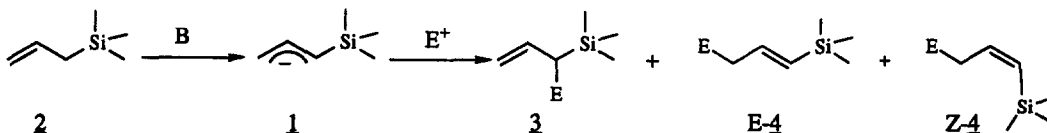


STERESELECTIVE REACTIONS OF α -SILYLALLYL ANIONS WITH CARBONYL COMPOUNDS.

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Abstracts: α -silylallyl anions of the type **1** react with carbonyl compounds at the γ -position, and stereoselectively to give the E- or Z-isomer depending on the reaction conditions. Solvent and reaction temperature play a critical role in the control of stereoselectivity.

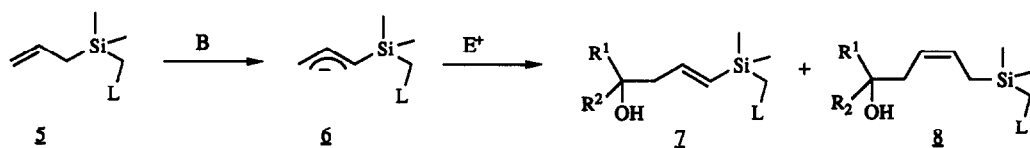
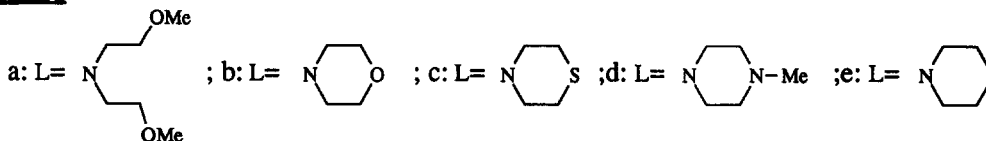
α -Silylallyl anions (**1**), first generated by Corriu *et. al* in the early 70's from the precursor allyl silanes **2**,¹ have been used extensively as synthetic intermediates.² In the reactions of **1** with various electrophiles E⁺, either the α -(**3**) or the γ -E-(**4**) regioisomeric products could be obtained (Scheme 1). Efforts to control the regioselection of these reactions have been reasonably successful.³



Scheme 1

In the case of γ -product, the double bond can assume either the E- or the Z-stereochemistry (E-**4** or Z-**4**). In nearly all the reactions examined so far, and independent of the nature of the electrophiles, the γ -products have inevitably the E- stereochemistry. The high stereoselectivity is ascribed to the structure of the silylallyl anion **1** which seems to adopt exclusively the exo-conformation as evident from recent NMR studies.⁴ Since the E-vinylsilane **4** can be converted to the corresponding Z-vinyl iodide with complete inversion of stereochemistry **2c**,⁵ the overall sequence of reactions has been used advantageously as a highly stereoselective synthesis of Z-alkenes.^{2c} It would be desirable to be able to prepare selectively the Z-vinylsilane **4** as well and to explore its synthetic potentials⁶. Recently in our study of the reaction of silylallyl anions of the type **6** where the silyl moiety contained a group L capable of internal chelation, **2d**,^c we observed a small but significant amount of γ -Z product.

Thus, when **6a** (L=bis-methoxyethylamino), generated from **5a** with *s*-BuLi in THF at -60° for 12 h, was allowed to react with a number of carbonyl compounds, the reactions took place at the γ -position giving the two geometrical isomers **7a** and **8a** in nearly equal proportions and the selectivities did not seem to be affected by the nature of the carbonyl electrophiles (Scheme 2, Table 1). Using acetone as the common electrophile, it was possible to probe the effect of temperature on the stereoselectivity and, by keeping the reaction temperature constant at -60°, the effect of the solvent was also studied (Table 2).

**Scheme 2****Table 1** Reactions of **6a** with Various Carbonyl Compounds

Entry	Reaction Condition ^a			Electrophile	E:Z:7a:8a ^d	Yield ^e
	Solvent	Temp. ^b	Time ^c			
1	THF	-60°	0.5h	Acetone	1.2:1	75%
2	THF	-60°	0.5h	Benzaldehyde	1.2:1	60%
3	THF	-60°	0.5h	Cinnamaldehyde	1.2:1	66%
4	THF	-60°	0.5h	β -ionone	1.2:1	56%
5	THF	-60	0.5h	Cyclohex-2-enone	1.2:1	64%

(a) The carbanion was generated by treating the allylsilane **5a** with *s*-BuLi in THF at -60° for 12h.

(b) The temperature of the reaction of the carbanion with the electrophile.

(c) Reaction time of the carbanion with the electrophile.

(d) Determined by proton NMR on the crude material.

(e) Combined yield of **7a** and **8a** after purification by flash chromatography.

Table 2 Reaction of **6a** with Acetone as Electrophile

Entry	Reaction condition ^a			E:Z: 7a:8a ^c	Yield ^d
	Solvent	Temp. ^b			
1	THF	-60°		1.2:1	75% ^e
2	THF-TMEDA	-60°		1:1	91%
3	THF-HMPA	-60°		2:1	89%
4	DME	-60°		5:1	82%
5	ETHER	-60°		7:1	74%
6	TOLUENE	-60°		>10:1	82%
7	THF	-30°		1.5:1	92%
8	THF	-80°		1:1.3	90%
9	THF	-100°		1:2	90%

(a)The deprotonation was carried out with **6a**, *s*-BuLi and the specified solvent at -25° for 12h.

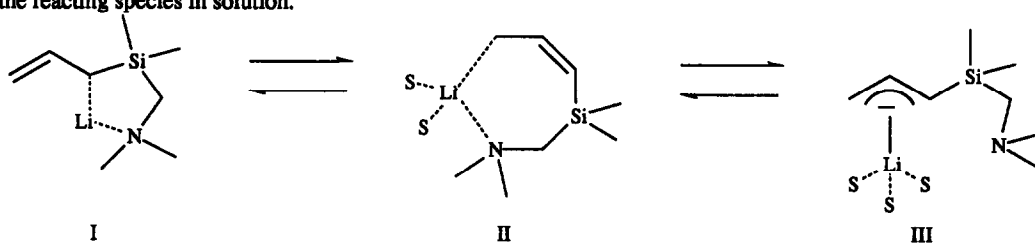
(b)The temperature of reaction of the carbanion with acetone. Reaction time was 15 min in all cases.

(c)The ratio was determined by integration of respective signals on proton NMR of the crude products.

(d)Crude yield.

(e)Combined yield of **7a** and **8a** after purification by chromatography.

These results suggest that silylallyl anions of this class can exist as the following exo-(I), endo-(II) and the open form (III) species. In solvents of high coordinating ability, the open form (III) is probably responsible for the formation of the E-vinylsilanes on reaction with the electrophiles. This is in agreement with the observation in table 2, as the solvent is changed from THF to THF-HMPA the ratio of E/Z increased (entries 1 and 3). In solvents of lower coordinating ability (e.g. ether and toluene, table 2), the exo-(I) structure can lead to a high E/Z ratio as well. The endo-(II) responsible for the formation of the Z products seems to be predominant only in specific complexation systems and solvents (table 2 and 4). The temperature effect observed in table 2 (entries 1,7-9) could be due to the change in relative reactivity between the species (I), (II) and (III) or to a change in relative concentration of these species when the temperature is changed. Further studies by such physical methods as low temperature ^1H and ^{13}C NMR spectroscopy are needed to determine the structures and the relative concentrations of the reacting species in solution.



Scheme 3

After considerable experimentation with a number of different amino derivatives, we found that the morpholino compound **6b** reacted with carbonyl compounds to give selectively either the E- or the Z-isomers depending on the specific reaction conditions (A or B) with even better specificity than with allylsilane **6a**, making the reaction synthetically useful. In method A, the silane **5b** (0.10g, 3.3 mmol) was dissolved in toluene (3.0 ml) and *s*-BuLi (1.3M in *c*-hexane, 1.5 eq) was added at -20°C under an argon atmosphere. After stirring for 24 h at this temperature, the carbonyl compound (1.5 eq) was added to the mixture at -78°C . After 15 mins., ether (20 ml) and conc. ammonium chloride solution (1.0 ml) were added. The organic layer was washed with brine, dried (MgSO_4) and evaporated to give predominantly the products with the E stereochemistry. In method B, the silane **5b** was deprotonated in toluene as before. After stirring for 24 h, dimethoxyethane (0.5 ml) was added and the mixture was stirred an additional 30 mins at -25°C . The carbonyl compound (1.5 eq.) was added slowly to the solution at -90°C .⁷ After 15 mins stirring at this temperature, hexane (20 ml) and conc. ammonium chloride solution (2 ml) were added. The organic layer was washed with brine, dried (MgSO_4) and evaporated to give the products with predominantly the Z-isomers. Separation and purification of the stereoisomers were achieved with flash chromatography using 20 % ethyl acetate in hexanes as eluent.

The critical element in the amino structure required for reversal of stereoselectivity under the two reaction conditions A and B appears to be the presence of the piperidine ring and not the heteroatom in the 4' position. Thus, in the reactions of the silylallyl anions **6b-e** with acetone under the same reaction conditions, the stereoselectivity was more or less the same (Table 3).

The profound differences between the selectivities of the reactions of the allylsilanes anions **6b-e** and the anion **6a** in the presence of DME can be explained by the complexation of the lithium with DME in the case **6b-e** as shown in structure (II) but not in the case of **6a** where the lithium cation is tightly complexed by the bis-methoxyethylamino moiety and where structure (I) should predominate (Scheme 3).

Since Z-vinylsilanes have recently found applications in total synthesis, where they were used in preference to the E-isomers.⁶ The present method represents a short viable route to this type of synthetic intermediates.

Table 3 Reaction of anion **6b-g** with Various Electrophiles Under Reaction Conditions A and B

Entry	anion	Electrophiles	Condition ^a	E:Z:7:8 ^b	Yield ^c
1	6b	Acetaldehyde	A	>10:1	66% (33%)
			B	1:6	92% (63%)
2	6b	Acetone	A	>10:1	95% (60%)
			B	1:6	90% (75%)
3	6b	Benzaldehyde	A	>10:1	95% (82%)
			B	1:7	83% (72%)
4	6b	Cinnamaldehyde	A	>10:1	90% (72%)
			B	1:5	97% (65%)
5	6b	2-Cyclohexen-1-one	A	>10:1	93% (85%)
			B	1:6	89% (61%)
6	6b	β -ionone	A	>10:1	83% (52%)
			B	1:8	74% (56%)
7	6c	Acetone	A	>10:1	80% (47%)
			B	1:6	94% (63%)
8	6d	Acetone	A	>4:1	55%
			B	1:7	68%
9	6e	Acetone	A	>10:1	85%
			B	1:7	76%

a) For reaction condition A and B, see text.

b) The ratio is determined by integration of the vinylic and methylic proton signals on the NMR of the crudes

c) Yields of crude material after work up and evaporation under vacuum. The crudes listed in entries 1-6 and 8 contained 10 to 15% of starting material, the ones listed in entries 7 and 9 contained up to 30% starting material. The combined yields of the pure products after flash chromatography are given in parenthesis.

References and Footnotes:

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7. The reaction flask containing the anion was suspended in a small dewar containing ether maintained at a temperature of -105 °C by addition of liquid nitrogen. The electrophiles were added slowly after 5 min equilibration time. Electronic thermometer reading inside the flask indicated that toluene with DME solidified at -90 °C.