REGIOSELECTIVE ALKYLATION OF 1-SILYL-2-METHYLALLYL CARBANIONS

L.-H. Li and D. Wang,* Institute of Chemistry, Academia Sinica, Beijing, 100080, People's Republic of China. T. H. Chan* Department of Chemistry, McGill University, Montreal, P. Q., Canada, H3A 2K6

<u>Summary</u>: Regioselective alkylations of 1-silyl-2-methylallyl carbanions were achieved by changing the substituents on silicon. γ -Alkylation was favoured by dialkylamino group on silicon, whereas α -alkylation was favoured by an alkoxy substituent on silicon.

Regiochemical control of the reactions of α -silylallyl anion (1) with electrophiles (scheme 1) has been a subject of much current interest. Corriu has shown that the α -trimethylsilylallyl anion (1a, R,Z=CH₃) reacted with carbonyl electrophiles regioselectively to give the γ -adducts¹ and the reaction has been developed as a general synthesis of γ -lactones.² Complexation of the carbonyl electrophiles or the silylallyl carbanion with a Lewis acid.³ on the other hand, often led to formation of the α -adducts and the reaction has been used as a method for the stereoselective synthesis of dienes.³ More complicated were reactions of 1 with alkyl halides. Mixtures of both α - and γ -alkylated products were usually obtained.⁴ Regiochemical control of the alkylation reactions can be achieved by manipulating the substituents on silicon. γ -Alkylation was usually favoured when the groups on silicon were sterically bulkier resulting in hindrance to the α -position.⁴ This observation has served as the basis of a useful method to prepare regio- and stereoselectively (E)-vinylsilanes and, after appropriate transformations, disubstituted alkenes.⁵ More recently, it was demonstrated that α -silylallyl carbanions having metal-ion complexing substituents on silicon reacted with alkyl halides to give α -alkylated allylsilanes regioselectively.⁶



SCHEME 1

In view of the extensive study on 1, it was rather surprising that the corresponding 2-methyl substituted anion 3 had not been investigated at all. Because of the potential application of the γ -alkylated product 4 (scheme 2) in the stereoselective synthesis of tri-substituted alkenes, we became interested in the reactions of 3.

The parent compound, (2-methylallyl)trimethylsilane (2a, R, Z=CH₃), had been prepared previously.⁷ We found that a convenient preparation of 2a was by a "one-pot" reaction of 3-chloro-2-methylpropene, trimethylchlorosilane and magnesium in tetrahydrofuran.⁸ Reaction of 2a with Schlosser's base (n-BuLi/t-BuOK)⁹ in ether at -78^o generated the anion 3a (R, Z=CH₃). Alkylation of 3a with a number of alkyl halides

gave a mixture of α - and γ -alkylated products in high yield (Table 1). The γ/α ratio was about 3 to 1 for the four alkyl halides examined (Table 1). This ratio is to be compared with the γ/α ratio of 4-9 to 1 observed in the alkylation of **1a** under identical conditions. The regioselection is favoured by a lower reaction temperature (entries 1-3, Table 1) and varied with the alkoxide used (entries 3-5). Interestingly, the γ -product **4** was formed as one stereoisomer. The stereochemistry was established to be the E-isomer by NOE. This suggests that the anion **3a** may have adopted the all trans- stereochemistry as in the silylallyl anion **1a**.¹⁰ The γ -product **4** could be purified readily from the regioisomeric mixture by treating the mixture with KF in DMSO which selectively protodesilylated the α -isomer **5** and leaving the compound **4** intact.⁵ As an illustration of the synthetic potential of these vinylsilanes, compound **6** reacted with iodine in CH₂Cl₂ to give stereoselectively the (E)-iodide **7**.¹¹



SCHEME 2

	TABLE 1	Regioselective Alky	-Trimethylsilyl-2-Meth	isilyl-2-Methylallyl Carbanion <u>3a</u> *	
Entry	R'-X	Base	T°	γ : α Ratio <u>(4</u> - <u>5</u>)	Combined Yield (4 + 5)
1	n-BuBr	n-BuLi/t-BuOK	-78°	3.3:1	95%
2	n-BuBr	n-BuLi/t-BuOK	-20°	2.4:1	-
3	n-BuBr	n-BuLi/t-BuOK	0	1.9:1	-
4	n-BuBr	n-BuLi/i-PrOK	-78°	4.7:1	-
5	n-BuBr	n-BuLi/EtOK	-78°	2.9:1	
6	\sim	n-BuLi/t-BuOK	-78°	3.2:1	90%
7	n-C ₈ H ₁₇ Br	n-BuLi/t-BuOK	-78°	3.4:1	93%

-78°

⁶General Procedure: To an ice-cooled suspension of potassium alkoxide (22 mmol) in dried hexane (15 ml) was added dropwise n-BuLi solution (C=1.6M in hexane, 22 mmol). The mixture was cooled to -78° . Ether (10 ml) was added followed with a solution of **2a** (20 mmol) in ether (10 ml). The mixture was allowed to warm to room temperature for 4h and cooled back to T^o before addition of alkyl halide (20 mmol) in ether (10 ml). The mixture was stirred at the specified temperature (T^o) for 6h, and then at room temperature for 12h. The mixture was poured into an aqueous saturated solution of ammonium chloride (50 ml). The organic layer was dried (MgSO₄) and evaporated to give the alkylated product which was purified by distillation. The ratio of **4:5** was determined by ¹H nmr and GC determinations.

3.4:1

95%



8

 $n-C_{12}H_{25}Br$

n-BuLi/t-BuOK

In order to improve the regioselection of the alkylation reaction, we examined the effect of different substituents on silicon. A number of dialkylamino-¹² and alkoxy-substituted⁶ 2-methylallylsilanes (**2b-e**) were prepared according to scheme 3. The corresponding carbanions **3b-e** were generated under similar conditions with Schlosser's base. Treatment of the anions with alkyl halides gave the alkylated products. It was clear from the results that the amino substituents on silicon favoured γ -alkylation (Table 2). With the more bulky di-ipropylamino-silyl compound, γ/α ratio as high as 14 to 1 could be obtained. On the other hand, with the alkoxy substituent on silicon, the regioselection was reversed, favouring the α -product with the less hindered n-butoxy group giving the most amount of the α -product.

It is clear from the results of this investigation that regiochemical control in the alkylation reactions of carbanions **3** can be achieved. Furthermore, the reactions offer a potentially convenient approach for the stereoselective synthesis of tri-substituted alkenes.



TABLE 2 Effect of Substituent on Regioselection in the Alkylation of Carbanian 3"

Entry	Carbanian 3	R'-X	γ:α Ratio (<u>4</u> : <u>5</u>)	Combined Yield (4 + 5)
1	3b R=Me,Z=Et ₂ N		4.7:1	85%
2	$\underline{\mathbf{3b}}_{R=Me,Z=Et_2N}$	n-BuBr	5.5:1	78%
3	3b R=Me,Z=Et ₂ N	n-Bul	4.7:1	85%
4	3c R=Mc,Z=1-Pr ₂ N		13:1	70%
5	3c R=Me,Z=i-Pr ₂ N	n-BuBr	14:1	80%
6	<u>3c</u> R=Me,Z=i-Pr ₂ N	n-C ₈ H ₁₇ Br	14:1	80%
7	3d R=Me,Z=i-Pr0		1:2	90%
8	3d R=Me,Z=i-PrO	n-BuBr	1:2	90%
9	3e R=Me,Z=n-Bu0	n-BuBr	1:2.4	60%
10	Se R=Me,Z=n-Bu0	n-C ₈ H ₁₇ Br	1:2.3	74%

[•]General procedure was the same as described for Table 1.

The base used was n-BuLi/t-BuOK and the reaction temperature was -78°.

<u>Acknowledgement</u>: We gratefully acknowledge the financial support of this research by the National Natural Science Foundation of China, and the Natural Science and Engineering Research Council of Canada.

References and Footnotes:

- Corriu, R. J. P.; Masse, J., J. Organomet. Chem., 1973, 57, C5; Corriu, R. J. P., Masse, J.; Samate, D., *Ibid.* 1975, 93, 71.
- 2. Ehlinger, E.; Magnus, P., J. Am. Chem. Soc., 1980, 102, 5004.
- Lau, P. W. K.; Chan, T. H., Tetrahedron Lett., **1978**, 2383; Yamamoto, Y.; Saito, Y.; Maruyama, Tetrahedron Lett., **1982**, 23, 4597; Sato, F.; Suzuki, Y.; Sato, M., Tetrahedron Lett., **1982**, 23, 4589; Eaborn, C.; Lickliss, P. D.; Chidsey, G. M.; Fhorli, E. Y., J. Chem. Soc., Chem. Commun., **1982**, 1326.
- 4. Koumagio, K.; Chan, T. H., Tetrahedron Lett., 1984, 25, 717.
- Chan, T. H.; Koumaglo, K., J. Organomet. Chem., 1985, 285, 109; Chan, T. H.; Koumaglo, K., Tetrahedron Lett., 1986, 27, 883.
- 6. Horvath, R. F.; Chan, T. H., J. Org. Chem., 1989, 54, 317.
- 7. Carr, S. A.; Weber, W. P., J. Org. Chem., 1985, 50, 2782 and references cited therein.
- *8. Experimental procedure: To a mixture of magnesium (10.0 g) in anhydrous tetrahydrofuran (30 ml), a few drops of 1,2-dibromoethane was added to initiate the reaction. A solution of 3-chloro-2-methylpropene (0.40 mol) and trimethylchlorosilane (0.30 mol) in THF (220 ml) was then added dropwise over 3 hrs. During addition, the mixture was heated to reflux with an oil bath. After addition, the mixture was refluxed for another 12 hrs. The mixture was then distilled under atmospheric pressure to remove the excess THF. The residue was extracted with petroleum ether. The organic extract was then distilled to give 2-methylallyltrimethylsilane (2), b. p. 110-2°, in 70% yield.
 - Schlosser, M.; Dahan, R.; Cottens, S., Helv. Chim. Acta, 1984, 67, 284; Schlosser, M., J. Organomet. Chem., 1967, 8, 9.
 - 10. Fraenkel, G.; Chow, A; Winchester, W. R., J. Am. Chem. Soc., 1990, 112, 2585; ibid, 1990, 112, 1382.
 - 11. Chan, T. H.; Lau, P. W. K.; Mychajlowskij, W., Tetrahedron Lett., 1977, 3317.
 - Tamao, K.; Nakajo, E.; Ito, Y., J. Org. Chem., 1987, 52, 4415, Tamao, K.; Nakajo, E.; Ito, Y., Synth. Commun., 1987, 17, 1637.

(Received in USA 1 February 1991)