

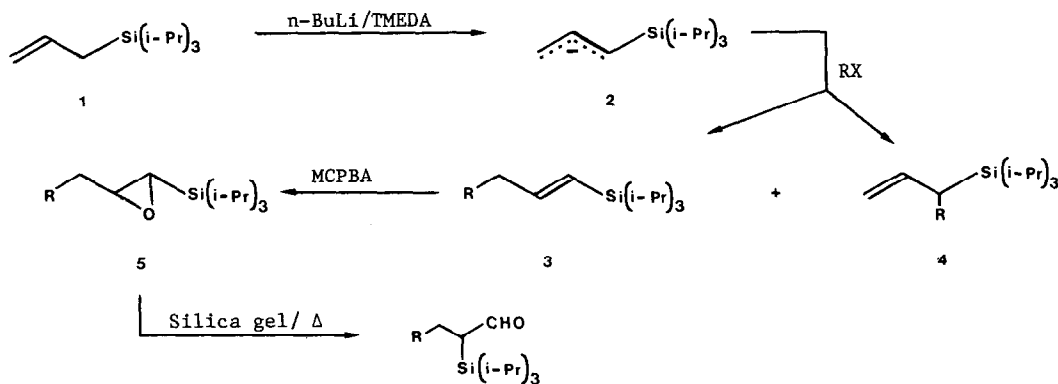
HIGHLY SELECTIVE γ -ALKYLATION OF TRIISOPROPYLSILYLALLYL ANION.
 SYNTHESIS OF α -TRIISOPROPYLSILYL ALDEHYDES.¹

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SUMMARY: The reaction of triisopropylsilylallyllithium with alkyl halides took place with considerably greater γ -selectivity than reported for trimethylsilyl allyllithium. Silica gel induced rearrangement of the epoxides **5** derived from the alkylation products **3** gave α -triisopropylsilyl aldehydes **6** by a process in which silyl group transposition occurred with predominant inversion at the migration terminus.

The utility of vinyltrialkylsilanes as intermediates in organic synthesis is well recognized^{3,4} and numerous studies have been devoted to the development of methods for the preparation of such compounds³. In this connection, it was recently reported⁵ that E-trimethylsilylalkenes are readily obtained by the selective γ -alkylation of the trimethylsilylallyl anion with primary alkyl halides. Enhanced γ : α product ratios (ca. 5) were crucially dependant on the use of "Schlosser's" base (KO-t-Bu/n-BuLi in hexane)⁶ but apparently were not significantly affected by the nature of the substituents on silicon (Me, Ph)⁷. This communication shows that a sterically demanding group on silicon, such as found in allyltriisopropylsilane (**1**), can in fact, profoundly increase the extent of γ -alkylation in the corresponding anion⁸, and that in this system, high γ : α ratios are not contingent upon the use of an exotic base system for the deprotonation of **1**. Furthermore the presence of the triisopropylsilyl moiety in the alkenylsilane **3** makes it possible to transform such substances into stable α -triisopropylsilyl aldehydes **6**.

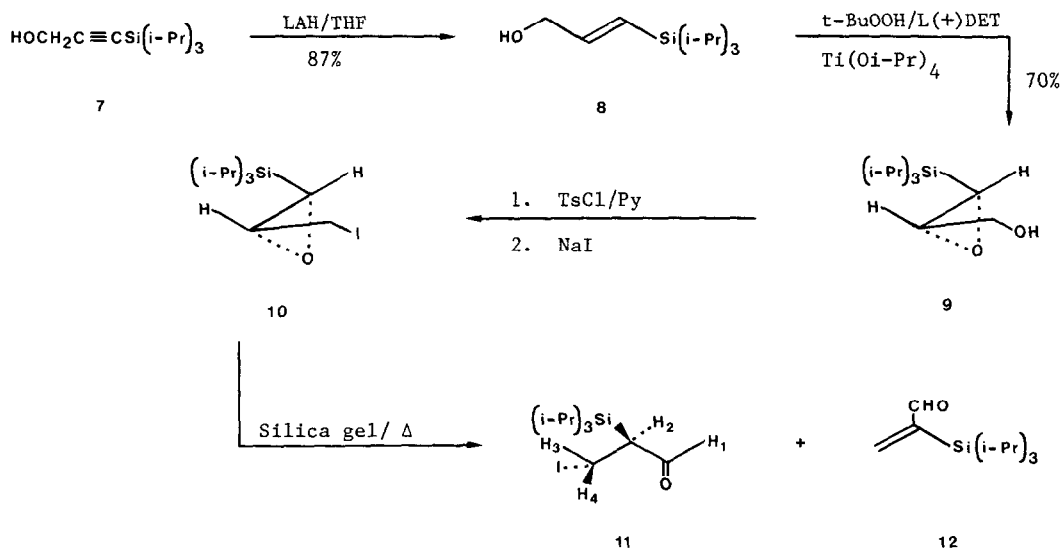


Scheme I

6

Allyltrisopropylsilane (1 b.p. 130 °C/16 torr, Kugelrohr) was prepared (96% yield)⁹ by stirring equimolar quantities of allylmagnesium chloride (2M in THF) and triisopropylsilyltrifluoromethanesulfonate under ambient conditions (5 h). The metalation of 1 (Scheme I) was effected with *n*-butyllithium (1 equiv.), in the presence of tetramethylethylenediamine (1.07 equiv.), in hexane solution over a 20 h period at room temperature. Reaction of the anion 2 with various alkyl halides (1.17 equiv., -80 °C to room temp.) gave mixtures of 3 and 4 in which the γ -product 3 always predominated, usually dramatically so (see Table). A particularly notable exception, however, was the case of 3-iodopentane which gave the expected products in poor yield (γ : α ca. 4) accompanied by a mixture of dimers (25%, at least three isomers) derived from coupling of the anion 2. This result is tentatively interpreted in terms of a change in the mechanism of the alkylation reaction, in part, from S_N2 displacement to a single electron transfer process¹⁰ and the formation of the dimers of 2 would seem to support this possibility. The low γ : α ratio (~ 6) observed for the benzyl bromide reaction can also be rationalized in this way.

The synthetic utility of the alkenylsilanes 3 was examined in a cursory manner. Thus, *m*-chloroperoxybenzoic acid (MCPBA) oxidation occurred rapidly and gave the epoxides 5 (e.g., R = *n*-C₁₂H₂₅, Me₃Si¹¹) in near quantitative yields (CH₂Cl₂/room temp.). When these epoxides were heated in boiling toluene, with an equal weight of activated silica gel (activated at 150-200 °C/0.2 torr, 2 h) for 1-2 h, the stable α -triisopropylsilyl aldehydes 6 were obtained (60-80%). Such α -silylated aldehydes have heretofore rarely¹² been isolated from acid catalysed epoxide rearrangements since protodesilylation usually takes place. The isolation of 6 in the cases described herein is attributed to the mildness of the reaction conditions (BF₃:OEt₂ or MgBr₂ gave mixtures of 6 and the corresponding desilylated aldehydes) and the steric properties of the triisopropylsilyl moiety¹³.



Scheme II

The nature of the silyl group transposition in the formation of 6 was investigated by the rearrangement of the 2(R),3(S) epoxide 10 which was synthesised as follows (Scheme II). Lithium aluminum hydride reduction of 7 gave the allylic alcohol 8 (b.p. 160 °C/16 torr) which was converted into the 2(S),3(S) glycidol derivative 9 {[α]_D - 12.7° (c 1.0, CHCl₃); \geq 98% ee¹⁴} under Sharpless¹⁵ conditions using (+)-diethyl tartrate. The alcohol 9 was reacted sequentially with p-toluenesulfonyl chloride/triethylamine (CH₂Cl₂, 0 °C) and sodium iodide in boiling acetone (3 h) to give the epiodohydrin derivative 10 {[α]_D + 17° (c 0.4, CHCl₃)} in 88% yield (from 9). Rearrangement of 10 under the usual conditions (2 h) produced an 85:15 mixture of the aldehyde 11 (mp 35 °C; [α]_D - 3.75° (c 3.2 CHCl₃); 80% yield at 10% conversion) and α -triisopropylsilylacrolein (12). The pmr spectrum¹⁶ showed, in addition to the expected peaks for the i-propyl groups, single proton multiplets centered at δ 3.35 (H₃), 3.39 (H₂), 3.88 (H₄) and 9.76 (H₁, formyl hydrogen) with J_{1,2} = 1.03 Hz, J_{1,3} = -2.31 Hz, J_{1,4} = 0.0 Hz, J_{2,3} = 1.99 Hz, J_{2,4} = 10.31 Hz and J_{3,4} = -12.91 Hz. The substantial long range W coupling (2.31 Hz) between the formyl proton and one of the hydrogens (H₃) of the iodomethyl group as well as the large vicinal coupling between H₂ and H₄ strongly support the relatively rigid conformation shown in 11. This data, in conjunction with the positive Cotton effect¹⁷ {(MeOH) [θ]₃₀₉ + 72, [θ]₂₉₈ + 132, [θ]₂₈₉ + 154, [θ]₂₇₉ + 154}, is fully consistent with the (S) configuration for the aldehyde 11. Even though the optical purity of 11 is not known, it nevertheless is obvious that transposition of the triisopropylsilyl moiety occurred with at least predominant inversion at the migration terminus. This result is analogous to that which has been observed for alkoxy-carbonyl migration in the rearrangement of glycidic esters¹⁸ and alkyl group transposition in pinacol-type rearrangements¹⁹.

Table. Product yields and γ : α ratios for alkylation of triisopropylsilyllallyl anion at -80 °C.

RX	%	γ : α ^a
n-PrI	86	17.4
n-BuI	90	99 ^b
n-Decyl Br	92	27.6
n-Dodecyl Br	82	17.5
PhCH ₂ Br	88 ^d	6.2
3-I-Pentane	44 ^e	4.1
Me ₃ SiCl	89	34.7

a) Ratios determined by capillary glc (SE 30) unless indicated otherwise.

b) The ratio was 33.5 at room temperature.

c) Ratio determined by NMR spectrometry (300 MHz).

d) Ca. 10% of a mixture of dimers derived from 2 was also formed.

e) Ca. 25% of a mixture of dimers derived from 2 was also obtained.

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References and Notes:

1. Contribution no. 692 from the Syntex Institute of Organic Chemistry.
2. Syntex Research Post-Doctoral Fellow, 1983-1984.
3. T.H. Chan and I. Fleming, *Synthesis*, 761, (1979).
4. L.A. Paquette, *Science*, 217, 793 (1982).
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7. In contrast, these authors recently reported [T.H. Chan and K. Koumaglo, *J. Organomet. Chem.*, 285, 109 (1985)] that alkylation of triethylsilyl- or tri-n-propylsilylallyl anions occurred with $\gamma:\alpha$ selectivities of 16-46 for some primary alkyl halides.
8. For other examples of the use of the triisopropylsilyl group to alter the regiochemical course of a reaction, see J.M. Muchowski and R. Naef, *Helv. Chim. Acta*, 67, 1168 (1984) and refs. therein.
9. All new compounds were characterized by the usual spectroscopic techniques and had satisfactory elemental analyses.
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11. β,γ -Epoxyasilanes are reported to be very sensitive to cleavage and/or rearrangement [P.F. Hudrlik and G.P. Withers, *Tetrahedron Letters*, 29 (1976); I. Fleming and B-W. Au-Yeung, *Tetrahedron*, 37, Supp. 1, 13 (1981); I. Fleming and N.K. Terrett, *J. Organomet. Chem.* 264, 99 (1984)]. None of these compounds were, however, silylated at the β - or the γ - carbon atom. We have also prepared 5 (R = *i*-Pr₃Si), a stable compound, and effected the rearrangement thereof to the corresponding aldehyde.
12. P.F. Hudrlik, A.M. Hudrlik, R.N. Misra, D. Peterson, G.P. Withers and A.K. Kulkarni, *J. Org. Chem.*, 45, 4444 (1980) and refs. therein.
13. The rearrangement is influenced by stereochemical and electronic effects since neither the *cis* isomer of 5 (R = C₇H₁₅) nor the benzyloxy compound 5 (R = PhCH₂O) reacted under these conditions. In contrast, the acetate 5 (R = OAc) was completely converted into α -triisopropylsilylacrolein (12).
14. Determined from the pmr spectrum in the presence of Eu(hfc)₃.
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