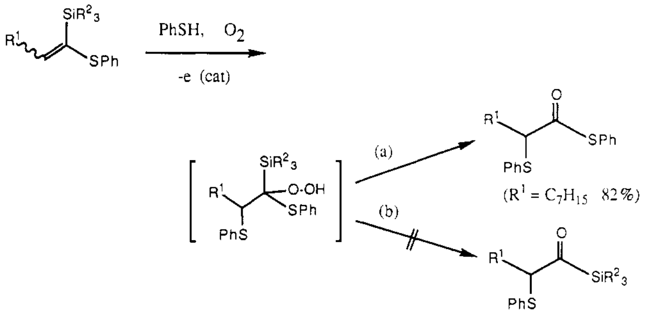
J. Org. Chem. 1989, 54, 5657-5659 5657

Scheme III



the radical with molecular oxygen gives the hydroperoxy radical, which abstracts hydrogen from another molecule of thiophenol to regenerate the phenylthio radical. The resulting hydroperoxide may decompose to give the corresponding α-phenylthio carbonyl compounds.[14]

Previously we have reported the oxygenation of alkenyl sulfides in the presence of thiophenol[4] and proposed a mechanism involving the hydroperoxide intermediate substituted by a phenylthio group,[15] which decomposed to give the carbonyl compounds. The following question then arises from a view point of decomposition mechanism of the hydroperoxide. If the hydroperoxide substituted by both a silyl group and a phenylthio group at the α-position is generated, which mode of decomposition would take place, (a) the carbon–silicon bond cleavage to give the thiolesters, or (b) the carbon–sulfur bond cleavage to give the acylsilanes (Scheme III)? Thus the oxygenation of alkenylsilanes substituted by the phenylthio group at the α-carbon[16] was examined. The reaction took place smoothly, and the corresponding α-phenylthio thiolesters were obtained as a sole product in high yields. The acylsilanes were not detected at all. This result indicates that the cleavage of the carbon–silicon bond took place exclusively without affecting the carbon–sulfur bond. Although more data should be accumulated before elucidation of the detailed mechanism, the present reaction gives an important insight into the chemistry of hydroperoxides,[17] as well as provides a convenient method for the synthesis of thiolesters activated at the α-position.

Acknowledgment. Financial support of this project by Grant-in-Aid, Scientific Research on Priority Areas (Advance Molecular Conversions) (No. 63607526), the Ministry of Education, Science and Culture, Japan is gratefully acknowledged.

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[14] Various reactions involving decomposition of silyl-substituted peroxides reported in the literature seems to relate the present reaction. (a) Silyl-substituted hypochlorites: Kuwajima, I.; Abe, T.; Minami, N. *Chem. Lett.* **1976**, 993. (b) Silyl-substituted peroxymetals: Knochel, P.; Xiao, C.; Yeh, M. C. P. *Tetrahedron Lett.* **1988**, *29*, 6697. (c) Endoperoxides of silyl-substituted furans: Katsumura, S.; Hori, K.; Fujiwara, S.; Isoe, S. *Tetrahedron Lett.* **1985**, *26*, 4625. (d) intermediate in ozonolysis of alkenylsilanes: Büchi, G.; Wüest, H. *J. Am. Chem. Soc.* **1978**, *100*, 294.

[15] (a) Takata, T.; Hoshino, K.; Takeuchi, E.; Tamura, Y.; Ando, W. *Tetrahedron Lett.* **1984**, *25*, 4767. (b) Takata, T.; Tamura, Y.; Ando, W. *Tetrahedron* **1985**, *41*, 2133. (c) Takata, T.; Ando, W. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1275.

[16] 1-(Phenylthio)-1-(trimethylsilyl)alkenes were readily prepared by the reaction of aldehydes with the anion of (phenylthio)bis(trimethylsilyl)methane in THF/hexane.

[17] Patai, S., Ed. *The Chemistry of Peroxides*; Wiley: Chichester, 1983.

γ-Lithioalkoxides via Reductive Lithiation of Oxetanes by Aromatic Radical Anions

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Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Received August 28, 1989

Summary: Oxetanes are cleaved at 0 °C in tetrahydrofuran by lithium 4,4'-di-*tert*-butylbiphenylide, giving lithium γ-lithioalkoxides which can provide 2-substituted tetrahydrofurans by trapping with aldehydes and ketones followed by acid cyclization of the resulting 1,4-diols; the cuprates of these dianions undergo conjugate addition and nucleophilic substitution reactions.

Sir: While the reductive cleavage of phenyl thioethers by aromatic radical anions is an efficient and general method for production of organolithium compounds,[1] the same procedure applied to simple acyclic ethers has only rarely been used.[2,3] However, it has recently been found that the reductive lithiation of oxiranes at −78 or −95 °C is a useful method for generating β-lithioalkoxides, which react with various electrophiles in moderate to good yields.[4]

We now report that γ-lithioalkoxides (**2**) can be efficiently generated by reductive lithiation of readily available oxetanes **1**[5] using lithium 4,4'-di-*tert*-butylbiphenylide (LDBB).[6] The temperature required (~0 °C) is substantially higher than that used for reductive cleavage of epoxides with the same reagent.[4b] Fortunately, the resulting γ-lithioalkoxides (**2**) do not undergo loss of lithium oxide as do β-lithioalkoxides[7] and are thus considerably more stable than the corresponding species derived from epoxides. The times required for the reductive cleavage range from 1 min to 4 h, depending on the substitution pattern; the reactivity order is **1d** > **1a** > **1b** >> **1c**. In unsymmetrical cases, the direction of opening is analogous to that observed in the reductive cleavage of epoxides.[4] Alkyl substituents at the 2-position lead to the least substituted carbanion (eq 1).[8] One explanation that has been put forth to explain this regiochemistry in the case of epoxides is that the greater stability of the more substituted alkoxide outweighs the lesser stability of the less

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[1] Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* **1989**, *22*, 152.

[2] Review: Maercker, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 972.

[3] A notable exception is the preparation of allyllithiums by reductive lithiation of allyl phenyl ethers: Eisch, J. J.; Jacobs, A. M. *J. Org. Chem.* **1963**, *28*, 2145.

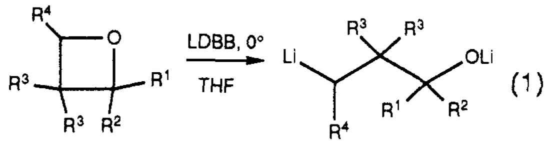
[4] (a) Bartmann, E. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 653. (b) Cohen, T.; Jeong, I.-H.; Mudryk, B.; Bhupathy, M.; Awad, M. A. A. *J. Org. Chem.*, in press.

[5] **2a** and **2b** are commercially available (Aldrich Co.). Other derivatives can easily be prepared. See, for example: (a) Okuma, K.; Tanaka, Y.; Kaji, S.; Ohta, H. *J. Org. Chem.* **1983**, *48*, 5133. (b) Picard, P.; Leclerq, D.; Bats, J. P.; Moulines, J. *Synthesis* **1981**, 550.

[6] Freeman, P.; Hutchinson, L. *J. Org. Chem.* **1980**, *45*, 1924.

[7] (a) Barluenga, J.; Flórez, J.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 3019. (b) Barluenga, J.; Fernández-Simón, J. L.; Concellón, J. M.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3339.

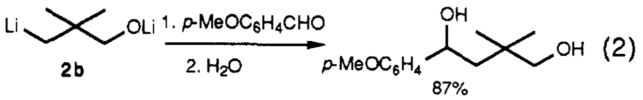
[8] Protonation of the reductive lithiation product of 2-octyloxetane provided 73% of 3-undecanol and 20% of 1-undecanol.



1 a: $R^1 = R^2 = R^3 = R^4 = H$ 2
b: $R^1 = R^2 = R^4 = H$; $R^3 = Me$
c: $R^1,R^2 = -(CH_2)_5-$; $R^3 = R^4 = H$
d: $R^1 = R^2 = R^3 = H$; $R^4 = Ph$

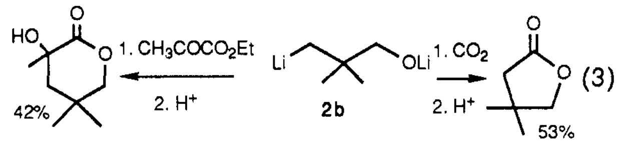
substituted radical thought to be formed upon rupture of the intermediate epoxide radical anion.[9] On the other hand, a phenyl group at the 2-position leads to the more substituted, benzylic anion (eq 1) as in the reductive lithiation of styrene oxide.[4a]

Equation 2 is an example of the reaction of the γ-lithioalkoxide cleavage products with aldehydes and ketones.[10,11] The dianion **2b** in this particular example is derived from the inexpensive 3,3-dimethyloxetane (**1b**).



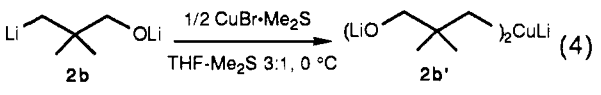
The reactions of the parent dianion **2a** with various aldehydes and ketones, including some conjugated unsaturated ones which undergo 1,2-addition, are shown in Scheme I. Similar reactions of **2c**, derived from the spirooxetane **1c**, and **2d** are shown in Schemes II and III. Alcohols, formed by hydride transfer from some of the β-lithioalkoxides to the aldehydes and ketones,[4b] are not observed in the case of γ-lithioalkoxides.

Equation 3 demonstrates one-pot syntheses of substituted γ-butyrolactones[12] and δ-valerolactones in moderate yields when **2b** is treated with carbon dioxide and ethyl pyruvate, respectively, followed by the acidic workup.

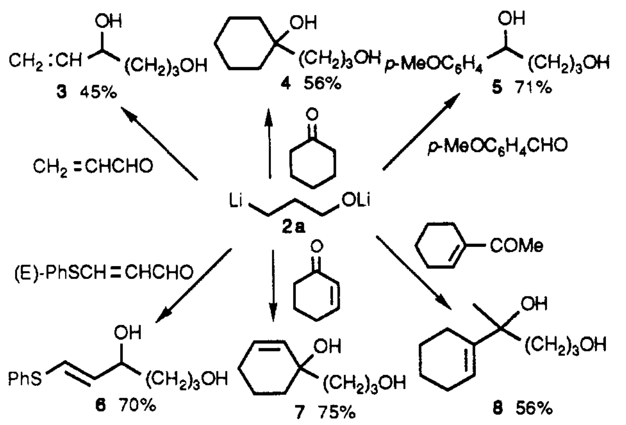


Most of the adducts, upon acid treatment, are able to form stabilized carbocations which are capable of internal capture by the second hydroxyl group to form 2-substituted tetrahydrofurans (Table I). This process constitutes an efficient ring expansion of oxetanes to substituted tetrahydrofurans. The 2-vinyltetrahydrofuran products should be capable of reacting with dichloroketene to form unsaturated 9-membered lactones.[13]

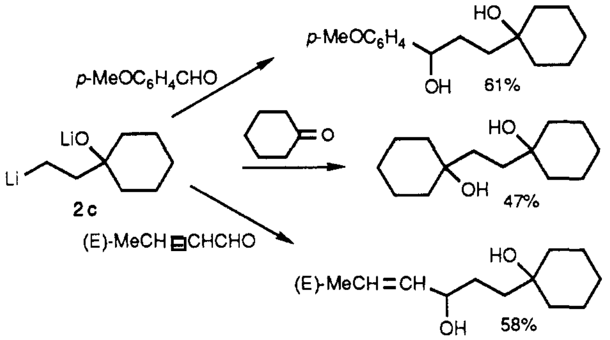
Dianion **2b** readily forms a cuprate **2b′** (eq 4). Its reactions with cyclohexenone, 1-oxaspiro[2,5]octane and alkyl bromides are shown in Table II.[14]



Scheme I



Scheme II



Scheme III

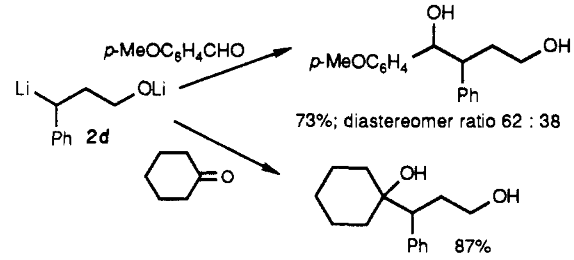
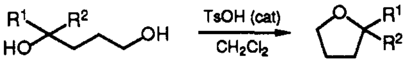
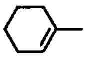


Table I. Cyclization of 1,4-Diols[a]



diol	R¹	R²	time	% yield
4	$-CH_2CH_2CH_2CH_2CH_2-$		5 h[b]	85
5	p-$MeOC_6H_4$	H	15 min	93
6	(E)-PhSCH=CH	H	2 min[c]	76
7	$-CH{=}CHCH_2CH_2CH_2-$		30 min	76
8		CH_3	10 min	75

[a] At 25 °C unless otherwise stated. [b] At reflux. [c] Longer stirring results in a complicated mixture of products.

There are two disadvantages, particularly in large scale runs, in the use of LDBB rather than the weaker reducing agent lithium 1-(N,N-dimethylamino)naphthalenide (LDMAN),[1] which cannot be used above −45 °C because of decomposition. One is the expense of the 4,4′-di-*tert*-butylbiphenyl (DBB) and the other is the chromatographic separation of this reduction byproduct from the desired product. Preliminary experiments have revealed a partial solution to these problems. A "catalyzed" reductive lithiation of **1b** was successful by using the stoichiometric quantity of lithium but only 20% of that (0.2 mol/g-atom

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(9) Dorigo, A. E.; Houk, K. N.; Cohen, T. *J. Am. Chem. Soc.*, in press.

(10) All products have been isolated by radial chromatography, and new compounds have been characterized by NMR and IR spectroscopy and high-resolution mass spectrometry.

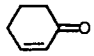
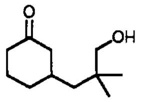
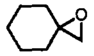
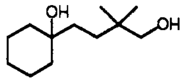
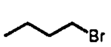
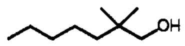
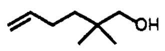
(11) The oxetane precursor of **2a** was used in 50% excess, the yields of **3–8** being based on the carbonyl compounds. This excess was not necessary in the case of the other oxetanes probably because of their lower acidity; see below.

(12) The use of another γ-lithioalkoxide in a γ-butyrolactone synthesis has been reported. Nájera, C.; Yus, M.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 289.

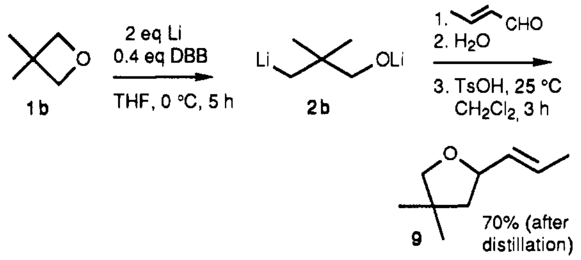
(13) Malherbe, R.; Bellus, D. *Helv. Chim. Acta* **1978**, *61*, 3096.

(14) 1,4-Addition and nucleophilic displacement reactions for $ClMg(CH_2)_3OMgCl$ in the presence of 5% CuBr have been reported: Cahiez, G.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1978**, 3013.

Table II. Reaction of 2b′ with Some Electrophiles

electrophile	product	yield, %
		78
		67
		60
		75

of Li) of DBB.[15] Equation 5 illustrates a one-pot synthesis of the vinyltetrahydrofuran **9** on a 6-g scale using this concept. However, when the unsubstituted **1a** was used instead, **2a** formed much less efficiently and a significant amount of 1-propanol was detected by GLC. It seems likely that in the latter case destruction of the dianion **2a** proceeded via abstraction of an α-proton from the sterically unhindered oxetane **1a**, a precedented type of deprotonation.[16]



(5)

This method of production of γ-lithioalkoxides nicely complements the other two methods that have been reported, reductive lithiation of a γ-chloroalkoxide[7a,12,17,18] and tin–lithium exchange of a γ-(tributylstannyl)alkoxide.[19] In the former method, the availability of substrates is severely limited and the yields are often poor, and only one example of the latter method has been reported. The major attraction of the present method is the ready availability of oxetanes and the ability to prepare them from epoxides;[5a] because the latter can frequently be obtained in optically active form,[20] optically active oxetanes and γ-lithioalkoxides should also become available.[21]

Acknowledgment. We thank the National Science Foundation for financial support and Professor Dennis Curran for a suggestion which stimulated this work.

Supplementary Material Available: Sample procedures for reductive lithiation of oxetanes and reactions of the dianions with electrophiles as well as spectral data for the products (19 pages). Ordering information is given on any current masthead page.

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(15) For the use of LDMAN in the reductive lithiation of thioketals by the catalytic method, see: Cohen, T.; Matz, J. R. *Synth. Commun.* **1980**, 311.

(16) Schakel, M.; Vrielink, J. J.; Klumpp, G. W. *Tetrahedron Lett.* **1987**, *28*, 5747.

(17) Barluenga, J.; Flõrez, J.; Yus, M. *Synthesis* **1983**, 378; **1985**, 846.

(18) The corresponding magnesium chloride derivatives have been prepared by an analogous procedure but reducing by magnesium rather than an aromatic radical anion.[14]

(19) Zidani, A.; Vaultier, M. *Tetrahedron Lett.* **1986**, *27*, 857.

(20) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765, and citations therein. Rao, A. S.; Palnikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323.

(21) Seebach has prepared optically active γ-lithioalkoxides from chloro alcohols.[12]

Stereoselective Addition Reactions of Chiral α-Sulfinyl Ketimine Anions with Ene Esters. Facile Asymmetric Syntheses of Indolo[2,3-*a*]quinolizidine and Yohimbanoid Alkaloids[†]

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Department of Chemistry, Kansas State University, Manhattan, Kansas 66506

Received September 5, 1989

Summary: A convenient route for the construction of chiral indolizidines and yohimbanoid alkaloids from the 1,4-addition/ring-closure reactions of chiral α-sulfinyl ketimine anions with ene esters is presented.

Sir: In the course of studies involving the enantioselective synthesis of functionalized indolizidines, such as (+)-castanospermine[2] via chiral sulfoxides,[3] the addition reactions of chiral α-sulfinyl ketimines with ene esters were investigated. Although the analogues silyl aldimines,[4a] tin aldimines,[4b] β-aminoalkenephosphonates,[4c] α-sulfinyl oxazolines,[5a,b] α-sulfinyl hydrazones,[5c–e] β-aminoalkenenitriles, and β-aminoalkene esters[6] have been reported, α-sulfinyl ketimines like **1** and **2** have not. Herein, we describe the preparation and stereoselective in situ addition/ring-closure reactions of α-sulfinyl ketimines and the utilization of **2** in the asymmetric syntheses of (−)-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine [(−)-**3**],[7] (−)-*allo*-

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[†] This paper is dedicated to Cal Y. Meyers on the occasion of his 60th birthday.

[‡] Fellow of the Alfred P. Sloan Foundation, 1989–1991.

(1) Department of Chemistry, University of Kansas, Lawrence, KS 66045.

(2) Isolation and structure: (a) Hohenschutz, L.; Bell, E. A.; Jewess, P. J.; Lewothy, D. P.; Pryce, R. J.; Arnold, E.; Clardy, J. *Phytochemistry* **1981**, *20*, 811. Synthesis: (b) Bernotas, R. C.; Ganem, B. *Tetrahedron Lett.* **1984**, *25*, 165. (c) Hamana, H.; Ikota, N.; Ganem, B. *J. org. Chem.* **1987**, *52*, 5492.

(3) Hua, D. H.; Venkataraman, S.; Chan-Yu-King, R.; Paukstelis, J. V. *J. Am. Chem. Soc.* **1988**, *110*, 4741 and references 5 cited therein.

(4) (a) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, *1*, 7 and references cited therein. (b) Brocas, J.-M.; De Jeso, B.; Pommier, J.-C. *J. Organomet. Chem.* **1976**, *120*, 217. (c) Nagata, W.; Hayase, Y. *J. Chem. Soc. C* **1969**, 460.

(5) (a) Annunziata, R.; Cinquini, M.; Gilardi, A.; Cozzi, F. *Synthesis* **1983**, 1016. (b) Bernardi, A.; Colombo, L.; Gennari, C.; Prati, L. *Tetrahedron* **1984**, *40*, 3769. (c) Annunziata, R.; Cozzi, F.; Cinquini, M.; Colombo, L.; Gennari, C.; Poli, G.; Scolastico, C. *J. Chem. Soc., Perkin Trans. I* **1985**, 251. (d) Annunziata, R.; Cinquini, M.; Cozzi, F.; Gilardi, A.; Cardani, S.; Poli, G.; Scolastico, C. *J. Chem. Soc., Perkin Trans. I* **1985**, 255. (e) Annunziata, R.; Cardani, S.; Gennari, C.; Poli, G. *Synthesis* **1984**, 702.