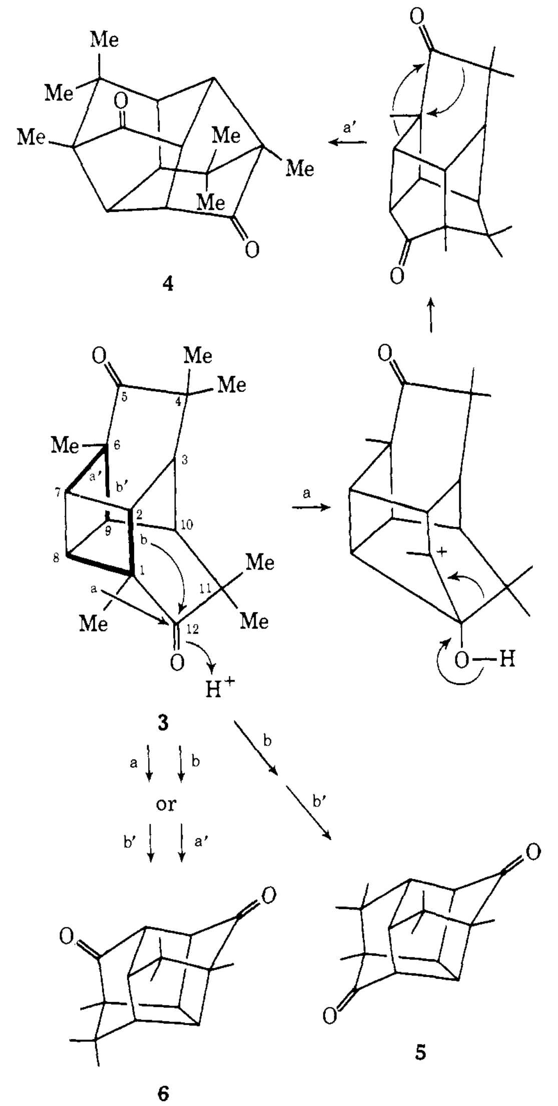

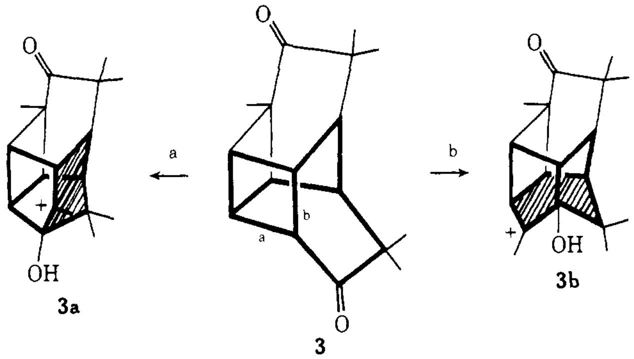

tion, whereas in **3b** the chair conformation is strongly distorted by a directly fused four-membered ring, destabilizing the structure of **3b**.

References and Notes

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Ken-ichi Hirao, Mikio Taniguchi
Takeo Iwakuma, Osamu Yonemitsu*
Faculty of Pharmaceutical Sciences, Hokkaido University
Sapporo, Japan

Judith L. Flippen, Isabella L. Karle
Laboratory for the Structure of Matter
Naval Research Laboratory
Washington, D.C. 20375

Bernhard Witkop*
Laboratory of Chemistry, NIAMDD,
National Institutes of Health
Bethesda, Maryland 20014

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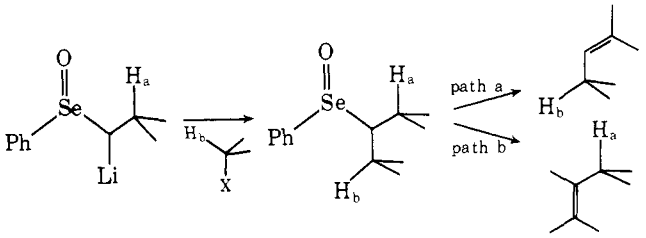
Organoselenium Chemistry. α-Lithio Selenoxides and Selenides. Preparation and Further Transformation to Olefins, Dienes, and Allylic Alcohols

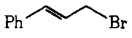
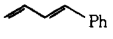
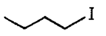
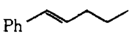
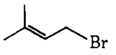
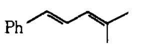
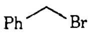
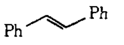
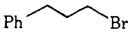
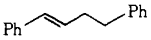
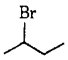
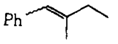
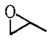
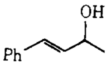
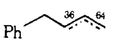
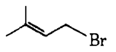
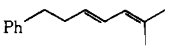
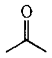
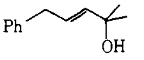
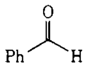
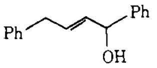
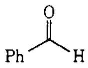
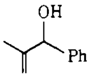
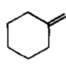
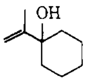
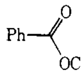
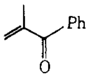
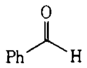
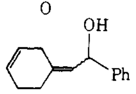
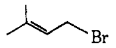
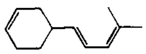
Sir:

Functionalized organolithium reagents have assumed an important role in synthetic organic chemistry. We report here the preparation and some reactions of several selenium stabilized organolithium reagents,[1] and synthetic applications based on the facile syn elimination of the selenoxide function.[2-4] The reaction products of selenium stabilized organolithium compounds with electrophiles could in general undergo selenoxide elimination in two directions.[5] Elimination away from the newly formed C–C bond (path a) results in an overall transformation synthetically equivalent to the operation of a vinyl anion; whereas, elimination across the new C–C bond (path b) results in a coupling of halides to form an olefin (alkyl selenides are usually prepared by nucleophilic displacements of halides or sulfonates by PhSeNa). To be synthetically useful, reactions of this type must have one pathway predominant, either because one elimination is blocked (no H_a or H_b) or by the operation of factors favoring one pathway over the other. We have found systems in which the exclusive operation of either path a or path b can be achieved.

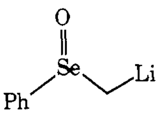


Methyl phenyl and benzyl phenyl[7] selenoxides cannot undergo selenoxide elimination, and so preparation and handling pose no special problems. They are rapidly deprotonated at −78° by lithium diisopropylamide (LDA) giving the anions **1** and **2**. Longer chain alkyl selenoxides having β-hydrogens must be handled below 0° to avoid the elimination reaction. We have developed procedures for the low temperature in situ oxidation of phenyl alkyl selenides (by ozonization in ether at −78°,[8] or reaction with *m*-chloroperbenzoic acid in THF at −10° [9]), and for deprotonation

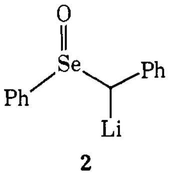
Table I. Preparation of Olefins by Reaction of Selenide and Selenoxide Stabilized Lithium Reagents with Electrophiles, Followed by Selenoxide Elimination

Anion[a]	Electrophile	Olefin[b]	% yield[a,b]
1			75
2			81
2			88
2			63
6			81[c]
6			78[d,e]
6			66[c]
3	CH_3I		59[e]
3			64[e]
3			81 (76)
3			72
4			81
4			55
4			73 (81)
5			(50)
5			(46)[e]

[a] For anions 1–5, yields given in parentheses were obtained using *m*-chloroperbenzoic acid as oxidant, the others using low temperature ozonization. [b] All compounds were adequately characterized by spectral methods, and new compounds gave satisfactory mass spectral or combustion elemental analysis. Yields quoted are for materials purified by short path distillation or preparative thin layer chromatography (1–10 mmol scale). [c] Oxidation and elimination was by the two-phase methylene chloride–hydrogen peroxide procedure (ref 4b). [d] Oxidation by ozonization at −78° in methylene chloride followed by addition to refluxing carbon tetrachloride. [e] Diphenyl diselenide was removed by oxidation with hydrogen peroxide to facilitate purification of the olefin.

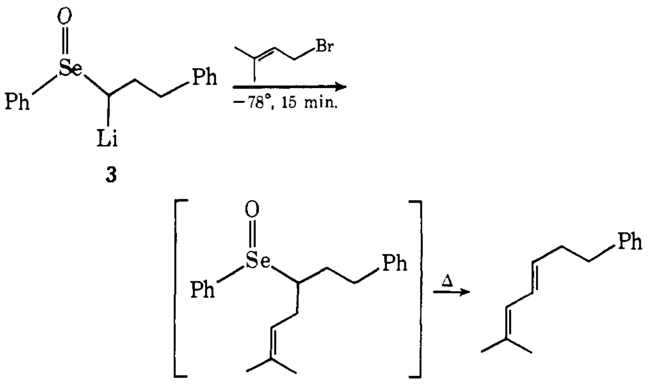


1



2

of the selenoxides using LDA. Both primary and secondary selenoxides are deprotonated rapidly at −78°, and the anions formed (e.g., **3** and **4**) react with aldehydes, ketones, and with the more reactive alkyl halides at −78°. The solutions are then neutralized and added to refluxing methylene chloride or carbon tetrachloride to cause selenoxide elimination[10] (see Table I). Alkylation products from **1** and **2** can only undergo selenoxide elimination across the new C–C bond (path b), but those from **3** and **4** can often give two products. When **3** is alkylated with methyl iodide two olefins are, in fact, obtained. With allyl halides, however, elimination to give conjugated dienes is strongly favored. The reaction products of **3** and **4** with ketones can only give allyl alcohols, but those from aldehydes could give either allyl alcohols (path a) or enols (path b). Only the former are observed. This remarkable reluctance of the selenoxide elimination to occur toward a carbon bearing a hydroxyl function was first observed by Sharpless and Lauer in their synthesis of allyl alcohols from epoxides and olefins.[4e] As also found previously, the preparation of disubstituted olefins by selenoxide elimination gives predominantly the trans isomer.[3,11] Application to a more complex system is illustrated by the anion **5**. Here ozonolysis cannot be used, but *m*-chloroperbenzoic acid selectively oxidizes the selenide in the presence of olefin.



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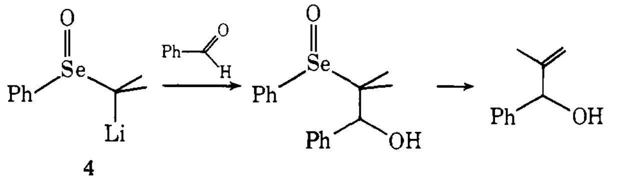

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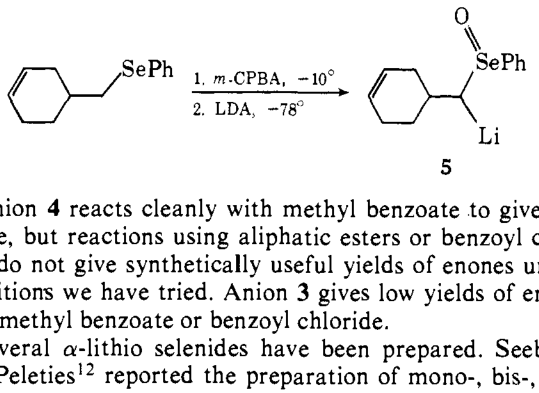


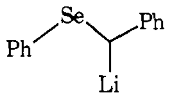
5

Anion **4** reacts cleanly with methyl benzoate to give the enone, but reactions using aliphatic esters or benzoyl chloride do not give synthetically useful yields of enones under conditions we have tried. Anion **3** gives low yields of enone with methyl benzoate or benzoyl chloride.

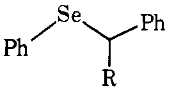
Several α-lithio selenides have been prepared. Seebach and Peleties[12] reported the preparation of mono-, bis-, and trisphenylselenomethyllithium, and made the observation that the phenylseleno group stabilizes anions to only a slightly lesser extent than the phenylthio group. They observed during the preparation of these reagents, and we have repeatedly observed with numerous other examples, that phenyl alkyl selenides (and selenoxides) are usually partially or completely cleaved rather than deprotonated by alkyllithium reagents. This reaction was used to good advantage in the preparation of $PhSeCH_2Li$ by cleavage of $PhSeCH_2SePh$ with *n*-butyllithium,[13] and has recently been extended to the preparation of more highly substituted systems.[14]

Lithium dialkylamides do not readily cleave selenides,[4h,12] and so are the preferred bases. We have found that simple alkyl selenides are not deprotonated, but benzyl and a variety of allyl selenides[15] can be deprotonated using LDA. The benzyl anion **6** is highly nucleophilic, and reacts cleanly with a range of electrophiles. Even 2-bromobutane and cyclohexene oxide react after 60–90 min at −78° (the alkylations are rapid at −30°, and are best done at this temperature), the other electrophiles shown react in a few minutes at −78°. No elimination occurs during any of these alkylations. Oxidation, either using the two-phase methylene chloride–hydrogen peroxide procedure,[4b] or by ozonolysis-pyrolysis[10] gives a variety of phenyl substituted olefins. Mitchell[4h] has recently reported the alkylation of **6** by several primary halides, and the oxidation-elimination of the products to give styrenes.

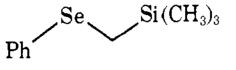
Compounds **7–8** are not deprotonated by LDA in THF, but **7b** gives the organolithium with lithium diethylamide (0°, 30 min). The trimethylsilyl substituent is apparently less kinetically acidifying than phenyl, phenylthio, or phenylseleno. The trimethylsilylmethyl selenide **8** is one of the few selenides that can be successfully deprotonated using alkyllithium reagents (*sec*-BuLi-TMEDA in hexane, 90 min, 25°). Only about 15% of cleavage products are obtained. Studies of the use of **7b** and **8** in the synthesis of vinyl silanes and/or carbonyl compounds[16] are in progress.



6



7a, R = CH_3
7b, R = $Si(CH_3)_3$



8

The selenide precursors for the systems **1–6** and **8** were prepared by reaction of PhSeNa (from reduction of PhSeSePh with sodium borohydride in ethanol) with the appropriate halide or mesylate, usually at room temperature. Selenides are thus easily prepared, and extension of the methods described here to more complex systems should be limited primarily by compatibility with the oxidizing[17] and deprotonation reagents used. In particular, the method allows the easy transformation of an alkyl halide or alcohol to the functional equivalent of a vinyl anion in reactions with carbonyl compounds.

Acknowledgment. We thank the National Science Foundation, the DuPont Company (DuPont Young Faculty Grant) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

References and Notes

(1) These results were presented in part at the American Chemical Society Midwest Regional Meeting, Iowa City, Iowa, Nov 8, 1974.
(2) (a) D. N. Jones, D. Mundy, and R. D. Whitehouse, *Chem. Commun.*, 86 (1970); (b) K. B. Sharpless, M. W. Young, and R. F. Lauer, *Tetrahedron Lett.*, 1979 (1973).
(3) Synthesis of α,β-unsaturated carbonyl compounds,[4a–f] allylic alcohols,[4e] α,β-unsaturated nitriles,[4f] exomethylene lactones,[4g] and styrenes[4h] have been reported using the selenoxide elimination.
(4) (a) H. J. Reich, I. L. Reich, and J. M. Renga, *J. Am. Chem. Soc.*, **95**, 5813 (1973); (b) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Org. Chem.*, **39**, 2133 (1974); (c) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973); (d) D. L. J. Clive, *J. Chem. Soc., Chem. Commun.*, 695 (1973); (e) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **95**, 2697 (1973); K. B. Sharpless and R. F. Lauer, *J. Org. Chem.*, **39**, 429 (1974); (f) D. N. Brattesani and C. H. Heathcock, *Tetrahedron Lett.*, 2279 (1974); (g) P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **39**, 120 (1974); (h) R. H. Mitchell, *J. Chem. Soc., Chem. Commun.*, 990 (1974).
(5) Only a single direction of elimination (path b) was possible for previous olefin syntheses using lithium reagents derived from α-phenylseleno esters,[4c,g] α-phenylselenino ketones,[4b] α-phenylsulfino esters,[6] and phenyl benzyl selenide.[4h]
(6) B. M. Trost, W. P. Conway, P. E. Strege, and T. J. Dietsche, *J. Am. Chem. Soc.*, **96**, 7165 (1974).
(7) M. Oki and H. Iwamura, *Tetrahedron Lett.*, 2917 (1966).
(8) Ether is used because it is somewhat less rapidly attacked by ozone than is THF. The blue color of excess ozone was used to detect the completion of the oxidation in ether, although the addition of the exact theoretical amount of ozone is preferable. The selenoxide usually precipitates as it is formed but redissolves when LDA is added. Reactions of the anions were usually performed in 1:1 ether–THF.
(9) The oxidation of alkyl phenyl selenides with *m*-chloroperbenzoic acid in THF is complete within 15 min at −10°. Anion formation requires the addition of 2 equiv of LDA.
(10) Sufficient acetic acid is added to neutralize strong base (alkoxide) and protonate half of the amine present, and the cold selenoxide solution is added to refluxing CCl_4 or CH_2Cl_2 under mildly basic conditions (HN-*i*-Pr_2). This procedure gives higher yields of purer products than simply warming the solution to room temperature. The elimination is complete essentially instantaneously in refluxing solvent.
(11) The preparation of α,β-unsaturated nitriles by selenoxide elimination is the only reported case where substantial amounts of cis isomer are formed.[4f]
(12) D. Seebach and N. Peleties, *Angew. Chem.*, **81**, 465 (1969); *Chem. Ber.*, **105**, 511 (1972).
(13) We have found that $PhSeCH_2Li$ can also be prepared from $PhSeCH_2Br$ and *t*-BuLi.
(14) W. Dumont, P. Bayet, and A. Krief, *Angew. Chem., Int. Ed. Engl.*, **13**, 804 (1974); D. Seebach and A. K. Beck, *ibid.*, **13**, 806 (1974). This work, which appeared after submission of our paper, describes the synthesis of allylic alcohols using α-lithio selenides.
(15) H. J. Reich, unpublished results.
(16) The rearrangement of phenyl trimethylsilylmethyl sulfoxide to (phenylthio)(trimethylsiloxy)methane has been reported by A. G. Brook and D. G. Anderson, *Can. J. Chem.*, **46**, 2115 (1968). See also F. A. Carey and O. Hernandez, *J. Org. Chem.*, **38**, 2670 (1973).
(17) G. Ayrey, D. Barnard, and D. T. Woodbridge, *J. Chem. Soc.*, 2089 (1962), have reported that selenides ozonize more rapidly than either 2-methyl-2-pentene or dibutyl sulfide. Ozonolysis of α-phenylseleno ketones[4b] and allyl phenyl selenide[15] occurs selectively at selenium. However, for 3-cyclohexenylmethyl phenyl selenide, *m*-chloroperbenzoic acid is more selective in oxidizing at selenium than ozone.

Hans J. Reich,* Shrenik K. Shah
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706

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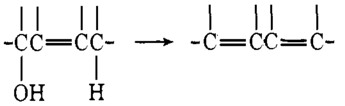
A General Method for the Synthesis of 1,3-Dienes. Simple Syntheses of β- and *trans*-α-Farnesene from Farnesol

Sir:

A highly stereospecific transformation of allylic alcohols into ethylenic derivatives has previously been described, as has the application of this reaction to the stereospecific synthesis of C_{18} *Cecropia* juvenile hormone.[1] The process is convenient and depending on the choice of reagent allows the synthesis of either olefinic isomer in good yields with high stereospecificity. We now wish to report a general method for an allylic alcohol → 1,3-diene conversion which depends crucially on the extraordinary effectiveness of organoaluminum reagent in oxirane ring opening.[2] The sequence shown in eq 1, which incorporates this reaction, constitutes a widely applicable method for the generation of 1,3-dienes in very mild conditions.[3]



$$-\underset{\underset{OH}{|}}{\overset{|}{C}}\overset{|}{C}=\overset{|}{C}\underset{\underset{H}{|}}{\overset{|}{C}}- \longrightarrow -\overset{|}{C}=\overset{|}{C}\overset{|}{C}=\overset{|}{C}- \qquad (1)$$

Reaction of nerol (**1**) with vanadium acetylacetonate–*tert*-butyl hydroperoxide in benzene at 25° for 2 hr[1,4] and subsequent treatment of trimethylchlorosilane–hexamethyldisilazane–pyridine at 25° for 30 min produces the epoxy silyl ether **2**. After washing with water and removing of the solvent, the crude product was subjected to the action of diethylaluminum 2,2,6,6-tetramethylpiperidide (DATMP) in benzene at 0° for 2 hr[2] followed by desilylation with excess potassium fluoride in aqueous methanol at 25° for 30 min[5] to produce the 3-substituted 3-butene-1,2-diol **3** (79% based on **1**), homogeneous by TLC and spectroscopically consistent with the indicated structure.[6] An analogous treatment of geraniol (**4**) furnished the isomeric diol **5** in 65% yield;[7] less than 6% of other isomers were determined by chemical degradation into conjugated aldehydes (IO_4^- in ethanol).[8] Thus, in the step of oxirane ring opening, *the site of attack of the organometallic reagent is enforced with remarkable*