Stereoselective Syntheses of *cis*- and *trans*-2-Substituted 1,3-Dithiane 1-Oxides

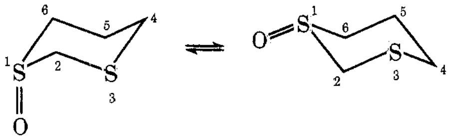
Francis A. Carey,* Oliver D. Dailey, Jr., Oscar Hernandez, and James R. Tucker

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901

Received March 29, 1976

Stereoselective syntheses of *cis*-2-deuterio- (**7b**), *cis*-2-methyl- (**4b**), *cis*-2-phenyl- (**4c**), and *trans*-2-deuterio- (**7a**), *trans*-2-methyl- (**3b**), and *trans*-2-phenyl-1,3-dithiane 1-oxide (**3c**) are described. Oxidation of 2-methyl-1,3-dithiane and 2-phenyl-1,3-dithiane with either sodium metaperiodate or *m*-chloroperoxybenzoic acid is consistently 92% stereoselective and gives pure **3b** and **3c** in good yield after recrystallization. The cis isomers **4b** and **4c**, as well as the specifically deuterated compounds **7a** and **7b**, were prepared by a reaction sequence involving *stereospecific* trimethylsilyl cleavage from C(2) of a 1,3-dithiane 1-oxide as a key step. Oxidation of 2-deuterio-2-trimethylsilyl-1,3-dithiane (**5b**) occurred trans to the trimethylsilyl substituent (cis to deuterium). Cleavage of the trimethylsilyl group with methanol–sodium methoxide occurred with retention of configuration at C(2) to give **7b**. An analogous process starting with 2-trimethylsilyl-1,3-dithiane (**5a**) and using CH_3OD in the cleavage step gave **7a**. The trimethylsilyl group was used as a stereospecifically removable substituent capable of influencing the stereoselectivity of oxidation in a similar manner in the synthesis of **4b** and **4c**. It is suggested that NMR provides a simple indicator of sulfoxide stereochemistry in 1,3-dithiane 1-oxides in certain circumstances. The chemical shift of the C(6) equatorial proton is in the range δ 3.2–3.5 ppm for *trans*-2-monosubstituted 1,3-dithiane 1-oxides. The applicability of the method is illustrated for the diastereomeric 2-(diphenylhydroxymethyl)-1,3-dithiane 1-oxides **3d** and **4d**.

Reactions involving carbanionic species stabilized by adjacent sulfur, sulfoxide, and sulfone have been the subject of numerous stereochemical investigations.[1] Recent emphasis on synthetic applications has served to stimulate interest in compounds containing two sulfur atoms.[2] In particular, the lithiation and subsequent reactions of 1,3-dithiane,[3] 1,3-dithiane 1-oxide (1),[4] methyl methylthiomethyl sulfoxide,[5] and related $-SCH_2S(O)-$ species[6] offer certain advantages in synthetic operations which require a nucleophilic carbonyl equivalent. The conformational properties of 1 have also attracted attention from a number of investigators interested in the interactions between polar groups in heterocyclic molecules.[7] The conformer having the sulfoxide oxygen equatorial is 0.63 kcal/mol more stable than the sulfoxide oxygen-axial conformer at −81 °C.

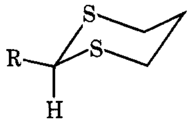


16% 1 84%

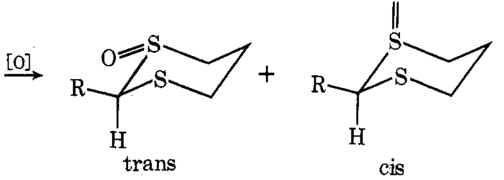
The metalation of 1 and subsequent reactions of its 2-lithio derivative with several electrophiles have been reported.[4] It was not possible, on the basis of the information available at the time, to determine the stereochemical courses of these reactions. The present work seeks to answer these questions. The approach which was employed is described in two parts. The first part is the subject of this paper and concerns the stereochemical relationships and stereoselective syntheses of the starting materials and products central to the study. The second paper[8a] reports the stereochemical course followed in the metalation of 1 and reactions of 2-lithio-1,3-dithiane 1-oxide with electrophiles. A subsequent paper will present a complete x-ray crystallographic study of the 1,3-dithiane 1-oxide system and will include several of the compounds described in this paper.[8b]

Results and Discussion

The preparation of *trans*-2-alkyl- and *trans*-2-aryl-1,3-dithiane 1-oxides presents no difficulties because oxidation of 2-substituted 1,3-dithianes is highly stereoselective (eq 1). Sodium metaperiodate oxidation of 2-*tert*-butyl-1,3-dithiane (**2a**) has been reported to afford a 9:1 trans/cis mixture of sulfoxides.[7a,c] When 2-methyl-1,3-dithiane (**2b**) was oxidized with either sodium metaperiodate in methanol–water or *m*-chloroperoxybenzoic acid in dichloromethane, a 92:8 mixture of diastereomers was obtained (analysis by liquid chromatography using authentic samples to calibrate the detector). The assignment of trans stereochemistry (**3b**) to the major isomer follows by analogy to the oxidation of **2a** to **3a**, and by the NMR spectra to be discussed later. An identical 92:8 trans/cis ratio was obtained on oxidation of 2-phenyl-1,3-dithiane (**2c**) with *m*-chloroperoxybenzoic acid. The configurational assignments to **3c** and **4c** were made on the same basis as those of **3b** and **4b** and are further supported by single crystal x-ray diffraction studies on each diastereomer.[8b] A single recrystallization usually suffices to give **3b**, mp 93–94 °C, and **3c**, mp 145–147 °C, in good yield.



2a, R = $(CH_3)_3C$
b, R = CH_3
c, R = C_6H_5
d, R = $Ph_2C(OH)$

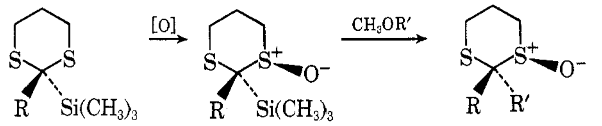


(1)

3a, R = $(CH_3)_3C$	**4a**, R = $(CH_3)_3C$
b, R = CH_3	**b**, R = CH_3
c, R = C_6H_5	**c**, R = C_6H_5
d, R = $Ph_2C(OH)$	**d**, R = $Ph_2C(OH)$

The identical direction and degree of stereoselectivity in oxidation of 1,3-dithianes with sodium metaperiodate and *m*-chloroperoxybenzoic acid contrasts markedly with that observed in thianes.[9] In thiane oxidation, sodium metaperiodate gives primarily the more stable axial sulfoxide. Peroxy acids give primarily equatorial thiane oxide, presumably corresponding to oxygen transfer from the less hindered direction.

It was reasoned that entry could be gained to the cis series of diastereomers (**4b** and **4c**) if C(2) bore a substituent which was sufficiently sterically demanding to direct oxidation trans to itself, and which could be replaced by hydrogen stereospecifically with retention of configuration. A trimethylsilyl substituent appeared a good candidate to meet both criteria,[10,11] and the scheme described by eq 2 was applied to the synthesis of *cis*-2-methyl- (**4b**) and *cis*-2-phenyl-1,3-dithiane 1-oxide (**4c**), as well as to the stereospecifically labeled *cis*- and *trans*-2-deuterio-1,3-dithiane 1-oxides **7a** and **7b**.



(2)

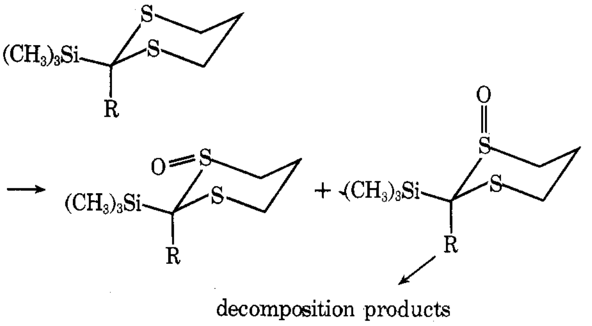
5a, R = H	**6a**, R = H	**7a**, R = H; R′ = D
5b, R = D	**6b**, R = D	**7b**, R = D; R′ = H
8, R = CH$_3$	**9**, R = CH$_3$	**4b**, R = CH$_3$; R′ = H
10, R = C$_6$H$_5$	**11**, R = C$_6$H$_5$	**4c**, R = C$_6$H$_5$; R′ = H

Oxidation of 2-trimethylsilyl-1,3-dithiane (**5a**) with sodium metaperiodate in methanol-water (4 h, 5 °C) is highly stereoselective, affording *trans*-2-trimethylsilyl-1,3-dithiane 1-oxide (**6a**) as a clear syrup in 92% yield. The stereoselectivity of this reaction has been confirmed by x-ray diffraction techniques using the corresponding 2-triphenylsilyl derivative which is crystalline.[8,12] Cleavage of the trimethylsilyl group occurred readily on treatment of **6a** with methanol-*O-d* in the presence of sodium methoxide (0.05 equiv, room temperature, 24 h) *with complete retention of configuration at C(2)* to give *trans*-2-deuterio-1,3-dithiane 1-oxide (**7a**) cleanly in 71% yield. The stereochemistry of deuterium incorporation can be determined readily by NMR analysis.[7] The proton at C(2) which is trans to oxygen, i.e., equatorial in the dominant conformation, appears at lower field than the proton at C(2) which is cis to oxygen (δ 4.02 and 3.64 ppm, respectively). This assignment can be made with confidence because it is the low-field signal which is further split by long-range coupling, and the required W orientation is met only when the proton is equatorial. The product obtained exhibited a one-proton signal (triplet, J = 1.8 Hz, due to geminal H–D coupling) at 3.6 ppm indicative of the C(2)-axial proton and showed no signal for the C(2)-equatorial proton.

The analogous sequence beginning with 2-deuterio-2-trimethylsilyl-1,3-dithiane (**5b**) and using CH$_3$OH in the cleavage step gave *cis*-2-deuterio-1,3-dithiane 1-oxide (**7b**) in 93% yield. NMR analysis confirmed its stereochemical integrity. Mass spectral analysis of **7a** and **7b** indicated that each was >93% monodeuterated.

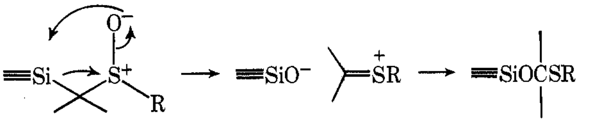
Application of the sequence to the synthesis of *cis*-2-methyl-1,3-dithiane 1-oxide (**4b**) proceeded smoothly. Reaction of 2-methyl-2-trimethylsilyl-1,3-dithiane (**8**) with sodium metaperiodate in methanol–water gave the sulfoxide **9** as a colorless oil in 85% yield. Analysis by NMR indicated that **9** was a single diastereomer. Treatment with methanol containing ammonium hydroxide (8:1) at room temperature for 12 h gave **4b**, mp 60–62 °C, in 77% yield.

The conversion of 2-phenyl-2-trimethylsilyl-1,3-dithiane (**10**) to *cis*-2-phenyl-1,3-dithiane 1-oxide (**4c**), mp 163.5–165.5 °C, proceeds in substantially lower overall yield (39%), presumably because the oxidation step is both more difficult and less stereoselective. The phenyl and trimethylsilyl substituents are comparable in their preference for the equatorial orientation.[10] It is reasonable to expect oxidation to produce comparable amounts of sulfoxide **11** and its diastereomer. The trimethylsilyl group in **11** is, however, very labile and the best conditions found (sodium metaperiodate in methanol–acetonitrile–water, 20 °C, 40 h) also led to cleavage of the trimethylsilyl group after oxidation. It should be mentioned that, in spite of the low absolute yield of **4c** isolated, the crude product contained only about 2% of the trans isomer. We believe that the high apparent stereoselectivity, as evidenced by product isolation, is a consequence of a rapid decomposition which takes place when a 2-trimethylsilyl group is cis to sulfoxide oxygen in a 1,3-dithiane 1-oxide (eq 3).



(3)

The thermal rearrangement of trimethylsilylmethyl sulfoxides has been observed several times and is presumed to involve fragmentation of a four-center intermediate or transition state (eq 4).[13] A marked stereochemical dependence has



(4)

been demonstrated, with one diastereomer of 1-trimethylsilylethyl phenyl sulfoxide being quantitatively converted to rearranged product after 1 h at 60 °C, and the other to the extent of only 7%.[13c] It is possible that the *cis*-2-trimethylsilyl-1,3-dithiane 1-oxide series shown in eq 3 rapidly undergoes this rearrangement reaction to Pummerer or other products which are, as yet, unidentified. The *cis*-2-substituted 1,3-dithiane 1-oxides which are isolated are derived from the more thermally stable *trans*-2-trimethylsilyl series of 1,3-dithiane oxides. It is noteworthy that the lability of silylmethyl sulfoxides is such that **6a** (and **6b**) and **9** are the first examples of such compounds reported to have been prepared by direct oxidation of silylmethyl thioethers.

As mentioned earlier, the stereochemical assignments have been made by analogy to the reported stereoselective formation of **3a** on oxidation of **2a**.[7a,c] In addition, the structures of **3c** and **4c** have been rigorously confirmed by single crystal x-ray diffraction techniques.[8] It would be desirable to have available a simple physical method for distinguishing *cis*- and *trans*-2-substituted 1,3-dithiane 1-oxides. Nuclear magnetic resonance spectroscopy can be applied to stereochemical assignments of *cis*- and *trans*-2-substituted 1,3-dithiane 1-oxides on the basis of previous observations[7] and the present results. The trans compounds **3a**, **3b**, **3c**, and **6a** (as well as the 2-triphenylsilyl analogue of **6a**), as well as **1**, all exhibit a one-proton multiplet centered between δ 3.2 and 3.5 ppm. This signal has been assigned to the C(6)-equatorial proton in **1** (δ 3.32)[7c] and in **3a** (δ 3.38).[7c] The corresponding signal appears at higher field in the cis series and is usually not clearly defined but overlaps with the other ring protons. The observation of a signal at 3.2–3.6 ppm, then may be taken as indicative of a *trans*-2-substituted 1,3-dithiane 1-oxide. The chemical shift of the C(6)-equatorial proton is sensitive to the torsional relationship between the proton and the sulfoxide oxygen, and the addition of a second substituent at C(2) apparently produces sufficient distortion of the ring to cause a shift of the signal to higher field. The generalization is therefore limited to monosubstituted derivatives. As an example of the application of the relationship, the case of the oxidation of 2-(diphenylhydroxymethyl)-1,3-dithiane (**2d**) is informative. Participation of neighboring hydroxyl in influencing the stereoselectivity of peroxy acid oxidations is well known, so while predominant equatorial oxidation is likely it is not assured.[14] Indeed, the ratio of diastereomers produced on oxidation with *m*-chloroperoxybenzoic acid was 3:1 by NMR analysis. Oxidation with sodium metaperiodate gave a 4:1 ratio of diastereomers. The NMR spectrum of the major diastereomer was well resolved in the region δ 2.7–4 ppm. A one-proton signal appeared as a doublet of triplets (J_{gem} = 13, J_{gauche} = 3.5 Hz) centered at 3.4 ppm, allowing the trans stereochemistry (**3d**) to be assigned to the major diastereomer. The corresponding multiplet is centered at 3.0 ppm in the minor diastereomer, which is accordingly assigned the cis stereochemistry **4d.**

Experimental Section

Nuclear magnetic resonance (NMR) spectra were recorded on Hitachi Perkin-Elmer R-20, Varian HA-100, and JEOL PS-FT spectrometers in $CDCl_3$, and chemical shifts are reported in parts per million (δ) from internal tetramethylsilane. Infrared spectra (ir) were obtained on a Perkin-Elmer 337 grating spectrometer as KBr disks and were calibrated with either the 1601-cm^{-1} or the 1028-cm^{-1} band of polystyrene. Melting points are corrected and were measured on a Thomas-Hoover apparatus. Boiling points are uncorrected. Mass spectra were obtained using a Hitachi Perkin-Elmer RMU-6E spectrometer at an ionizing potential of 70 eV (15 eV for isotope analyses). Liquid chromatography (LC) analyses were performed on a Waters Associates ALC-100 liquid chromatograph with a differential uv detector (254 nm). In all experiments a microporasil column was used, the solvent was 5% 2-propanol/methylene chloride, and the flow rate was 1.0 ml/min. Relative peak areas were determined by weighing of peaks cut from photostatic copies. The detector was calibrated using authentic samples of pure isomers prepared as described in this paper. Microanalyses were performed by Atlantic Microlab Inc., Atlanta, Ga., and by Alfred Bernhardt, Engelskirchen, West Germany.

Oxidation of 2-Methyl-1,3-dithiane (2b). A. Sodium Metaperiodate. A solution of 5.615 g (26.3 mmol) of sodium metaperiodate in 52 ml of water was added dropwise to a solution of 3.3565 g (25.0 mmol) of 2-methyl-1,3-dithiane[15] in 200 ml of methanol at −7 to 0 °C. The resulting white slurry was stirred at −5 °C for 1 h, then refrigerated at 0 °C overnight. The precipitated sodium iodate was removed by filtration and washed with chloroform, the chloroform being combined with the filtrate. The solvent was removed in vacuo, and the residue extracted with chloroform (2 × 100 ml). The combined organic layers were washed with brine (2 × 100 ml) and dried over potassium carbonate. A yellow-hued solid, 3.25 g, mp 81–88.5 °C, was isolated. LC analysis of the material showed it to contain 92% *trans*- (**3b**) and 8% *cis*- (**4b**) 2-methyl-1,3-dithiane 1-oxide.

Recrystallization from dichloromethane–ether gave 2.44 g (65%) of **3b:** mp 92–94 °C (lit. mp 93–94 °C);[4] ir (KBr) 3400, 2910, 1430, 1410, 1294, 1270, 1236, 1190, 1170, 1116, 1050, 1010 (vs), 914, 870, 830, 750, 715, 688, and 650 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 3.55 (q, 1, *J* = 7 Hz, $HCCH_3$), 3.2–3.5 [m, 1, eq H at C(6)], 2.2–2.9 (m, 5, ring protons), 1.60 (d, 3, *J* = 7 Hz, CH_3).

B. *m*-Chloroperoxybenzoic Acid. A solution of 1.34 g (10 mmol) of **2b** in 50 ml of dichloromethane was cooled in an ice bath while 2.03 g (10 mmol) of *m*-chloroperoxybenzoic acid in 75 ml of dichloromethane was slowly added. After standing for 12 h, the solution was washed with two 50-ml portions of 10% sodium carbonate solution and dried over magnesium sulfate. Evaporation of the solvent left 1.25 g of white solid, mp 77–88 °C, which on recrystallization from hexane–dichloromethane gave 790 mg (53%) of *trans*-2-methyl-1,3-dithiane 1-oxide (**3b**) as white needles, mp 91–95 °C.

In a separate experiment, carried out at −15 to −20 °C, analysis of the crude product by liquid chromatography showed a composition of 92% **3b** and 8% **4b.**

Oxidation of 2-Phenyl-1,3-dithiane (2c). A. Sodium Metaperiodate. The procedure used was similar to that employed for the oxidation of **2b** described above. The reaction was carried out on a 10-mmol scale and the solvent used was 100 ml of methanol–dioxane (9:1). The crude product (2.0 g), mp 139–142 °C, was recrystallized from dichloromethane–cyclohexane to give 1.98 g (94%) of **3c:** mp 140.5–142.5 °C; ir (KBr) 3400, 2900, 1490, 1440, 1420, 1290, 1270, 1175, 1060, 1030 (S=O), 750, 695, and 495 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (s, 5, aromatic), 4.5 (s, 1, C-2 H), 3.7–3.3 (m, 1, C-6 eq H), and 3.0–2.2 ppm (m, 5, ring H); mass spectrum (70 eV) *m/e* (rel intensity) 212 (M$^+$, 100), 196 (7), 163 (14), 135 (24), 122 (35), 121 (70), 106 (17), 91 (23), 90 (77).

The analytical sample, mp 145–147 °C, was obtained by recrystallization from dichloromethane–cyclohexane.

Anal. Calcd for $C_{10}H_{12}OS_2$: C, 56.57; H, 5.70; O, 7.52; S, 30.20. Found: C, 56.52; H, 5.66; O, 7.37; S, 30.22.

B. *m*-Chloroperoxybenzoic Acid. A similar procedure to that employed for **2b** was followed, using 4.91 g (25 mmol) of **2c**[15] and 5.08 g (25 mmol) of *m*-chloroperoxybenzoic acid in 210 ml of dichloromethane at −15 to −25 °C overnight. The crude product (5.56 g) was a white solid, mp 123.5–134 °C. Liquid chromatographic analysis showed it to consist of 92% *trans*- (**3c**) and 8% *cis*-2-phenyl-1,3-dithiane 1-oxide (**4c**). After recrystallizing from dichloromethane–cyclohexane, 3.37 g (63%) of **3c,** mp 143.5–145 °C, was obtained.

Oxidation of 2-(Diphenylhydroxymethyl)-1,3-dithiane (2d). These oxidations were performed on a 2-mmol scale.

A. Sodium Metaperiodate. The sodium metaperiodate was added as a solution in 45 ml of water to a solution of **2d** in 20 ml of 3:1 methanol–dioxane at 5 °C. Workup was as described for previous periodate oxidations to give 661 mg of crude product, mp 141–144 °C dec which appeared from its NMR spectrum to be a 4:1 mixture of **3d** and **4d.** After recrystallizing from chloroform–cyclohexane, 537 mg (84%) of white crystals, mp 131–133.5 °C, was obtained. This material was dissolved in warm acetonitrile, allowed to cool, and applied to four preparative TLC plates (silica gel). After allowing the acetonitrile to evaporate overnight, the plates were developed twice with 9:1 carbon tetrachloride–2-propanol to yield **3d** (289 mg), mp 150–155 °C dec, and **4d** (127 mg), mp 159–160 °C dec. The melting points are highly variable, and decomposition to a deep blue melt occurs for both diastereomers.

The major diastereomer, *trans*-2-(diphenylhydroxymethyl)-1,3-dithiane 1-oxide (**3d**), was recrystallized from chloroform–cyclohexane to afford 250 mg of pure material: mp 123–125 °C dec; ir (KBr) 3360, 3050, 2940, 2910, 1500, 1450, 1425, 1390, 1290, 1270, 1230, 1185, 1030 (vs), 1120 (vs), 1000, 930, 905, 820, 790, 760, 740, 700, 685, and 635 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 7.9–7.5 (m, 2), 7.5–7.1 (m, 8), 5.85 (s, 1, OH), 4.38 (s, 1, C-2 H), 3.6–3.1 (dt, 1, *J* = 13, 3 Hz, C-6 eq H), 3.1–2.7 (td, 1, *J* = 3.5, 13 Hz, C-6 ax H), 2.7–2.2 (m, 4, C-4, 5 ring H).

Anal. Calcd for $C_{17}H_{18}O_2S_2$: C, 64.12; H, 5.70; S, 20.14. Found: C, 63.94; H, 5.55; S, 20.26.

The minor diastereomer assigned cis stereochemistry **4d** had ir and NMR spectra identical with those of the compound reported previously by Carlson:[4,16] ir (KBr) 3400, 2920, 1500, 1450, 1050 (s), 1020, 990 (s), 970, 900, 780, 750, 735, 700, and 650 cm^{-1}; NMR ($CDCl_3$) δ 7.7–7.1 (m, 10, aromatic), 4.80 and 4.68 [each a one-proton singlet, C(2) H and OH], and 3.2–1.5 ppm (m, 6, CH_2).

B. *m*-Chloroperoxybenzoic Acid. The oxidation was carried out at −15 to −25 °C in 75 ml of dichloromethane. The crude product (450 mg), mp 123–129 °C, was a 3:1 mixture of **3d** and **4d.** Recrystallization from ethanol gave 104 mg of white crystals, mp 134–136 °C dec, which were at least 85% **3d** by NMR.

Oxidation of 2-Trimethylsilyl-1,3-dithiane (5a) with Sodium Metaperiodate. To 1.92 g (10 mmol) of 2-trimethylsilyl-1,3-dithiane (**5a**)[17] in 90 ml of methanol was added a solution of 2.14 g (10 mmol) of sodium metaperiodate in 20 ml of water while maintaining the temperature below 10 °C. After 4 h at 4–6 °C the solution was allowed to warm to room temperature and filtered. The methanol was removed by evaporation and the residue partitioned between brine and chloroform. Drying (sodium sulfate) and evaporation gave 1.91 g (92%) of *trans*-2-trimethylsilyl-1,3-dithiane 1-oxide (**6a**) as a light yellow oil: ir (neat) 2970, 2910, 1430, 1250, 1172, 1040 (S=O), 880, 850, 770, 730, 700, and 650 cm^{-1}; NMR ($CDCl_3$) δ 3.4–3.2 (m, 1, C-6 eq H), 3.19 (s, 1, C-2 H), 2.6–2.2 (m, 5, ring H), and 2.8 ppm (s 9, Me_3Si); mass spectrum (70 eV) *m/e* (rel intensity) 208 (5), 193 (14), 165 (11), 199 (66), 87 (34), 83 (18), 75 (100), and 73 (59).

The analytical sample was obtained by preparative TLC on silica gel using chloroform–ethanol (95:5) as the developing solvent.

Anal. Calcd for $C_7H_{16}OS_2Si$: C, 40.34; H, 7.74; S, 30.77. Found: C, 40.17; H, 7.51, S, 30.72.

Cleavage of 2-Trimethylsilyl-1,3-dithiane 1-Oxide (6a) in Methanol-*O-d*. A solution of 390 mg (1.87 mmol) of purified **6a** in 25 ml of CH_3OD (Diaprep, 99%) containing sodium methoxide (5 mg, 0.09 mmol) was stirred under nitrogen at 25 °C for 24 h. The solvent was removed and the residue was dissolved in chloroform (50 ml), washed with water and brine, and dried with sodium sulfate. The crude product was purified by preparative TLC on silica gel using chloroform–ethanol (95:5) to afford 182 mg (71%) of material, mp 88–89 °C. NMR analysis showed the product to be *trans*-2-deuterio-1,3-dithiane 1-oxide (**7a**). The NMR spectrum was consistent with all the deuterium being at the C-2 equatorial position. Recrystallization from dichloromethane–cyclohexane gave 160 mg of white crystals: mp 89–90.5 °C; ir (KBr) 2175 cm^{-1} (C–D); mass spectral analysis (15 eV) indicated 93.5% d_1, 6% d_0, and 0.5% d_2 material.

Preparation of *cis*-2-Deuterio-1,3-dithiane 1-Oxide (7b). A solution of 1.0 g (5.2 mmol) of 2-trimethylsilyl-1,3-dithiane (**5a**) in

20 ml of tetrahydrofuran was cooled to −25 °C and metalated with 2.7 ml (5.8 mmol) of *n*-butyllithium (2.2 M in *n*-hexane). After 45 min D_2O was added, the solvent evaporated, and the residue taken up in 50 ml of ether and washed with water. The aqueous extracts were washed with ether and the combined ether extracts dried over sodium sulfate. The ether was evaporated to leave 855 mg of 2-deuterio-2-trimethylsilyl-1,3-dithiane (**5b**) as a colorless oil. NMR analysis indicated complete exchange of protium by deuterium at C(2).

Oxidation of **5b** with sodium metaperiodate in methanol–water was carried out as described for the conversion of **5a** to **6a**, and the resulting sulfoxide dissolved in methanol and allowed to stand overnight. The solvent and volatile products were removed under vacuum to leave 563 mg (93%) of **7b**, mp 84–86 °C. The product was recrystallized from dichloromethane–cyclohexane to give 465 mg (76%) of material, mp 89–90 °C. The NMR spectrum of **7b** indicated exclusive and complete deuterium incorporation at C(2) cis to the sulfoxide oxygen. Mass spectral analysis (15 eV) gave an isotopic composition of 1.3% d_0, 98.3% d_1, and 0.4% d_2.

A similar reaction using 2-triphenylsilyl-2-deuterio-1,3-dithiane 1-oxide (319 mg, 0.79 mmol) afforded 95 mg (88%) of *cis*-2-deuterio-1,3-dithiane 1-oxide (**7b**), mp 89–90 °C; mass spectral analysis indicated 94% d_1 and 6% d_0 material.

Synthesis of *cis*-2-Methyl-1,3-dithiane 1-Oxide (4b). A. Oxidation of 2-Methyl-2-trimethylsilyl-1,3-dithiane (8) with Sodium Metaperiodate. Sodium metaperiodate (2.25 g, 10.5 mmol) was dissolved in 22 ml of water and added to a solution of 2.06 g (10 mmol) of 2-methyl-2-trimethylsilyl-1,3-dithiane[17] (**8**) in 90 ml of methanol while maintaining the temperature at −6 to −8 °C. A heavy white precipitate formed rapidly. After stirring overnight at 10 °C, the solution was allowed to warm to room temperature and filtered and the methanol removed by evaporation. The residue was partitioned between brine and dichloromethane, dried (Na_2SO_4), and evaporated to leave the sulfoxide **9** as a colorless oil (1.89 g, 85%): ir ($CHCl_3$, 5%) 3000, 1420, 1250, 1030 (s), 1020 (s), 880, and 850 cm^{-1} (s); NMR ($CDCl_3$) δ 3.0–2.0 (m, 6, ring CH_2), 1.70 (s, 3, CH_3), 0.25 (s, 9, $SiMe_3$).

The analytical sample was obtained by preparative TLC on silica gel using 95:5 chloroform–ethanol.

Anal. Calcd for $C_8H_{18}OS_2Si$: C, 43.20; H, 8.16; S, 28.83. Found: C, 43.05; H, 7.96; S, 28.63.

B. Methanol Cleavage of 9. After standing for 12 h, a solution of **9** (2.60 g, 11.7 mmol) in 40 ml of methanol containing 5 ml of concentrated ammonium hydroxide was evaporated and the volatile materials removed by vacuum pump to leave 1.78 g of soft, yellowish-white solid. The crude product was recrystallized from ether containing a trace of dichloromethane to give 1.36 g (77%) of *cis*-2-methyl-1,3-dithiane 1-oxide (**4b**): mp 60–63 °C; ir (KBr) 3400, 2910, 1450, 1410, 1280, 1260, 1250, 1200, 1170, 1125, 1060, 1030 (vs), 1000, 900, 865, 830, 670, and 630 cm^{-1}; NMR ($CDCL_3$, 100 MHz) δ 3.86 (q, 1, J = 7 Hz, $HCCH_3$), 1.9–3.0 (m, 6, ring protons), and 1.63 ppm (d, 3, J = 7 Hz, CH_3).

The analytical sample, mp 60–62 °C, was obtained by recrystallization from ether.

Anal. Calcd for $C_5H_{10}OS_2$: C, 39.97; H, 6.71; S, 42.68. Found: C, 39.84; H, 6.77; S, 42.72.

Synthesis of *cis*-2-Phenyl-1,3-Dithiane 1-Oxide (4c). 2-Phenyl-2-trimethylsilyl-1,3-dithiane[17] (**10**, 10.0 g, 37 mmol) was dissolved in a mixture of 200 ml of acetonitrile and 200 ml of methanol. It was necessary to heat on the steam bath to effect complete dissolution. A solution of sodium periodate (8.4 g, 39 mmol) in 100 ml of water was added dropwise at ca. 40 °C over a 10-min period. Midway through the addition, a white precipitate ($NaIO_3$) formed. After stirring at room temperature for 40 h, the reaction mixture was filtered, and the white precipitate washed with chloroform. The chloroform washings were combined with the yellow filtrate and the solvent removed *in vacuo*. The residue was partitioned between 150 ml of brine and 150 ml of chloroform. The layers were separated, and the aqueous layer extracted with 100- and 50-ml portions of chloroform. The combined organic extracts were dried over sodium sulfate; evaporation of solvent yielded 7.75 g of yellow solid, which was chromatographed on a column containing 90 g of silica gel 60. Elution with *n*-pentane and carbon tetrachloride gave 2.46 g of starting material. Further elution with 5% 2-propanol/carbon tetrachloride afforded 727 mg of a cloudy, pale yellow oil believed to be polymeric propylene disulfide[18] on the basis of its NMR spectrum. Elution with 8% 2-propanol/carbon tetrachloride gave 3.46 g (44%, 58% based upon recovered starting material) of crude **4c** as a white solid, mp 154–157.5 °C. The NMR spectrum indicated the presence of approximately 2% *trans*-2-phenyl-1,3-dithiane 1-oxide. Recrystallization from dichloromethane–cyclohexane afforded 3.06 g (39%, 51% based on recovered starting material) of pure **4c**: mp 163.5–165.5 °C; ir (KBr) 3400, 3030, 2900, 1500, 1450, 1420, 1050, 1040 (s), 1005, 910, 760, and 695 cm^{-1}; NMR ($CDCl_3$) δ 2.2–3.4 (m, 5, ring H), 4.72 (s, 1, PhCH), and 7.2–7.5 ppm (broad s, 5 aromatic); mass spectrum (70 eV) *m/e* (rel intensity) 212 (77), 173 (14), 146 (14), 145 (24), 132 (40), 131 (79), 101 (40), and 100 (100).

Anal. Calcd for $C_{10}H_{12}OS_2$: C, 56.57; H, 5.70; S, 30.20. Found: C, 56.66; H, 5.78; S, 30.20.

The same product was obtained in 24% yield when the oxidation was carried out with *m*-chloroperoxybenzoic acid in ether at reflux.

Registry No.—**2b**, 6007-26-7; **2c**, 5425-44-5; **2d**, 5849-23-0; **3b**, 60349-75-9; **3c**, 60349-76-0; **3d**, 60349-77-1; **4b**, 60349-78-2; **4c**, 60349-79-3; **4d**, 60349-80-6; **5a**, 13411-42-2; **5b**, 60349-81-7; **6a**, 60349-82-8; **6b**, 60349-83-9; **7a**, 60349-84-0; **7b**, 60349-85-1; **8**, 13411-43-3; **9**, 60349-86-2; **10**, 13411-45-5; sodium metaperiodate, 7790-28-5; *m*-chloroperoxybenzoic acid, 937-14-4; 2-triphenylsilyl-2-deuterio-1,3-dithiane 1-oxide, 60349-87-3.

References and Notes

(1) (a) D. J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York, N.Y., 1965, pp 71–113; (b) T. Durst and R. Viau, *Intra-Sci. Chem. Rep.*, **7**, 63 (1973), and references cited therein.

(2) Review: L. Field, *Synthesis*, 101 (1972).

(3) (a) D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975). (b) For a study of the stereoselectivity of these reactions see E. L. Eliel, A. A. Hartman, and A. G. Abatjoglou, *J. Am. Chem. Soc.*, **96**, 1807 (1974).

(4) R. M. Carlson and P. M. Helquist, *J. Org. Chem.*, **33**, 2596 (1968).

(5) K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, 3151 (1971), and succeeding papers in this series.

(6) J. L. Hermann, J. E. Richman, P. J. Wepplo, and R. H. Schlessinger, *Tetrahedron Lett.*, 4707 (1973), and succeeding papers.

(7) (a) M. J. Cook and A. P. Tonge, *Tetrahedron Lett.*, 849 (1973); (b) L. Van Acker and M. Anteunis, *Ibid.*, *225* (1974); (c) M. J. Cook, and A. P. Tonge, *J. Chem. Soc., Perkin Trans. 2*, 767 (1974); (d) S. A. Kahn, J. B. Lambert, O. Hernandez, and F. A. Carey, *J. Am. Chem. Soc.*, **97**, 1468 (1975); (e) K. Bergesen, M. J. Cook, and A. P. Tonge, *Org. Magn. Reson.*, **6**, 127 (1974).

(8) (a) F. A. Carey, O. D. Dailey, Jr., and O. Hernandez, *J. Org. Chem.*, *following* paper in this issue. (b) F. A. Carey, O. Hernandez, I. F. Taylor, Jr., P. Smith, R. Maher, and R. F. Bryan, to be submitted.

(9) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **87**, 1109 (1965).

(10) *A value of 3.41 kcal/mol has been calculated*, using molecular mechanics, for the preference of a trimethylsilyl substituent for the equatorial position on cyclohexane. This is comparable to the experimentally determined value for a phenyl substituent, but significantly smaller than that of *tert*-butyl (>5 kcal/mol). R. J. Ouellette, D. Baron, J. Stolfo, A A. Rosenblum, and P. Weber, *Tetrahedron*, **28**, 2163 (1972). The conformational preferences for substituents at C(2) in 1,3-dithianes is comparable to those in cyclohexanes; see E. L. Eliel and R. O. Hutchins, *J. Am. Chem. Soc.*, **91**, 2703 (1969).

(11) To the best of our knowledge, the stereochemical course at carbon had not been determined for the base-catalyzed cleavage of trimethylsilyl groups from carbon prior to this work.

(12) F. A. Carey, O. Hernandez, I. Taylor, and R. Bryan, Abstracts, 167th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1974, No. PETR-008.

(13) (a) A. G. Brook and D. G. Anderson, *Can. J. Chem.*, **46**, 2115 (1968); (b) F. A. Carey and O. Hernandez, *J. Org. Chem.*, **38**, 2670 (1973); (c) E. Vedejs and M. Mullins, *Tetrahedron Lett.*, 2017 (1975).

(14) (a) H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1958 (1957). (b) Hydroxyl participation has been cited in the periodate and peroxy acid oxidation of hydroxyalkyl sulfides: C. A. Kingsbury, *J. Org. Chem.*, **37**, 102 (1972).

(15) D. Seebach, *Synthesis*, 17 (1969).

(16) We thank Professor Carlson for an authentic sample.

(17) (a) A. G. Brook, J. M. Duff, P. F. Jones, and M. R. Davis, *J. Am. Chem. Soc.*, **89**, 431 (1967); (b) E. J. Corey, D. Seebach, and R. Freedman, *Ibid.*, **89**, 434 (1967).

(18) See R. Kuhn and F. A. Neugebauer, *Chem. Ber.*, **94**, 2629 (1961), for the isolation of polymeric propylene disulfide during the hydrolysis of 1,3-dithiane 1-oxides.