65-4; (±)-**10** (acid chloride), 89578-67-6; (±)-**10** (diazo ketone), 89578-81-4; (±)-**14**, 89578-66-5; (±)-**15**, 89578-68-7; (±)-**15** (acid), 89578-69-8; (±)-**16**, 89578-70-1; **17**, 13379-98-1; **17** (triflate), 89578-82-5; **18**, 89578-71-2; **19**, 89578-72-3; **20**, 89578-73-4; **21**, 89596-61-2; (±)-**23**, 89578-74-5; (±)-**24**, 89578-75-6; (±)-**24** (2,4,5-trichlorophenol), 89578-83-6; (±)-**25**, 89578-76-7; (±)-**26**, 89578-77-8; (±)-**27**, 89578-78-9; (±)-**28**, 89578-79-0; (±)-**29**, 89578-80-3; methyl glyoxylate, 922-68-9; 3-aminopropanol, 156-87-6; *N*-(4-bromobutyl)phthalimide, 5394-18-3; trifluoromethanesulfonic anhydride, 358-23-6; 4-aminobutanol, 13325-10-5.

Supplementary Material Available: Complete X-ray data for compound **10** (12 pages). Ordering information is given on any current masthead page.

A General Procedure for Preparing α-Lithiosilanes. Generalization of the Peterson Olefination[1]

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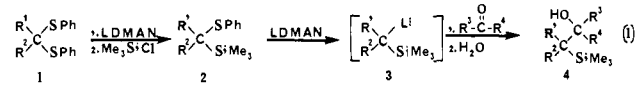
Abstract: A particularly convenient method for the preparation of α-lithiosilanes consists of the reductive lithiation of diphenyl thioacetals or thioketals with lithium 1-(dimethylamino)naphthalenide, treatment of the resulting anion with trimethylsilyl chloride, and reductive lithiation, with the same reducing agent, of the resulting α-(phenylthio)silane. The generality of the procedure is demonstrated by the preparation of α-lithiosilanes in which the negatively charged carbon atom is secondary, tertiary, vinylic, or part of a cyclopropyl ring. These species react with aldehydes and ketones to produce alcohols which, in all cases except the allylic alcohol produced from the vinylic α-lithiosilane, could be induced to form an olefin by loss of the elements of trimethylsilanol upon treatment with potassium hydride or acid.

The Peterson olefination,[2,3a] involving the reaction of an α-lithiosilane[3b] with an aldehyde or ketone followed by elimination of the hydroxide and silicon functions, is a potentially powerful alternative to the Wittig olefination, particularly because of the fact that the elimination step can usually be directed in either a syn or an anti manner.[4] However, the method has had the serious limitation that except in special cases α-lithiosilanes have not been readily available.[1a,3] Since early 1980[5], we have been studying the feasibility of preparing these organometallics by reductive lithiation, using lithium 1-(dimethylamino)naphthalenide[6] (LDMAN), of α-(phenylthio)silanes, a class of compounds two members of which we have reported to be available by reductive lithiation with lithium naphthalenide[7] or LDMAN[6] of diphenyl thioacetals followed by silylation; in addition to conventional procedures[8] for preparing such thioacetals, simple and versatile methods for preparing a variety of cyclopropanone thioketals[9] and ketene thioacetals[10] have recently been developed in our laboratory.

Results and Discussion

Preparation of α-Lithiosilanes. We now report that this method is completely general for the production of α-lithiosilanes (eq 1 and Table I).

We have found LDMAN to be far superior to lithium naphthalenide in the reductive lithiation steps for it obviates the necessity to separate the naphthalene byproduct from the neutral products; the 1-(dimethylamino)naphthalene is simply washed out with dilute acid.[11-13] We have found that even very acid sensitive groups can withstand this treatment.[14]



(1)

The reductive lithiation method is the only general one for the prepation of α-lithiosilanes containing no additional functionality.[15] An alternative procedure for the production of secondary α-lithiosilanes **3** ($R^1 \neq H$; $R^2 = H$) involves lithium–selenium exchange, but the yields are not entirely satisfactory and the method is not applicable to tertiary α-lithiosilanes (**3**, R^1 and $R^2 \neq H$)[16] except for the special case of 1-(lithiocyclopropyl)trimethylsilane.[17,18] The required α-(phenylthio)silane can be

(1) Taken in part (a) from the M.S. thesis of Paul R. Willey, University of Pittsburgh, 1981, and (b) from the Ph.D. thesis of James R. Matz, University of Pittsburgh, 1981.

(2) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780.

(3) (a) Chan, T.-H. *Acc. Chem. Res.* **1977**, *10*, 442. Colvin, E. "Silicon in Organic Synthesis"; Butterworths: Boston, 1975; Chapters 4 and 12. (b) Paquette, L. A. *Science* **1982**, *217*, 793.

(4) Hudrlik, P. F.; Peterson, D. *Tetrahedron Lett.* **1974**, 1133; *J. Am. Chem. Soc.* **1975**, *97*, 1464. Hudrlik, P. F.; Peterson, D.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2263.

(5) Many of the results reported here were discussed by T.C. in various lectures during 1981 and late 1980 in the United States and Europe; see footnote 3 of ref 17.

(6) Cohen, T.; Matz, J. R. *Synth. Commun.* **1980**, *10*, 311.

(7) Cohen, T.; Weisenfeld, R. B. *J. Org. Chem.* **1979**, *44*, 3601.

(8) Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

(9) (a) Cohen, T.; Daniewski, W. M. *Tetrahedron Lett.* **1978**, 2991. (b) Cohen, T.; Weisenfeld, R. B.; Gapinski, R. E. *J. Org. Chem.* **1979**, *44*, 4744. (c) Cohen, T.; Matz, J. R. *Ibid.* **1979**, *44*, 4816.

(10) Cohen, T.; Gapinski, R. E.; Hutchins, R. R. *J. Org. Chem.* **1979**, *44*, 3599.

(11) (a) Ager[12] has recently reported an analogous sequence for a specific subclass of **1**, namely diphenylthioacetals in which $R^1 = H$ and R^2 = phenyl or alkyl, using lithium naphthalenide rather than LDMAN. However, no mention was made of the problem of separating the α-silyl thioether from the naphthalene, one that has caused us and others[13] great grief before the LDMAN reagent was developed.[6] Also in this paper[12] it is implied that treatment of the α-lithiosilane with ketones or aldehydes yields olefins directly; no details are given. This does not correspond to our experience; as indicated, we found it necessary to treat the alcohols **4** with KH or with acid to effect elimination. (b) Paquette[13] prepared **3** ($R^1R^2 = CH_2CH_2$) from **2** ($R^1R^2 = CH_2CH_2$) using reductive lithiation with lithium naphthalenide, but the method was abandoned when the chromatography required to separate the alcohols (**4**, $R^1R^2 = CH_2CH_2$) from the naphthalene caused dehydration of the tertiary alcohols. Paquette also claimed that LDMAN gave incomplete reduction; we have found this not to be the case.

(12) Ager, D. J. *Tetrahedron Lett.* **1981**, *22*, 2983.

(13) (a) Paquette, L. A.; Horn, K. A.; Wells, G. J. *Tetrahedron Lett.* **1982**, *23*, 259. (b) Paquette, L. A.; Wells, G. J.; Horn, K. A.; Yau, T. H. *Tetrahedron* **1983**, *39*, 913.

(14) Cohen, T.; Bhupathy, M.; Matz, J. R. *J. Am. Chem. Soc.* **1983**, *105*, 520.

(15) Review of β-hetero-substituted organometallics: Krief, A. *Tetrahedron* **1980**, *36*, 2531.

(16) Dumont, W.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 161.

(17) Halazy, S.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1981**, *22*, 4737.

(18) A still less general method involves the addition of an alkyllithium to a triorganylvinylsilane. Cason, L. F.; Brooks, H. G. *J. Org. Chem.* **1954**, *19*, 1278. Chan, T.-H.; Chang, E.; Vinokur, E. *Tetrahedron Lett.* **1970**, 1137. See also ref 4.

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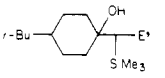
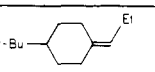
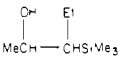
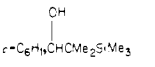
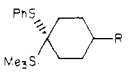
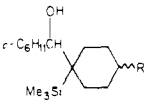
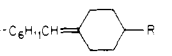
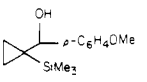
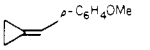
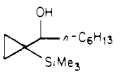
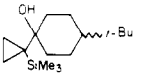
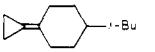
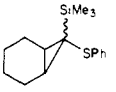
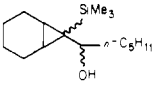
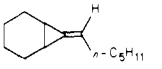
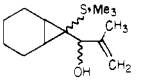
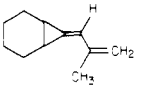
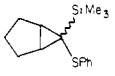
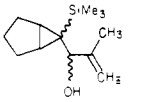
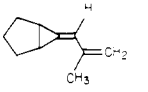
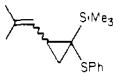
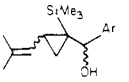
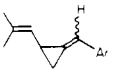
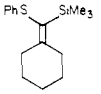
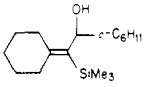
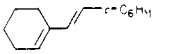
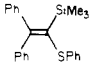
Table I. Preparation of α-(Phenylthio)trimethylsilanes and Their Use, via Reductive Lithiation, in the Peterson Olefination

α-(phenylthio)trimethylsilane[a]	% yield[b]	alcohol	% yield[b]	% olefin[b,c]	yield
$EtCH(SPh)SiMe_3$ (10)	86	 11	30[d]	 12	84[e] 62[f]
		 13	65[g]	*h*	
$c\text{-}C_6H_{11}CH(SPh)SiMe_3$ (14)	90	*i*			
$Me_2(SPh)CSiMe_3$ (15)	92	 16	79	$c\text{-}C_6H_{11}CH{=}CMe_2$ 17	92[j,k]
					
18, R = H 21, R = *t*-Bu	71 83	19, R = H 22, R = *t*-Bu	51[d] 58[d,m,n]	20, R = H 23, R = *t*-Bu	83,[l] 59[f] 80[o]
 24	95	 25	85	 26	90[p]
		 27	84	*h*	
		 28	86[q]	 29	86[r]
 30	86[n]	 31	92[q]	 32	98[s]
		 33	90[q]	 34	100[t]
 35	95[n]	 36	91[n]	 37	95[t]
 38	95[u]	 39	92	 40	95[v,w]
 41	96	 42	85	 43	72[x,y]
 48	87	*z*			

[a] Except where otherwise noted, all α-(phenylthio)trimethylsilanes were prepared from the corresponding thioacetal or thioketal. [b] For chromatographed material unless otherwise noted. [c] Yield for elimination step only unless otherwise noted. [d] Considerable decomposition of the alcohol occurred upon flash chromatography. [e] KH/THF, 19 h; 25 °C. [f] Overall yield of olefin from α-(phenylthio)silane; acid-catalyzed elimination performed on unpurified alcohol. [g] For distilled product. [h] Elimination step not performed. [i] Reduction to α-lithiosilane not performed. [j] Reference 53. [k] KH/diglyme, 2.5 h, 90 °C. [l] KH/THF; 0.5 h, 25 °C. [m] Reductive lithiation performed for 4 min at −78 °C. [n] Mixture of epimers. [o] Overall yield from α-(phenylthio)silane, using KH/THF, 1.5 h, 25 °C, for elimination on unpurified alcohol; yield 89% on the basis of consumed reactant. [p] KH/THF, 5 h, 90 °C. [q] A single isomer of unknown configuration. [r] KH/diglyme, 3.5 h, 90 °C. [s] KH/diglyme, 15 min, 25 °C. [t] KH/THF, 1.5 h, 25 °C. [u] Mixture of cis and trans isomers. [v] It is uncertain if this is one or more geometric isomer. [w] KH/THF, 25 °C. Reaction time: isomer A, 20 h; the mixture of isomers B, C, and D, 4 h. [x] Elimination carried out by Chan's procedure.[26d] [y] Isomerization product of allene isolated; see text. [z] The substrate did not undergo reductive lithiation in the presence of LDMAN.

prepared not only from the readily available diphenyl thioacetal group[8] as indicated in eq 1 but also by alkylation of the conjugate base of (phenylthio)(trimethylsilyl)methane (**2**, $R^1 = R^2 = H$)[12] and by addition of an alkyllithium to an appropriately substituted alkene.[19]

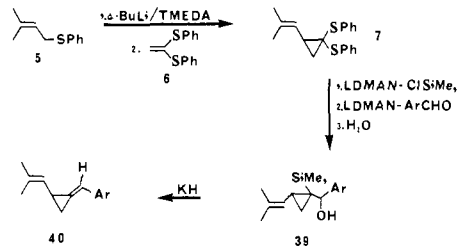
An attractive feature of the reductive lithiation route to organolithium compounds is the ability to produce tertiary α-lithiosulfides [by reductive lithiation of thioketals **1** (R^1 and $R^2 \neq H$)] and tertiary α-lithiosilanes [**3** (R^1 and $R^2 \neq H$)]. Such anionic species are not generally available by deprotonation or other exchange procedures. The instability of these tertiary lithio compounds necessitates certain precautions in their preparation and use and these are indicated in the Experimental Section.

A single silylation product was obtained when this procedure was applied to the thioketal of 4-*tert*-butylcyclohexanone. It is assigned the structure **21** (Table I) on the basis that its precursor anion is protonated exclusively to *trans*-1-(phenylthio)-4-*tert*-butylcyclohexane. This result is consistent with the concept that the organolithium is produced by reduction of a radical precursor[20]; in other reductions proceeding through tertiary cyclohexyl radicals, the latter apparently assume a conformation in which the substituent on the radical carbon atom assumes the equatorial position.[21]

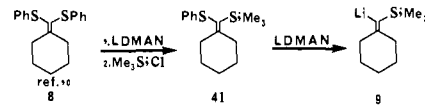
The silylation of the anion derived from the reductive lithiation of 7,7-bis(phenylthio)norcarane affords an epimeric mixture **30** in a ratio of 3:1 favoring the *endo*-7-trimethylsilyl epimer. This assignment is made on the basis that protonation of the same anion affords an identical ratio of *exo*- and *endo*-7-(phenylthio)norcarane, both of which are known compounds.[22] This can be understood on the basis that there is some preference for the initially produced radicals to interconvert very rapidly and to produce a mixture richer in the less sterically encumbered species possessing an exo substituent.[20b] A second electron is donated to form the anion which is configurationally stable.[20b] However, on this basis one would expect somewhat similar results in the formation of **35** but a 1:1 mixture of epimers is obtained instead.

The tertiary α-lithiosilane derived from the reductive lithiation of **21** is protonated or sulfenylated ($PhSSO_2Ph$) to an approximately 1:1 mixture of epimers. This may indicate that a flat configuration of the silicon-stablized anion is readily attainable, a conclusion which is consistent with the easily attained linearity of silicon stabilized vinyl anions[23] and the stereochemical instability of 7-lithio-7-(trimethylsilyl)norcarane at −90 °C.[24] Our results show this tendency in the norcarane system as the product of the reaction of the α-lithiosilane derived from the epimers of **30** with an aldehyde afforded a single epimeric alcohol (**31** or **33**) of unknown configuration. Similarly, the product from the epimers of **35** afforded primarily one epimeric product, **36** (>9:1). These results can be rationalized if it is assumed that the aldehyde approaches the flat silicon-stabilized anions from the accessible exo face of the fused ring systems.

Very recently (1-lithiocyclopropyl)trimethylsilanes have been prepared by selenium–lithium[17] and bromine–lithium exchange.[17,24a] The method reported here nicely complements these methods and will be particularly suitable in cases in which the cyclopropanone thioketal is available by one of the newer versatile procedures.[9,25] An example of such a procedure is the reaction of the sulfur stabilized conjugate base of **5** with **6** to produce the vinylcyclopropanone thioketal **7**.[9b] Subsequent formation of the β-silylcarbinol **39** affords the precursor of **40**, a member of an important class of alkylidenecyclopropanes (see below). It would be difficult or impossible to prepare the α-lithiosilane precursor to **39** by competing procedures[17,24a] or the β-silylcarbinol (**39**) by cyclopropanation of a diene.[13]



There has been considerable recent interest in the preparation and in a variety of uses of silyl-substituted vinyl anions.[26,27] The method of preparation reported here is in most cases a considerable improvement over existing methods[26,27] which all start from 1-silyl-1-halo-1-alkenes, a class of compounds the members of which are sometimes cumbersome to prepare.[26a,b,27-29] Reductive lithiation of 1-(phenylthio)-1-(trimethylsilyl)alkenes provides an attractive alternative as illustrated by the preparation of **9**:



Only one[29] of the previous methods[26-29] is applicable to the preparation of **9**. The ready availability of ketene thioacetals by the reaction of carboxylic acids or esters with aluminum thiophenoxide[10] and by certain Wittig-type connective methods,[30] as well as the ease of the reductive lithiation step, clearly makes the present procedure of value for preparing silicon-stabilized vinyllithium compounds.

It is of some interest to note an apparent minor limitation of this method. The 1-(phenylthio)-1-(trimethylsilyl)alkene **48**, formed in the usual way in two steps from diphenylacetic acid, fails to undergo reductive lithiation with LDMAN; only starting material is recovered. Apparently the radical anion, generated when **48** accepts an electron, has such great stability vis-a-vis the vinyl radical and the thiophenoxide ion that would be produced from it that it fails to irreversibly eject the thiophenoxide ion.

Reactions of α-Lithiosilanes with Aldehydes and Ketones. The α-lithiosilanes add in satisfactory yield to aldehydes and to 4-*tert*-butylcyclohexanone (Table I). The α-lithiosilane derived from **24** adds to 4-*tert*-butylcyclohexanone at −78 °C to afford an 86% yield of **28**. In preliminary experiments using cyclohexanone as the carbonyl compound, the yields of β-silylcarbinol decreased with increasing reaction temperature. Enolization is the only reaction observed when the α-lithiosilanes derived from **38** and

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(20) (a) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900. Cohen, T.; Lin, M.-T. *Ibid.* **1984**, *106*, 1130. (b) Freeman, P. K.; Hutchinson, L. L. *J. Org. Chem.* **1980**, *45*, 3191.

(21) House, H. O. "Modern Synthetic Reactions"; 2nd ed; Benjamin: New York, 1972; pp 155 and 156.

(22) Schöllkopf, U.; Lehman, G. J.; Paust, J.; Härtl, H.-D. *Chem. Ber.* **1964**, 1527.

(23) Zweifel, G.; Murray, R. E.; On, H. P. *J. Org. Chem.* **1981**, *46*, 1292. Cunico, R. F. *J. Organomet. Chem.* **1973**, *60*, 219.

(24) (a) Hiyama, T.; Kanakura, A.; Morizawa, Y.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 1279. (b) Brinker, U. H.; König, L. *J. Am. Chem. Soc.* **1979**, *101*, 4738.

(25) We shall soon disclose a new efficient connective method for the preparation of complex 1-(phenylthio)trimethylsilylcyclopropanes.

(26) (a) Ottolenghi, A.; Fridkin, M.; Silkha, A. *Can. J. Chem.* **1963**, *41*, 2977. (b) Gröbel, B. T.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 83; *Chem. Ber.* **1977**, *110*, 852, 867. (c) Stork, G.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 6152. Boeckman, R. K., Jr. *Ibid.* **1973**, *95*, 6867. Boeckman, R. K., Jr. *Tetrahedron Lett.* **1974**, 3365. (d) Chan, T. H.; Mychajlowskij, W.; Ong. B. S.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 1526.

(27) Miller, R. B.; McGarvey, G. *J. Org. Chem.* **1979**, *44*, 4623.

(28) Westmijze, H.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1977**, 1923.

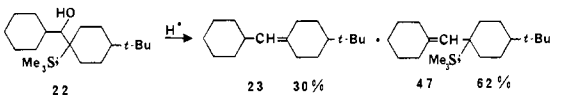
(29) Seyferth, D.; Lefferts, J. L.; Lambert, R. L., Jr. *J. Organomet. Chem.* **1977**, *142*, 39. These authors reported the preparation of the analogue of **41**, in which a bromine atom replaces the PhS group, in 34% yield, by reaction of cyclohexanone with $PhHgCBr_3$ and Ph_3P followed by *n*-butyllithium and then Me_3SiCl; presumably this compound could be used to generated **9**.

(30) (a) Seebach, D.; Kolb, M.; Gröbel, B.-T. *Chem. Ber.* **1973**, *106*, 2277. (b) Mendoza, A.; Matteson, D. S. *J. Org. Chem.* **1979**, *44*, 1352.

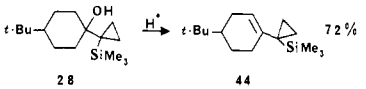
21 are treated with the noncyclic ketones acetone and 3-pentanone, respectively, at −78 °C.

Elimination to Olefin. The generally preferred method for performing the elimination uses KH in either THF or diglyme. With KH, eliminations to unstrained olefins and allylidenecyclopropanes often occur at 25 °C in THF. When unconjugated alkylidenecyclopropanes are the products, the eliminations must be performed in diglyme instead of THF. Alcohols **16** and **28**, which are particularly resistant to base-induced elimination, give good yields of olefin only when treated with KH in diglyme at 90 °C; it was later found that the base-induced elimination steps generally occur more rapidly in diglyme than in THF.

For comparison purposes, certain olefinations were carried out by using H_2SO_4; when **22** was subjected to acid treatment, both the expected olefin **23** and a larger amount of the allylic silane **47** were produced. The one 1-(trimethylsilyl)cyclopropylcarbinol



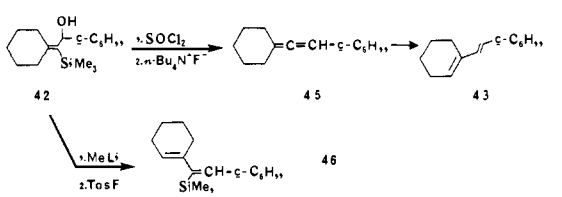
22 23 30% 47 62%



28 44

28 which was treated with acid also underwent dehydration to an allylsilane **44**. There are precedents for such behavior.[13,26d] However, in certain cases acid-induced eliminations were successful for the conversion of crude alcohols to the corresponding olefins. This procedure is a significant improvement over the usual olefination sequence from the α-(phenylthio)silane for compounds whose precursor alcohols are not stable to various chromatographic conditions. Treatment of crude alcohols **11** and **19** with a THF solution of H_2SO_4 afforded the olefins **12** and **20** in 62% and 59% overall yield from the α-(phenylthio)silane. Base-induced elimination was also successfully applied to one of the crude alcohols (see **22**, Table I).

The alcohol **42** posed a problem with regard to elimination. Chan[26d] has found that analogues of **42** are particularly resistant to the usual methods of elimination, and we could not induce elimination in the case of **42** by the use of KH. Chan[26d] was able to obtain phenylallene by treatment of the analogue of **42** with thionyl chloride and subjecting the mixture of allylic chlorides to reaction with fluoride ion. All of the examples studied were terminal olefins. When the allylic chlorides obtained by the reaction of **42** with thionyl chloride were treated with tetra-*n*-butylammonium fluoride, a 72% yield of the trans-diene **43** along with 15% of a mixture of the two geometric isomers of **46** was realized after chromatography. Diene **46** is the elimination product of the chlorides of **42**. (**46** was the major product obtained by treatment of the lithium salt of **42** with *p*-toluenesulfonyl fluoride.) The expected allene **45** probably undergoes a prototropic shift during the chromatographic procedure to yield **43**. A control experiment demonstrated that **43** did not arise by protodesilylation of **46**.



42 45 43 46

Alkylidenecyclopropanes. The excellent yields of alkylidenecyclopropanes indicate that this method compares favorably with extant procedures,[17,24,30a,31,32,33] none of which are applicable to the synthesis of **40**. Alkylidenecyclopropanes are very valuable intermediates in organic synthesis. Oxidation with peracid provides oxaspiropentanes which are capable of rearrangement to cyclobutanones.[34] Simple alkylidenecyclopropanes have been shown to undergo a variety of metal-catalyzed additions to olefins.[35] 2-Vinyl-1-alkylidenecyclopropanes undergo base-catalyzed rearrangement to 1,3-divinylcyclopropanes which, in turn, rearrange to 7-membered rings.[36] 2-Vinyl-1-alkylidenecyclopropanes and allylidenecyclopropanes undergo useful thermal rearrangements to 5-member rings.[32] Allylidenecyclopropanes undergo Diels–Alder reactions with some electrophilic olefins.[32i] Methylenecyclopropane can be metalated and alkylated directly on the ring.[37]

Conclusions

The reductive lithiation of diphenyl thioacetals and diphenyl thioketals with LDMAN, treatment of the resulting sulfur-stablized anions with trimethylsilyl chloride, and another reductive lithiation is an efficient method for the production of α-lithiosilanes. In this paper for the first time, details are given for the production of both secondary and tertiary α-lithiosilanes by reductive lithiation with this reagent. Precautions that should be observed for the successful preparation of tertiary organolithium species bearing sulfur or silicon on the negatively charged carbon atom are detailed in the experimental section. The procedure can be used for the production of silicon-stablized anions having sp^3, cyclopropyl, or sp^2 hybridization. The generality of this method, the ready availability of starting materials,[25] the ease of performing the experiments, and the generally satisfactory overall yields recommend this procedure for a significant role in synthetic chemistry. The use of these anions in the Peterson olefination,[38] particularly in the preparation of alkylidenecyclopropanes and allylidenecyclopropanes, is stressed, but there are many other uses for such anions; examples are the reactions with dimethylformamide to produce α-silylaldehydes which are useful as vinylating agents for anions,[39,40] reactions with sulfur dioxide to produce sulfines,[41] and in the case of the α-silylvinyl anions, protonation and alkylation to synthetically useful vinylsilanes.[42]

Experimental Section

In the ^1H NMR spectra of the (phenylthio)silanes (**2**) and β-silylcarbinols (**4**) the trimethylsilyl group in the molecule was generally used as an internal standard and its chemical shift was defined at δ 0.00. In

(31) Gröbel, B.-T.; Bürstinghaus, R.; Seebach, D. *Synthesis* **1976**, 121.

(32) (a) Shields, T. C.; Billups, W. E.; Lepley, A. R. *J. Am. Chem. Soc.* **1968**, *90*, 4749. (b) Kende, A. S.; Riecke, E. E. *Ibid.* **1972**, *94*, 1397. (c) Billups, W. E.; Leavell, K. H.; Lewis, E. S.; Vanderpool, S. *Ibid.* **1973**, *95*, 8096. (d) Semmelhack, M. F.; DeFranco, R. J. *Ibid.* **1972**, *94*, 8838. (e) Roth, W. R.; Schmidt, T. *Tetrahedron Lett.* **1971**, 3639. (f) Gilbert, J. C.; Higley, D. P. *Ibid.* **1973**, 1075. (g) Billups, W. E.; Baker, B. A.; Chow, W. Y.; Leavell, K. H.; Lewis, E. S. *Ibid.* **1975**, *40*, 1702. (h) Huber, M. D.; Martin, R.; Dreiding, A. S. *Helv. Chim. Acta* **1977**, *60*, 1811. (i) Zutterman, F.; Krief, A. *J. Org. Chem.* **1983**, *48*, 1135.

(33) (a) Bestman, H. J.; Denzel, T. *Tetrahedron Lett.* **1966**, 3591. Sisido, K.; Utimoto, K. *Ibid.* **1966**, 3267. Schweizer, E. E.; Berninger, C. J.; Thompson, J. G. *J. Org. Chem.* **1968**, *33*, 336. Gilbert, J. C.; Weerassoriya, U.; Giamalva, D. *Tetrahedron Lett.* **1979**, 4619. Halazy, S.; Krief, A. *Ibid.* **1979**, 4233; **1981**, 2135. Halazy, S.; Krief, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1136. Kitatani, K.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 949. (b) Hässig, R.; Siegel, H.; Seebach, D. *Chem. Ber.* **1982**, *115*, 1990.

(34) Crandall, J. K.; Conover, W. W. *J. Org. Chem.* **1978**, *43*, 3533 and references cited therein. For a recent example of the use of this procedure in synthesis, see: Slessor, K. N.; Oehlschlager, A. C.; Johnson, B. D.; Pierce, H. D., Jr.; Grewal, S. K.; Wickremesinghe, L. K. G. *J. Org. Chem.* **1980**, *45*, 2290.

(35) Binger, P.; Cetinkaya, M.; Doyle, M. J.; Germer, A.; Schuchard, U. In "Fundamental Research in Homogeneous Catalysis"; Tsutsui, M., Ed.; Plenum Press: New York, 1979; p 271. Noyori, R.; Odagi, T.; Takaya, H. *J. Am. Chem. Soc.* **1970**, *92*, 5780. Albrecht, T. A. *J. Organomet. Chem.* **1980**, *198*, 159. Binger, P.; Schuchardt, U. *Chem. Ber.* **1980**, *113*, 3334.

(36) (a) Billups, W. E.; Shields, T. C.; Chow, W. Y.; Deno, N. C. *J. Org. Chem.* **1972**, *37*, 3676. (b) Billups, W. E.; Chow, W. Y.; Cross, J. H. *J. Chem. Soc., Chem. Commun.* **1974**, 252.

(37) Thomas, E. W. *Tetrahedron Lett.* **1983**, *24*, 1467.

(38) In a recent paper the inability to prepare 1-lithio-1-(trimethylsilyl)-ethane for a Peterson olefination step in a total synthesis is lamented: Jung, M. E.; Hudsepth, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 2463.

(39) Unpublished observation of Paul Willey and James Sherbine.

(40) Hudrlik, P. F.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1981**, *103*, 6251.

(41) van der Leij, M.; Zwanenburg, B. *Tetrahedron Lett.* **1978**, 3383.

(42) Taylor, R. T.; Degenhardt, C. R.; Melega, W. P.; Paquette, L. A. *Tetrahedron Lett.* **1977**, 159.

instances in which this is not the case, it is noted that tetramethylsilane has been added and this was used as the internal standard.

Lithium 1-(Dimethylamino)naphthalenide (LDMAN). To a flame-dried 2-neck flask, which was continually purged with argon and was equipped with a glass coated stirring bar, was added THF (10 mL) and lithium ribbon (40 mg, 5.8 mmol).[43] The mixture was then cooled to between −45 and −55 °C with use of 1-hexanol/dry ice bath. 1-(Dimethylamino)naphthalene (0.84 mL, 0.87 g, 5.1 mmol) was slowly added. The dark green color of the radical anion appeared within 10 min, and the LDMAN was completely formed after 3.5 h of rapid stirring. It is suggested that the LDMAN be used soon after it is formed since at −45 °C it slowly decomposes to 1-lithionaphthalene. If the temperature is maintained below −55 °C, the formation of LDMAN will take considerably more time (i.e., ~8 h at −78 °C).

The above procedure should produce a 0.5 M solution of LDMAN. Generally 2.3 or 2.4 equiv (a 15–20% excess) of LDMAN are used to offset the effect of the lithium oxide formation.

Thioacetals and Noncyclopropyl Thioketals. These compounds were synthesized by the procedure of Campaigne and Leal.[44] This method involves passing dry HCl gas through a thiophenol solution of the appropriate carbonyl compound or acetal.

1,1-Bis(phenylthio)cyclohexane was prepared in 87% yield as a white solid: mp 81.5–82.0 °C; IR (KBr) 2930, 1450, 1340, 1100 cm^{-1}; ^1H NMR (CCl_4) δ 0.9 (s, 9 H, *tert*-butyl), 1.2–1.9 (m, 9 H, alicyclic), 7.1–7.8 (m, 10 H, phenyl). Anal. Calcd for $C_{18}H_{20}S_2$: C, 71.95; H, 6.71; S, 21.34. Found: C, 71.65; H, 6.70; S, 21.06.

2,2-Bis(phenylthio)propane[45] was prepared from the bis(methoxy)-propane in quantatative yield as a white solid: mp 56 °C (lit.[45] mp 56 °C); IR (KBr) 3050, 2950, 1480, 1420 cm^{-1}; ^1H NMR (CCl_4) δ 1.0 (s, 6 H, methyl), 7.0–7.3 (m, 10 H, phenyl); mass spectrum (15 eV) 260 (8, M), 151 (100, M − SPh), 134 (12), 123 (13), 117 (15), 111 (32), 73 (59).

1,1-Bis(phenylthio)propane[46] was prepared in 80% yield as an oil from propanal: IR (neat) 3050, 2950, 2900, 1580, 1475, 1460, 1440 cm^{-1}; ^1H NMR (CCl_4) δ 1.1 (t, J = 6 Hz, 3 H, methyl), 1.9 (m, 2 H, methylene), 4.3 (t, J = 6 Hz, 1 H, $HC(SPh)_2$), 7.0–7.5 (m, 10 H, phenyl); mass spectrum (15 eV) 260 (13, M), 151 (100, M − SPh), 123 (13).

1,1-Bis(phenylthio)-4-*tert*-butylcyclohexane was prepared in 84% yield as a white solid: mp 82.0–82.5 °C; IR (KBr) 2930, 2850, 1470, 1430, 1360, 1300, 1250, 1100 cm^{-1}; ^1H NMR (CCl_4) δ 0.9 (s, 9 H, *tert*-butyl), 1.2–1.9 (m, 9 H, alicyclic), 7.1–7.8 (m, 10 H, phenyl); mass spectrum (15 eV) 247 (100, M − SPh).

Bis(phenylthio)cyclohexylmethane was prepared from cyclohexanecarboxaldehyde in quantatative yield as an oil: IR (neat) 2950, 2900, 1590, 1480, 1440 cm^{-1}; ^1H NMR (CCl_4) δ 0.80–2.20 (m, 11 H, alicyclic), 4.27 (d, J = 2 Hz, 1 H, $HC(SPh)_2$), 6.87–7.43 (m, 10 H, phenyl); mass spectrum (15 eV) 314 (13, M), 205 (100), 123 (38), 95 (69).

1-(Phenylthio)-1-(trimethylsilyl)-4-*tert*-butylcyclohexane (21). A solution of 1,1-bis(phenylthio)-4-*tert*-butylcyclohexane (1.44 g, 4.05 mmol) in 5 mL of THF was added to a solution of 10.4 mmol of LDMAN in 20 mL of THF at −78 °C and the resulting mixture was stirred for 15 min. Freshly distilled trimethylsilyl chloride (0.60 mL, 0.51 g, 4.7 mmol) was added to the mixture and within 1 min the following standard workup procedure for non-cyclopropyl reductive lithiations was performed. The reaction was quenched with excess water at −78 °C.[47] The solvent was removed in vacuo, and the residue was taken up in ether. This mixture was washed twice with 5% NaOH, twice with 5% H_2SO_4, and finally with saturated aqueous $NaHCO_3$. The solvent was removed from the dried ($MgSO_4$) organic layer to yield a crude product. Column chromatography (silica gel, hexanes) afforded 1.08 g (83%) of **21** as a white solid: mp 83.1–83.9 °C; IR (CCl_4) 3090, 2950, 1440, 1400, 1370, 1250, 1120, 1020 cm^{-1}; ^1H NMR (CCl_4 + Me_4Si) δ 0.23 (s, 9 H, CH_3Si), 0.80 (s, 9 H, *tert*-butyl), 0.97–2.00 (m, 9 H, cyclohexyl); high resolution mass spectrum calcd for $C_{19}H_{32}SSi$ 320.1994, found 320.1994.

1-(Phenylthio)-1-(trimethylsilyl)propane (10). 1,1-Bis(phenylthio)-propane (10.0 g, 38.4 mmol) was treated with LDMAN for 2.5 h, and the resulting α-lithio thioether was silylated and the mixture worked up as usual to afford 7.4 g (86%) of **10** as a clear oil after Kugelrohr distillation (80–85°, 0.25 mm Hg): IR (neat) 3070, 3950, 1580, 1470, 1250 cm^{-1}; ^1H NMR (CCl_4 + Me_4Si) δ 0.13 (s, 9 H, CH_3Si), 1.05 (t, J = 7 Hz, 3 H, CH_3C), 1.43–1.97 (m, 2 H, CH_2), 2.40 (t, J = 5 Hz, 1 H, $HCSPh$), 7.03–7.53 (m, 5 H phenyl); high resolution mass spectrum calcd for $C_{12}H_{20}SSi$ 224.1055, found 224.1053.

Cyclohexyl(phenylthio)(trimethylsilyl)methane (14). Bis(phenylthio)cyclohexylmethane (3.93 g, 12.5 mmol) was treated as in the production of **21** to afford 3.15 g (90%) of spectroscopically pure **14** as an oil: IR (neat) 3075, 2925, 2850, 1580, 1470, 1250 cm^{-1}; ^1H NMR (CCl_4 + Me_4Si) δ 0.17 (s, 9 H, CH_3Si), 1.83–2.03 (m, 11 H, cyclohexyl), 2.30 (br d, J = 2 Hz, 1 H, $HCSPh$), 6.90–7.40 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{16}H_{26}SSi$ 278.1525, found 278.1523.

2-(Phenylthio)-2-(trimethylsilyl)propane (15). 2,2-Bis(phenylthio)-propane (9.94 g, 38.2 mmol) was treated as above to afford 2.96 g (92%) of **15** as an oil after both Kugelrohr distillation (70–80 °C (0.6 mmHg)) and flash chromatography (silica gel, hexanes): IR (neat) 3075, 2960, 1950, 1880, 1460, 1250 cm^{-1}; ^1H NMR (CCl_4 + Me_4Si) δ 0.13 (s, 9 H, CH_3Si), 1.13 (s, 6 H, CMe_2), 7.03–7.53 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{12}H_{20}SSi$ 224.1055, found 224.1055.

1-(Phenylthio)-1-(trimethylsilyl)cyclohexane (18). 1,1-Bis(phenylthio)cyclohexane (5.70 g, 19.0 mmol) was treated with LDMAN for 1.5 h at −78 °C; it was only after this experiment that it was found that far shorter reaction times provide better yields. (See preparation of **21**.) After silylation, the usual workup afforded 1.71 g (71%) of **18** as a white solid, with a room temperature melting point, after flash chromatography (silica gel, hexanes): IR (neat) 3075, 2925, 1580, 1470, 1440, 1260 cm^{-1}; ^1H NMR (CCl_4 + Me_4Si) δ 0.10 (s, 9 H, CH_3Si), 0.73–2.30 (m, 10 H, alicyclic), 6.97–7.53 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{15}H_{24}SSi$ 264.1368, found 264.1368.

1-(Phenylthio)-1-(trimethylsilyl)cyclopropane (24). A solution of 14.5 g (95.0 mmol) of 1,1-bis(phenylthio)cyclopropane[9a] was treated with LDMAN for 45 min at −45 °C. This is the standard reaction time and temperature for cyclopropanone thioketal reductive lithiations. Trimethylsilyl chloride (19.3 mL, 16.5 g, 15.2 mmol) was added, and the resulting mixture was stirred for 30 min.[48] Standard workup and purification by column chromatography (silica gel, 5% ethyl acetate–hexanes) afforded 20.0 g (95%) of **24** as an oil: IR (neat) 2990, 1595, 1375, 1250, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 1.0 (s, 4 H, cyclopropyl), 7.2–7.6 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{12}H_{18}SSi$ 222.0899, found 222.0893. This particular α-phenylthiosilane has also been prepared in our laboratory from 1,3-bis(phenylthio)propane by a method independently used by Paquette.[13]

6-(Phenylthio)-6-(trimethylsilyl)bicyclo[3.1.0]hexane (35). 6,6-Bis(phenylthio)bicyclo[3.1.0]hexane[49] (2.7 g, 9.2 mmol) was treated with LDMAN and the anion silylated to afford 2.3 g (95%) of **35** after purification by column chromatography (silica gel, hexanes): ^1H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 1.4–1.8 (m, 8 H. alicyclic), 6.9–7.1 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{15}H_{22}SSi$ 262.1212, found 262.1212.

7-(Phenylthio)-7-(trimethylsilyl)bicyclo[4.1.0]heptane (30). 7,7-Bis(phenylthio)bicyclo[4.1.0]heptane[50] (9.00 g, 28.8 mmol) was treated in the same way to afford 6.8 g (86%) of **30** after Kugelrohr distillation (145 °C (2 mmHg)): IR (neat) 2950, 1590, 1490, 1440, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.0–0.3 (s, 9 H, isomeric CH_3Si), 1.0–1.8 (m, 10 H, alicyclic), 7.3 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{16}H_{24}SSi$ 276.1368, found 276.1358. Likewise, 7-(phenylthio)norcarane was formed as an epimeric mixture of sulfides by protonation of the anion prepared as above. The sulfides were separated by medium-pressure chromatography and identified by the coupling constants of the cyclopropyl hydrogen atoms.[22]

(43) The lithium ribbon becomes coated with oxide while being stored under paraffin oil. Before it is weighed, both sides of the ribbon are scraped free of oxide while the ribbon is still under the oil. The piece of metal is then dipped into pentane to remove the oil and, after rapid air drying, placed in a tared vial of paraffin oil for weighing. However, varying degrees of lithium oxide formation reoccurs. Excessive oxidation can prevent formation of the radical anion. A widely used technique to strip lithium oxide by dipping the lithium into methanol followed by two or three dippings into successive vials of dry THF, then placing it in the reaction vessel, stripped the lithium oxide very well; however, this treatment seemed to deactivate the surface of the metal as radical anion formation was drastically inhibited and the reduction reaction was not complete. It is helpful to tear the lithium ribbon into small pieces in a dry, inert atmosphere prior to placing it in the reaction medium. This provides a fairly fresh area of lithium; scoring the metal is likewise helpful. On occasion, we have experienced difficulty in preparing LDMAN solutions in laboratory conditions of high humidity.

(44) Campaigne, E.; Leal, J. R. *J. Am. Chem. Soc.* **1954**, *76*, 1272.

(45) Schönberg, A.; Praefcke, K. *Chem. Ber.* **1967**, *100*, 778.

(46) Deljac, A.; Stefanoc, Z.; Bahenovič, K. *Tetrahedron Suppl.* **1966**, *8*, part I, 33.

(47) As discussed above, a slight excess of reducing agent is often used but, when this is the case, it is necessary to quench the reaction immediately after consumption of the anion by silylation since the silylation product can be rapidly reduced by excess radical anion. This "overreduction" is signaled by isolation of some geminal bis(trimethylsilyl) compound, and it is only observed with non-cyclopropanone thioketals.

(48) Bis silylation is not a problem with cyclopropanone thioketals.

(49) Cohen, T.; Ritter, R. H.; Ouellette, D. *J. Am. Chem. Soc.* **1982**, *104*, 7142.

(50) Braun, M.; Seebach, D. *Chem. Ber.* **1976**, *109*, 699. We have found[49] that the ring-closure step is best performed with methyllithium rather than butyllithium since the latter causes a significant amount of sulfur–lithium exchange in the product.

***exo*-7-(Phenylthio)norcarane**: ^{1}H NMR ($CDCl_3$ + Me_4Si) δ 1.208–1.288 (m, 6 H, alicyclic), 1.846–1.876 (m, 2 H, alicyclic), 1.876–1.903 (t, J = 4.05 Hz, 1 H, C*H*(SPh)), 1.925–2.060 (m, 2 H, alicyclic), 7.090–7.140 (m, 1 H, aromatic), 7.261–7.289 (m, 4 H, aromatic).

***endo*-7-(Phenylthio)norcarane**: ^{1}H NMR ($CDCl_3$ + Me_4Si) δ 1.255–1.546 (m, 8 H, alicyclic), 1.820–1.960 (m, 2 H, alicyclic), 2.251–2.304 (t, J = 8.0 Hz, 1 H, C*H*(SPh)), 7.060–7.127 (m, 1 H, aromatic), 7.237–7.289 (m, 2 H, aromatic), 7.329–7.361 (m, 2 H, aromatic).

***cis*- and *trans*-2-(2-Methyl-1-propenyl)-1-(phenylthio)-1-(trimethylsilyl)cyclopropane (38).** **7**[9b] (0.35 g, 1.12 mmol) was treated in a similar fashion to afford 0.30 g (95%) of **38** in an epimeric ratio of 2:1 after column chromatography: IR (neat) 2950, 2850, 1590, 1490, 1260, 860, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 and 0.1 (s, 9 H, epimeric CH_3Si), 0.8–1.6 (m, 3 H, cyclopropyl), 1.7–1.9 (m, 6 H, isomeric allylic methyl), 4.9–5.4 (m, 1 H, vinyl), 7.0–7.4 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{16}H_{24}SSi$ 276.1368, found 276.1363.

[Cyclohexylidene(phenylthio)methyl]trimethylsilane (41). **7**[10] (1.4 g, 4.5 mmol) was treated with LDMAN for 30 min at −45 °C. To this mixture was added trimethylsilyl chloride (0.68 mL, 0.58 g, 5.4 mmol), and the resulting solution was stirred for 1 h; the long reaction time was used because the vinyl lithium is silylated more slowly than the other anions in this study. This afforded 1.2 g (96%) of spectroscopically pure **41** as an oil: IR (neat) 3075, 2930, 1585, 1570, 1475 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H, CH_3Si), 1.34–1.70 (m, 6 H, nonallylic cyclohexyl), 2.23–2.73 (m, 4 H, allylic cyclohexyl), 6.85–7.10 (m, 5 H, phenyl); high resolution mass spectrum calcd for $C_{16}H_{24}SSi$ 276.1367, found 276.1360.

1-[1-(Trimethylsilyl)propyl]-4-*tert*-butylcyclohexanol (11). **10** (0.40 g, 1.8 mmol) was treated with LDMAN for 15 min at −78 °C.[51] A THF solution of 4-*tert*-butylcyclohexanone (0.27 g, 1.78 mmol) was added. After 1 min the mixture was worked up in the usual way. Flash chromatography (silica gel, 2% ethyl acetate–hexane) afforded 0.14 g (30%) of **11** as a pale yellow oil: IR (neat) 3630, 3500, 2950, 1480, 1370, 1255 cm^{-1}; ^{1}H NMR (CCl_4 + Me_4Si) δ 0.07 (s, 9 H, CH_3Si), 0.53 (t, J = 6 Hz, 1 H, *H*CSiMe$_3$), 0.83 (s, 9 H, *tert*-butyl), 0.67–1.87 (m, 24 H, alkyl and hydroxyl); mass spectrum (15 eV) 252 (44, M − H_2O), 180 (63, M − Me_3SiOH), 178 (100).

3-(Trimethylsilyl)pentan-2-ol (13). **10** (0.39 g, 1.73 mmol) was treated with LDMAN for 15 min at −78 °C. Acetaldehyde (0.13 mL, 0.10 g, 2.3 mmol) was added (see experiment above). Kugelrohr distillation (75–80 °C, aspirator) afforded 0.18 g (65%) of **13** as a clear oil: IR (neat) 3375, 2950, 1460, 1380, 1110, 1080 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.00 (s, 9 H, CH_3Si), 0.37–1.77 (m, 9 H, alkyl), 2.00–2.77 (br s, 1 H, OH), 3.67–4.20 (m, 1 H, *H*COH); mass spectrum (15 eV) 142 (25, M − H_2O), 70 (100, M − HOSiMe$_3$).

1-Cyclohexyl-2-methyl-2-(trimethylsilyl)propan-1-ol (16). **15** (0.20 g, 0.91 mmol) was treated with LDMAN for 15 min at −78 °C. Cyclohexanecarboxaldehyde (0.11 mL, 0.10 g, 0.91 mmol) was added, and the solution was treated in the usual way. Column chromatography (Silicar-CC-7, 4% ethyl acetate–hexanes) afforded 0.16 g (79%) of **16** as an oil which crystallized on standing: IR (CCl_4) 3650, 2950, 1460, 1250, 1080 cm^{-1}; ^{1}H NMR (CCl_4 + Me_4Si) δ 0.10 (s, 9 H, CH_3Si), 0.93 and 0.97 (two singlets, 6 H, enantiotopic methyls), 0.67–2.00 (m, 12 H, cyclohexyl and hydroxyl), 3.13–3.37 (m, 1 H, *H*COH).

[1-(Trimethylsilyl)cyclohexyl]cyclohexylmethanol (19). **18** (0.47 g, 1.79 mmol) was treated with LDMAN for 15 min at −78 °C. Cyclohexanecarboxaldehyde (0.24 mL, 0.21 g, 1.96 mmol) was added, and the solution was treated in the usual way. Column chromatography (Silicar-CC-7, 1% ethyl acetate–hexanes) afforded 0.24 g (51%) of **19** as an oil: ^{1}H NMR (CCl_4 + Me_4Si) δ 0.03 (s, 9 H, CH_3Si), 0.63–2.10 (m, 22 H, alkyl and hydroxyl), 3.60 (d, J = 6 Hz, 1 H, *H*COH); mass spectrum 250 (3, M − H_2O), 178 (100 M − Me_3SiOH).

(4-Methoxyphenyl)[1-(trimethylsilyl)cyclopropyl]methanol (25). **24** (0.55 g, 2.5 mmol) was treated with LDMAN for 1.5 h at −45 °C. *p*-Anisaldehyde (0.36 mL, 0.40 g, 3.0 mmol) was added, and the solution was treated in the usual way. Column chromatography (silica gel, 10% ethyl acetate–hexanes) afforded 0.53 g (85%) of **25** as an oil: IR (neat) 3450, 1240, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 0.6–0.7 (m, 4 H, cyclopropyl), 2.2 (br s, 1 H, OH), 4.0 (s, 3 H, OCH_3), 4.6 (m, 1 H, C*H*OH), 6.9–7.5 (m, 4 H, aromatic); high resolution mass spectrum calcd for $C_{14}H_{22}O_2Si$ 250.1389, found 250.1389.

[1-(Trimethylsilyl)cyclopropyl]-*n*-hexylmethanol (27). **24** (0.55 g, 2.5 mmol) was treated with LDMAN for 1.5 h at −45 °C. Heptanal (0.42 mL, 0.34 g, 3.0 mmol) was added, and the solution was treated in the usual way. Purification by column chromatography afforded 0.48 g (84%) of **27** as an oil: IR (neat) 3375, 2950, 2900, 1425, 1230, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 0.2–0.4 (m, 4 H, cyclopropyl), 1.0–1.8 (m, 14 H, hexyl and OH), 3.0 (t, J = 6 Hz, 1 H, *H*COH); high resolution mass spectrum calcd for $C_{13}H_{28}OSi$ 210.1804 (M − H_2O), found 210.1804.

1-[1-(Trimethylsilyl)cyclopropyl]-4-*tert*-butylcyclohexan-1-ol (28). **24** (0.47 g, 2.1 mmol) was treated with LDMAN for 1.5 h at −45 °C. The solution was cooled to −78 °C. A THF solution of 4-*tert*-butylcyclohexanone (0.38 g, 2.4 mmol) was added, and the solution was treated in the usual way. Column chromatography afforded 0.43 g (86%) of **28** as a solid (mp 98–100 °C): IR (KBr) 3600, 3500, 3000, 1340, 1220, 800 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 0.3–0.5 (m, 4 H, cyclopropyl), 0.8 (s, 9 H, *tert*-butyl), 1.2–1.6 (m, 9 H, alicyclic); high resolution mass spectrum calcd for $C_{16}H_{32}OSi$ 268.2222, found 268.2222.

***n*-Pentyl[7-(trimethylsilyl)bicyclo[4.1.0]hept-7-yl]methanol (31).** **30** (0.60 g, 2.2 mmol) was treated with LDMAN for 1.5 h at −45 °C. Hexanal (0.28 mL, 0.23 g, 2.4 mmol) was added, and the solution was treated in the usual way. Column chromatography afforded 0.53 g (92%) of **31** as an oil: IR (neat) 3500, 2950, 2900, 1500, 1280, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 0.8–1.5 (m, 22 H, alkyl, alicyclic and OH), 3.4 (m, 1 H, *H*COH); high resolution mass spectrum calcd for $C_{16}H_{32}OSi$ 253.1988 (M − CH_3), found 253.1988.

2-Propenyl[7-(trimethylsilyl)bicyclo[4.1.0]hept-7-yl]methanol (33). **30** (0.94 g, 3.4 mmol) was treated with LDMAN for 1.5 h at −45 °C. Methacrolein (0.46 mL, 0.38 g, 5.5 mmol) was added, and the solution was treated in the usual way. Column chromatography afforded 0.73 g (90%) of **33** as an oil: IR (neat) 3450, 2950, 1450, 1240, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 1.5–2.1 (m, 14 H, alicyclic H, and allylic methyl and OH), 3.8 (m, 1 H, C*H*OH), 4.9 (m, 1 H, vinyl), 5.2 (m, 1 H, vinyl); high resolution mass spectrum calcd for $C_{14}H_{16}OSi$ 238.1756, found 238.1746.

2-Propenyl[6-(trimethylsilyl)bicyclo[3.1.0]hex-6-yl]methanol (36). **35** (0.65 g, 2.5 mmol) was treated with LDMAN for 2 h at −45 °C. Methacrolein (0.30 mL, 0.25 g, 3.0 mmol) was added, and the solution was treated in the usual way. Column chromatography afforded 0.51 g (91%) of **36** as an oil: IR (neat) 3450, 2950, 2889, 1250, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 1.4–2.2 (m, 12 H, alicyclic H, allylic methyl and OH), 3.8 (m, 1 H, C*H*OH), 5.0 (m, 1 H, vinyl), 5.3 (m, 1 H, vinyl); high resolution mass spectrum calcd for $C_{13}H_{24}OSi$ 224.1596, found 224.1596.

***cis*- and *trans*-(4-Methoxyphenyl)[2-(2-methyl-1-propenyl)(1-trimethylsilyl)cyclopropyl]methanol (39).** **38** (0.10 g, 0.36 mmol) was treated with LDMAN for 40 min at −45 °C. *p*-Anisaldehyde (0.053 mL, 0.059 g, 0.043 mmol) was added, and the solution was treated in the usual way. Column chromatography (silica gel, 5% ethyl acetate–hexanes) afforded 0.10 g (92%) of **39** as three fractions comprised of four isomers whose R_f values in 5% ethyl acetate–hexanes are as follows: A (0.29), B (0.17), C (0.12), and D (0.09). These fractions consisted of pure A and pure B along with a mixture of B, C, and D. (It is necessary to note that the products of large-scale reactions (>1.5 g) should be flash chromatographed as decomposition occurs upon the longer chromatographic times necessary for open column silica gel chromatography; the yield for open column silica gel chromatography is ~70%.) The ^{1}H NMR spectrum of the mixture is very similar to that of pure A and pure B. The IR and mass spectrum are of a mixture of all of the isomers: IR (neat) 3450, 2950, 2900, 1610, 1510, 1250, 1175, 1040, 840 cm^{-1}. A: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H, CH_3Si), 1.25–1.30 (m, 1 H, cyclopropyl), 1.35–1.40 (m, 1 H, cyclopropyl), 1.85–1.95 (m, 1 H, tertiary cyclopropyl), 2.05 (s, 3 H, allylic methyl), 2.10 (s, 3 H, allylic methyl), 2.4 (br s, 1 H, OH), 4.05 (s, 3 H, OCH_3), 4.75 (m, 1 H, benzylic C*H*OH), 5.55–5.60 (m, 1 H, vinyl), 7.10–7.15 (d, J = 8 Hz, 2 H, aromatic), 7.65–7.70 (d, J = 8 Hz, 2 H, aromatic). B: ^{1}H δ 0.00 (s, 9 H, CH_3Si), 0.50–0.60 (m, 2 H, cyclopropyl), 1.50–1.60 (m, 1 H, tertiary cyclopropyl), 1.65 (s, 3 H, allylic methyl), 1.75 (s, 3 H, allylic methyl), 1.80–1.85 (m, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.75 (m, 1 H, C*H*OH), 4.85–4.95 (m, 1 H, vinyl), 6.80–6.85 (d, J = 8 Hz, 2 H, aromatic), 7.20–7.25 (d, J = 8 Hz, 2 H, aromatic); high resolution mass spectrum calcd for $C_{18}H_{28}O_2Si$ 304.1859, found 304.1852.

1-Cyclohexyl-2-cyclohexylidene-2-(trimethylsilyl)ethan-1-ol (42). **41** (1.9 g, 6.9 mmol) was treated with LDMAN for 1 h at −45 °C. Cyclohexanecarboxaldehyde (0.94 mL, 0.85 g, 7.6 mmol) was added, and the solution was treated in the usual way. Column chromatography afforded 1.6 g (85%) of **42** as an oil: IR (neat) 3550, 2900, 1470, 1270, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H, CH_3Si), 1.4–1.6 (m, 17 H, non-allylic cyclohexyl), 2.0–2.4 (m, 4 H, allylic cyclohexyl), 4.0 (d, J = 8 Hz, 1 H, *H*COH); high resolution mass spectrum calcd for $C_{17}H_{32}OSi$ 280.2222, found 280.2219.

(4-Methoxyphenyl)cyclopropylidenemethane (26). The following standard procedure was used for KH olefinations. In a 2-neck flask,

(51) It was later found that a reaction time of 4 min instead of 15 min improved the yield of alcohol for the preparation of **22**. See preparation of **23**.

continually being flushed with argon, a solution of **25** (0.090 g, 0.36 mmol) in 10 mL of THF was stirred as an excess of hexane-washed KH was slowly added through the argon outlet stream (until no further gas evolution was noticed). The reaction mixture was stirred for 20 h at room temperature. The resultant mixture was carefully poured onto ice water overlaid with ether. A preparative TLC plate of the residue of the dried ($MgSO_4$) organic layer, using hexanes as the eluent, afforded 0.060 g (90%) of **26** as an oil whose ^1H NMR spectrum was identical with that of an authentic sample:[52] ^1H NMR ($CDCl_3$) δ 1.0–1.5 (m, 4 H, cyclopropyl), 4.0 (s, 3 H, OCH_3), 6.6–6.7 (m, 1 H, vinyl), 6.7 (d, J = 8 Hz, 2 H, aromatic), 7.9 (d, J = 8 Hz, 2 H, aromatic).

4-*tert*-Butyl(propylidene)cyclohexane (12). A solution of **11** (0.10 g, 0.38 mmol) in 5 mL of THF was treated with KH by the usual procedure. After 19 h the starting material was consumed. Workup by the standard procedure followed by column chromatography (silica gel, hexanes) afforded 0.057 g (84%) of **12** as an oil: IR (neat) 2975, 2875, 2850, 1490, 1425, 1375 cm^{-1}; ^1H NMR (CCl_4) δ 0.83 (s, 9 H, *tert*-butyl), 0.63–2.77 (m, 14 H, alicyclic and alkyl), 5.02 (t broadened by allylic coupling, J = 7 Hz, 1 H, vinyl); mass spectrum (15 eV) 180 (100, M), 165 (20, M – CH_3).

Cyclohexylidenecyclohexylmethane (20). A solution of **19** (0.19 g, 0.73 mmol) in 5 mL of THF was treated with KH in the usual manner. After 0.5 h at room temperature the starting material was consumed. The reaction was worked up by the usual procedure. Kugelrohr distillation (85–95 °C, aspirator) afforded 0.10 g (83%) of **20** as an oil: IR (neat) 2925, 2850, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.57–2.57 (m, 21 H, alicyclic), 4.87 (d, broadened by allylic coupling, J = 9 Hz, 1 H, vinyl); mass spectrum (15 eV) 178 (100, M).

(4-*tert*-Butylcyclohexylidene)cyclohexylmethane (23). A solution of **21** (0.20 g, 0.64 mmol) in 1.0 mL of THF was added to a solution of 1.5 mmol of LDMAN in 3.0 mL of THF, and the resulting mixture was stirred for 4 min at −78 °C. Cyclohexanecarboxaldehyde (0.10 mL, 0.09 g, 0.08 mmol) was added. The resulting solution was stirred for 15 min and worked up by the standard procedure to provide crude **22** which was used directly in the elimination step. In another experiment, a sample of **22** was purified by flash chromatography: IR (CCl_4) 3625, 2925, 1440, 1335, 1225 cm^{-1}; ^1H NMR ($CDCl_3$ + Me_4Si) δ 0.13 (s, 9 H, CH_3Si), 0.83 (s, 9 H, *tert*-butyl), 0.66–1.97 (m, 21 H, cycloalkyl and hydroxyl), 3.13 (br m, 1 H, *H*COH); mass spectrum (15 eV) 306 (21, M – H_2O), 234 (100, M – Me_3SiOH). A solution of the crude **22** in 3.0 mL of THF was treated with KH by the usual procedure. After 1.5 h at room temperature all the starting material was consumed. After the usual workup column chromatography (silica gel, hexanes) afforded 0.12 g (80% overall) of **23** as an oil and 0.02 g (10%) of starting silane (**21**), **23**: IR (neat) 2950, 2850, 1485, 1395, 1250 cm^{-1}; ^1H NMR (CCl_4) δ 0.87 (s, 9 H, *tert*-butyl), 0.57–2.80 (m, 20 H, cycloalkyl), 4.75–4.97 (d broadened by allylic coupling, J = 9 Hz, 1 H, vinyl); high resolution mass spectrum calcd for $C_{17}H_{30}$: 234.2348. Found: 234.2345.

4-*tert*-Butyl-1-cyclopropylidenecyclohexane (29). A solution of **28** (0.11 g, 0.41 mmol) in 2 mL of diglyme was treated with KH by the standard procedure except that a reflux condenser was placed on the flask and the mixture was warmed to 90 °C for 3.5 h at which time the starting material was consumed. When diglyme is used as solvent, the following workup procedure is used. The cooled reaction mixture was partioned between hexanes and saturated NH_4Cl of pH 8. The organic layer was washed several times with saturated NH_4Cl of pH 8 and dried (Na_2SO_4), and the solvent was removed to yield a residue which, after purification by column chromatography (Silicar-CC-7, hexanes), afforded 0.062 g (86%) of **29** as an oil: IR (neat) 3000, 1400, 940 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + Me_4Si) δ 0.85 (s, 9 H, *tert*-butyl), 0.95–1.25 (m, 7 H), 1.85 (m, 2 H), 2.00 (m, 2 H), 2.55 (m, 2 H); high resolution mass spectrum calcd for $C_{13}H_{22}$ 178.1722, found 178.1722.

1-Cyclohexyl-2-methylpropene (17). A solution of **16** (0.20 g, 1.0 mmol) in 2 mL of diglyme was treated with KH by the standard procedure, and the reaction mixture was warmed to 90 °C. After 2 h, the starting material was consumed. The reaction mixture was worked up as in the previous diglyme reaction. Purification by column chromatography (Silicar-CC-7, hexanes) afforded 0.13 g (92%) of **17** whose spectral properties were identical with those of an authentic sample:[53] ^1H NMR ($CDCl_3$) δ 0.5–1.9 (m, 17 H, alicyclic H and allylic methyl groups), 4.8 (d broadened by allylic coupling, J = 9 Hz, 1 H, vinyl).

7-Hexylidenebicyclo[4.1.0]heptane (32). A solution of **31** (0.10 g, 0.40 mmol) in 5 mL of diglyme was treated with KH by the standard procedure. After 10 min the starting material was consumed. The reaction mixture was worked up as in the previous diglyme reaction. Purification by column chromatography afforded 0.064 g (98%) of **32** as an oil: IR (neat) 3000, 1500, 1480, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–2.3 (m, 21 H, alicyclic and alkyl H), 5.8 (7, 1 H, vinyl); high resolution mass spectrum calcd for $C_{13}H_{22}$ 178.1722, found 178.1722.

7-(2-Methyl-2-propenylidene)bicyclo[4.1.0]heptane (34). A solution of **33** (0.10, 4.2 mmol) in 15 mL of THF was treated with KH by the standard procedure. After 1.5 h the starting material was consumed. The solvent was removed from the washed and dried (Na_2SO_4) organic layer yielding 0.64 g (100%) of **34** which was spectroscopically pure: IR (neat) 2950, 2850, 1620, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–2.0 (m, 13 H, alicyclic H and methyl), 5.0 (m, 2 H, *gem*-vinyl), 6.6 (m, 1 H, vinyl); high resolution mass spectrum calcd for $C_{11}H_{16}$ 148.1252, found 148.1252.

6-(2-Methyl-2-propenylidene)bicyclo[3.1.0]hexane (37). A solution of **36** (1.14 g, 5.1 mmol) in 15 mL of THF was treated with KH by the standard procedure. After 2 h the starting material was consumed. Purification by column chromatography (wash column using Silicar-CC-7, hexanes) afforded 0.65 g (95%) of **37** as an oil: IR (neat) 3150, 3000, 2900, 1640, 1480, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–2.0 (m, 11 H, alicyclic H and methyl), 4.8 (m, 2 H, *gem*-vinyl), 6.4 (m, 1 H, vinyl); high resolution mass spectrum calcd for $C_{10}H_{14}$ 134.1096, found 134.1096.

***cis*- and *trans*-(*p*-Methoxyphenyl)[2-(2-methyl-1-propenyl)cyclopropylidene]methane (40).** A solution of isomer A of **39** (115 mg, 0.378 mmol) in 1 mL of THF was slowly added to a slurry of pentane-washed KH in 2 mL of THF at 0 °C. The resulting mixture was allowed to warm to ambient temperature. After the solution had been stirred for 20 h, no starting material remained (TLC). The reaction mixture was worked up in the usual manner, and column chromatography (Silicar CC-7, 5% ethyl acetate–hexanes, R_f 0.55) afforded 76 mg (94%) of **40** as a pale yellow oil. This olefin decomposes rapidly in the presence of $CDCl_3$; thus the NMR spectrum must be taken in CCl_4: IR (neat) 2950, 2900, 1610, 1510, 1250, 1170, 1040, 860, 840 cm^{-1}; ^1H NMR (CCl_4) δ 1.0–1.4 (m, 2 H, cyclopropyl), 1.7 (s, 3 H, methyl), 1.9 (s, 3 H, methyl), 2.1–2.3 (m, 1 H, tertiary cyclopropyl), 3.7 (s, 3 H, OCH_3), 4.5–4.7 (m, 1 H, vinyl), 6.3–6.5 (m, 3 H, aromatic and benzylic vinyl), 7.1–7.3 (d, J = 8 Hz, 2 H, aromatic); high resolution mass spectrum calcd for $C_{15}H_{18}O$ 214.1358, found 214.1356.

A solution of a mixture of isomers B, C, and D of **39** (115 mg, 0.378 mmol) in 1 mL of THF was treated, worked up, and chromatographed as for isomer A to afford 77 mg (95%) of a pale yellow oil with the same spectral properties as that of the olefin derived from A. It was not determined whether **40** is a mixture of cis and trans olefins or a single compound.

***trans*-1-(1-Cyclohexenyl)-2-cyclohexylethene (43).** In a 2-necked flask equipped with an argon inlet, a solution of **42** (0.47 g, 1.7 mmol) in 10 mL of CCl_4 was stirred and cooled to 0 °C. Freshly distilled thionyl chloride (0.16 mL, 0.26 g, 2.1 mmol) was slowly added, and the resulting solution was stirred for 2 h at 0 °C. The CCl_4 and excess thionyl chloride were removed in vacuo, and the crude chloride was taken up in 10 mL of 1:1 Me_2SO/THF and rapidly stirred. Tetra-*n*-butylammonium fluoride (1.85 mL of a 1.00 M solution in THF, 1.85 mmol) was added to the crude chloride solution, and the mixture was stirred for 1.5 h and partitioned between water and hexanes. Column chromatography (Silicar-CC-7, hexanes) of the dried (Na_2SO_4) organic layer afforded 0.23 g (72%) of **43** and 0.07 g (15%) of *cis*- and *trans*-**46**. **43**: IR (neat) 2900, 2850, 1450, 950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08–2.12 (m, 19 H, alicyclic), 5.51 (d of d, J = 15.8 Hz and 7.0 Hz, 1 H, 2-ethenyl H), 5.65 (m, 1 H, cyclohexenyl), 6.01 (d, J = 15.8 Hz, 1 H, 1-ethenyl H); high resolution mass spectrum calcd for $C_{14}H_{22}$ 190.1721, found 190.1721. **46**: IR (neat) 2910, 2840, 1430, 1230, 840, 820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.00–0.10 (s, 9 H, epimeric CH_3Si), 0.80–2.10 (m, 19 H), 5.05–5.15 (m, 1 H, endocyclic = CH), 5.40–5.65 (d, J = 11 Hz, 1 H, ethenyl H); mass spectrum (15 eV) 262 (100, M), 247 (10, M – CH_3), 188 (64, M – CH_3SiH).

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Registry No. 1 (R^1R^2 = $(CH_2)_5$), 37457-08-2; **1** (R^1R^2 = $(CH_2)_2$), 69519-84-2; **7**, 71987-46-7; **8**, 69190-57-4; **10**, 76200-34-5; **11**, 89656-93-9; **12**, 51197-95-6; **13**, 89656-94-0; **14**, 89656-95-1; **15**, 89656-96-2; **16**, 89656-97-3; **17**, 89656-98-4; **18**, 89656-99-5; **19**, 89657-00-1; **20**, 27428-33-7; **21**, 89657-01-2; **22**, 89657-02-3; **23**, 89657-03-4; **24**, 74379-74-1; **25**, 89657-04-5; **26**, 55088-84-1; **27**, 89657-05-6; **28**, 89657-06-7; **29**, 89657-07-8; **30** (dithioacetal), 83711-04-0; **30** (7-*endo*-Me_3Si), 89657-08-9; **30** (7-*exo*-Me_3Si), 89657-09-0; **31**, 81236-81-9; **32**, 81236-88-6; **33**, 89675-83-2; **34**, 89657-10-3; **35** (dithioacetal), 58681-

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16-6; **35** (6-*endo*-Me_3Si), 89657-11-4; **35** (6-*exo*-Me_3Si), 89657-12-5; **36**, 89657-13-6; **37**, 89657-14-7; *cis*-**38**, 89657-15-8; *trans*-**38**, 89657-16-9; *cis*-**39** (isomer 1), 89657-17-0; *cis*-**39** (isomer 2), 89708-66-7; *trans*-**39** (isomer 1), 89708-67-8; *trans*-**39** (isomer 2), 89708-68-9; **40**, 89657-18-1; **41**, 71342-13-7; **42**, 89657-19-2; **43**, 53723-46-9; (*E*)-**46**, 89657-21-6; (*Z*)-**46**, 89657-22-7; **48**, 87729-87-1; LDMAN, 74379-76-3; $(CH_3)_2C(SPh)_2$, 14252-46-1; $(CH_3)_2C(OMe)_2$, 77-76-9; $CH_3CH_2CH(SPh)_2$, 15486-58-5; CH_3CH_2CHO, 123-38-6; c-$C_6H_{11}CH(SPh)_2$, 54905-14-5; c-$C_6H_{11}CHO$, 2043-61-0; Me_3SiCl, 75-77-4; CH_3CHO, 75-07-0; $MeOC_6H_4$-*p*-CHO, 123-11-5; *n*-$C_6H_{13}CHO$, 111-71-7; *n*-$C_5H_{11}CHO$, 66-25-1; $CH_2{=}C(CH_3)CHO$, 78-85-3; KH, 7693-26-7; 1-(dimethylamino)naphthalene, 86-56-6; 1,1-bis(phenylthio)-4-*tert*-butylcyclohexane, 85895-63-2; 4-*tert*-butylcyclohexanone, 98-53-3; *exo*-7-(phenylthio)norcarane, 89657-20-5; *endo*-7-(phenylthio)norcarane, 37942-20-4.

Stereocontrolled Total Synthesis of (-)-Maytansinol

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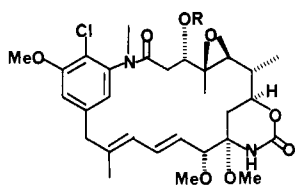
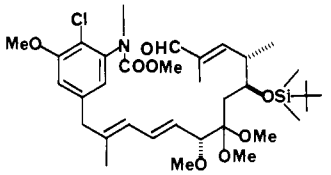
Abstract: Chiral maytansinol (**1**) was synthesized stereoselectively from D-mannose. Asymmetric centers of **1** were induced intramolecularly from an asymmetric carbon corresponding to C-7 via the common key intermediate **3** for maytansinoids. Key points are (i) the usage of a carbohydrate as a chiral template for acyclic asymmetric induction and (ii) a remote stereochemical control in aldol reaction to elaborate the C-3 asymmetric center by intramolecular asymmetric induction.

Maytansinol (**1**) is the key compound in preparing ansa macrolactams such as maytansine (**2a**) found in *Maytenus serrata*,[1]



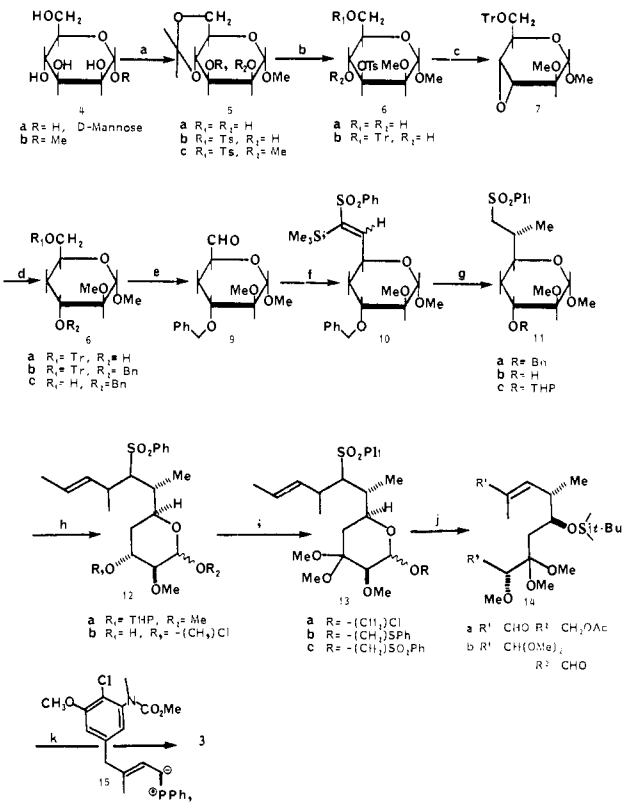
1 R= H
2a R= COCHMeNMeAc
b R= $COCHMe_2$



3

ansamitosin (**2b**) found in *Nocardia* sp. C-15003(N-1),[2] and others, which have remarkable antitumor activity with different accompanying toxicity depending upon the ester side chain at C-3 position.[3] We have recently reported the total synthesis of racemic maytansinol in a highly stereocontrolled manner involving diastereotopic induction of all the asymmetric centers of (±)-**1** from only one asymmetric carbon corresponding to C-7.[4] This success prompted us to the studies on the synthesis of optically active **1** via the same key intermediate **3** as the racemic case.

Scheme I[a]



[a] (a) $(CH_3)_2C(OMe)_2$-PPTS, TsCl/Py, NaH-MeI; (b) H^+, TrCl-Py; (c) *t*-BuOK/THF; (d) super hydride, BnBr-NaH, H^+; (e) $(COCl)_2$/Me_2SO/Et_3N; (f) $PhS(Me_3Si)_2CLi$/THF, *m*-CPBA; (g) MeLi/THF, KF-MeOH, H_2/Pd-black, DHP-PPTS; (h) *n*-BuLi-4-bromopent-2-ene/THF-HMPA, CSA/$HOCH_2CH_2Cl$; (i) CrO_3-2Py, CSA/HC-$(OMe)_3$-MeOH, PhSNa, *m*-CPBA; (j) $NaBH_4$, AcCl/Py, *t*-$BuMe_2$-SiCl-imidazole/DMF, O_3/CH_2Cl_2, Et_3N; (k) PPTS/$CH(OMe)_3$-MeOH, NaOMe/MeOH, CrO_3-2Py, 15/THF-DMF (2:1), AcOH-$THF-H_2O$ (4:1:1).

Synthesis of the Chiral Key Intermediate (-)-3. The key intermediate (-)-**3** was prepared from D-mannose (**4a**) both as the chiral starting material and as the chiral template for the induction

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