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Formation of Cyclic Sulfonium Salts by Me_3SiI-Promoted Intramolecular Displacement of Hydroxide or Methoxide by Sulfide. Ring contraction Thiepane → Thiolane

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Abstract. A suitably positioned (1,2-, 1,4-, and 1,5-) intramolecular sulfide interferes with the iodotrimethylsilane-promoted iodine for hydroxyl substitution, as well as the related alcohol deprotection procedure (regioselective cleavage of methyl ethers). The outcome may be a cyclic sulfonium salt or an iodide arising from cleavage of a sulfonium intermediate. Cyclization is especially favored with secondary and tertiary alcohols or ethers, and with an aliphatic more than an aromatic sulfide function. A transannular version of the reaction results in the facile ring contraction of a 7- to a 5-membered cyclic sulfide. Copyright © 1996 Elsevier Science Ltd

Trimethylsilyl iodide[1] is an effective reagent for the conversion of alcohols to iodides[2] as well as for the regioselective C-O bond cleavage, widely used in the latter capacity for the deprotection of hydroxyl groups protected as methyl ethers.[3,4]

$$\mathrm{R\text{-}OH} \xrightarrow{Me_3SiI} \mathrm{R\text{-}I}$$

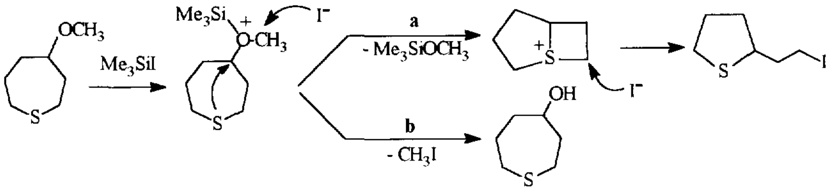
$$\mathrm{RCH_2OCH_3} \xrightarrow{Me_3SiI} \mathrm{RCH_2OH} + \mathrm{CH_3I}$$

Although this deprotection procedure is reported to be compatible with a variety of functional groups, including multiple carbon-carbon bonds, ketones, amines, aromatic halides,[3,4] certain limitations are apparently encountered with substrates carrying a nucleophilic functionality "soft" enough to maintain nucleophilic reactivity in the presence of trimethylsilyl iodide (a "hard" electrophile). This we have found to be the case of alcohols and ethers which carry a sulfide sulfur 2, 4 and 5 carbons away. Under such circumstances the expected substitution or ether cleavage may be accompanied, or be completely superseded, by an intramolecular displacement of the oxygen functionality with attending formation of a cyclic sulfonium salt or of products arising therefrom. Actually this turns out to be an effective one-step procedure for the synthesis of 5-and 6-membered cyclic sulfur compounds from δ-, or ε- hydroxy (-alkoxy) sulfides.

RESULTS AND DISCUSSION

We first encountered an example of this type of interaction while attempting to recover 4-hydroxythiepane from the corresponding methyl ether. Working under the usual conditions (Me_3SiCl/NaI/MeCN/reflux)[3,4] a ring contracted product was obtained, 2-(2-iodoethyl)-thiolane, instead of the expected alcohol (Table 2, compound **12**). If, consistent with the accepted mechanism for Me_3SiI-promoted ether cleavage, the reaction is assumed to proceed through an oxonium intermediate[5] (Scheme 1), this result

Scheme 1



can be accounted for in terms of competition between nucleophilic displacement of methyl trimethylsilyl ether by transannular sulfide (Scheme 1. path **a**), and intermolecular demethylation by iodide (path **b**). Path **a** leads to a 1-thioniabicyclo[3.2.0]heptane intermediate which will give the ring contracted product by iodide attack at the α position of the 4-membered ring moiety. It thus appears that, in the presence of a "soft"nucleophile such as sulfide, intramolecular demethoxylation may successfully compete with demethylation.

To establish the scope of this competition, its possible applications to the synthesis of cyclic sulfonium salts and sulfides, and the cautions to be exercised while using this reagent for alcohol deprotection, trimethylsilyl iodide (actually MeSiCl + NaI) has been reacted with a number of α,ω hydroxy- and methoxy-sulfides having a variety of structural features, such as the number of carbons separating the sulfur and the oxygen functions (i.e. the size of the ring potentially formed), the degree of substitution at the oxygen-carrying center, and the nature of the sulfide function. The results, collected in Tables 1 (alcohols) and 2 (methyl ethers), allow a number of observations.

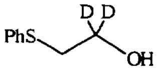
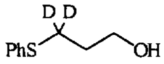
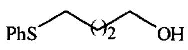
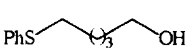
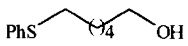
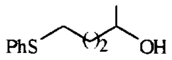
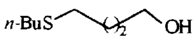
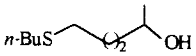
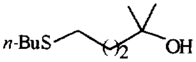
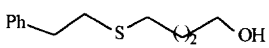
1. The relative position of the sulfide and oxygen functions is the all important factor. Thus (acyclic) 1,2-, 1,3-, and 1,6- *thiophenoxy primary* alcohols (Table 1, cmpds $\mathbf{1}_{d2}$, $\mathbf{2}_{d2}$, and **5**) which would give rise, respectively, to 3-, 4-, and 7-membered S-phenyl cyclic sulfonium salts, undergo iodide for hydroxy substitution exclusively, while 1,4- and 1,5-hydroxy sulfides (entry **3**, **4**) undergo, along with substitution, substantial cyclization to a 5- and 6-membered ring, respectively. The sulfonium salt product appears to arise directly from displacement of the OH group (coordinated with the silicon reagent) rather than from displacement of an iodide intermediate. Indeed no cyclic sulfonium salt was proven to be formed upon heating the 1,4- or 1,5- thiophenoxy iodides for 5 h under the conditions of the Me_3SiI reaction. Although for the 1,2-hydroxy-sulfide ($\mathbf{1}_{d2}$) no cyclic product is formed, complete deuterium scrambling is observed consistent with formation of a thiiranium intermediate which is subsequently cleaved by iodide at one or the other α position. On the other hand, for the 1,3-hydroxy-sulfide ($\mathbf{2}_{d2}$) no deuterium scrambling was observed. These observations are consistent with the neighboring group effect of sulfide-sulfur in solvolysis, which is known to depend on the size of the potential ring to be formed in the order: 3>5~6.[6,7]

2. Aliphatic sulfur appears to be considerably more effective at promoting cyclization than the aromatic one in agreement with the greater nucleophilicity of the former: unlike the aromatic sulfide counterpart, **3**, the aliphatic 1,4 hydroxy sulfide **7** gives raise to the cyclic product exclusively. Moreover, even for the 1,6-compound **10** cyclization appreciably competes with iodide substitution.

3. The cyclization path becomes more favorable as the degree of substitution at the reaction center increases (Table 1, cmpds **7-9**). For the secondary and tertiary alcohols cyclization occurs in few minutes, such

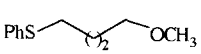
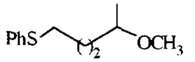
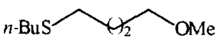
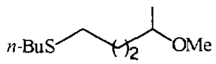
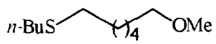
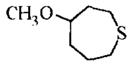
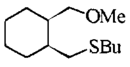
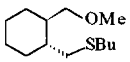
that it becomes the exclusive pathway. The dependence on the degree of substitution was confirmed by a competition experiment where an equimolar mixture of **8** and **9**, treated with a 50% deficit of Me_3SiI, yielded a product consisting almost exclusively (*ca.* 20 to 1) of the sulfonium salt arising from the tertiary alcohol. That the cyclization path becomes more favorable as the reaction center becomes more substituted, the greater steric encumbrance notwithstanding, suggests the transition state has considerable carbocation character. However, no inference is warranted at this stage on whether a carbocation may actually be involved.[8]

Table 1. Reaction of Me_3SiI (1.1 eq) with ω-Phenylthio- or -Alkylthio Alcohols

#	Substrate	Time, min	%	Products
1_{d2}		300	85	completely deuterium scrambled iodide **15**
2_{d2}		300	88	unscrambled iodide **16**
3		300	93	iodide **17** + 1-phenylthiolanium iodide **18** (*ca.* 3:7)
4		300	92	iodide **19** + 1-phenylthianium iodide **20** (*ca.* 1:3)
5		300	93	iodide **21**
6		15	90	*trans*- and *cis*-2-methyl-1-phenyl-thiolanium iodides **22** (*ca.* 4:1)
7		300	90	1-*n*-butylthiolanium iodide **23**
8		15	90	*trans*- and *cis*-1-*n*-butyl-2-methyl-thiolanium iodides **24** (*ca.* 4:1)
9		15	90	1-*n*-butyl-2,2-dimethylthiolanium iodide **25**
10		60	80	start. mat, *ca.* 30%; iodide **26**, *ca.* 55%; 1-*n*-butylthiepanium iodide **27**, *ca.* 15%
11		60	80	1-(2-phenylethyl)thiolanium iodide **28**

4. As to the feasibility of deprotecting alcohols protected as methyl ethers when intramolecular sulfide is present, the results in Table 2 indicate that with a *thiophenoxide* group at positions δ (**3a**) and, presumably, γ or ε, deprotection can be carried out with primary, but not with secondary or (*a fortiori*) tertiary methyl ethers (Table 2, **6a**), further evidence of how cyclization is favored by branching at the reaction center. However, with

Table 2. Reactions of Me_3SiI (1.1 eq) with ω-Phenylthio- or -Alkylthio alkyl Methyl Ethers

#	Substrate	Time, min	%	Products
3a		120	80	start. mat. + iodide **17** (*ca* 1:1)
6a		60	90	*trans*- and *cis*-2-methyl-1-phenyl-thiolanium iodide **22** (*ca* 4:1)
7a		120	82	start. mat., *ca.* 25%, alcohol, **7** *ca.* 10%, 1-*n*-butylthiolanium iodide **23**, *ca.* 65%
8a		15	90	*trans*- and *cis*-1-*n*-butyl-2-methyl-thiolanium iodide **24** (95:5)
10a		60	80	start.mat., *ca.* 25%; alcohol **10**, *ca.* 60%; 1-*n*-butylthiepanium iodide **27**, *ca.* 15%
12		15	95	2-(2-iodoethyl)thiolane **29**
13		15	80	*cis*-7-*n*-butyl-7-thioniabicyclo[4.3.0]no-nane iodide **30** (*ca.* 7:1 diastereomeric mixture)
14		180	80	*trans*-7-*n*-butyl-7-thioniabicyclo[4.3.0]-nonane iodide **31**

an aliphatic sulfide deprotection is not feasible even with a primary methyl ether, for which cyclization is the highly predominant path (entries **7a**, **10a**, **13**, **14**).

5. The intramolecular cyclization may be subject to geometrical constraints other than ring size. A pertinent case is that of entries **13** and **14**: *cis*-1-(methoxymethyl)-2-(thiabutoxymethyl)cyclohexane cyclizes considerably more readily than the trans isomer even though the trans thiahydrindane product is thermodynamically more stable.[10] This can be explained on the basis of the transition state for intramolecular S_N2 reaction requiring the sulfur atom, the oxonium leaving group, and the carbon center to be approximately collinear, a conformation which models suggest to be considerably more strained for the trans than for the cis isomer.

Two main conclusions can be drawn from our results: 1) Alcohols protected as methyl ethers and carrying a sulfide function at position 2, 4, or 5 cannot in general be deprotected by the Me_3SiI method, but give cyclic sulfonium salts either as final products or as intermediates. However, methyl ethers of primary (but not of secondary or tertiary) alcohols may be deprotected in the presence of intramolecular *aromatic sulfide*. 2) Me_3SiI may be a practical reagent for the synthesis of cyclic 5- and 6-membered sulfonium salts directly from 1,4- and 1,5-thioalkoxy alcohols and ethers. The procedure can be of particular interest for the preparation of the S-aryl salts, which are otherwise difficult to prepare. It can be used also for the preparation of cyclic sulfides. In this latter capacity, compounds such as **11**, where the sulfur atom carries a phenylethyl group, may be especially useful since the sulfonium salt will give the cyclic sulfide simply by base catalyzed elimination of styrene.[11]

EXPERIMENTAL

General. All moisture sensitive reactions were performed in flame-dried glassware equipped with rubber septa under a positive pressure of dry nitrogen. Organic extracts were dried over $CaSO_4$. Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} the spots being developed with an aqueous solution of $(NH_4)_6Mo_7O_{24}$ (2.5%), $(NH_4)_4Ce(SO_4)_4$ (1%) in 10% H_2SO_4. Preparative liquid chromatography was performed on Merck Kieselgel 60 (0.040-0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 at 200 and 50.3 MHz respectively. Chemical shifts, unless otherwise specified, were measured in δ, and referenced to $CDCl_3$ (7.25 ppm for ^1H NMR and 77.20 ppm for ^{13}C NMR). Signal multiciplities were established by DEPT experiments. Melting points are uncorrected. Solvents were reagent grade. Solvents and reagents were obtained dry as follows: tetrahydrofuran (THF) was distilled from benzophenone ketyl, CH_3CN and CH_2Cl_2 were refluxed over, and distilled from CaH_2 then stored over molecular sieves (3Å), pyridine was distilled from KOH, CH_3OH from Mg. NaI was heated at 100°C and 0.1 mm Hg for 48 h.

Preparation of 1,n thioalkoxy alcohols and their methyl ethers. The hydroxy sulfides employed in this work have been prepared from the pertinent thiols and 1,n choro alcohols (for details see the preparation of phenyl 4-hydroxybutyl sulfide, **3**) according to a published procedure.[12] A number of them (**2-5**) had already been reported.[12] The preparations of the few which required a different procedure are specified below. The methyl ethers were obtained from the alcohols as described below for phenyl 4-methoxybutyl sulfide (**3a**).

Reactions of alcohols or ethers with Me_3SiCl/NaI. Sodium iodide (1.1 mmol) was added to 10 mL of a 0.1 M acetonitrile solution of the alcohol or ether substrate, followed by 1.1 mmol of freshly distilled Me_3SiCl added dropwise, the mixture being refluxed for the time indicated in the Tables. After cooling to rt, few drops of aq 10% NH_4Cl were added, followed by CH_2Cl_2 extraction. The organic layer was sequentially washed with aq 20% $Na_2S_2O_3$ and brine, dried, and evaporated. The nature, composition and product yields were determined by ^1H and ^{13}C NMR spectroscopy as reported in the sequel.

Phenyl 2,2-dideutero-2-hydroxyethyl sulfide, 1_{d2}. Was obtained by $LiAlD_4$ (0.20 g, 4.8 mmol) reduction of commercial phenyl carboxymethyl sulfide (1.00 g, 5.9 mmol, in THF, 25 mL) for 2h at reflux. After cooling, excess hydride was spent with 10% aq NH_4Cl added dropwise and the solution filtered. The solid was washed with CH_2Cl_2 and the combined organic solution was concentrated to a small volume and flash chromatographed (SiO_2, ether:light petroleum ether 1:1) to give the title compound as an oil (0.84 g, 91%). ^1H NMR: 7.39-7.11 (m, 5H), 3.51 (br s, 1H), 3.05 (s, 2H); ^{13}C NMR: 135.45 (s), 130.18, 129.23, 126.71 (d's), 36.72 (t).

Phenyl 1,1-dideutero-3-hydroxypropyl sulfide, 2_{d2}. Was obtained by $LiAlD_4$[13] (0.04 g, 0.09 mmol) reduction of the corresponding sulfoxide (see below) (0.45 g, 2.4 mmol, in THF, 20 mL). After 4 hours at room temperature, 10 % aq NH_4Cl solution was added dropwise to destroy the unreacted hydride. The organic layer, obtained by filtration of solid, was concentrated to give the sulfide as an oil (0.35 g, 85%). ^1H NMR: 7.40-7.10 (m, 5 H), 3.77 (t, 2 H), 3.15 (br s, 1 H), 1.82 (t, 2 H); ^{13}C NMR: 136.26 (s), 128.94, 128.84, 125.82 (d's), 60.87, 31.43 (t's).

Phenyl 1,1-dideutero-3-hydroxypropyl sulfoxide was obtained from the corresponding protio-compound, by H/D exchange with 2M NaOD in D_2O for 48 h at reflux. The mixture was repeatedly extracted with CH_2Cl_2 and the organic extract was washed with brine, dried, and evaporated (0.46 g, 98%). ^1H NMR: 7.50-7.25 (m, 5 H), 4.20 (br s, 1 H), 3.50 (m, 2 H), 1.77 (m, 2 H); ^{13}C NMR: 142.57 (s), 130.88, 129.03, 123.84 (d's), 60.03, 25.01 (t's).

Phenyl 3-hydroxypropyl sulfoxide was obtained by $NaIO_4$ oxidation (1.05 g, 4.9 mmol in 9 mL H_2O) of the corresponding sulfide (**2**)[12] (0.77 g, 4.6 mmol, in 2 mL MeOH). The mixture was stirred for 5 h at 0 °C and extracted with CH_2Cl_2. The organic layer was washed with brine, dried and chromatographed (SiO_2, ether:methanol 9:1) to give the sulfoxide as an oil, 0.69 g, 71%. ^1H NMR: 7.45 (m, 2 H), 7.35 (m, 3 H), 4.18 (s, 1 H), 3.52 (m, 2 H), 2.80 (m, 2 H), 1.75 (m, 2 H); ^{13}C NMR: 142.57 (s), 130.88, 129.04, 123.83 (d's), 60.18, 53.73, 25.23 (t's).

Phenyl 4-hydroxybutyl sulfide, 3.[12] Commercial 4-chlorobutanol (2.17 g, 20.0 mmol) was added dropwise to a solution of PhSNa previously prepared from thiophenol (2.20 g, 20 mmol) and Na (0.46 g, 20 mmol) in 10 mL of CH_3OH. After 2 h at reflux, 2 mL of H_2O were added and the solvent evaporated. The residue, extracted with CH_2Cl_2 dried and evaporated, gave 3.17 g, 87 % of product as an oil. ^1H NMR: 7.22 (m, 5 H), 3.55 (t, 2 H), 3.00 (br s, 1 H), 2.88 (t, 2 H), 1.67 (m, 4 H); ^1H NMR: 136.74 (s), 128.98 (2 signals), 125.88 (d's), 61.85, 33.13, 31.44, 25.26 (t's).

Phenyl 4-methoxybutyl sulfide, 3a, was obtained by adding **3** (0.73 g, 4.0 mmol) to a suspension of NaH (0.10 g, 4.0 mmol) in THF (5 mL) and, after stirring for 1 h at rt, MeI (0.85 g, 6.0 mmol). After 12 h at rt water was added (2 mL) and the mixture extracted with light petroleum ether. Evaporation of the solvent gave the title compound (0.67 g, 85%) as an oil. ^1H NMR: 7.25 (m, 5 H), 3.37 (t, 2 H), 3.10 (s, 3 H), 2.92 (t, 2 H), 1.70 (m, 4 H); ^{13}C NMR: 137.134 (s), 129.30, 129.11, 125.99 (d's), 72.27 (t), 58.57 (q), 33.45, 28.68, 25.91 (t's).

Phenyl 4-hydroxypentyl sulfide, 6. The pertinent iodo-alcohol, obtained as *t*-butyldimethylsilyl ether by *t*-$BuMe_2SiI$ cleavage of 2-methyltetrahydrofuran,[14] was reacted directly with sodium thiophenoxide, and desilylated by reaction with tetrabutylammonium fluoride to give the title compound (81%). ^1H NMR: 7.30-7.05 (m, 5 H), 3.72 (m, 1 H), 2.85 (t, 2 H), 2.67 (br s, 1 H), 1.80-1.40 (m, 4 H), 1.10 (d, 3 H); ^{13}C NMR: 136.93 (s), 129.14, 129.04, 125.93, 67.41 (d's), 38.04, 33.49, 29.57 (t's), 23.35 (q).

Phenyl 4-methoxypentyl sulfide, 6a, (88 %). ^1H NMR: 7.32-7.07 (m, 5 H), 3.17 (m, 1 H), 3.15 (s, 3 H), 2.88 (t, 2 H), 1.77-1.48 (m, 4 H), 1.09 (d, 3 H); ^{13}C NMR: 137.36 (s), 129.34, 129.21, 126.06, 76.46 (d's), 56.08 (q), 35.51, 33.82, 25.21 (t's), 19.07 (q).

***n*-Butyl 4-hydroxybutyl sulfide, 7.** From *n*-BuSNa and 4-chlorobutanol (92 %). ^1H NMR: 3.48 (t, 2H), 3.18 (br s, 1 H), 2.45 (t, 4 H), 1.60-1.20 (m, 8 H), 0.78 (t, 3H). ^{13}C NMR: 62.05, 31.82 (3 signals), 26.02, 22.08 (t's), 13.76 (q).

***n*-Butyl 4-methoxybutyl sulfide, 7a,** (92 %). ^1H NMR: 3.32 (t, 2 H), 3.28 (s, 3 H), 2.45 (m, 4 H), 1.55-1.25 (m, 8 H), 0.85 (t, 3 H); ^{13}C NMR: 72.29 (t), 58.53 (q), 31.90, 31.74 (2 signals), 28.86, 26.36, 22.06 (t's), 13.73 (q).

***n*-Butyl 4-hydroxypentyl sulfide, 8,** (88 %). ^{1}H NMR: 3.70 (m, 1 H), 2.95 (br s, 1 H), 2.45 (m, 4 H), 1.65-1.25 (m, 8H), 1.10 (d, 3H), 0.80 (t, 3H); ^{13}C NMR: 67.39 (d), 38.27 (s), 32.10, 31.74, 25.83, 25.67 (t's), 23.36 (q), 21.95 (t), 13.61 (q).

***n*-Butyl 4-methoxypentyl sulfide, 8a,** (87 %). ^{1}H NMR: 3.28 (s, 3 H), 3.25 (m, 1 H), 2.47 (2 overlapping t's, 4 H), 1.65-1.15 (m, 8 H), 1.10 (d, 3 H), 0.85 (t, 3H); ^{13}C NMR: 76.42 (d), 55.95 (q), 35.58 (2 signals), 32.30, 31.87, 25.65, 22.06 (t's), 19.07, 13.71 (q's).

***n*-Butyl 4-hydroxy-4-methylpentyl sulfide, 9.** To Mg (0.06 g, 2.4 mmol) in 2 mL of THF, under nitrogen, was added *n*-butyl 3-chloropropyl sulfide (0.43 g, 2.4 mmol) (see below). The mixture was refluxed for 3 h then $(CH_3)_2CO$ (0.17 g, 3.0 mmol) was added and reflux was continued for 3 h. The reaction mixture was quenched with 0,5 mL of NH_4Cl and filtered; the organic layer, dried and evaporated, gave the product (0.37 g, 80 %). ^{1}H NMR: 2.40 (m, 4H), 1.65-1.15 (m, 8H), 1.10 (m, 6H), 0.80 (t, 3H); ^{13}C NMR: 70.49 (s), 43.03, 32.81, 31.86 (t's), 29.29 (q), 24.64, 21.89 (t's), 13.50 (q).

***n*-Butyl 3-chloropropyl sulfide.** To a solution of 1-bromo-4-chlorobutane (0.50 g, 3.0 mmol) in 2 mL of CH_3OH was added *n*-BuSNa previously prepared from Na (0.07 g, 3.0 mmol) in 2 mL of CH_3OH and 1-butanethiol (0.27 g, 3.0 mmol) under N_2. After 12 h at rt the solvent was evaporated, the residue treated with H_2O and extracted with CH_2Cl_2. The organic layer, dried and evaporated, yielded the title compound (0.49 g, 90 %). ^{1}H NMR: 3.61 (t, 2 H), 2.60 (t, 2 H) ,2.47 (t, 2 H), 1.88 (m, 2 H), 1.60-1.28 (m, 4 H), 0.88 (t, 3 H); ^{13}C NMR: 43.54, 32.42, 31.92, 31.81, 29.10, 22.01 (t's), 13.68 (q).

***n*-Butyl 6-hydroxyhexyl sulfide, 10,** (84%). ^{1}H NMR: 3.42 (t, 2 H), 3.20 (br s, 1 H), 2.35 (2 t, 4 H), 1.52-1.15 (m, 12 H), 0.77 (t, 3 H); ^{13}C NMR: 62.07, 32.34, 31.86, 31.61, 29.46, 28.55, 25.28, 21.85 (t's), 13.55 (q).

***n*-Butyl 6-methoxyhexyl sulfide, 10a.** (81%). ^{1}H NMR: 3.33 (t, 2 H), 3.28 (s, 3 H), 2.47 (2t, 4 H), 1.55 (m, 6 H), 1.33 (m, 6 H), 0.88 (t, 3 H); ^{13}C NMR: 72.86 (t), 58.62 (q), 32.14, 31.89 (2 signals), 29.72, 29.63, 28.86, 25.88, 22.13 (t's), 13.79 (q).

2-Phenylethyl 4-hydroxybutyl sulfide, 11, from 4-chlorobutanol and sodium 2-phenylethanethiolate, (85 %). ^{1}H NMR: 7.27 (m, 5 H), 3.62 (m, 2 H), 2.90 (m, 2 H), 2.78 (m, 2 H), 2.67 (m, 2 H), 2.05 (br s, 1 H), 1.68 (m, 4H); ^{13}C NMR: 140.66 (s), 128.53, 126.39, 62.25, 36.38, 33.65, 32.12, 31.84, 25.94 (t's).

4-methoxy thiepane, 12, from 4-hydroxy thiepane[15] (92 %). ^{1}H NMR: 3.40 (m, 1 H), 3.22 (s, 3 H), 2.58 (m, 4 H), 2.18-1.60 (m, 6 H); ^{13}C NMR: 80.50 (t), 56.09 (q), 36.79, 33.02, 31.94, 27.73, 25.94 (t's).

***cis*-1-Methoxymethyl-2-*n*-thiobutoxymethylcyclohexane, 13,** was obtained by reacting (rt overnight) cis-1-methoxymethyl-2-tosyloxymethylcyclohexane (1.64 g, 5.0 mmol) with a MeOH solution of sodium *n*-butanethiolate, prepared from *n*-BuSH (0.45 g, 5.0 mmol) and Na (0.12 g, 5.0 mmol) in 5 mL of MeOH. The residue after solvent evaporation was extracted with H_2O and CH_2Cl_2 . The residue after evaporation of the organic layer was evaporaed and purified by flash chromatography (SiO_2, light petroleum ether:ether 95:5) to give 1.68 g, 90%, of the title compound. ^{1}H NMR: 3.18 (s, 3 H), 3.18 (m, 2 H), 2.34 (m, 4 H), 1.98-1.65 (m, 2 H), 1.60-1.10 (m, 12 H), 0.78 (t, 3 H); ^{13}C NMR: 73.31 (t), 58.46 (q), 38.72, 36.56 (d's), 32.30, 31.79, 31.57, 28.01, 26.01, 23.60, 22.90, 21.76 (t's), 13.39 (q).

***cis*-1-Methoxymethyl-2-tosyloxymethylcyclohexane** was obtained by tosylation of *cis*-1-methoxymethyl-2-hydroxymethylcyclohexane and tosyl chloride under standard conditions (tosyl chloride, pyridine, 0 °C to 5 °C, 12 h) and purified by flash chromatography (SiO_2, 95:5 light petroleum ether:ether), (80 %). ^{1}H NMR: 7.70 (d, 2 H), 7.26 (d, 2 H), 3.91 (m, 2 H), 3.12 (s, 3 H), 3.12 (m, 2 H), 2.37 (s, 3 H), 2.05-1.78 (m, 2 H), 1.50-1.10 (m, 8 H); ^{13}C NMR: 144.86, 133.31 (s's), 129.95, 127.99, 73.26, 71.42 (d's), 58.54 (q), 36.97, 36.82, 26.56, 25.58, 23.20, 22.99 (t's), 21.40 (q).

***cis*-1-Methoxymethyl-2-hydroxymethylcyclohexane**. Commercial *cis*-1,2-cyclohexanedimethanol (2.88 g, 20.0 mmol) dissolved in THF (10 mL) was added dropwise to a suspension of NaH (0.53 g, 22.0 mmol) in 10 mL of THF at 0°C. After warming to rt MeI (3.55 g, 25.0 mmol) was added quickly. After 2 h, 2 mL of H_2O were added and the solvent evaporated. The residue consisted of the mono methyl and the dimethyl ethers in a *ca* 5:1 ratio, which were separated by flash chromatography (SiO_2, light petroleum ether:ether 9:1). The second eluted material was the title product (2.20 g, 70%). ^{1}H NMR: 3.42 (br s, 1 H), 3.24 (m, 4 H), 3.05 (s, 3 H), 3.05 (m, 1 H), 1.78 (m, 1 H), 1.57 (m, 1 H), 1.40-1.00 (m, 8 H,); ^{13}C NMR: 73.62, 63.38, (t's), 58.15 (q), 40.08, 36.24 (d's), 27.48, 25.48, 23.83, 22.97 (t's).

***trans*-1-Methoxymethyl-2-*n*-thiobutoxymethylcyclohexane, 14,** (92 %). Was prepared as described above for the cis isomer starting from *trans*-1,2-cyclohexanedimethanol *via* the mono methyl ether and monomethyl ether monotosylate. ^{1}H NMR: 3.28 (s, 3 H), 3.30 (m, 2H), 2.78-2.25 (m, 4 H), 1.98-1.00 (m, 14 H), 0.88 (t, 3 H); ^{13}C NMR: 76.32 (t), 58.99 (q), 41.89, 39.84 (d's), 37.22, 32.94, 32.03, 31.89, 30.24, 26.08 (2 signals), 22.16 (t's), 13.82 (q).

***trans*-1-Methoxymethyl-2-tosyloxymethylcyclohexane**, (83 %). ^{1}H NMR: 7.70 (d, 2 H), 7.28 (d, 2 H), 4.05, 3.85 (m, 2 H), 3.28-3.00 (m, 2 H), 3.12 (s, 3 H), 2.38 (s, 3 H), 1.70-0.96 (m, 10 H); ^{13}C NMR: 144.92, 138.32 (s's), 129.91, 128.03, 75.90, 73.44 (d's), 58.52 (q), 39.57, 38.81 (d's), 29.63, 29.18, 25.52, 25.32 (t's), 21.27 (q).

***trans*-1-Hydroxymethyl-2-methoxymethylcyclohexane**, (70 %). ^{1}H NMR: 3.65-3.20 (m, 5 H), 3.30 (s, 3H), 1.78-1.55 (m, 2 H), 1.40-1.15 (m, 8 H); ^{13}C NMR: 77.76, 66.46 (t's), 58.43 (q), 44.33, 40.34 (d's), 29.77, 29.61, 25.77 (t's).

1,1-Dideutero-2-iodoethyl phenyl sulfide and 2,2-Dideutero-2-iodoethyl phenyl sulfide, 15. The 1:1 composition of crude reaction mixture from $\mathbf{1}_{d2}$ was established by ^{1}H NMR and confirmed by integration of the ^{13}C NMR spectrum. ^{1}H NMR: 7.42-7.15 (m, 10 H), 3.30 (br s, 2 H), 3.25 (br s, 2 H); ^{13}C NMR: 134.39 (s), 130.91, 129.49, 126.88 (d's), 37.16, 2.14 (t's).

1,1-Dideutero-3-iodopropyl phenyl sulfide, 16 . ^{1}H NMR: 7.35-7.10 (m, 5 H), 3.20 (t, 2 H), 1.63 (t broad, 2H); ^{13}C NMR: 134.16 (s), 129.90, 129.31, 126.14 (d's), 32.43, 4.73 (t's).

4-Iodobutyl phenyl sulfide, 17[16]. ^{1}H NMR: 7.35-7.10 (m, 5 H), 3.15 (t, 2 H), 2.95 (t, 2 H), 1.95 (m, 2 H), 1.75 (m, 2 H); ^{13}C NMR: 136.85 (s), 129.52, 126.03, 125.95 (d's), 32.54, 32.17, 29.75,29.59, 5.73 (t's).

1-Phenyl thiolanium iodide, 18[16]. ^{1}H NMR (acetone-d_6): 8.18 (m, 2 H), 7.90 (m, 3 H), 4.45 (m, 2 H), 4.15 (m, 2 H), 2.78 (m, 4 H), 2.10 (s, 3 H); ^{13}C NMR (acetone-d_6): 137.37 (s), 134.34, 131.59, 130.70 (d's), 49.21, 29.78 (t's).

5-Iodopentyl phenyl sulfide, 19[16]. ^{1}H NMR: 7.20 (m, 5H), 3.18 (t, 2 H), 2.88 (t, 2 H), 2.00-1.60 (m, 6 H); ^{13}C NMR: 131.25 (s), 129.47, 129.03, 125.97 (d's), 32.51, 28.59, 24.55, 22.94, 5.68 (t's)

1-Phenyl thianium iodide, 20[16]. ^{1}H NMR (acetone-d_6): 7.95 (m, 5 H), 4.30 (m, 2 H), 4.05 (m, 2 H), 3.75 (m, 6 H); ^{13}C NMR (acetone-d_6): 131.40 (s), 129.47, 129.03, 125.97 (d's), 49.39, 29.49, 27.99 (t's).

6-Iodohexyl phenyl sulfide, 21. ^{1}H NMR: 7.18 (m, 5 H), 3.15 (t, 2 H), 2.80 (t, 2 H), 2.00-1.65 (m, 8 H); ^{13}C NMR: 132.50 (s), 128.62, 128.31, 125.28 (d's), 33.05, 32.44 (2 signals), 29.49, 27.10, 7.02 (t's).

2-Methyl-1-phenylthiolanium iodide, 22. Major isomer ^{1}H NMR (acetone-d_6): 7.95 (m, 2 H), 7.68 (m, 3 H), 4.15 (m, 2 H), 3.90 (m, 2 H), 2.48 (m, 4 H); ^{13}C NMR (acetone-d_6): 134.39 (s), 130.91, 129.49, 126.88, 58.84 (d's), 44.60, 28.97 (t's), 21.66 (q), 18.92 (t).

1-*n*-Butylthiolanium iodide, 23.[16] ^{1}H NMR (acetone-d_6): 3.90-3.60 (m, 6 H), 2.50 (m, 4 H), 1.78 (m, 2H), 1.50 (m, 2 H), 0.90 (t, 3 H); ^{13}C NMR (acetone-d_6): 43.95, 41.88, 28.87, 27.07, 21.17 (t's), 13.37 (q).

1-*n*-Butyl-2-methylthiolanium iodide, 24. Major isomer ^{1}H NMR (acetone-d_6): 4.42 (m, 1 H), 4.00-3.63 (m, 4 H), 2.80-2.35 (m, 4 H), 1.90-1.45 (m, 2 H), 1.65 (d, 3 H), 1.60-1.45 (m, 2 H), 0.92 (t, 3 H). ^{13}C NMR (acetone-d_6): 58.84 (d) , 44.60, 42.79, 37.73, 28.97, 27.56 (t's), 21.66 (q), 18.92 (t), 13.74 (q).

1-*n*-Butyl-2,2-dimethylthiolanium iodide, 25. ^{1}H NMR (acetone-d_6): 4.20-3.45 (m, 4 H), 2.68-2.30 (m, 4 H), 1.75-1.50 (m, 4H), 1.88 (s, 3 H), 1.78 (s, 3 H), 0.70 (t, 3 H); ^{13}C NMR (acetone-d_6): 71.57 (s), 43.54 (2 signals), 39.45, 27.89, 27.77 (t's), 24.22 (2 signals, q), 22.18 (t), 13.76 (q).

***n*-Butyl 6-iodohexyl sulfide, 26.**[16] ^{1}H NMR: 3.15 (t, 2 H), 2.45 (2t, 4 H), 1.78 (m, 2 H), 1.60-1.28 (m, 10 H), 0.87 (t, 3H); ^{13}C NMR: 33.38, 32.00, 31.84 (2 signals), 30.12, 29.45, 27.78, 22.06 (t's), 13.77 (q), 7.14 (t).

1-*n*-Butylthiepanium iodide, 27.[16] ^{1}H NMR (acetone-d_6): 4.05-3.65 (m, 6 H), 2.30-1.45 (m, 12 H), 0.97 (t, 3 H); ^{13}C NMR (acetone-d_6): 42.70, 42.34, 27.67, 27.27, 26.08, 22.74, (t's), 14.38 (q).

1-(2-Phenylethyl)thiolanium iodide, 28, was obtained as a white solid, mp 67-8°C. ^{1}H NMR (acetone-d_6): 7.40 (m, 5 H), 3.65-3.40 (m, 6 H), 3.15 (t, 2 H), 2.47-2.25 (m, 4 H); ^{13}C NMR (acetone-d_6): 136.87 (s), 128.67, 127.14, 43.43, 42.96, 30.57, 28.35 (d's). The sulfonium salt, treated with *t*-BuOK/*t*-BuOH in THF at 80°C for 3 h, gave thiolane (75 % by glc, 50% isolated). ^{1}H NMR: 2.75 (m, 4 H), 1.85 (m, 4 H); ^{13}C NMR: 31.72, 31.03 (t's)

2-(2-Iodoethyl)thiolane, 29. ^{1}H NMR: 3.38 (m, 1 H), 3.13 (m, 2 H), 2.80 (t, 2 H), 2.20-1.80 (m, 5 H), 1.55 (m, 1 H); ^{13}C NMR: 49.48 (d), 41.28, 36.65, 32.14, 30.17, 4.41 (t's

***cis*-7-*n*-Butyl-7-thioniabicyclo[4.3.0]nonane iodide, 30.** Major isomer ^{13}C NMR: 46.42. 43.76 (t's), 41.56 (d), 27.51, 25.85, 21.98, 21.45 (t's), 13.58 (q). The sulfonium salts, treated with *t*-BuOK/*t*-BuOH at 80°C for 3 hours, gave the *cis*-7-thiabicyclo[4.3.0]nonane. ^{1}H NMR: 2.87 (dd, 2 H), 2.68 (dd, 2 H), 2.28 (m, 2 H), 1.65-1.25 (m, 8 H); ^{13}C NMR: 43.03 (d), 35.04, 26.41, 23.06 (t's).

***trans*-7-*n*-Butyl-7-thioniabicyclo[4.3.0]nonane iodide, 31.** ^{1}H NMR: 4.02 (m, 1 H), 3.57 (m, 2 H), 3.35-3.03 (m, 2 H), 2.10-1.10 (m, 15 H), 0.88 (t, 3 H); ^{13}C NMR: 48.68, 47.55(t's), 46.83, 44.76 (d's), 43.51, 29.69 (2 signals), 27.40, 24.59, 24.50, 21.24 (t's), 13.34 (q). The sulfonium salt, treated with *t*-BuOK/*t*-BuOH at

80°C for 3 h, gave the *trans*-7-thiabicyclo[4.3.0]nonane. ^{1}H NMR: 2.75 (dd, 2 H), 2.42 (m, 2 H), 2.00-1.65 (m, 4 H), 1.50-0.95 (m, 6 H); ^{13}C NMR: 48.47 (d), 37.08, 31.63, 25.84 (t's)

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