Silylallyl Anions in Organic Synthesis: A Study in Regio- and Stereoselectivity

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1. Introduction

Silicon-substituted carbanions have attracted considerable interest because of their multiple synthetic utilities.[1] While such carbanions undergo reactions similar to those expected of other heteroatom-substituted carbanions,[2] the silyl group is believed to stabilize the carbanions.[3] Furthermore, the silyl group can be subsequently transformed to other electrophile equivalents thus enhancing its usefulness in synthesis.[4] When the carbanion is allylic in nature, the silylallyl anion (**1**) offers a high degree of complexity in terms of its possible reactions. In this review, we examine in detail the reactions of **1** with various electrophiles E^+. In such reactions, there is first of all the question of regioselectivity. The reaction can occur at either the α- or the γ-position giving the products **2** or **3**, respectively. In the case of the γ-product **3**, there is the additional complexity in terms of the stereochemistry of the double bond which can be either *E* or *Z*. If the electrophile E^+ is an aldehyde or an unsymmetrical ketone, then, in addition to the regioselectivity question of giving products **4** and **5**, there is the question of relative stereochemistry of the two new stereogenic centers in the α-products **4**. Finally, in either **2**, **4**, or **5**, since new chiral centers are being created, there are the issues of enantioselectivity and diastereoselectivity if either chiral reagent or substrate is being used (Scheme 1).

Research over the last two decades has allowed us to know the structures of various silylallyl anions, their reactions, and the factors which govern their reactivities and selectivities. Furthermore, by changing the substituents on silicon, it has been possible

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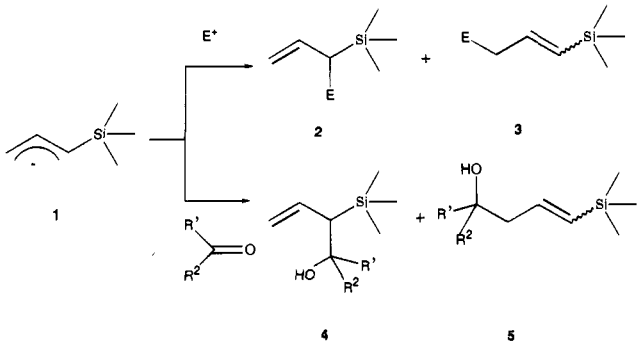
Scheme 1

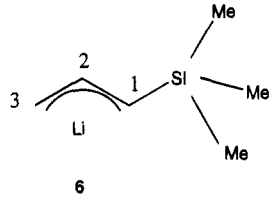


to control the regioselectivity, the stereoselectivity, and the enantioselectivity of these reactions. The lessons learned may well have general applications in other heterosubstituted allyl anions.

2. Structures of α-Silylallyl Anions

The first reported α-silylallyl anion was prepared by Corriu and his co-workers in 1973.[5] Since then, numerous α-silylallyl anions have been obtained by metalation of allylsilanes or alkyl-substituted vinylsilanes,[6] either of which can be prepared by a wide array of methods.[7] Organolithium compounds, such as alkyllithium or lithium dialkylamide are generally used as the base for the proton abstraction reaction to form the lithiated anions in solution. Since the counterion often plays an important role in the control of selectivity of the reaction, exchange of the lithium ion into other counterions or into an ate complex is carried out by the addition of appropriate metal halide or organometallic compound to the silylallyl lithium compound in solution.

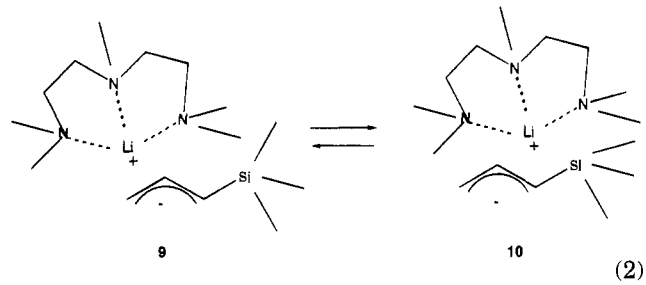
The structures of α-silylallyl anions in solution have been extensively studied by Fraenkel and his co-workers using NMR.[8] The following salient features can be drawn. The (trimethylsilyl)allyl anion seemed to adopt exclusively an exo orientation as represented in **6** in a variety of media. This is to be



contrasted with simple alkylallyl anions which tend to exist as mixture of exo and endo isomers **7** and **8** (eq 1),with the latter isomer generally predominat-

(1)

ing.[9] Secondly, when the coordinating solvent molecule was pentamethyldiethylenetriamine (PMDTA), the symmetrical pattern of the NMR at low temperature was interpreted to be consistent with rapidly equilibrating monomeric close contact ion pairs **9** and **10** with the lithium ion near C1 or C3 (eq 2). Thirdly,



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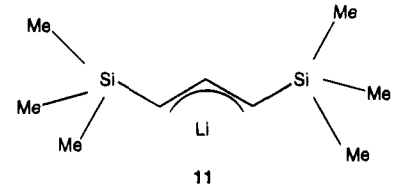
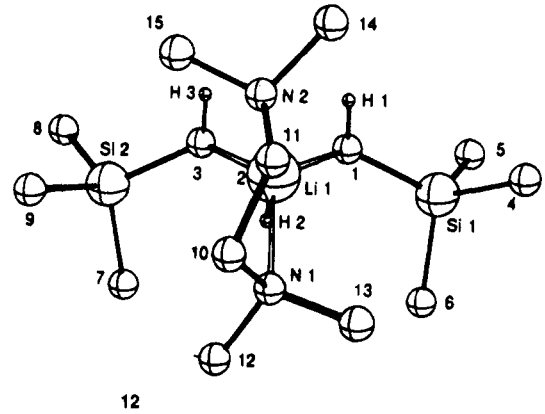
the exo orientation was extended to the symmetrical 1,3-bis(trimethylsilyl)allyl anion **11**. The X-ray struc-



ture of **11**–lithium–TMEDA complex was obtained which showed that the essentially symmetrical allyl anion moiety was slightly perturbed by the complexation of Li^+ with TMEDA in a twisted conformation as shown in **12**.[10] This symmetry reduction was



consistent with the NMR of **12** in solution at low temperature. The dynamic NMR behavior, i.e., coalescence of C1 and C3, was explained by rotation of the Li^+–TMEDA with respect to the anion component, and inversion of the Li^+–TMEDA five-membered ring (Figure 1).

The structures of the silylallyl anions in solution as revealed by NMR have clear implication in the reactions of these compounds. Particularly important is the exo orientation of these anions where the silyl moiety assumes a trans relationship with the C3 carbon.

3. Alkylation Reactions

[(Trimethylsilyl)allyl]lithium, generated readily from the reaction of trimethylallylsilane and *n*-butyllithium in TMEDA–THF at low temperature, reacted with a number of primary alkyl halides to give a mixture of α- and γ-alkylated products (**13** and **14**) in a ratio around 1:2 (Scheme 2). The ratio did not seem to vary significantly with the solvent system used, by addition of DABCO or crown ethers, or by

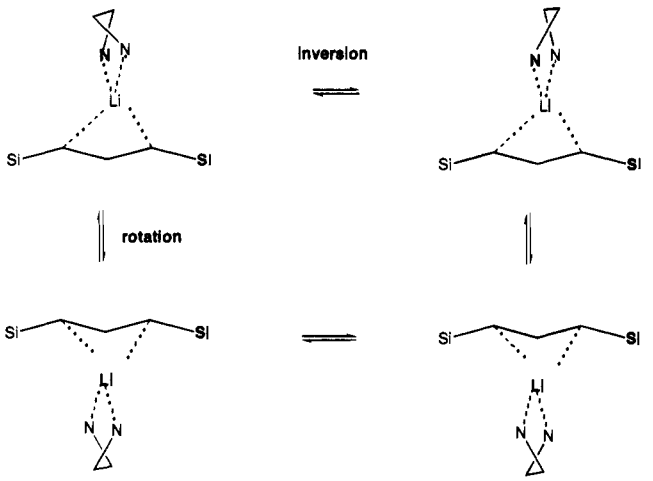
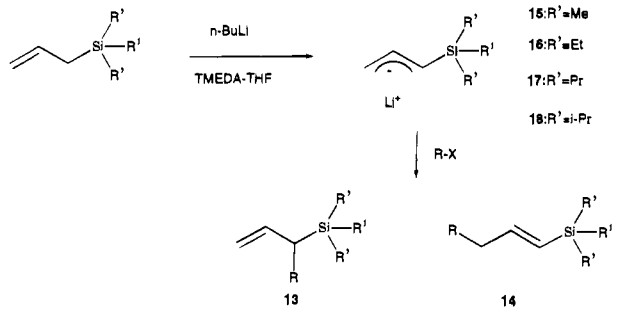


Figure 1.

Scheme 2



addition of various metal salts.[11] The lack of regioselectivity can be understood from the structure of the anion **6** or more specifically **8** and **9**. Reactions at either C1 or C3 are presumably of comparable rates (depending of course on the relative proportion of **8** and **9**), with a slight preference for reactions at C3 giving rise to a slight excess of the γ-products. The stereochemistry of the double bond in the γ-alkylation product **14** was found to be exclusively *E*, consistent with the exo structure observed for **6** in solution.

3.1. γ-Regioselectivity

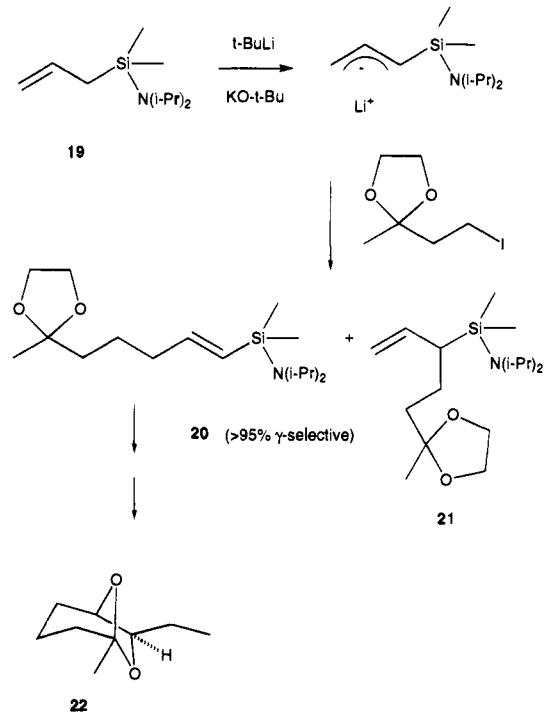
In order to make the reactions synthetically useful, improvement in the regioselection was required. It was found that when the (trimethylsilyl)allyl anion was generated using KO-*t*-Bu/*n*-BuLi in hexane (Schlosser's base),[12] alkylation of the anion so generated with the same primary alkyl halides gave an improved ratio (about 1:4) of α to γ, favoring the γ-product **14**. Since KO-*t*-Bu/*n*-BuLi is believed not to be the same as *n*-BuK,[13] the change in regioselectivity cannot be due to a change in the counterion from Li^+ to K^+ alone, nor can one ascribe the change to a greater dissociation of the ion pair since crown ethers had no effect on the regioselection. A possible role is the association of the *tert*-butoxide anion with either the metal ion, or with the silicon moiety, thus giving greater steric hindrance to α-alkylation.

A series of silylallyl anions were prepared where the substituents on silicon were varied.[14] When the substituents changed from methyl to ethyl to propyl, it was found that on alkylation of the corresponding anions (**15**, **16**, and **17** respectively), the ratio of γ- to α-alkylation increased to nearly 40:1 with increasing bulk (Table 1). With the even bulkier (triisopropylsilyl)allyl anion (**18**),[15] the selectivity of γ- to α-alkylation can be as high as 99:1 (Scheme 2).

Table 1. Steric Effect on Regioselection of Alkylation of Silylallyl Anions Generated from Schlosser's Base (For reaction conditions, see ref 14)

silylallyl anion	alkyl halides	ratio 14:13
15: R^1 = Me	$(Me)_2CH(CH_2)_3Cl$	4/1
	$THPO(CH_2)_6Br$	7/1
16: R^1 = Et	n-$C_{12}H_{25}Br$	18/1
	$THPO(CH_2)_6Br$	22/1
17: R^1 = Pr	n-PrBr	46/1
	$THPO(CH_2)_6Br$	36/1

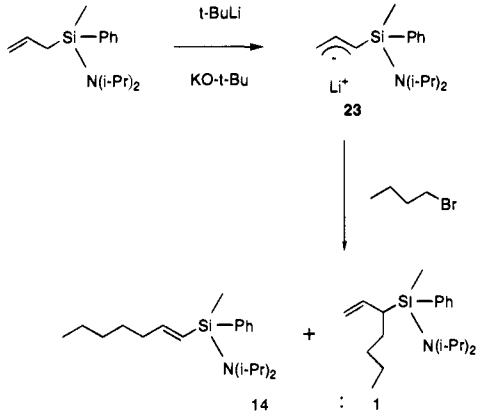
Scheme 3



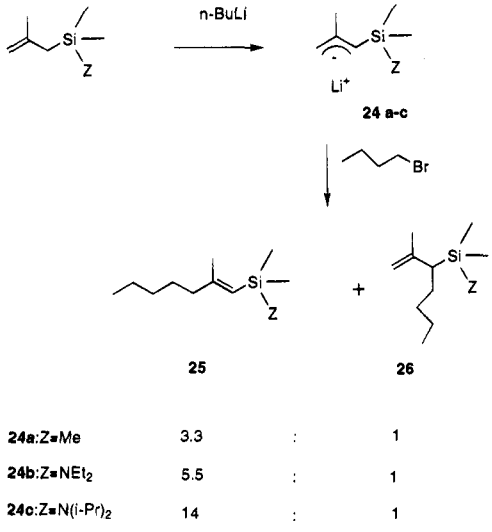
It is clear that by taking advantage of the steric effect on silicon, highly regioselective γ-alkylation of silylallyl anions can be achieved. Furthermore, the γ-isomers formed in these reactions are always exclusively the *E*-isomers, suggesting that the exo orientation of these anions has been maintained as the substituents on silicon become bulkier. In the context of synthesis, the γ-alkylation products are (*E*)-vinylsilanes, and their stereospecific transformations into disubstituted alkenes have been applied to the syntheses of a number of insect sex pheromones.[16]

A similar steric effect was in play in the alkylation of aminosilylallyl anions. It was found that the diisopropylaminosilyl compound **19**, in conjunction with the use of Schlosser's base, provided high γ-selectivity in the reactions with alkyl halides, leading preferentially to **20** over **21** with >95% γ-selectivity (Scheme 3).[17] This approach has been used in the preparation of *exo*-brevicomin (**22**).[18] It should be noted that in the case of (diisopropylaminosilyl)allyl anion, replacing the methyl groups on silicon by phenyl groups (**23**) did not lead to much greater γ-selectivity in the alkylation reactions (Scheme 4).[19]

Scheme 4



Scheme 5



The alkylation of 1-silyl-2-methylallyl anion **24**, prepared by treatment of the parent allylsilanes with Schlosser's base, has been examined.[20] It was found that replacement of a methyl group (**24a**) on silicon by a diethylamino group (**24b**) raised the γ:α (**25**:**26**) ratio from 3.3:1 to 5.5:1 (Scheme 5). Introduction of the bulkier diisopropylamino group **24c** allowed the γ:α ratio to reach 14:1. Equally important is the observation that the vinylsilanes **25** have the *E* stereochemistry, thus suggesting that the anions **24** probably retain the exo stereochemistry in spite of the presence of the methyl group at C2 position. The γ-regioselective alkylation of **24c** allowed the facile construction of **27**, from which the vinylsilanol was easily obtained. Sharpless asymmetric epoxidation followed by protodesilylation gave the optically active compound **28** which was easily converted to the aggregation pheromone of female southern pine beetle, (*S*)-(−)-frontalin (**29**) with 85% ee (Scheme 6).[21]

Scheme 7

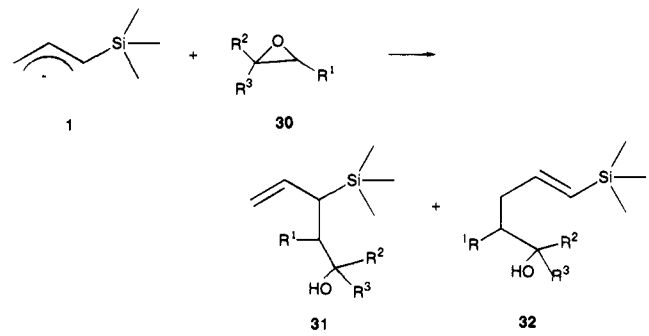


Table 2. Regioselectivity of Reaction of Silylallyl Anion 1 with Epoxides

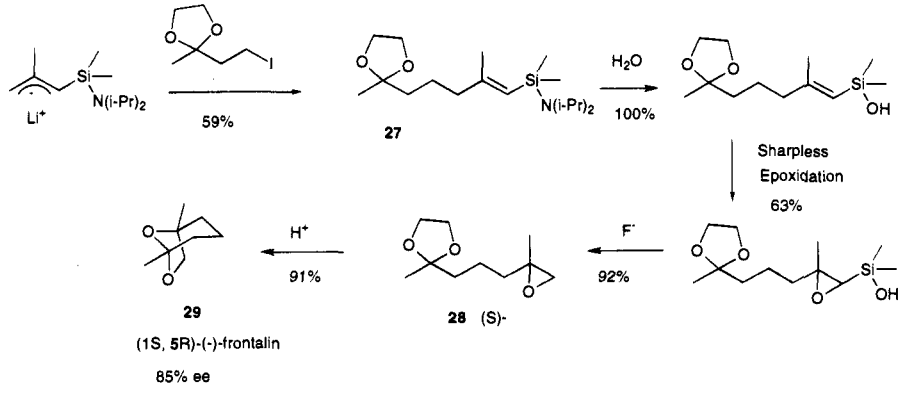
oxirane **30**		ratio **31**:**32**
$R^1 = R^2 = R^3 = H$		>10:<1
$R^1 = R^3 = H$, $R^2 = Me$		4.5:1
$R^1 = R^2 = H$, $R^2 = Et$		2:1
$R^1 = R^2 = Me$, $R^3 = H$	cis	1:2
	trans	1:2.5
$R^1 = R^2 = -(CH_2)_4-$, $R^3 = H$		1:6
$R^1 = R^2 = -(CH_2)_4-$, $R^3 = Me$		<1:>10

Steric effect appeared to be the controlling factor as well in the ring opening of oxiranes by silylallyl anions. [(Trimethylsilyl)allyl]lithium reacted with epoxides **30** to give a mixture of the α- and γ-alkylation products **31** and **32** respectively (Scheme 7). When ethylene oxide and monosubstituted derivatives were used, the reaction showed a preference for α-adducts. However, for 1,2-disubstituted and 1,1,2-trisubstituted epoxides, the reaction gave predominantly the γ-adducts (Table 2). Similarly, sterically demanding substituents on silicon showed a directing effect favoring the γ-adducts.[22]

3.2. α-Regioselectivity

More demanding is the question of whether the alkylation of the silylallyl anion can be controlled to give regioselectively the α-isomer. Since complex-induced proximity effect has been proven to be useful in controlling regioselection in reactions of organo-

Scheme 6



Scheme 8

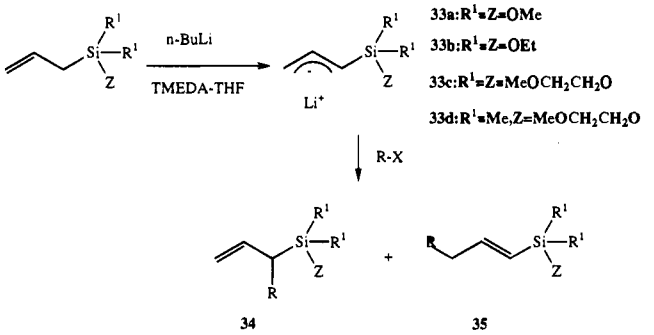
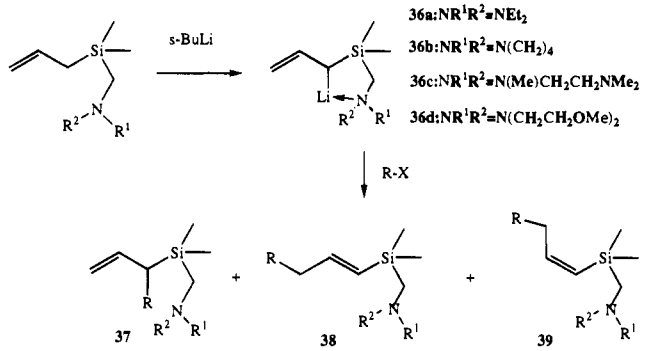


Table 3. Ratios of Products on Alkylation of Anion 33

anion	R–X	α:γ = 34:35
33a	MeI	91:9
33b	MeI	82:18
33c	MeI	74:26
33d	MeI	86:14
33b	n-$C_6H_{13}I$	34:66
33d	n-$C_6H_{13}I$	65:35

Scheme 9



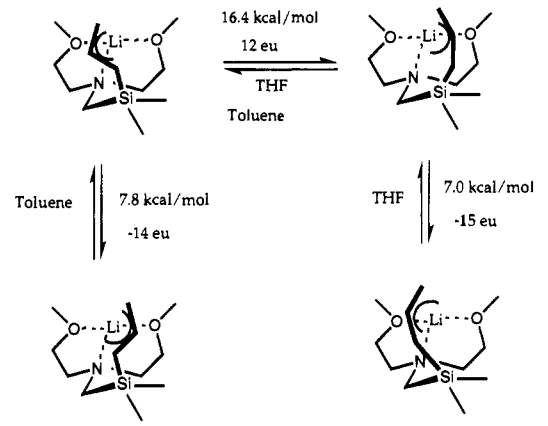
metallic species,[23] the reactions of silylallyl anions **33** with alkoxy groups attached to silicon were examined (Scheme 8). The results are summarized in Table 3. It is interesting to note that, first of all, in all cases, α-selectivity has been improved over those of simple alkyl-substituted (on silicon) silylallyl anions. Secondly, the important factor responsible for the improved α-selectivity (**34**) is not due to the inductive effect of the alkoxy substituent, since the anion **33c**, with three methoxyethoxy groups, is less α-selective in its reaction with methyl iodide than the anion **33d**, with only one methoxyethoxy group on silicon. The improved α-selectivity was attributed to the chelation of the lithium ion with the alkoxy group thus localizing the lithium ion at the C1 position, and favoring α-alkylation.

That being the explanation, a series of aminomethyl-substituted silylallyl anions (**36**) was prepared and their alkylation reactions were examined, on the expectation that the substituents in **36** may well be more effective ligands for the lithium ion (Scheme 9).[24] The results are summarized in Table 4. α-Regioselection indeed improved substantially in these cases, with methylation giving nearly 100% the α-isomer. The regioselection was quite sensitive to solvent effect, with ether a much better solvent than tetrahydrofuran in giving enhanced α-regioselection. Finally, for the first time, in addition to obtaining the γ-*E*-alkylation products **38**, some γ-*Z*-alkylation

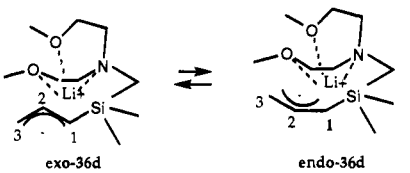
Table 4. Ratios of Products on Alkylation of Anion 36

anion	R–X	solvent	α:γ-*E*:γ-*Z* = 37:38:39
36a	MeI	THF	68:26:6
36b	MeI		58:38:4
36c	MeI		89:5:6
36d	MeI		87:3:10
36a	n-$C_6H_{13}Br$	THF	42:58:0
36c	n-$C_6H_{13}I$		59:37:4
36c	MeI	ether	87:7:6
36d	MeI		100:0:0
36c	n-$C_6H_{13}I$	ether	75:25:0
36d	n-$C_6H_{13}I$		95:3:2

Scheme 10



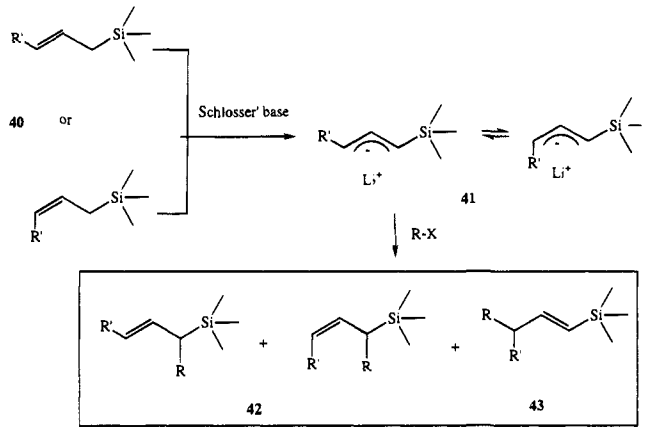
products **39** were observed as well. This led to the suggestion that in these silylallyl anions, there was an equilibrium of both the exo and the endo stereoisomers. Recently, a careful NMR analysis of the anion **36d** confirmed the existence of the exo and endo structures.[25] Furthermore, the **36d**-*exo*/**36d**-



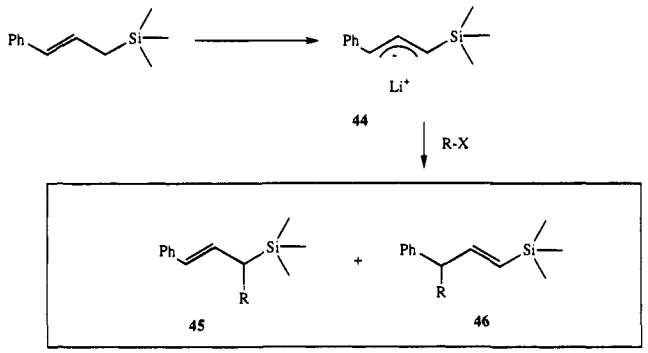
endo ratio changed depending on the solvents, being 0.49 in THF-d_8 and 7.3 in toluene-d_8. These ratios appeared to change very little between 160 and 320 K, less than 3%. The dynamic NMR behavior gave the activation parameters governing the equilibration (Scheme 10). NMR line-shape analysis established that for rotation around the SiC_1-C_2 allyl bond, $\Delta H^{\ddagger}$ was found to be 16 ± 0.5 kcal/mol. In addition, there was rotation of the coordinated Li^+ around the Si–C_1 (allyl) bond, $\Delta H^{\ddagger}$ of which was found to be about 7 ± 0.4 kcal/mol.

In the absence of internal chelation, substituents in the γ-position of the silylallyl anion tend to favor α-alkylation. Thus, (*E*)- or (*Z*)-allylsilanes **40** (R = Me or Pr) were converted to the corresponding anions **41** by Schlosser's base. Alkylation of **41** with alkyl halides gave mainly the α-isomers **42** (Scheme 11). The interesting feature in this system is that the stereochemistry of the double bond in **42** can be controlled depending apparently on the equilibration of the anion **41** between the endo and the exo forms.[26] On the other hand, when the substituent was phenyl, methylation of the anion **44** gave a nearly equal

Scheme 11



Scheme 12



mixture of α- and γ-products (**45** and **46**).[27] Interestingly, the double-bond geometry in either **45** or **46** was *E*, suggesting that the anion **44** existed solely in the exo,exo conformation (Scheme 12).

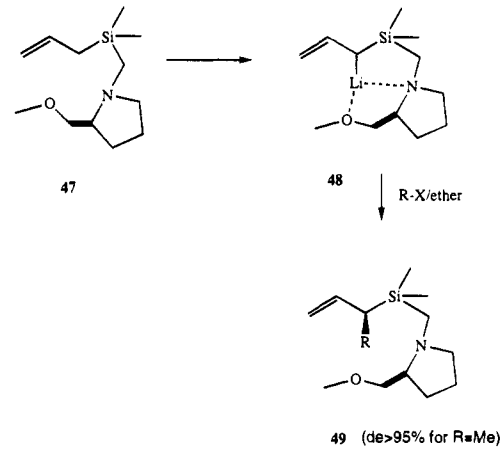
3.3. Asymmetric Induction

The enhanced α-regioselectivity and the NMR study both indicated that in anions such as **36**, the coordinating ligand, the cation, and the anion were tightly bound. If the coordinating ligand is chiral, one might expect the alkylation to be stereoselective.

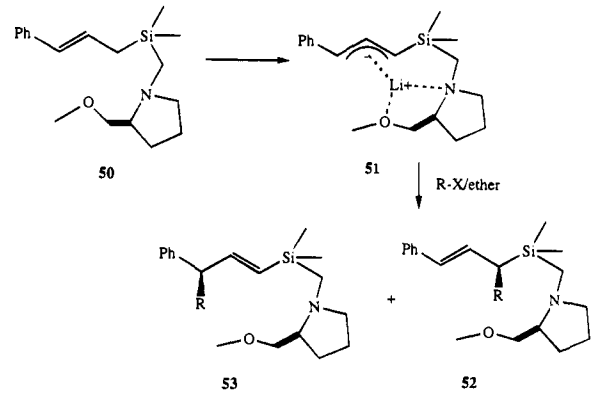
Chiral (aminomethyl)allylsilane **47** was deprotonated to the corresponding anion **48**. Methylation of **48** in ether not only gave the α-product **49** predominantly (87%), but as one diastereomer (de > 98%). A bulkier alkylating agent such as *n*-hexyl iodide gave somewhat lower α-selectivity (63%) but still excellent diastereoselectivity (Scheme 13).

A more thorough investigation was carried out with the chiral silylcinnamyl system **50**. With (*S*)-(+)-(methoxymethyl)pyrrolidinyl moiety as the chiral component, the anion **51**, on alkylation with primary alkyl halide, gave largely α-alkylation product **52** with excellent diastereoselectivity (de > 90%) if the alkylation was carried out in ether, pentane, or toluene as solvent (Scheme 14). With THF or DME as the solvent, the alkylation of the same anion gave both poor α-selectivity as well as poor diastereoselectivity in the α-product formed. Alkylation of **51** with isopropyl iodide, a secondary halide, gave predominantly the γ-product **53** irrespective of the solvent used. However, diastereoselectivity of the γ-product **53** remained quite high (de = 64−78%) if the reaction was carried out in ether or toluene, but

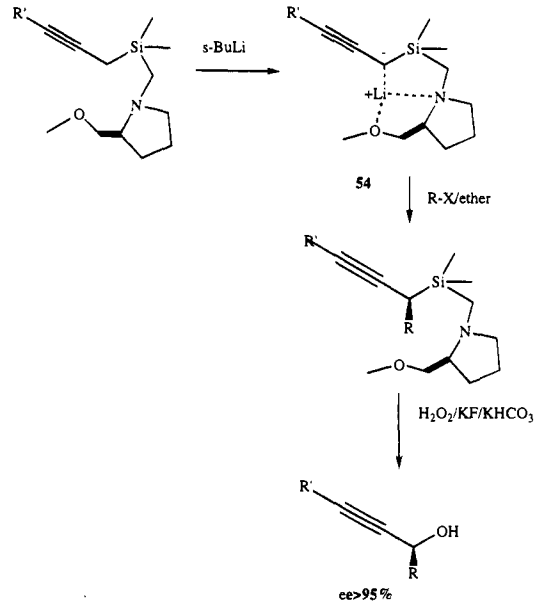
Scheme 13



Scheme 14

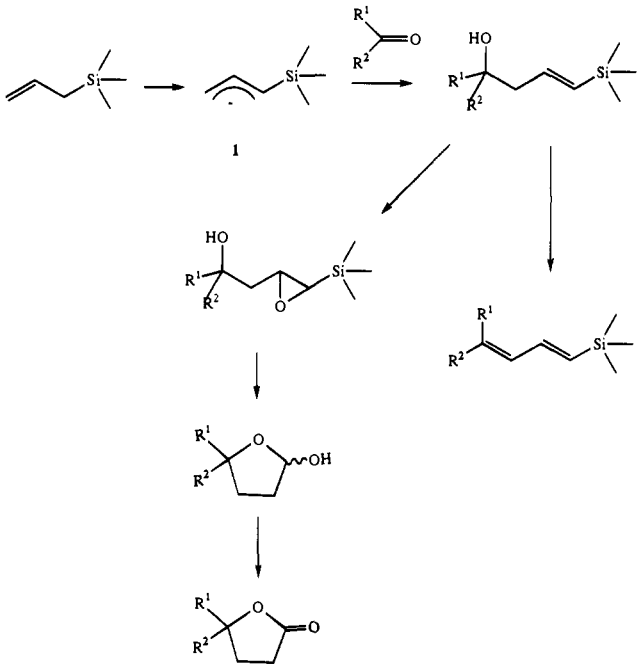


Scheme 15

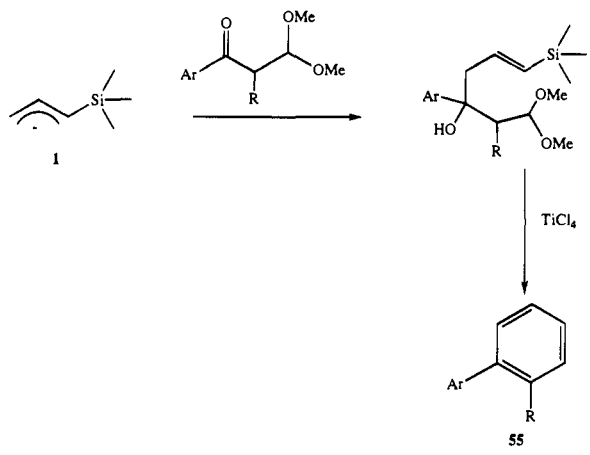


became poor if the reaction was carried out in THF.[28] From the absolute configurations of the products obtained, it can be concluded that for reactions occurring in less coordinating solvents (toluene or ether), the *exo,exo*-silylcinnamyl anion **51** is alkylated from the same face whether the electrophile is large (γ-selective) or small (α-selective). It is worth noting that in the case of **53**, asymmetric induction took place at a site quite remote from the existing chiral center.

Scheme 16



Scheme 17



Silylpropargyl anions **54** bearing the same chiral auxiliary on silicon have been alkylated with excellent regio- and diastereoselectivity as well.[29] Oxidative cleavage[30] of the silyl moiety gave the corresponding chiral (*S*)-propargyl alcohols in high optical purity (ee > 95%) (Scheme 15).

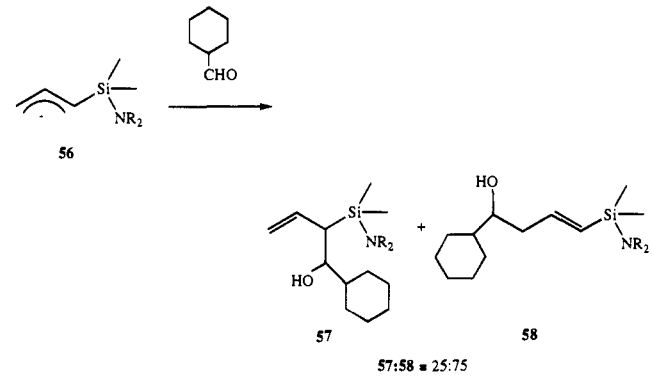
4. Addition to Carbonyl Compounds

4.1. γ-Regioselectivity

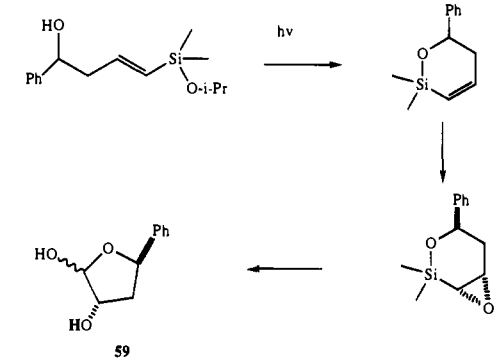
The early work by Corriu[31] and Magnus[32] establish clearly that α-silylallyl anions react with carbonyl compounds to give preferentially the γ-addition products (Scheme 16) and this has been developed as a useful synthetic approach for the syntheses of γ-lactols, γ-lactones, and 1-silyl 1,3-dienes.[33]

The vinylsilanes thus obtained can also undergo intramolecular electrophilic substitution to form cyclic compounds. An example of this is the synthesis of unsymmetrical biphenyls **55** according to Scheme 17. In this case the regiospecificity of the aromatic ring being formed is determined by the γ-selectivity of the silylallyl anion and the relative reactivities of the electrophilic components of the ketoacetal.[34]

Scheme 18



Scheme 19

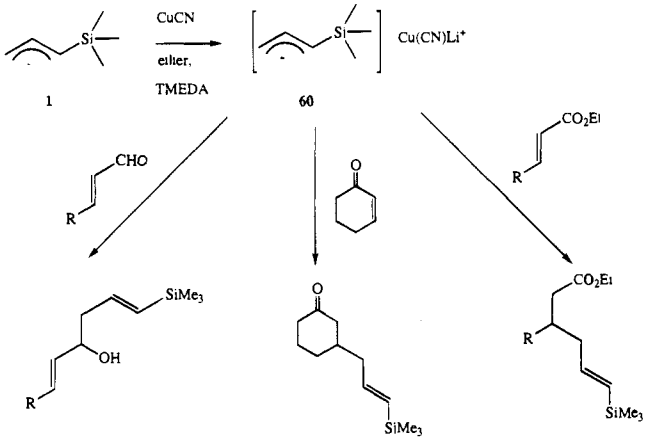


With (aminosilyl)allyl anion **56**, reactions with aldehydes (e.g. cyclohexanecarboxaldehyde) gave a mixture of α- and γ-products (**57** and **58**) in a 25:75 ratio (Scheme 18). The γ-selectivity was further improved by adding copper cyanide to the anion in the reaction system.[35] The regioselectivity was also found to be dependent on the nature of the amino group on silicon. The γ-selectivity increased with a decrease of steric bulkiness of the amino group. These results were interpreted by the suggestion that the counterion was located at the α-position, whereas the attack on the carbonyl compounds took place at the γ-position via a S_E2' type process. The silafunctional vinylsilane thus obtained has been transformed into 2-deoxy-C-nucleoside **59** by a photoisomerization–oxidation sequence (Scheme 19).[35]

Similar copper species of (trimethylsilyl)allyl anion (**60**) reacted with α,β-unsaturated esters and ketones in a 1,4-addition fashion at the γ-position. However, reactions with α,β-unsaturated aldehydes took place in a 1,2-addition mode (Scheme 20).[36] [(Timethylsilyl)allyl]lithium also added at the γ-position to naphthyloxazolines in good yields.[37]

In all the reactions examined thus far, the γ-adduct vinylsilanes have inevitably the *E* stereochemistry at the double bond. The high stereoselectivity is ascribed to the structure of the silylallyl anion which adopts the exo conformation **6**. It is clear from the alkylation studies mentioned in section 3, silylallyl anions with a pendant ligand on silicon can adopt the endo conformation as well. This raises the possibility of having γ-(*Z*)-vinylsilanes as products in these reactions. Reactions of **36d** with a number of carbonyl compounds indeed gave the γ-products (Scheme 21) as a mixture of *E* and *Z* geometrical isomers (**61** and **62**).[38] Furthermore, using acetone

Scheme 20



Scheme 21

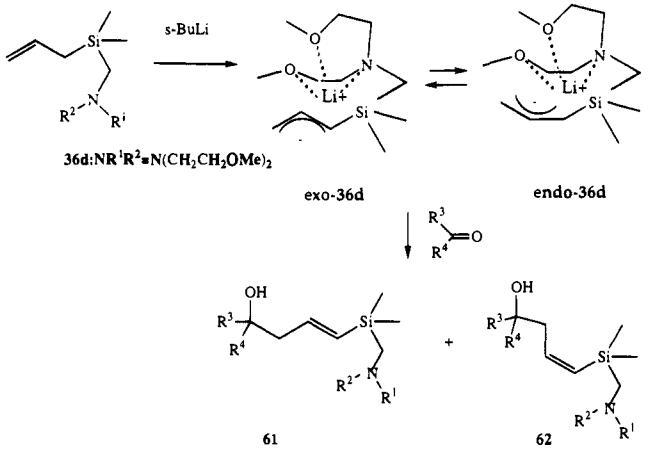


Table 5. Ratios of Products on Reactions of Anion 36d with Acetone

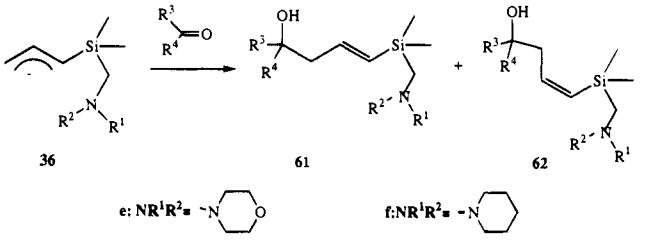
solvent	temp, °C	yield, %	*E*:*Z* = **61**:**62**
THF	−60	75	1.2:1
THF−TMEDA	−60	91	1:1
THF−HMPA	−60	89	2:1
DME	−60	82	5:1
ether	−60	74	7:1
toluene	−60	82	>10:1
THF	−30	92	1.5:1
THF	−80	90	1:1.3
THF	−100	90	1:2

as the common electrophile, it was possible to study the ratio of **61**/**62** as a function of reaction solvent and temperature (Table 5). It was interesting to note that the highest *E*/*Z* ratio was obtained in toluene, and the lowest in THF, results which are in agreement with the exo/endo ratio of **36d** observed by NMR.[25] By changing the pendant ligand from the bis(2-methoxyethyl)amino group to the morpholinyl (**36e**) or piperidinyl (**36f**) group, it was possible to develop specific reaction conditions to obtain predominantly (*E*)- or (*Z*)-vinylsilanes (Table 6). Presumably, the somewhat less effective ligand on the silicon permitted more effective participation of the DME molecule to favor the endo conformation of the anion.

4.2. α-Regioselectivity

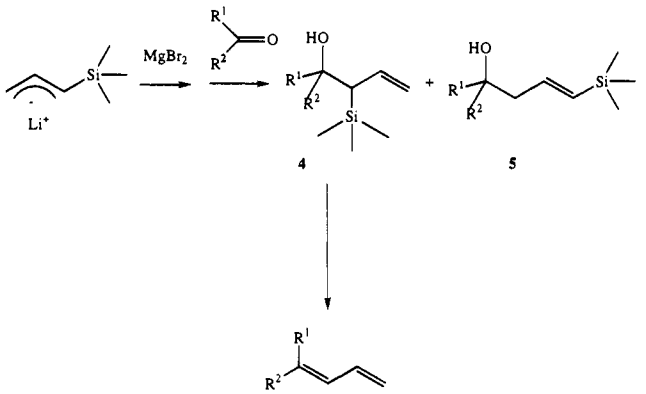
While α-silylallyl lithium reacts with carbonyl compounds to give regioselectively the γ-addition

Table 6. Ratios of Products on Reactions of Anion 36 with Carbonyl Compounds



anion	carbonyl	solvent	temp, °C	yield, %	*E*:*Z* = **61**:**62**
36e	acetaldehyde	toluene	−78	66	>10:1
		toluene−DME	−90	92	1:6
36e	acetone	toluene	−78	95	>10:1
		toluene−DME	−90	90	1:6
36e	benzaldehyde	toluene	−78	95	>10:1
		toluene−DME	−90	83	1:7
36f	acetone	toluene	−78	85	>10:1
		toluene−DME	−90	76	1:7

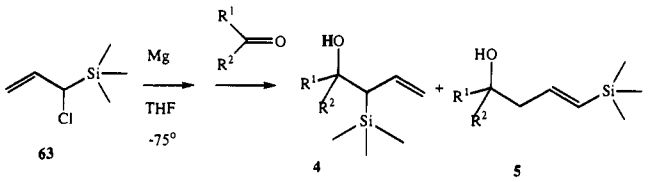
Scheme 22



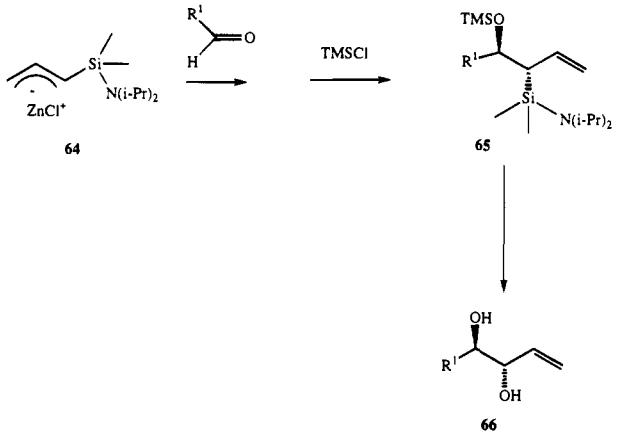
products, it is possible to direct the regioselectivity to α-addition by the proper use of counterion or ate complex. As early as 1978, Chan and Lau reported that addition of freshly prepared anhydrous magnesium bromide to a solution of [α-(trimethylsilyl)allyl]-lithium (Scheme 22) followed by addition of the carbonyl compounds gave preferentially the α-addition products **4**, in addition to the γ-addition products **5**. The extent of α-addition depended on the nature of the carbonyl compound. For ketones, α-selectivity could be as high as 95%, but with aldehydes it was about 60%. Interestingly, the α-adduct derived from aldehyde was found to be one diastereomer which could be converted stereospecifically to one stereoisomer of the 1,3-diene.[39] Subsequently, Shimizu and co-workers found that if the Grignard reagent was generated from the precursor chloride **63**, the reaction with ketones occurred only at the γ-position giving the product **5** regardless of solvent or temperature used. However, for aldehydes, the α-addition predominated, giving the β-hydroxysilane **4** (Scheme 23).[40] An explanation that was put forward to account for these different results was that in Chan's case, a mixed bimetallic complex with Mg and Li was formed, whereas in Shimizu's case, a Grignard reagent of solely Mg complex was involved. Presumably, the two species displayed different regioselectivity.[40]

The reverse selectivity for reactions with ketones and aldehydes was also investigated using zinc

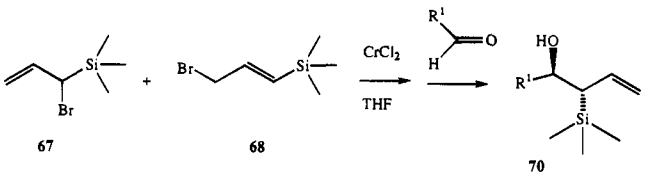
Scheme 23



Scheme 24



Scheme 25



chloride. While it was known that adding zinc chloride seemed to have little effect on the γ-selectivity in the reaction of [(trimethylsilyl)allyl]lithium with ketones, the case was different with (aminosilyl)allyl anion. The [(aminosilyl)allyl]zinc chloride **64**, generated from the precursor lithium species and zinc chloride, reacted with aldehydes to give the anti-α-addition product **65** (Scheme 24). The presence of the bulky diisopropylamino group in the zinc reagent **64** was essential for the isolation of **65**. Otherwise formation of 1,3-dienes under the reaction conditions occurred from the Peterson olefination. The silyl moiety in **65** can be conveniently oxidized to the corresponding hydroxy group stereospecifically with retention. The sequence of reactions was therefore a good method for the synthesis of erythro 1,2-diol (**66**) skeleton.[41]

Similar to the case of Grignard reagent, [(trimethylsilyl)allyl]chromium reagent, generated from a 2:1 mixture of the allyl bromides **67** and **68** with $CrCl_2$, reacted with aldehydes to give α-addition products **70**. Again, in this case, only the anti-isomer was obtained (Scheme 25).[42] One assumes that in the Mg, Zn, or Cr cases, a chair transition state **69** was involved to account for the anti stereochemistry observed in the α-addition products.

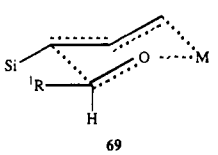
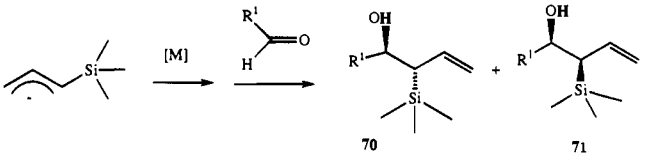
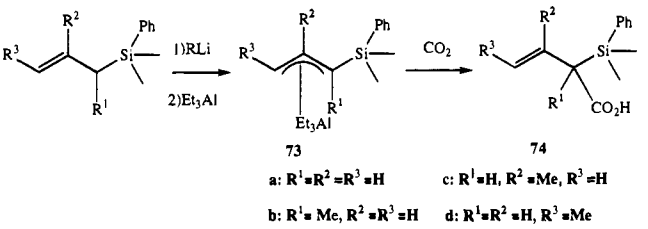


Table 7. Influence of [M] on the ratio of 70:71

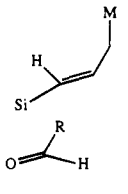


[M]	R^1	anti:syn = **70:71**
Et_3Al	Ph	43:37
Et_3Al	*n*-Pr	100:0
Et_3Al	*i*-Pr	50:35
$EtAlCl_2$	Ph	88:4
$EtAlCl_2$	*n*-Pr	100:0
$Ti(O\text{-}i\text{-}Pr)_4$	Ph	99:1
Cp_2TiCl	Et	100:0
Cp_2TiCl	*t*-Bu	100:0
Bu_3SnCl	Ph	0:100
Bu_3SnCl	$n\text{-}C_9H_{19}$	0:100
n-Bu-9-BBN	Ph	96:2
$c\text{-}C_5H_9BCl_2$	Ph	100:0

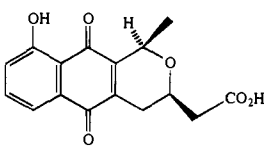
Scheme 26



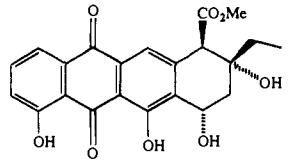
Addition of various organoaluminum,[43] -boron,[44] -titanium,[45] -zinc,[46] and -tin[41] reagents to the silylallyl anion also directed its reactions with aldehydes to the α-addition products. In these cases, the silyl group acted as a γ-substituent in the allylmetal systems. The stereochemical course of the reactions of these allylmetals with aldehydes followed that expected of the parent allylmetal systems (Table 7). That is, in the cases of boron, aluminum, titanium, and zinc complexes, the reactions gave anti stereochemistry presumably via a cyclic transition state similar to **69**, leading to the diastereoisomer **70**. On the other hand, the tin compounds induced a syn preference via an acyclic transition state **72**, forming the syn-isomer **71**.



Carboxylation of silylallyl anion–triethylaluminum ate complex **73a–d** gave the carboxylic acids **74a–d** with high α-selectivity (Scheme 26).[47] The introduction of a phenyl substituent on silicon served to increase the α-selectivity to virtually 100%. This method is quite useful for the preparation of α-silyl β,γ-unsaturated carboxylic acids and has been used for the synthesis of the antibiotics **75** and the anthracyclinone **76**.



75



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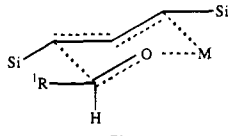
4.3. Reactions of Substituted Silylallyl Anions

For the symmetrically substituted 1,3-bis(trimethylsilyl)allyl anion **11**, there is no issue regarding regioselectivity, but there is interesting stereochemical consideration. The reactions of **11**, as the lithium compound, with carbonyl compounds were reported to give low yield and low stereoselectivity.[48] Both the yield and the stereoselectivity were substantially improved by the addition of $MgBr_2$, or trimethyl borate,[49] or Cp_2TiCl[50] to the lithium compound **11** prior to the addition of the aldehydes. In all these cases, the products were mainly the anti-isomer **77**, with the anti selectivity as high as 98% (Scheme 27). This high stereoselectivity can be explained on the basis of a six-membered chair transition state **79** with the bis-silylallyl system adopting the extended exo, exo conformation as reported by X-ray structure determination.[10]



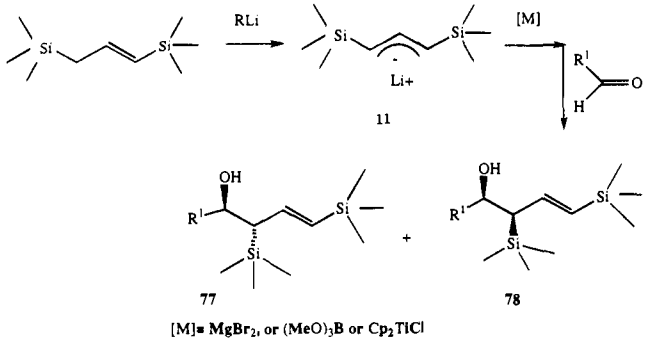
79

Alkyl-substituted silylallyl anions present additional complexity with regard to both regio- and stereochemistry. It was found that the reaction of 1-(trimethylsilyl)-but-2-enyl anion **80** with Cp_2TiCl afforded presumably the titanium complex **81** which then reacted with propanol with exclusive γ-regioselectivity. The products were the anti- and syn-alcohols **82** and **83** in a 86:14 ratio (Scheme 28).[48]

On the other hand, if the analogous system was generated from the mixture of allyl bromides **84** and **85** with $CrCl_2$, followed by reaction with benzaldehyde, the products were a mixture of the γ-adducts **86**–**88**, as well as the α-adducts **89** and **90**. In this particular example, the α/γ regioselectivity was 10:90, and the anti-/syn diastereoselection was 71:19 for the γ-adducts, but entirely anti for the α-adducts (Scheme 29).[40] In both the α- and the γ-adducts, *E*- and *Z*-stereoisomers for the double bond were formed. These results tend to suggest that the silylallyl chromium system may exist in a number of conformations.

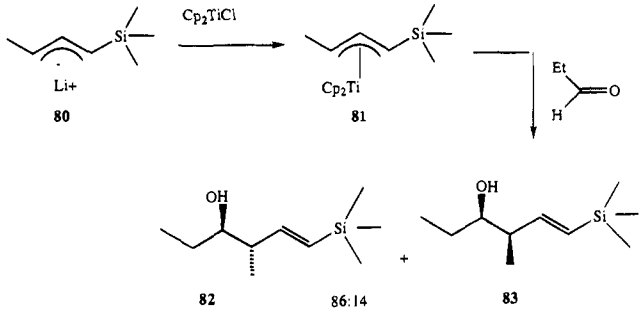
The highly substituted silylallyl anion **91** could be generated from the precursor **92** with *sec*-BuLi/TMEDA (Scheme 30).[51] The anion **91** reacted with alkyl halides, ketones and *N*,*N*-dimethylbenzamide to give the corresponding γ-adducts **93**, **94**, and **95**, respectively. Reaction of **91** with benzaldehyde gave, however, a mixture of products **96**–**98**. The diene **96** was believed to be formed via the α-adduct **99**

Scheme 27

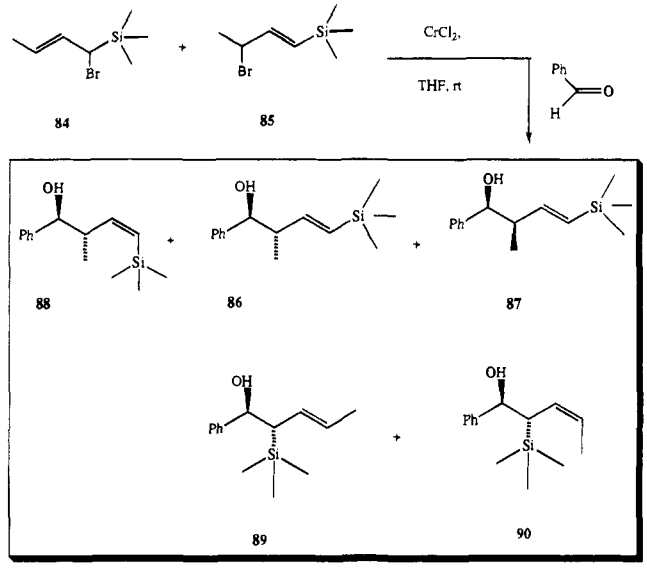


[M]= $MgBr_2$, or $(MeO)_3B$ or Cp_2TiCl

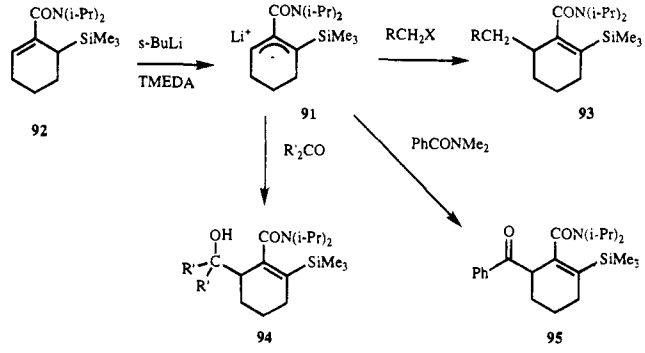
Scheme 28



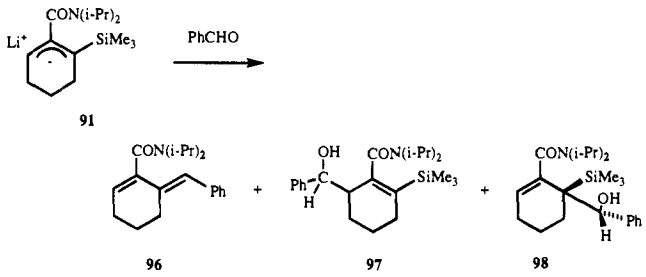
Scheme 29



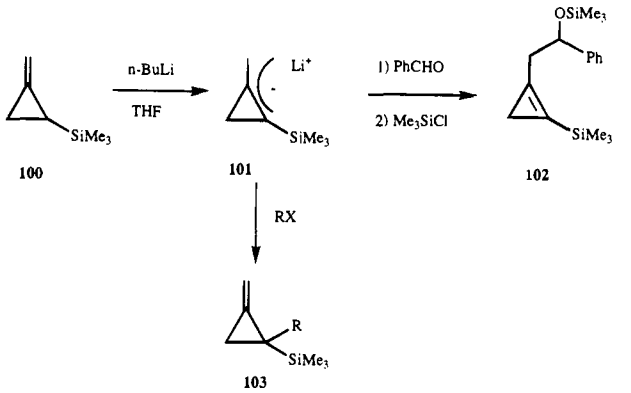
Scheme 30



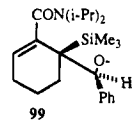
Scheme 31



Scheme 32



followed by an in situ Peterson elimination (Scheme 31).

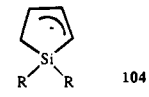


Another interesting example is the silylated methylenecyclopropane **100**. Treatment of **100** with *n*-BuLi in THF generated the anion **101**. Reaction of **101** with benzaldehyde followed by quenching the reaction mixture with trimethylchlorosilane gave the γ-product **102**, in spite of the highly strained cyclopropene structure. On the other hand, alkylation of **101** gave the α-alkylation product **103** (Scheme 32).[52] In the case of alkylation, the strained cyclopropene structure was sufficient to direct the reaction to the α-position over the competing γ-alkylation.

5. Cyclenic and Polyenic Silylallyl Anions

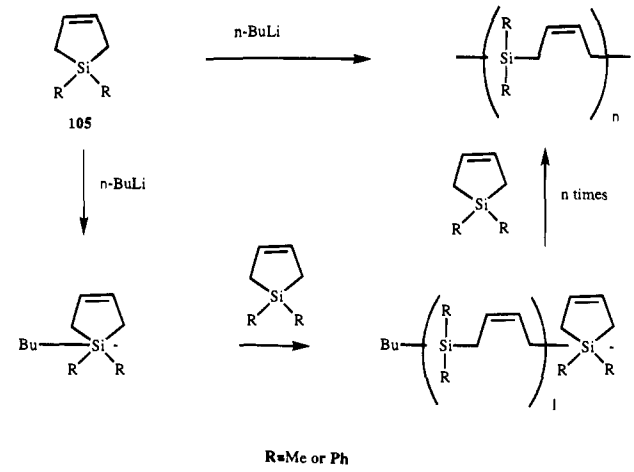
5.1. Cyclenic Silylallyl Anions

The anion **104**, derived from the metalation of 1-silacyclo-3-pentane (**105**), must have an endo orientation for the silylallyl system. When the substit-

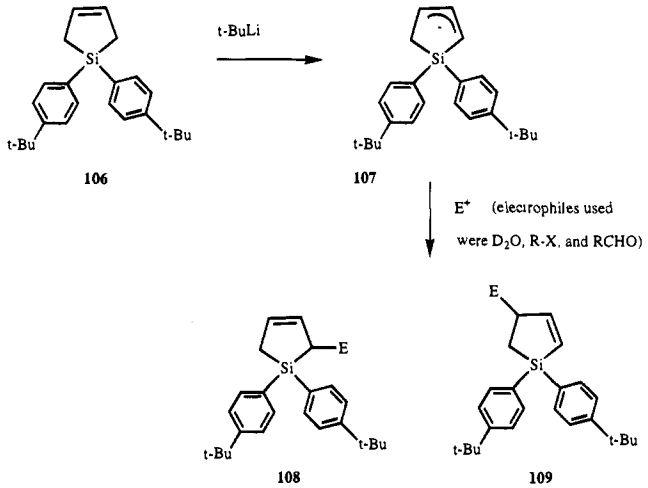


uents on silicon were methyl or phenyl, treatment of **105** with *n*-BuLi led to polymerization,[53] presumably by a ring-opening process outlined in Scheme 33. The polymer was characterized by ^1H and ^{13}C NMR and the ring-opening process may well serve as a general method for the preparation of silicon-containing polymers. The polymerization reaction could be suppressed by the use of an electron-donating sub-

Scheme 33



Scheme 34



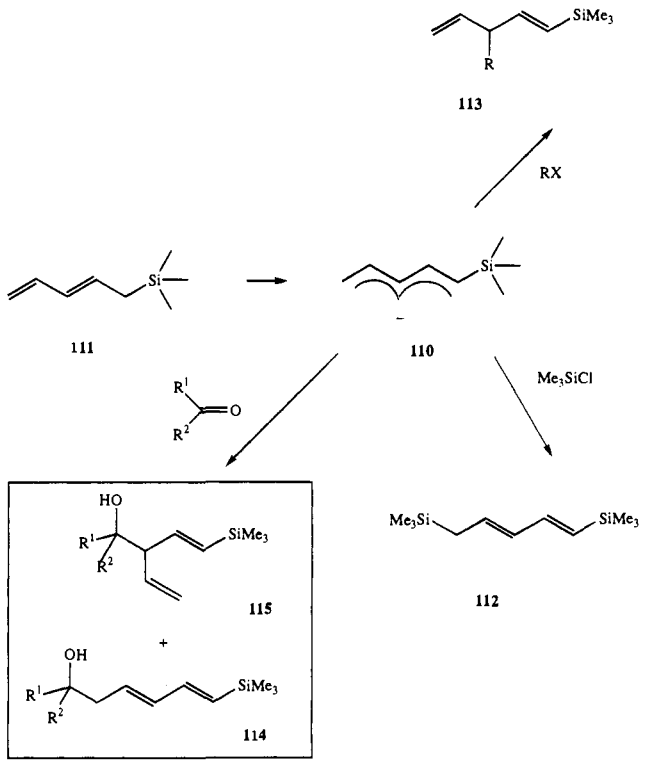
stituent on the phenyl ring. Thus, the bis(*p-tert*-butylphenyl)silacyclopentene (**106**) was cleanly deprotonated to give the anion **107** which reacted with a number of electrophiles such as D_2O, R–X, or RCHO (Scheme 34) to give a mixture of α- and γ-products **108** and **109**, respectively. The regioselection appeared to be dependent on the size of the electrophile, with the bulkier electrophile preferring reaction at the γ-position.[54]

5.2. Polyenic Silylallyl Anions

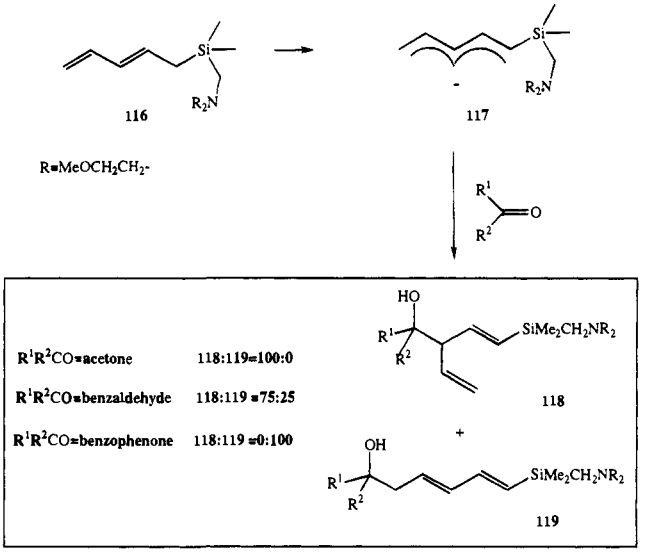
The extended conjugation in polyenic silylallyl anions gives rise to greater complexity in the question of regioselectivity. The anion **110**, derived from the metalation of the pentadienylsilane **111** using lithium dialkylamides, reacted with trimethylchlorosilane to give exclusively the ϵ-product **112**. When alkyl halides were the electrophiles, the reaction gave the γ-products **113**.[55] With carbonyl compounds as the electrophiles, a mixture of ϵ- and γ-addition products (**114** and **115**) were obtained with the ϵ-adduct being favored (Scheme 35).[56] A similar trend was observed by Nakamura and co-workers who also reported that γ-selectivity could be enhanced by the use of magnesium, boron, or copper reagents.[57]

The behavior of **110** could be compared with the anion **117** where the silicon bears a pendant ligand. Reactions of **117** with carbonyl compounds showed

Scheme 35



Scheme 36



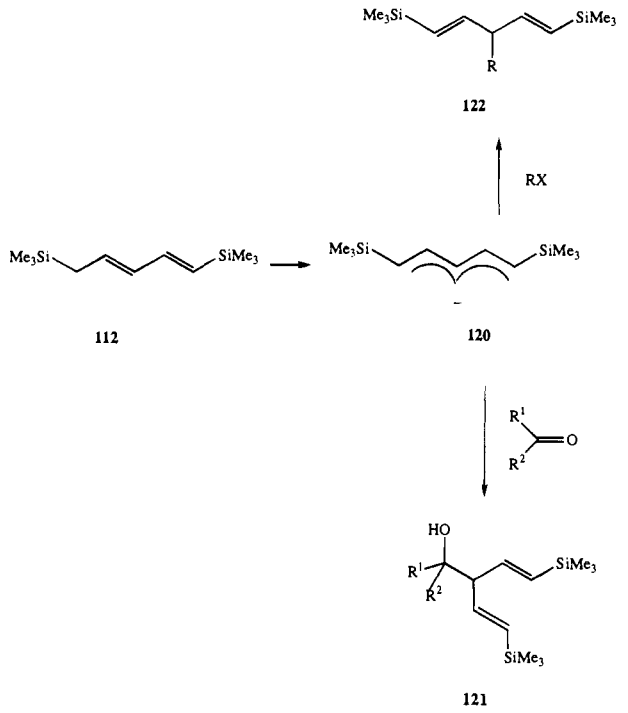
greater preference for γ-addition products **118** over the ϵ-adducts **119** for the sterically less bulky carbonyl compounds (Scheme 36).[58]

The symmetrical 1,5-bis-silylpentadienyl anion **120**, derived from the deprotonation of **112**, reacted with either carbonyl compounds or alkyl halides to give regioselectively the γ-products **121** or **122** (Scheme 37).[55]

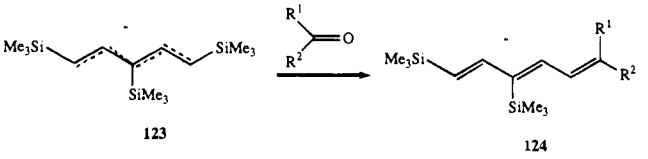
In the case of the 1,3,5-tris-silylpentadienyl anion **123**, it reacted cleanly with aldehydes and ketones to give the trienes **124** (Scheme 38).[55] Here, the regiochemistry can of course be considered as α-, γ-, or ϵ-selective depending on which of the silyl groups is used as the reference.

The reaction of [(trimethylsilyl)cyclopentadienyl]-lithium (**126**) with dimethyldichlorosilane followed by

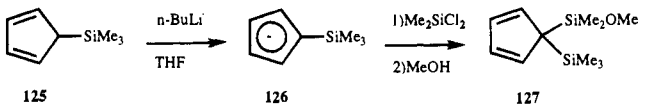
Scheme 37



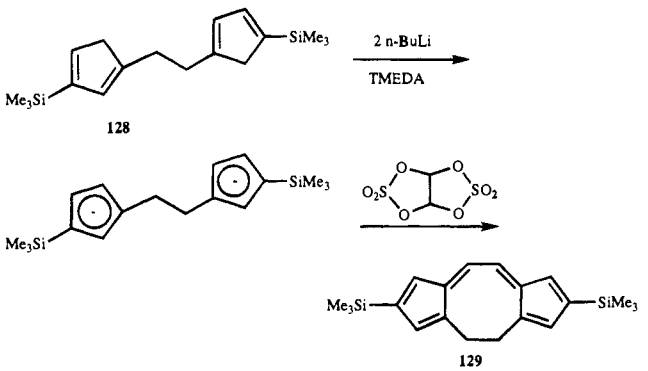
Scheme 38



Scheme 39

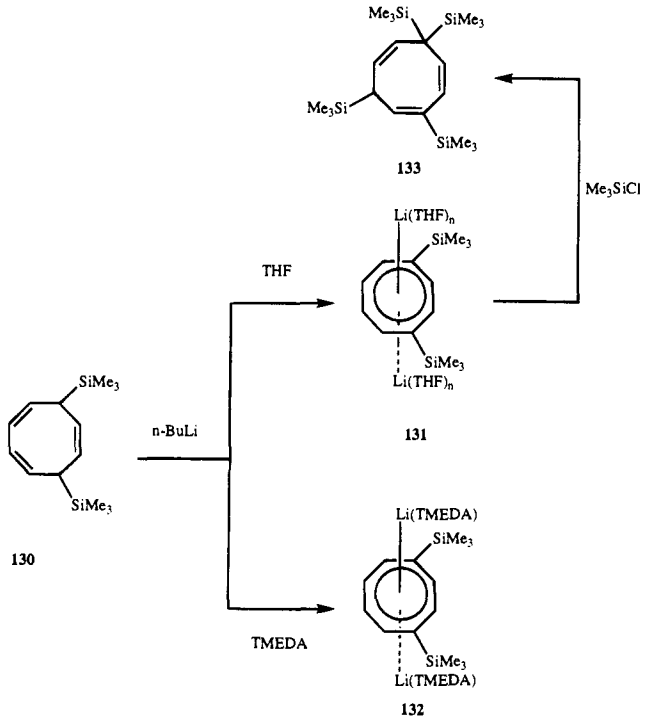


Scheme 40

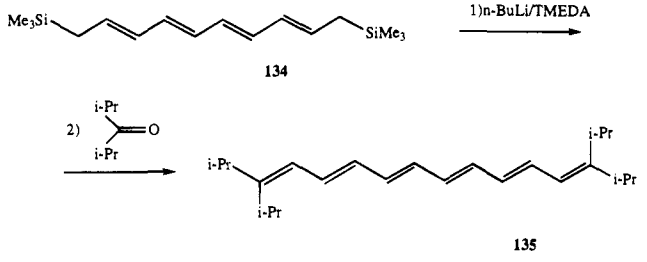


methanolysis in the presence of pyridine yielded the product **127** (Scheme 39).[59] The regiochemistry, while seemingly α-selective, should be considered as ϵ-selective especially in light of the reaction of **110** with trimethylchlorosilane. In that sense, the coupling product **129** obtained from the deprotonation of 1,2-bis[(trimethylsilyl)cyclopentadienyl)]ethane (**128**) and then condensation with glyoxal sulfate (Scheme 40)[60] can be understood as a γ-selective reaction in agreement with the regioselection in the reactions of **110** with carbonyl compounds.

Scheme 41



Scheme 42

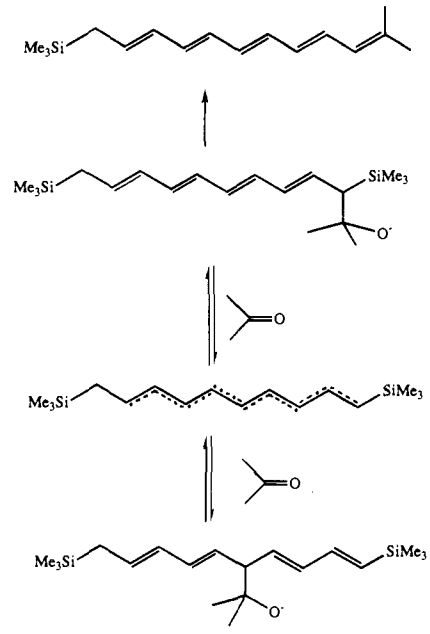


Deprotonation of 5,8-bis(trimethylsilyl)cycloocta-1,3,6-triene **130** with *n*-BuLi/THF or *n*-BuLi/TMEDA gave the dianions **131** and **132**, respectively. The ^{7}Li NMR spectra of the dianions were consistent with a lithium ion symmetrically bound to an aromatic 10π-system as shown in **131** and **132** (Scheme 41).[61] Silylation of **131** with excess trimethylchlorosilane gave the tetrasilyl product **133**. In here, again, it may not be meaningful to refer to the reaction as being α- or γ-selective.

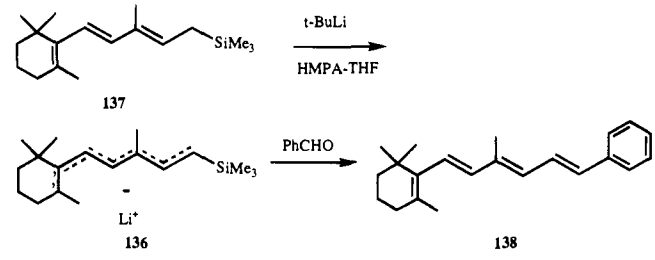
Metalation of the tetraene **134** and subsequent reaction with diisopropyl ketone provided the polyene **135** in 25% yield (Scheme 42).[55] The reaction involved double Peterson olefination. What is surprising in this case is the rather high α-selective addition, somewhat contrary to the situation with the anion **110** which showed ε- or γ-selectivity. It is possible that as the conjugation becomes more extended, the addition reaction becomes reversible. The product distribution is then governed by thermodynamical control upon Peterson elimination (Scheme 43).

This may well explain the reaction of the anion **136**, derived from deprotonation of **137**, with benzaldehyde in giving a good yield of the olefin **138**, again with good α-selectivity (Scheme 44).[62] Steric hindrance at the other positions is probably also a factor in making α-attack more favorable in this case.

Scheme 43



Scheme 44



6. Conclusions

It is clear from this review that reactions of silylallyl anions can now be controlled in some cases to be regio- and stereoselective. The factors governing these selectivities are understood and can be manipulated. This ability to direct the course of the reactions has greatly enhanced the synthetic utility of the silylallyl anions. The challenge in the future is to extend this control to the more complicated polyenic silylallyl systems and to other heteroatom-substituted allylic systems.[2]

7. Acknowledgments

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