9

Carbon-Carbon Bond-Forming Reactions of Compounds of Boron, Silicon, and Tin

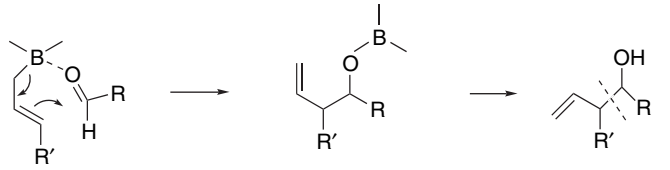
Introduction

In this chapter we discuss the use of boron, silicon, and tin compounds to form carbon-carbon bonds. These elements are at the metal-nonmetal boundary, with boron being the most and tin the least electronegative of the three. The neutral alkyl derivatives of boron have the formula R_3B, whereas silicon and tin are tetravalent compounds, R_4Si and R_4Sn. These compounds are relatively volatile nonpolar substances that exist as discrete molecules and in which the carbon-metal bonds are largely covalent. By virtue of the electron deficiency at boron, the boranes are Lewis acids. Silanes do not have strong Lewis acid character but can form pentavalent adducts with hard bases such as alkoxides and especially fluoride. Silanes with halogen or sulfonate substituents are electrophilic and readily undergo nucleophilic displacement. Stannanes have the potential to act as Lewis acids when substituted by electronegative groups such as halogens. Either displacement of a halide or expansion to pentacoordinate or hexacoordinate structures is possible.

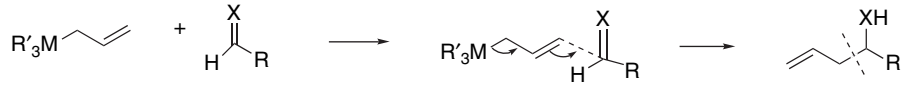
In contrast to the transition metals, where there is often a change in oxidation level at the metal during the reaction, there is usually no change in oxidation level for boron, silicon, and tin compounds. The synthetically important reactions of these three groups of compounds involve transfer of a carbon substituent with one (radical equivalent) or two (carbanion equivalent) electrons to a reactive carbon center. Here we focus on the nonradical reactions and deal with radical reactions in Chapter 10. We have already introduced one important aspect of boron and tin chemistry in the transmetallation reactions involved in Pd-catalyzed cross-coupling reactions, discussed

in Section 8.2.3. This chapter emphasizes the use of boranes, silanes, and stannanes as sources of nucleophilic carbon groups toward a variety of electrophiles, especially carbonyl compounds.

Allylic derivatives are particularly important in the case of boranes, silanes, and stannanes. Allylic boranes effect nucleophilic addition to carbonyl groups via a cyclic TS that involves the Lewis acid character of the borane. 1,3-Allylic transposition occurs through the cyclic TS.

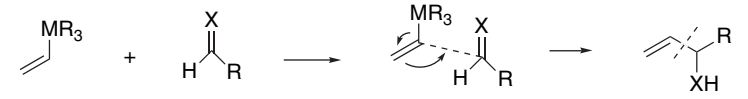


Allylic silanes and stannanes react with various electrophiles with demetallation. These reactions can occur via several related mechanisms. Both types of reagents can deliver allylic groups to electrophilic centers such as carbonyl and iminium.



M = Si, Sn X = O, NY

Alkenyl silanes and stannanes have the potential for nucleophilic delivery of vinyl groups to a variety of electrophiles. Demetallation also occurs in these reactions, so the net effect is substitution for the silyl or the stannyl group.

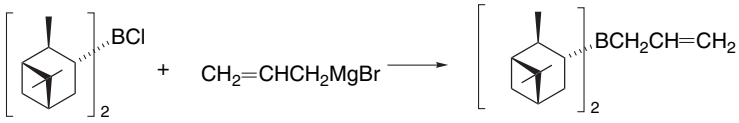


M = Si, Sn X = O, NY

9.1. Organoboron Compounds

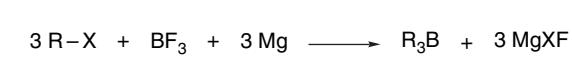
9.1.1. Synthesis of Organoboranes

The most widely used route to organoboranes is hydroboration, introduced in Section 4.5.1, which provides access to both alkyl- and alkenylboranes. Aryl-, methyl-, allylic, and benzylboranes cannot be prepared by hydroboration, and the most general route to these organoboranes is by reaction of an organometallic compound with a halo- or alkoxyboron derivative.[1]



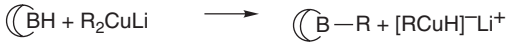
[1] H. C. Brown and P. K. Jadhar, *J. Am. Chem. Soc.*, **105**, 2092 (1983).

Alkyl, aryl, and allyl derivatives of boron can be prepared directly from the corresponding halides, BF_3, and magnesium metal. This process presumably involves in situ generation of a Grignard reagent, which then displaces fluoride from boron.[2]

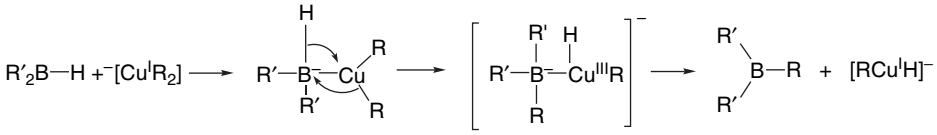


Alkoxy groups can be displaced from boron by alkyl- or aryllithium reagents. The reaction of diisopropoxy boranes with an organolithium reagent, for example, provides good yields of unsymmetrically disubstituted isopropoxyboranes.[3]

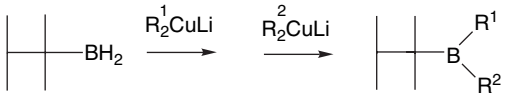
Organoboranes can also be made using organocopper reagents. One route to methyl and aryl derivatives is by reaction of a dialkylborane, such as 9-BBN, with a cuprate reagent.[4]



These reactions occur by oxidative addition at copper, followed by decomposition of the Cu(III) intermediate.



Two successive reactions with different organocuprates can convert thexylborane to an unsymmetrical trialkylborane.[5]

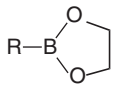


In addition to trialkylboranes, various alkoxyboron compounds have prominent roles in synthesis. Some of these, such as catecholboranes (see. p. 340) can be made by hydroboration. Others are made by organometallic or related substitution reactions. Alkoxyboron compounds are usually named as esters. Compounds with one alkoxy group are esters of borinic acids and are called *borinates*. Compounds with two alkoxy groups are called *boronates*. Trialkoxyboron compounds are *borates*.

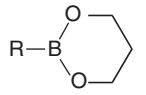
R_2BOH	R_2BOR'	$RB(OH)_2$	$RB(OR')_2$	$B(OH)_3$	$B(OR')_3$
borinic acid	borinate	boronic acid	boronate	boric acid	borate

2. H. C. Brown and U. S. Racherla, *J. Org. Chem.*, **51**, 427 (1986).
3. H. C. Brown, T. E. Cole, and M. Srebnik, *Organometallics*, **4**, 1788 (1985).
4. C. G. Whiteley and I. Zwane, *J. Org. Chem.*, **50**, 1969 (1985).
5. C. G. Whiteley, *Tetrahedron Lett.*, **25**, 5563 (l984).

The cyclic five- and six-membered boronate esters are used frequently. Their systematic names are 1,3,2-dioxaborolane and 1,3,2-dioxaborinanes, respectively.



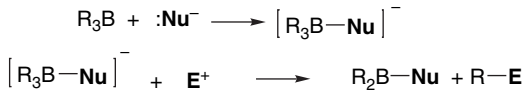
1,3,2-dioxaborolane



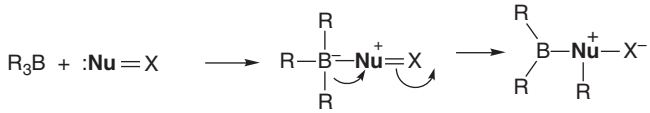
1,3,2-dioxaborinane

9.1.2. Carbonylation and Other One-Carbon Homologation Reactions

The reactions of organoboranes that we discussed in Chapter 4 are valuable methods for introducing functional groups such as hydroxy, amino, and halogen into alkenes. In this section we consider carbon-carbon bond-forming reactions of boron compounds.[6] Trivalent organoboranes are not very nucleophilic but they are moderately reactive Lewis acids. Most reactions in which carbon-carbon bonds are formed involve a tetracoordinate intermediate that has a negative charge on boron. Adduct formation weakens the boron-carbon bonds and permits a transfer of a carbon substituent with its electrons. The general mechanistic pattern is shown below.



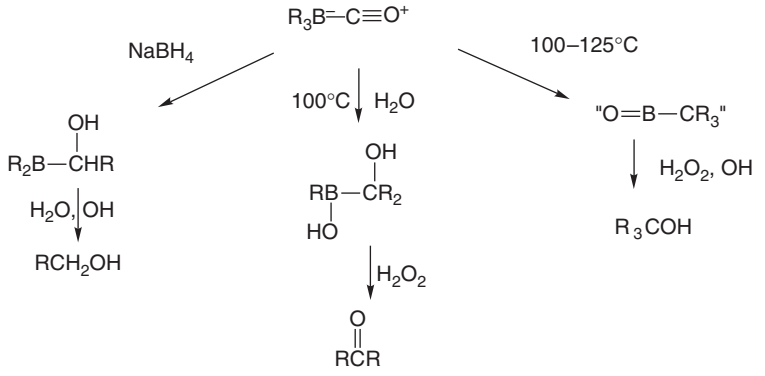
The electrophilic center is sometimes generated from the Lewis base by formation of the adduct, and the reaction proceeds by migration of a boron substituent.



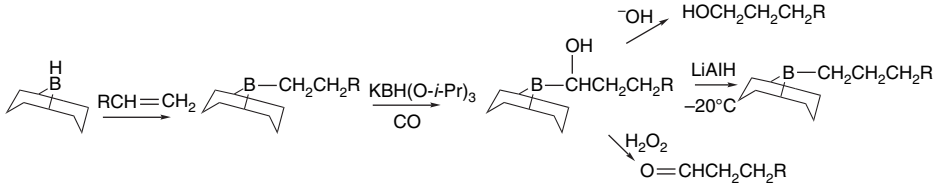
A significant group of reactions of this type involves the reactions of organoboranes with carbon monoxide, which forms Lewis acid-base complexes with the organoboranes. In these adducts the boron bears a formal negative charge and carbon is electrophilic because the triply bound oxygen bears a formal positive charge. The adducts undergo boron to carbon migration of the alkyl groups. The reaction can be controlled so that it results in the migration of one, two, or all three of the boron substituents.[7] If the organoborane is heated with carbon monoxide to 100°–125 °C, all of the groups migrate and a tertiary alcohol is obtained after workup by oxidation. The presence of water causes the reaction to cease after migration of two groups from boron to carbon. Oxidation of the reaction mixture at this stage gives a ketone.[8] Primary alcohols are obtained when the carbonylation is carried out in the presence of

6. For a review of this topic, see E. Negishi and M. Idacavage, *Org. React*., **33**, 1 (1985).
7. H. C. Brown and M. W. Rathke, *J. Am. Chem. Soc*., **89**, 2737 (1967).
8. H. C. Brown and M. W. Rathke, *J. Am. Chem. Soc*., **89**, 2738 (1967).

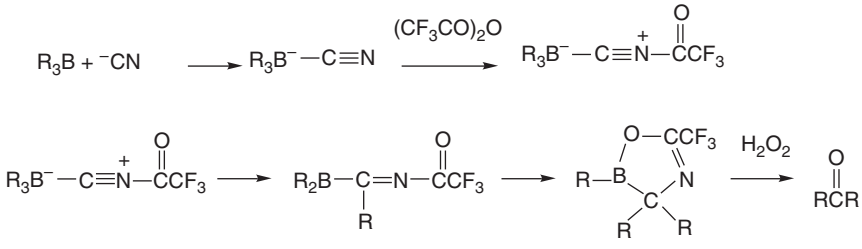
sodium borohydride or lithium borohydride.[9] The product of the first migration step is reduced and subsequent hydrolysis gives a primary alcohol.



In this synthesis of primary alcohols, only one of the three groups in the organoborane is converted to product. This disadvantage can be overcome by using a dialkylborane, particularly 9-BBN, in the initial hydroboration. (See p. 338 to review the abbreviations of some of the common boranes.) After carbonylation and B → C migration, the reaction mixture can be processed to give an aldehyde, an alcohol, or the homologated 9-alkyl-BBN.[10] The utility of 9-BBN in these procedures is the result of the minimal tendency of the bicyclic ring to undergo migration.



Several alternative procedures have been developed in which other reagents replace carbon monoxide as the migration terminus.[11] The most generally applicable of these methods involves the use of cyanide ion and trifluoroacetic anhydride (TFAA). In this reaction the borane initially forms an adduct with cyanide ion. The migration is induced by N-acylation of the cyano group by TFAA. Oxidation and hydrolysis then give a ketone.

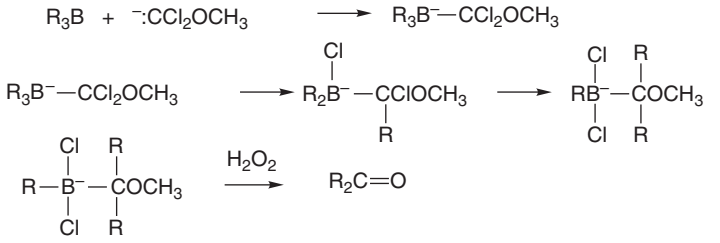


[9] M. W. Rathke and H. C. Brown, *J. Am. Chem. Soc.*, **89**, 2740 (1967).

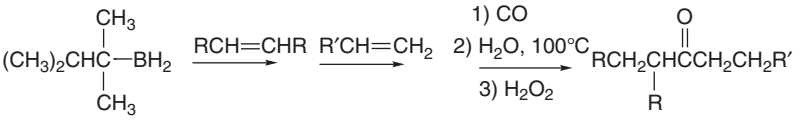
[10] H. C. Brown, E. F. Knights, and R. A. Coleman, *J. Am. Chem. Soc.*, **91**, 2144 (1969); H. C. Brown, T. M. Ford, and J. L. Hubbard, *J. Org. Chem.*, **45**, 4067 (1980).

[11] H. C. Brown and S. M. Singh, *Organometallics*, **5**, 998 (1986).

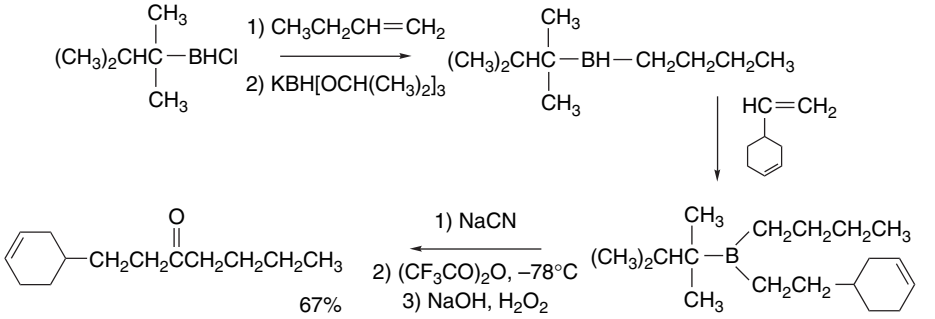
Another useful reagent for introduction of the carbonyl carbon is dichloromethyl methyl ether. In the presence of a hindered alkoxide base, it is deprotonated and acts as a nucleophile toward boron. Rearrangement then ensues with migration of two boron substituents. Oxidation gives a ketone.



Unsymmetrical ketones can be made by using either thexylborane or thexylchloroborane.[12] Thexylborane works well when one of the desired carbonyl substituents is derived from a moderately hindered alkene. Under these circumstances, a clean monoalkylation of thexylborane can be accomplished, which is then followed by reaction with a second alkene and carbonylation.



Thexylchloroborane can be alkylated and then converted to a dialkylborane by a reducing agent such as $KBH[OCH(CH_3)_2]_3$, an approach that is preferred for terminal alkenes.

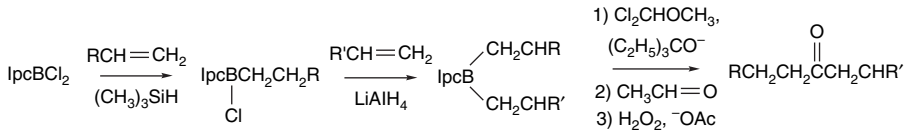


The success of both of these methods depends upon the thexyl group being noncompetitive with the other groups in the migration steps.

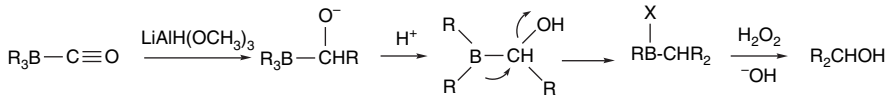
The formation of unsymmetrical ketones can also be done starting with $IpcBCl_2$. Sequential reduction and hydroboration are carried out with two different alkenes. The first reduction can be done with $(CH_3)_3SiH$, but the second stage requires $LiAlH_4$.

[12] H. C. Brown and E. Negishi, *J. Am. Chem. Soc*., **89**, 5285 (1967); S. U. Kulkarni, H. D. Lee, and H. C. Brown, *J. Org. Chem*., **45**, 4542 (1980).

In this procedure, dichloromethyl methyl ether is used as the source of the carbonyl carbon.[13]



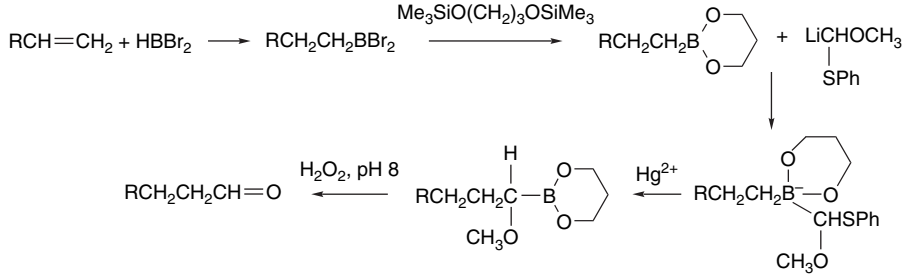
Scheme 9.1 shows several examples of one-carbon homologations involving boron to carbon migration. Entry 1 illustrates the synthesis of a symmetrical tertiary alcohol. Entry 2 involves interception of the intermediate after the first migration by reduction. Acid then induces a second migration. This sequence affords secondary alcohols.



Entries 3 to 5 show the use of alternative sources of the one carbon unit. In Entry 3, a tertiary alcohol is formed with one of the alkyl groups being derived from the dithioacetal reagent. Related procedures have been developed for ketones and tertiary alcohols using 2-lithio-2-alkyl-1,3-benzodithiole as the source of the linking carbon.[14] Problem 9.3 deals with the mechanisms of these reactions.

Section B of the Scheme 9.1 shows several procedures for the synthesis of ketones. Entry 6 is the synthesis of a symmetrical ketone by carbonylation. Entry 7 illustrates the synthesis of an unsymmetrical ketone by the thexylborane method and also demonstrates the use of a functionalized olefin. Entries 8 to 10 illustrate synthesis of ketones by the cyanide-TFAA method. Entry 11 shows the synthesis of a bicyclic ketone involving intramolecular hydroboration of 1,5-cyclooctadiene. Entry 12 is another ring closure, generating a potential steroid precursor.

Section C illustrates the synthesis of aldehydes by boron homologation. Entry 13 is an example of synthesis of an aldehyde from an alkene using 9-BBN for hydroboration. Entry 14 illustrates an efficient process for one-carbon homologation to aldehydes that is based on cyclic boronate esters. These can be prepared by hydroboration of an alkene with dibromoborane, followed by conversion of the dibromoborane to the cyclic boronate. The homologation step is carried out by addition of methoxy(phenylthio)methyllithium to the boronate. The migration step is induced by mercuric ion. Use of chiral boranes and boronates leads to products containing groups of retained configuration.[15]



13. H. C. Brown, S. V. Kulkarni, U. S. Racherla, and U. P. Dhokte, *J. Org. Chem.*, **63**, 7030 (1998).
14. S. Ncube, A. Pelter, and K. Smith, *Tetrahedron Lett.*, 1893, 1895 (1979).
15. M. V. Rangaishenvi, B. Singaram, and H. C. Brown, *J. Org. Chem.*, **56**, 3286 (1991).

Scheme 9.1. Homologation and Coupling of Organoboranes by Carbon Monoxide and Other One-Carbon Donors

A. Formation of alcohols

1[a] $\left(CH_3CH_2\underset{CH_3}{CH}\right)_3B$ 1) CO, 125°C; 2) H_2O_2, ^-OH → $\left(CH_3CH_2\underset{CH_3}{CH}\right)_3COH$ 87%

2[b] $CH_3CH{=}CHCH_3$ B_2H_6; 1) $LiAlH(OCH_3)_3$, 2) CO; 1) H_2O, H^+; 2) H_2O_2, ^-OH → $CH_3CH_2\underset{CH_3}{CH}\underset{OH}{CH}\underset{CH_3}{CH}CH_2CH_3$ 82%

3[c] $(C_4H_9)_3B$ + $CH_3CH_2CH_2\underset{Li}{C}(SPh)_2$ → 1) $HgCl_2$; 2) H_2O_2, ^-OH → $(C_4H_9)_2\underset{OH}{C}CH_2CH_2CH_3$ 90%

4[d] $CH_3(CH_2)_5B(OCH_3)$–c-C5H9 1) $LiCHCl_2$; 2) $NaOCH_3$; 3) H_2O_2 → $CH_3(CH_2)_5\underset{OH}{CH}$–c-C5H9 63%

5[e] $CH_3(CH_2)_3$, $(CH_2)_3CH_3$ boronate 1) CH_2Cl_2; 2) *n*-BuLi; 3) H_2O_2, OH → $CH_3(CH_2)_3$, $(CH_2)_3CH_3$ alkene, H, CH_2OH 80%

B. Formation of ketones

6[f] $(C_6H_5)_3B$ 1) CO, 125°C, H_2O; 2) H_2O_2, ^-OH → $(C_6H_5)_2C{=}O$ 90%

7[g] $(CH_3)_2C{=}CH_2$ thexylborane $CH_2{=}CHCO_2C_2H_5$ 1) CO, 50°C; 2) H_2O_2, ^-OAc → $(CH_3)_2CHCH_2\underset{O}{\overset{\|}{C}}CH_2CH_2CO_2C_2H_5$ 81%

8[h] $CH_3(CH_2)_5CH{=}CH_2$ 1) thexylchloroborane; 2) $KBH(OR)_3$; $CH_2{=}CH(CH_2)_7CH_3$; 1) NaCN; 2) $(CF_3CO)_2O$ → $CH_3(CH_2)_7\underset{O}{\overset{\|}{C}}(CH_2)_9CH_3$ 74%

9[g] $CH_3(CH_2)_7CH{=}CH_2$ 1) thexylchloroborane; 2) $KBH(OR)_3$; c-C5H5N; 1) ^-CN; 2) $(CF_3CO)_2O$; NaOH, H_2O_2 → $CH_3(CH_2)_9\underset{O}{\overset{\|}{C}}$–c-C5H9 67%

10[i] $(CH_3)_2CHC(CH_3)BH_2$ + c-C5H5N; $(CF_3CO)_2O$, ^-CN; H_2O_2 → $C_6H_5\underset{O}{\overset{\|}{C}}$–c-C5H9 80%

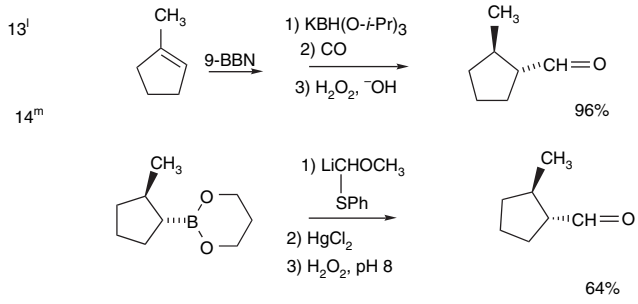
11[j] c-C8H8 $H_2BCl{-}SMe_2$; 2,6-dimethylphenol; 1) Cl_2CHOCH_3; 2) $LiOCR_3$; H_2O_2 → c-C8H12O 71%

12[k] $CH_2{=}CH$, CH_3, CH_3O 1) siamylborane; 2) CO, 50°C; 3) H_2O_2 → CH_3, O, H, CH_3O 53%

(Continued)

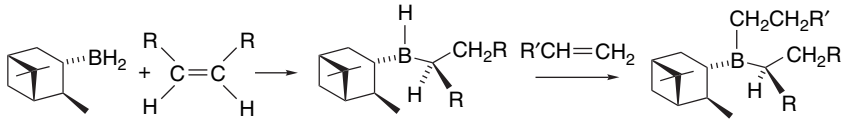
Scheme 9.1. (*Continued*)

C. Formation of aldehydes

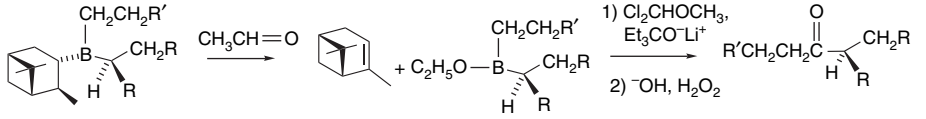


a. H. C. Brown and M. W. Rathke, *J. Am. Chem. Soc*., **89**, 2737 (1967).
b. J. L. Hubbard and H. C. Brown, *Synthesis*, 676 (1978).
c. R. J. Hughes, S. Ncube, A. Pelter, K. Smith, E. Negishi, and T. Yoshida, *J. Chem. Soc., Perkin Trans. 1*, 1172 (1977); S. Ncube, A. Pelter, and K. Smith, *Tetrahedron Lett*., 1893, 1895 (1979).
d. H. C. Brown, T. Imai, P. T. Perumal, and B. Singaram, *J. Org. Chem*., **50**, 4032 (1985).
e. H. C. Brown, A. S. Phadke, and N. G. Bhat, *Tetrahedron Lett*., **34**, 7845 (1993).
f. H. C. Brown and M. W. Rathke, *J. Am. Chem. Soc*., **89**, 2738 (1967).
g. H. C. Brown and E. Negishi, *J. Am. Chem. Soc*., **89**, 5285 (1967).
h. S. U. Kulkarni, H. D. Lee, and H. C. Brown, *J. Org. Chem*., **45**, 4542 (1980).
i. A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe, *J. Chem. Soc., Perkin Trans. 1*, 129 (1975).
j. H. C. Brown and S. U. Kulkarni, *J. Org. Chem*., **44**, 2422 (1979).
k. T. A. Bryson and W. E. Pye, *J. Org. Chem*., **42**, 3214 (1977).
l. H. C. Brown, J. L. Hubbard, and K. Smith, *Synthesis*, 701 (1979).
m. H. C. Brown and T. Imai, *J. Am. Chem. Soc*., **105**, 6285 (1983).

As can be judged from the preceding discussion, organoboranes are versatile intermediates for formation of carbon-carbon bonds. An important aspect of all of these synthetic procedures involving boron to carbon migration is that they occur with *retention of the configuration of the migrating group*. Since effective procedures for enantioselective hydroboration have been developed (see Section 4.5.3), these reactions offer the opportunity for enantioselective synthesis. A sequence for enantioselective formation of ketones starts with hydroboration by mono(isopinocampheyl)borane, ($IpcBH_2$), which can be obtained in high enantiomeric purity.[16] The hydroboration of a prochiral alkene establishes a new stereocenter. A third alkyl group can be introduced by a second hydroboration step.

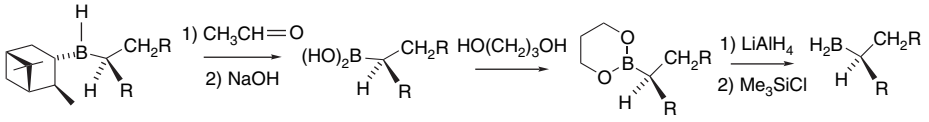


The trialkylborane can be transformed to a dialkyl(ethoxy)borane by heating with acetaldehyde, which releases the original chiral α-pinene. Finally application of one of the carbonylation procedures outlined in Scheme 9.1 gives a chiral ketone.[17] The enantiomeric excess observed for ketones prepared in this way ranges from 60–90%.

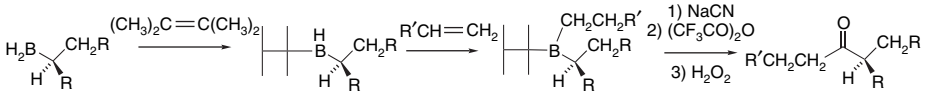


16. H. C. Brown, P. K. Jadhav, and A. K. Mandal, *J. Org. Chem*., **47**, 5074 (1982).
17. H. C. Brown, R. K. Jadhav, and M. C. Desai, *Tetrahedron*, **40**, 1325 (1984).

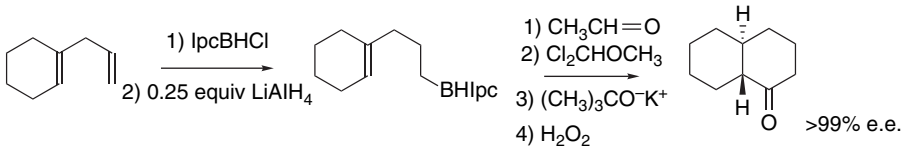
Higher enantiomeric purity can be obtained by a modified procedure in which the monoalkylborane intermediate is prepared by reduction of a cyclic boronate.[18]



Subsequent steps involve introduction of a thexyl group and then the second ketone substituent. Finally, the ketone is formed by the cyanide-TFAA method.

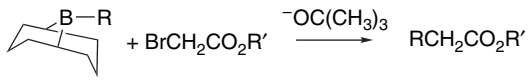


By starting with enantiomerically enriched IpcBHCl, it is possible to construct chiral cyclic ketones. For example, stepwise hydroboration of 1-allylcyclohexene and ring construction provides *trans*-1-decalone in greater than 99% e.e.[19]



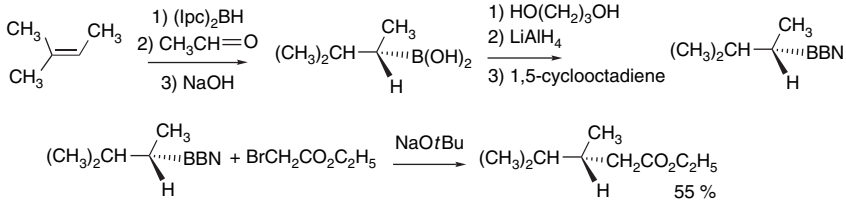
9.1.3. Homologation via α-Haloenolates

Organoboranes can also be used to construct carbon-carbon bonds by several other types of reactions that involve migration of a boron substituent to carbon. One such reaction involves α-halo carbonyl compounds.[20] For example, ethyl bromoacetate reacts with trialkylboranes in the presence of base to give alkylated acetic acid derivatives in excellent yield. The reaction is most efficiently carried out with a 9-BBN derivative. These reactions can also be effected with β-alkenyl derivatives of 9-BBN to give β,γ-unsaturated esters.[21]

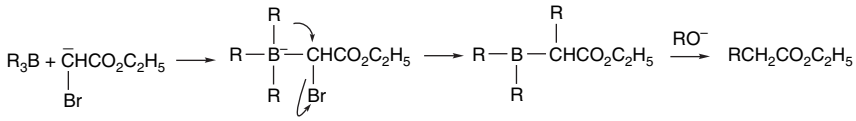


18. H. C. Brown, R. K. Bakshi, and B. Singaram, *J. Am. Chem. Soc.*, **110**, 1529 (1988); H. C. Brown, M. Srebnik, R. K. Bakshi, and T. E. Cole, *J. Am. Chem. Soc.*, **109**, 5420 (1987).
19. H. C. Brown, V. K. Mahindroo, and U. P. Dhokte, *J. Org. Chem.*, **61**, 1906 (1996); U. P. Dhokte, P. M. Pathare, V. K. Mahindroo, and H. C. Brown, *J. Org. Chem.*, **63**, 8276 (1998).
20. H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, **90**, 818 (1968); H. C. Brown and M. M. Rogic, *J. Am. Chem. Soc.*, **91**, 2146 (1969).
21. H. C. Brown, N. G. Bhat, and J. B. Cambell, Jr., *J. Org. Chem.*, **51**, 3398 (1986).

The reactions can be made enantioselective by using enantiomerically pure $IpcBH_2$ for hydroboration of alkenes and then transforming the products to enantiomerically pure derivatives of 9-BBN by reaction with 1,5-cyclooctadiene.[22]



The mechanism of these alkylations involves a tetracoordinate boron intermediate formed by addition of the enolate of the α-bromo ester to the organoborane. The migration then occurs with displacement of bromide ion. In agreement with this mechanism, retention of configuration of the migrating group is observed.[23]



α-Halo ketones and α-halo nitriles undergo similar reactions.[24]

A closely related reaction employs α-diazo esters or α-diazo ketones.[25] With these compounds, molecular nitrogen acts as the leaving group in the migration step. The best results are achieved using dialkylchloroboranes or monoalkyldichloroboranes.

$$RBCl_2 + N_2CHCO_2CH_3 \longrightarrow RCH_2CO_2CH_3$$

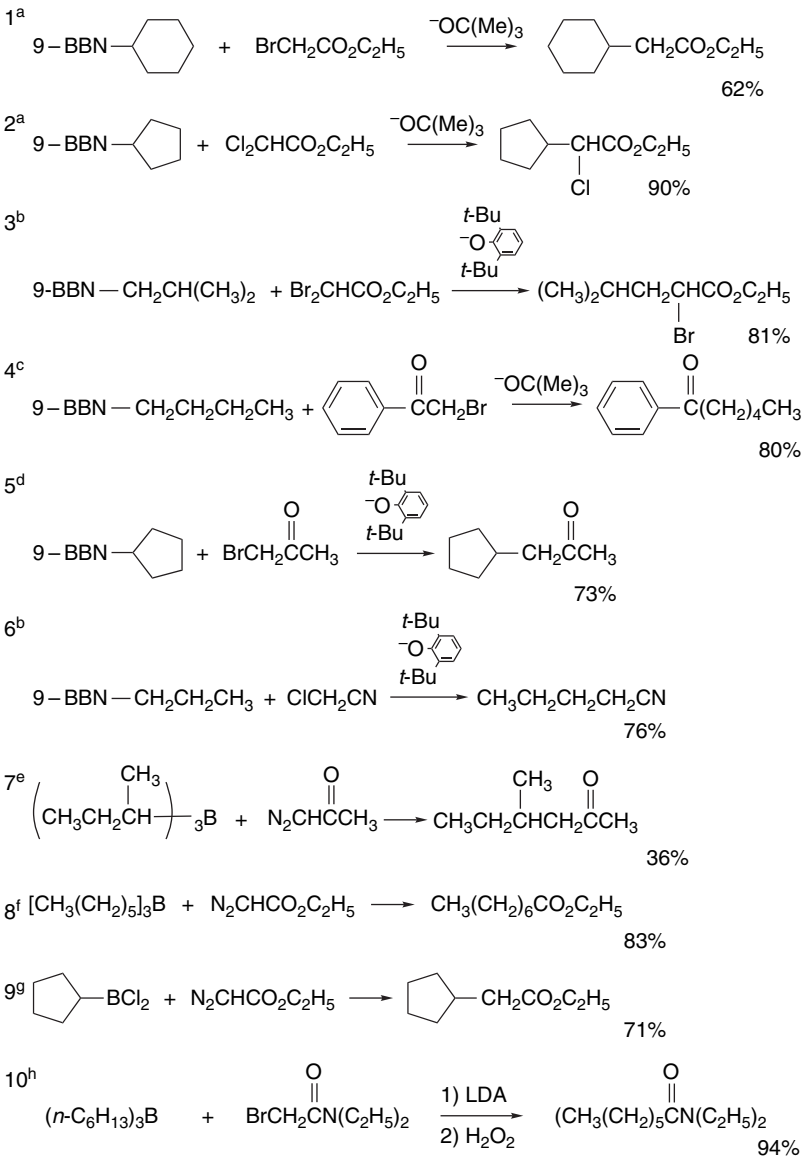
A number of these alkylation reactions are illustrated in Scheme 9.2. Entries 1 and 2 are typical examples of α-halo ester reactions. Entry 3 is a modification in which the highly hindered base potassium 2,6-di-*t*-butylphenoxide is used. Similar reaction conditions can be used with α-halo ketones (Entries 4 and 5) and nitriles (Entry 6). Entries 7 to 9 illustrate the use of diazo esters and diazo ketones. Entry 10 shows an application of the reaction to the synthesis of an amide.

9.1.4. Stereoselective Alkene Synthesis

Several methods for stereoselective alkene synthesis are based on boron intermediates. One approach involves alkenylboranes, which can be prepared from terminal alkynes. Procedures have been developed for the synthesis of both *Z*- and *E*-alkenes.

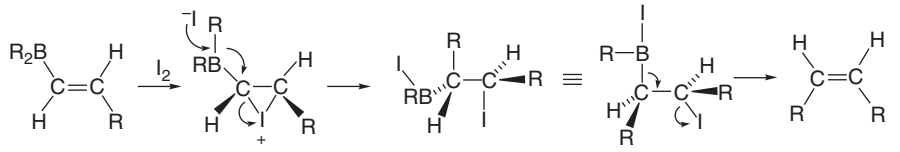
22. H. C. Brown, N. N. Joshi, C. Pyun, and B. Singaram, *J. Am. Chem. Soc*., **111**, 1754 (1989).
23. H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc*., **91**, 2151 (1969).
24. H. C. Brown, M. M. Rogic, H. Nambu, and M. W. Rathke, *J. Am. Chem. Soc*., **91**, 2147 (1969); H. C. Brown, H. Nambu, and M. M. Rogic, *J. Am. Chem. Soc*., **91**, 6853, 6855 (1969).
25. H. C. Brown, M. M. Midland, and A. B. Levy, *J. Am. Chem. Soc*., **94**, 3662 (1972); J. Hooz, J. N. Bridson, J. G. Calzada, H. C. Brown, M. M. Midland, and A. B. Levy, *J. Org. Chem*., **38**, 2574 (1973).

Scheme 9.2. Homologation of Boranes by α-Halocarbonyl and Related Compounds

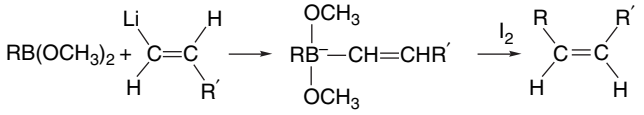


a. H. C. Brown and M. M. Rogic, *J. Am. Chem. Soc.*, **91**, 2146 (1969).
b. H. C. Brown, H. Nambu, and M. M. Rogic, *J. Am. Chem. Soc.*, **91**, 6855 (1969).
c. H. C. Brown, M. M. Rogic, H. Nambu, and M. W. Rathke, *J. Am. Chem. Soc.*, **91**, 2147 (1969).
d. H. C. Brown, H. Nambu, and M. M. Rogic, *J. Am. Chem. Soc.*, **91**, 6853 (1969).
e. J. Hooz and S. Linke, *J. Am. Chem. Soc.*, **90**, 5936 (1968).
f. J. Hooz and S. Linke, *J. Am. Chem. Soc.*, **90**, 6891 (1968).
g. J. Hooz, J. N. Bridson, J. G. Caldaza, H. C. Brown, M. M. Midland, and A. B. Levy, *J. Org. Chem.*, **38**, 2574 (1973).
h. N.-S. Li, M.-Z. Deng, and Y.-Z. Huang, *J. Org. Chem.*, **58**, 6118 (1993).

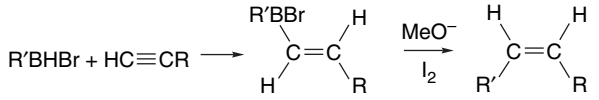
Treatment of alkenyldialkylboranes with iodine results in the formation of the *Z*-alkene with migration of one boron substituent.[26]



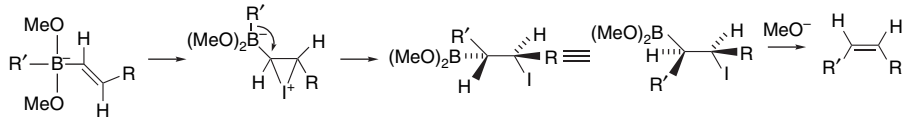
Similarly, alkenyllithium reagents add to dimethyl boronate to give adducts that decompose to *Z*-alkenes on treatment with iodine.[27]



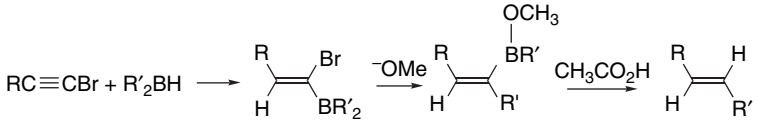
The synthesis of *Z*-alkenes can also be carried out starting with an alkylbromoborane, in which case migration presumably follows replacement of the bromide by methoxide.[28]



The stereoselectivity of these reactions arises from a base-induced *anti* elimination after the migration. The elimination is induced by addition of methoxide to the boron, generating an anionic center.

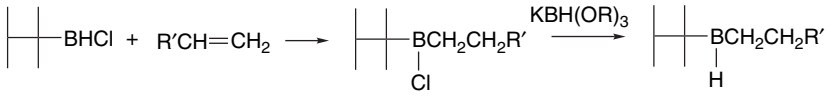


E-Alkenes can be prepared by several related reactions.[29] Hydroboration of a bromoalkyne generates an α-bromoalkenylborane. On treatment with methoxide ion these intermediates undergo B → C migration to give an alkyl alkenylborinate. Protonolysis generates an *E*-alkene.

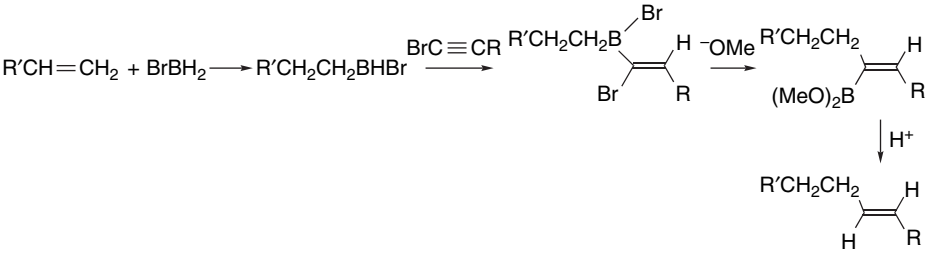


26. G. Zweifel, H. Arzoumanian, and C. C. Whitney, *J. Am. Chem. Soc*., **89**, 3652 (1967); G. Zweifel, R. P. Fisher, J. T. Snow, and C. C. Whitney, *J. Am. Chem. Soc*., **93**, 6309 (1971).
27. D. A. Evans, T. C. Crawford, R. C. Thomas, and J. A. Walker, *J. Org. Chem*., **41**, 3947 (1976).
28. H. C. Brown, D. Basavaiah, S. U. Kulkarni, N. G. Bhat, and J. V. N. Vara Prasad, *J. Org. Chem*., **53**, 239 (1988).
29. H. C. Brown, D. Basavaiah, S. U. Kulkarni, H. P. Lee, E. Negishi, and J.-J. Katz, *J. Org. Chem*., **51**, 5270 (1986).

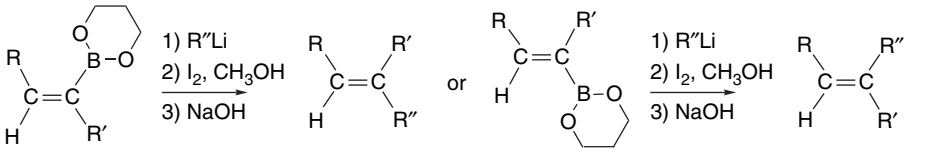
The dialkylboranes can be prepared from thexylchloroborane. The thexyl group does not normally migrate.



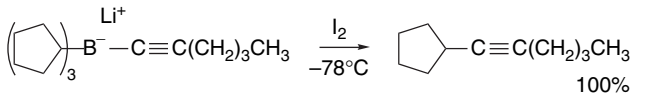
A similar strategy involves initial hydroboration by $BrBH_2$.[30]



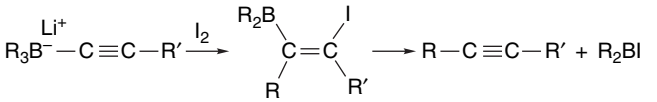
Stereoselective syntheses of trisubstituted alkenes are based on *E*- and *Z*-alkenyldioxaborinanes. Reaction with an alkyllithium reagent forms an "ate" adduct that rearranges on treatment with iodine in methanol.[31]



Both alkynes and alkenes can be obtained from adducts of terminal alkynes and boranes. Reaction with iodine induces migration and results in the formation of the alkylated alkyne.[32]

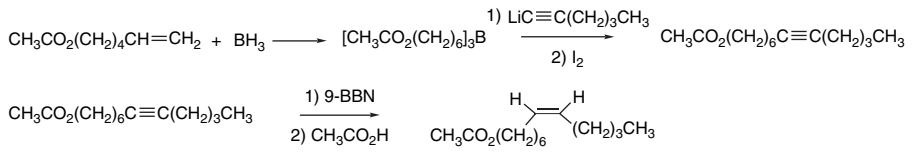


The mechanism involves electrophilic attack by iodine at the triple bond, which induces migration of an alkyl group from boron. This is followed by elimination of dialkyliodoboron.



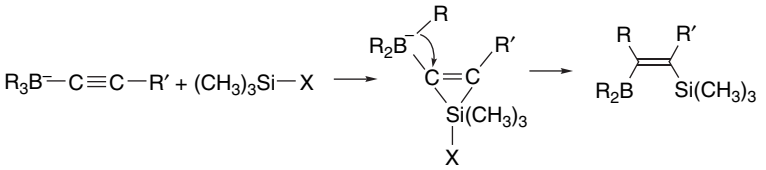
30. H. C. Brown, T. Imai, and N. G. Bhat, *J. Org. Chem.*, **51**, 5277 (1986); H. C. Brown, D. Basavaiah, and S. U. Kulkarni, *J. Org. Chem.*, **47**, 3808 (1982).
31. H. C. Brown and N. G. Bhat, *J. Org. Chem.*, **53**, 6009 (1988).
32. A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, H. C. Brown, J. A. Sinclair, and M. M. Midland, *J. Am. Chem. Soc.*, **95**, 3080 (1973); A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, M. M. Midland, J. A. Sinclair, and H. C. Brown, *J. Org. Chem.*, **51**, 4507 (1986).

If the alkyne is hydroborated and then protonolyzed a *Z*-alkene is formed. This method was used to prepare an insect pheromone containing a *Z*-double bond.

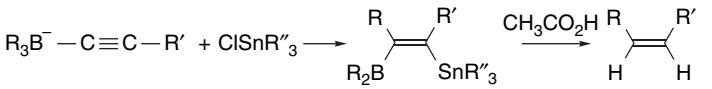


Ref. 33

The B → C migration can also be induced by other types of electrophiles. Trimethylsilyl chloride or trimethylsilyl triflate induces a stereospecific migration to form β-trimethylsilyl alkenylboranes having *cis* silicon and boron substituents.[34] It has been suggested that this stereospecificity arises from a silicon-bridged intermediate.

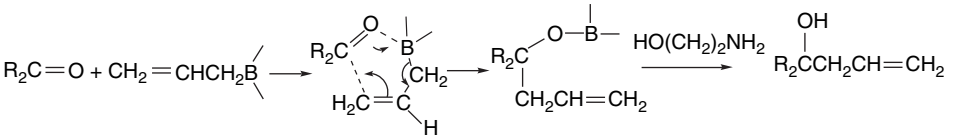


Tributyltin chloride also induces migration and gives the product in which the C–Sn bond is *cis* to the C–B bond. Protonolysis of both the C–Sn and C–B bonds by acetic acid gives the corresponding *Z*-alkene.[35]



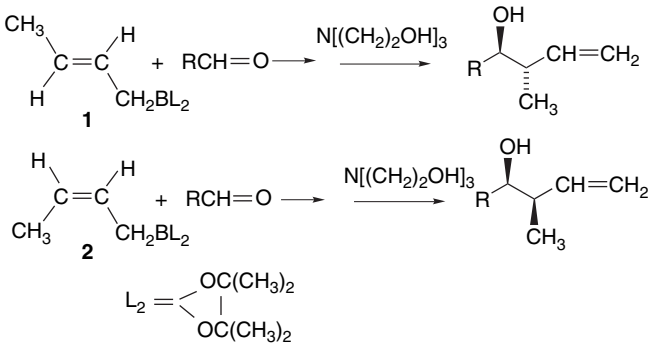
9.1.5. Nucleophilic Addition of Allylic Groups from Boron Compounds

Allylic boranes such as 9-allyl-9-BBN react with aldehydes and ketones to give allylic carbinols. The reaction begins by Lewis acid-base coordination at the carbonyl oxygen, which both increases the electrophilicity of the carbonyl group and weakens the C–B bond to the allyl group. The dipolar adduct then reacts through a cyclic TS. Bond formation takes place at the γ-carbon of the allyl group and the double bond shifts.[36] After the reaction is complete, the carbinol product is liberated from the borinate ester by displacement with ethanolamine. Yields for a series of aldehydes and ketones were usually above 90% for 9-allyl-9-BBN.

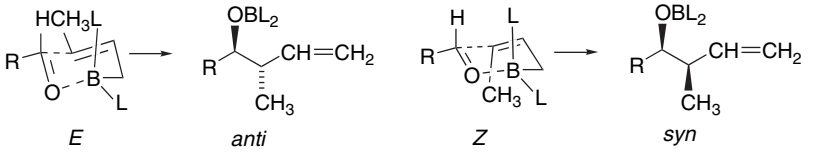


33. H. C. Brown and K. K. Wang, *J. Org. Chem.*, **51**, 4514 (1986).
34. P. Binger and R. Koester, *Synthesis*, 309 (1973); E. J. Corey and W. L. Seibel, *Tetrahedron Lett.*, **27**, 905 (1986).
35. K. K. Wang and K.-H. Chu, *J. Org. Chem.*, **49**, 5175 (1984).
36. G. W. Kramer and H. C. Brown, *J. Org. Chem.*, **42**, 2292 (1977).

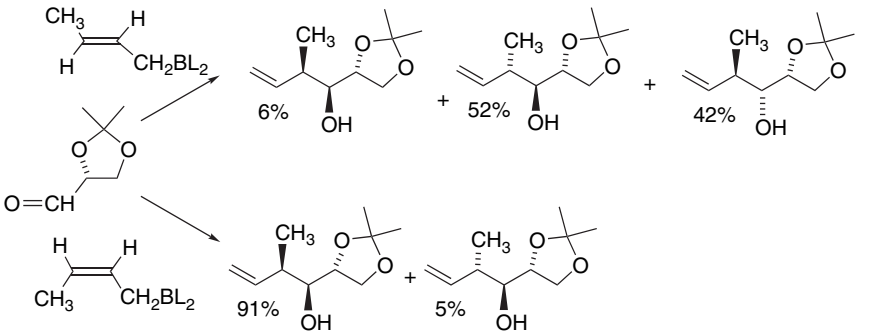
The cyclic mechanism predicts that the addition reaction will be stereospecific with respect to the geometry of the double bond in the allylic group, and this has been demonstrated to be the case. The *E*- and *Z*-2-butenyl cyclic boronates **1** and **2** were synthesized and allowed to react with aldehydes. The *E*-boronate gave the carbinol with *anti* stereochemistry, whereas the *Z*-boronate resulted in the *syn* product.[37]



This stereochemistry is that predicted by a cyclic TS in which the aldehyde substituent occupies an equatorial position.



The diastereoselectivity observed in simple systems led to investigation of enantiomerically pure aldehydes. It was found that the *E*- and *Z*-2-butenylboronates both exhibit high *syn-anti* diastereoselectivity with chiral α-substituted aldehydes. However, only the *Z*-isomer also exhibited high selectivity toward the diastereotopic faces of the aldehyde.[38]

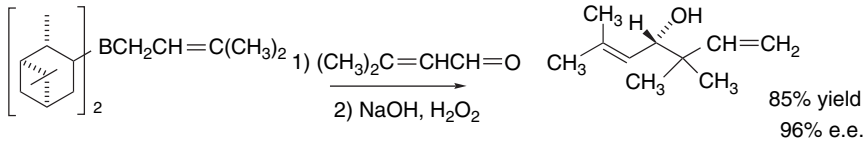


The allylation reaction has been extended to enantiomerically pure allylic boranes and borinates. For example, the 3-methyl-2-butenyl derivative of $(Ipc)_2BH$ reacts with aldehydes to give carbinols of greater than 90% e.e. in most cases.[39]

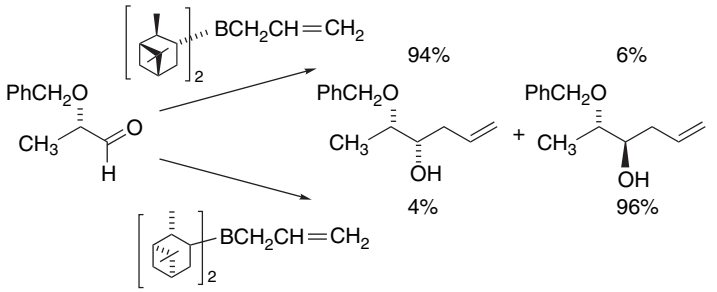
[37] R. W. Hoffmann and H.-J. Zeiss, *J. Org. Chem.*, **46**, 1309 (1981); K. Fujita and M. Schlosser, *Helv. Chim. Acta*, **65**, 1258 (1982).

[38] W. R. Roush, M. A. Adam, A. E. Walts, and D. J. Harris, *J. Am. Chem. Soc.*, **108**, 3422 (1986).

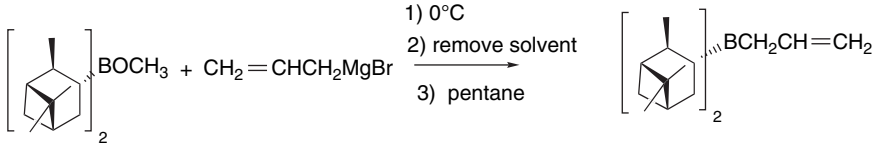
[39] H. C. Brown and P. K. Jadhav, *Tetrahedron Lett.*, **25**, 1215 (1984); H. C. Brown, P. K. Jadhav, and K. S. Bhat, *J. Am. Chem. Soc.*, **110**, 1535 (1988).



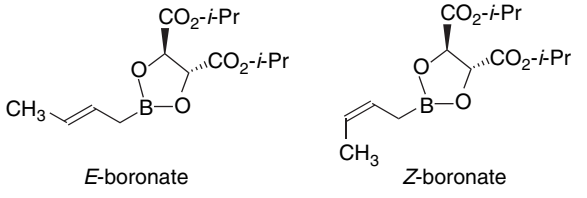
β-Allyl-*bis*-(isopinocampheyl)borane exhibits high stereoselectivity in reactions with chiral α-substituted aldehydes.[40] The stereoselectivity is *reagent controlled*, in that there is no change in stereoselectivity between the two enantiomeric boranes in reaction with a chiral aldehyde. Rather, the configuration of the product is determined by the borane. Both enantiomers of $(Ipc)_2BH$ are available, so either enantiomer can be prepared from a given aldehyde.



It has been found that conditions in which purified allylic boranes are used give even higher enantioselectivity and faster reactions than the reagents prepared and used in situ. The boranes are prepared from Grignard reagents and evidently the residual Mg^{2+} salts inhibit the addition reaction. Magnesium-free borane solutions can be obtained by precipitation and extracting the borane into pentane. These purified reagents react essentially instantaneously with typical aldehydes at $-100\,^{\circ}C$.[41]

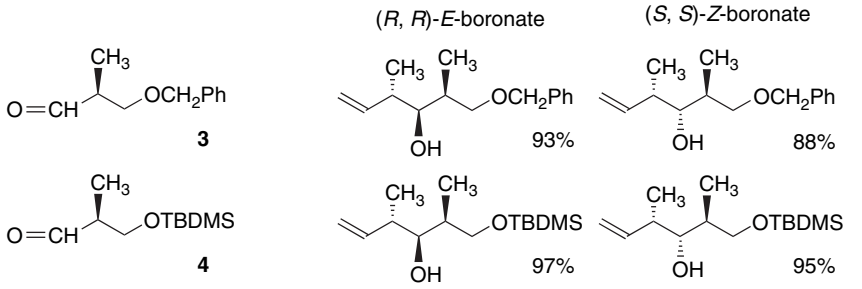


Another extensively developed group of allylic boron reagents for enantioselective synthesis is derived from tartrates.[42]



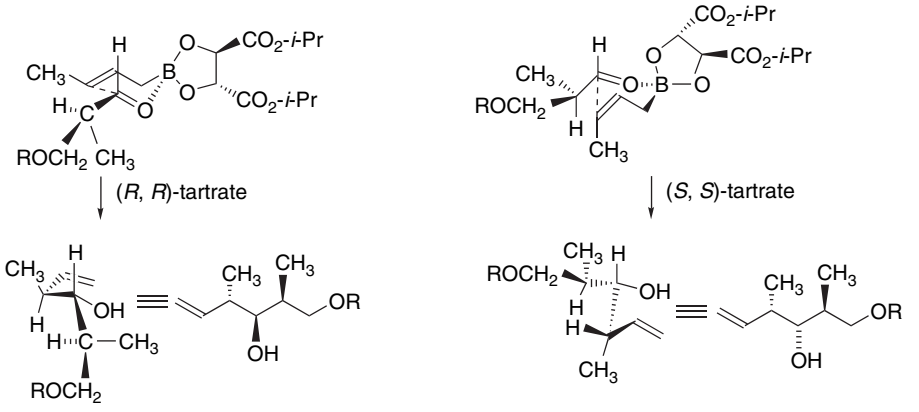
40. H. C. Brown, K. S. Bhat, and R. S. Randad, *J. Org. Chem.*, **52**, 319 (1987); H. C. Brown, K. S. Bhat, and R. S. Randad, *J. Org. Chem.*, **54**, 1570 (1989).
41. U. S. Racherla and H. C. Brown, *J. Org. Chem.*, **56**, 401 (1991).
42. W. R. Roush, K. Ando, D. B. Powers, R. L. Halterman, and A. Palkowitz, *Tetrahedron Lett.*, **29**, 5579 (1988); W. R. Roush, L. Banfi, J. C. Park, and L. K. Hong, *Tetrahedron Lett.*, **30**, 6457 (1989).

With unhindered aldehydes such as cyclohexanecarboxaldehyde, the diastereoselectivity is higher than 95%, with the *E*-boronate giving the *anti* adduct and the *Z*-boronate giving the *syn* adduct. Enantioselectivity is about 90% for the *E*-boronate and 80% for the *Z*-boronate. With more hindered aldehydes, such as pivaldehyde, the diastereoselectivity is maintained but the enantioselectivity drops somewhat. These reagents also give excellent double stereodifferentiation when used with chiral aldehydes. For example, the aldehydes **3** and **4** give at least 90% enantioselection with both the *E*- and *Z*-boronates.[43]



These reagents exhibit reagent control of stereoselectivity and have proven to be very useful in stereoselective synthesis of polyketide natural products, which frequently contain arrays of alternating methyl and oxygen substituents.[44]

The enantioselectivity is consistent with cyclic TSs. The key element determining the orientation of the aldehyde within the TS is the interaction of the aldehyde group with the tartrate ligand.



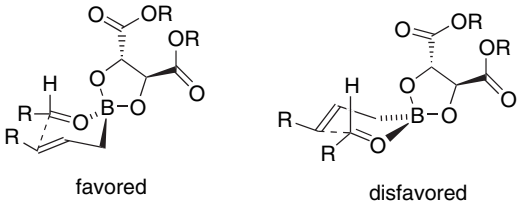
The preferred orientation results from the greater repulsive interaction between the carbonyl groups of the aldehyde and ester in the disfavored orientation.[45] There is also an attractive electrostatic interaction between the ester carbonyl and the aldehyde

[43] W. R. Roush, A. D. Palkowitz, and M. A. J. Palmer, *J. Org. Chem.*, **52**, 316 (1987); W. R. Roush, K. Ando, D. B. Powers, A. D. Palkowitz, and R. L. Halterman, *J. Am. Chem. Soc.*, **112**, 6339 (1990); W. R. Roush, A. D. Palkowitz, and K. Ando, *J. Am. Chem. Soc.*, **112**, 6348 (1990).

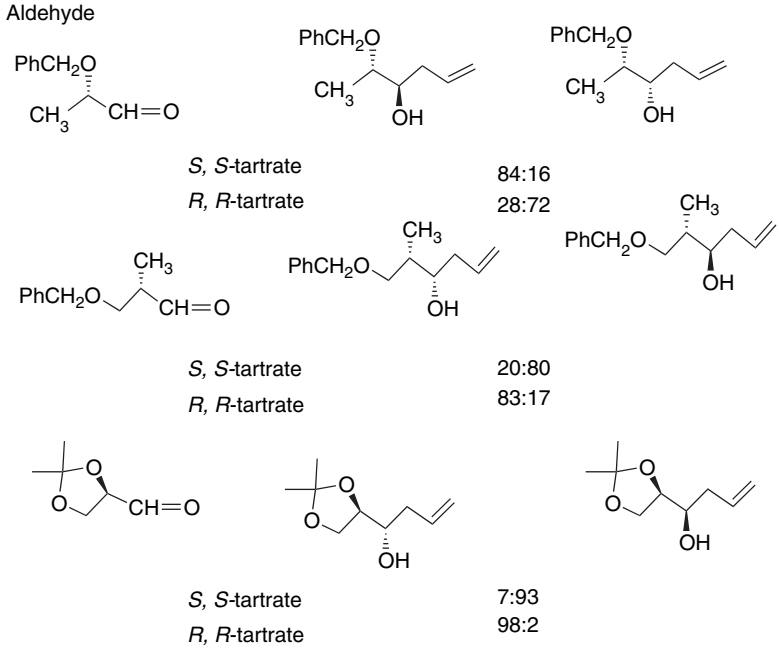
[44] W. R. Roush and A. D. Palkowitz, *J. Am. Chem. Soc.*, **109**, 953 (1987).

[45] W. R. Roush, A. E. Walts, and L. K. Hoong, *J. Am. Chem. Soc.*, **107**, 8186 (1985); W. R. Roush, L. K. Hoong, M. A. J. Palmer, and J. C. Park, *J. Org. Chem.*, **55**, 4109 (1990).

carbon.[46] This orientation and the *E*- or *Z*-configuration of the allylic group as part of a chair TS determine the stereochemistry of the product.



Detailed studies have been carried out on the stereoselectivity of α- and β-substituted aldehydes toward the tartrate boronates.[47] α-Benzyloxy and β-benzyloxy-α-methylpropionaldehyde gave approximately 4:1 diastereoselectivity with both the *R*, *R*- and *S*, *S*- enantiomers. The stereoselectivity is reagent (tartrate) controlled. The acetonide of glyceraldehydes showed higher stereoselectivity.



The tartrate-based allylboration reaction has been studied computationally using B3LYP/6-31G* calculations.[46] The ester groups were modeled by formyl. It was concluded that the major factor in determining enantioselectivity is a favorable electrostatic interaction between a formyl oxygen lone pair and the positively polarized carbon of the reacting aldehyde. This gives rise to a calculated energy difference of 1.6 kcal/mol between the best *si* and the best *re* TS (see Figure 9.1). In the preferred conformation of the TS, the formyl carbonyl is nearly in the plane of the dioxaborolane ring. This orientation has been calculated to be optimal for α-oxy esters[48] and is observed in the crystal structure of the tartrate ligands.[49]

46. B. W. Gung, X. Xue, and W. R. Roush, *J. Am. Chem. Soc*., **124**, 10692 (2002).
47. W. R. Roush, L. K. Hoong, M. A. J. Palmer, J. A. Straub, and A. D. Palkowitz, *J. Org. Chem*., **55**, 4117 (1990).
48. K. B. Wiberg and K. E. Laiding, *J. Am. Chem. Soc*., **109**, 5935 (1987).
49. W. R. Roush, A. M. Ratz, and J. A. Jablonowski, *J. Org. Chem*., **57**, 2047 (1992).

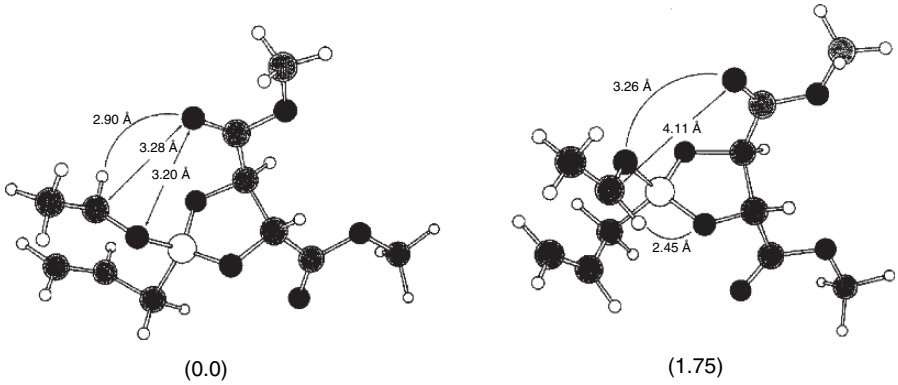
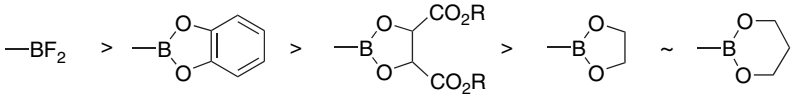


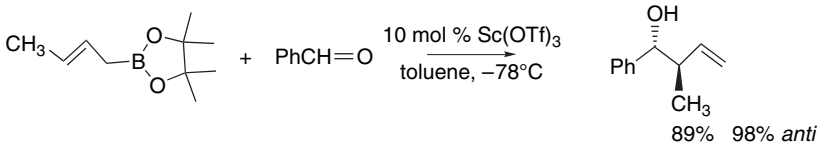
Fig. 9.1. Most favorable *si* and *re* transition structures for allylboration of acetaldehyde. The *si* TS is favored by 1.75 kcal/mol, which is attributed to an electrostatic attraction between a formyl carbonyl oxygen lone pair and the acetaldehyde carbonyl carbon. In the *re* TS, there is a repulsive interaction between lone pairs on the formyl and acetaldehyde carbonyl oxygens. Reproduced from *J. Am. Chem. Soc*., **124**, 10692 (2002), by permission of the American Chemical Society.

Visual models, additional information and exercises on Allylboration can be found in the Digital Resource available at: Springer.com/carey-sundberg.

Another computational study examined the effect that the boron ligands might have on the reactivity of allyl derivatives.[50] The order found is shown below and is related to the level of the boron LUMO. The dominant factor seems to be the π-donor capacity of the ligands. The calculated order is consistent with experimental data.[51]



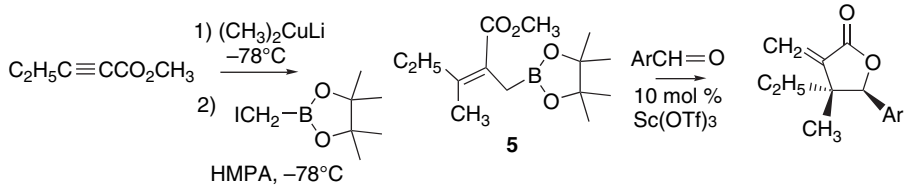
Recently the scope of the allylboration has been expanded by the discovery that it is catalyzed by certain Lewis acids, especially $Sc(OTf)_3$.[52] The catalyzed reaction exhibits the same high diastereoselectivity as the uncatalyzed reaction, which indicates that it proceeds through a cyclic TS.



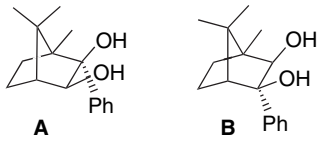
Ref. 52b

50. K. Omoto and H. Fujimoto, *J. Org. Chem*., **63**, 8331 (1998).
51. H. C. Brown, U. S. Racherla, and P. J. Pellechia, *J. Org. Chem*., **55**, 1868 (1990).
52. (a) J. W. J. Kennedy and D. G. Hall, *J. Am. Chem. Soc*., **124**, 11586 (2002); (b) T. Ishiyama, T.-A. Ahiko, and N. Miyaura, *J. Am. Chem. Soc*., **124**, 12414 (2002).

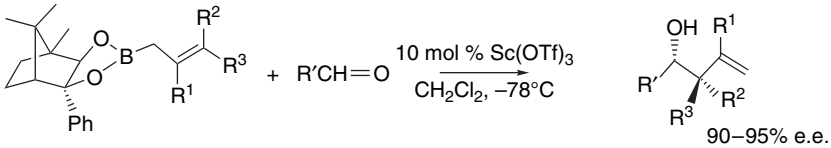
The catalysis has made reactions of certain functionalized boronates possible. For example, a carbocupration and alkylation allowed the synthesis of boronate **5**. Reaction with aldehydes gave α-methylene lactones with high stereoselectivity.[53]



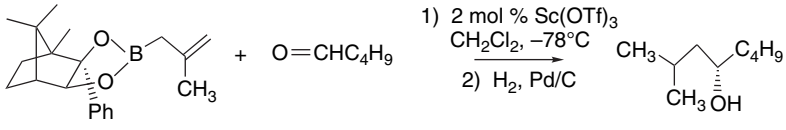
The catalysis has been extended for use with chiral boronates and those from the phenyl-substituted bornane diol derivatives **A** and **B**[54] have been found to be particularly effective.[55]



These reagents have been utilized for allyl-, 2-methylallyl-, and *E*- and *Z*-2-butenyl derivatives. Enantioselectivity of 90–95% is achieved with alkyl- and aryl-, as well as α- and β-siloxy aldehydes.



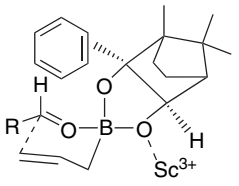
This method has been applied to the synthesis of (*S*)-2-methyl-4-octanol, an aggregation pheromone of *Metamasius hemipterus*.[56]



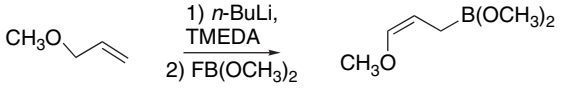
Mechanistic studies have suggested that the TS involves bonding of Sc^{3+} to one of the boronate oxygens,[57] which is consistent with the observation that the catalysts do not have much effect on the rate of allylic boranes. The phenyl substituent on the

53. J. W. J. Kennedy and D. G. Hall, *J. Org. Chem.*, **69**, 4412 (2004).
54. T. Herold, U. Schrott, and R. W. Hoffmann, *Chem. Ber.*, **114**, 359 (1981).
55. H. Lachance, X. Lu, M. Gravel, and D. G. Hall, *J. Am. Chem. Soc.*, **125**, 10160 (2003).
56. M. Gravel, H. Lachance, X. Lu, and D. G. Hall, *Synthesis*, 1290 (2004).
57. V. Rauniyar and D. G. Hall, *J. Am. Chem. Soc.*, **126**, 4518 (2004).

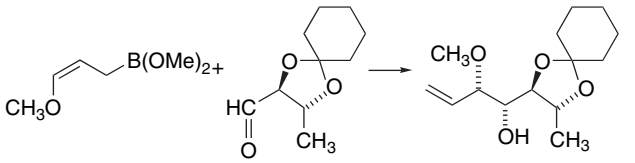
boronate is thought to assist in the aldehyde binding through a π-π^* interaction with the aromatic ring.



Various functionalized allylic boronates have been prepared.[58] *Z*-3-Methoxy derivatives can be prepared by lithiation of allyl methyl ether and substitution.[59]

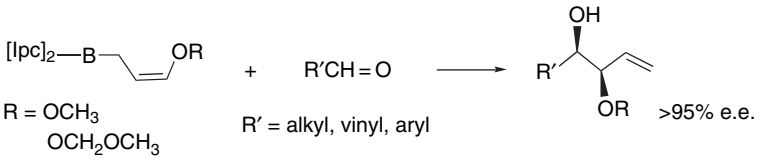


They react with aldehydes to give α-methoxy alcohols.

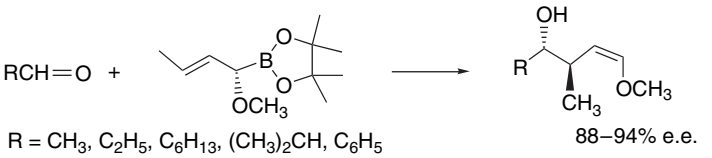


Ref. 60

Oxygenated allylic derivatives of $(Ipc)_2BH$ also show excellent diastereoselectivity.

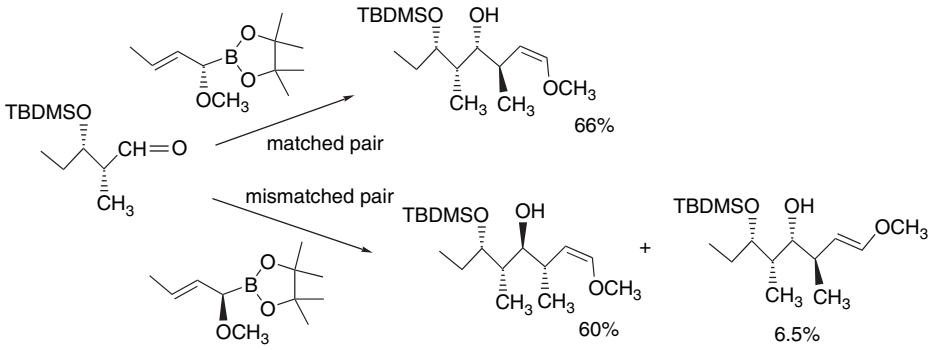


1-Methoxy-2-butenyl pinacol boronates show good stereoselectivity toward achiral aldehydes.[61]

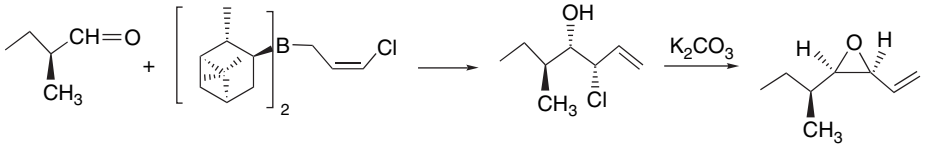


These reagents were also examined with chiral α-substituted aldehydes. The allylboration reagent dominates the enantioselectivity in both matched and mismatched pairs.

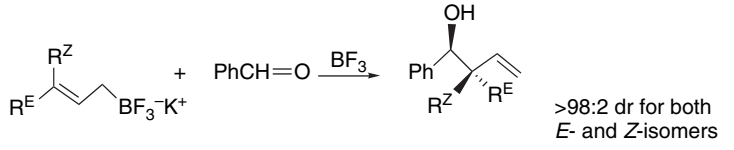
58. P. G. M. Wuts, P. A. Thompson, and G. R. Callen, *J. Org. Chem.*, **48**, 5398 (1983); E. Moret and M. Schlosser, *Tetrahedron Lett.*, **25**, 4491 (1984).
59. P. G. M. Wuts and S. S. Bigelow, *J. Org. Chem.*, **47**, 2498 (1982); K. Fujita and M. Schlosser, *Helv. Chim. Acta*, **65**, 1258 (1982).
60. W. R. Roush, M. R. Michaelides, D. F. Tai, and W. K. M. Chong, *J. Am. Chem. Soc.*, **109**, 7575 (1987).
61. R. W. Hoffmann and S. Dresely, *Chem. Ber.*, **122**, 903 (1989).



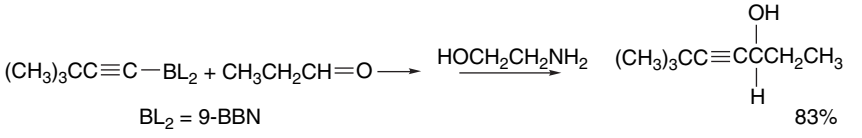
Chloro-substituted $[Ipc]_2BH$ derivatives have proven useful for enantioselective synthesis of vinyl epoxides.[62]



Allyl tetrafluoroborates are also useful allylboration reagents. They can be made from allylic boronic acids and are stable solids.[63] The reaction with aldehydes is mediated by BF_3, which is believed to provide the difluoroborane by removing a fluoride. The addition reactions occur with high stereoselectivity, indicating a cyclic TS.



β-Alkynyl derivatives of 9-BBN act as mild sources of nucleophilic acetylenic groups. Reaction occurs with both aldehydes and ketones, but the rate is at least 100 times faster for aldehydes.[64]



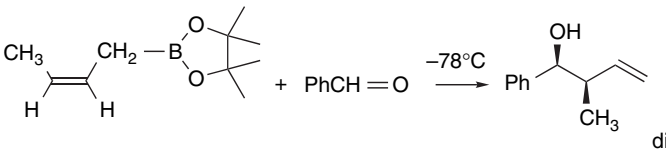
The facility with which the transfer of acetylenic groups occurs is associated with the relative stability of the *sp*-hybridized carbon. This reaction is an alternative to the more common addition of magnesium or lithium salts of acetylides to aldehydes.

Scheme 9.3 illustrates some examples of syntheses of allylic carbinols via allylic boranes and boronate esters. Entries 1 and 2 are among the early examples that

62. S. Hu, S. Jayaraman, and A. C. Oehschlager, *J. Org. Chem.*, **63**, 8843 (1998).
63. R. A. Batey, A. N. Thandani, D. V. Smil, and A. J. Lough, *Synthesis*, 990 (2000).
64. H. C. Brown, G. A. Molander, S. M. Singh, and U. S. Racherla, *J. Org. Chem.*, **50**, 1577 (1985).

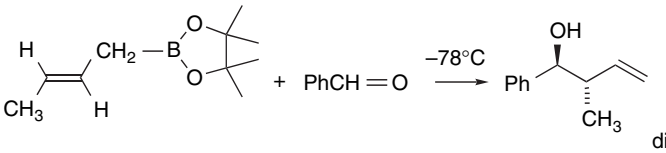
Scheme 9.3. Addition Reactions of Allylic Boranes and Carbonyl Compounds

1[a]



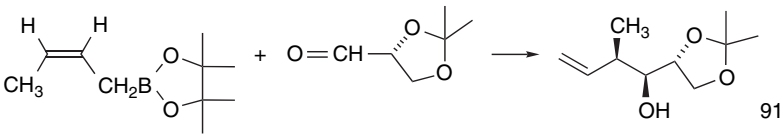
diastereoselectivity >95%

2[a]



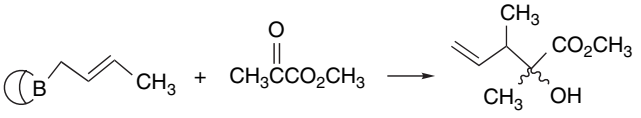
diastereoselectivity >95%

3[b]



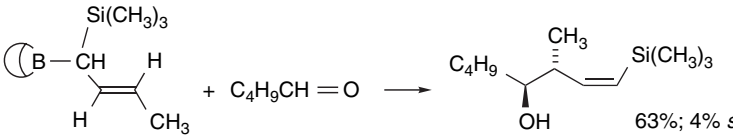
91%

4[c]



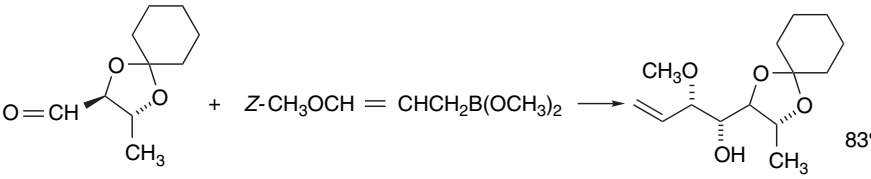
96% yield,
73:27 *anti-syn* mixture

5[d]



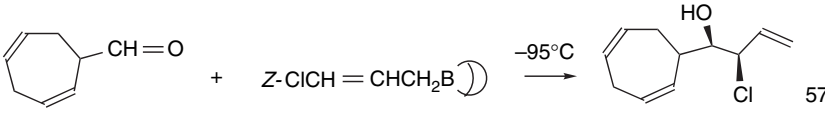
63%; 4% *syn*-isomer

6[e]



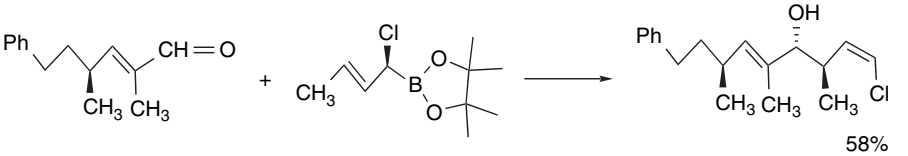
83%

7[f]



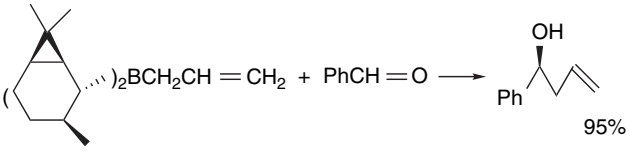
57%

8[g]



58%

9[h]

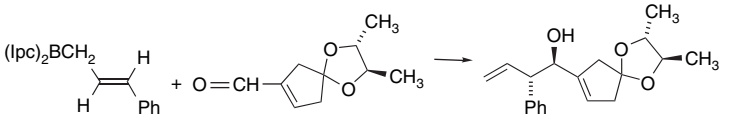


95% e.e.

(*Continued*)

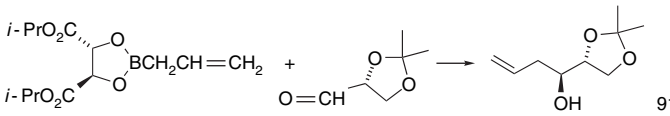
Scheme 9.3. (*Continued*)

10[i]



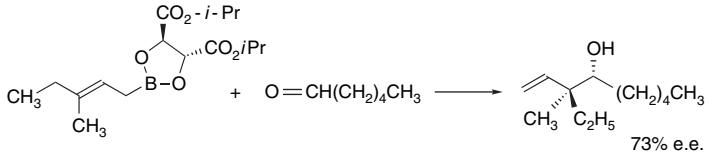
96:4 diastereoselectivity, 89% e.e.

11[j]



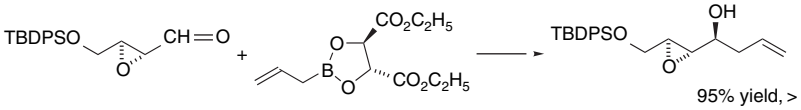
91% yield
96:4 diastereoselectivity

12[k]



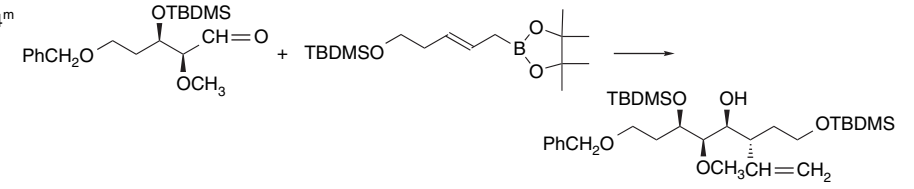
73% e.e.

13[l]



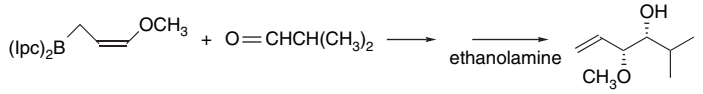
95% yield, > 96% e.e.

14[m]



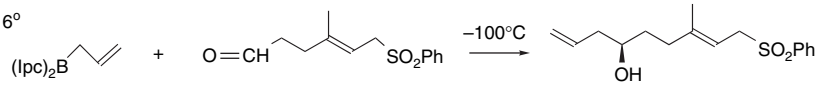
85% total yield,
major isomer of mixture

15[n]



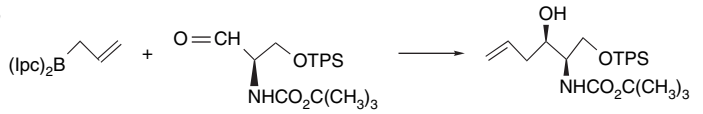
57% yield,
100% *anti*, 88% e.e.

16[o]

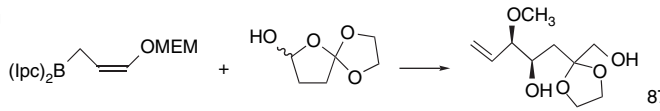


62% yield, 86% e.e.

17[p]

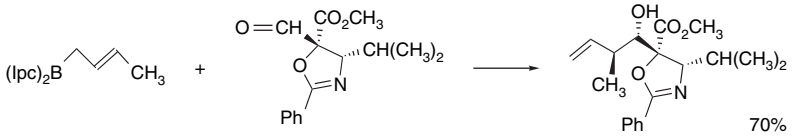


18[q]



87% >98% e.e.

19[r]



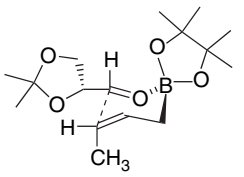
70%

(*Continued*)

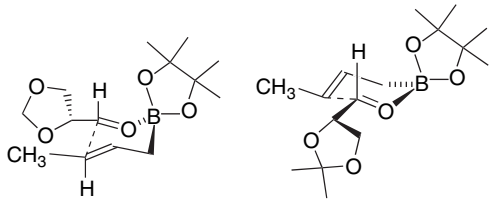
Scheme 9.3. (*Continued*)

a. R. W. Hoffmann and H.-J. Zeiss, *J. Org. Chem*., **46**, 1309 (1981).
b. W. R. Roush and A. E. Walts, *Tetrahedron Lett*., **26**, 3427 (1985); W. R. Roush, M. A. Adam, and D. J. Harris, *J. Org. Chem*., **50**, 2000 (1985).
c. Y. Yamamoto, K. Maruyama, T. Komatsu, and W. Ito, *J. Org. Chem*., **51**, 886 (1986).
d. Y. Yamamoto, H. Yatagai, and K. Maruyama, *J. Am. Chem. Soc*., **103**, 3229 (1981).
e. W. R. Roush, M. R. Michaelides, D. F. Tai, and W. K. M. Chong, *J. Am. Chem. Soc*., **109**, 7575 (1987).
f. C. Hertweck and W. Boland, *Tetrahedron Lett*., **53**, 14651 (1997).
g. H. C. Brown, R. S. Randad, K. S. Bhat, M. Zaidlewicz, and U. S. Racherla, *J. Am. Chem. Soc*., **112**, 2389 (1990).
h. R. W. Hoffmann, E. Haeberlin, and T. Rolide, *Synthesis*, 207 (2002).
i. L. K. Truesdale, D. Swanson, and R. C. Sun, *Tetrahedron Lett*., **26**, 5009 (1985).
j. W. R. Roush, A. E. Walts, and L. K. Hoong, *J. Am. Chem. Soc*., **107**, 8186 (1985).
k. Y. Yamamoto, S. Hara, and A. Suzuki, *Synlett*, 883 (1996).
l. W. R. Roush, J. A. Straub, and M. S. Van Nieuwenhze, *J. Org. Chem*., **56**, 1636 (1985).
m. P. G. M. Wuts and S. S. Bigelow, *J. Org. Chem*., **53**, 5023 (1988).
n. H. C. Brown, P. K. Jadhav, and K. S. Bhat, *J. Am. Chem. Soc*., **110**, 1535 (1988).
o. M. Z. Hoemann, K. A. Agrios, and J. Aube, *Tetrahedron*, **53**, 11087 (1997).
p. K. C. Nicolaou, M. E. Bunnage, and K. Koide, *Chem. Eur. J*., **1**, 454 (1995).
q. A. L. Smith, E. N. Pitsinos, C.-K. Hwang, Y. Mizuno, H. Saimoto, G. R. Scarlato, T. Suzuki, and K. C. Nicolaou, *J. Am. Chem. Soc*., **115**, 7612 (1993).
r. T. Sunazuka, T. Nagamitsu, K. Matsuzaki, H. Tanaka, S. Omura, and A. B. Smith, III, *J. Am. Chem. Soc*., **115**, 5302 (1993).

demonstrate the high diastereoselectivity of the allylboration reaction. Entry 3 examines the facial selectivity of glyceraldehyde acetonide toward the achiral reagents derived from butenyl pinacol borane. It was found that the reaction with the *Z*-2-butenyl derivative is highly enantioselective, the *E*-isomer was much less so. It was suggested that steric interaction of the *E*-methyl group with the dioxolane in the expected TS ring led to involvement of a second transition structure.

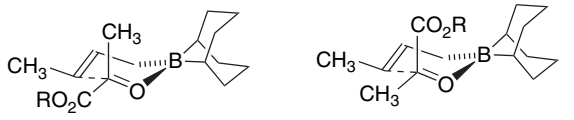


strongly favored for *Z*-boronate



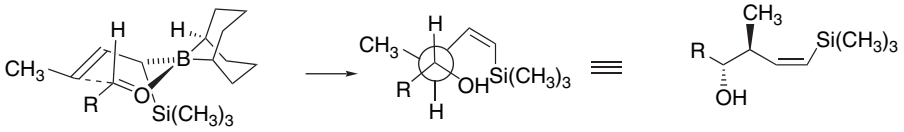
two competing transition structures for *E*-boronate

Entry 4 shows the reaction of 9-(*E*-2-butenyl)-9BBN with methyl pyruvate. This reaction is not very stereoselective, which is presumably due to a modest preference for the orientation of the methyl and methoxycarbonyl groups in the TS. Only use of an extremely sterically demanding pyruvic ester achieved high diastereoselectivity.



R	product ratio	
CH_3	73	27
Ph	80	20
2,6-diMePh	75	25
2,4,6-tri-*t*-BuPh	100	0

Entry 5 is an example of use of an α-trimethylsilylallyl group to prepare a vinylsilane. The stereochemistry is consistent with a cyclic TS having the trimethylsilyl substituent in a quasi-axial position to avoid interaction with the bridgehead hydrogen of the bicyclic ring.



Entries 6 and 7 involve functionalized allyl groups, with a Z-γ-methoxy group in Entry 6 and a Z-γ-chloro group in Entry 7. Both give *syn* products; in the case of Entry 7 the chlorohydrin was cyclized to the *cis* epoxide, which is a pheromone (lamoxirene) of a species of algae. Entry 8 is another example of the use of a chloro-substituted allylic borane. Entry 9 involves one of the alternatives to $(Ipc)_2BH$ for enantioselective allylation. In Entry 10, both the aldehyde and allyl group contain chiral centers, but the borane is presumably the controlling factor in the stereoselectivity. Entries 11 to 13 demonstrate several enantioselective reactions using the tartrate-derived chiral auxiliaries. Entry 14 is an example of *reactant-controlled* stereochemistry involving the achiral β-allyl pinacol borane. This reaction proceeded with low stereochemical control to give four isomers in a ratio of 18:3.4:1.4:1. Entry 15 shows high diastereoselectivity and enantioselectivity in a reaction with a *Z*-γ-methoxyallyl-$(Ipc)_2$-borane. Entries 16 to 19 are examples of the use of allylboration in multistage syntheses. Entry 16 involves magnesium-free conditions (see p. 799). Entry 17 was used to construct balanol, a PKC inhibitor, and demonstrates *reagent control* of stereochemistry by allyl-$B(Ipc)_2$ without interference from the protected α-amino and β-hydroxy substituents. Entries 18 and 19 also involve functionalized aldehydes.

9.2. Organosilicon Compounds

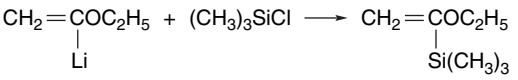
9.2.1. Synthesis of Organosilanes

Silicon is similar in electronegativity to carbon. The carbon-silicon bond is quite strong (~75 kcal) and trialkylsilyl groups are stable to many of the reaction conditions that are used in organic synthesis. Much of the repertoire of synthetic organic chemistry can be used for elaboration of organosilanes.[65] For example, the Grignard reagent derived from chloromethyltrimethylsilane is a source of nucleophilic $CH_2Si(CH_3)_3$ units. Two of the most general means of synthesis of organosilanes are nucleophilic displacement of halogen from a halosilane by an organometallic reagent and addition of silanes at multiple bonds (*hydrosilation*). Organomagnesium and organolithium compounds react with trimethylsilyl chloride to give the corresponding tetrasubstituted silanes.

$$CH_2{=}CHMgBr + (CH_3)_3SiCl \longrightarrow CH_2{=}CHSi(CH_3)_3$$ Ref. 66

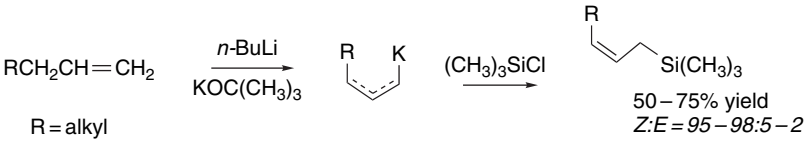
[65] L. Birkofer and O. Stuhl, in *The Chemistry of Organic Silicon Compounds*, S. Patai and Z. Rappoport, eds., Wiley-Interscience, 1989, New York, Chap. 10.

[66] R. K. Boeckman, Jr., D. M. Blum, B. Ganem, and N. Halvey, *Org. Synth.*, **58**, 152 (1978).

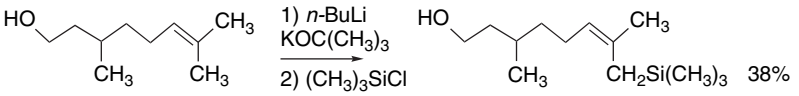


Ref. 67

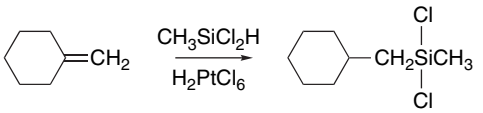
Metallation of alkenes with *n*-BuLi-$KOC(CH_3)_3$ provides a route that is stereoselective for *Z*-allylic silanes.[68] (See p. 632 for discussion of this metallation method.)



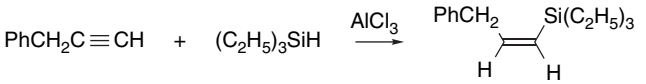
These conditions are also applicable to functionalized systems that are compatible with metallation by this "superbase."[69]



Silicon substituents can be introduced into alkenes and alkynes by hydrosilation.[70] This reaction, in contrast to hydroboration, does not occur spontaneously, but it can be carried out in the presence of catalysts such as H_2PtCl_6, hexachloroplatinic acid. Other catalysts are also available.[71] Halosilanes are more reactive than trialkylsilanes.[72]



Alkenylsilanes can be made by Lewis acid–catalyzed hydrosilation of alkynes. Both $AlCl_3$ and $C_2H_5AlCl_2$ are effective catalysts.[73] The reaction proceeds by net *anti* addition, giving the *Z*-alkenylsilane. The reaction is regioselective for silylation of the terminal carbon.



67. R. F. Cunico and C.-P. Kuan, *J. Org. Chem.*, **50**, 5410 (1985).
68. O. Desponds, L. Franzini, and M. Schlosser, *Synthesis*, 150 (1997).
69. E. Moret, L. Franzini, and M. Schlosser, *Chem. Ber.*, **130**, 335 (1997).
70. J. L. Speier, *Adv. Organomet. Chem.*, **17**, 407 (1979); E. Lukenvics, *Russ. Chem. Rev.* (Engl. Transl.), **46**, 264 (1977); N. D. Smith, J. Mancuso, and M. Lautens, *Chem. Rev.*, **100**, 3257 (2000); M. Brunner, *Angew. Chem. Int. Ed. Engl.*, **43**, 2749 (2004); B. M. Trost and Z. T. Ball, *Synthesis*, 853 (2005).
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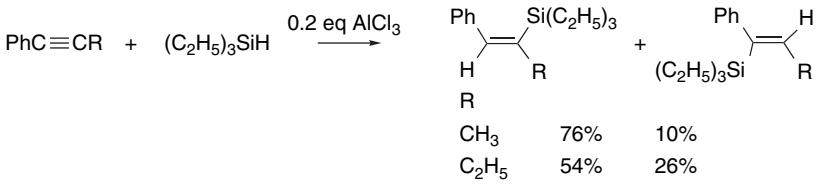
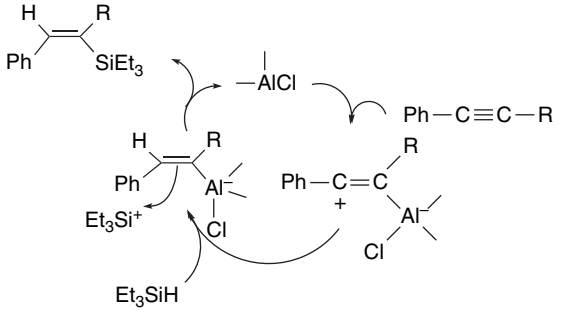
72. T. G. Selin and R. West, *J. Am. Chem. Soc.*, **84**, 1863 (1962).
73. N. Asao, T. Sudo, and Y. Yamamoto, *J. Org. Chem.*, **61**, 7654 (1996); T. Sudo, N. Asoa, V. Gevorgyan, and Y. Yamamoto, *J. Org. Chem.*, **64**, 2494 (1999).

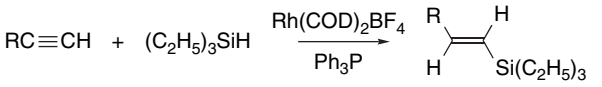
These conditions can also be applied to internal alkynes and show a regiochemical preference for silylation β to aryl substituents.



The reaction is formulated as an electrophilic attack by the aluminum halide, followed by hydride abstraction and transmetallation. A vinyl cation intermediate can account for both the regiochemistry and the stereochemistry.

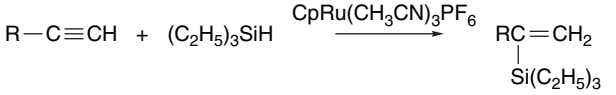


A variety of transition metal complexes catalyze hydrosilylation of alkynes. Catalysis of hydrosilylation by rhodium gives *E*-alkenylsilanes from 1-alkynes.[74]

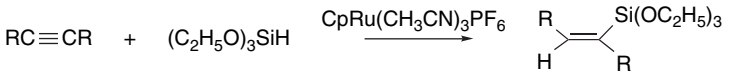


Ref. 75

$CpRu(CH_3CN)_3PF_6$ catalyzes hydrosilylation of both terminal and internal alkynes. With this catalyst, addition exhibits the opposite regiochemistry.

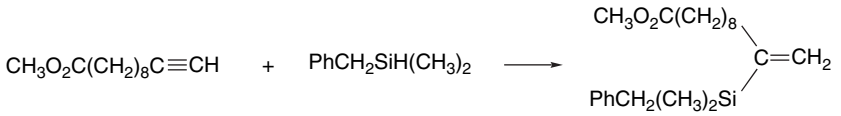


With internal alkynes, the stereochemistry of addition is *anti*.

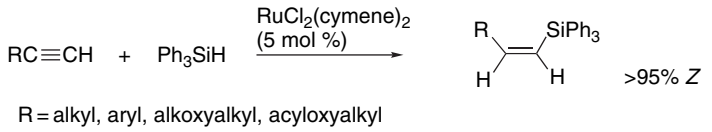


[74.] R. Takeuchi, S. Nitta, and D. Watanabe, *J. Org. Chem.*, **60**, 3045 (1995).
[75.] B. M. Trost and Z. T. Ball, *J. Am. Chem. Soc.*, **123**, 12726 (2001).

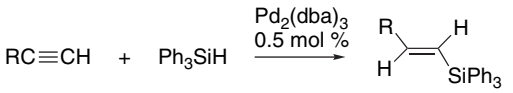
This method has been used to prepare alkenyl benzyldimethylsilanes.[76] These derivatives are amenable to synthetic transformation involving F^--mediated debenzylation.



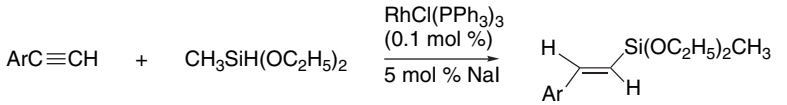
Other ruthenium-based catalysts are also active. Ruthenium dichloride–cymene complex is stereoselective for formation of the *Z*-vinyl silanes from terminal alkynes.



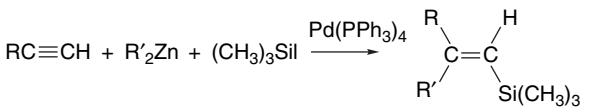
Palladium-phosphine catalysts have also been used in the addition of triphenylsilane.[77] In this case, the *E*-silane is formed.



High stereoselectivity was noted with Wilkinson's catalyst in the reaction of arylalkynes with diethoxymethylsilane. Interestingly, the stereoselectivity was dependent on the order of mixing of the reagents and the catalyst. When the alkyne was added to a mixture of catalyst and silane, the *Z*-isomer was formed. Reversing the order and adding the silane to an alkyne-catalyst mixture led to formation of the *E*-product.[78]



Tandem *syn* addition of alkyl and trimethylsilyl groups can be accomplished with dialkylzinc and trimethylsilyl iodide in the presence of a Pd(0) catalyst.[79]



76. B. M. Trost, M. R. Machacek, and Z. T. Ball, *Org. Lett*., **5**, 1895 (2003).
77. D. Motoda, H. Shinokubo, and K. Oshima, *Synlett*, 1529 (2002).
78. A. Mori, E. Takahisa, H. Kajiro, K. Hirabayashi, Y. Nishihara, and T. Hiyama, *Chem. Lett*., 443 (1998).
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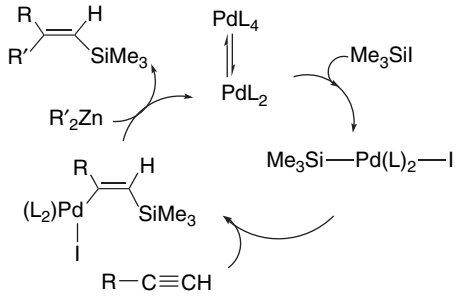
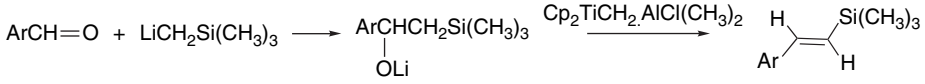
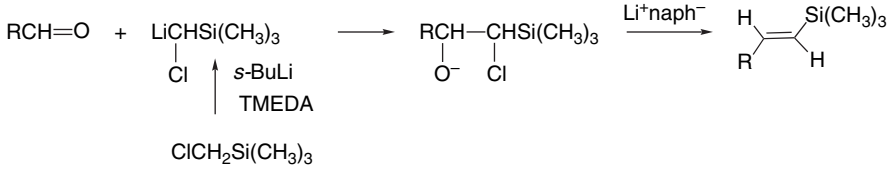
A possible mechanism involves formation of a Pd(II) intermediate that can undergo cross coupling with the zinc reagent.



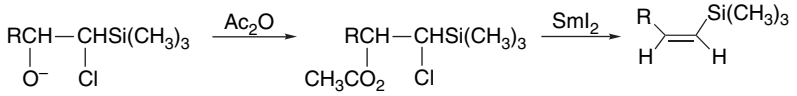
Several variations of the Peterson reaction have been developed for synthesis of alkenylsilanes.[80] *E*-β-Arylvinylsilanes can be obtained by dehydration of β-silyloxy alkoxides formed by addition of lithiomethyl trimethylsilane to aromatic aldehydes. Specific Lewis acids have been found to be advantageous for the elimination step.[81]



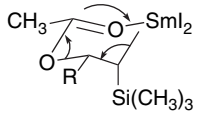
Alkenylsilanes can be prepared from aldehydes and ketones using lithio(chloromethyl)trimethylsilane. The adducts are subjected to a reductive elimination by lithium naphthalenide. This procedure is stereoselective for the *E*-isomer with both alkyl and aryl aldehydes.[82]



The adducts can be directed toward *Z*-alkenylsilanes by acetylation and reductive elimination using SmI_2.[83]

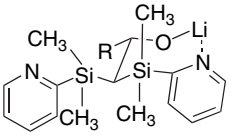


The stereoselectivity in this case is attributed to elimination through a cyclic TS, but is considerably reduced with aryl aldehydes.

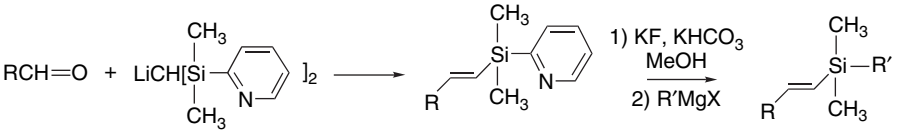


80. C. Trindle, J.-T. Hwang, and F. A. Carey, *J. Org. Chem*., **38**, 2664 (1973); P. F. Hudrlik, E. L. Agwaramgbo, and A. M. Hudrlik, *J. Org. Chem*., **54**, 5613 (1989).
81. M. L. Kwan, C. W. Yeung, K. L. Breno, and K. M. Doxsee, *Tetrahedron Lett*., **42**, 1411 (2001).
82. J. Barluenga, J. L. Fernandez-Simon, J. M. Concellon, and M. Yus, *Synthesis*, 234 (1988).
83. J. M. Concellon, P. L. Bernad, and E. Bardales, *Org. Lett*., **3**, 937 (2001).

Specialized silyl substituents have been developed. High yields of *E*-alkenylsilanes were obtained using *bis*-(dimethyl-2-pyridyl)silylmethyllithium.[84] The stereoselectivity is attributed to a cyclic TS for the addition step.

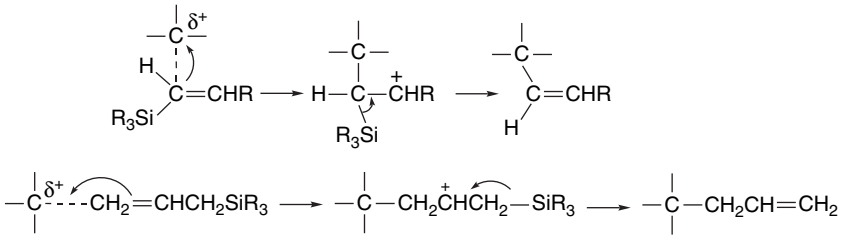


If necessary for further applications, the 2-pyridyl group can be exchanged by alkyl in a two-step sequence that takes advantage of the enhanced leaving-group ability of the 2-pyridyl group.

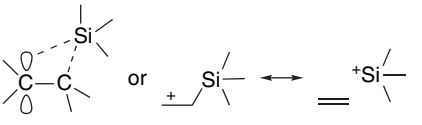


9.2.2. General Features of Carbon-Carbon Bond-Forming Reactions of Organosilicon Compounds

Alkylsilanes are not very nucleophilic because there are no high-energy electrons in the sp^3-sp^3 carbon-silicon bond. Most of the valuable synthetic procedures based on organosilanes involve either alkenyl or allylic silicon substituents. The dominant reactivity pattern involves attack by an electrophilic carbon intermediate at the double bond that is followed by desilylation. Attack on alkenylsilanes takes place at the α-carbon and results in overall replacement of the silicon substituent by the electrophile. Attack on allylic groups is at the γ-carbon and results in loss of the silicon substituent and an allylic shift of the double bond.



The crucial influence on the reactivity pattern in both cases is the *very high stabilization that silicon provides for carbocationic character at the ß-carbon atom*. This stabilization is attributed primarily to hyperconjugation with the C–Si bond (see Part A, Section 3.4.1).[85]

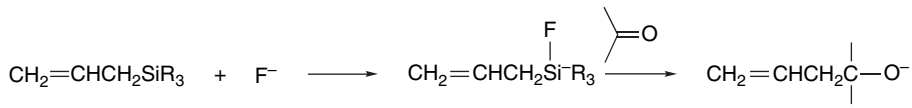


[84] K. Itami, T. Nokami, and J. Yoshida, *Org. Lett*., **2**, 1299 (2000).

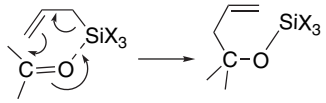
[85] S. G. Wierschke, J. Chandrasekhar, and W. L. Jorgensen, *J. Am. Chem. Soc*., **107**, 1496 (1985); J. B. Lambert, G. Wang, R. B. Finzel, and D. H. Teramura, *J. Am. Chem. Soc*., **109**, 7838 (1987).

Most reactions of alkenyl and allylic silanes require strong carbon electrophiles and Lewis acid catalysts are often involved. The most useful electrophiles from a synthetic standpoint are carbonyl compounds, iminium ions, and electrophilic alkenes.

There are also some reactions of allylic silanes that proceed through anionic silicate species. These reactions usually involve activation by fluoride and result in transfer of an allylic anion.

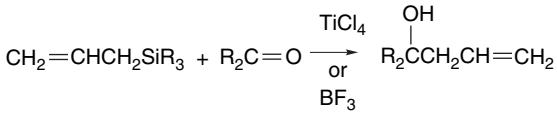


Trichloro- and trifluorosilanes introduce another dimension into the reactivity of allylic silanes. The silicon in these compounds is electrophilic and can expand to pentacoordinate and hexacoordinate structures. These reactions can occur through a cyclic or chelated TS.

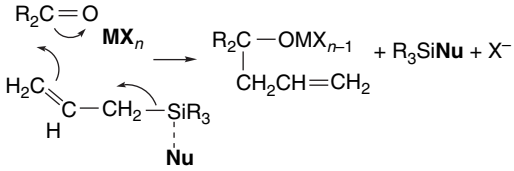


9.2.3. Addition Reactions with Aldehydes and Ketones

A variety of electrophilic catalysts promote the addition of allylic silanes to carbonyl compounds.[86] The original catalysts included typical Lewis acids such as $TiCl_4$ or BF_3.[87] This reaction is often referred to as the *Sakurai reaction*.



These reactions involve activation of the carbonyl group by the Lewis acid. A nucleophile, either a ligand from the Lewis acid or the solvent, assists in the desilylation step.

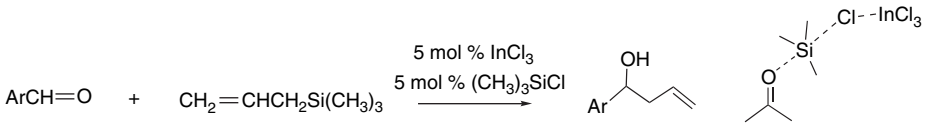


Various other Lewis acids have been explored as catalysts, and the combination $InCl_3$-$(CH_3)_3SiCl$ has been found to be effective. [88] The catalysis requires both components and is attributed to assistance from O-silylation of the carbonyl compound.

[86.] A. Hosomi, *Acc. Chem. Res*., **21**, 200 (1988); I. Fleming, J. Dunoques, and R. Smithers, *Org. React*., **37**, 57 (1989).

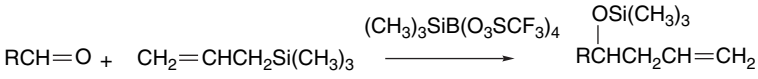
[87.] A. Hosomi and H. Sakurai, *Tetrahedron Lett*., 1295 (1976).

[88.] Y. Onishi, T. Ito, M. Yasuda, and A. Baba, *Eur. J. Org. Chem*., 1578 (2002); Y. Onishi, T. Ito, M. Yasuda, and A. Baba, *Tetrahedron*, **58**, 8227 (2002).

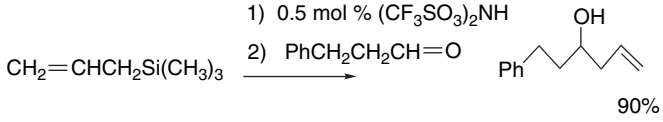


Lanthanide salts, such as $Sc(O_3SCF_3)_3$, are also effective catalysts.[89]

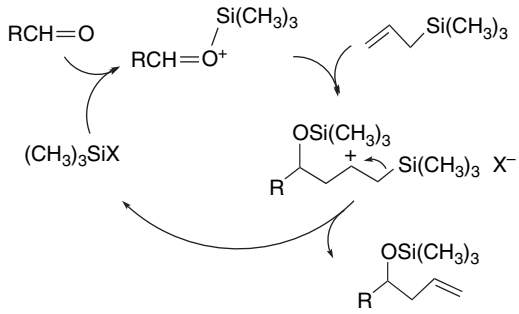
Silylating reagents such as TMSI and TMS triflate have only a modest catalytic effect, but the still more powerful silylating reagent $(CH_3)_3SiB(O_3SCF_3)_4$ does induce addition to aldehydes.[90]



In another procedure, $(CH_3)_3SiN(O_3SCF_3)$ is generated in situ from triflimide.[91]



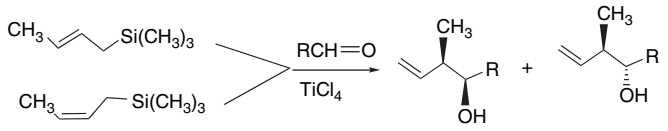
These reagents initiate a catalytic cycle that regenerates the active silyation species.[92] (See p. 83 for a similar cycle in the Mukaiyama reaction.)



Although the allylation reaction is formally analogous to the addition of allylic boranes to carbonyl derivatives, it does not normally occur through a cyclic TS. This is because, in contrast to the boranes, the silicon in allylic silanes has little Lewis acid character and does not coordinate at the carbonyl oxygen. The stereochemistry of addition of allylic silanes to carbonyl compounds is consistent with an acyclic TS. The *E*-stereoisomer of 2-butenyl(trimethyl)silane gives nearly exclusively the product in

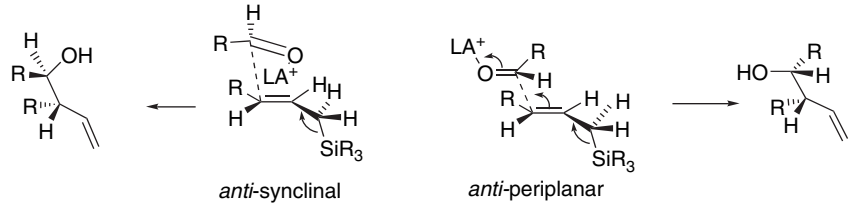
89. V. K. Aggarwal and G. P. Vennall, *Tetrahedron Lett*., **37**, 3745 (1996).
90. A. P. Davis and M. Jaspars, *Angew. Chem. Int. Ed. Engl*., **31**, 470 (1992).
91. K. Ishihara, Y. Hiraiwa, and H. Yamamoto, *Synlett*, 1851 (2001).
92. T. K. Hollis and B. Bosnich, *J. Am. Chem. Soc*., **117**, 4570 (1995).

which the newly formed hydroxyl group is *syn* to the methyl substituent; the *Z*-isomer is also modestly selective for the *syn* isomer.[93]



R	*E*-silane *syn:anti*	*Z*-silane *syn:anti*
Et	>95:5	65:35
i-Pr	>97:3	64:36
t-Bu	>99:1	69:31

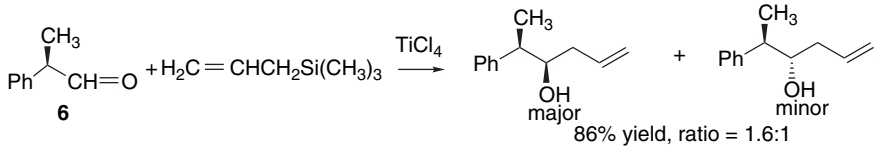
Both *anti*-synclinal and *anti*-periplanar TSs are considered to be feasible. These differ in the relative orientation of the C=C and C=O bonds. The *anti*-synclinal arrangement is usually preferred.[94]



anti-synclinal *anti*-periplanar

The addition reaction of allylsilane to acetaldehyde with BF_3 as the Lewis acid has been modeled computationally.[95] The lowest-energy TSs found, which are shown in Figure 9.2, were of the synclinal type, with dihedral angles near 60°. Although the structures are acyclic, there is an apparent electrostatic attraction between the fluorine and the silicon that imparts some cyclic character to the TS. Both *anti* and *syn* structures were of comparable energy for the model. However, steric effects that arise by replacement of hydrogen on silicon with methyl are likely to favor the *anti* TS.

When chiral aldehydes such as **6** are used, there is a modest degree of diastereoselectivity in the direction predicted by an open Felkin TS.[96]



93. T. Hayashi, K. Kabeta, I. Hamachi, and M. Kumada, *Tetrahedron Lett.*, **24**, 2865 (1983).
94. S. E. Denmark and N. G. Almstead, *J. Org. Chem.*, **59**, 5130 (1994).
95. A. Bottoni, A. L. Costa, D. Di Tommaso, I. Rossi, and E. Tagliavini, *J. Am. Chem. Soc.*, **119**, 12131 (1997).
96. M. Nakada, Y. Urano, S. Kobayashi, and M. Ohno, *J. Am. Chem. Soc.*, **110**, 4826 (1988).

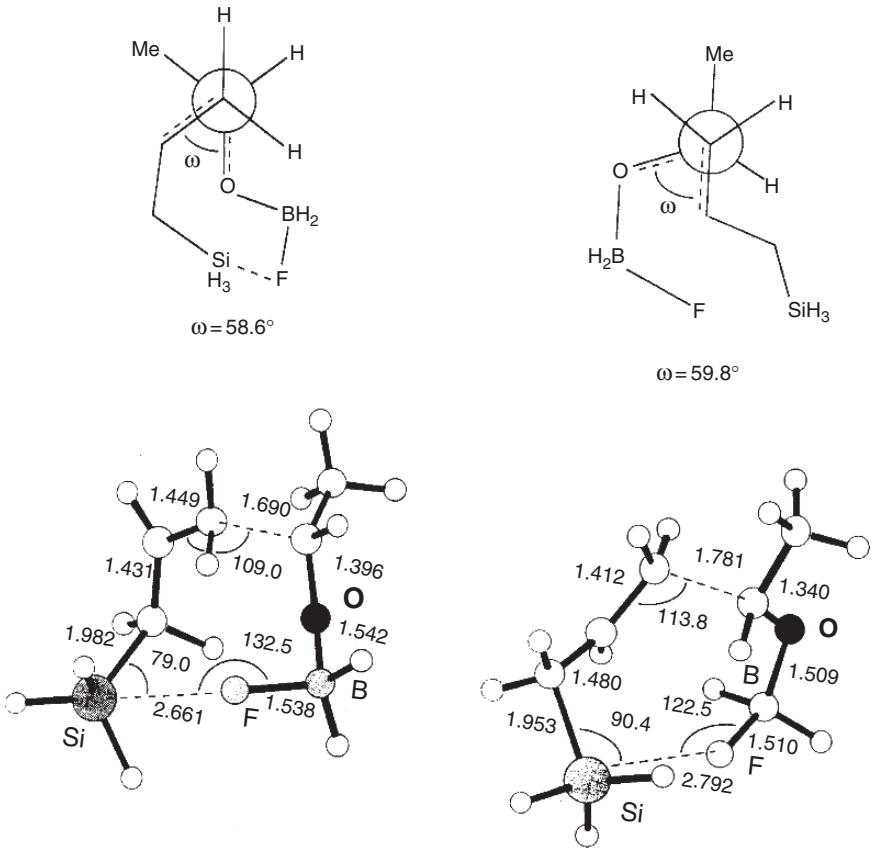
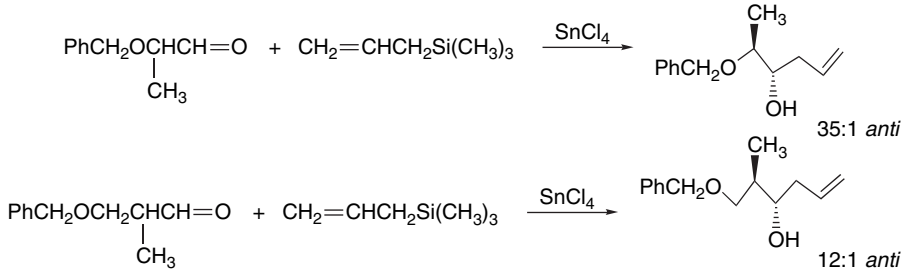


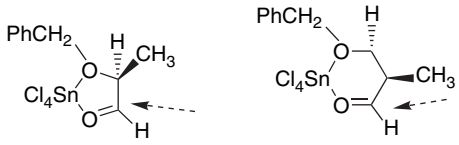
Fig. 9.2. Most favorable transition structures for reaction of allylsilane with acetaldehyde-fluoroborane: (left) *anti* synclinal; (right) *syn* synclinal. Reproduced from *J. Am. Chem. Soc*., **119**, 12131 (1997), by permission of the American Chemical Society.

Aldehydes with α- or β-benzyloxy substituents react with allyltrimethylsilane in the presence of $SnCl_4$ to give high yields of product resulting from chelation control.[97]



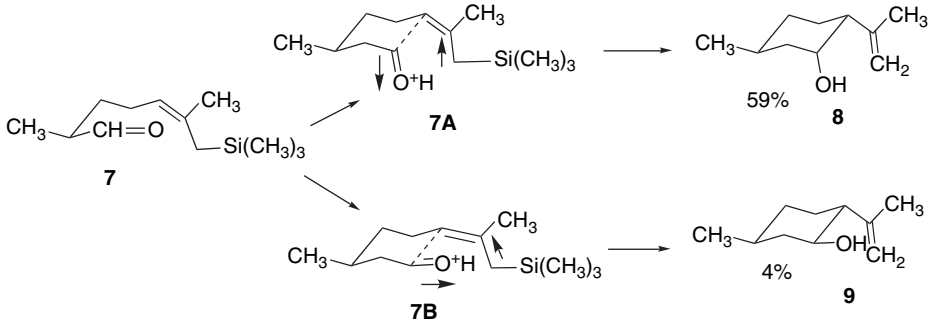
97. C. H. Heathcock, S. Kiyooka, and T. Blumenkopf, *J. Org. Chem*., **49**, 4214 (1984).

The stereochemistry is consistent with approach of the silane *anti* to the methyl substituent.

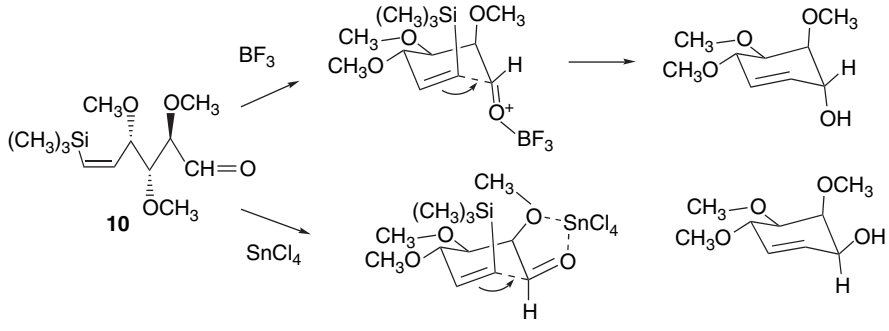


In contrast, BF_3 showed very low stereoselectivity, consistent with its inability to form a chelate.

Intramolecular reactions can also occur between carbonyl groups and allylic silanes. These reactions frequently show good stereoselectivity. For example, **7** cyclizes primarily to **8** with 4% of **9** as a by-product. The two other possible stereoisomers are not observed.[98] The stereoselectivity is attributed to a preference for TS **7A** over TS **7B**. These are both synclinal structures but differ stereoelectronically. In **7A**, the electron flow is approximately *anti* parallel, whereas in **7B** it is skewed. It was suggested that this difference may be the origin of the stereoselectivity.



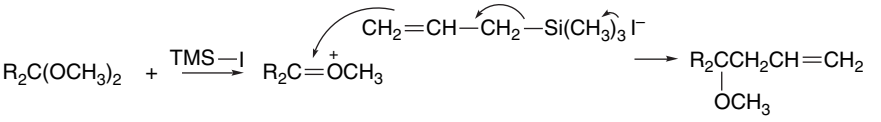
The differential in chelation capacity between BF_3 and $SnCl_4$ was used to control the stereochemistry of the cyclization of the vinyl silane **10**.[99] With BF_3, the reaction proceeds through a nonchelated TS and the stereochemistry at the new bond is *trans*. With $SnCl_4$, a chelated TS leads to the *cis* diastereomer.



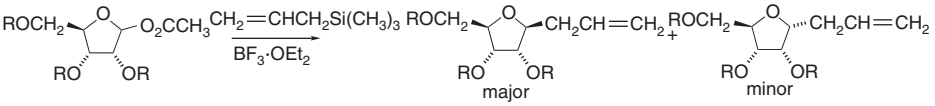
Both ketals[100] and enol ethers[101] can be used as electrophiles in place of aldehydes with appropriate catalysts. Trimethylsilyl iodide can be used in catalytic quantities

98. M. Schlosser, L. Franzini, C. Bauer, and F. Leroux, *Chem. Eur. J.*, **7**, 1909 (2001).
99. M. C. McIntosh and S. M. Weinreb, *J. Org. Chem.*, **56**, 5010 (1991).
100. T. K. Hollis, N. P. Robinson, J. Whelan, and B. Bosnich, *Tetrahedron Lett.*, **34**, 4309 (1993).
101. T. Yokozawa, K. Furuhashi, and H. Natsume, *Tetrahedron Lett.*, **36**, 5243 (1995).

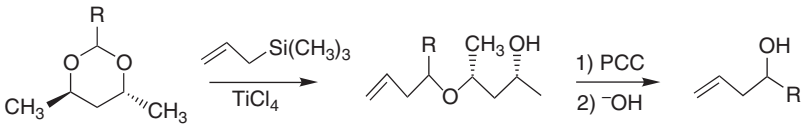
because it is regenerated by recombination of iodide ion with silicon in the desilylation step.[102]



This type of reaction has been used for the extension of the carbon chain of protected carbohydrate acetals.[103]

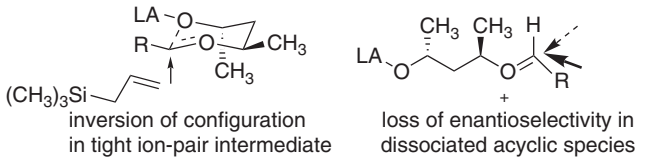


Reaction of allylic silanes with enantiomerically pure 1,3-dioxanes has been found to proceed with moderate enantioselectivity.[104] The homoallylic alcohol can be liberated by oxidation followed by base-catalyzed β-elimination. The alcohols obtained in this way are formed in 70 ± 5% e.e.

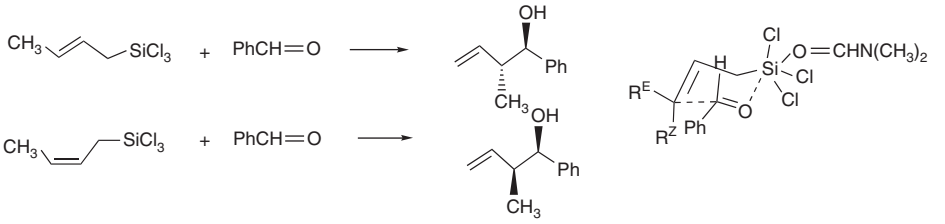


The enantioselectivity is dependent on several reaction variables, including the Lewis acid and the solvent. The observed stereoselectivity appears to reflect differences in the precise structure of the electrophilic species generated. Mild Lewis acids tend to react with inversion of configuration at the reaction site, whereas very strong Lewis acids cause loss of enantioselectivity. The strength of the Lewis acid, together with related effects of solvent and other experimental variables, determines the nature of the electrophile. With mild Lewis acids, a tight ion pair favors inversion, whereas stronger Lewis acids cause complete dissociation to an acyclic species. These two species represent extremes of behavior and intermediate levels of enantioselectivity are also observed.[105]

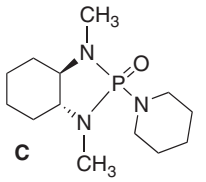
102. H. Sakurai, K. Sasaki, and A. Hosomi, *Tetrahedron Lett*., **22**, 745 (1981).
103. A. P. Kozikowski, K. L. Sorgi, B. C. Wang, and Z. Xu, *Tetrahedron Lett*., **24**, 1563 (1983).
104. P. A. Bartlett, W. S. Johnson, and J. D. Elliott, *J. Am. Chem. Soc*., **105**, 2088 (1983).
105. S. E. Denmark and N. G. Almstead, *J. Am. Chem. Soc*., **113**, 8089 (1991).



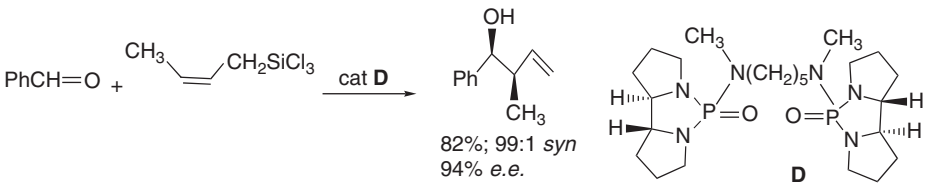
Although most studies of alkenyl and allylic silanes have been done with trialkylsilyl analogs, the reactivity of the system can be adjusted by varying the silicon substituents. Allylic trichlorosilanes react with aldehydes in DMF to give homoallylic alcohols.[106] The reactions are highly stereoselective with respect to the silane geometry and give the product expected for a cyclic TS. The reaction is thought to proceed through a hexacoordinate silicon intermediate.



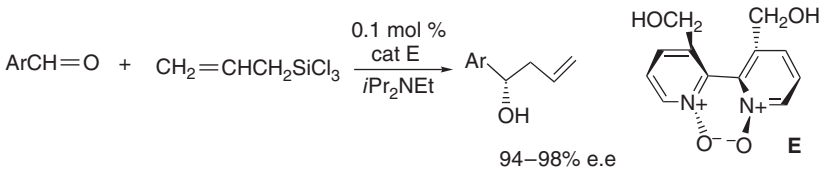
Allylic trichlorosilanes have shown promise in the development of methods for enantioselective reactions by use of chiral phosphoramides such as **C**.



Mechanistic studies suggested that two phosphoramide molecules were involved.[107] This led to the development of linked phosphoramides such as **D**.[108]

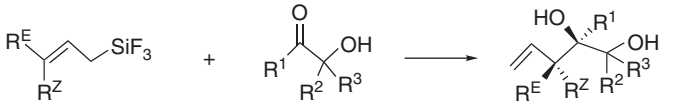


The axially chiral 2, 2′-bipyridine **E** is also an effective enantioselective catalyst for addition of allyltrichlorosilane to aldehydes.[109]

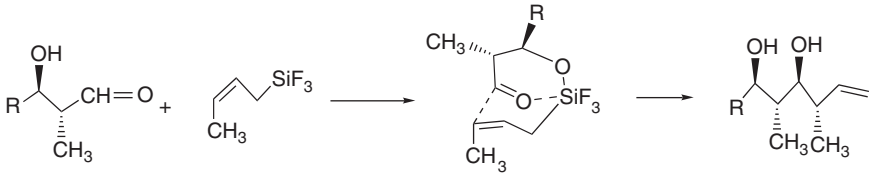


106. S. Kobayashi and K. Nishio, *J. Org. Chem.*, **59**, 6620 (1994).
107. S. E. Denmark and J. Fu, *J. Am. Chem. Soc.*, **123**, 9488 (2001).
108. S. E. Denmark and J. Fu, *J. Am. Chem. Soc.*, **125**, 2208 (2003).
109. T. Shimada, A. Kina, S. Ikeda, and T. Hayashi, *Org. Lett.*, **4**, 2799 (2002).

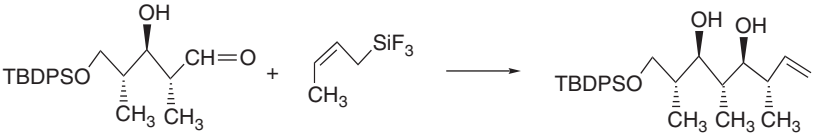
The use of trifluorosilanes permits reactions through hexacoordinate silicon, which presents an opportunity for chelation control. For example, α-hydroxy ketones give *syn* diols.[110]



Advantage of this chelation has been taken in the construction of compounds with several contiguous chiral centers. *Z*-2-Butenyl trifluorosilanes give *syn*-1,3-diols on reaction with *anti*-β-hydroxy-α-methyl aldehydes.[111] The stereoselectivity is consistent with a chelated bicyclic TS.

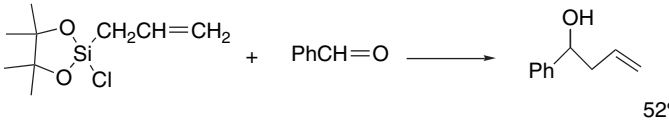


This methodology was applied to construct the all *anti* stereochemistry for a segment of the antibiotic zincophorin.



The corresponding *syn*-β-hydroxy-α-methyl aldehydes do not react through a chelated TS,[112] which appears to be due to steric factors that raise the bicyclic TS by several kcal relative to the *anti* isomers. The monocyclic six-membered TS does not incorporate these factors and the *syn* isomer reacts through a monocyclic TS. Figure 9.3 depicts the competing TSs and their relative energies as determined by MNDO calculations.

The electrophilicity of silicon is enhanced in five-membered ring structures. Chloro dioxasilolanes, oxazasilolidines, and diazasilolidines react with aldehydes in the absence of an external Lewis acid catalyst.[113]



52%

110. K. Sato, M. Kira, and H. Sakurai, *J. Am. Chem. Soc.*, **111**, 6429 (1989).
111. S. R. Chemler and W. R. Roush, *J. Org. Chem.*, **63**, 3800 (1998).
112. S. R. Chemler and W. R. Roush, *J. Org. Chem.*, **68**, 1319 (2003).
113. J. W. A. Kinnaird, P. Y. Ng, K. Kubota, X. Wang, and J. L. Leighton, *J. Am. Chem. Soc.*, **124**, 7920 (2002).

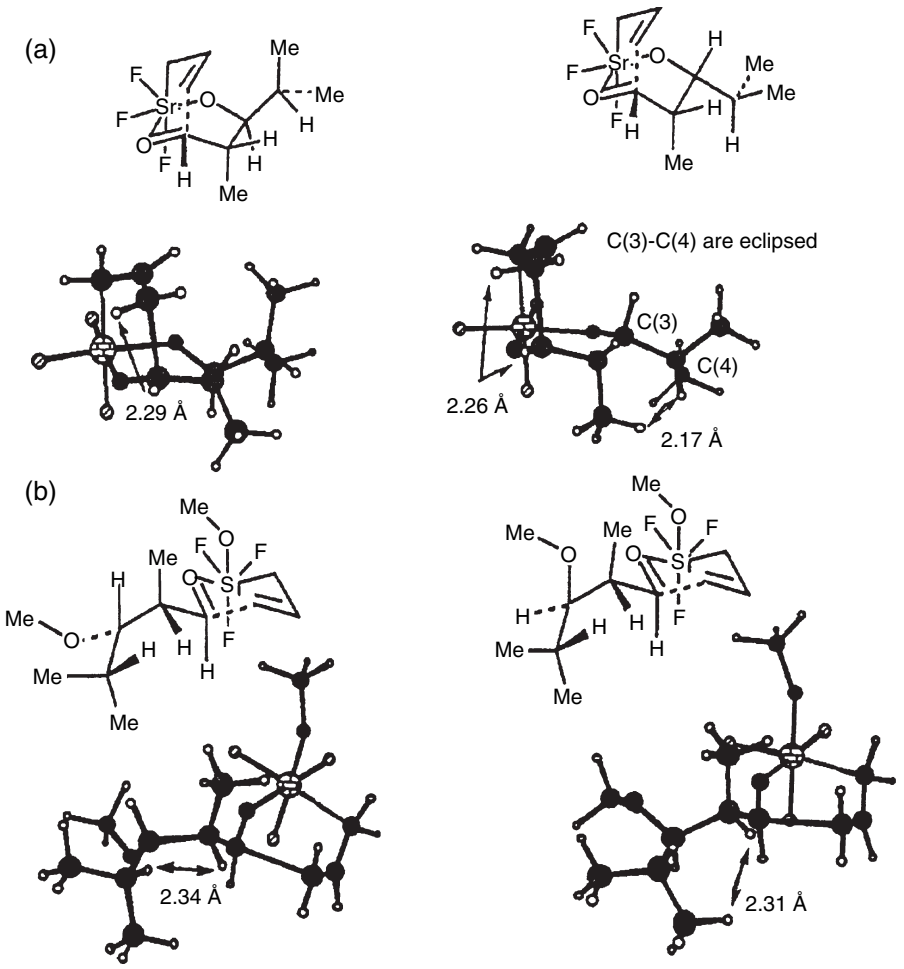
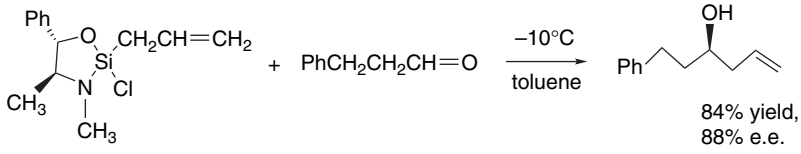


Fig. 9.3. Comparison of chelated bicyclic and nonchelated monocyclic transition structures for addition of allyl trifluorosilane to *syn*- and *anti*-3-methoxy-2,4-dimethylpentanal based on MNDO computations: (a) chelated bicyclic transition structures differ by 6 kcal/mol owing to nonbonded interactions in the *syn* case; (b) nonchelated monocyclic transition structures are of comparable energy for both isomers. Reproduced from *J. Org. Chem*., **68**, 1319 (2003), by permission of the American Chemical Society.

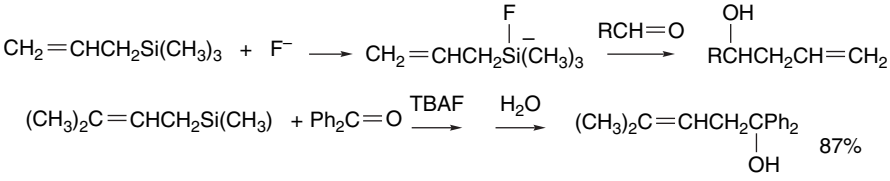
The oxazasilolidine derived from pseudoephedrine incorporates chirality around the silicon and leads to enantioselective addition.



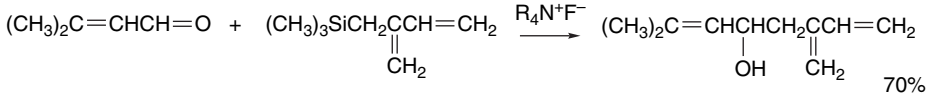
While trifluoro and other halosilanes function by increased *electrophilicity* at silicon, *nucleophilic* reactivity of allylic silanes can be enhanced by formation of anionic adducts (silicates). Reaction of allylic silanes with aldehydes and ketones can

be induced by fluoride ion. Fluoride adds at silicon to form a hypervalent anion having enhanced nucleophilicity.[114]

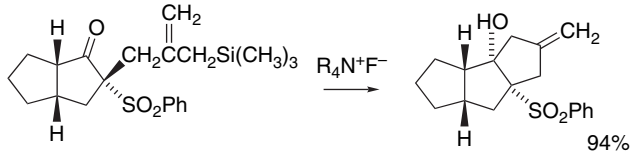
The THF-soluble salt tetrabutylammonium fluoride (TBF) is a common source of fluoride. An alternative reagent is tetrabutylammonium triphenyldifluorosilicate (TBAF).[115] Unsymmetrical allylic anions generated in this way react with ketones at their less-substituted terminus.



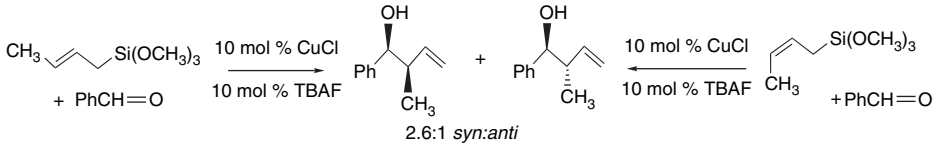
An allylic silane of this type serves as a reagent for the introduction of isoprenoid structures.[116]



Fluoride-induced desilylation has also been used to effect ring closures.[117]



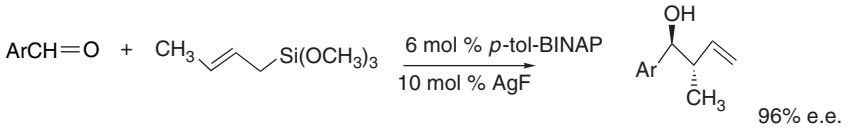
Allylic trimethoxysilanes are activated by a catalytic combination of CuCl and TBAF.[118] The mechanism of this reaction is not entirely clear, but it seems to involve fluoride activation of the silane. These reactions are stereoconvergent for the isomeric 2-butenyl silanes, indicating that reaction occurs through an acyclic TS.



2.6:1 *syn:anti*

114. A. Hosomi, A. Shirahata, and H. Sakurai, *Tetrahedron Lett*., 3043 (1978); G. G. Furin, O. A. Vyazankina, B. A. Gostevsky, and N. S. Vyazankin, *Tetrahedron*, **44**, 2675 (1988).
115. A. S. Pilcher and P. De Shong, *J. Org. Chem*., **61**, 6901 (1996).
116. A. Hosomi, Y. Araki, and H. Sakurai, *J. Org. Chem*., **48**, 3122 (1983).
117. B. M. Trost and J. E. Vincent, *J. Am. Chem. Soc*., **102**, 5680 (1980); B. M. Trost and D. P. Curran, *J. Am. Chem. Soc*., **103**, 7380 (1981).
118. S. Yamasaki, K. Fujii, R. Wada, M. Kanai, and M. Shibasaki, *J. Am. Chem. Soc*., **124**, 6536 (2002).

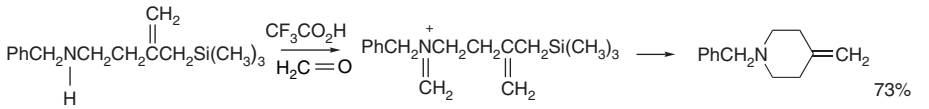
p-Tol-BINAP-AgF effects enantioselective additions with trimethoxysilanes.[119] These reactions give *anti* products, regardless of the configuration of the allylic silane.



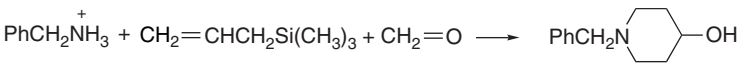
The combination BINAP-Ag_2O-KF with 18-crown-6 also leads to high enantioselectivity.[120]

9.2.4. Reactions with Iminium Ions

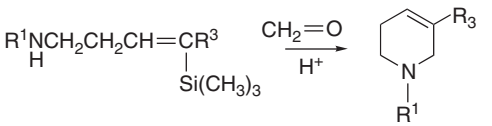
Iminium ions are reactive electrophiles toward both alkenyl and allylic silanes. Useful techniques for closing nitrogen-containing rings are based on in situ generation of iminium ions from amines and formaldehyde.[121]



When primary amines are employed, the initially formed 3-butenylamine undergoes a further reaction forming 4-piperidinols.[122]

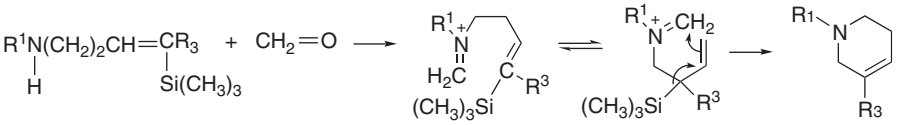


Reactions of this type can also be observed with 4-(trimethylsilyl)-3-alkenylamines.[123]

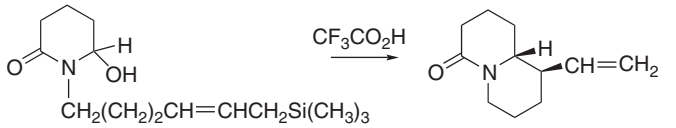


Mechanistic investigation in this case has shown that there is an equilibrium between an alkenyl silane and an allylic silane by a rapid 3,3-sigmatropic process. The cyclization occurs through the more reactive allylic silane.

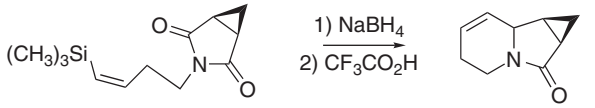
119. A. Yanagisawa, H. Kageyama, Y. Nakatsuka, K. Asakawa, Y. Matsumoto, and H. Yamamoto, *Angew. Chem. Int. Ed. Engl*., **38**, 3701 (1999).
120. M. Wadamoto, N. Ozasa, A. Yanagisawa, and H. Yamamoto, *J. Org. Chem*., **68**, 5593 (2003).
121. P. A. Grieco and W. F. Fobare, *Tetrahedron Lett*., **27**, 5067 (1986).
122. S. D. Larsen, P. A. Grieco, and W. F. Fobare, *J. Am. Chem. Soc*., **108**, 3512 (1986).
123. C. Flann, T. C. Malone, and L. E. Overman, *J. Am. Chem. Soc*., **109**, 6097 (1987).



N-Acyliminium ions, which are even more reactive toward allylic and alkenylsilanes, are usually obtained from imides by partial reduction (see Section 2.2.2). The partially reduced *N*-acylcarbinolamines can then generate acyliminium ions. Such reactions have been employed in intramolecular situations with both allylic and vinyl silanes.



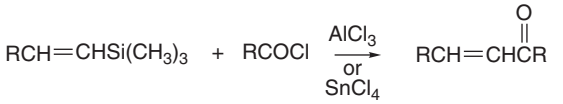
Ref. 124



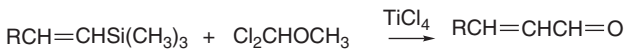
Ref. 125

9.2.5. Acylation Reactions

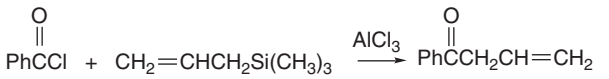
Reaction of alkenyl silanes with acid chlorides is catalyzed by aluminum chloride or stannic chloride.[126]



Titanium tetrachloride induces reaction with dichloromethyl methyl ether to give α, β-unsaturated aldehydes.[127]

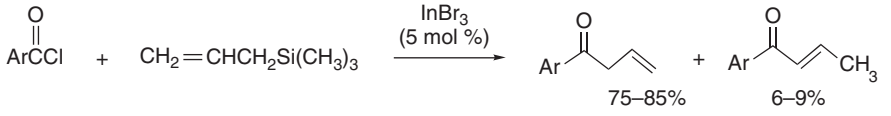


Similar conditions are used to effect reactions of allylsilanes with acyl halides, resulting in β,γ-unsaturated ketones.[128]



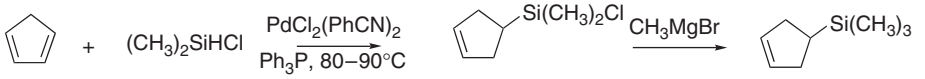
[124.] H. Hiemstra, M. H. A. M. Sno, R. J. Vijn, and W. N. Speckamp, *J. Org. Chem*., **50**, 4014 (1985).
[125.] G. Kim, M. Y. Chu-Moyer, S. J. Danishefsky, and G. K. Schulte, *J. Am. Chem. Soc*., **115**, 30 (1993).
[126.] I. Fleming and A. Pearce, *J. Chem. Soc., Chem. Commun*., 633 (1975); W. E. Fristad, D. S. Dime, T. R. Bailey, and L. A. Paquette, *Tetrahedron Lett*., 1999 (1979).
[127.] K. Yamamoto, O. Nunokawa, and J. Tsuji, *Synthesis*, 721 (1977).
[128.] J.-P. Pillot, G. Deleris, J. Dunogues, and R. Calas, *J. Org. Chem*., **44**, 3397 (1979); R. Calas, J. Dunogues, J.-P. Pillot, C. Biran, F. Pisciotti, and B. Arreguy, *J. Organomet. Chem*., **85**, 149 (1975).

Indium tribromide also gives good yields, with minor isomerization to the α,β-isomers.[129]

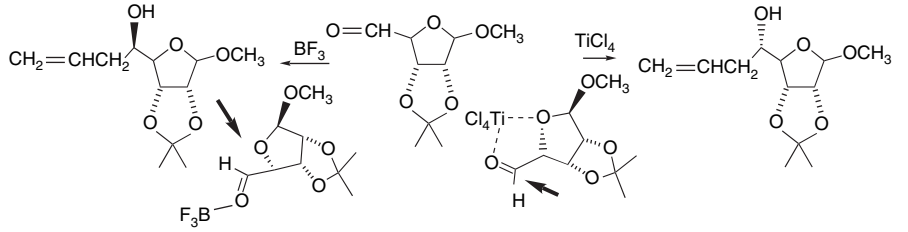


These reactions probably involve acylium ions as the electrophiles.

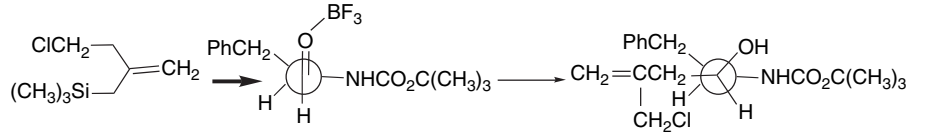
Scheme 9.4 shows some representative reactions of allylic and alkenyl silanes. Entry 1 involves 3-trimethylsilylcyclopentene, which can be made by hydrosilylation of cyclopentadiene by chlorodimethylsilane, followed by reaction with methylmagnesium bromide.



Entry 2 was reported as part of a study of the stereochemistry of addition of allyltrimethylsilane to protected carbohydrates. Use of BF_3 as the Lewis acid, as shown, gave the product from an open TS, whereas $TiCl_4$ led to the formation of the alternate stereoisomer through chelation control. Similar results were reported for a protected galactose.



In Entry 3, BF_3-mediated addition exhibits a preference for the Felkin stereochemistry.



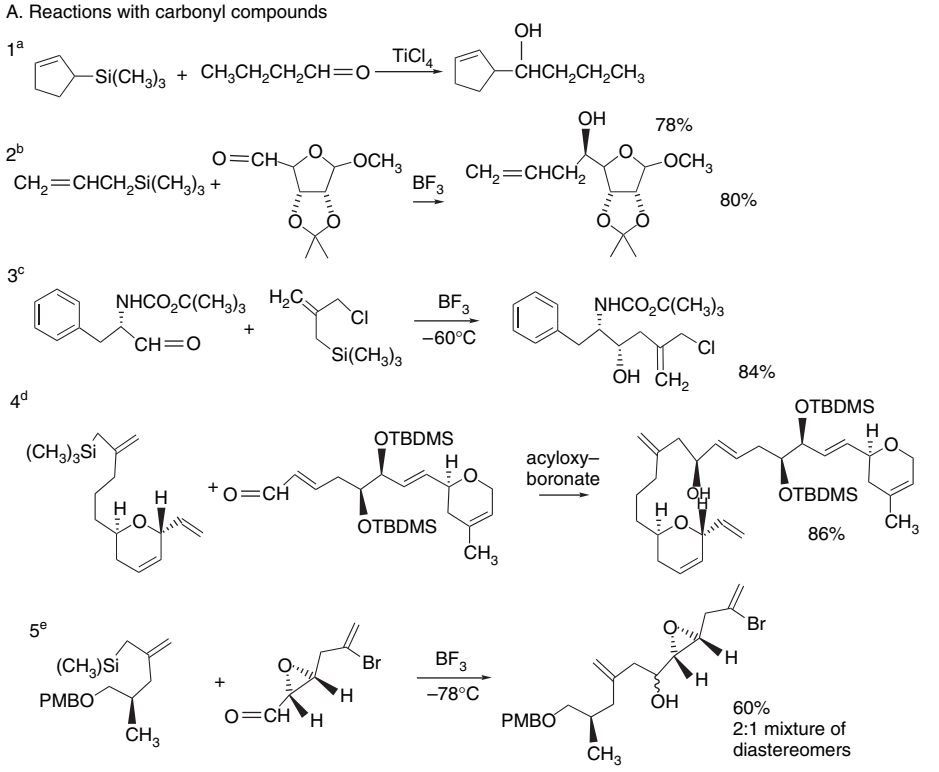
Entries 4 and 5 are examples of use of the Sakurai reaction to couple major fragments in multistage synthesis. In Entry 4 an unusual catalyst, a chiral acyloxyboronate (see p. 126) was used to effect an enantioselective coupling. (See p. 847 for another application of this catalyst.) Entry 5 was used in the construction of amphidinolide P, a compound with anticancer activity.

Entries 6 to 8 demonstrate addition of allyl trimethylsilane to protected carbohydrate acetals. This reaction can be a valuable method for incorporating the chirality of carbohydrates into longer carbon chains. In cases involving cyclic acetals, reactions occur through oxonium ions and the stereochemistry is governed by steric and stereoelectronic effects of the ring. Note that Entry 8 involves the use of trimethylsilyl

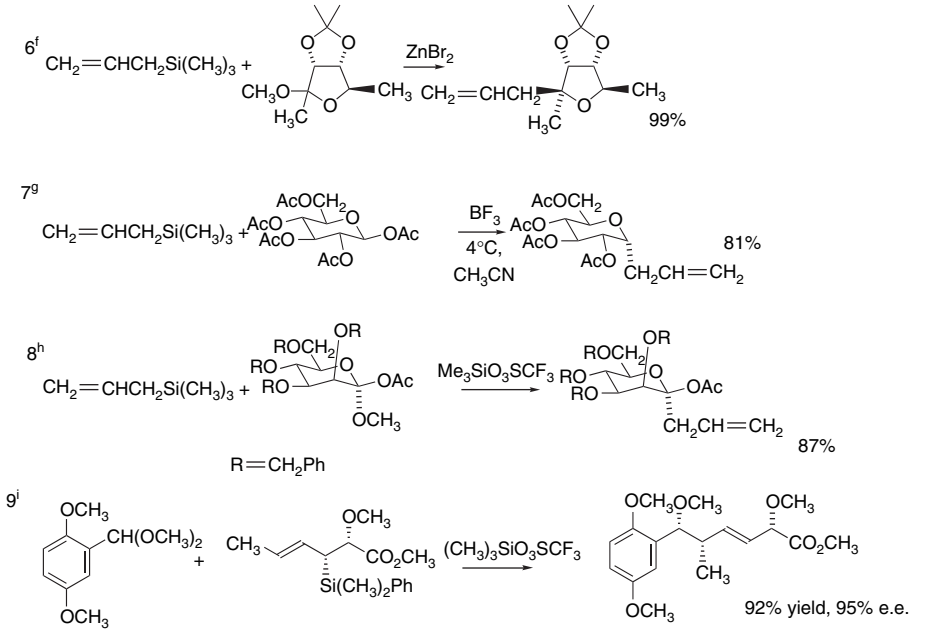
[129] J. S. Yadav, B. V. S. Reddy, M. S. Reddy, and G. Parimala, *Synthesis*, 2390 (2003).

Scheme 9.4. Reactions of Alkenyl and Allylic Silanes with Aldehydes, Ketones, Acetals, Iminium Ions, and Acyl Halides

A. Reactions with carbonyl compounds

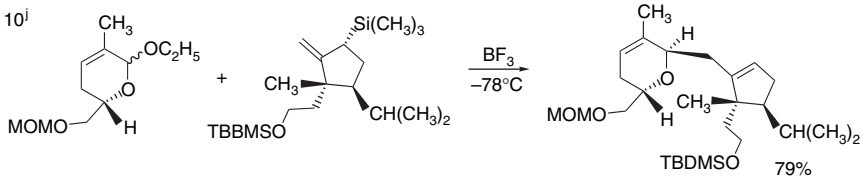


B. Reactions with acetals and related compounds



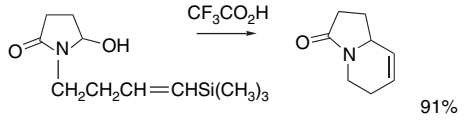
(Continued)

10[j]

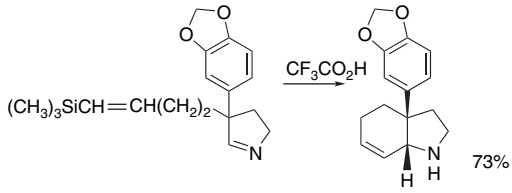


C. Reactions with Iminium ions

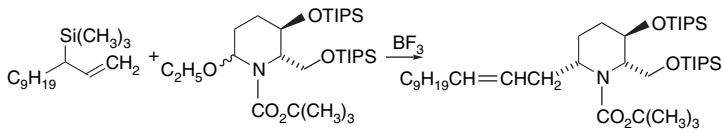
11[k]



12[l]

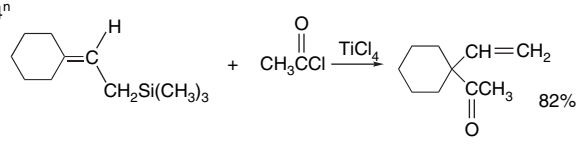


13[m]

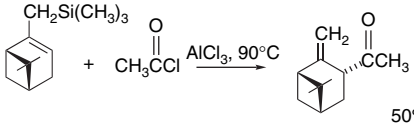


D. Acylation reactions

14[n]

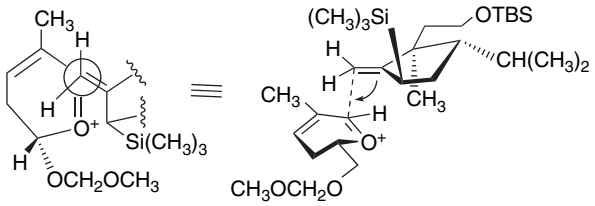


15[o]



a. I. Ojima, J. Kumagai, and Y. Miyazawa, *Tetrahedron Lett*., 1385 (1977).
b. S. Danishefsky and M. De Ninno, *Tetrahedron Lett*., **26**, 823 (1985).
c. F. D'Aniello and M. Taddei, *J. Org. Chem*., **57**, 5247 (1992).
d. P. A. Wender, S. G. Hegde, R. D. Hubbard, and L. Zhang, *J. Am. Chem. Soc*., **124**, 4956 (2002).
e. D. R. Williams, B. J. Myers, and L. Mi, *Org. Lett*., **2**, 945 (2000).
f. H. Suh and C. S. Wilcox, *J. Am. Chem. Soc*., **110**, 470 (1988).
g. A. Giannis and K. Sanshoff, *Tetrahedron Lett*., **26**, 1479 (1985).
h. A. Hosomi, Y. Sakata, and H. Sakurai, *Tetrahedron Lett*., **25**, 2383 (1984).
i. J. S. Panek and M. Yang, *J. Am. Chem. Soc*., **113**, 6594 (1991).
j. D. R. Williams and R. W. Heidebrecht, Jr., *J. Am. Chem. Soc*., **125**, 1843 (2003).
k. C. Flann, T. C. Malone, and L. E. Overman, *J. Am. Chem. Soc*., **109**, 6097 (1987).
l. L. E. Overman and R. M. Burk, *Tetrahedron Lett*., **25**, 5739 (1984).
m. I. Ojima and E. S. Vidal, *J. Org. Chem*., **63**, 7999 (1998).
n. I. Fleming and I. Paterson, *Synthesis*, 446 (1979).
o. J. P. Pillot, G. Deleris, J. Dunogues, and R. Calas, *J. Org. Chem*., **44**, 3397 (1979).

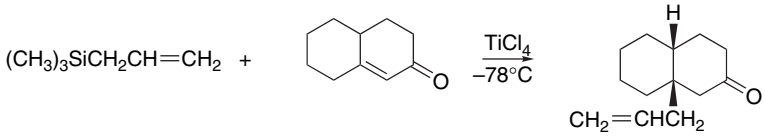
triflate as the catalyst. Entry 9 is a case of substrate control of enantioselectivity. Both high diastereoselectivity and enantioselectivity at the new chiral center were observed. The reaction is believed to proceed through an *O*-methyloxonium and to involve an open TS. Entry 10 involves generation of a cyclic oxonium ion. The observed stereochemistry is consistent with a synclinal orientation in the TS.



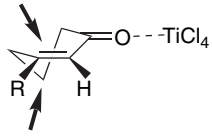
Entries 11 to 13 are examples of iminium ion and acyliminium ion reactions. Note that in Entries 11 and 12, vinyl, rather than allylic, silane moieties are involved. Entries 14 and 15 illustrate the synthesis of β, γ-unsaturated ketones by acylation of allylic silanes.

9.2.6. Conjugate Addition Reactions

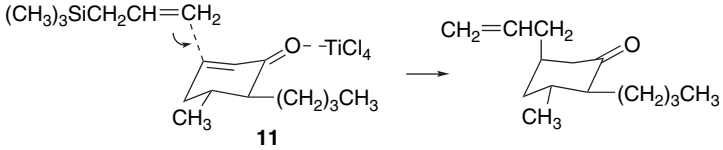
Allylic silanes act as nucleophilic species toward α, β-unsaturated ketones in the presence of Lewis acids such as $TiCl_4$.[130]



The stereochemistry of this reaction in cyclic systems is in accord with expectations for stereoelectronic control. The allylic group approaches from a trajectory that is appropriate for interaction with the LUMO of the conjugated system.[131]

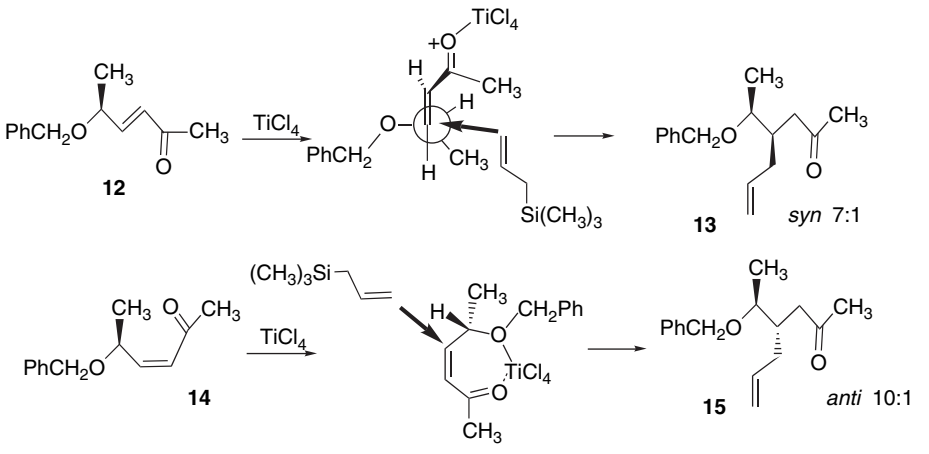


The stereoselectivity then depends on the conformation of the enone and the location of substituents that establish a steric bias for one of the two potential directions of approach. In the ketone **11**, the preferred approach is from the β-face, since this permits maintaining a chair conformation as the reaction proceeds.[132]

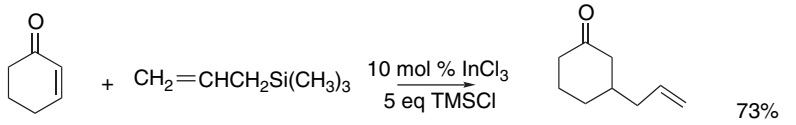


130. A. Hosomi and H. Sakurai, *J. Am. Chem. Soc*., **99**, 1673 (1977).
131. T. A. Blumenkopf and C. H. Heathcock, *J. Am. Chem. Soc*., **105**, 2354 (1983).
132. W. R. Roush and A. E. Walts, *J. Am. Chem. Soc*., **106**, 721 (1984).

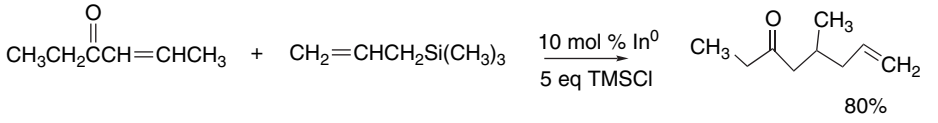
Conjugate addition to acyclic enones is subject to chelation control when $TiCl_4$ is used as the Lewis acid. Thus, whereas the *E*-enone **12** gives *syn* product **13** via an acyclic TS, the *Z*-isomer **14** reacts through a chelated TS to give **15**.[133]



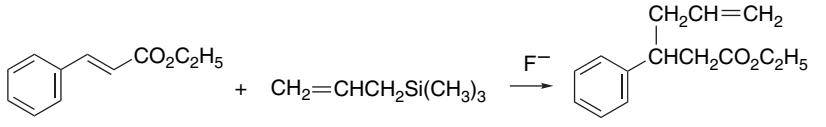
Conjugate additions of allylic silanes to enones are also catalyzed by $InCl_3$-TMSCl.[134]



The reaction can also be carried out using indium metal. Under these conditions $InCl_3$ is presumably generated in situ.[135]

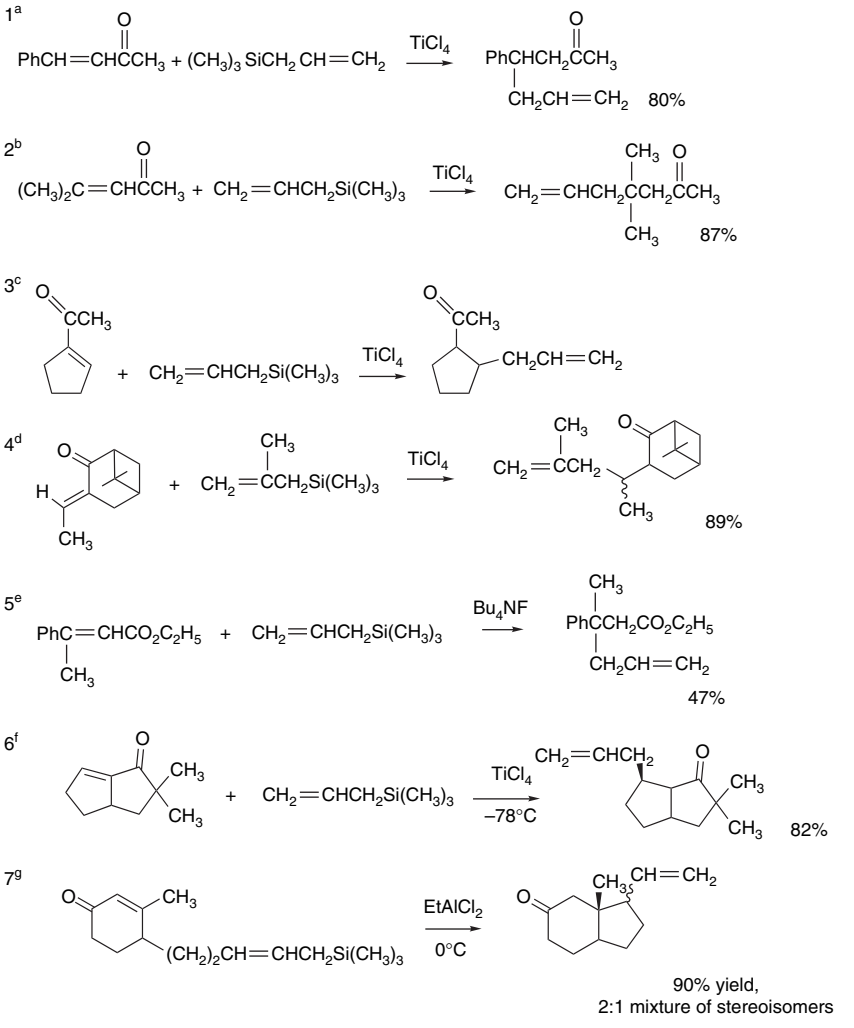


Conjugate addition can also be carried out by fluoride-mediated disilylation. A variety of α,β-unsaturated esters and amides have been found to undergo this reaction.[136]



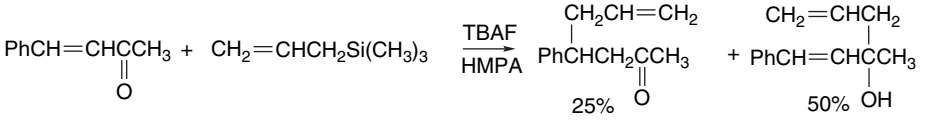
133. C. H. Heathcock, S. Kiyooka, and T. A. Blujenkopf, *J. Org. Chem.*, **49**, 4214 (1984).
134. P. H. Lee, K. Lee, S.-Y. Sung, and S. Chang, *J. Org. Chem.*, **66**, 8646 (2001); Y. Onishi, T. Ito, M. Yasuda, and A. Baba, *Eur. J. Org. Chem.*, 1578 (2002).
135. P. H. Lee, D. Seomoon, S. Kim, K. Nagaiah, S. V. Damle, and K. Lee, *Synthesis*, 2189 (2003).
136. G. Majetich, A. Casares, D. Chapman, and M. Behnke, *J. Org. Chem.*, **51**, 1745 (1986).

Scheme 9.5. Conjugate Addition of Allylic Silanes to α, β-Unsaturated Enones



a. H. Sakurai, A. Hosmoni, and J. Hayashi, *Org. Synth*., **62**, 86 (1984).
b. D. H. Hua, *J. Am. Chem. Soc*., **108**, 3835 (1986).
c. H. O. House, P. C. Gaa, and D. Van Derveer, *J. Org. Chem*., **48**, 1661 (1983).
d. T. Yanami, M. Miyashita, and A. Yoshikoshi, *J. Org. Chem*., **45**, 607 (1980).
e. G. Majetich, A Casares, D. Chapman, and M. Behnke, *J. Org. Chem*., **51**, 1745 (1986).
f. C. E. Davis, B. C. Duffy, and R. M. Coates, *Org. Lett*., **2**, 2717 (2000).
g. D. Schinzer, S. Solyom, and M. Becker, *Tetrahedron Lett*., **26**, 1831 (1985).

With unsaturated aldehydes, 1,2-addition occurs and with ketones both the 1,2- and 1,4-products are formed.



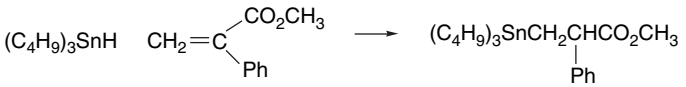
Some examples of conjugate addition reactions of allylic silanes are given in Scheme 9.5. Entries 1 to 3 illustrate the synthesis of several β-allyl ketones. Note that Entry 2 involves the creation of a quaternary carbon. Entry 4 was used in the synthesis of a terpenoid ketone, (+)-nootkatone. Entry 5 illustrates fluoride-mediated addition using tetrabutylammonium fluoride. These conditions were found to be especially effective for unsaturated esters. In Entry 6, the addition is from the convex face of the ring system. Entry 7 illustrates a ring closure by intramolecular conjugate addition.

9.3. Organotin Compounds

9.3.1. Synthesis of Organostannanes

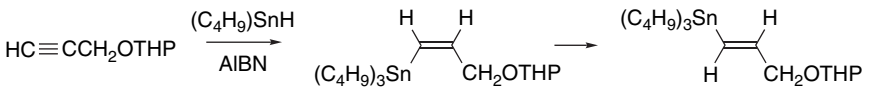
The readily available organotin compounds include tin hydrides (stannanes) and the corresponding chlorides, with the tri-*n*-butyl compounds being the most common. Trialkylstannanes can be added to carbon-carbon double and triple bonds. The reaction is usually carried out by a radical chain process,[137] and the addition is facilitated by the presence of radical-stabilizing substituents.

Ref. 138



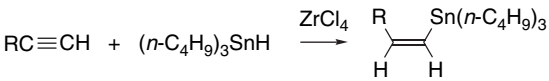
Ref. 139

With terminal alkynes, the stannyl group is added at the unsubstituted carbon and the *Z*-stereoisomer is initially formed but is readily isomerized to the *E*-isomer.[140]



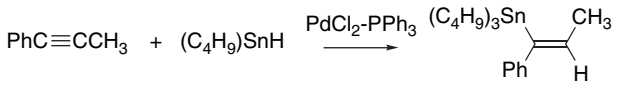
The reaction with internal acetylenes leads to a mixture of both regioisomers and stereoisomers.[141]

Lewis acid–catalyzed hydrostannylation has been observed using $ZrCl_4$. With terminal alkynes the *Z*-alkenylstannane is formed.[142] These reactions are probably similar in mechanism to Lewis acid–catalyzed additions of silanes (see p. 811).

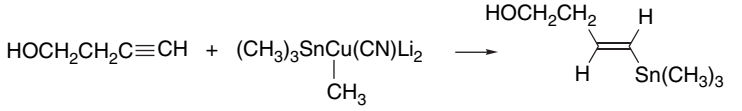


137. H. G. Kuivila, *Adv. Organomet. Chem.*, **1**, 47 (1964).
138. A. J. Leusinsk and J. G. Noltes, *Tetrahedron Lett.*, 335 (1966).
139. I. Fleming and C. J. Urch, *Tetrahedron Lett.*, **24**, 4591 (1983).
140. E. J. Corey and R. H. Wollenberg, *J. Org. Chem.*, **40**, 2265 (1975).
141. H. E. Ensley, R. R. Buescher, and K. Lee, *J. Org. Chem.*, **47**, 404 (1982).
142. N. Asao, J.-X. Liu, T. Sudoh, and Y. Yamamoto, *J. Org. Chem.*, **61**, 4568 (1996).

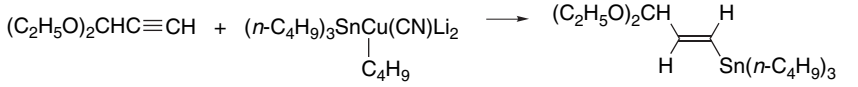
Palladium-catalyzed procedures have also been developed for addition of stannanes to alkynes,[143] and these reactions usually occur by *syn* addition.



Hydrostannylation of terminal alkynes can also be achieved by reaction with stannyl-cyanocuprates.

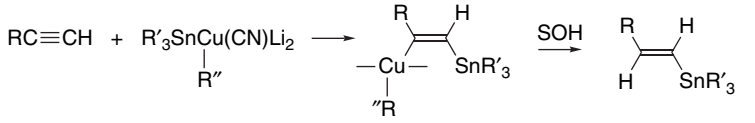


Ref. 144



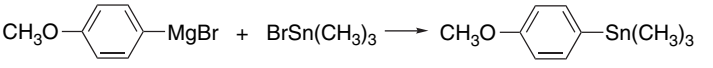
Ref. 145

These reactions proceed via a *syn* addition followed by protonolysis.



Allylic stannanes can be prepared from allylic halides and sulfonates by displacement with or $LiSnMe_3$ or $LiSnBu_3$.[146] They can also be prepared by Pd-catalyzed substitution of allylic acetates and phosphates using $(C_2H_5)_2AlSn(n\text{-}C_4H_9)_3$.[147]

Another major route for synthesis of stannanes is reaction of an organometallic reagent with a trisubstituted halostannane, which is the normal route for the preparation of aryl stannanes.



Ref. 148

143. H. X. Zhang, F. Guibe, and G. Balavoine, *Tetrahedron Lett*., **29**, 619 (1988); M. Benechie, T. Skrydstrup, and F. Khuong-Huu, *Tetrahedron Lett*., **32**, 7535 (1991); N. D. Smith, J. Mancuso, and M. Lautens, *Chem. Rev*., **100**, 3257 (2000).

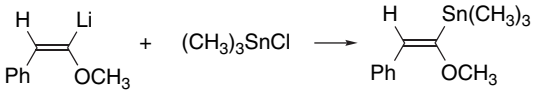
144. I. Beaudet, J.-L. Parrain, and J.-P. Quintard, *Tetrahedron Lett*., **32**, 6333 (1991).

145. A. C. Oehlschlager, M. W. Hutzinger, R. Aksela, S. Sharma, and S. M. Singh, *Tetrahedron Lett*., **31**, 165 (1990).

146. E. Winter and R. Bruckner, *Synlett*, 1049 (1994); G. Naruta and K. Maruyama, *Chem. Lett*., 881 (1979); G. E. Keck and S. D. Tonnies, *Tetrahedron Lett*., **34**, 4607 (1993); S. Weigand and R. Bruckner, *Synthesis*, 475 (1996).

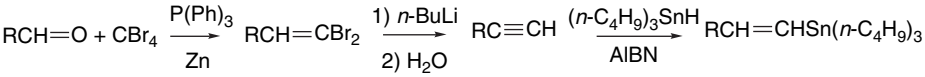
147. B. M. Trost and J. W. Herndon, *J. Am. Chem. Soc*., **106**, 6835 (1984); S. Matsubara, K. Wakamatsu, J. Morizawa, N. Tsuboniwa, K. Oshima, and H. Nozaki, *Bull. Chem. Soc. Jpn*., **58**, 1196 (1985).

148. C. Eaborn, A. R. Thompson, and D. R. M. Walton, *J. Chem. Soc. C*, 1364 (1967); C. Eaborn, H. L. Hornfeld, and D. R. M. Walton, *J. Chem. Soc. B*, 1036 (1967).

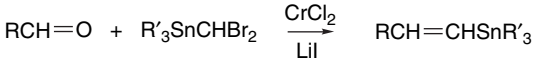


Ref. 149

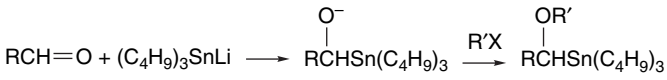
There are several procedures for synthesis of terminal alkenyl stannanes that involve addition to aldehydes. A well-established three-step sequence culminates in a radical addition to a terminal alkyne.[150]



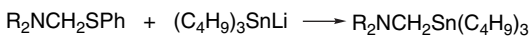
Another sequence involves a dibromomethyl(trialkyl)stannane as the starting material. On reaction with $CrCl_2$, addition to the aldehyde is followed by reductive elimination.[151]



Deprotonated trialkylstannanes are potent nucleophiles. Addition to carbonyl groups or iminium intermediates provides routes to α-alkoxy- and α-aminoalkylstannanes.

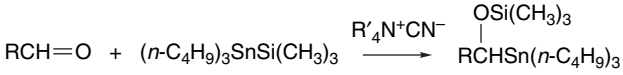


Ref. 152

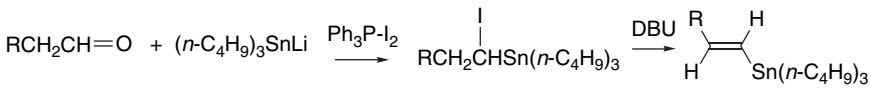


Ref. 153

α-Silyoxystannanes can be prepared directly from aldehydes and tri-*n*-butyl (trimethylsilyl)stannane.[154]



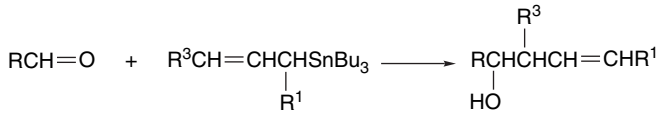
Addition of tri-*n*-butylstannyllithium to aldehydes followed by iodination and dehydrohalogenation gives primarily *E*-alkenylstannanes.[155]



149. J. A. Soderquist and G. J.-H. Hsu, *Organometallics*, **1**, 830 (1982).
150. E. J. Corey and P. L. Fuchs, *Tetrahedron Lett*., 3769 (1972).
151. M. D. Cliff and S. G. Payne, *Tetrahedron Lett*., **36**, 763 (1995); D. M. Hodgson, *Tetrahedron Lett*., **33**, 5603 (1992); D. M. Hodgson, L. T. Boulton, and G. N. Maw, *Tetrahedron Lett*., **35**, 2231 (1994).
152. W. C. Still, *J. Am. Chem. Soc*., **100**, 1481 (1978).
153. D. J. Peterson, *J. Am. Chem. Soc*., **93**, 4027 (1971).
154. R. M. Bhatt, J. Ye, and J. R. Falck, *Tetrahedron Lett*., **35**, 4081 (1994).
155. J. M. Chong and S. B. Park, *J. Org. Chem*., **58**, 523 (1993).

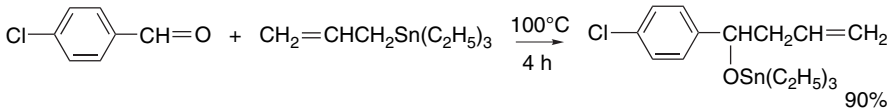
9.3.2. Carbon-Carbon Bond-Forming Reactions

As with the silanes, the most useful synthetic procedures involve electrophilic attack on alkenyl and allylic stannanes. The stannanes are considerably more reactive than the corresponding silanes because there is more anionic character on carbon in the C–Sn bond and it is a weaker bond.[156] The most useful reactions in terms of syntheses involve the Lewis acid–catalyzed addition of allylic stannanes to aldehydes.[157] The reaction occurs with allylic transposition.



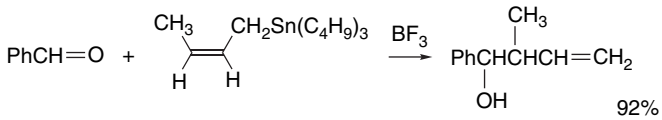
There are also useful synthetic procedures in which organotin compounds act as carbanion donors in transition metal–catalyzed reactions, as discussed in Section 8.2.3.3. Organotin compounds are also very important in free radical reactions, as is discussed in Chapter 10.

9.3.2.1. Reactions of Allylic Trialkylstannnanes. Allylic organotin compounds are not sufficiently reactive to add directly to aldehydes or ketones, although reactions with aldehydes do occur with heating.



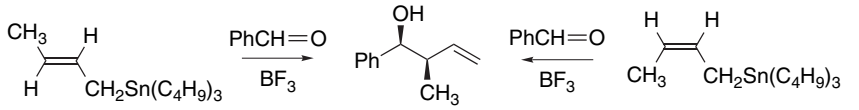
Ref. 158

Use of Lewis acid catalysts allows allylic stannanes to react under mild conditions. As is the case with allylic silanes, a double-bond transposition occurs in conjunction with destannylation.[159]



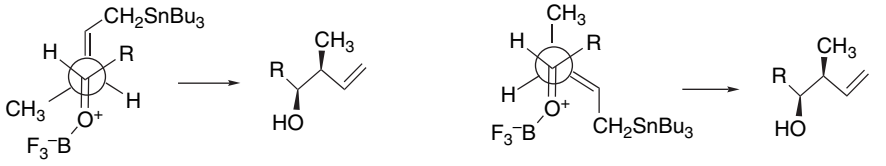
The stereoselectivity of addition to aldehydes has been of considerable interest.[160] With benzaldehyde the addition of 2-butenylstannanes catalyzed by BF_3 gives the *syn* isomer, irrespective of the stereochemistry of the butenyl group.[161]

156. J. Burfeindt, M. Patz, M. Mueller, and H. Mayr, *J. Am. Chem. Soc*., **120**, 3629 (1998).
157. B. W. Gung, *Org. React*., **64**, 1 (2004).
158. K. König and W. P. Neumann, *Tetrahedron Lett*., 495 (1967).
159. H. Yatagai, Y. Yamamoto, and K. Maruyama, *J. Am. Chem. Soc*., **102**, 4548 (1980); Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *J. Am. Chem. Soc*., **102**, 7107 (1989).
160. Y. Yamomoto, *Acc. Chem. Res*., **20**, 243 (1987); Y. Yamoto and N. Asao, *Chem. Rev*., **93**, 2207 (1993).
161. (a) Y. Yamamoto, H. Yatagai, H. Ishihara, and K. Maruyama, *Tetrahedron*, **40**, 2239 (1984); (b) G. E. Keck, K. A. Savin, E. N. K. Cressman, and D. E. Abbott, *J. Org. Chem*., **59**, 7889 (1994).



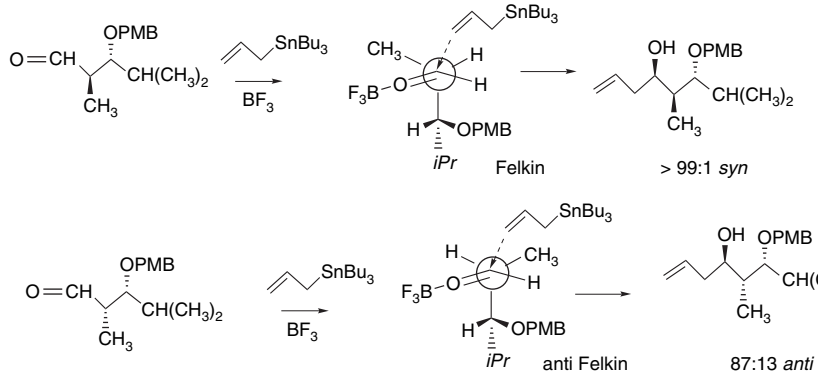
>98% *syn*

Synclinal and antiperiplanar conformations of the TS are possible. The two TSs are believed to be close in energy and either may be involved in individual systems. An electronic π interaction between the stannane HOMO and the carbonyl LUMO, as well as polar effects appear to favor the synclinal TS and can overcome the unfavorable steric effects.[161b, 162] Generally the synclinal TS seems to be preferred for intramolecular reactions. The steric effects that favor the antiperiplanar TS are not present in intramolecular reactions, since the aldehyde and the stannane substituents are then part of the intramolecular linkage.



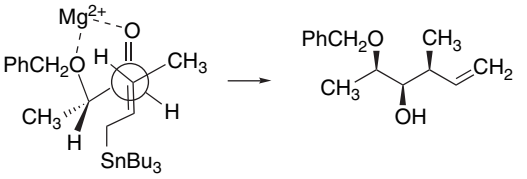
antiperiplanar *syn* synclinal *syn*

With chiral aldehydes, reagent approach is generally consistent with a Felkin model.[163] This preference can be reinforced or opposed by the effect of other stereocenters. For example, the addition of allyl stannane to 1,4-dimethyl-3-(4-methoxybenzyloxy)pentanal is strongly in accord with the Felkin model for the *anti* stereoisomer but is anti-Felkin for the *syn* isomer.

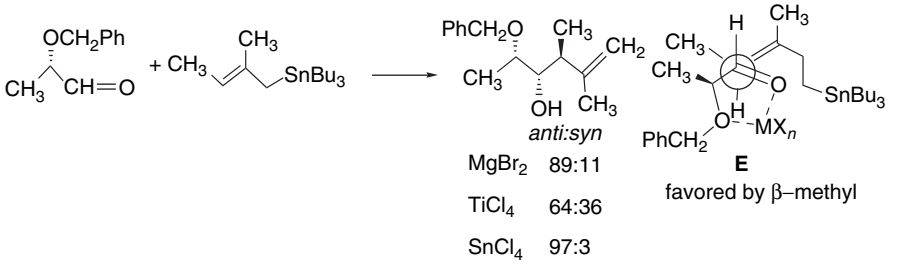


When an aldehyde subject to chelation control is used, the *syn* stereoisomer dominates, with $MgBr_2$ as the Lewis acid.[164]

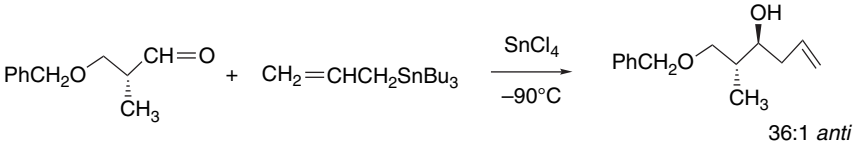
162. S. E. Denmark, E. J. Weber, T. Wilson, and T. M. Willson, *Tetrahedron*, **45**, 1053 (1989).
163. D. A. Evans, M. J. Dart, J. L. Duffy, M. G. Yang, and A. B. Livingston, *J. Am. Chem. Soc*., **117**, 6619 (1995); D. A. Evans, M. J. Dart, J. L. Duffy, and M. G. Yang, *J. Am. Chem. Soc*., **118**, 4322 (1996).
164. G. E. Keck and E. P. Boden, *Tetrahedron Lett*., **25**, 265 (1984); G. E. Keck, D. E. Abbott, and M. R. Wiley, *Tetrahedron Lett*., **28**, 139 (1987).



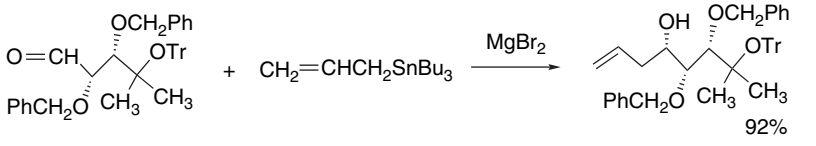
The introduction of a β-methyl group shifts the stereoselectivity to *anti*, indicating a preference for TS **E**. There is some dependence on the Lewis acid. For example, the reaction below gives a high ratio of chelation control with $MgBr_2$ and $SnCl_4$, but not with $TiCl_4$.[165]



β-Oxy substituents can also lead to chelation control. Excellent stereoselectivity is observed using $SnCl_4$ at low temperature.[166]

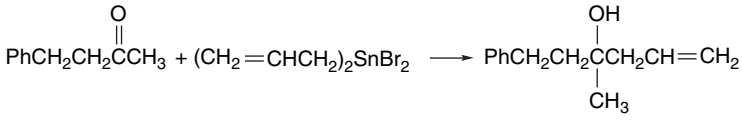


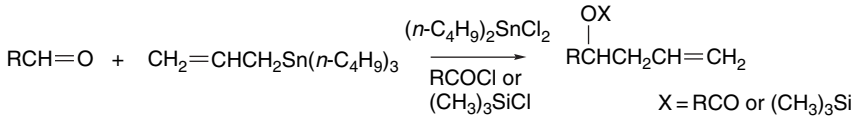
The chelation control approach has been used during the synthesis of the C(13)–C(19) fragment of a marine natural product called calculin A-D.[167]



9.3.2.2. Reactions of Allylic Halostannanes. Various allyl halostannanes can transfer allyl groups to carbonyl compounds. In this case the reagent acts both as a Lewis acid and as the source of the nucleophilic allyl group. Reactions involving halostannanes are believed to proceed through cyclic TSs.

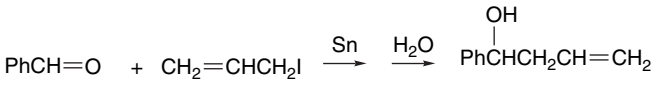
165. K. Mikami, K. Kawamoto, T.-P. Loh, and T. Nakai, *J. Chem. Soc., Chem. Commun*., 1161 (1990).
166. G. E. Keck and D. E. Abbott, *Tetrahedron Lett*., **25**, 1883 (1984); R. J. Linderman, K. P. Cusack, and M. R. Jaber, *Tetrahedron Lett*., **37**, 6649 (1996).
167. O. Hara, Y. Hamada, and T. Shiori, *Synlett*, 283 285 (1991).



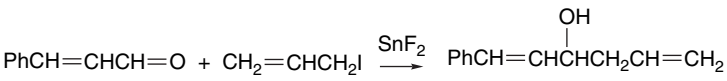


Ref. 168

The halostannanes can also be generated in situ by reactions of allylic halides with tin metal or stannous halides.

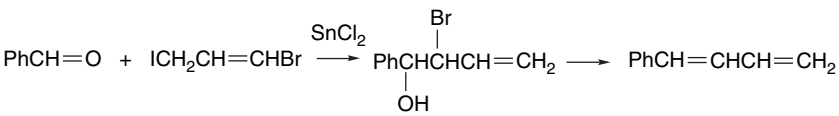


Ref. 169



Ref. 169

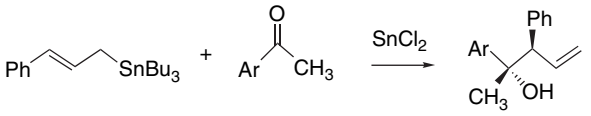
The allylation reaction can be adapted to the synthesis of terminal dienes by using 1-bromo-3-iodopropene and stannous chloride. The elimination step is a reductive elimination of the type discussed in Section 5.8. Excess stannous chloride acts as the reducing agent.



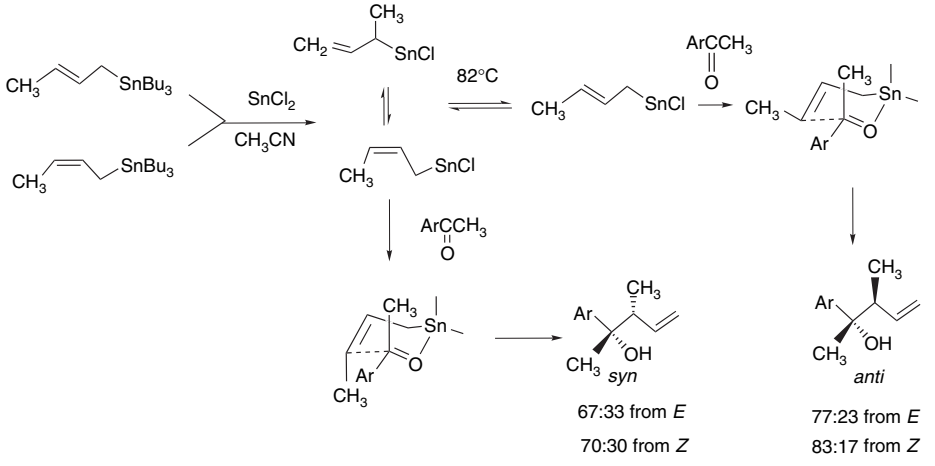
Ref. 170

Allylic Sn(II) species are believed to be involved in reactions of allylic trialkyl stannanes in the presence of $SnCl_2$. These reactions are particularly effective in acetonitrile, which appears to promote the exchange reaction. Ketones as well as aldehydes are reactive under these conditions.[171]

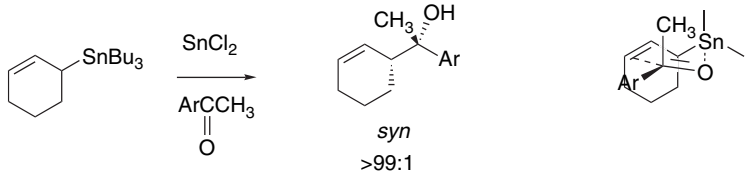
168. T. Mukaiyama and T. Harada, *Chem. Lett*., 1527 (1981).
169. T. Mukaiyama, T. Harada, and S. Shoda, *Chem. Lett*., 1507 (1980).
170. J. Auge, *Tetrahedron Lett*., **26**, 753 (1985).
171. (a) M. Yasuda, Y. Sugawa, A. Yamamoto, I. Shibata, and A. Baba, *Tetrahedron Lett*., **37**, 5951 (1996); (b) M. Yasuda, K. Hirata, M. Nishino, A. Yamamoto, and A. Baba, *J. Am. Chem. Soc*., **124**, 13442 (2002).



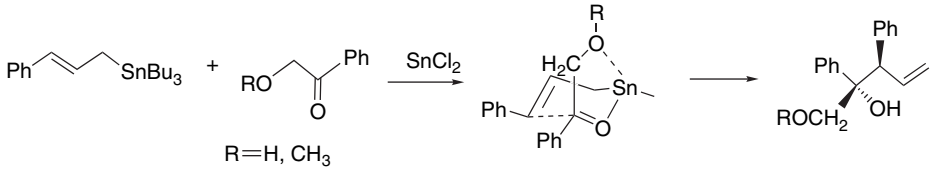
The *anti* stereochemistry is consistent with a cyclic TS, but the reaction is stereoconvergent for the *E*- and *Z*-2-butenylstannanes, indicating that isomerization must occur at the transmetallation stage. The adducts are equilibrated at 82 °C and under these conditions the *anti* product is isolated on workup.



Cyclic allylstannanes give *syn* products with high selectivity.



The reaction with α-hydroxy and α-methoxy ketones under these conditions are chelation controlled.

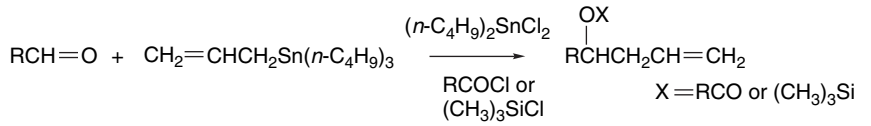


Use of di-(*n*-butyl)stannyl dichloride along with an acyl or silyl halide leads to addition of allylstannanes to the aldehydes.[172a, 172] Reaction is also promoted by butylstannyl trichloride.[173] Both $SnCl_4$ and $SnCl_2$ also catalyze this kind of addition.

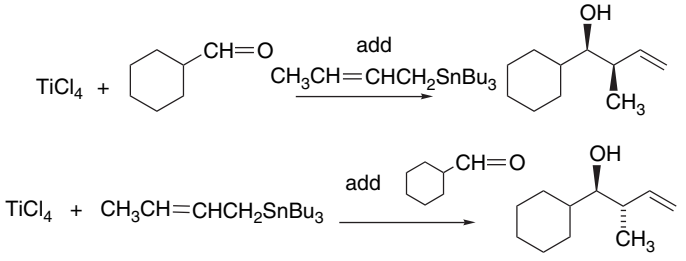
172. J. K. Whitesell and R. Apodaca, *Tetrahedron Lett*., **37**, 3955 (1996).

173. H. Miyake and K. Yamamura, *Chem. Lett*., 1369 (1992); H. Miyake and K. Yamamura, *Chem. Lett*., 1473 (1993).

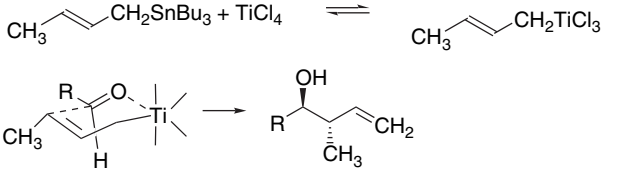
Reactions of tetraallylstannanes with aldehydes catalyzed by $SnCl_4$ also appear to involve a halostannane intermediate. It can be demonstrated by NMR that there is a rapid redistribution of the allyl group.[174] Reactions with these halostannanes are believed to proceed through a cyclic TS.



9.3.2.3. Reactions Involving Transmetallation. With certain Lewis acids, the reaction may involve a prior transmetallation. This introduces several additional factors into the analysis of the stereoselectivity, as the stereochemistry of the transmetallation has to be considered. Reactions involving halo titanium and halo tin intermediates formed by transmetallation can proceed through a cyclic TS. When $TiCl_4$ is used as the catalyst, the stereoselectivity depends on the order of addition of the reagents. When *E*-2-butenylstannane is added to a $TiCl_4$-aldehyde mixture, *syn* stereoselectivity is observed. When the aldehyde is added to a premixed solution of the 2-butenylstannane and $TiCl_4$, the *anti* isomer predominates.[175]

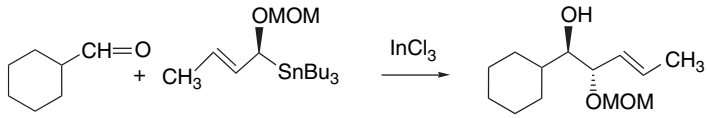


The formation of the *anti* stereoisomer is attributed to involvement of a butenyltitanium intermediate formed by rapid exchange with the butenylstannane. This intermediate then reacts through a cyclic TS.

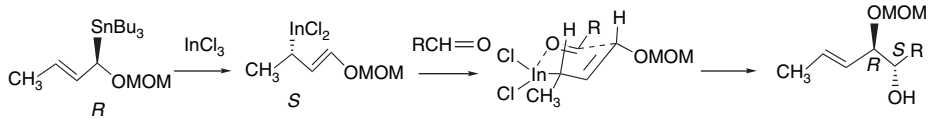


Indium chloride in polar solvents such as acetone or acetonitrile leads to good diastereoselectivity with cyclohexanecarboxaldehyde and other representative aldehydes.[176]

174. S. E. Denmark, T. Wilson, and T. M. Willson, *J. Am. Chem. Soc*., **110**, 984 (1988); G. E. Keck, M. B. Andrus, and S. Castellino, *J. Am. Chem. Soc*., **111**, 8136 (1989).
175. G. E. Keck, D. E. Abbott, E. P. Boden, and E. J. Enholm, *Tetrahedron Lett*., **25**, 3927 (1984).
176. J. A. Marshall and K. W. Hinkle, *J. Org. Chem*., **60**, 1920 (1995).

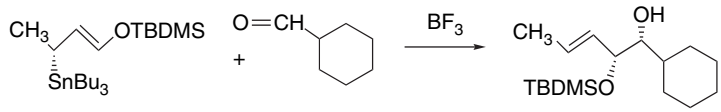


These reactions are believed to proceed via transmetallation. Configurational inversion occurs at both the transmetallation and addition steps, leading to overall retention of the allylic stereochemistry.



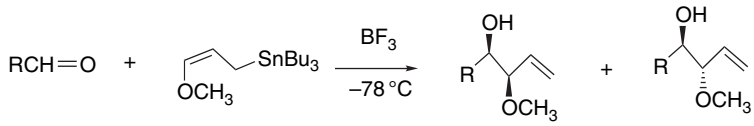
These reagents are useful in enantioselective synthesis and are discussed further in the following section.

9.3.2.4. γ-*Oxygen-Substituted Stannanes.* Oxygenated allylic stannanes have been synthesized and used advantageously in several types of syntheses. Both α- and γ-alkoxy and silyloxy stannane can be prepared by several complementary methods.[177] *E*-γ-Alkoxy and silyloxy allylic stannanes react with aldehydes to give primarily *syn* adducts.[178]



79% yield, 98:2 *syn*

Allylic silanes with γ-alkoxy substituents also give a preference for the *syn* stereochemistry.[179]

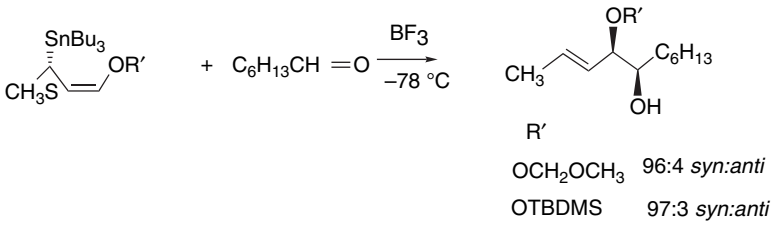


syn *anti*

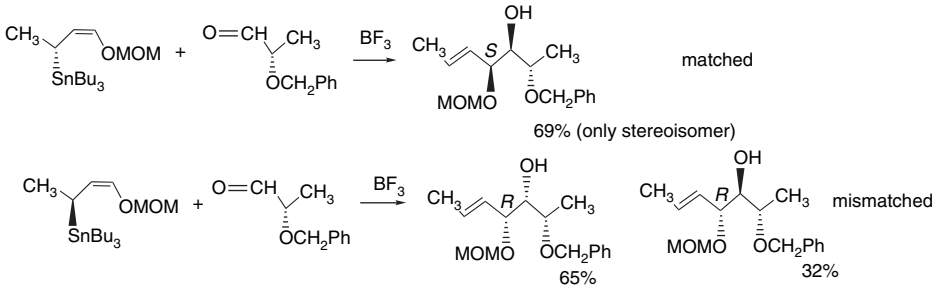
R	*syn:anti*
Ph	10:1
i-Pr	25:1
c-C_6H_{11}	5:1

Improved stereoselectivity is observed with methoxymethoxy (MOM) and TBDMSO substituents.[180]

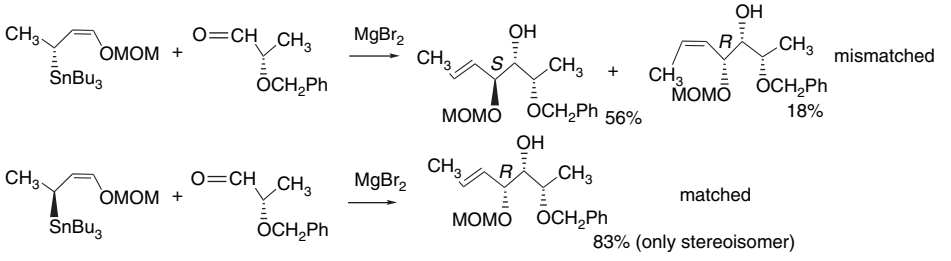
177. J. A. Marshall, *Chem. Rev.*, **96**, 31 (1996).
178. J. A. Marshall, J. A. Jablonowski, and L. M. Elliott, *J. Org. Chem.*, **60**, 2662 (1995).
179. M. Koreeda and Y. Tanaka, *Tetrahedron Lett.*, **28**, 143 (1987).
180. J. A. Marshall and J. A. Welmaker, *J. Org. Chem.*, **57**, 7158 (1992).



Use of oxygenated stannanes with α-substituted aldehydes leads to matched and mismatched combinations.[181] For example, with the γ-MOM derivative and α-benzyloxypropanal, the matched pair gives a single stereoisomer of the major product, whereas the mismatched pair gives a 67:33 *syn:anti* mixture. The configuration at the alkoxy-substituted center is completely controlled by the chirality of the stannane.

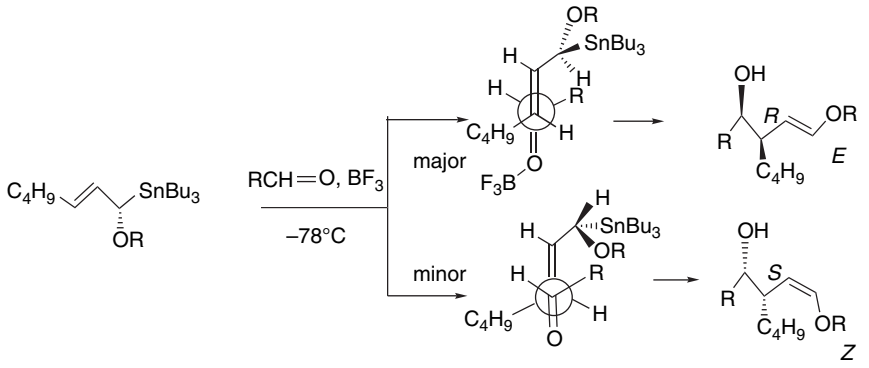


Use of $MgBr_2$, which results in chelation control, reverses the matched and mismatched combinations.



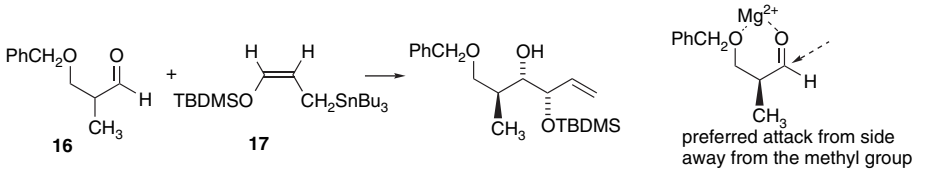
9.3.2.5. Enantioselective Addition Reactions of Allylic Stannanes. There have been several studies of the enantiomers of α-oxygenated alkenyl stannanes. The chirality of the α-carbon exerts powerful control on enantioselectivity with the preference for the stannyl group to be *anti* to the forming bond. This is presumably related to the stereoelectronic effect that facilitates the transfer of electron density from the tin to the forming double bond.[182]

[181] J. A. Marshall, J. A. Jablonowski, and G. P. Luke, *J. Org. Chem.*, **59**, 7825 (1994).
[182] J. A. Marshall and W. Y. Gung, *Tetrahedron*, **45**, 1043 (1989).



anti relationship between stannyl substituent and developing bond exerts control on double bond configuration

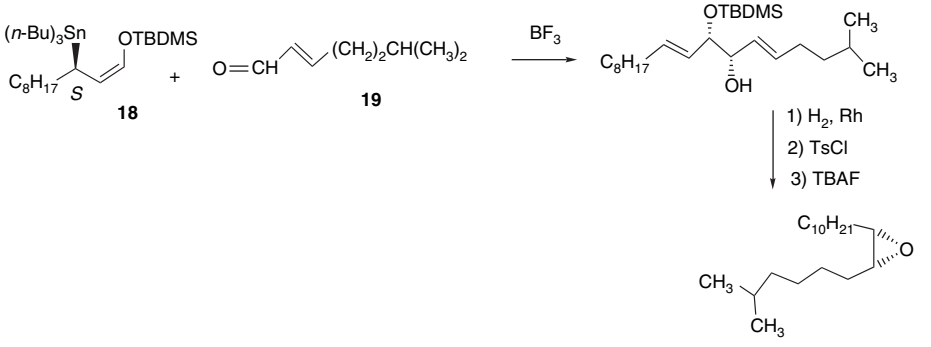
Allylic stannanes with γ-oxygen substituents have been used to build up polyoxygenated carbon chains. For example, **16** reacts with the stannane **17** to give a high preference for the stereoisomer in which the two oxygen substituents are *anti*. This stereoselectivity is consistent with chelation control.[183]



16 **17**

preferred attack from side away from the methyl group

The substrate-controlled addition of **18** to **19** proceeded with good enantioselectivity and was used to prepare the epoxide (+)-dispalure, a gypsy moth pheromone.[184]

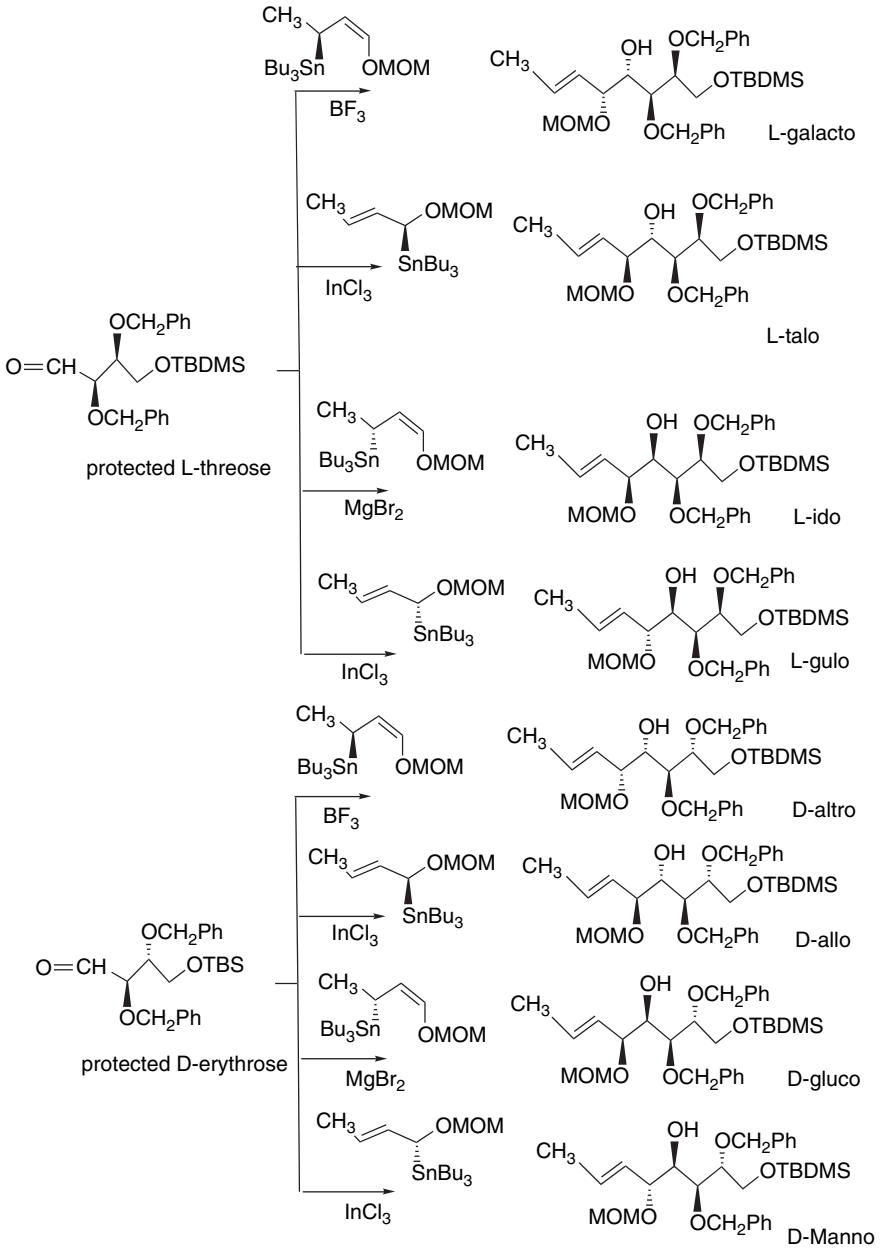


18 **19**

Reagent-controlled stereoselectivity can provide stereochemical relationships over several centers when a combination of acyclic and chelation control and cyclic TS resulting from transmetallation is utilized. In reactions mediated by BF_3 or $MgBr_2$ the new centers are *syn*. Indium reagents can be used to create an *anti* relationship between two new chiral centers. The indium reagents are formed by transmetallation and react

183. G. E. Keck, K. A. Savin, E. N. K. Cressman, and D. E. Abbott, *J. Org. Chem.*, **59**, 7889 (1994).
184. J. A. Marshall, J. A. Jablonowski, and H. Jiang, *J. Org. Chem.*, **64**, 2152 (1999).

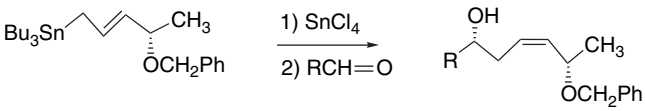
through cyclic TSs leading to *anti* stereochemistry at the new bond. The complementary relationship has been used to construct all eight possible hexose configurations.[185]



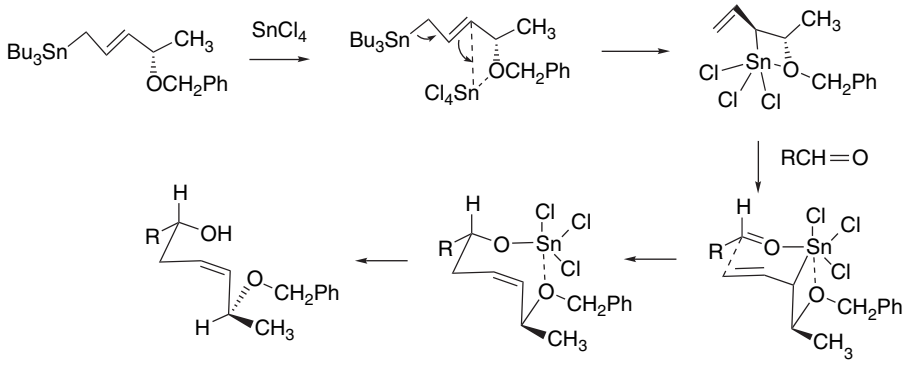
More remote oxygen substituents can also influence stereochemistry. 4-Benzyloxy-2-pentenyl tri-*n*-butylstannane exhibits excellent enantioselectivity in reactions with aldehydes.[186] This reaction is believed to involve chelation of the

185. J. A. Marshall and K. W. Hinkle, *J. Org. Chem.*, **61**, 105 (1996).
186. E. J. Thomas, *J. Chem. Soc. Chem. Commun.*, 411 (1997); A. H. McNeill and E. J. Thomas, *Synthesis*, 322 (1998).

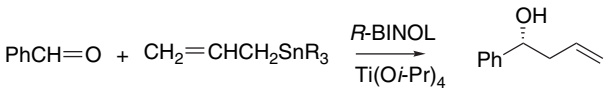
benzyloxy group in both the transmetallation and addition steps. The transmetallation is thought to involve coordination with $SnCl_4$ through the benzyloxy group that is maintained in the addition step.



>90% 1,5-*syn*

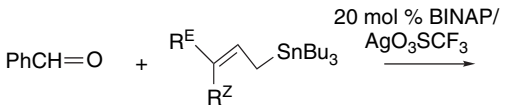


Allylstannane additions to aldehydes can be made enantioselective by use of chiral catalysts. A catalyst prepared from the chiral binaphthols *R*- or *S*-BINOL and $Ti(O\text{-}i\text{-}Pr)_4$ achieves 85–95% enantioselectivity.[187]



87–96% e.e.

BINAP-AgF gives good enantioselectivity, especially for the major *anti* product in the addition of 2-butenylstannanes to benzaldehyde.[188] This system appears to be stereoconvergent, suggesting that isomerization of the 2-butenyl system occurs, perhaps by transmetallation.

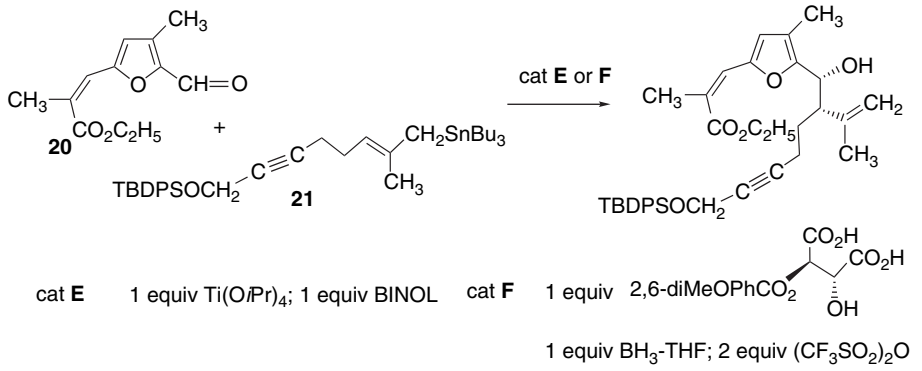


	anti (e.e.)	*syn* (e.e.)
E	85 (94)	15 (64)
Z	85 (91)	15 (50)

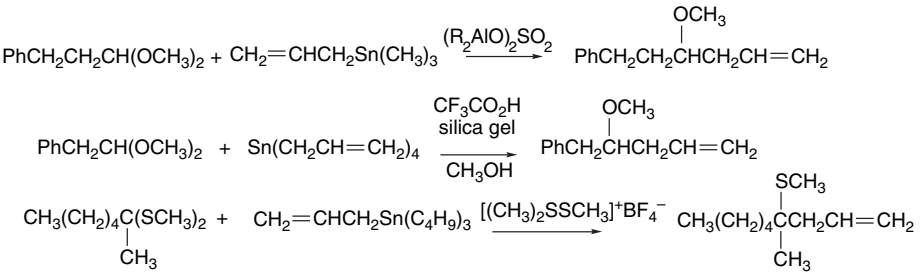
[187] G. E. Keck, K. H. Tarbet, and L. S. Geraci, *J. Am. Chem. Soc*., **115**, 8467 (1993); A. L. Costa, M. G. Piazza, E. Tagliavini, C. Trombini, and A. Umani-Ronchi, *J. Am. Chem. Soc*., **115**, 7001 (1993); G. E. Keck and L. S. Geraci, *Tetrhahedron Lett*., **34**, 7827 (1993); G. E. Keck, D. Krishnamurthy, and M. C. Grier, *J. Org. Chem*., **58**, 6543 (1993).

[188] A. Yanagisawa, H. Nakashima, Y. Nakatsuka, A. Ishiba, and H. Yamamoto, *Bull. Chem. Soc. Jpn*., **74**, 1129 (2001).

The coupling of the achiral stannane **20** and aldehyde **21** was achieved with fair to good enantioselectivity and fair yield using chiral catalysts. Ti-BINOL gave 52% e.e. and 31% yield, whereas an acyloxyborane catalyst (see p. 127) gave 90% e.e. and 24% yield.[189]



Lewis acid–mediated ionization of acetals also generates electrophilic carbon intermediates that react readily with allylic stannanes.[190] Dithioacetals can be activated by the sulfonium salt $[(CH_3)_2SSCH_3]^+BF_4^-$.[191]

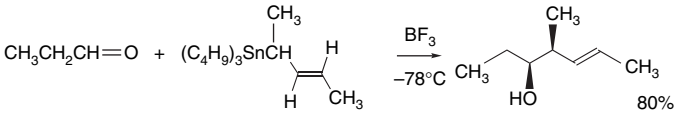


Scheme 9.6 gives some other examples of Lewis acid–catalyzed reactions of allylic stannanes with carbonyl compounds. Entry 1 demonstrates the *syn* stereoselectivity observed with *E*-allylic systems. Entries 2 and 3 illustrate the use of mono- and dihalostannanes in reactions with acetone. Entry 4 involves addition to acrolein, using Bu_2SnCl_2 as the catalyst. This reaction was run at room temperature for 24 h and gave exclusively the *Z*-configuration of the new double bond. It seems likely that this is the result of thermodynamic control. Entry 5 involves an α-ethoxyallylstannane and shows *syn* stereoselectivity. Entry 6 involving an α-benzyloxy aldehyde occurred with high chelation control. The addition in Entry 7 involves in situ generation of an allylic stannane and favored the *anti* stereoisomer by about 4:1. Entry 8 was used to establish relative stereochemistry in a short synthesis of racemic Prelog-Djerassi lactone. Although the methoxycarbonyl group is a potential chelating ligand, the use of

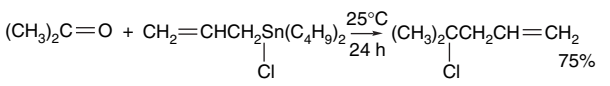
189. J. A. Marshall and J. Liao, *J. Org. Chem*., **63**, 5962 (1998).
190. A. Hosomi, H. Iguchi, M. Endo, and H. Sakurai, *Chem. Lett*., 977 (1979).
191. B. M. Trost and T. Sato, *J. Am. Chem. Soc*., **107**, 719 (1985).

Scheme 9.6. Reactions of Allylic Stannanes with Carbonyl Compounds

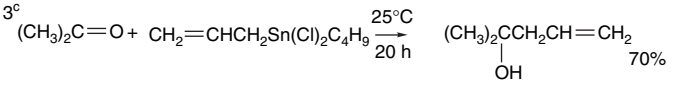
1[a]



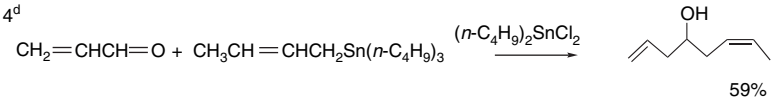
2[b]



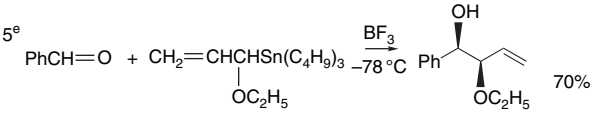
3[c]



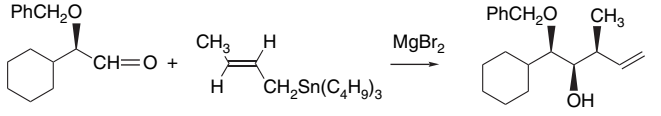
4[d]



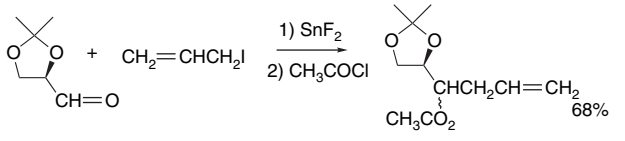
5[e]



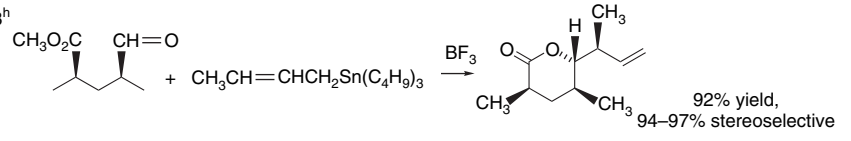
6[f]



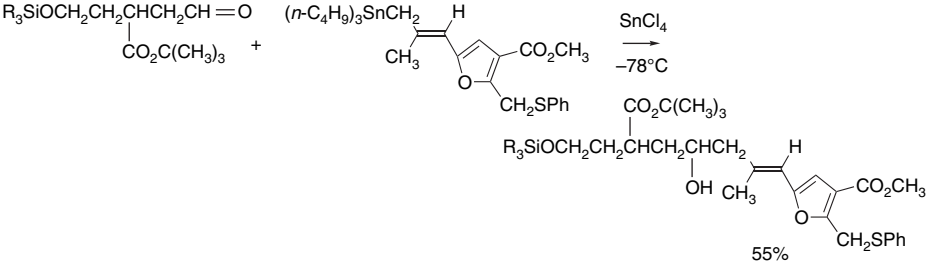
7[g]



8[h]

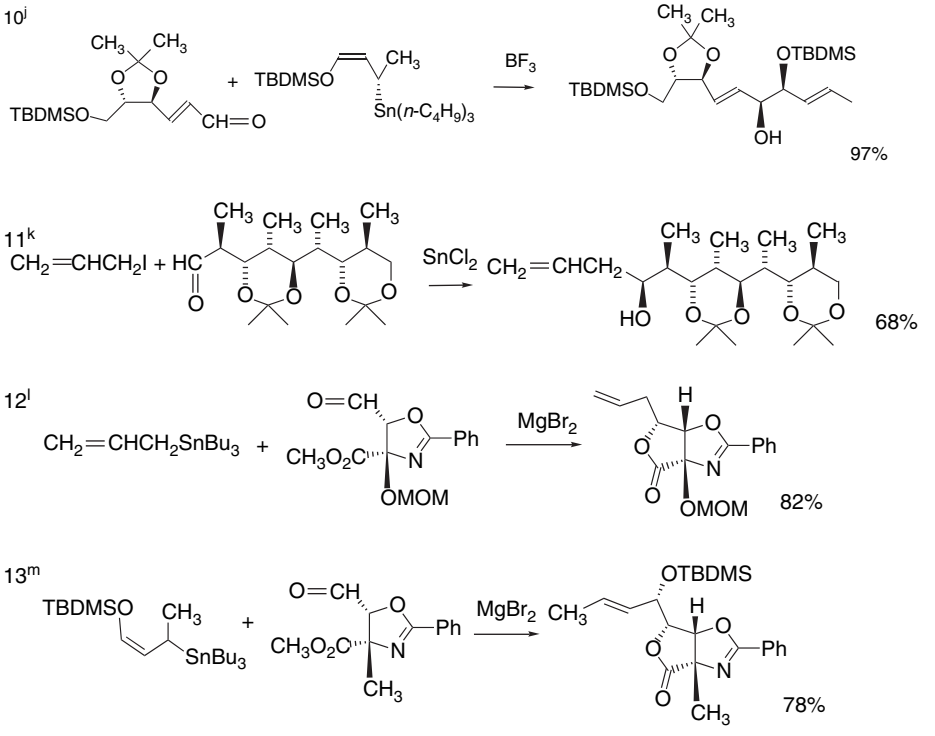


9[i]



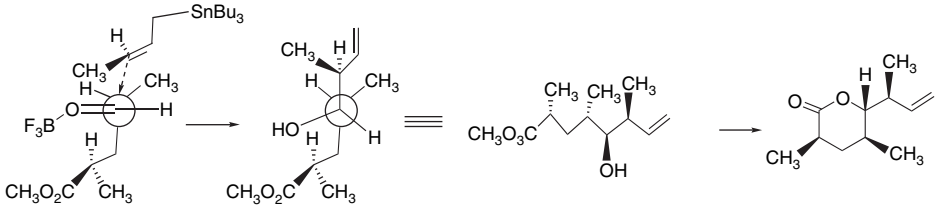
(*Continued*)

Scheme 9.6. (*Continued*)



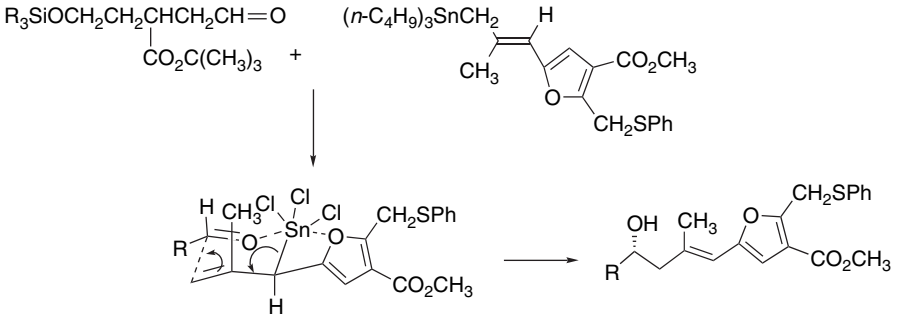
a. M. Koreeda and Y. Tanaka, *Chem. Lett*., 1297 (1982).
b. V. Peruzzo and G. Tagliavini, *J. Organomet. Chem*., **162**, 37 (1978).
c. A. Gambaro, V. Peruzzo, G. Plazzogna, and G. Tagliavini, *J. Organomet. Chem*., **197**, 45 (1980).
d. L. A. Paquette and G. D. Maynard, *J. Am. Chem. Soc*., **114**, 5018 (1992).
e. D.-P. Quintard, B. Elissondo, and M. Pereyre, *J. Org. Chem*., **48**, 1559 (1983).
f. G. E. Keck and E. P. Boden, *Tetrahedron Lett*., **25**, 1879 (1984).
g. T. Harada and T. Mukaiyama, *Chem. Lett*., 1109 (1981).
h. K. Maruyama, Y. Ishiara, and Y. Yamamoto, *Tetrahedron Lett*., **22**, 4235 (1981).
i. L. A. Paquette and P. C. Astles, *J. Org. Chem*., **58**, 165 (1993).
j. J. A. Marshall, S. Beaudoin, and K. Lewinski, *J. Org. Chem*. **58**, 5876 (1993).
k. H. Nagaoka, and Y. Kishi, *Tetrahedron*, **37**, 3873 (1981).
l. K.-Y. Lee, C.-Y. Oh, Y.-H. Kim, J. E. Joo, and W.-H. Ham, *Tetrahedron Lett*., **43**, 9361 (2002).
m. K.-Y. Lee, C.-Y. Oh, and W.-H. Ham, *Org. Lett*., **4**, 4403 (2002).

BF_3 should involve an open TS. The observed stereochemistry is *syn* but the approach is anti-Felkin.

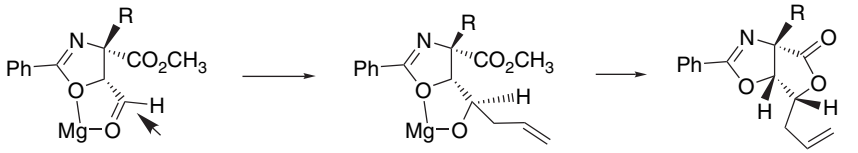


Entry 9 was used in the synthesis of a furanocembranolide. This reaction presumably proceeds through a trichlorostannane intermediate and involves allylic

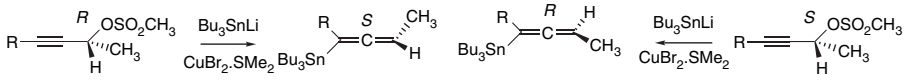
shift at both the transmetallation and addition steps, resulting in restoration of the original allylic structure.



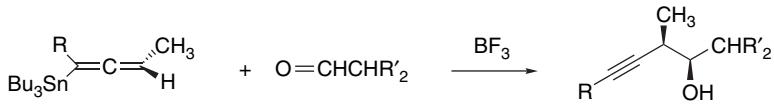
Entry 10 was used in conjunction with dihydroxylation in the enantiospecific synthesis of polyols. Entry 11 illustrates the use of $SnCl_2$ with a protected polypropionate. Entries 12 and 13 result in the formation of lactones, after $MgBr_2$-catalyzed additions to heterocyclic aldehyde having ester substituents. The stereochemistry of both of these reactions is consistent with approach to a chelate involving the aldehyde oxygen and oxazoline oxygen.



9.3.2.6. Allenyl Stannanes. Allenyl stannanes are a useful variation of the allylic stannanes.[192] They can be made in enantiomerically pure form by S_N2' displacements on propargyl tosylates.[193]



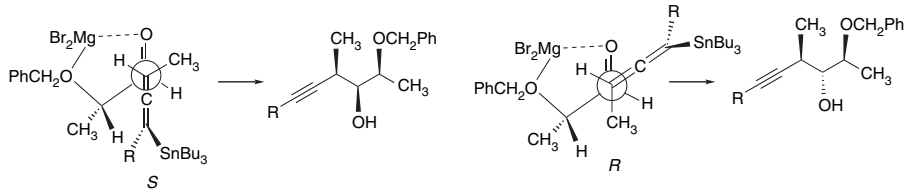
The allenic stannanes react with aldehydes under the influence of Lewis acids such as BF_3 and $MgBr_2$. Unbranched aldehydes are not very stereoselective, but branched aldehydes show a strong preference for the *syn* adduct.



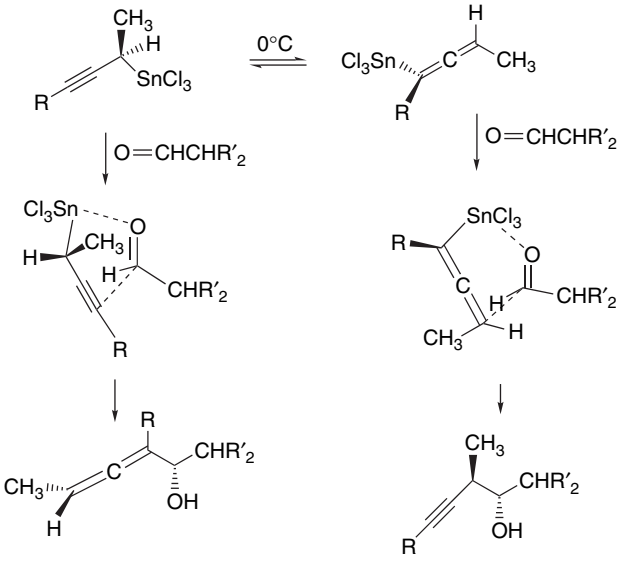
With α-benzyloxypropanal, using $MgBr_2$ as the Lewis acid, chelation control is observed. The stereospecificity is determined by an *anti* orientation of the C–Sn bond

192. J. A. Marshall, *Chem. Rev.*, **96**, 31 (1996).
193. J. A. Marshall and X. Wang, *J. Org. Chem.*, **56**, 3211 (1991).

and the forming C–C bond. As a result, the (*S*) reactant gives a *syn* adduct, whereas the (*R*) reactant gives the *anti* isomer.



The allenic stannanes can be transmetallated by treatment with $SnCl_4$, a reaction that results in the formation of the a propargyl stannane. If the transmetallation reaction is allowed to equilibrate at 0 °C, an allenic structure is formed. These reagents add stereospecifically to the aldehyde through cyclic TSs.[194]



The combination of reagents and methods can provide for stereochemical control of addition to α-substituted aldehydes.[195] An application of the methodology can be found in the synthesis of (+)-discodermolide that was carried out by J. A. Marshall and co-workers and is described in Scheme 13.69.

9.4. Summary of Stereoselectivity Patterns

In this chapter, we have seen a number of instances of stereoselectivity. Although they are affected by specific substitution patterns, every case can be recognized as conforming to one of several general patterns.

1. Reactions proceeding through a monocyclic TS with substrate control: These reactions exhibit predictable stereoselectivity determined by the monocyclic

194. J. A. Marshall and J. Perkins, *J. Org. Chem.*, **60**, 3509 (1995).
195. J. A. Marshall, J. F. Perkins, and M. A. Wolf, *J. Org. Chem.*, **60**, 5556 (1995).

Scheme 9.7. Summary of Stereoselectivity of Allylic Reagents in Carbonyl Addition Reactions

Monocyclic TS	Open TS	Chelation TS	Stereoconvergent
Allylboration with β-allylic boranes and boronates	Lewis acid–catalyzed addition of allylic silanes	Lewis acid–catalyzed addition of allylic silanes and stannanes α- and β-oxy aldehydes	$SnCl_2$- mediated addition of allylic to stannanes aryl methyl ketones
Addition of allylic trihalo stannanes to aldehydes	Lewis Acid-catalyzed addition of allylic stannanes		

TS, which is usually based on the chair (Zimmerman-Traxler) model. This pattern is particularly prevalent for the allylic borane reagents, where the Lewis acidity of boron promotes a tight cyclic TS, but at the same time limits the possibility of additional chelation. The dominant factors in these cases are the *E*- or *Z*-configuration of the allylic reagent and the conformational preferences of the reacting aldehyde (e.g., a Felkin-type preference.)

2. Reactions proceeding through open TS: In this group, exemplified by BF_3-catalyzed additions of allylic silanes and stannanes, the degree of stereochemical control is variable and often moderate. The stereoselectivity depends on steric factors in the open TS and can differ significantly for the *E*- and *Z*-isomers of the allylic reactant.
3. Reactions through chelated TS: Reactions of α- or β-oxy-substituted aldehydes often show chelation-controlled stereoselectivity with Lewis acids that can accommodate five or six ligands. Chelation with substituents in the allylic reactant can also occur. The overall stereoselectivity depends on steric and stereoelectronic effects in the chelated TS.
4. Stereoconvergence owing to reactant or product equilibration: We also saw several cases where the product composition was the same for stereoisomeric reactants, e.g., for *E*- and *Z*-allylic reactants. This can occur if there is an intermediate step in the mechanism that permits *E*- and *Z*-equilibration or if the final stereoisomeric product can attain equilibrium.

Scheme 9.7 gives examples of each of these types of stereoselectivities. The analysis of any particular system involves determination of the nature of the reactant, e.g., has transmetallation occurred, the coordination capacity of the Lewis acid, and the specific steric and stereoelectronic features of the two reactants.

General References

Organoborane Compounds

H. C. Brown, *Organic Synthesis via Boranes*, Wiley, New York, 1975.

A. Pelter, K. Smith, and H. C. Brown, *Borane Reagents*, Academic Press, New York, 1988.

A. Pelter, in *Rearrangements in Ground and Excited States*, Vol. 2, P. de Mayo, ed., Academic Press, New York, 1980, Chap. 8.

B. M. Trost, ed., *Stereodirected Synthesis with Organoboranes*, Springer, Berlin, 1995.

E. W. Colvin, *Silicon Reagents in Organic Synthesis*, Academic Press, London, 1988.
I. Fleming, J. Dunogves, and R. Smithers, *Org. React.*, **37**, 57 (1989).
W. Weber, *Silicon Reagents for Organic Synthesis*, Springer, Berlin, 1983.

Organotin Compounds

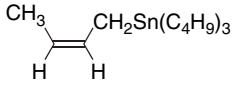
A. G. Davies, *Organotin Chemistry*, VCH, Weinheim, 1997.
S. Patai, ed., *The Chemistry of Organic Germanium, Tin and Lead Compounds*, Wiley-Interscience, New York, 1995.
M. Pereyre, J.-P. Quintard, and A. Rahm, *Tin in Organic Synthesis*, Butterworths, London, 1983.

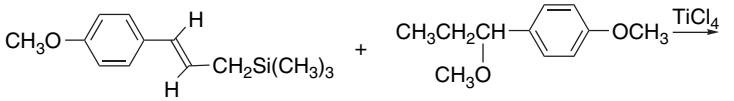
Problems

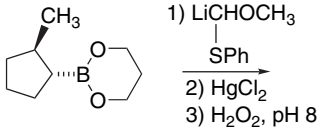
(*References for these problems will be found on page 1286.*)

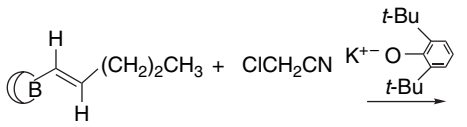
9.1. Give the expected product(s) for the following reactions:

(a) $[CH_3CO_2(CH_2)_5]_3B + LiC{\equiv}C(CH_2)_3CH_3 \longrightarrow \xrightarrow{I_2}$

(b) $PhCH{=}O +$  $\xrightarrow{BF_3}$

(c) 

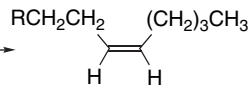
(d) 

(e) 

9.2. Starting with an alkene $RCH{=}CH_2$, indicate how an organoborane intermediate could be used for each of the following synthetic transformations:

(a) $RCH{=}CH_2 \longrightarrow RCH_2CH_2CH_2C(=O)C_6H_5$

(b) $RCH{=}CH_2 \longrightarrow RCH_2CH_2CH{=}O$

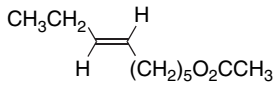
(c) $RCH{=}CH_2 \longrightarrow$ 

(d) $RCH{=}CH_2 \longrightarrow RCH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2R$

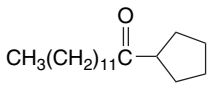
(e) $RCH{=}CH_2 \longrightarrow RCH_2CH_2CH_2CO_2C_2H_5$

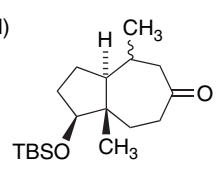
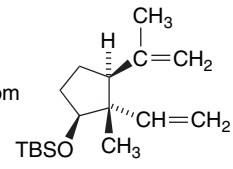
9.3. Scheme 9.1 describes reactions with several lithiated compounds, including dichloromethane, dichloromethyl methyl ether, phenylthiomethyl methyl ether, and phenylthioacetals. Compare the structure of these reagents and the final products for these reactions. Develop a mechanistic outline that encompasses these reactions. Discuss the features that these reagents have in common with one another and with carbon monoxide.

9.4. Each of the following transformations was performed advantageously with a thexylborane derivative. Give appropriate reactants, reagents, and reaction conditions for effecting the following syntheses in a one-pot" process.

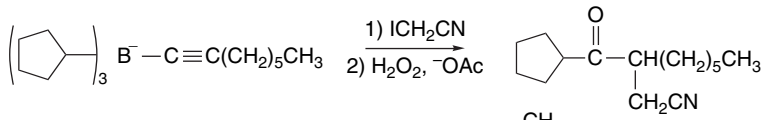
(a)  from $IC{\equiv}CCH_2CH_3$ and $CH_2{=}CH(CH_2)_3O_2CCH_3$

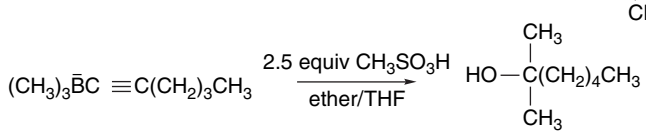
(b) $CH_3(CH_2)_3C{\equiv}C(CH_2)_7CH_3$ from $CH_2{=}CH(CH_2)_5CH_3$ and $HC{\equiv}C(CH_2)_3CH_3$

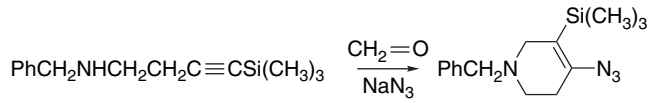
(c)  from $CH_2{=}CH(CH_2)_9CH_3$ and 

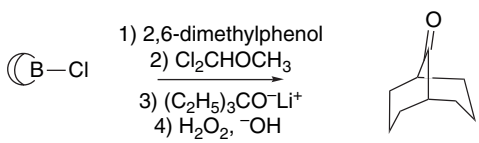
(d)  from 

9.5. Provide mechanisms for the formation of the new carbon-carbon bonds in each of the following reactions:

(a) 

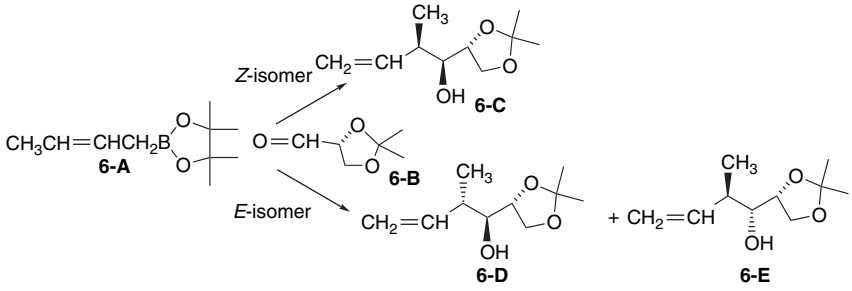
(b) 

(c) 

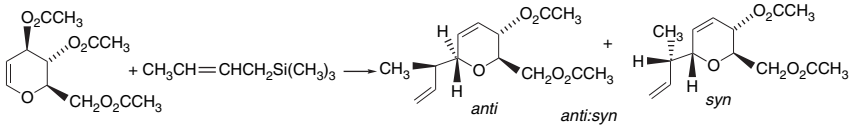
(d) 

9.6. Offer a detailed mechanistic explanation for the following observations.

a. When the *E*- and *Z*-isomers of 2-butenyl-1,3,2-dioxaborolane **6-A** react with aldehyde **6-B**, the *Z*-isomer gives *syn* product **6-C** with greater than 90% stereoselectivity. The *E*-isomer, however, gives a nearly 1:1 mixture of two *anti* products **6-D** and **6-E**.

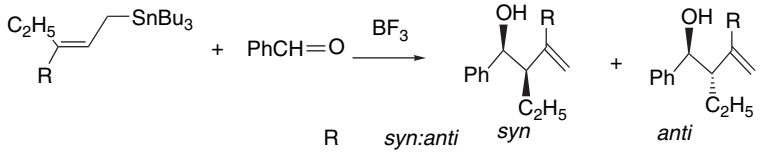


b. The reaction of several $\Delta^{2,3}$-pyranyl acetates with allyl trimethylsilane under the influence of Lewis acids gives 2-allyl-$\Delta^{3,4}$-pyrans. The stereochemistry depends on whether the *E*- or *Z*-allylsilane is used. There is a preference for *anti* stereochemistry at the new bond with the *E*-silane but *syn* stereochemistry with the *Z*-silane. The preference for the *syn* stereochemistry is increased by use of a more bulky silyl substituent. Analyze the competing transition structures for the *E*- and *Z*-silanes and suggest an explanation for the observed stereoselectivity.



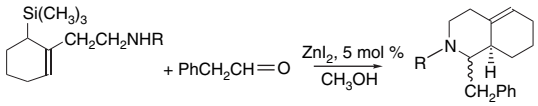
		anti:syn
E	$SiMe_3$	3:1
Z	$SiMe_3$	1:3
Z	$SiMe_2Ph$	1:3.2
Z	$SiMePh_2$	1.4.5
Z	$Si(tBu)Ph_2$	1:7

c. In the reaction of 2-pentenyl tri-*n*-butylstannanes with benzaldehyde and BF_3, the diastereoselectivity is dependent on the identity of the 3-substituent group. Offer an explanation in terms of possible transition structures.



R	*syn:anti*
H	78:22
CH_3	91:9
i-Pr	84:16
t-Bu	13:87

d. It is observed that the stereoselectivity of cyclizative condensation of aminoalkyl silane **6-F** depends on the steric bulk of the amino substituent. Offer an explanation for this observation in terms of the transition structure for the addition reaction.

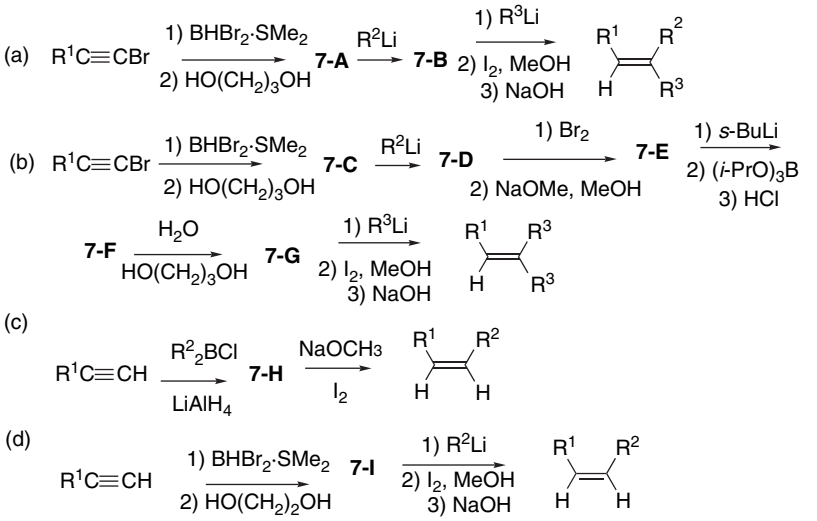


6-F

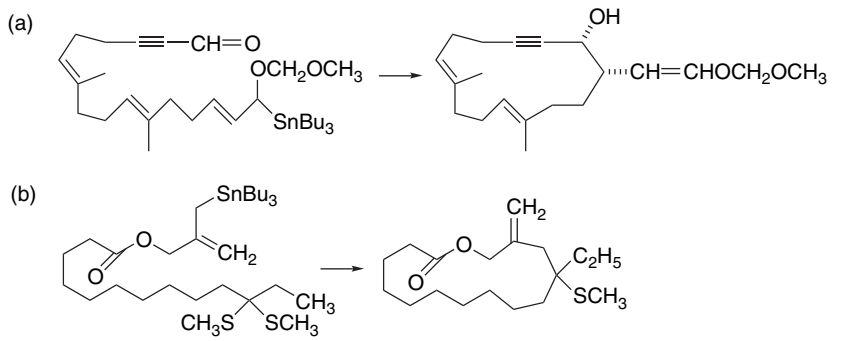
R	Yield (%)	*trans*:*cis* ratio
CH_3[a]	68	20:80
$PhCH_2$	88	58:42
Ph_2CH	73	>99:1
Dibenzocycloheptyl	67	>99:1

[a] $Ph(CH_3)_2Si$ instead of $(CH_3)_3Si$.

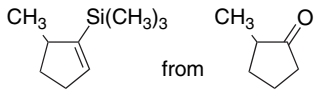
9.7. A number of procedures for stereoselective synthesis of alkenes involving alkenylboranes have been developed. For each of the reactions given below, show the structure of the intermediates and outline the mechanism in sufficient detail to account for the observed stereoselectivity.

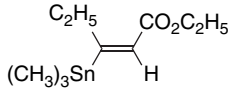


9.8. Suggest reagents and reaction conditions that would be effective for the following cyclization reactions:

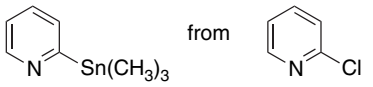


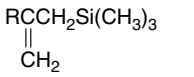
9.9. Show how the following silanes and stannanes can be synthesized from the suggested starting material.

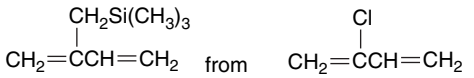
(a) 

(b)  from $CH_3CH_2C{\equiv}CCO_2C_2H_5$

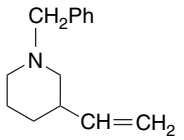
(c) $Bu_3SnCH{=}CHSnBu_3$ from $HC{\equiv}CH$, Bu_3SnCl, and Bu_3SnH

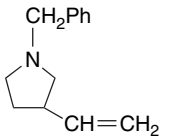
(d) 

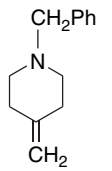
(e) 

(f) 

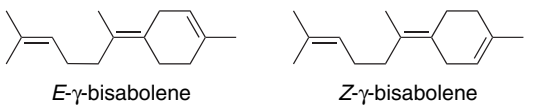
9.10. Each of the unsaturated cyclic amines shown below has been synthesized by reaction of an amino-substituted allylic silane under iminium ion cyclization conditions ($CH_2{=}O$, TFA). By retrosynthetic analysis, identify the appropriate precursor for each cyclization. Suggest a method of synthesis of each of the required amines.

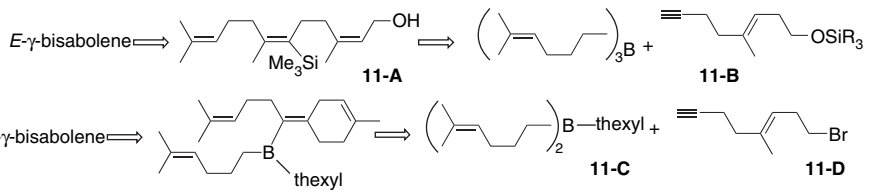
(a) 

(b) 

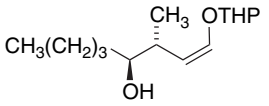
(c) 

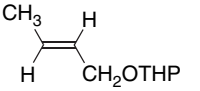
9.11. Both *E*- and *Z*-isomers of the terpene γ-bisabolene have been isolated from natural sources. The synthesis of these compounds can be achieved by stereoselective alkene syntheses using borane intermediates. An outline of each synthesis is given below. Indicate the reaction conditions that would permit the stereoselective synthesis of each isomer.

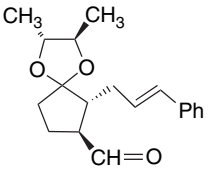


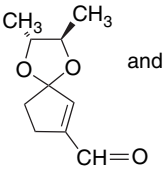


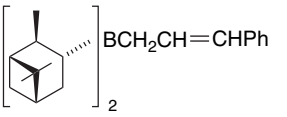
9.12. By retrosynthetic analysis, devise a sequence of reactions that would provide the desired compound from the indicated starting materials.

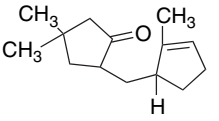
(a) 

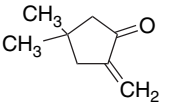
from $CH_3(CH_2)_3CH{=}O$ and 

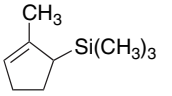
(b) 

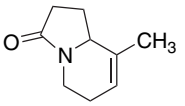
from 

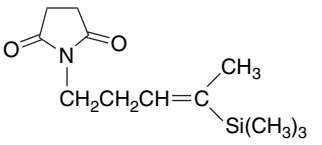
and 

(c) 

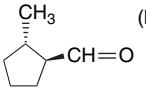
from 

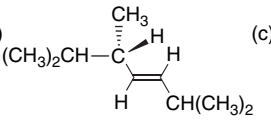
and 

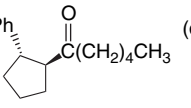
(d) 

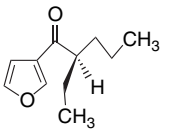
from 

9.13. Show how the following compounds could be prepared in high enantiomeric purity using enantiopure boranes as reactants.

(a) 

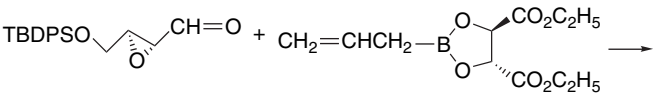
(b) 

(c) 

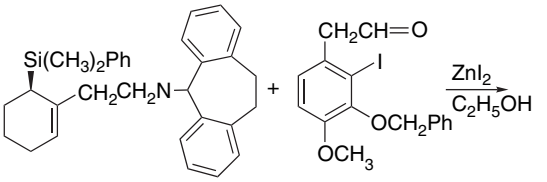
(d) 

9.14. Show how organoborane intermediates can be used to synthesize the gypsy moth pheromone E,Z-$CH_3CO_2(CH_2)_4CH{=}CH(CH_2)_2CH{=}CH(CH_2)_3CH_3$ from hept-6-ynyl acetate, allyl bromide, and 1-hexyne.

9.15. Predict the major stereoisomer that will be formed in the following reactions. Show the transition structure that is the basis for your response.

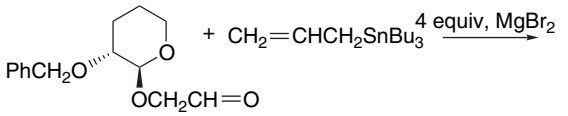
(a) 

(b) $CH_2{=}CHCH{=}O + CH_3CH{=}CHCH_2Sn(n\text{-}C_4H_9)_3 \xrightarrow[25^\circ C,\ 24\ h]{(n\text{-}C_4H_9)_2SnCl_2}$ (3:1 *E*:*Z*-mixture)

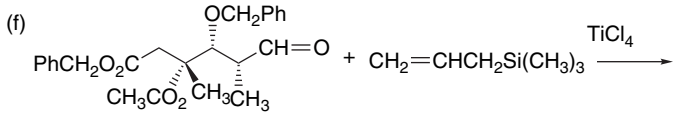
(c) 

(d)

(e)

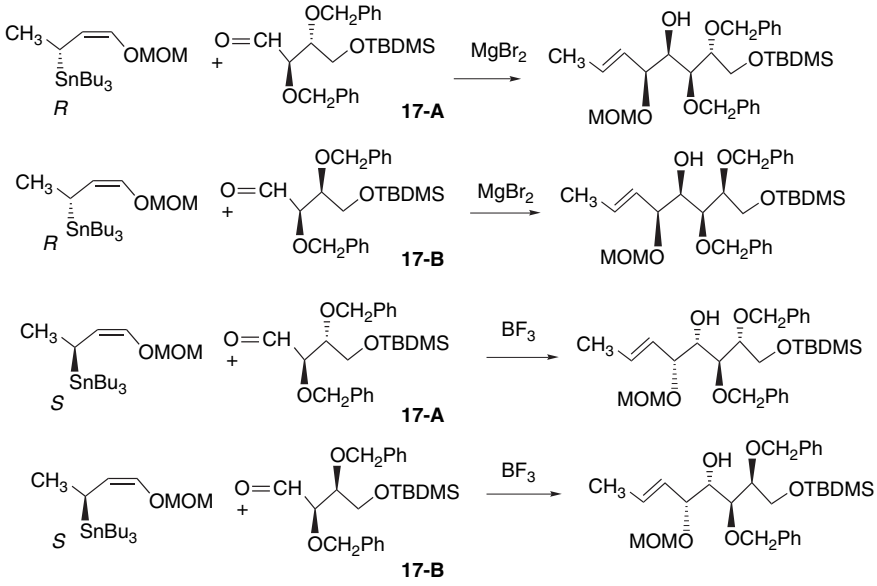


(f)

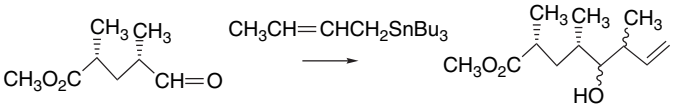


9.16. The stereoselectivity of the β-carboethoxyallylic boronate derived from the *endo*-phenyl auxiliary **A** (p. 803) toward *R*- and *S*-glyceraldehyde acetonide has been investigated. One enantiomer gives the *anti* product in 98:2 ratio, whereas the other favors the *syn* product by a 65:35 ratio. Based on the proposed transition structure for this boronate, determine which combination leads to the higher stereoselectivity and which to the lower. Propose the favored transition structure in each case.

9.17. The *R*- and *S*-enantiomers of *Z*-3-methoxymethyl-1-methylpropenylstannane have been allowed to react with the protected erythrose- and threose-derived aldehydes **17-A** and **17-B**. The products are shown below. Indicate the preferred transition structure for each combination.



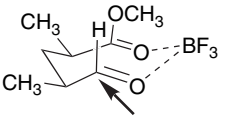
9.18. In the original report of the reaction in Entry 8 of Scheme 9.6, it was found that use of three equivalents of BF_3 led to loss of stereoselectivity, but not yield.



Product Composition

Equiv BF_3	Total Yield	*anti* anti-Felkin	*anti* Felkin	*syn* Felkin	*syn* anti-Felkin
1	92	94–97	3–4	1	1
2	90	83–91	5–9	1–3	2–5
3	90	41	10	17	32

These results were attributed to a preference for an eight-membered chelated transition structure that was lost in the presence of excess BF_3 because of coordination of a second BF_3 at the ester group. What objections would you raise to this explanation? What alternative would you propose?



9.19. The aldehyde **19-A** shows differential stereoselectivity toward the enantiomeric stannanes (*S*)-**19-B** and (*R*)-**19-B**. The former aldehyde gives a single product in high yield, whereas the latter gives a somewhat lower yield and a mixture of two stereoisomers under the same conditions and is a mixture of two stereoisomers. Propose TSs to account for each product and indicate the reasons for the enhanced stereoselectivity of (*S*)-**19-B**.