry*, Oxford University Press, 2001.

P. Wyatt, S. Warren, *Organic Synthesis*, John Wiley & Sons Ltd, West Sussex, 2007.