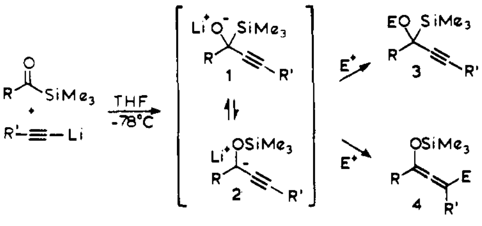
Silyl Ketone Chemistry.[1] Preparation of Siloxyallenyl- and -allyllithium Reagents

Sir:

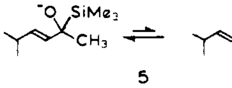
We report here a new connective route to siloxy substituted allenic, allylic, and pentadienylic lithium reagents[2,3] which provides an efficient procedure for the regiospecifc and stereoselective assembly of allenol, enol, and dienol silyl ethers, and the ketones derived from them by hydrolysis. The process is illustrated in Scheme I. It involves the addition of organolithium reagents to silyl ketones,[4] followed by carbon to oxygen silyl shift (Brook rearrangement[5]) of the first-formed intermediate alkoxide **1** to the propargylic–allenic lithium reagent **2**. Reaction with electrophiles can lead to either **3** or the allenol silyl ethers **4**.

Scheme I



If a vinyllithium is used instead of the acetylenic lithium of Scheme I, siloxyallyllithium reagents[2a,3b] are formed. These can also be prepared by organometallic additions to vinyl silyl ketones[5] (runs 15–17, Table I).

The success of these procedures depends crucially on the position of the equilibrium between the α-silyl alkoxide and the siloxy carbanion (e.g., between **1** and **2**). If the carbanion is inadequately stabilized, its rate of formation will be so slow that successful derivatization at carbon becomes difficult. This is the case when there is more than one alkyl group at the termini of an allyl system,[8,9] as in the anions **5** for which no detectable methylation with methyl iodide or C-protonation with 1-pentyne occurred. Only dimethyl and diphenyl sulfides gave useful amounts of reaction at carbon with **5** (run 17, Table I). Since the rate of reaction of **5** was identical with dimethyl or diphenyl disulfide and only varied slightly when the concentration of dimethyl disulfide was changed by a factor of 4,[10] we conclude that here the [1,2]-sigmatropic rearrangement of the silyl group is rate determining.



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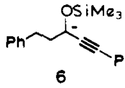

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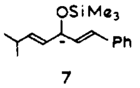

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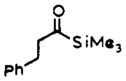
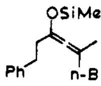
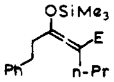
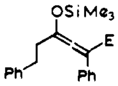
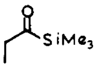
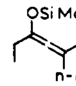
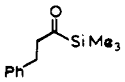
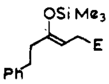
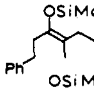
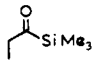
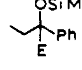
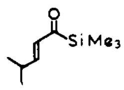
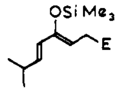
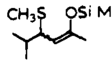
On the other hand, a highly stabilized carbanion (e.g., **6** or **7**) can exist as a significant or even predominant species in the equilibrium mixture[8] and a different problem emerges. As the carbanion is formed it rapidly attacks unreacted silyl ketone to form oligomeric and polymeric materials. Successful utilization of the anion **6** is possible when silyl ketone is slowly added to a solution containing lithium phenylacetylide and alkyl iodide at −78 °C, so that **6** is immediately removed by alkylation (runs 4 and 5, Table I). The anion **7** is even more highly stabilized, and we have not been able to find conditions under which it can be successfully formed and derivatized. Anions **5** and **7** thus bracket the range of carbanion stabilities that our method will tolerate in its present form.

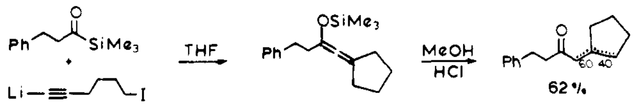
The site of electrophilic attack on anions such as **1**, **2**, or **5** is dependent on the choice of electrophile. Very reactive hard electrophiles such as water or trimethylchlorosilane react at oxygen.[3] Protonation on carbon can be achieved by using a terminal acetylene as proton source. Sulfenylations occur at carbon and are the cleanest reactions which we have encountered. Alkylations proceed well with methyl and ethyl iodides, more poorly with less reactive halides.[11] All of these derivatizations proceed predominantly or exclusively γ to the siloxy group. With the exception of run 12, only *Z* isomers of the enol silyl ethers are formed.

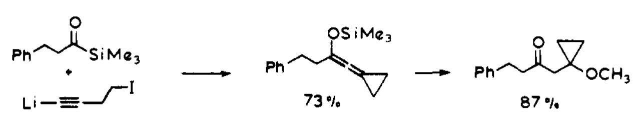
Table I. Preparation of Allenol and Enol Silyl Ethers

RUN NO	SILYL KETONE	ORGANOLITHIUM (ELECTROPHILE)	PRODUCT	E-	YIELD[a]
1		n-Bu–≡–Li (CH_3I)			71[b]
2		n-Pr–≡–Li (CH_3CH_2I)		CH_3CH_2-	60[b,c]
3		(n-Pr–≡–H)		H-	63[b]
4		Ph–≡–Li (CH_3I)		CH_3-	70[b,d]
5		(CH_3CH_2I)		CH_3CH_2-	54[b,d]
6		n-Bu–≡–Li (CH_3I)			74
7		CH_2=CHLi[e] (CH_3SSCH_3)		CH_3S-	89
8		(n-Pr–≡–H)		H-	79
9		(CH_2=CH-CH_2-Br)		Allyl-	62[b]
10		(CH_3CH_2I)		CH_3CH_2-	86[b]
11		(CH_3I)		CH_3-	83[b]
12		CH_2=C(CH_3)Li[e] (CH_3CH_2I)			64[b]
13		PhLi[e] (CH_3SSCH_3)		CH_3S-	79
14		(CH_3CH_2I)		CH_3CH_2-	67
15		CH_2=CHLi[e] (n-Pr–≡–H)		H-	81
16		(CH_3I)		CH_3-	79
17		CH_3Li[e] (CH_3SSCH_3)			85[f,g]

[a] Yields are for material purified by bulb-to-bulb distillation unless indicated otherwise. [b] Yields reported are for the ketones or enones (cis–trans mixture, as well as β, γ isomer in some cases) obtained by hydrolysis with HCl-MeOH. The enol and allenol silyl ethers were characterized spectroscopically. [c] One equivalent of HMPA was added to facilitate alkylation. [d] Silyl ketone was added over a 40-min period to a mixture of PhC≡CLi and alkyl iodide at −78 °C. [e] Silyl ketone was added to a solution of the organolithium in ether, and the electrophile dissolved in an equal volume of THF was added. The alkenyllithium reagents (runs 10–12, 15, 16) were prepared by addition of vinyl bromide or 2-bromopropene to 2 equiv of *tert*-butyllithium in ether at −78 °C: H. Neumann and D. Seebach, *Chem. Ber.*, **111**, 2785 (1978). [f] NMR yield. [g] The product was a 55:35 ratio of γ- (shown) and α-sulfenylated products.

It is possible to perform intramolecular alkylations leading to the unusual enol ethers and ketones shown below. The reaction can also be used to prepare the cyclobutane analogue, 1-methoxy-1-(2-oxo-4-phenylbutyl)cyclobutane (58% yield).





Simple enol silyl ethers have a broad spectrum of applications as enolate equivalents.[13] The procedures developed here expand the range of such compounds available. They also provide an efficient route to a previously almost unknown type, the allenol silyl ethers **8**,[12] formally derived from α,β-unsaturated ketones by enolization of the vinyl hydrogen (**9**).

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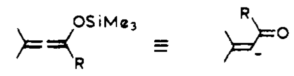
Utilization of **8** as a synthetic equivalent of **9** has so far been limited to protonation (hydrolysis) and halogenation, but other more useful electrophiles are being studied.



8 **9**

A typical experimental procedure for the preparation of allenol silyl ethers is as follows (run 6). To a stirred solution of 0.37 mL (3.2 mmol) of 1-hexyne in 5 mL of dry THF at 0 °C was added 2.8 mL (3.2 mmol, 1.15 M) of MeLi (1:1 LiBr complex in ether). After 15 min, the solution was cooled to −78 °C and 0.47 mL (3.0 mmol) of ethyl trimethylsilyl ketone was added dropwise. A white precipitate formed. After 15 min, 0.25 mL (4.0 mmol) of MeI was added and the flask was warmed to 0 °C and stirred for 30 min. The contents were then partitioned between cold aqueous 7% $NaHCO_3$ and ether–pentane (1:1) and washed with saturated NaCl. After drying (Na_2SO_4, then K_2CO_3) and concentration of the organic layer, distillation of the residue (Kugelrohr, 24 mm, bath temperature 89–91 °C) gave 0.50 g (74%) of 3-trimethylsilyloxy-5-methyl-3,4-nonadiene as a clear, mobile liquid: NMR ($CDCl_3$) δ 0.12 (s, 9 H), 0.80–1.12 (m, 6 H), 1.20–1.68 (m, 4 H), 1.74 (s, 3 H), 1.92–2.36 (m, 4 H); IR (salt plate) 2960, 1962, 1628, 1467, 1260, 1201, 1178, 855 cm^{-1}; MS calcd for $C_{13}H_{26}OSi$ 226.1753, found 226.1738.

Acknowledgment. The authors thank the National Science Foundation for a research grant in support of this work and Cristina Montes for the preparation of several silyl ketones.

References and Notes

(1) For the previous paper in this series see: Reich, H. J., Rusek, J. J., Olson, R. E. *J. Am. Chem. Soc.* **1979,** *101*, 2225.

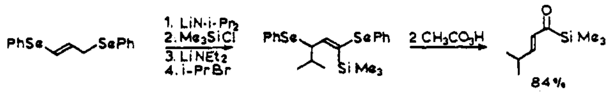
(2) Several siloxyallyllithium reagents have been previously prepared by deprotonation of allyl silyl ethers: (a) Still, W. C., Macdonald, T. L. *J. Am. Chem. Soc.* **1974,** *96*, 5561. (b) Hosomi, A., Hashimoto, H., Sakurai, H. *J. Organomet. Chem.* **1979,** *175*, C1. (c) Oppolzer, W., Snowden, R. L. *Tetrahedron Lett.* **1976,** 4187.

(3) (a) The derivatization of siloxybenzyllithium formed by Brook rearrangement of the silyl carbinol has been reported: Wright, A., West, R. *J. Am. Chem. Soc.* **1974,** *96*, 3214. Reaction occurs at oxygen or carbon depending on electrophile. (b) Kuwajima, I., Kato, M. (*Chem. Commun.* **1979,** 708) have recently shown that vinyltrimethylsilylcarbinols, prepared by vinyl Grignard addition to silyl ketones, serve as precursors for siloxyallyllithium reagents.

(4) (a) Brook, A. G., Quigley, M. A., Peddle, G. J. D., Schwartz, N. V., Warner, C. M. *J. Am. Chem. Soc.* **1960,** *82*, 5102. (b) Brook, A. G., Pascal, J. D. *Ibid.* **1971,** *93*, 6224. (c) Corriu, R. J. P., Masse, J. P. *J. Organomet. Chem.* **1970**, *22*, 321. (d) Sato, T., Abe, T., Kuwajima, I. *Tetrahedron Lett.* **1978,** 259.

(5) Brook, A. G. *Acc. Chem. Res.* **1974,** *7*, 77.

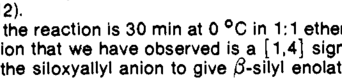
(6) Only a small number of vinyl silyl ketones have been reported.[1,7] The enone used in runs 12–15 was prepared as shown. A number of related enones



have been prepared by similar procedures (M. C. Clark, unpublished results).

(7) (a) Mantione, R., Leroux, Y. *J. Organomet. Chem.* **1971,** *31*, 5. (b) Reich, H. J., Shah, S. K., *J. Am. Chem. Soc.* **1977,** *99*, 263. (c) Minami, N., Abe, T., Kuwajima, I. *J. Organomet. Chem.* **1978,** *145*, C1.

(8) Earlier work[3a] has shown that the equilibrium i ⇌ ii lies on the right for R = H and on the left for R = Ph.



i ii

(9) Note that a second alkyl substituent at the *center* of the allyl system is tolerated (run 12).

(10) The half-life of the reaction is 30 min at 0 °C in 1:1 ether–THF.

(11) One side reaction that we have observed is a [1,4] sigmatropic O to C silicon shift in the siloxyallyl anion to give β-silyl enolate. Similar rearrangements have been reported for related systems: Still, W. C. *J. Org. Chem.* **1976,** *41*, 3063. Evans, D. A., Takacs, J. M., Hurst, K. M. *J. Am. Chem. Soc.* **1979,** *101*, 371.

(12) Merault, G., Bourgeois, P., Donogues, J., Duffaut, N. (*J. Organomet. Chem.* **1974,** *76*, 17) have prepared several allenol silyl ethers by reductive silylation of acetylenic ketones.

(13) For a recent review of enol silane chemistry, including many applications in organic synthesis, see Rasmussen, J. K. *Synthesis* **1977,** 91.

(14) Fellow of Alfred P. Sloan Foundation, 1975–1979.

(15) Deceased Oct 4, 1979.

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Molecular Mechanics Calculations of Reactivity Differences between Alicyclic Compounds

Sir:

The *I*-strain explanation of Brown for the differences in nucleophilic substitution, ketone reduction, cyanohydrin equilibria, etc., between alicyclic compounds represents one of the earliest attempts to relate steric energy changes accompanying $sp^3 \rightleftharpoons sp^2$ interconversions to chemical reactivity.[1a] Thus Brown suggested that relief of torsional angle or Pitzer strain and of transanular repulsions eases the formation of an sp^2 center in medium-ring compounds, opposite to strain-free cycloalkanes. Molecular mechanics force fields[2] allow calculations not only on ground states but in principle also on transition states and thus in particular on steric hindrance in reactivity. Other than in related earlier force-field approaches to reaction rates,[3] a rigorous test of the *I*-strain hypothesis requires strain energy calculations of a large number of conformations for each ring compound. This is illustrated with methylcyclodecane (Figure 1), where minimizations using the Allinger force field[2] yield the following conformer distribution. TCCC: Me in position 2, 16%; in position 3, 30%; in position 4, 14%. BCB: Me in position 2, 15%; in position 3, 22%; in position 4, 3%. Low-temperature ^{13}C NMR measurements have so far offered limited information supporting conformational equilibria of medium-ring compounds.[4]

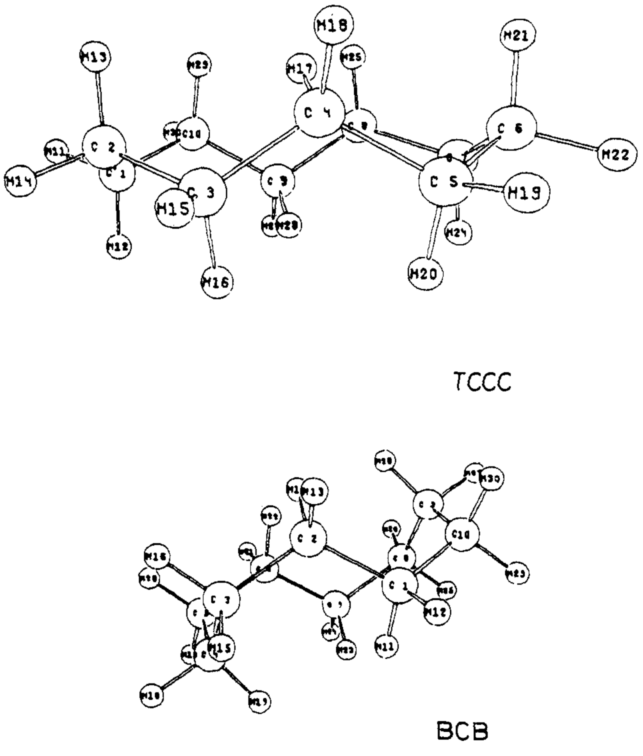

Figure 1. Cyclodecane conformations: TCCC, twist chair chair chair; BCB, boat chair boat.