

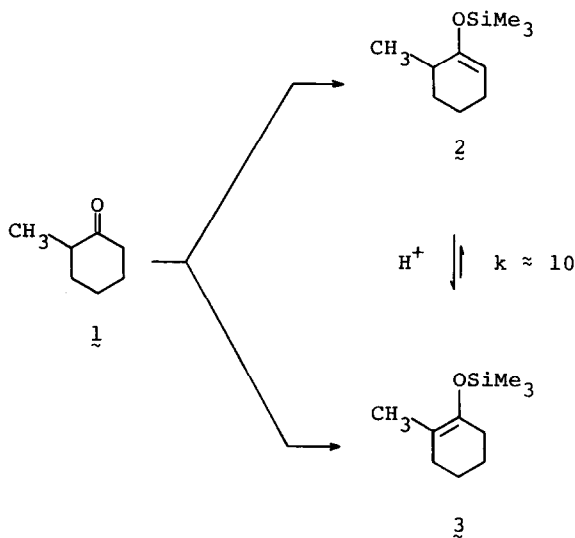
OZONIZATION OF SILYLOXYALKENES

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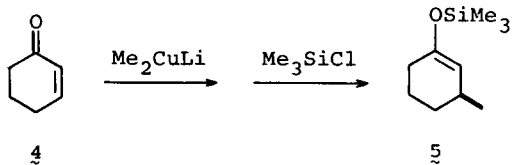
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(Received in USA 18 March 1974; received in UK for publication 2 May 1974)

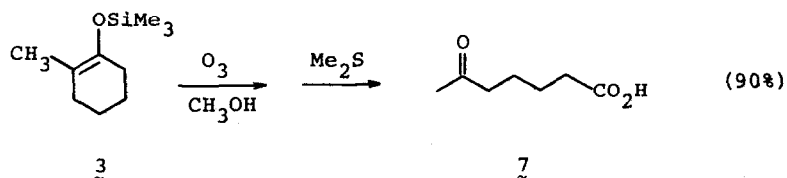
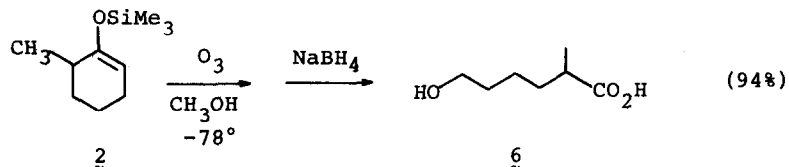
Silyloxyalkenes may be generated from ketones by trapping the kinetic or thermodynamic enolate with a trialkylsilyl chloride (e.g., $1 \rightarrow 2$ or 3).^{1,2} In general, when the ketone is unsymmetrically substituted, the more highly substituted silyloxyalkene predominates under equilibrating conditions (e.g., $2 \rightleftharpoons 3$).^{1,2}



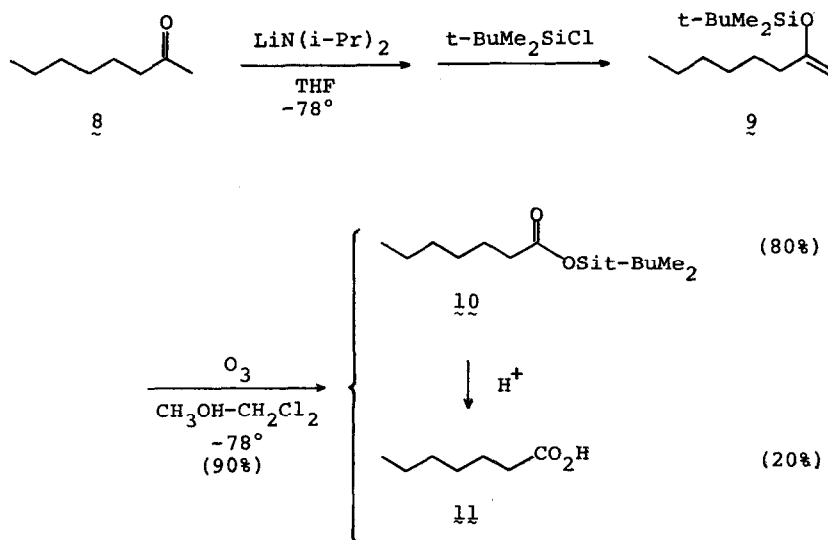
Silyloxyalkenes may also be prepared by trapping the kinetic enolate generated in the conjugate addition of organometallic reagents to enones (e.g., $4 \rightarrow 5$).¹



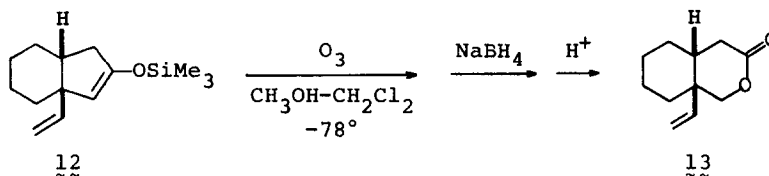
We have found that some of these silyloxyalkenes may be oxidized by ozone in methanolic solution. The ozonization products may be worked up with NaBH_4 to give hydroxyacids (e.g., $\underline{2} \rightarrow \underline{6}$) or with dimethylsulfide to give ketoacids (e.g., $\underline{3} \rightarrow \underline{7}$).



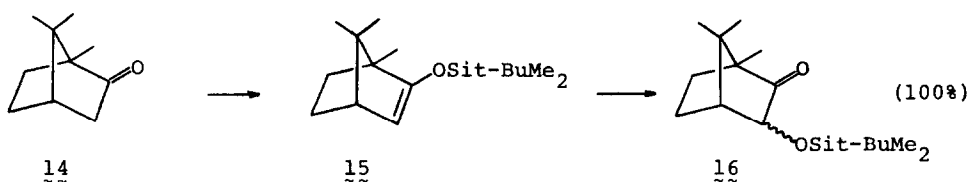
The overall two-step process of forming and cleaving the kinetic enolate provides a way of oxidatively cleaving an unsymmetrical ketone away from the more highly alkylated side. In this respect, the method complements the Baeyer-Villiger oxidation. The method may also be applied to acyclic ketones (e.g., $\underline{8} \rightarrow \underline{9}^3 \rightarrow \underline{10} + \underline{11}$).⁴



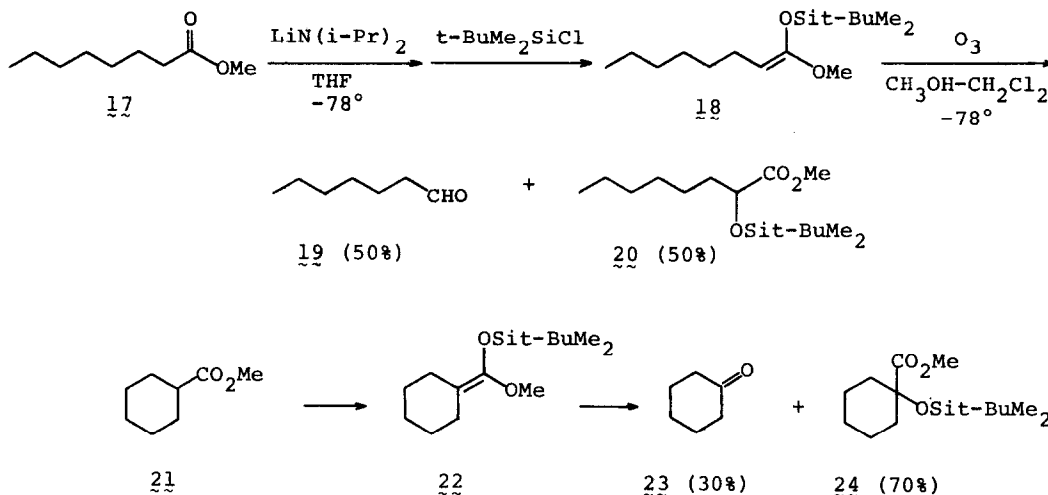
Because of the extreme nucleophilicity of the silyloxyalkenes, it is possible to ozonize this bond even in the presence of other olefinic groups (e.g., 12 → 13).⁶



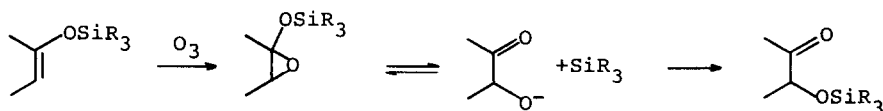
In one silyloxyalkene we have studied, the oxidation is anomalous, yielding the silylated α -hydroxyketone rather than a cleavage product (e.g., 15 → 16).



Similar reactions are observed, in varying amounts, with the silylated ketone acetals 18 and 22.⁷



The abnormal oxidation products may be formulated as arising in the following manner.



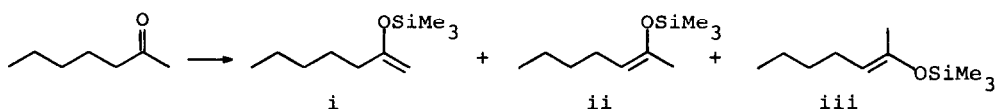
A typical procedure for the oxidation of a silyloxyalkene is given below:

Oxidation of 6-Methyl-1-trimethylsilyloxy-cyclohexene (2): A solution of 5.48 g of silyloxyalkene **2** in a mixture of 5 ml CH_2Cl_2 and 20 ml CH_3OH is ozonized, using a Welsbach Ozonator, at -78° . After the calculated amount of ozone has been added, the blue solution is treated with 1.13 g of NaBH_4 . After stirring at -78° for 1 hr, a second 1.13 g portion of NaBH_4 is added and the solution is allowed to warm to room temperature. The solvent is evaporated and the remaining residue is worked up by partitioning between dilute acid and CHCl_3 . Upon drying and evaporating the solvent, hydroxyacid **6** is obtained as a colorless oil (4.10 g, 94.3%).

Acknowledgement: We thank the National Institutes of Health (CA 12617) for financial support.

References

1. G. Stork and P.F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462 (1968).
2. H.O. House, L.J. Czuba, M. Gall, and H.D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).
3. The *t*-butyldimethylsilyloxyalkene **9** is the sole product of this reactions. Neither of the isomeric 2-alkenes can be detected by glpc or by nmr. This result is in contrast to the results of House and co-workers,² who formed the kinetic enolate from 2-heptanone with lithium diisopropylamide in 1,2-dimethoxyethane. Upon quenching with trimethylsilyl chloride, silyloxyalkenes **i**, **ii**, and **iii** were produced in a ratio of 84:7:9.



4. Since the *t*-butyldimethylsilyloxy grouping is more stable to nucleophilic cleavage than the trimethylsilyloxy grouping,⁵ it is necessary to hydrolyze the reaction product with mild acid to obtain acid **11**.
5. E.J. Corey and A. Venkateswarlu, *J. Amer. Chem. Soc.*, **94**, 6190 (1972).
6. R.D. Clark and C.H. Heathcock, *Tetrahedron Lett.*, in press.
7. M.W. Rathke and D.F. Sullivan, *Syn. Commun.*, **3**, 67 (1973).