C.2 Type II Allyl Metals

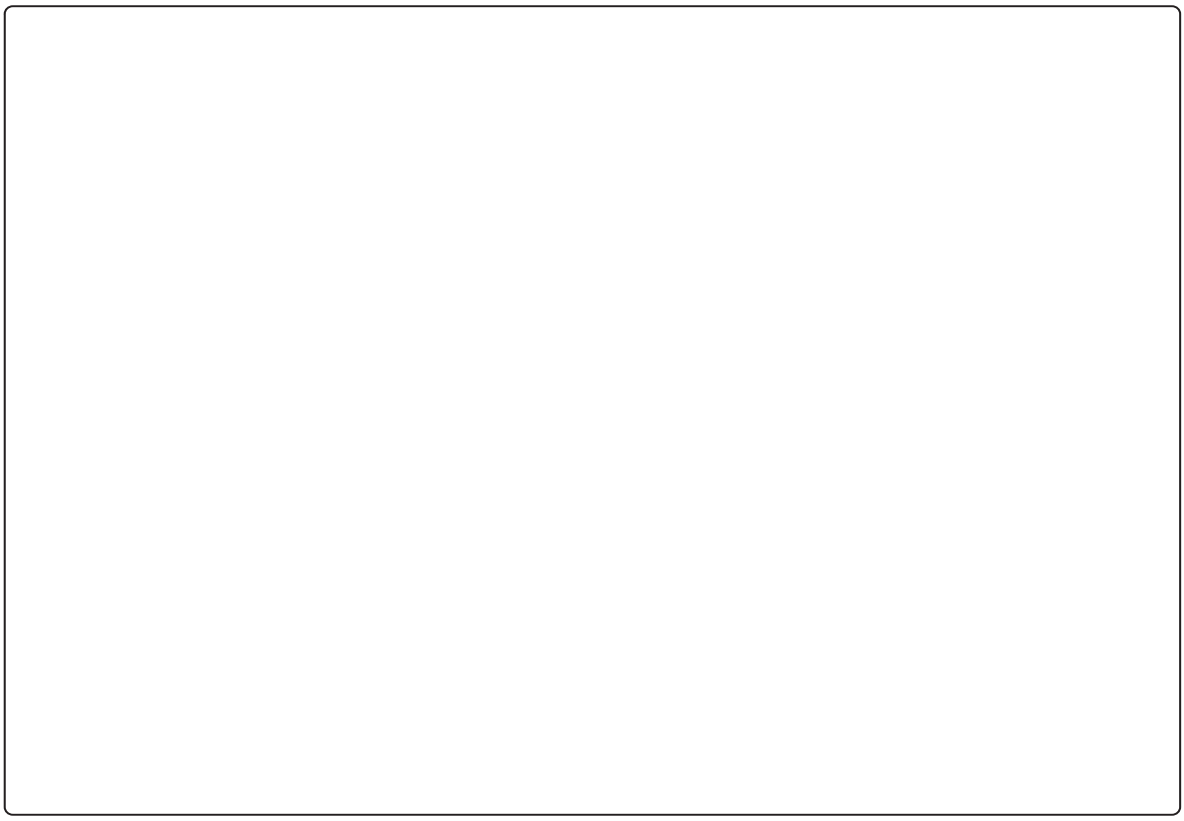
Exemplified by the reaction of allylstannanes with aldehydes under BF_3 catalysis (allylsilanes react similarly although are less nucleophilic (Si is less electropositive than Sn) and tend to require more forcing conditions.)

General reviews:

1. I. Fleming in *Comprehensive Organic Synthesis*, eds B. M. Trost and I. Fleming, Pergamon, New York, 1991, vol 2, p 563-593.
2. J. A. Marshall, *Chem. Rev*., 1996, **96**, 31-47.

IN GENERAL, reaction proceeds through an OPEN or ACYCLIC Transition State.

Basic reaction mechanism:

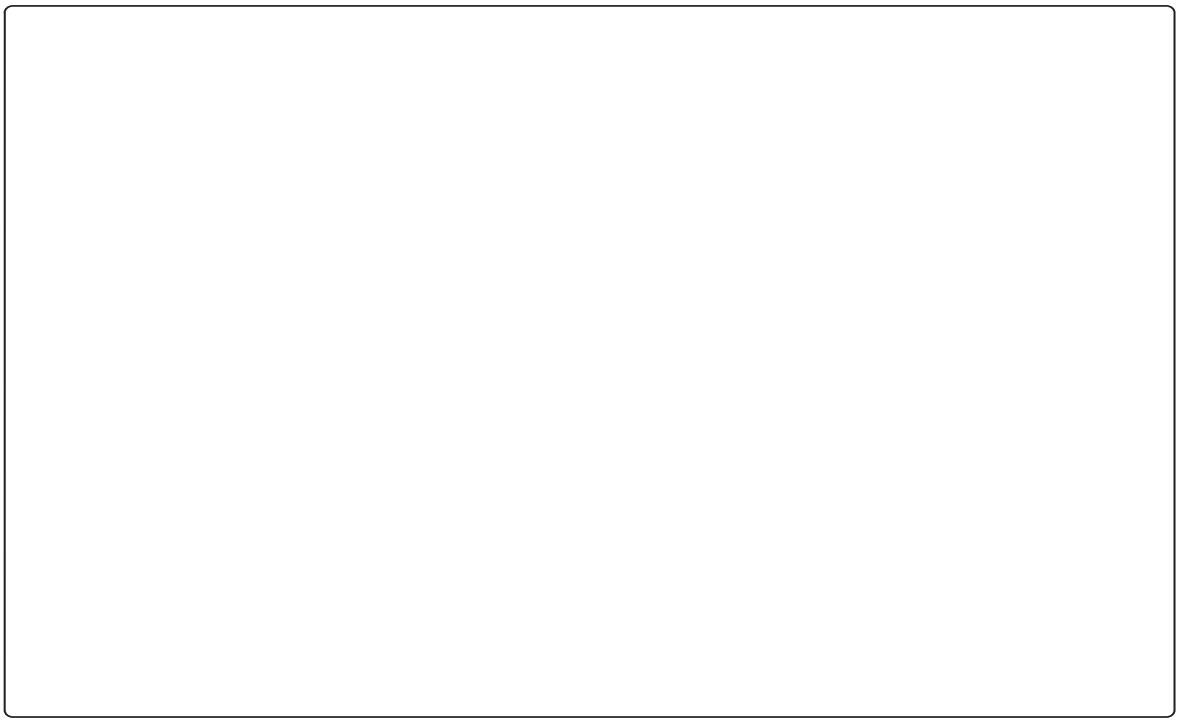


Notes:

1. Allylstannanes, and even more so allylsilanes, are not very nucleophilic so even aldehydes require activation before they can react. This is best accomplished using a Lewis acid *e.g.* $BF_3{\cdot}OEt_2$, $TiCl_4$, $SnCl_4$ *etc.*

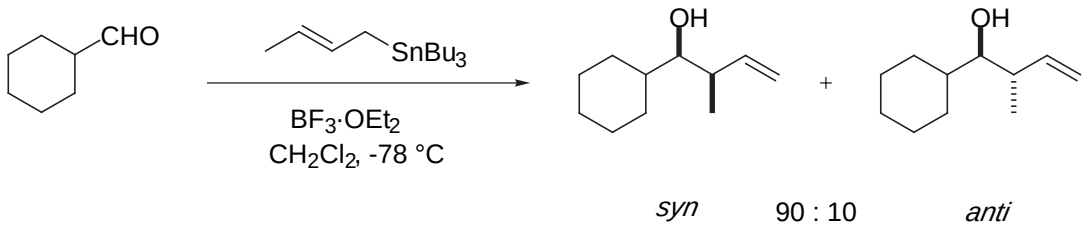
2. Allylation may be regarded as a stepwise process (although the intermediate **A** is extremely short-lived). Reaction proceeds in an S_E2' fashion (usually!) with reaction at the distal end of the allyl species away from the Bu_3Sn group (steric grounds).

3. The intermediate **A** possesses a positive charge β to the Sn. Just as Si exerts a stabilising effect on β-carbocations, Sn does the same (even more so therefore lowering the energy of the transition state of this, the rate-determining step). Note that to stabilise this charge, the C–Sn bond must align parallel to the empty p AO. This point is important as the bulkiest part of the allyl nucleophile is at a maximum distance away from the reacting electrophile.



4. Intermediate **A** readily collapses by attack of a nucleophile on the Sn atom and formation of the olefin (*c.f.* Si-mediated olefination).

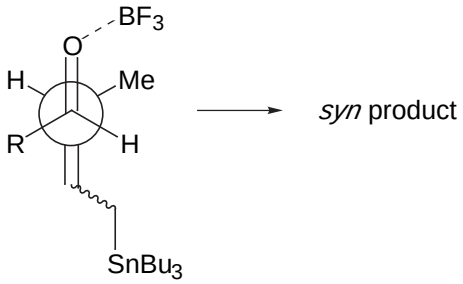
5. The open T.S. ensures that the reaction is *not stereospecific* like it is for Type I allylating reagents such as allyl boranes discussed earlier; nevertheless it can still be *highly stereoselective*. In the case of crotyl stannanes, reaction with aldehydes is invariably *syn* selective.

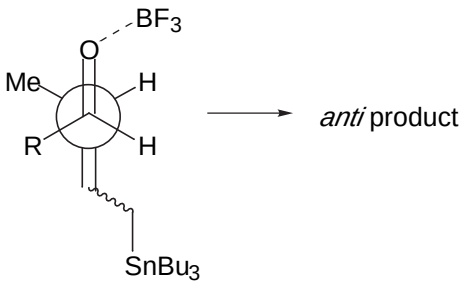


A First Attempt at Rationalising the Stereoselectivity

Y. Yamamoto provided one of the earliest attempts at rationalising the stereoselectivity. He proposed that crotyltributylstannane reacted through an open T.S. and as a result, the geometry of the crotyl metal species was unimportant. Use of $BF_3{\cdot}OEt_2$ as the Lewis acid provided the best results.

A transition state with an antiperiplanar arrangement of π-systems, in a staggered reactive conformation, was proposed and the *syn* selectivity arose through minimising steric interactions between the methyl group on the crotyl reagent and the aldehyde substituent.





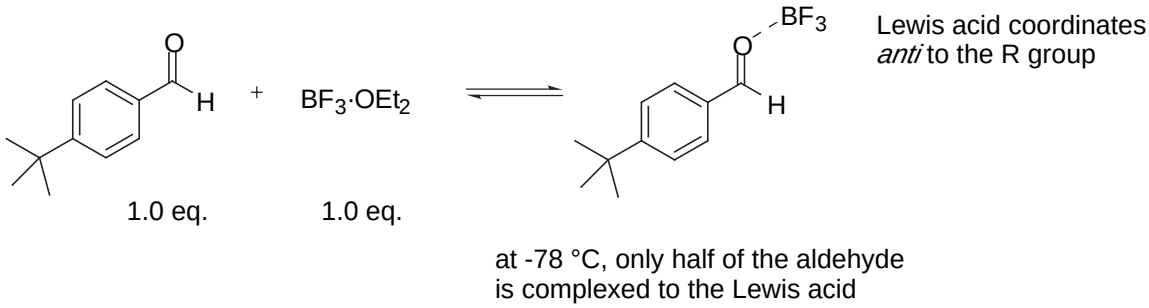
The role and bonding mode of the Lewis acid was not considered in detail and a proper study of the effect of double bond geometry was hindered (at the time) by the difficulty in obtaining stereochemically pure (*E*)- and (*Z*)-crotylstannanes.

The Importance of the Lewis Acid

Coordination of the Lewis acid to the aldehyde oxygen polarises the C=O bond, making it more electrophilic and susceptible to nucleophilic attack.

Denmark recognised that the Lewis acid was probably very important in governing the stereochemical outcome of the reaction and consequently used NMR spectroscopy to investigate the effect of different Lewis acids on the reaction of allyltributylstannane with a variety of aldehydes.

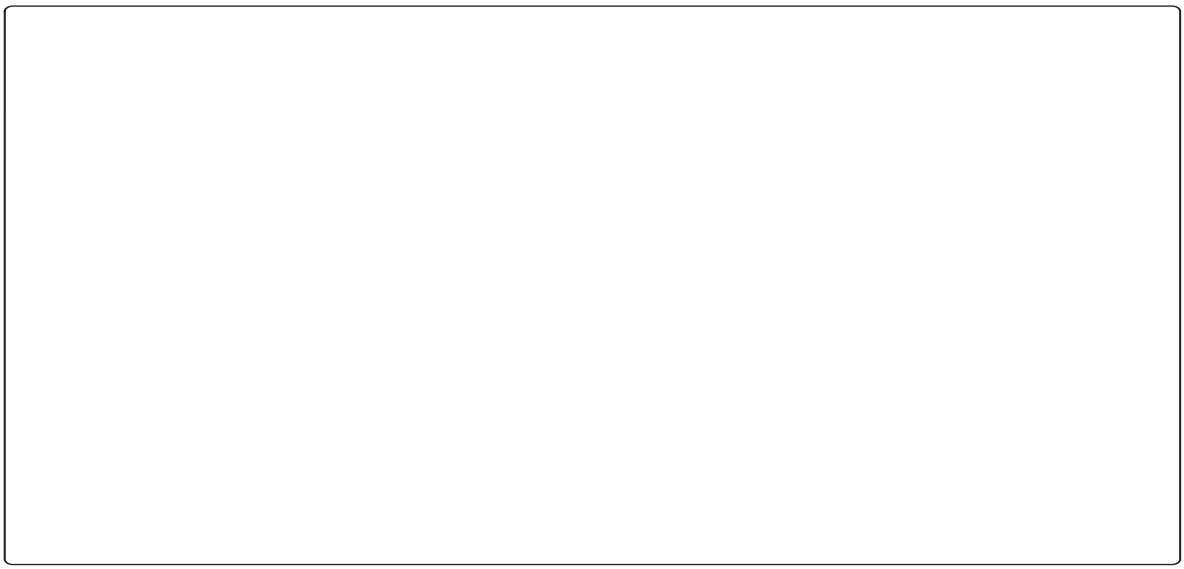
In the case of $BF_3{\cdot}OEt_2$, the degree of complexation was dependent on the aldehyde; in this case, Lewis acid complexation to the aldehyde is an equilibrium process.



In contrast, reaction of all aldehydes with an equimolar amount of $SnCl_4$ effected rapid and complete complexation.

Reaction of the Lewis acid with the allyl metal reagent

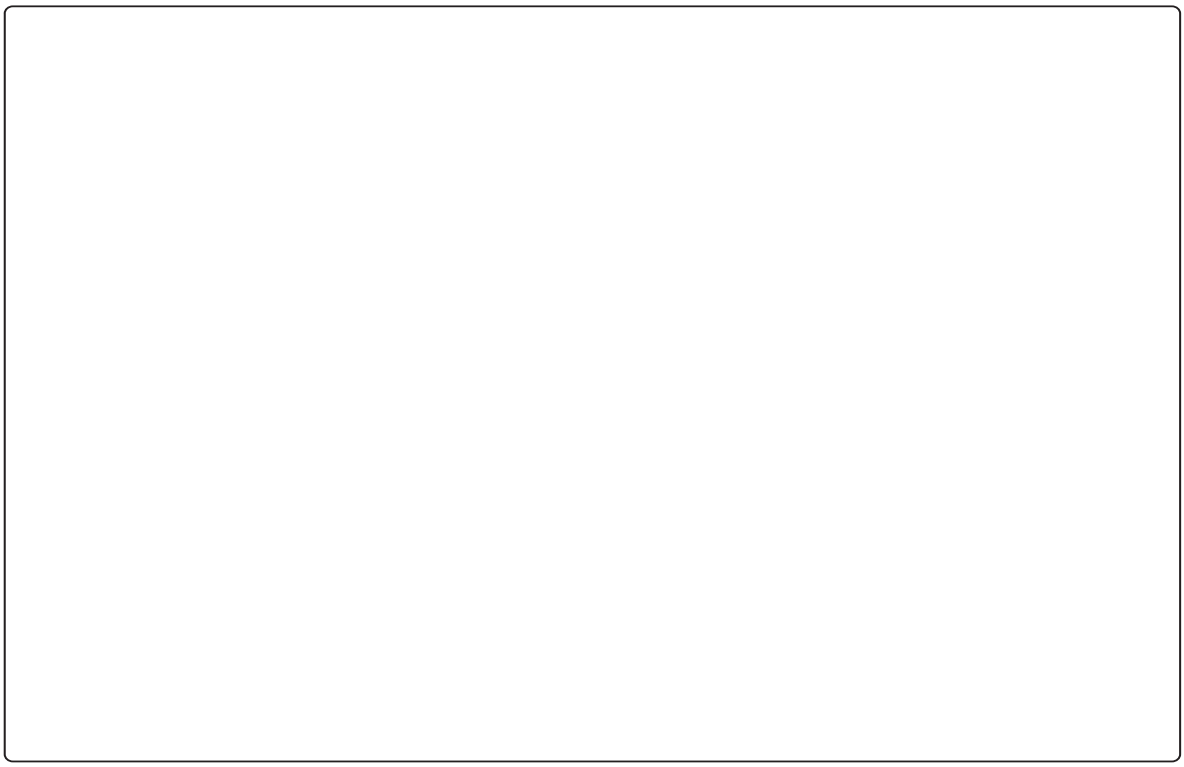
The presence of a Lewis acid can also have profound effects on the nature of the allyl metal species. For example, $SnCl_4$ reacts with allyltributylstannane instantaneously at –78 °C to provide the corresponding allyltrichlorostannane and Bu_3SnCl.



The resulting allyltrichlorostannane is appreciably more Lewis acidic than allyltributylstannane and therefore reacts through a CLOSED T.S. analogously to allyl boranes and boronates (*i.e.* it is now a Type I allyl metal reagent).

Allyltributylstannane can react through an open T.S. using $SnCl_4$. The key is to *pre*-complex the Lewis acid to the aldehyde *prior* to adding the allyl tin reagent.

BF_3 does not react with allyltributylstannane to afford the corresponding difluoro(allyl)borane. However $BF_3 \cdot OEt_2$ (and other Lewis acids) can scramble the double bond geometry of a crotyl metal species by catalysing a reversible 1,3-shift of the metal.

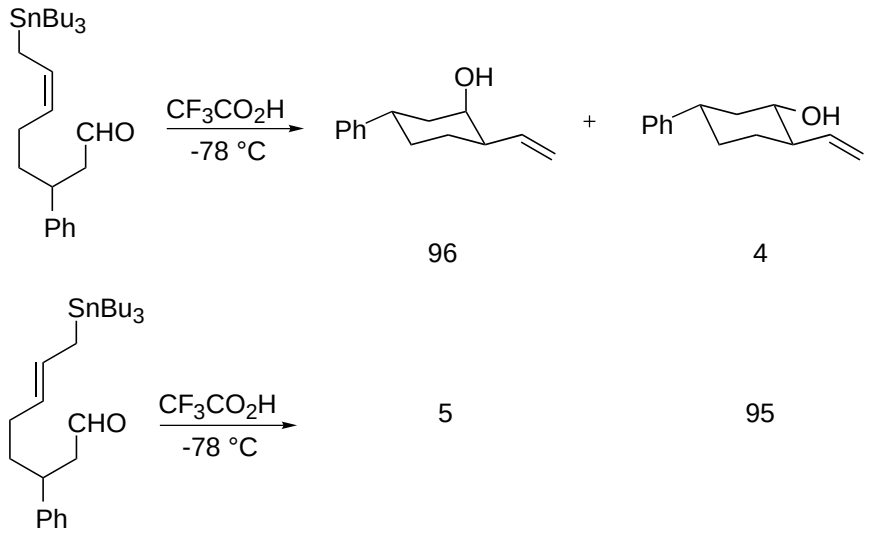


A More In-Depth Study of the Origins of Stereoselectivity – a Modified T.S.

The reaction is clearly more complicated than it first appears. Denmark and Keck have investigated the reaction mechanism in more detail and both groups propose a modified T.S. in which certain synclinal arrangements of π-systems are preferred over the alternative antiperiplanar arrangements proposed by Yamamoto.

S. E. Denmark, E. J. Weber, T. M. Wilson, T. M. Willson, *Tetrahedron*, 1989, **45**, 1053-1065.
G. E. Keck, K. A. Savin, E. N. K. Cressman, D. E. Abbott, *J. Org. Chem*., 1984, **59**, 7889-7896.
G. E. Keck, S. M. Dougherty, K. A. Savin, *J. Am. Chem. Soc*., 1995, **117**, 6210-6223.

Keck synthesised two allylstannanes which reacted *intramolecularly* with a tethered aldehyde under Brønsted acid activation. The results were in sharp contrast to Yamamoto's claim that olefin geometry was unimportant:



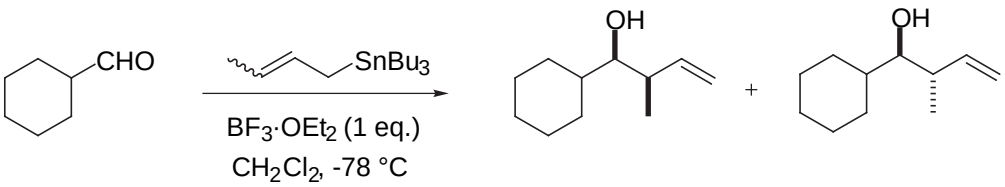
Clearly the double bond geometry *in this example* has a profound effect on the stereochemical outcome of the addition reaction. In both cases, the transition states leading to the observed major products have a synclinal arrangement of π-systems in which the Sn-CH_2 is *gauche* to the carbonyl group.

The reaction is not under thermodynamic control (*i.e.* governed by product stability) since the major product arising from the (*Z*)-stannane has an axial hydroxyl group – the minor product comes from a T.S. in which all substituents are in pseudoequatorial positions:

minor

The reaction is similarly not controlled by simple steric arguments ((*Z*)-stannane has a pseudoaxial OH substituent in the T.S.). Keck proposed that a *stereoelectronic effect* based on *Frontier Molecular Orbitals* could account for the observed stereochemical outcome. The dominant molecular orbitals in the reaction are the LUMO of the aldehyde and the HOMO of the allylstannane. The *syn* synclinal arrangement in the T.S. s shown allows a secondary stabilising interaction not possible in either the antiperiplanar or the other synclinal arrangements.

What about intermolecular reactions??



(*E*) / (*Z*)	
90 : 10	94 : 6
12 : 88	58 : 42

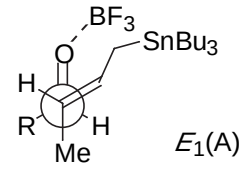
The results with cyclohexanecarboxaldehyde and $BF_3{\cdot}OEt_2$ as the Lewis acid (same effect was observed with other types of aldehydes) clearly show a strong correlation between the geometry of the stannane and the stereoselectivity of the product. **In both cases the reaction is *syn* selective although with (*Z*)-crotylstannane, the stereoselectivity is very poor.**

Assuming only staggered, open T.S.s with the Lewis acid coordinating *anti* to the aldehyde substituent (plenty of evidence for this with BF_3), there are *six* possible T.S.s – three give *anti* products, three give *syn* products.

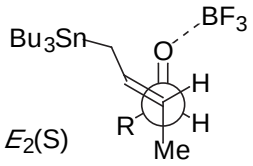
E_3(A) and E_4(S) are the T.S.s proposed by Yamamoto. If these were important we have to make the assumption (valid ???) that the Me/R interaction is more significant than the Me/BF_3 interaction. These T.S.s also do not account for the observation that the *syn* selectivity is higher when R = sp^2-hybridised (*eg*. PhCHO) than when R = sp^3-hybridised (and therefore bulkier) – should be the other way round if these T.S.s were significant.

E_1(A) and E_2(S) are the two *syn* synclinal T.S.s which can benefit from a secondary orbital overlap. E_2(S) is the energetically more favoured of the two since E_1(A) suffers unfavourable steric interactions between the Lewis acid and the CH_2Sn group.

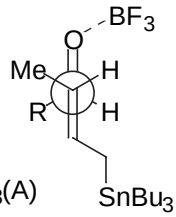
In the case of the (*E*)-stannane:



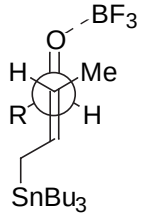
*E*1(A)



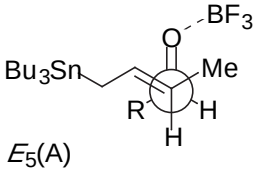
*E*2(S)



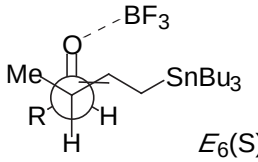
*E*3(A)



*E*4(S)



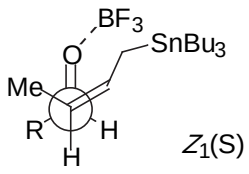
*E*5(A)



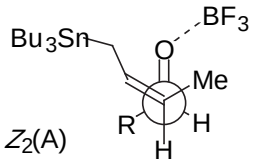
*E*6(S)

In the case of the (*Z*)-stannane:

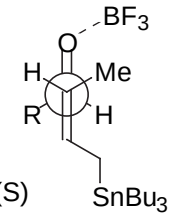
Compared with the possible T.S.s for the (*E*)-stannane, the S/A pairs for the (*Z*)-analogue appear to be similar in terms of steric interactions; no T.S. stands out as being much more favourable than the rest. The T.S.s may be much more comparable in energy leading to decreased levels of stereocontrol. Note these arguments are based on non-bonded steric repulsions that are difficult to quantify.



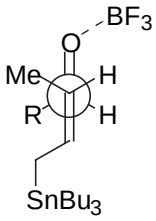
Z_1(S)



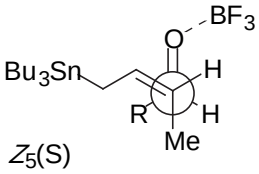
Z_2(A)



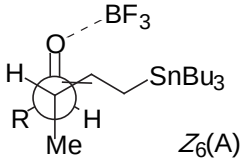
Z_3(S) SnBu$_3$



Z_4(A)



Z_5(S)



Z_6(A)

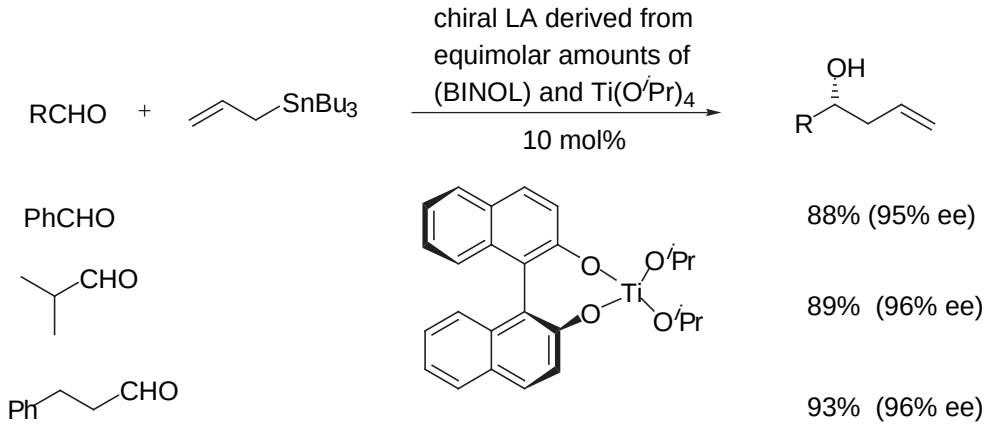
In the words of Ian Fleming (*Chemtracts: Org. Synth.* 1991, **4**, 21):

"We are still far from understanding the reasons for the high diastereoselectivity often shown in reactions of this type, in spite of their fundamental nature. It is likely that synclinal and antiperiplanar transition structures are inherently close in energy, and that it is indeed subtle balances among the substituents that determine which pathway is followed."

Asymmetric Type II Allylation reactions

The easiest method for incorporating asymmetry into a Type II allylation is to use a chiral Lewis acid for activating the aldehyde electrophile. Keck and co-workers have developed a Ti-Lewis acid derived from BINOL and Ti(O^iPr)$_4$. This has been used to prepare homoallylic alcohols with high enantioselectivities using allyltributylstannane (and methallyltributylstannane). It has not been applied to crotyl reagents.

A variety of other chiral Lewis acids have also been investigated and there are a growing number of possibilities for enantioselective synthesis using chiral Lewis acids and allylstannanes.



G. E. Keck, K. H. Tarbet, L. S. Geraci, *J. Am. Chem. Soc.*, 1993, **115**, 8467-8468.

Summary

1. Allylstannanes and allylsilanes are not very Lewis acidic although they both have vacant d AOs into which they can accept electron density and form hypervalent species. This is not observed at room temperatures.
2. Reaction with carbonyl groups (aldehydes are the most important electrophiles) therefore requires external Lewis acid activation to increase their electrophilicity.
3. The Lewis acid can affect the reaction mechanism through reaction with the allyl metal species (*e.g.* $SnCl_4$ reacting with allyltributylstannane to generate allyltrichlorostannane).
4. The reaction mechanism contrasts sharply with that of Type I allyl metals (*e.g.* allylboranes) in that it proceeds through an open T.S. As a result, the reaction is not stereospecific although it can be highly stereoselective.
5. Allylation with allylstannanes and allylsilanes proceeds through an S_E2' reaction mechanism. Alignment of the C–Sn/Si bond with developing positive charge on the β-carbon provides a stabilising effect in the T.S.
6. Detailed investigations by Keck and Denmark suggest that a *syn* synclinal arrangement of the π-systems (C=O and C=C) in the T.S. is favoured as this allows further stabilisation of the T.S. through energetically favourable frontier orbital interactions.
7. Control of the relative stereoselectivity using crotylstannanes is good for the (*E*)-stannane and favours the *syn* product. The level of stereocontrol with (*Z*)-crotylstannane is poor although still favours the *syn* product.
8. The best method for achieving absolute stereocontrol with Type II allyl metals is to use a chiral Lewis acid.