Sulfinic Acids and Related Compounds. 18. Synthesis and Properties of Derivatives of 2-Mercaptoethanesulfinic Acid[1]

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Use of thiirane 1,1-dioxide (**2**) affords a useful synthesis of ethanesulfinates with the following functions in the 2-position: thiol, disulfide, trisulfide, thiosulfate, thiosulfonate, and phosphorothioate. The sulfinic esters generally were rather stable, but in several instances the salts gave unexpected results because of involvement of the sulfinate function with the sulfur atom of the 2-substituent; for example, the thiosulfonate *p*-$MeC_6H_4SO_2S(CH_2)_2SO_2Na$ (**17**) in water quickly liberated sodium *p*-toluenesulfinate (**15**) and gave an insoluble polymer shown by mass spectra to have the structure *p*-$MeC_6H_4SO_2[S(CH_2)_2SO_2]_nS(CH_2)_2SO_2Na$ (**26**). Aryl disulfides of the structure $ArSS(CH_2)_2S(O)OMe$ were reasonably stable thermally but were quite sensitive to light.

Derivatives of 4-mercaptobutanesulfinic acid (**1**) have been studied at length.[2] One motivation has been the development of agents that will protect animals against otherwise lethal effects of ionizing radiation; these radioprotective agents have been of particular interest since they are atypical in containing no nitrogen.[3,4] Another

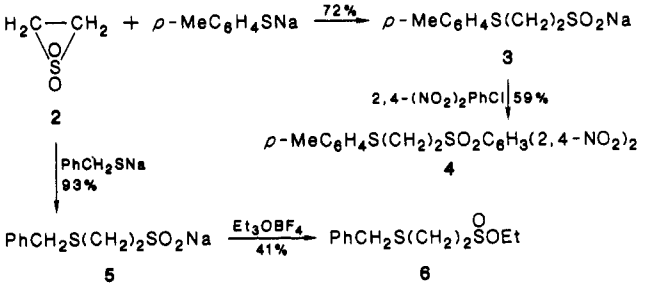
$$HS(CH_2)_4SO_2H$$
1

important motivation, however, has been interest in interactions of the SO_2H and SH functions and their derivatives. The present paper reports the synthesis and properties of counterparts of the butanesulfinic series where the sulfinic acid function is separated from divalent sulfur functions by two carbon atoms rather than four. Entry into this two-carbon series was afforded by cleavage reactions of thiirane 1,1-dioxide (**2**). These new cleavages complement earlier ones studied by Vilsmaier and Becker that involved RS^-, S^{2-}, and thioamides.[5] The chemistry of thiirane 1,1-dioxides has been reviewed recently.[6]

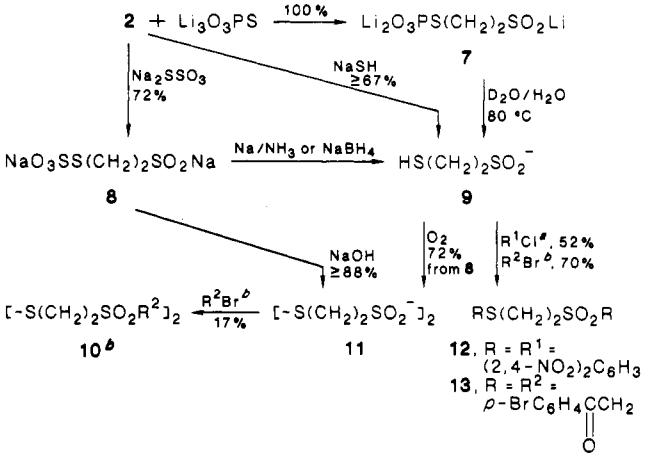
Results and Discussion

Reactions of the Dioxide 2 with Thiolate Salts. In contrast to carbanions and alkali, which attack **2** at the sulfur atom, the S-nucleophiles studied by Vilsmaier and Becker attacked a carbon atom specifically and led to 2-thio-substituted ethanesulfinates.[5] As a basis for later work, we recently showed that a thiolate ion would attack a camphor-based thiirane 1,1-dioxide at the CH_2 of the thiirane ring rather than at the CH, to give an ethanesulfinate;[1a] however, the chemistry of the two-carbon series seemed better developed by concentrating initially on the unsubstituted dioxide **2**.

Scheme I



Scheme II[a]



[a] R^1 = 2,4-$(NO_2)_2C_6H_3$. [b] *p*-$BrC_6H_4C(O)CH_2$.

We first confirmed the conclusions of Vilsmaier and Becker by reaction of **2** with sodium *p*-toluenethiolate to give the sulfinate **3**, which, as expected of a sulfinate, could be converted for further confirmation to the sulfone **4** (Scheme I). Similarly, **2** was converted to the benzyl counterpart **5**, which was desired for possible debenzylation to the thiol (vide infra); since the salt **5** was difficult to purify, it was converted to the ethyl ester **6**.

Reaction of the Dioxide 2 with Thiophosphate and Thiosulfate Ions. Ring-cleavage reactions of **2** offered attractive possibilities for introducing a phosphorothioate or thiosulfate (Bunte salt) function at the 2-position of an ethanesulfinate, to give **7** and **8**, respectively (Scheme II).

(1) (a) Part 17: Lenhert, P. G.; Morales, A. E.; Harmon, J. P.; Field, L. *Acta Crystallogr., Sect. B: Struct. Sci.*, in press. (b) Abstracted from part of the Ph.D. dissertation of J.P.H., Vanderbilt University, May 1985, which may be consulted for further details. (c) This investigation was supported by the U.S. Army Medical Research and Development Command, Department of the Army, under Research Contracts No. DAMD17-79-C-9039 and No. DAMD17-85-C-5181; this paper has been designated as Contribution No. 1790 to the U.S. Army Drug Development Program. (d) We thank J. H. Hillhouse and J. R. Piper for helpful suggestions and B. J. Sweetman for mass spectra.

(2) (a) See previous papers in the present series and also in the series entitled "Organic Disulfides and Related Substances."[2b] (b) Part 46: Chandra, R.; Field, L. *J. Org. Chem.* **1986**, *51*, 1844.

(3) For reviews of much of our earlier work, see: (a) Klayman, D. L.; Copeland, E. S. In *Drug Design*; Ariëns, E. J., Ed.; Academic: New York, 1975; Vol. 6, Chapter 2. (b) Klayman, D. L.; Copeland, E. S. In *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed.; Grayson, M., Ed.; Wiley: New York, 1982; Vol. 19, pp 801–832. (c) Foye, W. O. In *Burger's Medicinal Chemistry*, 4th ed.; Wolff, M. E., Ed.; Wiley: New York, 1981; Part III, Chapter 37. (d) Sweeney, T. R. *A Survey of Compounds from the Antiradiation Drug Development Program of the U.S. Army Medical Research and Development Command*; Walter Reed Army Institute of Research: Washington, D.C., 1979; see especially pp 5, 769–770.

(4) Bowman, G T.; Clement, J. J.; Davidson, D. E., Jr.; Eswarakrishnan, V.; Field, L.; Hoch, J. M.; Musallam, H. A.; Pick, R. O.; Ravichandran, R.; Srivastava, P. K. *Chem.-Biol. Interact.* **1986**, *57*, 161.

(5) Vilsmaier, E.; Becker, G. *Synthesis* **1975**, 55.

(6) Zoller, U. In *Small Ring Heterocycles—Part 1*; Hassner, A., Ed.; Wiley: New York, 1983; pp 499–535.

0022-3263/86/1951-5235$01.50/0

Since the classes of aminoalkyl phosphorothioates and thiosulfates include promising antiradiation drugs,[3] it was desirable to determine whether ethanesulfinic acids containing these functions might be useful nonnitrogen radioprotective counterparts of **1**. Furthermore, the phosphorothioate and thiosulfate functions are chemically interesting in being potentially convertible to a variety of other sulfur functions.

For the synthesis of a phosphorothioate (cf. **7**, Scheme II), commercial trisodium phosphorothioate was found to be unsatisfactory, as was material prepared by standard procedures.[7] On the other hand, trilithium phosphorothioate gave **7** in good yield when prepared according to Åkerfeldt (Scheme II).[8]

The Bunte salt **8** was prepared without incident (Scheme II). It was considerably more resistant to hydrolysis than the phosphorothioate **7** (cf. the Experimental Section).

2-Mercaptoethanesulfinates as Synthons. Interest in **9** was prompted by antiradiation activity of the salt of **1**,[4] as well as by the promise of **9** for synthesis. Reduction of the *S*-benzyl derivative **5** by sodium or lithium in liquid ammonia gave very little **9** (with sodium, only 13% by Ellman analysis),[9] however, and sodium hydrosulfide with **2** gave a maximum yield of only 67% by Ellman analysis (Scheme II).[9]

Acidic or basic hydrolysis of the phosphorothioate **7** in H_2O also was preparatively unpromising. Hydrolysis of **7** in (neutral) D_2O was about half complete at 25 °C in 3 days and at 55 °C in about 3 h (considerably more rapidly than in H_2O). Despite indications that inorganic products might precipitate cleanly, however, and although hydrolysis of **7** in D_2O at 80 °C did indeed give **9** [NMR, conversion to the 2,4-dinitrophenyl sulfone (**12**, 52%)], NMR indicated 5–10% content of the disulfide **11**, and elemental analysis indicated presence of ca. 0.5 molar proportion of Li_2HPO_4.

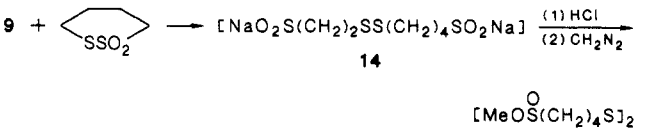
Basic hydrolysis of the Bunte salt **8** led principally to the disulfide **11**, probably because of thioalkylation of the thiolate salt of **9** by **8** (eq 1). An effort was made to stop this hydrolysis at optimum formation of the thiol salt **9**, by using Ellman analysis,[9] but the maximum yield was only 57%.

$$\underset{\mathbf{8}}{NaO_3SS(CH_2)_2SO_2Na} + \underset{\mathbf{9}}{NaS(CH_2)_2SO_2Na} \rightarrow Na_2SO_3 + \underset{\mathbf{11}}{[-S(CH_2)_2SO_2Na]_2} \quad (1)$$

On the other hand, **8** could be reduced to **9** (Scheme II). Ellman analysis indicated that sodium in liquid ammonia reduced **8** quantitatively. Sodium borohydride also was effective, and reduction to **9** followed by derivatization with *p*-bromophenacyl bromide gave **13** in 70% yield from **9** (this yield may have been reduced by loss of **9** to form the disulfide **11** via eq 1; on the other hand, part of the **9** might have originated by a neighboring-group expulsion of the thiol **9** *from* the disulfide **11**).

The disulfide **11** from the thiol **9** is of interest as an antiradiation drug, since it is a two-carbon counterpart of the radioprotective disulfide from **1**.[4] Treatment of the Bunte salt **8** with $NaBH_4$, followed by air oxidation of the thiol **9**, gave **11** (part of the **11** may have resulted from the thioalkylation of **9** as shown in eq 1). The identity of the **11** was confirmed by conversion to the sulfone **10**. Another counterpart, the unsymmetrical disulfide–sulfinate **14** shown in Scheme III, could not be obtained by reducing the Bunte salt **8** to the thiol **9** with either $NaBH_4$ or Na/NH_3, followed by reaction with 1,2-dithiane 1,1-dioxide. After acidification and esterification with diazomethane (Scheme III), only the ester shown could be isolated (along with 1,2-dithiane 1,1-dioxide). The apparent lack of any diester corresponding to **14** seems likely to be a result of facile disproportionation of **14** facilitated by neighboring-group attack(s) of the sulfinate group(s) on the SS bond.

Scheme III



Salts and Esters of 2-(*p*-Tolylsulfonylthio)ethanesulfinic Acid. The thiosulfonate **17** seemed likely to be an effective thioalkylating agent that would introduce the $S(CH_2)_2SO_2Na$ moiety. Hence it was a particularly attractive target for synthesis because of this potential as a synthon, as well as for potential antiradiation activity. As Scheme IV shows, **17** was prepared by converting sodium *p*-toluenesulfinate (**15**) to the thiosulfonate **16**, which then was used to cleave thiirane 1,1-dioxide (**2**) in methanol; evaporation of the methanol under reduced pressure left the salt **17**.

To our surprise, dissolution of **17** in D_2O quickly led to much precipitate. NMR spectra showed that the residual solute was largely the sulfinate **15** (Scheme V; confirmed by conversion to **27**). We concluded that Scheme V explained the results, i.e., that neighboring-group attack in **17** expels the sulfinate ion **15**. The thiosultone **25** formed then polymerizes to give **26** (with nucleophilic initiation, mainly by **15**). The polymer **26** had appropriate IR and NMR spectra and showed mass peaks for **17** and for each of the peaks of **26** with n = 0–5. In methanol-d_4, the **17** was more stable than in water. Thus, with 1.0 equiv of **16** and 1.4 equiv of **2** in MeOH-d_4, **17** began to appear in 1.5 h (by NMR, from the CH_3 peak at δ 2.43 of **17**; the CH_3 peaks of **15** and **16** are at ca. δ 2.36). In 1.5 h more, the sulfinate **15** began to appear (doublets at δ 7.54 and 7.31; confirmed by peak enhancement; the aryl peaks of **15**–**17** all are distinguishable); however, the **15** increased only to ca. 30% after ca. 48 h. A similar result occurred at 0 °C, although more slowly. After trial of several solvents, we conclude that **17** is best prepared by reaction of **2** and **16** in a minimum of methanol for a day (the best compromise between the time for reaction of **2** with **16** and that at which the loss of **17** becomes significant), followed by precipitation with ether.

Since **17** is so unstable, use of an ester seemed a better approach to the synthesis of unsymmetrical disulfides, such as **20**–**22**, which were desired as analogues of promising antiradiation agents.[4] Esterification of **17** with triethyloxonium tetrafluoroborate gave the ethyl ester **18** (Scheme IV). However, a suspicion that residual fluoride might have increased the toxicity of a similarly prepared ethyl sulfinate (**28**, R = Et)[4] led us to work with the methyl ester **19** instead. The methyl ester was prepared by the route of Scheme IV, which does not seem to have a toxic liability.[4] The ethyl and methyl esters **18** and **19** proved to be reasonably stable in solution (see the Experimental Section).

Preparation of Di- and Trisulfides 20–24. Reaction of **19** with *p*-methylthiophenol gave the unsymmetrical

(7) (a) Piper, J. R.; Johnston, T. P. *J. Org. Chem.* **1967**, *32*, 1261. (b) Åkerfeldt, S. *Acta Chem. Scand.* **1960**, *14*, 1980.

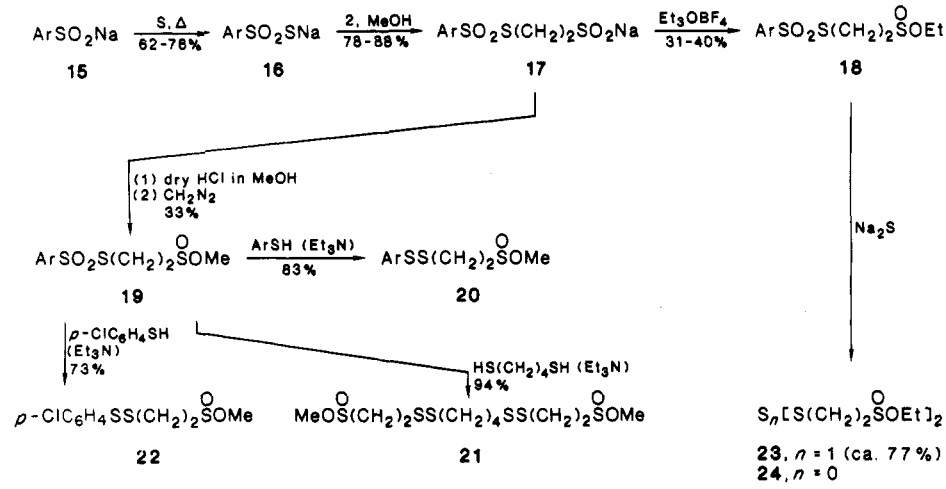
(8) Åkerfeldt, S. *Acta Chem. Scand.* **1962**, *16*, 1897. We are indebted to J. R. Piper for suggesting the use of the lithium salt.

(9) Ellman, G. L. *Arch. Biochem. Biophys.* **1959**, *82*, 70.

(10) Srivastava, P. K.; Field, L. *J. Chem. Eng. Data* **1986**, *31*, 252.

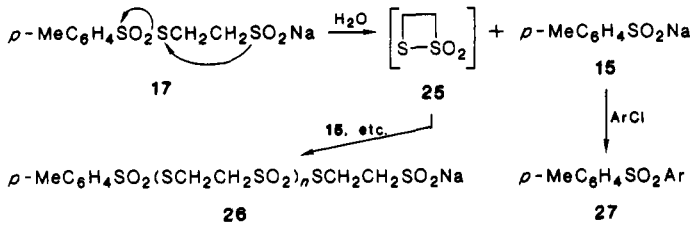
(11) Field, L.; Parsons, T. F.; Pearson, D. E. *J. Org. Chem.* **1966**, *31*, 3550.

Scheme IV[a]



[a] Ar = p-MeC_6H_4.

Scheme V[a]



[a] Ar = 2,4-$(NO_2)_2C_6H_3$. A reviewer kindly suggested the following sulfinate exchange as a plausible alternative to Scheme V (cf. also Field, L.; Lacefield, W. B. *J. Org. Chem.* **1966**, *31*, 599): 17 + 17 $\xrightarrow{-15}$ p-$MeC_6H_4SO_2[S(CH_2)_2SO_2]_2^-$ $\xrightarrow{+17,\ -15}$ **26**.

disulfide **20** (Scheme IV), a two-methylene counterpart of radioprotective **29**.[4] The p-chlorophenyl disulfide **22** was prepared to compare effects of Cl and CH_3, and **21** was prepared because of the radioprotectivity of **30**.[4] All three

$[RO_2S(CH_2)_4S]_2S$ (**28**, R = Na, Me, Et) p-$MeC_6H_4SS(CH_2)_4SO_2Na$ (**29**)

$[NaO_2S(CH_2)_4SS(CH_2)_2]_2$ (**30**)

disulfides **20–22** were stable at ambient conditions, at least for a week, and in $CDCl_3$, **21** and **22** were stable for a week even at 50 °C (ca. 10% of **20** decomposed); **21** and **22** thus seemed roughly comparable in thermal stability, with **20** being somewhat less stable. Under UV light, **20** and **22** began to disproportionate in 5 min. Since the alkylene disulfide **21** was unchanged after an hour, **20** and **22** thus seem notably more susceptible to homolysis. Such behavior has been noted before for disulfides containing the ArSS moiety (cf. ref 10 and 11) and indicates the desirability of protecting such disulfides from strong light.

Trisulfide-disulfinates **28** are promisingly radioprotective.[4] A small-scale reaction gave the two-methylene counterpart **23** reasonably pure and in good yield (Scheme IV), but a larger scale led only to a mixture of **23** and **24** (respective yields of 23% and 44%), and neither gave a good analysis.[1b] Since **23** was not readily converted to **24**,[1b] the **24** must have originated in the reaction itself, probably through a neighboring-group mechanism like that invoked for a very similar reaction of a benzylsulfinylethyl trisulfide.[2b]

Experimental Section

Melting points were determined by using a Thomas-Hoover stirred-liquid apparatus and are corrected. ^1H NMR spectra, reported in parts per million (δ), were obtained with a JEOL Model JNM-MH-100 (100 MHz) or JEOL-FX-90Q (90 MHz) spectrometer with Me_4Si as an internal standard in organic solvents or in D_2O with $Me_3Si(CH_2)_3SO_3Na$ (DSS). ^{13}C NMR spectra were obtained at 22.5 MHz with the JEOL-FX-90Q spectrometer. ^1H and ^{13}C NMR spectra were consistent with values reported.[12] IR spectra were obtained with a Perkin-Elmer Model 727 spectrometer; bands not shown as strong (s) or weak (w) were medium intensity (br = broad). Mass spectra (FAB) were obtained with use of a VG 70-250 GC-MS instrument equipped with a VG 11/250 data system and capability for fast atom bombardment (FAB) by Prof. B. J. Sweetman (Department of Pharmacology, Vanderbilt University; funds were provided by the NIH, Division of Research Resources Grant No. RR 01688). Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Solvent was removed by using a Büchi rotary-flask evaporator and then an oil pump. Analytical TLC was performed on silica gel (Eastman Chromagram, catalog no. 13181) with visualization by UV or I_2 vapor, and preparative TLC was done on Whatman PLK5F or PK6F silica gel plates. Flash chromatography was performed essentially as described by Still et al. with use of Baker 7024 silica gel (40-μm average particle size).[13]

For our preparation of thiirane 1,1-dioxide (**2**), the reaction of CH_2N_2, $MeSO_2Cl$, and Et_3N[14] gave **2** containing impurities that were difficult to remove because of the instability of **2**. Preparation according to Hesse et al. succeeded well;[15] the **2** thus obtained had an appropriate IR spectrum[15] and was used without purification: ^1H NMR ($CDCl_3$) δ 3.19 (s); ^{13}C NMR ($CDCl_3$) δ 31.6. All other chemicals mentioned were commercial unless otherwise stated.

Sodium 2-(p-Tolylthio)ethanesulfinate (3). Sodium methoxide (16.1 mmol) in MeOH (10 mL) was added dropwise with stirring to p-thiocresol (2.02 g, 16.3 mmol) and the dioxide **2** (1.50 g, 16.3 mmol) in 50 mL of MeOH at 25 °C over 5 min. After 25 min at 0 °C (owing to slight warming of the solution), the mixture was stirred for 16 h at 25 °C under Ar. After concentration under reduced pressure, Et_2O was added to the residue. Solid was separated by filtration and washed with Et_2O (3 × 50 mL) to give 2.80 g (73%) of **3**: IR (KBr) 2920 (w), 1600 (w), 1490, 1080 (w), 1000 (s), 930 (w), 790 cm^{-1}; ^1H NMR (D_2O) δ 7.35 (d, 2 H), 7.19 (d, 2 H), 3.16 (A_2B_2, 2 H), 2.59 (A_2B_2, 2 H), 2.32 (s, 3 H).

For further confirmation of the identity of the sulfinate salt **3**, a solution of **3** (1.00 g, 4.20 mmol) and 2,4-dinitrochlorobenzene (0.77 g, 3.80 mmol) in absolute EtOH (50 mL) was stirred at reflux for 21 h. The precipitate was isolated and washed with cold H_2O (2 × 25 mL), hot H_2O (2 × 25 mL), and Et_2O (3 × 15 mL) to give 0.85 g (58%) of yellow 2,4-dinitrophenyl 2-(p-tolylthio)ethyl

(12) Freeman, F.; Angeletakis, C. N.; Maricich, T. *Org. Magn. Reson.* **1981**, *17*, 53.
(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(14) Opitz, G.; Fischer, K. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 70.
(15) Hesse, G.; Reichold, E.; Majmudar, S. *Chem. Ber.* **1957**, *90*, 2106.

sulfone (4), which was recrystallized from Me_2CO–benzene: mp 120.5–124 °C; IR (KBr) 3100, 1600, 1560 (s), 1540 (s), 1495, 1420, 1350 (s), 1325 (s), 1210, 1155 (s), 1120, 1100, 1015, 945 (w), 910, 850 (w), 830, 800, 780, 750, 715; ^1H NMR (Me_2CO-d_6) δ 8.92–8.53 (m, 3 H), 7.36 (d, 2 H), 7.20 (d, 2 H), 4.02–3.87 (m, 2 H), 3.45–3.25 (m, 2 H), 2.34 (s, 3 H).

Anal. Calcd for $C_{15}H_{14}N_2O_6S_2$: C, 47.11; H, 3.69; S, 16.77. Found: C, 47.38; H, 3.88; S, 16.99.

Ethyl 2-(Benzylthio)ethanesulfinate (6). As with 3, NaOMe (21.7 mmol) in MeOH (15 mL) was added to 2 (2.00 g, 21.7 mmol) and phenylmethanethiol (2.70 g, 21.7 mmol) in MeOH (40 mL). A little was added at 25 °C, but when slight warming occurred, most was added at 0 °C over 5 min. After stirring periods and isolation as with 3, 3.5 g (68%) of **sodium 2-(benzylthio)-ethanesulfinate (5)** was obtained: IR (KBr) 3400 (br, H_2O), 3070, 3020, 2920, 1600 (H_2O), 1490, 1450, 1410, 1235, 1190, 1005 (s), 760, 690 cm^{-1}; ^1H NMR (D_2O) δ 7.45 (s, 5 H), 3.85 (s, 2 H), 2.68 (t, 2 H), 2.63 (t, 2 H). For conversion of the salt 5 to the ester 6, $Et_3O^+BF_4^-$ (2.81 g, 14.8 mmol; Fluka) in CH_2Cl_2 (15 mL) was added over 10 min to a suspension of 5 (3.20 g, 13.4 mmol) in 40 mL of CH_2Cl_2 stirred at 0 °C. After being stirred for 30 min at 0 °C, the mixture was washed with saturated aqueous NaCl (3 × 50 mL) and cold H_2O (1 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo to give 2.25 g (69%) of the crude ester 6 as a mobile yellow oil. IR spectra and TLC indicated the presence of impurities (mostly the sulfonate ester); however, preparative TLC (R_f 0.32, 15% EtOAc in hexane) of 240 mg of the crude ester gave 130 mg (37% from 5) of pure 6: n^{23}_D 1.5540; IR (neat) 3070, 3040, 2990, 2930, 1600 (w), 1490, 1450, 1420, 1385, 1370 (w), 1280, 1240, 1200, 1120 (s), 1070, 1010 (s), 880 (s), 760, 700 (s); ^1H NMR ($CDCl_3$) δ 7.43 (s, 5 H), 4.11 (m, 2 H), 3.82 (s, 2 H), 3.04–2.64 (m, 4 H), 1.33 (t, 3 H); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) δ 137.57 (s), 129.82 (d), 127.17 (d), 64.87 (t), 56.79 (t), 36.53 (t), 22.88 (t), 15.79 (q); MS (CI), m/z 199 (M – EtO).

Anal. Calcd for $C_{11}H_{16}O_2S_2$: C, 54.06; H, 6.60; S, 26.24. Found: C, 53.81; H, 6.72; S, 26.14.

On a larger scale, a similar preparation gave crude 5 in 93% yield; reaction of 5 with $Et_3O^+BF_4^-$, followed by flash chromatography, led to 6 in 41% yield from 5.

Trilithium *S*-(2-Sulfinoethyl)phosphorothioate (7). Trilithium phosphorothioate was prepared essentially as described.[8] Titration of 0.2550 g in 50 mL of HOAc with 0.1 N aqueous KI_3 required 12.2 mL (calcd for $Li_3SPO_3 \cdot 4.25H_2O$, 12.2 mL). This result indicated the product to be $Li_3SPO_3 \cdot 4.25H_2O$: IR (KBr) 3600–3100 (br, H_2O), 2050 (w), 1630 (H_2O), 1050 (s), 950 (s), 650 (br) cm^{-1}. The product was stored in several portions under Ar at −65 °C.

Anal. Calcd for $Li_3O_3PS \cdot 4H_2O$: P, 15.19; S, 15.72; H, 3.95. Found: P, 14.92; S, 15.82; H, 4.08.

Thiirane 1,1-dioxide (2, 0.50 g, 5.43 mmol) in 5 mL of H_2O was added over 2–3 min to $Li_3SPO_3 \cdot 4H_2O$ (1.01 g, 4.95 mmol) in 10 mL of H_2O at ca. 0 °C. The mixture was stirred at 0 °C until, after 3 h, the solution, when acidified with HNO_3, gave no black precipitate with aqueous $AgNO_3$.[8] The mixture then was poured through glass wool (to remove a little insoluble material). EtOH (300 mL) was added, and the white precipitate was isolated via centrifugation and decantation and washed with EtOH (100 mL). A solution of the solid product in H_2O (20 mL) was centrifuged, decanted, and lyophilized to give 0.74 g (67%) of 7: mp 220 °C dec; IR (KBr) 3400 (br, H_2O), 1630 (H_2O), 1430, 1405, 1280, 1120 (s), 1060 (s), 990 (s), 775 cm^{-1}; ^1H NMR (D_2O) δ 3.04–2.58 (m, A_2B_2); ^{13}C NMR (D_2O, MeOH as reference) δ 63.54 [d(split by P), 3.6 Hz], 24.18 (s).

Anal. Calcd for $C_2H_4Li_3O_5PS_2$: C, 10.72; H, 1.80; S, 28.63; P, 13.83. Found: C, 10.62; H, 1.87; S, 28.31; P, 13.62. Calcd for $C_2H_4Li_3O_5PS_2 \cdot 0.4H_2O$ (initial product) to $C_2H_4Li_3O_5PS_2$: H_2O, 3.12. Found: 3.18.

A large-scale preparation from 2 (8.00 g, 86.9 mmol) and $Li_3SPO_3 \cdot 4H_2O$ (16.0 g, 78.5 mmol) in 50 mL of H_2O gave 17.6 g (100%) of the phosphorothioate 7, part of which was lyophilized and had appropriate spectra.

A sample of the phosphorothioate 7 in D_2O at 0 °C over 18 days showed no change (^1H NMR and no formation of a precipitate). When this sample was warmed to ca. 25 °C, hydrolysis of the phosphorothioate moiety was approximately one-half complete in 3 days (^1H NMR, from the ratio of the peaks centered at δ ca. 2.68 for 9 to those for 7 at δ ca. 2.82. In one week, hydrolysis was virtually complete.

In a second experiment, the reaction of the thiirane dioxide 2 (23 mg, 0.250 mmol) and $Li_3SPO_3 \cdot 4H_2O$ (50 mg, 0.245 mmol) in 1 mL of D_2O was followed via NMR. The reaction was complete in ca. 5 min (disappearance of the peak at δ 3.19 of 2). After 2 h at ca. 25 °C, the spectrum was unchanged, but after heating of the reaction mixture at 55 °C for 1 h, ^1H NMR spectra showed that approximately one-third of the material had hydrolyzed and after 3 h about one-half had hydrolyzed. The hydrolysis was complete in 5.5 h.

Disodium *S*-(2-Sulfinoethyl)thiosulfate (8). Thiirane 1,1-dioxide (2, 5.00 g, 54.4 mmol) in 25 mL of H_2O was added to Na_2SSO_3 (7.80 g, 49.3 mmol) in 25 mL of H_2O over 5 min at ca. 25 °C. The mixture was stirred for 2 h at ca. 25 °C, and Me_2CO (350 mL) then was added. After the mixture had been vigorously stirred for a few minutes, gum was separated via centrifugation and decantation and was taken up in ca. 50 mL of MeOH. Addition of Et_2O (ca. 300 mL) then gave the Bunte salt 8 as a white precipitate. Centrifugation and decantation gave 11.22 g of 8 (91%, calcd as anhydrous 8). A solution in MeOH was centrifuged and decanted to remove insoluble material, and Et_2O (350 mL) was added to give 8.88 g (72%) of 8. NMR showed peaks corresponding to those expected for the Bunte salt 8 plus a singlet at δ 3.2 corresponding to a little residual MeOH. For removal of MeOH, 0.50 g of the white powder was taken up in 10 mL of H_2O and lyophilized during 19 h at ca. 0.1 torr to give 0.43 g of solid that gave an analysis corresponding to $8 \cdot 1.25H_2O$. After the sample had been dried rigorously, it still contained moisture (0.25 H_2O): IR (KBr) 3600 (s, H_2O), 3350–2900 (br, H_2O), 2100, 1620 (H_2O), 1400, 1205 (s), 1000 (s), 850 (w), 770 cm^{-1}; ^1H NMR (D_2O) δ 3.27 (m, 2 H), 2.76 (m, 2 H); ^{13}C NMR (D_2O, Me_2SO) δ 61.01, 28.88; mp 178 °C dec.

Anal. Calcd for $C_2H_4Na_2O_5S_3 \cdot 1.25H_2O$: C, 8.81; H, 2.40; S, 35.27. Found: C, 8.98; H, 2.30; S, 35.05. Calcd for loss of 1 H_2O upon drying: 6.61. Found: 6.95. Calcd for $C_2H_4O_5S_3Na \cdot 0.25H_2O$: C, 9.43; H, 1.78; S, 37.76. Found: C, 9.55; H, 1.77; S, 37.81.

A sample of the Bunte salt 8 in D_2O showed no change (^1H NMR) after ca. 1 month at 25 °C nor after the sample had been heated in solution at 50 °C for 1 day.

Lithium 2-Mercaptoethanesulfinate (9). The phosphorothioate 7 (2.0 g, 8.9 mmol) was heated in 10 mL of D_2O (with use of a condenser) at ca. 80 °C for 2 h. Solid that formed was separated via centrifugation after the solution was cooled; ^1H and ^{13}C NMR showed that no 7 remained in solution but that 5–10% of the disulfide 11 was present, despite efforts to exclude O_2. The mixture was chilled at 0 °C for 15 h, centrifuged to remove a little precipitate, diluted to 100 mL with H_2O (Ar bubbled through beforehand), and freeze-dried to give 1.14 g (97% calcd as pure 9) of the mercaptosulfinate 9: IR (KBr) 3400 (br, H_2O), 2900, 1640 (H_2O), 1550 (w), 1405, 1390, 1170, 1010 (s), 930, 900, 740 cm^{-1}; ^1H NMR (D_2O) δ 2.68 (m, A_2B_2); ^{13}C NMR (D_2O) δ 66.58, 19.45. Elemental analysis gave results 5% low in C and 14% low in S, consistent with presence of ca. 0.5 molar proportion of Li_2HPO_4; a qualitative $(NH_4)_2MoO_4$ test showed the presence of phosphate.[16] Attempts to purify this crude 9 were successful; the ^1H NMR was unchanged after 1 day at 55 °C in D_2O.

In order to confirm that the product was largely 9, 0.250 g (1.89 mmol, calcd as the mono-Li salt of 9) was heated with 0.340 g (1.68 mmol) of 2,4-dinitrochlorobenzene in 1:3 H_2O–EtOH under reflux for 3 h. Product was removed, washed with H_2O, EtOH, and Et_2O, and then taken up in warm Me_2CO, concentrated slightly, and crystallized to give, after being washed with Et_2O, 200 mg (52%) of yellow **2,4-dinitrophenyl 2-(2,4-dinitrophenylthio)ethyl sulfone (12)**: mp 195–196.5 °C; TLC using 50% EtOAc in hexane gave one spot (R_f 0.44). The crude product was recrystallized to a constant mp of 195.5–196.5 °C: IR (KBr) 3100, 1570, 1550, 1500, 1340–1300, 1150, 1110, 1040, 910, 830, 740, 710 cm^{-1}; ^1H NMR (CD_3CN) δ 8.89 (d, 1 H), 8.68 (d, 1 H), 8.56 (d, 1 H), 8.41 (m, 2 H), 7.70 (d, 1 H), 3.98 (m, 2 H), 3.59 (m, 2 H); ^{13}C NMR (Me_2CO-d_6) δ 144.22, 137.82, 135.44, 128.99, 128.45, 122.22, 121.63, 55.37, 25.52.

(16) McAlpine, R. K.; Soule, B. A. *Qualitative Chemical Analysis*; D. Van Nostrand: New York, 1933; p 565.

Anal. Calcd for $C_{14}H_{10}N_4O_{10}S_2$: C, 36.68; H, 2.20; S, 13.99; N, 12.22. Found: C, 36.69; H, 2.31; S, 13.97; N, 11.94.

Reactions of the Bunte Salt 8. (a) With NaOH. The Bunte salt **8** (4.50 g, 18.0 mmol) and NaOH (1.03 g, 25.8 mmol) were stirred for 20 h at 25 °C in 50 mL of H_2O (pH ca. 12). The reaction mixture was concentrated to dryness under reduced pressure, and the residue was taken up in 25 mL of warm MeOH. Insoluble material was removed by centrifugation and decantation, and Me_2CO (300 mL) was added; weight of precipitate, 2.34 g (88% of expectation for the disulfide **11** as the anhydrous Na salt): ^1H NMR (D_2O) δ 3.08–2.92 (m, 4 H), 2.80–2.63 (m, 4 H), cf. **11** in (d) below, δ 2.56 (s, $NaO_2SCH_2CH_2SO_2Na$?); ^{13}C NMR (D_2O) δ 60.50, 31.25 [cf. **11** in (d) below], δ 53.46 ($NaO_2SCH_2CH_2SO_2Na$?); IR (KBr) 1430, 990, 950 cm^{-1}.

(b) With Na–NH_3. Sodium (ca. 0.3 g, 13 mmol) was added in small pieces to 0.50 g (2.00 mmol, if anhydrous) of **8** in 75 mL of liquid NH_3 during 1.5 h, until a blue color persisted for more than 15 min. After destruction of excess sodium with NH_4Cl and removal of NH_3 under Ar, the residue was taken up in MeOH and centrifuged to remove insoluble material. The thiol content of an aliquot was ca. 100% of theory by Ellman analysis.[9]

(c) With $NaBH_4$, for Reduction to 9 and Derivatization as 13. In order to determine whether $NaBH_4$ would reduce the Bunte salt **8**, at least in considerable part, to the mercaptosulfinate **9**, *p*-bromophenacyl bromide (0.43 g, 1.55 mmol) and *n*-Bu_4NI (0.03 g, 0.08 mmol) in 10 mL of dimethoxyethane (DME) were added to a suspension in 25 mL of DME of 0.30 g (2.03 mmol, calcd as the Na salt of **9**) of the product obtained by reducing 1.80 g (7.20 mmol) of **8** with 0.34 g (8.99 mmol) of $NaBH_4$ essentially as described under (d); this crude **9** probably contained some of the disulfide **11**, as predicted by eq 1. The mixture with the bromide was heated under reflux for 30 min, cooled, and diluted with 200 mL of ice–water; yield of crude ***p*-bromobenzoylmethyl 2-(*p*-bromobenzoylmethylthio)ethyl sulfone (13)**, 0.28 g (70%): mp ca. 125–140 °C. Recrystallization ($CHCl_3$) gave pure **13**: mp 144–146 °C; IR (Nujol) 1670, 1580, 1310, 1280, 1220, 1200, 1150, 1115, 1070, 990, 805, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (d, 2 H), 7.83 (d, 2 H), 7.66 (d, 2 H), 7.61 (d, 2 H), 4.64 (s, 2 H), 3.88 (s, 2 H), 3.67–3.49 (m, 2 H), 3.13–2.96 (m, 2 H).

Anal. Calcd for $C_{18}H_{16}Br_2O_4S_2$: C, 41.55; H, 3.10; S, 12.32. Found: C, 41.43; H, 3.06; S, 12.48.

(d) With $NaBH_4$ and O_2, for the Preparation of Disodium 2,2′-Dithiobis(ethanesulfinate) (11). $NaBH_4$ (1.33 g, 35.1 mmol) was added over 5 min to a solution of the Bunte salt **8** (8.00 g, 32.0 mmol) in 75 mL of H_2O at ca. 0 °C. The mixture then was stirred for 1 h (no H_2 was evolved when 1 N HCl was added to 2–3 drops of the reaction mixture). Solid was removed by centrifugation, H_2O was evaporated at 0.1 torr, and the residue was taken up in 40 mL of MeOH. After removal of insoluble material, ca. 25 mL of Et_2O was added to precipitate an estimated 5–10% of the salt present. This precipitate was removed, and 450 mL of Et_2O was added. The abundant precipitate of **11** was collected (centrifugation), washed with Et_2O, and dried. A solution in H_2O (125 mL) was poured through glass wool, air was bubbled through it for 8 h (a test for thiol with nitroprusside then was negative), and the solution was freeze-dried; yield of **11**, 3.38 g (72%, calcd as the anhydrous Na salt from **8**): IR (KBr) 3600–3000 (br, H_2O), 2900, 1640 (H_2O), 1480, 1450, 1420, 1400, 1010 (s), 980 (s), 880, 740–620 cm^{-1}; ^1H NMR (D_2O) δ 3.07–2.92 (m, 4 H), 2.80–2.63 (m, 4 H); ^{13}C NMR (D_2O, MeOH as reference) δ 60.53, 31.23.

Anal. Calcd for **11**·3.75H_2O to **11**·0.25H_2O: H_2O, 17.43. Found: 17.66. Calcd for $C_4H_8Na_2O_4S_4$·0.25H_2O: C, 16.08; H, 2.87; S, 42.92. Found: C, 15.90; H, 2.57; S, 42.94.

For confirmation of identity, 0.10 g (0.276 mmol) of the disulfide **11** (Na salt·3.75H_2O) was stirred with 0.38 g (1.37 mmol) of *p*-bromophenacyl bromide in 4 mL of DMF at ca. 25 °C for 18 h. Addition of H_2O (100 mL) precipitated 0.11 g of solid. TLC showed several spots (including one with the R_f value of **13**). The solid was washed with hot $CHCl_3$ (in which **13** is soluble) and recrystallized from MeCN to give 30 mg (17%) of **bis-2-(*p*-bromobenzoylmethylsulfonyl)ethyl disulfide (10)**: mp 193.5–195.5 °C; IR (KBr) 2960 (w), 2920 (w), 1670 (s), 1580, 1570, 1500 (w), 1400, 1310 (s), 1280, 1200, 1180, 1130 (s), 850 (w), 810 (w), 780 (w), 730 (w) cm^{-1}; ^1H NMR (CD_3CN) δ 7.92 (d, 2 H), 7.73 (d, 2 H), 5.82 (s, 2 H), 3.52–3.41 (m, 4 H). Further recrystallization from MeCN gave pure **10**: mp 193–194 °C.

Anal. Calcd for ($C_{20}H_{20}Br_2O_6S_4/2$)–H: ^{79}Br, 319.9177; ^{81}Br, 321.9157. Found (HRMS): ^{79}Br, 319.9200; ^{81}Br, 321.9153 (fragment ions were appropriate).

Sodium 2-(*p*-Toluenesulfonylthio)ethanesulfinate (17). Sodium *p*-toluenethiosulfonate (**16**) was prepared by a procedure based on one of Buckman,[17] in turn based on an undetailed one of Otto,[18] by vigorously stirring 30 g of **15** (assumed to be **15**·2H_2O; 140 mmol) and 4.50 g of sulfur (140 mmol) in 250 mL of 1:1 H_2O–EtOH under reflux for 3 days at 80–90 °C. The mixture was cooled, filtered to remove unreacted sulfur (ca. 0.3–0.5 g), and concentrated to a mush. 2-Propanol (100 mL) was added, the mixture was cooled (2 °C, 42 h), and 100 mL of Et_2O was added; yield, 26.1 g (76%, assuming the product to be **17**·2H_2O); the lowest yield was ca. 62%. Thiirane 1,1-dioxide (**2**, 2.50 g, 27.1 mmol) in 50 mL of MeOH then was added over 10 min to a solution of the thiosulfate **16**·2H_2O (6.19 g, 25.1 mmol) in 60 mL of MeOH stirred at 0 °C. After the thiirane **2** had been added, the reaction mixture was stirred for 30 min at 0 °C and then for 16 h at ca. 25 °C in a flask fitted with a drying tube. Concentration to dryness and addition of Et_2O (100 mL) gave a gummy solid. After removal of the Et_2O, the residue was dried under vacuum (1 h, 1 torr), washed (Et_2O, 100 mL), and again dried (2 h, 1 torr) to give 5.91 g (78%) of **17** as a white hygroscopic solid, which initially was soluble in water, although solid soon appeared. ^1H NMR indicated that the crude **17** contained impurity (mostly the sulfinate **15** and the thiosulfate **16**).

A partial solution of 0.50 g of the crude **17** in D_2O (2 mL) was shaken for 6 min. Centrifugation, decantation, and drying gave 0.1 g of insoluble solid, the polymer **26** (only ca. 10–20 mg more appeared in the supernatant later): IR (KBr) 1320 (s), 1110 (s), 1070, 1020, 940 (the foregoing are consistent with SO_2 and SO_2Na); NMR (Me_2SO-d_6, the only good solvent for **26**) δ 7.90–7.09 (m), 4.10–3.05 (m), 2.44 (s), 2.37 (s), 2.29 (s); mass spectrum (FAB+), *m/z* 302 (*p*-$MeC_6H_4SO_2SCH_2CH_2SO_2Na$), and 426, 550, 674, 798, 922 [*p*-$MeC_6H_4SO_2'(SCH_2CH_2SO_2)_nS(CH_2)_2SO_2Na$ with n = 1–5, respectively]. The supernatant liquid from the centrifugation had an NMR spectrum that contained all the peaks of the sulfinate **15**, and no new peaks appeared upon addition of **15**; for confirmation, the **15** obtained by evaporating the supernatant from similar treatment of another 1.50 g of **17** (4.96 mmol) was heated with 0.51 g (2.52 mmol) of 2,4-dinitrochlorobenzene in 50 mL of EtOH under reflux for 15 h to give 0.29 g (36%) of *p*-tolyl 2,4-dinitrophenyl sulfone (**27**), mp 184–186 °C [after recrystallization, mp and mixture mp with authenic **27** 187–188.5 °C (lit.[19] mp 189.5 °C); IR spectrum congruent with that of authentic **27**].

Ethyl 2-(*p*-Toluenesulfonylthio)ethanesulfinate (18). By a method used previously for esterifying alkanesulfinate salts,[20] a solution of $Et_3O^+BF_4^-$ (2.07 g, 10.9 mmol; 1.1 equiv) in CH_2Cl_2 (40 mL) was added over 10 min to a suspension of the crude thiosulfonate–sulfinate **17** (3.0 g, 9.9 mmol) in 80 mL of CH_2Cl_2 stirred at ca. 25 °C. After a stirring period of 30 min at ca. 25 °C, the reaction mixture was washed with H_2O (3 × 40 mL), dried ($MgSO_4$), and concentrated in vacuo to give 2.74 g (90%) of oil. Flash chromatography (25% EtOAc in hexane) of 2.5 g of the oil using 100 g of silica gel (Baker 7024) in a 50-mm (diameter) column gave 0.86 g (31% based on **17**) of the ethyl ester **18** as a viscous pale yellow oil: n^{26}_D 1.5662; IR (neat) 3070, 2990, 2950, 2900, 1590, 1490, 1440, 1400, 1320 (s), 1300, 1140 (s), 1120 (s), 1080, 1010 (s), 890 (s), 810, 700, 650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (d, 2 H), 7.39 (d, 2 H), 4.10 (q, 2 H), 3.33 (m, 2 H), 3.05 (m, 2 H), 2.49 (s, 3 H), 1.34 (t, 3 H); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) δ 145.15 (s), 141.20 (s), 129.87 (d), 127.00 (d), 65.14 (t), 55.22 (t), 26.73 (t), 21.53 (q), 15.68 (q); MS (CI), *m/z* 263 (M – EtO).

Anal. Calcd for $C_{11}H_{16}O_4S_3$: C, 42.83; H, 5.22; S, 31.19. Found: C, 42.63; H, 5.35; S, 31.32.

A larger scale preparation of **18** from 3.50 g (38.0 mmol) of the episulfone **2** and 9.40 g (38.2 mmol) of the thiosulfate **16**·2H_2O

(17) Buckman, J. D. Ph.D. Dissertation, Vanderbilt University, 1966, p 114.
(18) Otto, R. *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 121.
(19) *Handbook of Tables for Organic Compound Identification*, 3rd ed.; compiled by Rappoport, Z.; The Chemical Rubber Co.: Cleveland, 1967; p 416.
(20) Srivastava, P. K.; Field, L. *Phosphorus Sulfur* **1985**, *25*, 161.

gave 10.08 g (88%) of the thiosulfonate salt **17**, of which 10.0 g (33.1 mmol) with $Et_3O^+BF_4^-$ (6.92 g, 36.4 mmol) gave 9.02 g (88% based on **17**) of the crude ester **18**. Flash chromatography (35% EtOAc in hexane) with 3.0 g of the crude oil on 120 g of silica gel gave 1.35 g (40% from **17**) of pure **18**: n^{27}_D 1.5656.

TLC showed that neat **18** could be kept unchanged for 5 days at ca. 25 °C (but was much decomposed after a week) or for 2 weeks at 2 °C. In CH_2Cl_2 at ca. 25 °C, **18** was unchanged in 2 weeks but precipitation began in 2.5 weeks. In refluxing EtOAc, decomposition was slight after 2 days but complete after 5 days.

Methyl 2-(*p*-Toluenesulfonylthio)ethanesulfinate (19). By a method based on a reported one,[21] an ethereal solution of diazomethane at ca. 0 °C was added in small portions to a solution of the thiosulfonate **17** (18.20 g, 60.2 mmol) in MeOH (100 mL), to which 39 mL of 1.9 M methanolic HCl (74.1 mmol) had been added. Addition of CH_2N_2 was continued until a slight yellow color from excess CH_2N_2 persisted. After 2–3 drops of HOAc had been added to destroy excess CH_2N_2, the reaction mixture was poured through glass wool and concentrated under reduced pressure. The residue was taken up in EtOAc (250 mL) and washed with H_2O (2 × 100 mL). The aqueous layers then were extracted with 50 mL of EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 12.21 g (69%) of the crude ester **19** as a viscous pale yellow oil. TLC (25% EtOAc in hexane) showed three spots at R_f 0.25 (**19**), 0.35, and 0.51. The crude ester **19** (12.21 g) was divided into two portions. Each was flash chromatographed on 120 g of silica gel in a 50-mm (diameter) column with use of 40% EtOAc in hexane. The combined samples of pure thiosulfonate–sulfinate ester **19** isolated amounted to 5.84 g (33% from the thiosulfonate salt **17**) of the ester **19** as a pale yellow oil: n^{26}_D 1.5789; IR (neat) 3050 (w), 2975, 2940, 1510, 1475, 1430 (s), 1350 (s), 1315, 1305, 1215 (w), 1145 (s), 1085 (s), 1025, 1000 (s), 940, 825, 710, 665, 590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.89 (d, 2 H), 7.43 (d, 2 H), 3.82 (s, 3 H), 3.37 (m, 2 H), 3.09 (m, 2 H), 2.51 (s, 3 H). Preparative TLC on 200 mg of this **19** using 40% EtOAc in hexane gave 110 mg of analytically pure methyl ester **19**: n^{27}_D 1.5763.

Anal. Calcd for $C_{10}H_{14}O_4S_3$: C, 40.79; H, 4.79; S, 32.67. Found: C, 40.70; H, 4.70; S, 32.48.

Methyl 2-(*p*-Tolyldithio)ethanesulfinate (20). *p*-Thiocresol (0.63 g, 5.07 mmol) in 15 mL of CH_2Cl_2 was added to thiosulfonate **19** (1.50 g, 5.09 mmol) and Et_3N (0.51 g, 5.04 mmol) in ca. 25 mL of CH_2Cl_2 at 0 °C. TLC (25% EtOAc in hexane) showed the reaction to be complete (no **19** remaining) in 15 min (product at R_f 0.37, thiol at 0.65). Then, CH_2Cl_2 (100 mL) was added, and the reaction mixture was washed with H_2O (2 × 50 mL). The H_2O layers were extracted with 25 mL of $CHCl_3$, and the combined organic layers were dried ($MgSO_4$) and concentrated to give 1.42 g of a pale yellow oil. Flash chromatography of this oil on 50 g of silica gel on a 30-mm (diameter) column using 25% EtOAc in hexane gave 1.09 g (82%) of pure disulfide **20**: n^{23}_D 1.5954; IR (neat) 2995, 2960, 2925, 2820, 1590 (w), 1490, 1450, 1420, 1400, 1310 (w), 1285, 1260, 1215 (w), 1200, 1185, 1130 (s), 1085, 1020, 995 (s), 940, 810 (s), 760, 695 (s), cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47 (d, 2 H), 7.18 (d, 2 H), 3.78 (s, 3 H), 3.08 (m, 4 H), 2.36 (s, 3 H); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) δ 137.78 (s), 132.96 (s), 129.87 (d), 129.17 (d), 55.60 (t), 54.52 (q), 29.27 (t), 20.93 (q). Similar **20** after preparative TLC using 30% EtOAc in hexane gave analytically pure **20**: n^{27}_D 1.5958.

Anal. Calcd for $C_{10}H_{14}O_2S_3$: C, 45.77; H, 5.38; S, 36.66. Found: C, 45.42; H, 5.50; S, 36.41.

Compound **20** in $CHCl_3$ at ca. 25 °C remained virtually unchanged (TLC) after 1 week in ambient (diffuse) light. At 50 °C in $CDCl_3$ after 1 week, ca. 10% of **20** had decomposed (NMR), and after 3.5 weeks at 50 °C, ca. 75% had decomposed. Within 5 min after exposure to UV light (sample dissolved in $CHCl_3$ in a Pyrex tube suspended ca. 13 cm from a Hanovia 100-W UV quartz lamp, No. 30620), the disulfide **20** began to disproportionate (two extra spots in TLC); after 2–4 h, essentially no **20** remained.

Methyl 2-(*p*-Chlorophenyldithio)ethanesulfinate (22). Essentially the procedure for **20** was used but with 1.47 g (10.2 mmol) of *p*-chlorothiophenol, 3.00 g (10.2 mmol) of **19**, and 1.03 g (10.2 mmol) of Et_3N.[1b] Flash chromatography of the oily **22** (3.21 g, 111%) on 120 g of silica gel in a 50-mm (diameter) column using 30% EtOAc in hexane gave 2.09 g (73%) of pure **22** as a pale yellow oil: IR (neat) 2950, 2920, 2815 (w), 1575 (w), 1475, 1425, 1400, 1280 (w), 1130 (s), 1090 (s), 1010 (s), 990 (s), 935 (w), 815, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (d, 2 H), 7.35 (d, 2 H), 3.80 (s, 3 H), 3.10 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 135.02, 129.66, 129.28, 55.55, 54.74, 29.33. The oily **22** in Et_2O–hexane at −70 °C gave 1.35 g (47%) of white crystalline **22** (mp 32–33.5 °C), which after recrystallization at −70 °C had mp 32.5–33 °C.

Anal. Calcd for $C_9H_{11}ClO_2S_3$: C, 38.22; H, 3.92; Cl, 12.54; S, 34.01. Found: C, 38.08; H, 4.18; Cl, 12.42; S, 33.94.

Compound **22** in $CHCl_3$ at ca. 25 °C was virtually unchanged (TLC) after 1 week in ambient light. At 50 °C in $CDCl_3$, **22** was essentially unchanged after 1 week, but ca. 10–20% decomposed after 3.5 weeks (NMR). When exposed to strong UV light, as with **20**, **22** behaved much like **20**.

Dimethyl (1,4-Butylenedithio)bis(2-ethanesulfinate) (21). 1,4-Butanedithiol (62 mg, 0.51 mmol) in 5 mL of CH_2Cl_2 was added over 2–3 min to the thiosulfonate **19** (300 mg, 1.02 mmol) and Et_3N (103 mg, 1.02 mmol) in 10–15 mL of CH_2Cl_2 with stirring at ca. 0 °C. After 30 min, some of the **19** remained (TLC), so more dithiol (ca. 10 mg) was added. When after 10 min TLC showed no **19**, the product was isolated as with **20**. Preparative TLC of the oil (370 mg), obtained by the usual concentration, with 50% EtOAc in hexane gave 190 mg (94%) of **21** as colorless oil (R_f 0.09–0.20). TLC showed a small amount of impurity. A second preparative TLC (75% EtOAc in hexane) gave 150 mg (74%) of **21**, which crystallized in Et_2O–hexane at −70 °C to give 120 mg (59%) of solid **21** that liquefied again at ca. 25 °C: n^{27}_D 1.5782; IR (neat) 2930, 1410, 1400, 1270, 1240, 1110 (s), 990, 890 (s), 730, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80 (s, 3 H), 3.08 (m, 2 H), 3.02 (m, 2 H), 2.73 (m, 2 H), 1.81 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 55.98; 54.57, 38.16, 29.06, 27.70.

Anal. Calcd for $C_{10}H_{22}O_4S_6$: C, 30.13; H, 5.56; S, 48.26. Found: C, 30.10; H, 5.72; S, 48.27.

The disulfide **21** was stable at 50 °C in $CDCl_3$ in the dark for 2 weeks (NMR); ca. 10–20% decomposition occurred in 3.5 weeks. In $CHCl_3$ under UV light, TLC showed no change up to 1 h, but new spots appeared at 1–2 h.

(21) Eswarakrishnan, V.; Field, L. *J. Org. Chem.* **1981**, *46*, 4182.