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Free Radical Rearrangement of Alkenyl Epoxy Silanes. Isolation of α-Trimethylsilyl Aldehydes.

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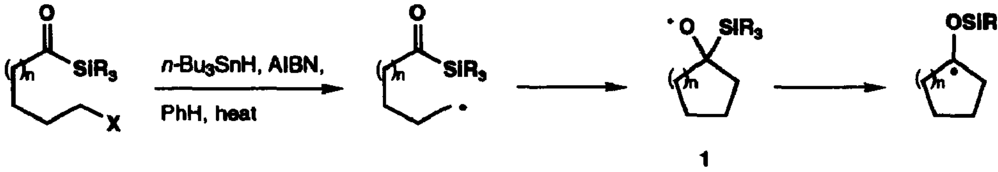
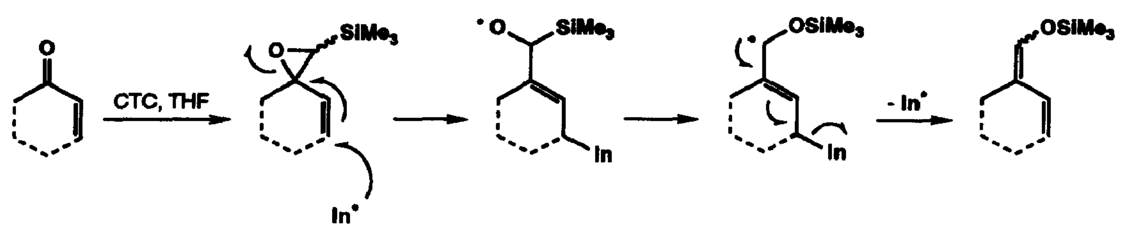
Abstract: The thiyl-radical induced fragmentation of alkenyl epoxy silanes has been found to afford α-trimethylsilyl aldehydes as the immediate products. These may be isolated, rearranged to trimethylsilyl dienol ethers, or converted to 1,3-dienes with high stereoselectivity.

Recent reports by Tsai *et al.* have described the use of a homolytic Brook rearrangement of silyl-substituted alkoxy radicals as a means of generating carbon-centred radicals.[1] Alkoxy radicals of general structure 1 were generated by 5-*exo*- cyclisation of 1°-carbon radicals derived from ω-haloalkyl acyl silanes (Scheme 1).



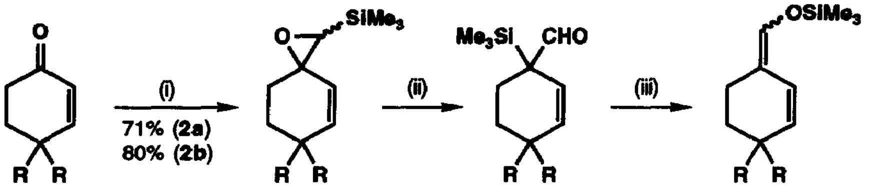
Scheme 1

We were attracted to the possibility that this type of intermediate could be generated by the fragmentation of an epoxy silane under free radical conditions[2] and employing the carbon-centred radical, derived from subsequent homolytic Brook rearrangement, in C-C bond forming processes. To establish the viability of this proposal we wished to devise precursors that were readily prepared and that would undergo isomerisation in the presence of a catalytic quantity of a radical initiator. These criteria were met by the preparation of epoxy silanes derived from α,β-unsaturated ketones using the chloromethyltrimethylsilyl carbanion (CTC) methodology of Magnus[3] since these products could conceivably undergo a sequence of steps to generate trimethylsilyl dienol ethers[4], *viz.* i) addition of a radical In• to the alkene, ii) epoxide fragmentation, iii) homolytic Brook rearrangement, and iv) ejection of In• to continue the radical chain process (Scheme 2).



Scheme 2

Accordingly, two rearrangement precursors **2a,b** were prepared and their behaviour on treatment with various radical initiating reagents investigated. In the event, it was found that the predicted TMS-dienol ethers **4a,b** were, indeed, formed on heating with small quantities of thiophenol and AIBN in benzene.[5] However, these compounds are not the primary products from the reaction but are derived from rapidly-formed intermediates which undergo subsequent slow thermal conversion to the dienol ethers. Running the free radical isomerisations more carefully allowed conditions to be optimised to the obtention and identification of these intermediates. On the basis of spectroscopic analysis the primary products in these processes were identified as the α-trimethylsilyl aldehydes **3a,b** (Scheme 3).[6]



R = H, **2a**
R = Me, **2b**

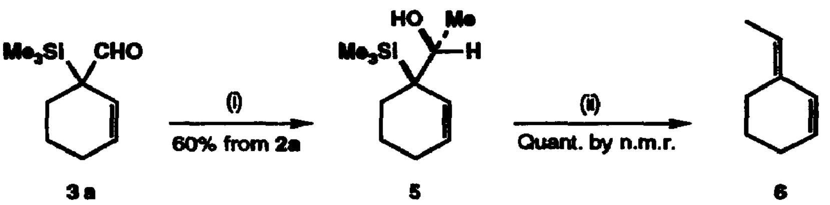
R = H, **3a**
R = Me, **3b**

R = H, **4a**
R = Me, **4b**

Conditions: (i) CTC (2.0 equiv.), -55° → RT, 2h; (ii) PhSH (0.1 equiv.), AIBN (0.1 equiv.), PhH, For **2a**: RT, 15h (or 80°C, 0.5h). For **2b**: 80°C, 8h; (iii) PhH, 80°C, 15-24h

Scheme 3

We were initially sceptical as to the identity of compounds **3a,b** in the light of the reputedly unstable nature of trimethylsilyl aldehydes[7] and therefore strove to confirm their structure by chemical means additional to their thermal isomerisation to dienes **4a,b**.[8] Thus, treatment of compound **3a** with methyl magnesium bromide afforded β-hydroxy silane **5** in an isolated yield of 60% from **2a**. The relative stereochemistry of this compound was assigned by treatment with sodium hydride[9] to generate the known diene **6** having an *E*-configured exocyclic double bond (Scheme 4).[10] Additionally, the reaction of compound **5** with *p*-toluene sulphonyl chloride and pyridine in dichloromethane provided a 1:2 mixture of diene **6** and the corresponding *Z*-isomer for comparison purposes.



Conditions: (i) MeMgBr, THF, -78°C → 0°C then AcOH; (ii) NaH, THF, RT, 1.5h

Scheme 4

The addition of the Grignard reagent to the carbonyl group in **3a** proved to be stereoselective.[11] By ^{1}H n.m.r. analysis of the crude product the stereoisomer shown (**5**, Scheme 4) was formed with a selectivity of at least 12:1 as a result of preferred addition of the nucleophile *via* a trajectory eclipsing the flattened β-CH= rather than the tetrahedral β-CH$_2$- groups of the cyclohexenyl ring in a simple Felkin-Anh treatment (Figure 1).

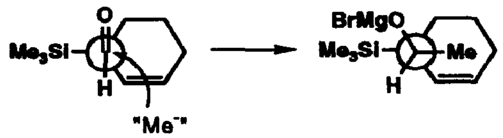
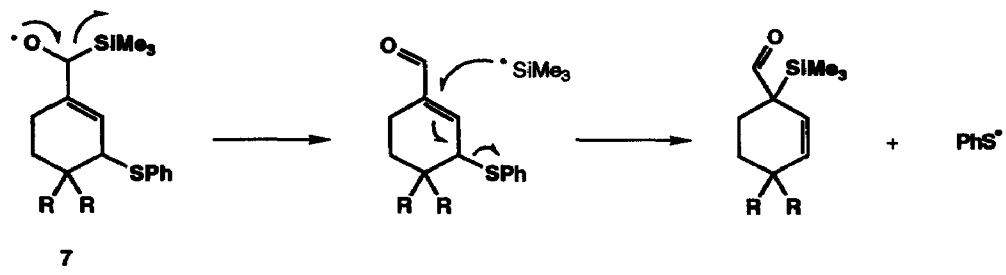


Figure 1

Regarding the mechanism of this process, we suggest that an ionic pathway[12] is not followed:

- The reaction may also be effected thermally with tributyltin hydride or diphenyl disulphide.
- A rate determining addition of an initiating species is implied by the finding that increased substitution adjacent to the alkene functionality retards the reaction rate; this is not consistent with a purely acid-catalysed process.
- Control experiments with compound **2a** indicate that isomerisation does not ensue at room temperature without additives however the reaction does proceed slowly at room temperature with thiophenol alone (0.1 equiv.) and is accelerated by a factor of at least five on addition of AIBN (0.1 equiv.).
- The isomerisation of compound **2a** does not take place using NaSPh (0.1 equiv., benzene, 20°C).



Scheme 5

On the basis of this evidence we feel it is reasonable to invoke a homolytic pathway and that the expected course of the reaction is followed up to intermediate **7**. A concerted 1,2-shift of a silyl group, whilst conceivable, seems unlikely in the light of the dearth of authentic homolytic 1,2-shifts.[13] A possible mechanism involves ejection of a silyl radical[14] followed by its re-addition to the α-position of the resulting α,β–unsaturated aldehyde (presumably addition to the β-position is reversible although kinetically more favourable) with concomitant ejection of PhS$^\bullet$ (Scheme 5).[15]

In conclusion, we have demonstrated that cycloalkenyl epoxy silanes may be isomerised homolytically affording α-trimethylsilyl aldehydes by way of an overall 1,2-silyl shift from carbon to carbon. Full experimental details of these reactions and further studies concerning the mechanism, scope, and limitations of the rearrangement, and of the chemistry of the cycloalkenyl α-trimethylsilyl aldehydes will be reported in due course.

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