Cyclodehydration and Selective Chlorination of *trans*-2-Hydroxycyclohexyl 2-Hydroxyethyl Sulfide with Triphenylphosphine and Tetrachloromethane

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Introduction

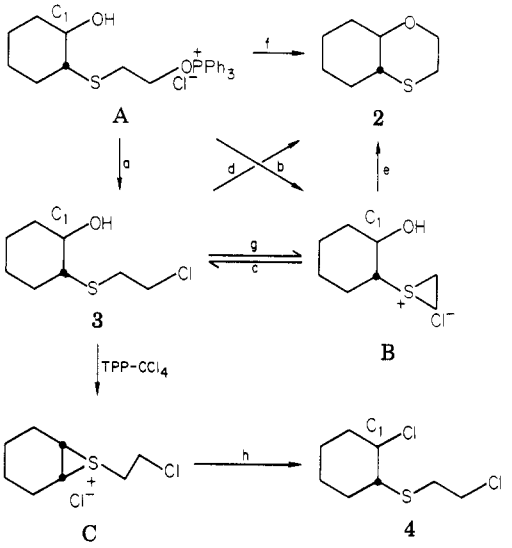
Reaction of primary and secondary alcohols with triphenylphosphine (TPP) and tetrahalomethane (e.g., CCl_4, CBr_4) has become a useful and convenient synthetic method for the conversion of alcohols to halides (e.g., RCl, RBr).[1-6] These displacement reactions of triphenylphosphine oxide (TPPO) by chloride ion are often characterized as mild and highly stereoselective, occurring with predominant inversion of stereochemistry at the carbinyl carbon.[7] Polar solvents (e.g., MeCN, Me_2SO) also allow for "nucleophile transposition" via the alkoxytriphenylphosphonium chloride intermediate with subsequent displacement of TPPO by other nucleophiles.[7b,d,e]

Recently, we reported that relatively simple diols undergo chlorination to the chlorohydrins and dichlorides as well as cyclodehydration to the cyclic ethers with TPP–CCl_4.[8] In this present paper, we describe the results of our efforts to prepare *trans*-1,4-oxathiadecalin (**2**), a *conformationally homogeneous* model for conformational studies of substituted oxathiadecalins[9] and precursor to a series of *trans*-tetrahydro-1,4-benzoxathiins possessing possible systemic fungicidal properties,[10] from *trans*-2-hydroxycyclohexyl 2-hydroxyethyl sulfide (**1**) and TPP–CCl_4.

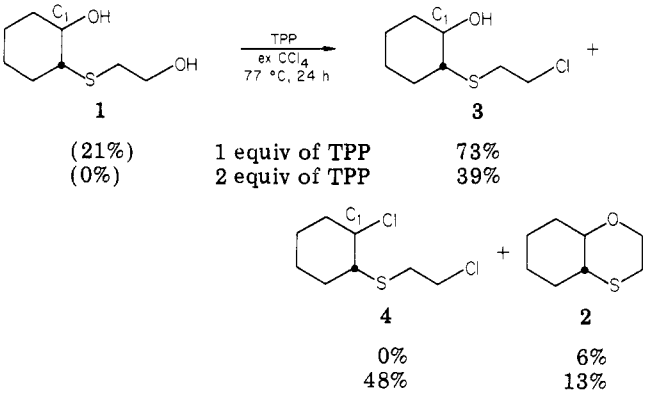
Results and Discussion

In an attempt to prepare *trans*-1,4-oxathiadecalin (**2**)[9] by the cyclodehydration of *trans*-2-hydroxycyclohexyl 2-hydroxyethyl sulfide (**1**)[11] with 1 equiv of TPP in CCl_4, we discovered a selective chlorination of the primary hydroxy group to afford *trans*-2-hydroxycyclohexyl 2-chloroethyl sulfide (**3**) in 73% yield (^1H and ^{13}C NMR analyses). Formation of chlorohydrin **3** may result from path a, chloride ion displacement[12] of TPPO from the intermediate hydroxy oxyphosphonium ion A (i.e., the Lee reaction[6e,13]), or path c, by chloride ion capture of thiiranium ion B formed by path b, neighboring-group displacement of TPPO by sulfenyl sulfur (Scheme I). Formation of oxathiane **2** (6%) in this reaction may come from path d, intramolecular cyclization of chlorohydrin **3**; e, capture of a thiiranium ion by the C_1 hydroxy group; f, collapse of the hydroxy oxyphosphonium ion A to oxathiane **2** and TPPO (Scheme I).

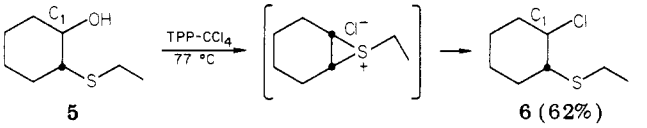
Scheme I



When diol **1** was allowed to react with 2 equiv of TPP in CCl_4, 39% chlorohydrin **3** and 13% oxathiadecalin **2** were formed as well as 48% *trans*-2-chloro-cyclohexyl 2-chloroethyl sufide (**4**). It is apparent that employing



1 or 2 equiv of TPP offers no synthetic advantage for preparing **2**. However, it does seem evident that formation of dichloride **4**, presumably from precursor **3**, must arise by path h, demonstrating the intermediacy and capture of thiiranium ion C, which allows for retention of stereochemistry at C_1 during the OH → Cl conversion. This conclusion is supported by the observation that *trans*-2-(ethylthio)cyclohexanol (**5**) in the presence of equimolar TPP in CCl_4 gives only *trans*-2-(ethylthio)cyclohexyl chloride (**6**;[14] 62% by ^1H and ^{13}C NMR). By contrast, the



(1) Brett, D.; Downie, I.M.; Lee, J. B.; Matough, M. F. S. *Chem. Ind. (London)* **1969**, 1017.
(2) Axelrod, E. H.; Milne, G. M.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139–41.
(3) Stork, G.; Jung, M. E.; Calvin, E.; Noel, Y. *J. Am. Chem. Soc.* **1974**, *96*, 3684.
(4) Georgoulis, C.; Ville, G. *Bull. Soc. Chim. Fr.* **1975**, 607.
(5) Goering, H. L.; Trenbeath, S. L. *J. Am. Chem. Soc.* **1976**, *98*, 5016.
(6) (a) Kocienski, P. J.; Cernigliaro, G.; Feldstein, G. *J. Org. Chem.* **1977**, *42*, 353. (b) Miller, R. D.; Schneider, M.; Dolce, D. L. *J. Am. Chem. Soc.* **1973**, *95*, 8468–8469. (c) Hunt, C. B.; MacSweeny, D. F.; Ramage, R. *Tetrahedron* **1971**, *27*, 1491. (d) Friederang, A. W.; Tarbell, D. S. *J. Org. Chem.* **1968**, *33*, 3797. (e) Appel, R. *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 801.
(7) (a) Jones, L. A.; Sumner, C. E., Jr.; Franzus, B.; Huang, T. t.-S. *J. Org. Chem.* **1978**, *43*, 2821–2827. (b) Slagle, J. D.; Huang, T. T.-S.; Franzus, B. *Ibid.* **1981**, *46*, 3526–3530. (c) Ramos, S.; Rosen, W. *Ibid.* **1981**, *46*, 3530–3533. (d) Brett, D.; Downie, I. M.; Lee, J. B. *Ibid.* **1967**, *32*, 855.
(8) Barry, C. N.; Evans, S. A., Jr. *J. Org. Chem.* **1981**, *46*, 3361–3364.
(9) Frieze, D. M.; Hughes, P. F.; Merrill, R. L.; Evans, S. A., Jr. *J. Org. Chem.* **1977**, *42*, 2206–2211.
(10) Rooney, R. P.; Dyer, J. C.; Evans, S. A., Jr. *Org. Magn. Reson.* **1981**, *16*, 266–271.
(11) Rooney, R. P.; Evans, S. A., Jr. *J. Org. Chem.* **1980**, *45*, 180–183.
(12) It is noteworthy that Slagle et al.[7b] and Ramos and Rosen[7c] have presented convincing evidence that the mechanism of the TPP–CCl_4 promoted chlorination of alcohols involves *ion-pair* clusters.
(13) For a recent review, see Appel, R.; Halstenberg, M. in "Organophosphorus Reagents in Organic Sythesis"; Cadogen, J. I. G., Ed.; Academic Press: New York, 1979; pp 378–424.

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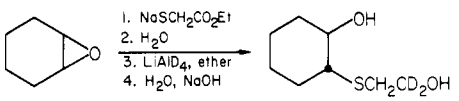
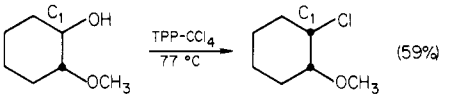
Scheme II



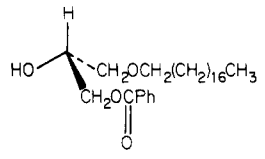
1-d_2

reaction of *trans*-2-methoxycyclohexanol (**7**) with TPP–CCl_4 gives exclusively *cis*-2-methoxycyclohexyl chloride (**8**)



7 **8**

from chloride ion displacement of TPPO with complete inversion of stereochemistry at C_1. This latter result is in harmony with the findings of Aneja et al.[16] where it was determined that chlorination of 3-benzoyl-1-octadecyl-*sn*-glycerol (**9**) with TPP–CCl_4 occurred with inversion of



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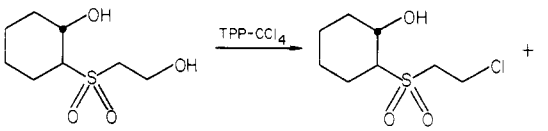
stereochemistry at the C_2-hydroxyl group. Apparently, neither neighboring-group interactions by the ethereal oxygen nor the ester carbonyl are influential determinants in the stereochemical outcome during the TPP–CCl_4 chlorination at C_2.

To gather insight as to how chlorohydrin **3** is formed, we prepared *trans*-2-hydroxycyclohexyl 2-hydroxyethyl-d_2 sulfide (1-d_2), employing the series of reactions shown in Scheme II, and examined the results of its reaction with TPP–CCl_4. If **3** is formed exclusively by reaction involving an intermediate episulfonium ion and Cl^-, one might expect a nearly equal distribution of the deuterium label on both methylene carbons of the 2-chloroethyl fragment of **3**: SCD_2CH_2Cl and SCH_2CD_2Cl. Alternatively, direct Cl^- displacement of TPPO would give **3** without intervention of a thiiranium ion; consequently, the deuterium label would be maintained in the SCH_2CD_2Cl portion of the chlorohydrin product. The ^1H NMR spectra in Figure 1 are of (i) diol **1**, (ii) 1-d_2, (iii) the reaction mixture consisting of 1-d_2 and **3**-d_2, and (iv) chlorohydrin **3**. The ^1H NMR chemical shifts at δ 2.92 and 3.62 with equivalent integrated intensities correspond to the methylene hydrogens in **3**-d_2 and it is clear that the deuterium label is nearly equally distributed between C_1 and C_2 of the chloroethyl group. We view this result as evidence for the intermediacy of thiiranium ion B with the suggestion that formation of chlorohydrin **3** from diol **1** and TPP–CCl_4 follows paths b and c rather than a.

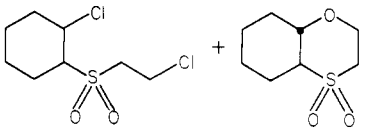
Our present findings for both 1-d_2 and **5** corroborate the results of Billington and Golding where it was determined that the reaction between $MeSCH_2{}^*CH_2OH$ and TPP–CCl_4 gave a 1:1 mixture of $MeS^*CH_2CH_2Cl$ and $MeSCH_2{}^*CH_2Cl$ ($^*CH_2$ is a ^{13}C enriched methylene carbon).[17]

Unfortunately, the relatively low concentrations of oxathiadecalin **2** formed in these reactions prohibited accurate ^1H and ^{13}C NMR analyses to determine the extent of deuterium incorporation at C_2 and C_3 in **2**. There are several mechanistic possibilities leading to formation of **2** from reaction of **1** with TPP–CCl_4. Heating *trans*-chlorohydrin **3** in CCl_4 solution for 72 h showed only starting material (^{13}C NMR). This result indicates that under the experimental conditions, direct conversion of **3** → **2** (path d) and/or equilibration of **3** and B then conversion to **2** (paths c, g, then e) are unlikely. This, of course, implies that formation of **2** comes largely from paths f and b, e.

Oxidation of sulfide **1** with 30% hydrogen peroxide in acetic acid gives *trans*-2-[(2-hydroxyethyl)sulfonyl]cyclohexanol (**11**). Treatment of **11** with 1.1 equiv of TPP in CCl_4 affords 54% of *trans*-2-[(2-chloroethyl)sulfonyl]-cyclohexanol (**12**), 30% of *trans*-1,4-oxathiadecalin (**13**), and presumably 8% of *cis*-2-[(2-chloroethyl)sulfonyl]-cyclohexanol (**14**; analytical HPLC analysis).



11 (8%) **12** (54%)



14 (8%) **13** (30%)

It is apparent that formation of sulfone **13** from **11** (or **12**) is considerably more favorable than formation of ether **2** from **1** (or **3**). Activation of the carbinyl carbon in the $CH_2OP^+Ph_3$ fragment toward nucleophilic displacement caused by the inductive effect of the sulfonyl group may be responsible. Formation of cis dichloride **14** is expected in the absence of neighboring-group participation by sulfenyl sulfur.

Experimental Section

Melting points were obtained with a Mel-Temp melting point apparatus with an open capillary tube, and they are uncorrected.

Proton magnetic resonance (^1H NMR) spectra were recorded on Varian Model XL-100-12 and Perkin-Elmer Model R24B NMR spectrometers. The ^{13}C NMR FT spectra were recorded on Varian Model XL-100-12 and Bruker Model WM-250 NMR spectrometers. All FT spectra were obtained at ambient temperature (approximately 30 °C) with noise decoupling. All ^1H and ^{13}C NMR chemical shifts of samples as 5–15 w/w % deuteriochloroform ($CDCl_3$) solutions are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si). The ^{13}C NMR spectra of the 1,2-disubstituted cyclohexanes reported here are shown in Table I.

Gas chromatographic analyses were obtained on a Hewlett-Packard Model 5754B research gas chromatograph with a stainless steel column [0.125 in. (i.d.) × 6 ft packed with 20% Carbowax 20M on Chromosorb W-HP-AW-DMCS, 100–120 mesh]. Preparative gas chromatographic separations were performed on a Gow-Mac Series 550 research gas chromatograph with an aluminum column [0.375 in. (i.d.) × 5.5 ft, packed with 15% Car-

(14) The stereochemistry of **6** was assigned by comparing its ^{13}C NMR shifts with those of **1**, **4**, and **5**. The ^1H NMR spectrum of **6** was also consistent with the assigned structure (e.g., $W_{1/2}$ for CHCl = 19 Hz, which is characteristic of an axial hydrogen).[15]

(15) (a) Eliel, E. L. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 761–774. (b) Franklin, N. C.; Feltkamp, H. *Ibid.* **1965**, *4*, 774–783.

(16) Aneja, R.; Davies, A. P.; Knaggs, J. A. *J. Chem. Soc., Chem. Commun.* **1973**, 110–111.

(17) Billington, D. C.; Golding, B. T. *J. Chem. Soc., Chem. Commun.* **1978**, 208.

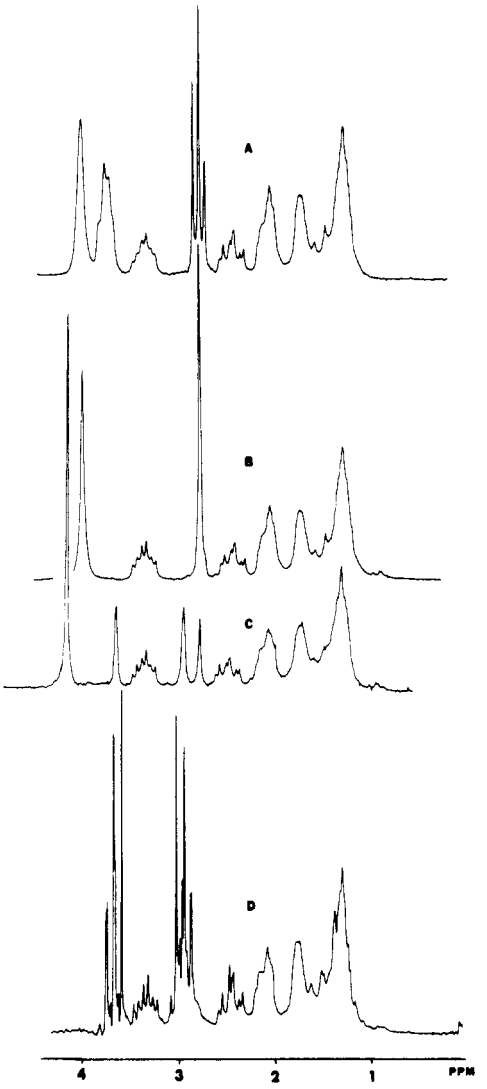


Figure 1. A, diol 1; B, 1-d_2; C, reaction mixture consisting of 1-d_2 and an equimolar mixture of the chlorohydrin 3-d_2 isomers having SCD_2CH_2Cl and SCH_2CD_2Cl groups; D, chlorohydrin 3 obtained by reaction of diol 1 with *p*-toluenesulfonyl chloride in pyridine solvent.

bowax 20M (0.1% KOH) on Chromosorb A (20–30 mesh)].

Preparative high-performance liquid chromatography (HPLC) was performed on a Waters Prep LC500A instrument with two Teflon columns [2.0 in. (i.d.) × 11.25 in. packed with silica (Waters Prepak-500/Silica)]. Analytical HPLC was performed in a Waters Model 6000A instrument with a stainless steel column [4.60 mm (i.d.) × 250 mm packed with silica (Waters Partisil-10)].

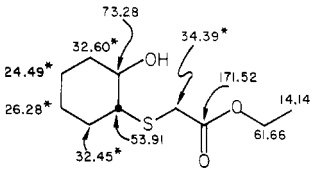
Triphenylphosphine was obtained from M & T Chemicals, Inc. (TPP-VWVAH-27k) and the Aldrich Chemical Co. Tetrachloromethane was dried and distilled over phosphorus pentoxide.[8] Cyclohexene oxide was obtained from Research Organic/Inorganic Chemical Corp. and the Aldrich Chemical Co. The preparations of *trans*-2-hydroxycyclohexyl 2-hydroxyethyl sulfide (1) and *trans*-2-chlorocyclohexyl 2-chloroethyl sulfide (4) have been previously reported;[11] however, an improved preparation for 1 is included here. *trans*-1,4-Oxathiadecalin (2) and *trans*-1,4-oxathiadecalin 4,4-dioxide (13) have been previously prepared.[9]

***trans*-2-(Ethylthio)cyclohexanol (5).** Sodium metal (1.5 g-atom, 0.065 mol) was dissolved in 200 mL of absolute ethanol under a nitrogen atmosphere. Ethanethiol (31 g, 37 mL, 0.50 mol) was added in one portion to the solution. Cyclohexene oxide (49.0 g, 0.50 mol) was added dropwise to this solution and the reaction mixture was refluxed overnight (ca. 18 h). The reaction mixture was cooled to ambient temperature, diluted with 400 mL of water, and extracted with diethyl ether (3 × 150 mL), and the ethereal solution was dried ($MgSO_4$). The ethereal solution was concentrated (rotary evaporator) to give an oil that was distilled to give 52.36 g (65%) of cyclohexanol 5: bp 93–100 °C (1 torr) [lit.[18] bp 117 °C (2 torr)]; ^1H NMR ($CDCl_3$) δ 1.28 (t, 3 H, J = 7 Hz, CH_3), 1.05–2.26 (m, 8 H, ring CH_2), 2.30 (m, 1 H, CHS), 2.60 (q, 2 H, J = 7 Hz, SCH_2), 2.98 (br s, 1 H, OH), 3.36 (m, 1 H, CHOH).

***cis*-2-Methoxy-1-chlorocyclohexane (8).** A solution containing a catalytic quantity of fluoroboric acid (0.5 mL) and a 3:1 ratio of anhydrous ether and dichloromethane (88 mL) was added to a solution of *cis*-2-chlorocyclohexanol[8] (15 mL, 20 g, 0.15 mol) in dichloromethane (400 mL). A solution of 0.5 M diazomethane[19] (400 mL) was added slowly with magnetic stirring. After the addition was completed, the mixture was allowed to stir at ambient temperature for 1 h and then filtered. The filtrate was washed with a 10% aqueous sodium bicarbonate solution (500 mL) and water (3 × 500 mL). The organic layer was dried (sodium sulfate) and concentrated to dryness (rotary evaporator) to afford an oil, which was distilled under reduced pressure to give an oil: bp 78–82 °C (20 torr). A homogeneous sample of chloro ether 8 was obtained by preparative GLC separation: ^1H NMR ($CDCl_3$) δ 1.01–2.60 (m, 8 H, ring CH_2), 3.37 (m, 1 H, $CHOCH_3$), 3.41 (s, 3 H, OCH_3), 4.40 (m, 1 H, CHCl).

***trans*-2-Hydroxycyclohexyl 2-Hydroxyethyl Sulfide (1).** Sodium metal (1.50 g-atom, 0.0652 mol) was dissolved in absolute ethanol (200 mL) under a nitrogen atmosphere and 2-mercaptoethanol (46.3 mL, 51.6 g, 0.660 mol) was added in one portion. Cyclohexene oxide (61.4 mL, 58.9 g, 0.600 mol) was added dropwise and the resulting mixture was refluxed overnight (approximately 18 h). Ethanol was removed (rotary evaporator), the residue diluted with water (150 mL), and the aqueous mixture saturated with sodium chloride. The aqueous mixture was extracted with diethyl ether (4 × 250 mL) and the ethereal solution was dried ($MgSO_4$) and concentrated to dryness (rotary evaporator). Diol 1 was obtained as a colorless solid (98.5 g, 93%) by distillation: bp 120–133 °C (0.5 torr); mp 45–48 °C (lit.[11] mp 45 °C); ^1H NMR ($CDCl_3$) δ 1.04–2.22 (m, 8 H, ring CH_2), 2.43 (m, 1 H, CHS), 2.82 (t, 2 H, J = 6 Hz, SCH_2), 3.36 (m, 1 H, CHOH), 3.74 (br s, 2 H, OH), 3.78 (t, 2 H, J = 6 Hz, CH_2OH).

***trans*-2-Hydroxycyclohexyl (Carboethoxy)methyl Sulfide (10).** Sodium metal (887 mg-atom, 39 mmol) was dissolved in absolute ethanol (100 mL), under a nitrogen atmosphere, and ethyl mercaptoacetate (38.6 g, 0.322 mol) was added in one portion. Cyclohexene oxide (27.8 g, 0.284 mol) was added dropwise and the resulting mixture was refluxed overnight (ca. 25 h). Ethanol was removed (rotary evaporator) and diethyl ether (100 mL) was added to the residue. The ethereal solution was washed with water (3 × 50 mL), dried (anhydrous magnesium sulfate), and concentrated (rotary evaporator and then high vacuum) to afford 58.73 g (99%) of a clear liquid: ^1H NMR ($CDCl_3$) δ 0.90–2.17 (m, 8 H, ring CH_2), 1.16 (t, 3 H, J = 7 Hz, OCH_2CH_3), 2.37 (m, 1 H, CH_a), 3.10 (m, 1 H, CHOH), 3.20–3.23 (br s, 2 H, SCH_2CO_2), 4.06 (q, 2 H, J = 7 Hz, OCH_2). The ^{13}C NMR shifts and assignments of crude 10 are shown below.

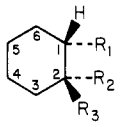


***trans*-Heptahydro-1,4-benzoxathian-2-one** Attempted purification of the hydroxy ethyl ester 10 by distillation [bp 110–155 °C (0.5 torr)] gave a green oil, which was dissolved in petroleum ether (boiling range, 60–90 °C) and crystallized (ice bath) to afford a colorless solid: mp 87–89 °C. Sublimation of this material at reduced pressure gave homogeneous material: mp 88.0–89.5 °C; ^1H NMR ($CDCl_3$) δ 1.08–2.42 (m, 8 H, CH_2), 3.00 (m, 1 H, $CHSCH_2$), 3.22 (d, 1 H, J = 14 Hz, $SCH_AH_BCO_2$), 3.70 (d, 1 H, J = 14 Hz, $SCH_AH_BCO_2$), 4.17 (m, 1 H, CHOCO). Anal.

(18) Shilov, G. I.; Zil'berman, E. N.; Pomerantseva, E. G. *J. Org. Chem. (USSR)* **1967**, *3*, 1694–6.

(19) Arndt, F. In "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 165.

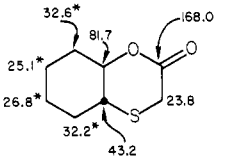
Table I. ^{13}C NMR Spectral Data of 1,2-Disubstituted Cyclohexanes[a]



compd	R_1	R_2	R_3	C1	C2	C3	C4	C5	C6	other carbons
1	OH	H	SCH_2CH_2OH	73.59	53.23	34.53	26.35*	26.55*	33.87	SCH_2CH_2OH, 33.50 SCH_2CH_2OH, 61.82
3	OH	H	SCH_2CH_2Cl	72.90	53.62	32.80*	26.15*	24.32*	33.12*	SCH_2CH_2Cl, 34.15 SCH_2CH_2Cl, 43.48
4	Cl	H	SCH_2CH_2Cl	63.99	51.17	31.46	23.38*	23.90*	34.48	SCH_2CH_2Cl, 34.48 SCH_2CH_2Cl, 43.27
5	OH	H	SCH_2CH_3	72.33	53.33	33.09*	24.07*	24.52*	33.93*	SCH_2CH_3, 26.38 SCH_2CH_3, 15.47
7	OH	H	OCH_3	73.67	85.08	28.63	24.19*	24.35*	32.51	OCH_3, 56.54
8	Cl	OCH_3	H	61.09	79.71	26.86	22.45*	21.43*	32.24	OCH_3, 56.10
11	OH	H	$SO_2CH_2CH_2OH$	69.70	67.70	24.58	23.32*	23.99	35.27	$SO_2CH_2CH_2OH$, 57.11 $SO_2CH_2CH_2OH$, 56.26
12	OH	H	$SO_2CH_2CH_2Cl$	69.45	67.58	24.52	23.07*	23.87*	35.25	$SO_2CH_2CH_2Cl$, 56.91 $SO_2CH_2CH_2Cl$, 35.76

[a] Experimental details of the ^{13}C NMR data collection process are given in the Experimental Section. Carbons whose chemical shifts cannot be assigned with a high level of certainty and may be interchangeable are labeled with an asterisk.

Calcd for $C_8H_{12}O_2S$: C, 55.79; H, 7.02. Found: C, 55.73; H, 7.04. On the basis of the ^1H and ^{13}C NMR chemical shifts we have assigned the structure of this new substance as that shown below.



***trans*-2-Hydroxycyclohexyl 2-Hydroxyethyl-d_2 Sulfide (1-d_2).** A solution of hydroxy ester **10** (8.00 g, 0.039 mol) in dry tetrahydrofuran (100 mL) was added dropwise to a suspension of lithium aluminum deuteride (1.00 g, 0.024 mol) in dry tetrahydrofuran (100 mL) under a nitrogen atmosphere at 0–5 °C (ice bath). The resulting mixture was stirred at ambient temperature for 1 h and then heated at reflux for 1 h. The mixture was cooled to ambient temperature, treated with water (1 mL), 15% aqueous sodium hydroxide (1 mL), and water (3 mL), and filtered. The filtrate was diluted with diethyl ether (200 mL) and washed with water (500 mL). The organic layer was dried (sodium carbonate) and concentrated to dryness (rotary evaporator). The crude diol was purified by preparative HPLC (solvent system: 65% ethyl acetate–35% hexanes): mp 44–46 °C; ^1H NMR ($CDCl_3$) δ 1.02–2.22 (m, 8 H, ring CH_2), 2.45 (m, 1 H, CHS), 2.80 (s, 2 H, SCH_2), 3.37 (m, 1 H, CHOH), 3.74 (s, 1 H, OH). The ^1H NMR spectrum of 1-d_2 is also included in Figure 1 for comparison with 1.

***trans*-2-Hydroxycyclohexyl 2-Chloroethyl Sulfide (3).** A solution of *p*-toluenesulfonyl chloride (41.94 g, 0.22 mol) in dry pyridine (95 mL) was added to a cold solution (0–5 °C; ice bath) of diol **1** (35.24 g, 0.20 mol) in 295 mL of pyridine with cooling. The mixture was stored at 0 °C overnight (approximately 24 h) and then poured into an ice-cold mixture of 10% aqueous hydrochloric acid (1.5 L) and ether (500 mL). The resulting mixture was shaken in a separatory funnel, the ethereal layer removed, and the aqueous phase extracted with ether (500 mL). The combined ethereal portions were dried ($MgSO_4$, K_2CO_3), filtered, and concentrated to yield light-purple crystals (15.28 g, 39%): mp 46–51 °C; ^1H NMR ($CDCl_3$) δ 1.04–2.29 [m, 8 H, $(CH_2)_4$], 2.45 (m, 1 H, CHS), 2.94 (m, 2 H, SCH_2), 2.97 (s, 1 H, OH), 3.32 (m, 1 H, CHOH), 3.66 (m, 2 H, CH_2Cl). Anal. Calcd for $C_8H_{15}SOCl$: C, 49.35; H, 7.76. Found: C, 49.20; H, 7.88.

***trans*-2-[(2-Hydroxyethyl)sulfonyl]cyclohexanol (11).** A solution containing 30% hydrogen peroxide (14.0 g, 0.12 mol) and 40 mL of glacial acetic acid was added to a solution of 2-hydroxycyclohexyl 2-hydroxyethyl sulfide (8.80 g, 0.05 mol) in glacial acetic acid (40 mL). The resulting solution was stirred overnight (ca. 12 h) and finally concentrated to a yellow oil by distillation under reduced pressure. The oil was diluted with ethyl acetate and subjected to preparative HPLC analysis [solvent system: 10% hexanes, 90% ethyl acetate; sulfone **11** was eluted over a broad range, centered around 3 column volumes]. The first fraction containing sulfone **11** was impure and was not used in the yield calculation. The remaining fractions were concentrated (rotary evaporator) to afford 6.3 g (31%) of crude sulfone **11**: mp 57–62 °C. A sample of this material was recrystallized (hexanes–ethyl acetate): mp 66.5–67.0 °C. Anal. Calcd for $C_8H_{16}SO_4$: C, 46.14; H, 7.74. Found: C, 46.13; H, 7.79.

***trans*-2-[(Chloroethyl)sulfonyl]cyclohexanol (12).** A solution of chlorohydrin **2** (7.79 g, 40 mmol) in 32 mL of glacial acetic acid was added to a mixture of 30% hydrogen peroxide (11.20 g, 99 mmol) in 30 mL of glacial acetic acid. The resulting solution was stirred at ambient temperature (ca. 22 °C) for 24 h and concentrated by distillation under reduced pressure to give an oil. The residue was dissolved in 50 mL of dichloromethane, washed with 10% aqueous sodium bicarbonate 2 × 25 mL), dried (anhydrous K_2CO_3), and filtered. The dichloromethane solution was concentrated (rotary evaporator) to give an oil. ^{13}C NMR analysis of the oil indicated the presence of sulfone **12** as well as the diastereoisomeric sulfoxides. Separation of this three-component mixture was accomplished by use of preparative HPLC (100% ethyl acetate; sulfone **12** eluted in 1.3 column volumes) to afford 2.70 g (30%) of *trans*-chlorohydrin **12**. Recrystallization of sulfone **12** from hexanes–ethyl acetate gave homogeneous material: mp 75–76 °C. Anal. Calcd for $C_8H_{15}SO_3Cl$: C, 42.38; H, 6.67. Found: C, 42.11; H, 6.86.

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Registry No. 1, 71989-47-4; 1-d_2, 82622-20-6; **2**, 62015-71-8; **3**, 82622-15-9; **4**, 71989-48-5; **5**, 58198-41-7; **6**, 20556-30-3; **7**, 7429-40-5; **8**, 51332-49-1; **10**, 82622-17-1; **11**, 82338-34-9; **12**, 82622-18-2; **13**, 62015-76-3; **14**, 82622-19-3; *trans*-heptahydro-1,4-benzoxathian-2-one, 82622-16-0; cyclohexene oxide, 286-20-4; ethanethiol, 75-08-1; *cis*-2-chlorocyclohexanol, 17002-09-4; 2-mercaptoethanol, 60-24-2; ethyl mercaptoacetate, 623-51-8; triphenylphosphine, 603-35-0; tetrachloromethane, 56-23-5.