5-55511-318) and the National Institutes of Health (Grant No. DA 02037) for support of this work.

Registry No. 2a, 76916-18-2; **2b**, 77415-78-2; **2c**, 77415-79-3; **4**, 2201-33-4; **5**, 77415-80-6; **6a**, 3485-84-5; **6b**, 5428-09-1; **6c**, 52898-32-5; **7**, 76916-13-7; **8**, 77415-81-7; (*E*)-**9a**, 77415-82-8; (*E*)-**9b**, 77415-83-9; (*E*)-**9c**, 77415-84-0; (*E*)-**10**, 77415-85-1; (*E*)-**11**, 77415-86-2; **12a**, 76916-26-2; **12b**, 77415-87-3; **12c**, 77415-88-4; (*E*)-**13**, 77415-89-5; (*Z*)-**13**, 77415-90-8; **13a**, 76916-30-8; **13b**, 77415-91-9; **13c**, 77482-41-8; **14**, 77415-92-0; **16a**, 77482-42-9; **16b**, 77415-93-1; **18**, 77415-94-2; (*E*)-**19**, 77415-95-3; (*Z*)-**19**, 77415-96-4; **20**, 77415-97-5; **21**, 77415-98-6; (*E*)-**22**, 77415-99-7; 1,4-diiodobenzene, 624-38-4; 1-piperidyl-1-cyanocyclohexane, 3867-15-0; *N*-(2-bromoethyl)phthalimide, 574-98-1; palladium acetate, 33571-36-7; phenyl isothiocyanate, 103-72-0; acrylonitrile, 107-13-1; methyl acrylate, 96-33-3; acrolein ethylene ketal, 3984-22-3.

Organic Disulfides and Related Substances. 43. Properties of a Mercaptoalkyl Sulfoxide, a Novel Class of Structure[1]

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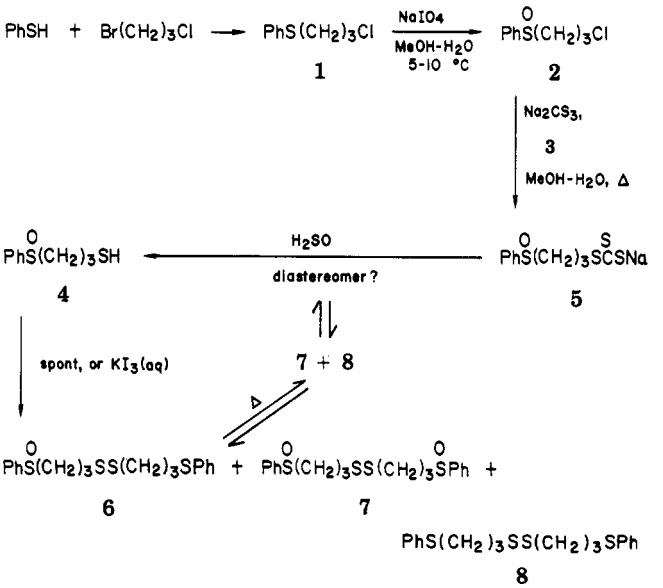
Received January 26, 1981

3-Mercaptopropyl phenyl sulfoxide (**4**) was prepared by reaction of 3-chloropropyl phenyl sulfoxide (**2**) with sodium trithiocarbonate (**3**). The mercaptopropyl sulfoxide **4** could be obtained only in a maximum purity of 93% (and yield of 75%) because it underwent rapid oxidation at ~25 °C of the SH function, with reduction of the S(O) function; however, **4** is more stable neat or in chloroform. The thiol **4** could be converted to the 2,4-dinitrophenyl sulfide in 47% yield. Oxidation with iodine gave the corresponding monosulfoxide–disulfide **6**, the disulfoxide–disulfide **7**, and the disulfide–disulfide **8** in respective yields of up to 27%, 38%, and 12%. The intermediary 3-chloropropyl sulfoxide (**2**) was obtained by oxidizing the sulfide with $NaIO_4$ in methanol–water; it (very slowly) disproportionated to the sulfide and sulfone. The chloro sulfoxide **2** reacted far more rapidly than the chloro sulfide **1** with **3**, but use of the chloro sulfide **1** afforded the preferred route to the disulfide–disulfide **8** (26% yield).

Studies on the chemistry of disulfides have led us to an interest in the properties of disulfides containing sulfoxide functions. When an effort to synthesize a sulfoxide–disulfide from a chloroalkyl sulfoxide by using Na_2S_2 gave an unpromising mixture, a mercapto sulfoxide seemed an attractive starting material. Since thiols are well-known to be oxidized to disulfides by sulfoxides (which are reduced thereby to sulfides),[2] our interest in mercapto sulfoxides was stimulated further by curiosity about the compatibility of S(O) and SH functions in the same molecule, a question that seems not to have been addressed heretofore. Mercapto sulfoxides apparently have not been reported previously, although a thiolate salt of one has been invoked as an intermediate.[3] In this paper we report the properties of 3-mercaptopropyl phenyl sulfoxide (**4**), a compound that undergoes redox reactions readily in water or methanol, together with conversion of **4** to the corresponding monosulfoxide–disulfide **6**, disulfoxide–disulfide **7**, and disulfide–disulfide **8**.

For synthesis of the intermediary chloro sulfoxide **2** (Scheme I), oxidation of the known sulfide **1**[4] with ozone[5] was unattractive because large amounts of **2** were desired, and use of SO_2Cl_2–wet silica gel[6] or Me_2SO[7] proved unpromising. Oxidation of **1** with $NaIO_4$ in water or aqueous dioxane[8] gave **2** but also the sulfone. However, use of

Scheme I



$NaIO_4$ in methanol–water with the sulfide **1** gave the pure sulfoxide **2** in 100% yield;[8] the striking improvement effected by methanol warrants special emphasis. It is worth remarking also that the sulfoxide **2** underwent a redox reaction, although slowly, to give the sulfide **1** and the sulfone.

Conversion of the chloride **2** to a thiol derivative first was attempted by using sodium *p*-toluenethiosulfate (*p*-$CH_3C_6H_4SO_2SNa$; 5 days, 70 °C, DMF). The product contained 61% of a thiolsulfonate,[9] but impurities could not be removed. Scheme I shows the route to **4** that proved successful, reaction of the chloro sulfoxide **2** with

(1) (a) Paper 42: Field, L.; Ravichandran, R. *J. Org. Chem.* **1979**, *44*, 2624–2629. (b) Abstracted from the Ph.D. Dissertation of G.T.B., Vanderbilt University, 1981, which can be consulted for further detail.
(2) For leading references, see: Oae, S. "Organic Chemistry of Sulfur"; Plenum Press: New York, 1977; pp 159, 318, 404.
(3) Huynh, C.; Ratovelomanana, V.; Julia, S. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1975**, *280*, 1231–1234.
(4) Zimmerman, H. E.; Thyagarajan, B. S. *J. Am. Chem. Soc.* **1960**, *82*, 2505–2511.
(5) Bordwell, F. G.; Brannen, W. T., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 4645–4650.
(6) Hojo, M.; Masuda, R. *Tetrahedron Lett.* **1976**, 613–614.
(7) Roush, P. B.; Musker, W. K. *J. Org. Chem.* **1978**, *43*, 4295–4298.
(8) Johnson, C. R.; Keiser, J. E. *Org. Synth.* **1966**, *46*, 78–80.
(9) Barnard, D.; Cole, E. R. *Anal. Chim. Acta* **1959**, *20*, 540–547.

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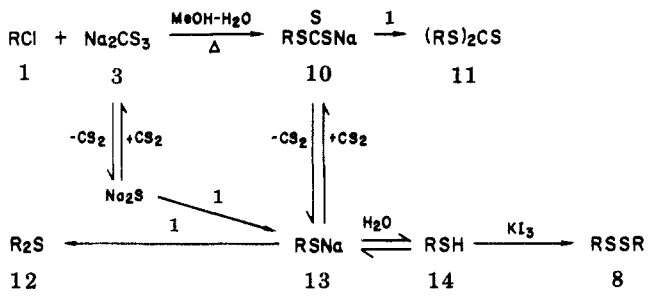
Scheme II[a]



[a] R = $PhS(CH_2)_3$

sodium trithiocarbonate,[10] although extraction of water-insoluble material after the reaction suggests that dialkylation was significant. Acidification of the aqueous layer gave the mercapto sulfoxide **4**. TLC showed several components, but NMR indicated ca. 70% content of the thiol. In addition to the NMR peak for PhSO (δ ~7.5–7.4), however, a peak for PhS was present (δ ~7.3–7.2), although none for $PhSO_2$ (δ ~7.9). That redox reactions of **4** had occurred was confirmed in efforts to purify **4** by extraction from CH_2Cl_2 into alkali and reacidification (34% mass recovery; SH decrease to 39%; increased ratio of PhS/PhSO by NMR); these results are understandable in terms of partition into the CH_2Cl_2 of disulfide rapidly formed through oxidation of the SH of the **4** and reduction of the SO (spectra and TLC were consistent). When all materials were combined and oxidized with KI_3, chromatography separated the monosulfoxide **6** (27% yield), the disulfoxide **7** (19%), and the disulfide **8** (12%). A delay after formation of **4**, before its oxidation with KI_3, appears to favor formation of **6**.

The disulfoxide–disulfide **7** was best obtained by minimizing the delay. Thus a shorter reaction time and immediate oxidation led to pure solid **7** in 16% yield. Other fractions of **7** (NMR; about 19% yield) seemed to be a mixture of **7** with an oily diastereomer attributable to the chiral sulfoxide functions, but only suggestive evidence (NMR) could be obtained for the diastereomer. Another fraction on the basis of spectra appeared to be the sulfone **9** (5%). Since the monosulfoxide **6** and disulfoxide **7** showed no change in NMR, IR, or TLC over several days **9** probably was formed either from a disproportionation

$$\underset{\mathbf{9}}{PhSO_2(CH_2)_3SS(CH_2)_3S(O)Ph}$$

product of **2** or by oxidation of **7** by the aqueous KI_3. The stability of **6** (by TLC) shows also that it was not the source of **7** and **8**; furthermore, when **6** was tested for the disproportionation to two symmetrical disulfides typical of unsymmetrical disulfides (Scheme I), it gave new TLC spots for **7** and **8** much too slowly to account for **7** and **8** in the syntheses.

The disulfide–disulfide **8** was best prepared by adapting the approach for the chloro sulfoxide **2** (Scheme I) to the chloro sulfide **1** (Scheme II). An incidental but noteworthy point is that reaction of **1** with the trithiocarbonate **3** required over 75 h (NMR), although less than 1 h sufficed with **2** and 1–5 h with earlier alkyl chlorides;[10] this result is surprising in view of the slight difference in rates of reaction of **1** and **2** with iodide ion in acetone.[5]

NMR spectra of the product from **1** and **3**, after oxidation (Scheme II), indicated formation of the sulfide **12**, along with **8**; presumably **10** decomposed to **13** and **3** to Na_2S, both of which led to **12**. Addition of excess **3** in

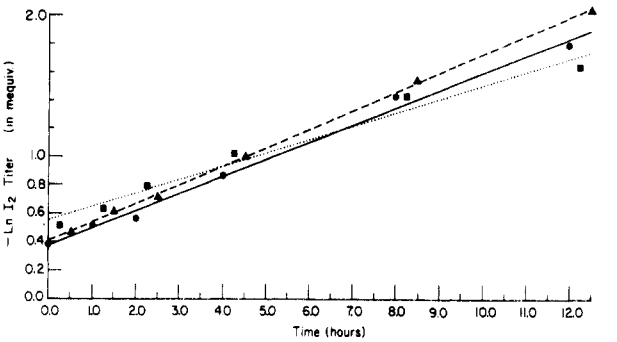
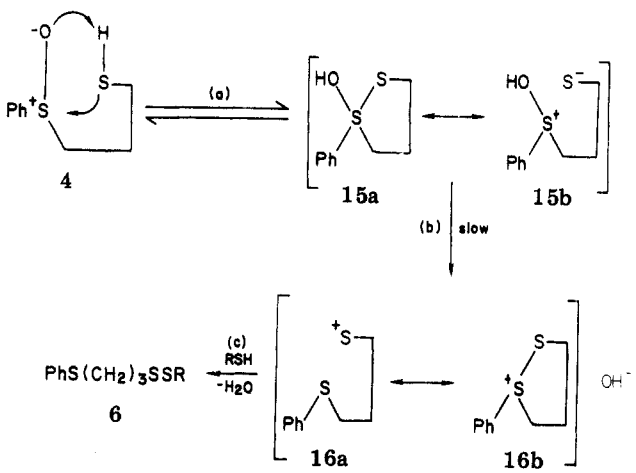


Figure 1. Rate of reaction of the mercaptoalkyl sulfoxide **4** in methanol (0.50 M) at 23–24 °C, as reflected by titration of unreacted **4** with aqueous KI_3 (least-squares treatment): circles and solid line, solution as such; triangles and dashed line, solution adjusted to pH 2; squares and dotted line, solution adjusted to pH 10.

Scheme III[a]



[a] R = $PhS(O)(CH_2)_3$

portions proved advantageous, evidently by offsetting decomposition of **3** and minimizing alkylation of **10** to form **11**. After extraction of the reaction mixture from **1** and **3** with CH_2Cl_2, *without acidification* (cf. Experimental Section), oxidation with KI_3 and chromatography produced pure **8** (26%), along with the sulfide **12** (5%).

The foregoing results show that SH and S(O) functions of the thiol **4** are indeed incompatible. To gain information about redox reactions of **4**, fresh preparations of **4** were isolated quickly and studied. Reaction with 2,4-dinitrochlorobenzene gave the 2,4-dinitrophenyl sulfide in 47% yield, confirming the identity of the **4**. The KI_3 titer showed 78–93% thiol content (47–75% yield). The KI_3 titer for thiol then was followed at ~23–24 °C in methanol alone and after adjustment to pH 2 and 10. Figure 1 shows the results. From Figure 1, we conclude that the reaction is first order ($t_{1/2}$ = 5.0–5.8 h) and not significantly affected by acid or base ($t_{1/2}$, respectively, of 5.2 and 6.9–8.7 h). The reaction products of this rate study were **6** (chiefly), **7**, and **8**. However, although **4** reacts readily in H_2O or methanol, it is considerably more stable neat or (especially) in chloroform (see Experimental Section).

Wallace and Mahon showed that the stoichiometry for oxidation of a thiol by a sulfoxide is that of eq 1,[11] that the reaction shows second-order kinetics overall,[12] that it is catalyzed by amines and somewhat by acids,[13] and that

(10) Martin, D. J.; Greco, C. C. *J. Org. Chem.* **1968**, *33*, 1275–1276.

(11) Wallace, T. J. *J. Am. Chem. Soc.* **1964**, *86*, 2018–2021.
(12) Wallace, T. J.; Mahon, J. J. *J. Am. Chem. Soc.* **1964**, *86*, 4099–4103.
(13) Wallace, T. J.; Mahon, J. J. *J. Org. Chem.* **1965**, *30*, 1502–1506.

the rate-determining step appears to be formation of an unstable adduct that is rapidly destroyed by thiol (eq 2).[13] Since the reaction of the mercapto sulfoxide **4** is first-order

$$2RSH + R_2SO \rightarrow R_2S + RSSR + H_2O \quad (1)$$

$$RSH + R_2SO \xrightarrow{slow} [R_2S(OH)SR] \xrightarrow{RSH(fast)} RSSR + R_2S + H_2O \quad (2)$$

but not subject to significant acid or base catalysis, formation of an ionized cyclic structure such as **16a** ↔ **16b**, made possible by the favorable juxtaposition of groups, may play the rate-determining role (step b, Scheme III); a thiosulfonium ion will react with a thiol to give a disulfide (cf. **16b**).[14] In Scheme III, hydrogen bonding of **4** may precede a (four-center?)[13] reaction that leads to an intermediate, **15a** ↔ **15b**, which then undergoes a rate-determining ionization of OH^- and thiosulfonium salt formation blended with ring cleavage (**16a** ↔ **16b**), followed by rapid reaction of **16a** ↔ **16b** with the thiol **4**. Internal favoring of cyclization may account for the insignificant effects of acid and base, since catalysis by amines and acids of eq 1 was explained by cyclic complexes;[13] the slight inhibitory action of sodium methoxide (Figure 1) may result from its depletion of thiol in step a. Scheme III shows the monosulfoxide **6** as the major product; oxidation after prolonged standing did give **6** in 27% yield, with **7** and **8** in 19% and 12% yields, respectively, but perhaps only coincidentally. Since pure **6** resisted a redox reaction, formation of **7** and **8** seems best explained by interaction of **4** and **6** through thiol interchange and/or perhaps redox reactions (reaction of **4** and **6** led to at least a slight increase in intensity of a TLC spot for **8** already present in a sample of **4**). It is noteworthy that the reaction of **4** occurs so readily at room temperature, since "oxidation of aliphatic thiols at reasonable rates (by sulfoxides) requires temperatures in excess of 100 °C".[11]

Experimental Section

Techniques and General Materials. Melting points were determined by using a Thomas-Hoover stirred-liquid apparatus and are corrected. NMR spectra, reported in parts per million (δ), were obtained with a JEOLCO Model JNM-MH-100 spectrometer using Me_4Si as an internal standard [or in D_2O using DSS, $Me_3Si(CH_2)_3SO_3Na$]. IR spectra were obtained by using Nujol mulls, neat liquids, or KBr pellets with a Perkin-Elmer 727 spectrometer. Elemental analyses were performed by Galbraith Laboratories. Moist extracts were dried by using Na_2SO_4 or $MgSO_4$, and solvent then was removed under reduced pressure with a rotary-flask evaporator. TLC was performed on Eastman Chromagram No. 6060 by using the solvents as stated, with visualization by UV or development by I_2 vapor. Brinkmann 7729 (<230 mesh) silica gel was used for column chromatography; the volumes of solvents reported refer to effluent. Sodium trithiocarbonate (**3**) was prepared as described[10] in argon-deaerated water and diluted to give 1.72–2.98 M solutions of **3**. All other materials were commercial unless otherwise stated.

3-Chloropropyl Phenyl Sulfoxide (2). 3-Chloropropyl phenyl sulfide (**1**) was prepared in 90% yield from thiophenol and 1-bromo-3-chloropropane;[4] n^{25}_D 1.5722 (lit.[4] n^{25}_D 1.5725). Sodium metaperiodate (12.02 g, 56.2 mmol) in H_2O (110 mL) was added over 0.5 h at 5–10 °C to a solution of **1** (10.0 g, 53.6 mmol) in MeOH (400 mL). After 24 h at 5–10 °C, H_2O (100 mL) was added as an aid in stirring. After 24 h more of stirring at 5–10 °C, TLC (50% EtOAc in pentane) showed only a spot corresponding to authentic **2**. Precipitated $NaIO_3$ was removed by filtration. The filtrate then was concentrated to 400 mL and was extracted with CH_2Cl_2. Concentration of the dried (Na_2SO_4) CH_2Cl_2 extract gave 10.9 g (100%) of **2**: n^{26}_D 1.5693 (lit.[5] n^{20}_D 1.5710); NMR ($CDCl_3$) δ 7.55 (m, 5 H), 3.62 (t, 2 H), 2.96 (m, 2 H), 2.22 (m, 2 H); IR (neat) 3460, 3070, 2990, 2950, 1580, 1490, 1460, 1410, 1320, 1280, 1160, 1100, 1050, 1010, 960, 760, 700, 660 cm^{-1}.

Essentially the same result occurred with an up to 7.5-fold increase in scale.

After 2 months at ambient conditions, TLC of **2** (R_f 0.3, 1:3 EtOAc–pentane) showed weak spots for the sulfide **1** (R_f 0.7) and 3-chloropropyl phenyl sulfone [R_f 0.5; n^{25}_D 1.5454 (lit.[15] n^{18}_D 1.5489)]. Heating fresh **2** at 50 °C for 5 h caused the spots for **1** and the sulfone to appear and become increasingly intense; NMR indicated 3–9% of disproportionation. Even storage of **2** below 5 °C caused the appearance in 6 months of small NMR peaks for **1** (δ 7.34) and the sulfone (δ 7.94) (3–5% disproportionation).

1,10-Diphenyl-1,5,6,10-tetrathiadecane 1-Oxide (6). A solution of **2** (15.0 g, 74.0 mmol) in MeOH (30 mL) was added to **3** (86 mL of a 1.72 M solution, 148 mmol) under Ar. The mixture was stirred at 50 °C for 4 h and then was concentrated to remove CH_3OH. The aqueous solution was washed once with CH_2Cl_2 (50 mL) and then was acidified to pH 1–2 with concentrated H_2SO_4. The CS_2 and H_2S liberated were removed at reduced pressure. The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL). The combined CH_2Cl_2 extracts were dried (Na_2SO_4) and then concentrated, leaving 11.2 g of yellow oil. Attempted extraction of the thiol **4** from this oil in CH_2Cl_2 with 10% aqueous NaOH was unpromising (see the previous discussion). Hence all fractions derived from this oil were recombined to be oxidized fully. The recovered oil (10.34 g) was dissolved in 95% EtOH (75 mL), and 0.4 N KI_3 was added dropwise until persistence of the purple color assured oxidation of all sulfhydryl species. After addition was complete, the mixture was stirred for 1 h, diluted with water, and extracted with CH_2Cl_2. The organic extract was washed with 5% $NaHSO_3$ and water and then was dried (Na_2SO_4). Evaporation left 10.31 g of an oil which was chromatographed on 400 g of silica gel in a 10-cm-diameter column with 30% EtOAc–hexane (first 3.5 L), EtOAc (next 1 L), and acetone as eluants. At volumes of effluent of 0.6–0.9 L, 1.69 g (12%) of **8** appeared, at 0.9–2.4 L, 0.72 g of unidentified material appeared, at 3.8–4.5 L, 3.83 g (27%) of **6** appeared, at 4.6–5.4 L, 0.30 g of unidentified material appeared, and at 5.8–6.7 L, 2.85 g (19%) of **7** appeared. Identifications of **6**–**8** were made by NMR and IR.

The monosulfoxide disulfide **6** (3.6 g, TLC R_f 0.19 with 30% EtOAc in hexane) was purified by additional chromatography on 160 g of silica gel in a 8-cm-diameter column with 35% EtOAc in pentane as eluant. The effluent volume from 1.5 to 2.3 L contained analytically pure **6** as an oil: 2.95 g (21%); n^{25}_D 1.6317; NMR ($CDCl_3$) δ 7.41 (m, 5 H), 7.17 (m, 5 H), 2.94 (t, 4 H), 2.70 (m, 4 H), 2.00 (m, 4 H); IR (neat) 3460, 3070, 2930, 1580, 1480, 1445, 1415, 1340, 1300, 1250, 1180, 1085, 1070, 1050, 1000, 745, 690 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}OS_4$: C, 56.50; H, 5.81; S, 33.51. Found: C, 56.36; H, 5.78; S, 33.71.

Further chromatography of the disulfoxide–disulfide **7** portion gave pure **7**, but **7** was best prepared as described below.

1,10-Diphenyl-1,5,6,10-tetrathiadecane 1,10-Dioxide (7). Much as with **6**, a solution of **2** (40.0 g, 197 mmol) in CH_3OH (90 mL) was added (45 min) to **3** (230 mL of a 1.74 M solution, 400 mmol) at 45 °C under Ar. The reaction mixture was stirred for an additional 1.5 h at 45 °C (NMR showed that the CH_2Cl peak remained after 0.5 h but not after 1 h). The mixture was cooled, washed with CH_2Cl_2 (50 mL), and acidified to pH 1–2 with concentrated H_2SO_4, and H_2S and CS_2 were removed. After addition of CH_2Cl_2 (50 mL) and H_2O (300 mL), the water layer was separated and further extracted with CH_2Cl_2 (4 × 50 and 1 × 100 mL). The combined organic extracts were washed with H_2O (2 × 50 and 4 × 25 mL), dried (Na_2SO_4), and concentrated at ~25 °C to 25.58 g of yellow oil.

A portion (22.98 g) of this oil was dissolved immediately in EtOH (170 mL) and oxidized by adding 0.4 N aqueous KI_3 until the color of I_2 persisted. Water (300 mL) was added, followed by extraction with CH_2Cl_2 (5 × 50 mL). The organic extract was washed with 5% aqueous $NaHSO_3$ (to remove I_2) and water and dried (Na_2SO_4). Evaporation gave 22.2 g of yellow oil, which was

(14) Tanikaga R.; Tanaka, K.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1978**, 865–866.

(15) Bird, R.; Stirling, C. J. M. *J. Chem. Soc. B* **1968**, 111–114.

chromatographed on 700 g of silica gel in a 10-cm-diameter column with 50% EtOAc–hexane (first 5 L) and then 100% EtOAc as eluant. At volumes of effluent of 1–1.8 L, 0.60 g (2%) of the disulfide–disulfide **8** appeared and at 2.3–3.5 L, 4.02 g (12%) of the monosulfoxide **6**; both were identified by comparison of TLC behavior with authentic **8** and **6**. At 4.1–5.2 L, 1.69 g of pasty solid appeared, which was assigned the structure of the sulfone–sulfoxide–disulfide **9** (5%) on the basis of NMR ($CDCl_3$): δ 7.90 (m, 2 H), 7.56 (m, 8 H), 3.21 (t, 2 H), 2.90 (m, 2 H), 2.72 (t, 4 H), 2.10 (m, 4 H). A volume of 6.7–8.5 L gave 3.21 g (9%) of product with δ 7.43, characteristic of the disulfoxide **7**; it was believed to contain an oily diastereomer of **7** on the basis of NMR, although this could not be purified. A volume of 8.5–9.9 L gave 3.52 g (10%) of impure **7** (δ 7.43), and the final volume of 9.9–12.9 L gave 6.74 g (19%) of solid **7**. This **7** was rubbed with 20 mL of Et_2O and then was washed with Et_2O (2 × 20 mL) to yield 5.81 g (16%) of **7** (mp 64–65 °C); the **7** could be recrystallized from CCl_4 but only in yields of 18%, and this **7** was therefore analyzed directly: NMR ($CDCl_3$) δ 7.43 (m, 10 H), 2.86 (m, 4 H), 2.70 (t, 4 H), and 2.08 (m, 4 H); IR (Nujol) 3070, 2950, 1580, 1470, 1445, 1415, 1330, 1300, 1245, 1190, 1180, 1085, 1070, 1040, 995, 910, 830, 745, 690 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}O_2S_4$: C, 54.23; H, 5.57; S, 32.17. Found: C, 54.35; H, 5.56; S, 32.25.

Stability of the Tetrathiadecane 1-Monoxide 6 and 1,10-Dioxide 7. The 1-monoxide **6**, 1,10-dioxide **7**, and disulfide **8** can be distinguished readily by TLC using 50% EtOAc in hexane [R_f 0.10 (**7**), 0.44 (**6**), 0.66 (**8**)]. Differences in the aromatic region permit distinction by NMR of the disulfoxide **7** (PhSO, δ 7.43) and the disulfide **8** (PhS, δ 7.28). Use of these differences in TLC and NMR to assess whether the SO function of **6** and **7** was likely to undergo redox conversion to S and SO_2 revealed no change under ordinary conditions. For example, the NMR spectra of **6** and **7** showed no change after 9 days at ~25 °C or 1 month at 0 °C. The TLC behavior of **6** and **7** showed no change during 6 weeks at 25 °C. In using TLC behavior to assess the rapidity of disproportionation of **6** (as an unsymmetrical disulfide to form **7** and **8**), a solution of 19.1 mg (0.05 mmol) of **6** in 2 mL of MeOH was heated under reflux. The first indication of two new TLC spots (50% EtOAc/hexane) for the symmetrical disulfides **7** and **8** occurred in the interval of 31–42 h. The spots were identified as **7** and **8** by simultaneously doing authentic samples.

1,10-Diphenyl-1,5,6,10-tetrathiadecane (8). A solution of **1** (10.0 g, 53.6 mmol) in MeOH (30 mL) was added (0.5 h) to **3** (80 mL of a 2.25 M solution, 180 mmol) at 55 °C. Additional **3** (25 mL of a 2.25 M solution, 56 mmol, at each addition) was added to the resulting suspension at 55 °C at 5, 10, 20, 29, and 53 h. After a total stirring period at 55 °C of 95 h, the reaction mixture was cooled to ~25 °C. For determination of the reaction period, aliquots were removed from time to time, were acidified, were extracted with $CDCl_3$, and were examined by NMR for the CH_2Cl peak at δ 3.54; the size of this peak slowly decreased (28 h, 71% of **1**; 51 h, 21%) until at 75 h the size suggested that 9% of **1** remained. *Without acidification*, the reaction mixture was extracted with CH_2Cl_2 (3 × 35 mL). The organic layer was dried (Na_2SO_4) and then was concentrated to yield 8.62 g of yellow oil. The presence of a considerable amount of thiol in this oil was evidenced by a strong SH peak in the NMR at δ 1.30; when a $CDCl_3$ solution of material from a previous preparation was shaken with D_2O, the triplet at δ 1.30 disappeared, and the quartet for CH_2S became a triplet. The presence of the thiol without acidification probably results from decomposition of **10** to **13** during the prolonged reaction, followed by displacement of the following hydrolytic equilibrium in favor of the thiol **14** by extraction of the thiol into CH_2Cl_2: **13** + H_2O ⇄ **14** + NaOH. The oil was dissolved in EtOH (85 mL) and oxidized by adding 0.4 N aqueous KI_3 until the color of I_2 persisted. After addition of H_2O, the mixture was extracted with CH_2Cl_2. The organic layer was washed with 5% aqueous $NaHSO_3$ and water, dried (Na_2SO_4), and concentrated to 7.46 g of oil. This oil was chromatographed on 310 g of silica gel in a 8-cm-diameter column with 1% EtOAc in pentane as eluant, since separation of the mixture of **8** and presumed **12** by chemical means proved unpromising. Material contained in the eluant from 2.9 to 4.6 L amounted to 2.57 g (26%) of analytically pure **8**: n^{25}_D 1.6324; NMR ($CDCl_3$) δ 7.27 (m, 10 H), 2.97 (t, 4 H), 2.74 (t, 4 H), 1.96 (m, 4 H); IR (neat) 3070, 2930, 2250, 1585, 1480, 1440, 1420 (sh), 1340, 1295, 1250, 1090, 1070, 1030, 1000, 830, 740, 690 cm^{-1}.

Anal. Calcd for $C_{18}H_{22}S_4$: C, 58.96; H, 6.06; S, 34.98. Found: C, 59.16; H, 6.00; S, 35.16.

After a fraction (3.22 g) containing a mixture of the disulfide–disulfide **8** and the disulfide–sulfide **12** appeared at volumes of 4.6–5.4 L, material (0.42 g, 5%) appeared at volumes of 5.4–6.2 L; it was judged to be **12** by NMR ($CDCl_3$): δ 7.31 (m, 10 H), 3.01 (t, 4 H), 2.61 (t, 4 H), 1.87 (m, 4 H); n^{26}_D 1.6180.

3-Mercaptopropyl Phenyl Sulfoxide (4). Preparation and Properties. The sulfoxide **4** was freshly prepared by the following procedure, which is that preferred for **4**. A solution of **2** (14.0 g, 69.1 mmol) in MeOH (50 mL) was added (0.75 h) under Ar to freshly prepared **3** (50 mL of a 2.98 M solution, 149 mmol) at 55 °C. The resulting suspension was stirred at 55 °C for 1.5 h more, was cooled to ~25 °C, and then was washed with CH_2Cl_2 (1 × 200 and 2 × 50 mL). The clear solution was acidified to pH 1 by adding concentrated H_2SO_4 (~7 mL) with cooling and vigorous stirring. Considerable oil precipitated and was extracted immediately with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with H_2O (1 × 100 and 1 × 50 mL), dried (Na_2SO_4), and concentrated to constant weight (1.5 torr, 0.33 h): apparent yield of **4** as oil 8.29 g (60%); 0.1140 g of **4** consumed 4.8 mL of 0.0922 N KI_3 (78% thiol; therefore the actual yield of **4** was 47%). Determination of the amount of thiol by Ellman's technique[16] gave a value of 75% thiol. All of the following data then were obtained as rapidly as possible (about 1 h). This **4** gave an immediate strong Feigl test (loss of color and vigorous evolution of N_2 from the I_2–azide reagent):[17] n^{26}_D 1.5917; NMR ($CDCl_3$) δ 8.0–7.2 [m, 5 H; with δ 7.95 ($PhSO_2$ impurity), 7.60 (PhS(O) and $PhSO_2$ impurity), and 7.33 (PhS impurity)], 2.91 (m, 2 H), 2.66 (q, collapses to t on addition of D_2O, 2 H), 2.05 (m, 2 H), 1.35 (t, 1 H, disappears on addition of D_2O, SH); IR (neat) 3460, 3060, 2940, 2540, 1580, 1515, 1480, 1440, 1300, 1260, 1145, 1085, 1040, 995, 745, 690 cm^{-1}. The **4** was soluble in MeOH, EtOH, $CHCl_3$, and CH_2Cl_2 but was insoluble in H_2O. A sample of this **4** stored at ~25 °C for 8 days gave a value of 74% thiol by titration with KI_3.

3-[(2′,4′-Dinitrophenyl)thio]propyl phenyl sulfoxide, the 2,4-dinitrophenyl sulfide derivative of **4**, was prepared by addition of **4** (0.50 g, 2.5 mmol assuming 100% purity) in EtOH (10 mL) containing 1 mL of 10% NaOH to a solution of 2,4-dinitrochlorobenzene (0.50 g, 2.5 mmol) in EtOH (2.5 mL). The mixture was heated on a steam bath for 10 min and then was subjected to filtration while hot. The yellow-orange product that precipitated upon cooling was collected by filtration (0.43 g, 47%); this material sintered at ~109 °C, melted at ~114–117 °C, showed orange to deep red color changes from ~117–~132 °C, and then remained a deep red liquid. This product, recrystallized twice from 95% EtOH (~25 mL), amounted to 0.21 g (23%): the melting point behavior was exactly that of the product before recrystallization; NMR ($CDCl_3$) δ 9.04 (d, 1 H), 8.36 (dd, 1 H), 7.53 (m, 6 H), 3.30–2.70 (m, 4 H), 2.23 (m, 2 H); IR (KBr) 3120, 1590, 1520, 1510, 1445, 1390, 1340, 1310, 1270, 1240, 1185, 1130, 1090, 1045, 1025, 1000, 960, 915, 830, 745, 730, 685 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}N_2O_5S_2$: C, 49.16; H, 3.86; N, 7.65; S. 17.50. Found: C, 49.19; H, 3.94; N, 7.54; S, 17.40.

When the preparation of **4** was attempted similarly with 20.0 g of **2** but with omission of MeOH, no reaction occurred. Recovery of the **2** and use of a procedure much as that above then gave 16.0 g (81%) of **4** (93% thiol by KI_3 titration; hence the actual yield of **4** was 75%).

In an attempt to study the interaction of **4** with the disulfides **6** and **7**, samples of **4** were mixed with analytically pure **6** and analytically pure **7**. The mixtures of **4** with **6** and of **4** with **7** as well as a sample of **4** alone were dissolved in $CHCl_3$ and monitored by TLC (50%; EtOAc in hexane). Initially, the sample of **4** had a major spot for **4** at R_f 0.38, with spots corresponding to **6** (R_f 0.46), **7** (R_f 0.05), and **8** (R_f 0.71) and unidentified spots at R_f 0.61 and R_f 0.18. The mixture of **4** with **6** demonstrated a slight increase in intensity of the spot corresponding to **8** after ~16 h at ~25 °C. The mixture of **4** with **7** gave inconclusive results.

(16) Ellman, G. L. *Arch. Biochem. Biophys.* **1959**, *82*, 70–77.
(17) Feigl, F. "Spot Tests in Organic Analysis"; Elsevier: New York, 1960; pp 242–245.

To study the rate of reaction of 4, we divided 6.01 g of the reaction product (78% by I_2 titration) dissolved in 60 mL of MeOH (previously purged with Ar) into parts A–D. Part A (6 mL) was stored at −26 °C under Ar as a control. Part B (18 mL) was allowed to stir at 23–24 °C under Ar. Concentrated H_2SO_4 (25 μL, 0.9 mequiv) was added to part C (18 mL); this MeOH solution of 4 contained ~9 mmol of 4 (on a weight basis) and had a pH of 2. To part D (18 mL) was added 329 μL of 4.1 N $NaOCH_3$ (1.35 mequiv) to give a pH of 10. The solutions containing H_2SO_4 and $NaOCH_3$, as well as the solution containing only 4, were stored at 23–24 °C under Ar, and 2-mL aliquots were titrated with 0.0922 N KI_3 at various time intervals. The pH of the solutions was checked periodically, with no change being observed. Rate constants were obtained by taking the slope of the least-square lines in Figure 1; Figure 1 shows the I_2 titer after subtraction of the infinity titer determined at 72 h. The rate constants (with check values from a different preparation of 4 in parentheses) were 0.12 h^{-1} (0.14 h^{-1}) for 4 alone, 0.13 h^{-1} (0.13 h^{-1}) for 4 in the presence of H_2SO_4, and 0.10 h^{-1} (0.08 h^{-1}) for 4 in the presence of $NaOCH_3$. The half-lives (calculated as $t_{1/2} = 0.693/k$) were 5.8 (5.0), 5.3 (5.3), and 6.9 h (8.7 h), respectively.

Inspection of the materials, isolated from the infinity titer samples, by TLC (50% EtOAc in hexane), indicated 6 (R_f 0.49) to be the principal component, along with significant amounts of 7 (R_f 0.10) and 8 (R_f 0.74); minor unidentified components were observed at R_f 0.67 and R_f 0.24. The ratios by NMR of the moieties PhS/PhS(O) were 1.0 for 4 alone, 1.0 for 4 in the presence of H_2SO_4, and 0.5 for 4 in the presence of $NaOCH_3$.

Initial attempts were made to study the redox reaction of 4 by NMR. These experiments, done in $CDCl_3$ instead of MeOH, led to significantly slower rates [thus a solution of 4 in $CHCl_3$ (119.7 mg in 1 mL) showed no change by NMR and titration during 8 days (79% SH by I_2 titration vs. 78% initially)]. For example, in early experiments an average of the percent SH based on integrals of SH/all aromatic protons and of SH/CH_2 β to S showed a decrease from an initial ~27% to ~17% in 240 h and to ~11% in 596 h; the ratio for PhS/PhSO increased meanwhile from 0.46 to 0.66 to 0.68, respectively. NMR spectra thus proved useful for qualitatively assessing trends in the loss of SH and the increase of PhS. For several reasons, however, they were unpromising for quantitative work.

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Vinyl Selenides and Selenoxides: Preparation, Conversion to Lithium Reagents, Diels–Alder Reactivity, and Some Comparisons with Sulfur Analogues[1]

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A variety of aryl vinyl selenides are prepared by reaction of vinyl Grignard reagents with aryl selenenyl bromides or by reductive elimination of the adducts of [bis(arylseleno)methyl]lithiums with carbonyl compounds. Deprotonation of phenyl vinyl selenide is achieved with LDA at −78 °C in THF. Vinyl selenides with β-alkyl groups require LiTMP and warmer temperatures (−50 °C) for complete deprotonation. Allylic lithium reagents were obtained from 1-propenyl and 2-methyl-1-propenyl selenides whereas 1-butenyl or 3-methyl-1-butenyl selenides gave vinyl lithium reagents. Reaction with electrophiles proceeds in good to excellent yield. Primary halides require HMPA to react well. Unhindered carbonyl compounds react without enolization. Deprotonation with LDA is shown to be reversible, and during competitive deprotonation studies with LDA, aryl vinyl sulfides are found to be thermodynamically less acidic than aryl vinyl selenides ($K_{S/Se}$ = 0.21 for phenyl vinyl and 0.3 for *m*-(trifluoromethyl)phenyl vinyl). Deprotonation with LiTMP is shown to be irreversible, and competitive deprotonation studies showed vinyl selenide to be kinetically more acidic as well [$k_{S/Se}$ = 0.37 (phenyl vinyl), 0.42 (*m*-(trifluoromethyl)phenyl vinyl)]. Most studies have shown sulfur compounds to be more acidic. *m*-(Trifluoromethyl)phenyl allyl sulfide, as expected, is more acidic than the selenium compound ($k_{S/Se}$ = 3.8). Vinyl selenoxides can be prepared with *m*-chloroperbenzoic acid. They are not thermally stable enough to serve as acetylene equivalents in Diels–Alder reactions. Phenyl vinyl selenide gives a Diels–Alder addition product with 1,4-diphenylisobenzofuran but failed to give cycloaddition products with less reactive dienes. Phenyl vinyl selenoxide does not give a useful yield of lithium reagent upon reaction with amide bases.

A number of useful functional group transformations can be achieved by the introduction and removal of selenium functions.[2] Vinyl selenides and selenoxides have the potential of combining such processes with carbon–carbon bond-forming reactions involving the vinyl group. We report here our results on the preparation and deprotonation of vinyl selenides and selenoxides, on the further transformations of the lithium reagents so formed, and on the relative kinetic and thermodynamic acidities of several vinyl and allyl selenides and sulfides. We also report on

(1) For previous papers in our series on organoselenium chemistry see: (a) H. J. Reich, F. Chow, and S. K. Shah, *J. Am. Chem. Soc.*, **101**, 6638 (1979); (b) H. J. Reich and J. M. Renga, *J. Org. Chem.*, **40**, 3313 (1975); (c) H. J. Reich, *ibid.*, **39**, 428 (1974); (d) H. J. Reich, J. M. Renga, and J. E. Trend, *Tetrahedron Lett.*, 2217 (1976); (e) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Org. Chem.*, **39**, 2133 (1974); (f) H. J. Reich and M. L. Cohen, *J. Am. Chem. Soc.*, **101**, 1307 (1979); (g) S. K. Shah, Ph.D. Thesis, University of Wisconsin, Madison, 1977; (h) H. J. Reich and F. Chow, *J. Chem. Soc., Chem. Commun.*, 790 (1975); (i) H. J. Reich and S. K. Shah, *J. Org. Chem.*, **42**, 1773 (1977); (j) H. J. Reich, *ibid.* **40**, 2570 (1975); (k) H. J. Reich, S. K. Shah, and F. Chow, *J. Am. Chem. Soc.*, **101**, 6648 (1979); (l) H. J. Reich and W. W. Willis, Jr., *ibid*, **102**, 5967 (1980).

(2) (a) H. J. Reich in "Oxidation in Organic Chemistry, Part C", W. Trahanovsky, Ed., Academic Press, New York, 1978, p 1; (b) H. J. Reich, *Acc. Chem. Res.*, **12**, 22 (1979); (c) D. L. J. Clive, *Tetrahedron*, **34**, 1049 (1978).

0022-3263/81/1946-2775$01.25/0