to an accuracy of ±0.5% on an Isocap 300 liquid scintillation spectrometer using the ESR method for dpm calculations.

(15) L. Melander, "Isotope Effects on Reaction Rates", Ronald Press, New York, N.Y., 1960, pp 51, 52.

Yusuke Wataya, Daniel V. Santi*
Department of Biochemistry and Biophysics and
Department of Pharmaceutical Chemistry
University of California, San Francisco, California 94143

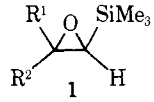
Received December 6, 1976

α-Chloro-α-trimethylsilyl Carbanion, a Reagent for Homologation of Ketones and Aldehydes via α,β-Epoxysilanes

Sir:

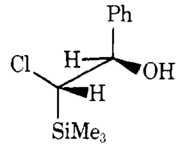
α,β-Epoxysilanes **1** have recently enjoyed conspicuous use in synthetic procedures that require a masked carbonyl group or vinyl cation equivalent.[1] Unfortunately, without exception all the methods used to prepare this functional group proceed via the epoxidation of vinylsilanes, and, since vinylsilanes are not readily available, the chemistry of α,β-epoxysilanes, while useful, remains a specialist area. Here we describe a general solution that enables aldehydes and ketones, the most ubiquitous functional groups, to be converted directly into α,β-epoxysilanes **1**.

α-Chloromethyltrimethylsilane (**2**) was deprotonated by treatment with *sec*-butyllithium in THF containing TMEDA (1 equiv) at −78 °C to give a species whose reactions indicate it to be α-chloro-α-trimethylsilyl carbanion (**3**, CTC).[2] Surprisingly **3** was comparatively stable to −40 °C and then only decomposed slowly (~1 h).[3] Table I lists a number of ketones and an aldehyde that have been treated with **2** to establish its scope in this particular type of reaction. If the reaction of CTC (**3**) with benzaldehyde is quenched at −55 °C, then a mixture


1

Me_3SiCH_2Cl
2

$Me_3SiCH(Li)Cl$
3


erythro-**4a**

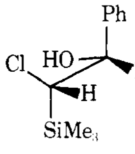
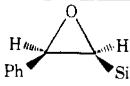
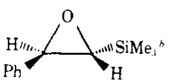
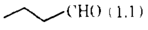
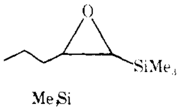
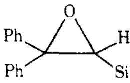
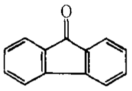
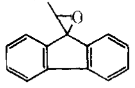
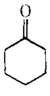
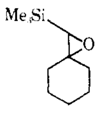
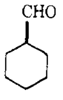
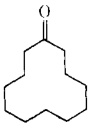
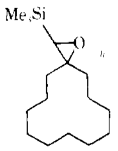
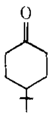
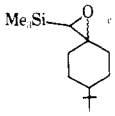
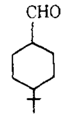
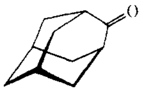
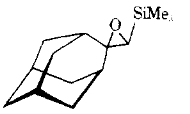
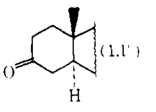
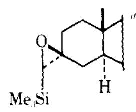
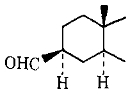
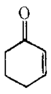
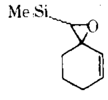
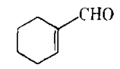
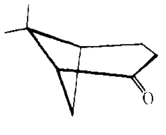
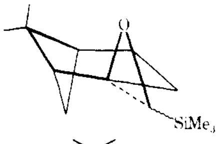
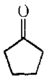
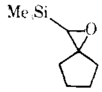
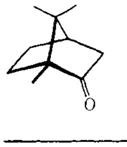
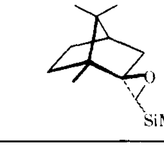

threo-**4b**

Table I[a]

Substrate (equiv of CTC)	Epoxysilane	% Yield	Aldehyde	Substrate (equiv of CTC)	Epoxysilane	% Yield	Aldehyde
PhCHO (1)	 **6**  **5** [b]	≥95	$PhCH_2CHO$	 (1.1)		≥75	
PhCOPh (3)		≥95		 (3)	 [g]	≥60	
 (1.1)	 **7**	≥95		 (2)	 [h]	≥70	
	 [c]	≥95	 (1:1)	 (1.1)		≥90	
 (1.1') cholestanone	 [d] + 3 α epimer	≥95	 + 3 α epimer	 (1.1)		≥80	
		~40		 (1.1)		≥90	
		≥20					

[a] All compounds were identified by IR, NMR, and accurate mass spectral measurements. Known compounds (aldehydes) were derivatized (2,4-DNP). Yields refer to isolated material at least 90% pure (NMR, TLC). A representative experiment follows. Chloromethyltrimethylsilane (0.75 g, 6.14 mmol) in dry THF (8 mL) at −78 °C under N_2 was treated with *sec*-butyllithium in cyclohexane (4.50 mL, 6.75 mmol, 1.5 M solution) followed by TMEDA (0.97 mL, 6.45 mmol). After this mixture was stirred at −78 °C for 40 min the solution was warmed to −55 °C and cyclohexanone (0.59 mL, 5.68 mmol) added. The mixture was kept at −40 °C for 0.5 h, then allowed to warm to 20°. Work-up by pouring the mixture into sat. ammonium chloride, extraction, and drying gave the epoxysilane 7 (95%), bp 32–35 °C (0.35 mm). Anal. C, H. [b] J. J. Eisch and J. E. Galle, *J. Org. Chem.*, 41, 2615 (1976). [c] No assignment of stereochemistry could be made from the available data. [d] A 1:1 mixture of epimers was formed. [e] Attempts to increase the yield were unsuccessful. It should be noted that isopropyllithium adds to the extent of only 2–5%. [f] A mixture of cis and trans epoxides. [g] For complete formation of the epoxide the reaction mixture (chlorohydrin) is left at room temperature for 15 h. [h] Incomplete reaction owing to ~30% enolization. [i] 2-Adamantanecarboxaldehyde is unstable: D. Farcasin, *Synthesis*, 615 (1972).

of chlorohydrins **4a** and **4b** can be isolated. The major diastereomer is the threo adduct which on treatment with NaH/THF at 50 °C gave only the cis epoxide **5**, δ 0.31 (9 H, s), 2.78 (1 H, d, $J = 5.0$ Hz), 4.40 (1 H, d, $J = 5.0$ Hz), 7.5 (5 H, s). No vinyl chlorides were formed from the elimination of trimethylsilanol, which could have been a competing reaction. When the reaction mixture of CTC (**3**) with benzaldehyde is warmed from −55 to 20 °C, the initially formed chlorohydrins **4a** and **4b** are converted in situ into the trans and cis epoxides, **5** and **6** (1:3.4), respectively. The threo chlorohydrin **4b** is converted more slowly into the cis epoxide **6** than the erythro chlorohydrin **4a** is converted into the trans epoxide **5**.

All of the substrates listed in Table I react rapidly and cleanly with CTC (**3**) to give α,β-epoxysilanes. The only limitations noted from the examples are that sterically hindered or readily enolizable carbonyl groups cause a lowering of yields. We have not examined the direct hydrolysis of the epoxides listed in Table I using optimum conditions with respect to yield and purity. The conditions described in the literature appear to suffice, and in all cases gave clean and rapid conversion of the α,β-epoxysilanes into aldehydes.[4] Treatment of the epoxides **5** and **6** with $MeOH/BF_3{\cdot}OEt_2$ gave phenylacetaldehyde dimethyl acetal (90%), whereas 5% aqueous $HClO_4$ in THF or 10% aqueous $H_2SO_4/MeOH$ gave phenylacetaldehyde (80%). Furthermore we have converted the α,β-epoxysilane **7** into cyclohexanecarboxaldehyde ethylene acetal, dithioethylene acetal, and 1,3-dithiopropane acetal by treatment with $HOCH_2CH_2OH/TSOH/PhH$, $HSCH_2CH_2SH/TSOH/PhH$, and $HSCH_2CH_2CH_2SH/TSOH/PhH$, respectively.[5] All conversions proceed in excellent yields ($\geq$95%), thus providing a homologation procedure that leads directly to a protected aldehyde or derivative (dithiane) capable of further elaboration. No existing procedure has this simple versatility.

Apart from α,β-epoxysilanes being precursors to carbonyl groups they can react with dialkyl cuprates to give β-hydroxysilanes which can be stereospecifically converted into alkenes.[6] α,β-Epoxysilanes serve as useful precursors to vinyl ethers, bromides, and enamides.[7] Recently α,β-epoxysilanes have been deprotonated to give an α-lithio epoxide synthon.[8]

The α-chloro-α-trimethylsilyl carbanion serves as a nucleophilic acylating species ($\ominus$ CHO synthon) where reduction has occurred at the original electrophilic carbonyl group—*reductive nucleophilic acylation.* While reagents exist for this transformation, none offer the flexibility for further conversion nor the mild and specific conditions that provide the homologated aldehyde.[9] Furthermore the new method described here for making α,β-epoxysilanes uses a commercially available reagent[10] and the only other product formed in their hydrolysis to an aldehyde is trimethylsiloxane.

The procedure described here requires no special techniques or experience with organosilicon chemistry and should find wide use in organic synthesis.

The chemistry of the α-chloro-α-trimethylsilylcarbanion is being actively pursued in these laboratories.

References and Notes

(1) For a leading review covering general organosilicon chemistry, see C. Eaborn and R. W. Bott, "Organometallic Compounds of the Group IV Elements", Part I, A. G. MacDiarmid, Ed., Marcel Dekker, New York, N.Y., 1968; R. F. Cunico, *J. Organomet. Chem.*, **109,** 1 (1976). For reviews describing the synthetic uses of organosilicon chemistry, see I. Fleming, *Chem. Ind.* (*London*), 449 (1975); S. S. Washburne, *J. Organomet. Chem.*, **83,** 115 (1974), and **123,** 1 (1976).
(2) Several silicon stabilized carbanions have been used in synthesis. $Me_3SiCH_2^-$: D. J. Peterson, *J. Org. Chem.*, **33,** 780 (1968); T. H. Chan, E. Chang, and E. Vinokur, *Tetrahedron Lett.*, 1137 (1970). Me_3SiC^-HSR and $Me_3SiC^-HPR_2$: F. A. Casey and A. S. Court, *J. Org. Chem.*, **37,** 939 (1972); H. Gilman and R. Tomasi, *ibid.*, **27,** 3647 (1962); N. E. Miller, *J. Inorg. Chem.*, **4,** 1458 (1965). $Me_3SiCHSeR$: K. Sachdev and H. S. Sachdev, *Tetrahedron Lett.*, 4223 (1976). $Me_3SiC^-HSiMe_3$: B.-T. Gröbel and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **13,** 83 (1974).
(3) R. L. Kreeger, Ph.D. dissertation, The Ohio State University, 1976 (with Professor Shecter) has studied the reactions of bases with trimethylsilyl bromide to give α-bromo-α-trimethylsilylcarbanion which undergoes efficient alkylation with *tert*-butylbromide. Seyferth has prepared the carbanions $Me_3SiCCl_2^-$, $(Me_3Si)_2CCl^-$, $Me_3SiCBr_2^-$, and $Me_3SiCHBr^-$: D. Seyferth, E. M. Hansen, and F. M. Armbrecht, Jr., *J. Organomet. Chem.*, **23,** 361 (1970); D. Seyferth, R. L. Lambert, Jr., and E. M. Hansen, *ibid.*, **24,** 647 (1970). No products from α-elimination of CTC have been observed.
(4) G. Stork and B. Ganem, *J. Am. Chem. Soc.*, **95,** 6152 (1973); G. Stork and E. Colvin, *ibid.*, **93,** 2080 (1971); G. Stork and M. E. Jung, *ibid.*, **96,** 3682 (1974); R. K. Boeckman, Jr., and K. J. Burza, *Tetrahedron Lett.*, 3365 (1974).
(5) Mr. Glenn Roy is thanked for carrying out these experiments.
(6) P. F. Hudrlik, D. Peterson, and R. J. Rona, *J. Org. Chem.*, **40,** 2263 (1975).
(7) P. F. Hudrlik, A. M. Hudrlik, R. J. Rona, R. N. Misra, and G. P. Withers, *J. Am. Chem. Soc*, **99,** 1993 (1977).
(8) J. J. Eisch and J. E. Galle, *J. Am. Chem. Soc.*, **98,** 4646 (1976).
(9) O. W. Lever, Jr., *Tetrahedron Rep.*, **No. 19,** 1943 (1976). This review describes in detail the reagents that have been used for nucleophilic acylation.
(10) α-Chloromethyltrimethylsilane is commercially available from Petrarch Systems, Inc.
(11) The Upjohn Co. is gratefully acknowledged for supporting this work.

Cliff Burford,[11] Frank Cooke, Ed Ehlinger, Philip Magnus*
The Evans Chemistry Laboratory, The Ohio State University
Columbus, Ohio 43210

Received February 8, 1977

Book Reviews

Fluorocarbon and Related Chemistry. Volume 3. By R. E. BANKS and M. G. BARLOW (University of Manchester, England). The Chemical Society, London. 1976. ix + 491 pp. £35.00.

For that small band of chemists who concern themselves primarily with highly fluorinated compounds, this book is indispensable. The third volume in a biennial series, it is a 450-page running abstract of new work in fluorine chemistry appearing in 1973 and 1974. It maintains and may even improve the high standard set by its predecessors.

The literature coverage is excellent and an astonishing amount of information is conveyed, not only concerning reaction conditions and yields but also about secondary products, mechanisms (where possible), and related or previous work. This is not a book which tantalizes one with offhand references; insofar as the extremely condensed format permits, the data are given.

The faults of the book are not attributable to the authors but are inherent in its nature. Although it contains a tremendous amount of information valuable to nonfluorine chemists, this is very difficult to disinter since there is no index and the arrangement of chapters is rather rudimentary, being generally based on structure rather than process. There are, however, a few subject headings such as "The Chlorofluorocarbon-Ozone Question" and "Inhalation Anaesthetics", as well as a good number of cross-references. The style of writing is so dense as to require more nearly translation than reading; this is not a volume to be picked up for a little technical browsing. In places, the British habit of using a dot for an electron-pair bond, in conjunction with efforts to save an em here and an em there, make comprehension momentarily difficult for an American reader; it would certainly be less confusing if a slash were used rather than a hyphen to denote a mixture in $CF_2{:}CF_2$-$CF_2{:}CFOCF_3$, and the symbol R_F is employed