Sulfinic Acids and Related Compounds. 19. Synthesis and Properties of 1-Propane-, 1-Butane-, and 1-Pentanesulfinates Terminally Substituted with Di- and Trisulfide Functions[1,2]

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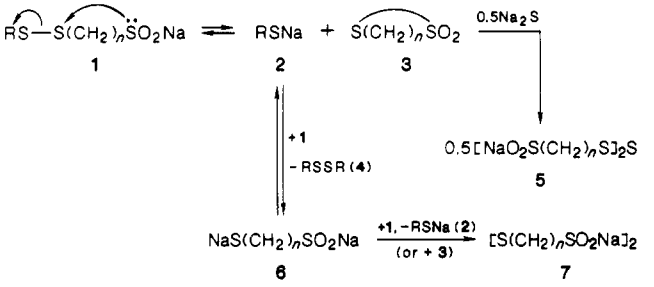
Preparation and reactions are compared, for n = 3–5, of disulfide sulfinates with the structure $RSS(CH_2)_nSO_2Na$ (**1**) and of trisulfide bisalkanesulfinates with the structure $[NaO_2S(CH_2)_nS]_2S$ (**5**). The di- and trisulfides were prepared by reaction of cyclic thiosulfonates, and optimum preparations of the thiosulfonates are considered. For **1**, R was $HO_2CCH_2CH_2$ (**10–12**), p-$CH_3C_6H_4$ (**13–15**), C_6H_5 (**16** and **17**), 2,4,6-$(CH_3O)_3C_6H_2$ (n = 4; **18**), and $H_2N(CH_2)_2$ (n = 4; H in lieu of Na; **19**). Several of the di- and trisulfides were sensitive to light (the trisulfides about equally). Much faster conversion for the disulfides occurred with heat for R = p-$CH_3C_6H_4$ when n was 3 (**13**) or 4 (**14**) than when n was 5 (**15**); these results with **13–15** point as principal processes to homolysis with light but heterolysis with heat, the latter with operation of a neighboring-group effect of SO_2Na on the SS bond. Sodium methanesulfinate readily forms a thiosulfonate with sulfur, and the implications of this reaction are developed for the chemistry of the trisulfide bissulfinates (**5**), where a novel rearrangement produces disulfide thiosulfonates (**21**, n = 3–5).

Disulfides with the general structure of **1** and trisulfides with that of **5**, both with n = 4, have shown promise for protecting mammals against otherwise lethal effects of ionizing radiation; they are of particular interest since they lack nitrogen, which typically is present in antiradiation agents.[3] As shown in Scheme I, a significant feature of the chemistry of the disulfides (**1**) has been cyclization in solution to produce a thiolate ion (**2**) and a cyclic thiosulfonate (**3**); subsequent reactions of the kind in Scheme I then can lead to the two symmetrical disulfides **4** and **7**.[4] This paper reports a study of compounds with the general structure of **1** and **5**, where results are compared for n = 3–5 so that the effects of varied chain length could be ascertained. Also reported is an astonishing new rearrangement of the trisulfide sulfinate **5**, which apparently has its origin in a neighboring-group effect for **5** resembling that shown for the disulfide **1** in Scheme I.

Disulfides of type **1** are made by reactions of a thiolate ion (**2**) and a cyclic thiosulfonate (**3**),[4a] and trisulfides of type **5** are made by reaction of Na_2S and **3** (Scheme I).[5] With both the disulfides **1** and trisulfides **5**, reactions usually go virtually to completion very rapidly, so that these products can be precipitated with Et_2O before equilibria of the kind shown in Scheme I become established. Isolation of **1** and **5** thus depend on kinetic control and subsequent equilibrations in solution on thermodynamic control. Since we have been unable to purify the salts produced by recrystallization or chromatography,

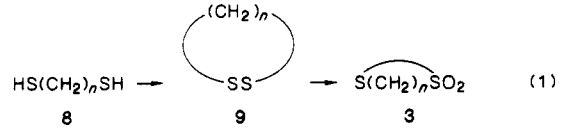
Scheme I



preparation of pure products depends on pure starting materials. The best purification found so far for compounds of types **1** and **5** is dissolution in a minimum of methanol, precipitation and removal of ca. 5–10% with ether, and then precipitation of ca. 80%, leaving a little of the salt in solution.

Preparation of Cyclic Thiosulfonates (3).[2] Since our yields of the thiosulfonates (**3**) used as starting materials often have been low and inconsistent, determination of the best routes for preparing these thiosulfonates was an important first step in synthesizing members of the classes **1** and **5**.

In our early work, numerous methods were investigated for converting the dithiol **8** (n = 3) to 1,2-dithiolane (**9**, n = 3) and then the dithiolane to the cyclic thiosulfonate **3** (n = 3).[6] For our present purposes, however, a one-step oxidation of the dithiol **8** (n = 3) to **3** (n = 3), with H_2O_2 in AcOH, as later developed by Harpp, Gleason, and Ash,[7] gave about the same yield (31%) as that overall from the two-step sequence of eq 1 and ordinarily was used. Sim-



(1)

ilarly, we previously studied several methods for preparing 1,2-dithiane (**9**, n = 4) and converting it to 1,2-dithiane 1,1-dioxide (**3**, n = 4).[6] Here also, the one-step oxidation

(1) (a) Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Louisville, KY, November 3–5, 1986. (b) Paper 18: Harmon, J. P.; Field, L. *J. Org. Chem.* **1986**, *51*, 5235. (c) This investigation was supported by the U.S. Army Medical Research and Development Command, Department of the Army, under Research Contracts Nos. DAMD 17-79-C-9039 and DAMD 17-85-C-5181; this paper has been designated as Contribution No. 1812 to the U.S. Army Drug Development Program. (d) We thank Prof. B. J. Sweetman for mass spectra.

(2) The doctoral dissertation of J.D.M., from which this paper was abstracted, can be consulted for further details (Vanderbilt University, May 1987).

(3) (a) Srivastava, P. K.; Field, L.; Grenan, M. M. *J. Med. Chem.* **1975**, *18*, 798. (b) 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.

(4) See 4a and 4b and references cited in each: (a) Chandra, R.; Field, L. *Phosphorus Sulfur* **1986**, *27*, 247. (b) R. Chandra; Field, L. *J. Org. Chem.* **1986**, 51, 1844.

(5) Field, L.; Eswarakrishnan, V. *J. Org. Chem.* **1981**, *46*, 2025.

(6) Field, L.; Barbee, R. B. *J. Org. Chem.* **1969**, *34*, 36.

(7) Harpp, D. N.; Gleason, J. G.; Ash, D. K. *J. Org. Chem.* **1971**, *36*, 322.

0022-3263/88/1953-0396$01.50/0

of Harpp et al. gave much the same result (31%) as that overall from the two steps of eq 1 and ordinarily was used to prepare the dithiane dioxide (**3**, $n = 4$).

The low yield in the overall conversion of dithiols (**8**) to the cyclic thiosulfonates undoubtedly is caused by a poor result in the second step of eq 1 rather than in the first (cf. relative results in ref 6), perhaps because S–S cleavage and recombination are required. Accordingly, we initially attempted to improve the oxidation of the intermediary cyclic disulfides (**9**). In common with extensive earlier such efforts,[6] however, we obtained unpromising results with *m*-chloroperoxybenzoic acid, Oxone (a potassium hydrogen persulfate product), or 2-(phenylsulfonyl)-3-phenyloxaziridine.[8] Also unavailing was a possibility suggested by Oae and co-workers that two types of oxidant can be recognized for converting *SS*-monoxides to *SS*-1,1-dioxides, viz. electrophilic and nucleophilic, and that the latter differ in attacking an S(O)S system at S(O) rather than S.[9] Since most of our present and earlier oxidants probably have been electrophilic ones, we tried a mixture reported to effect nucleophilic attack without S–S cleavage,[9] i.e. $NaIO_4$–AcOH–H_2O, for the oxidation of 1,2-dithiane 1-monoxide. Here too, a yield of 40% offered little advantage over the 31% mentioned for direct oxidation of the dithiol 8 ($n = 4$) to the 1,1-dioxide by the procedure of Harpp et al.[7]

For the preparation of 1,2-dithiepane 1,1-dioxide (**3**, $n = 5$), on the other hand, the direct oxidation of 1,5-pentanedithiol (**8**, $n = 5$) with H_2O_2 in AcOH failed. Extensive polymerization occurred, and no dioxide could be isolated, no doubt because of the relatively difficulty of closing the seven-membered ring. 1,2-Dithiepane 1,1-dioxide (**3**, $n = 5$) was prepared best by resorting to the two-step sequence of eq 1. The dithiol was oxidized to the cyclic disulfide (**9**, $n = 5$) with $FeCl_3$ by a high-dilution method of Schöberl and Gräfje;[6,10] Schöberl and Gräfje improved the yield from 30% to 80% by using high-dilution conditions (2-day addition) and, without their special precautions of quartzware and exclusion of light,[10] we improved the yield from 54%[6] to 75% by extending the addition from 1.5 to 5 days at still higher dilution.[2] For the second step, H_2O_2 in AcOH previously led to 1,2-dithiepane 1,1-dioxide (**3**, $n = 5$) in low yield (17%, mp ca. 25 °C).[6] Although we were able to improve the yield by this means on occasion to 49% (mp 50.5–52 °C),[2] results were inconsistent and the yield sometimes dropped to 20%. The best oxidant proved to be sodium perborate, which oxidizes sulfides to sulfoxides or sulfones.[11] Although our yields were only ca. 35%, they were consistent. Furthermore, very little monoxide or polymer were formed, and the isolation was cleaner and more convenient than with H_2O_2–AcOH (emulsions). Use of the Oae procedure ($NaIO_4$–AcOH–H_2O) with 1,2-dithiepane monoxide gave mostly polymer, along with the 1,1-dioxide in only 9% yield,[9] and *m*-chloroperoxybenzoic acid led only to polymer.

Disulfide Sulfinates (1). The cyclic thiosulfonates (**3**) were converted to unsymmetrical disulfides (**1**), for comparison of the effects of chain length, by the reaction of **2** with **3** (Scheme I). The procedure used for earlier compounds of structure **1** was satisfactory, where NaOMe was added to a solution of the thiol (RSH) and cyclic thiosulfonate (**3**, $n = 4$) in methanol, followed by the precipitation outlined above.[4a,12] Table I shows the disulfides prepared. A puzzling difference arose in repetition of the preparation of **11** ($n = 4$).[12] The product showed a very strong new IR band at 1550 cm^{-1}, although TLC and NMR spectra still were consistent with **11**. The cause was traced to precipitation from methanol by acetone rather than ether. When **11**, precipitated with ether (no 1550-cm^{-1} band), was reprecipitated with acetone, it developed the band at 1550 cm^{-1}. The carboxyl group of **11** presumably interacts with the carbonyl group of the acetone strongly, since the band decreased only to 20% after 2 days at 100 °C under reduced pressure.

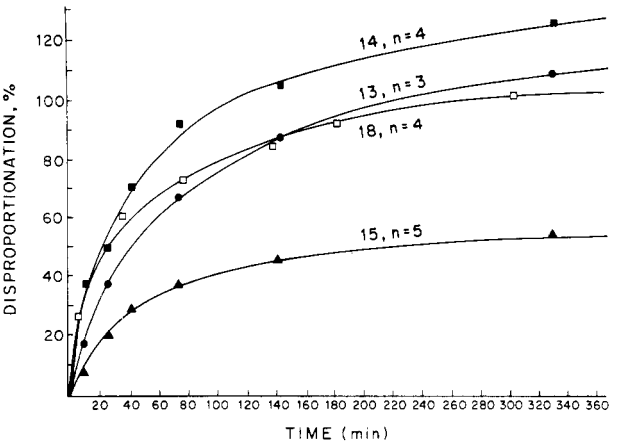


Figure 1. Plot of percent disproportionation at ca. 25 °C vs time for *p*-$CH_3PhSS(CH_2)_nSO_2Na$ (**13**, $n = 3$, ●; **14**, $n = 4$, ■; **15**, $n = 5$, ▲) and 2,4,6-$(CH_3O)_3C_6H_2(CH_2)_4SO_2Na$ (**18**, □). Results exceeding 100% are attributable to small sample sizes and the difficulty of drying without loss of the disulfide.

As Table I shows, the three carboxy sulfinates **10–12** were surprisingly alike in being considerably resistant to disproportionation, whether induced by heat or light, perhaps because $HO_2C(CH_2)_2S^-$ is a relatively poor leaving group for the disproportionation of **1** shown in Scheme I; this feature was noted before for **11**.[12] Thus, as indicated by NMR and TLC, change in aqueous solutions in the dark at 68 °C was first noted only at ca. 80 min. The cyclic thiosulfonate **3** ($n = 4$) was isolated previously from **11** at ca. 25 °C,[12] but NMR did not permit clearcut conclusions as to the products produced under the present more vigorous conditions. Under UV light, **10–12** behaved quite like one another and were affected enough to indicate the advisability of protecting such disulfides from strong light.

The aryl disulfides **13–18** were far less resistant to heat than **10–12** (Table I), and aqueous solutions became turbid within a few minutes at ca. 25 °C owing to formation of the insoluble diaryl disulfides. Changes in **13–15** and **18** were followed by periodic removal and weighing of the diaryl disulfide. Although this precipitation of course precluded equilibration, the relative amounts afford a realistic view of the behavior and lifetimes of the aryldithio compounds in water. Figure 1 shows the results.

As Table I shows, the pentamethylene disulfide **15** was far more resistant to disproportionation at either ca. 25 or 68 °C than were **13** and **14** with three and four methylene groups. These results appear to support a heterolytic mechanism for the thermal reactions, since homolysis should involve cleavage and intermolecular reactions essentially independent of chain length. They also support the neighboring-group effect illustrated for **1** in Scheme

(8) We are indebted to Prof. Franklin A. Davis of Drexel University for a sample of the oxaziridine; cf. Davis, F. A.; Jenkins, R., Jr.; Yocklovich, S. G. *Tetrahedron Lett.* **1978**, 5171.
(9) (a) Kim, Y. H.; Takata, T.; Oae, S. *Tetrahedron Lett.* **1978**, 2305. (b) Oae, S.; Takata, T. *Tetrahedron Lett.* **1980**, *21*, 3213.
(10) Schöberl, A.; Gräfje, H. *Justus Liebigs Ann. Chem.* **1958**, *614*, 66.
(11) McKillop, A.; Tarbin, J. A. *Tetrahedron Lett.* **1983**, *24*, 1505.
(12) Srivastava, P. K.; Field, L. *J. Chem. Eng. Data* **1986**, *31*, 252.
(13) Field, L.; Grimaldi, J. A. R., Jr.; Hanley, W. S., Holladay, M. W.; Ravichandran, R.; Schaad, L. J.; Tate, C. E. *J. Med. Chem.* **1977**, *20*, 996.
(14) Field, L.; Barbee, R. B. *J. Org. Chem.* **1969**, *34*, 1792.

Table I. Preparation and Properties of Disulfide Sulfinate Salts, $RSS(CH_2)_nSO_2Na$ (1)[a]

no.	for $RSS(CH_2)_nSO_2Na$ R	n	yield, %	% disproportionation (min)[b] dark ca. 25 °C	dark ca. 68 °C	UV	spectra[c] IR, cm^{-1}	^1H NMR, δ	^{13}C NMR, δ	ref to prev report
10	$HO_2C(CH_2)_2$	3	71	*d*	ca. 5 (80)[e,f]	ca. 10 (20)[e]	3700–3200, 1700, 1260, 1200, 1010, 980, 930, 720	(D_2O) 2.87 (m, 6), 2.46 (m, 2), 2.00 (m, 2)	(D_2O) 179.86, 61.87. 40.12, 37.30, 36.11, 24.05	
11		4	70	*d*	ca. 5 (80)[f]	ca. 10 (20)[e]			(D_2O) 179.78, 62.92, 40.55, 37.27, 36.13, 30.47, 23.19	12
12[a]		5	76	*d*	ca. 5 (80)[e,f]	ca. 10 (20)[e]	3650–3200, 1710, 1590, 1420, 1230, 1040, 1030, 1010, 980	(D_2O) 316–2.64 (m, 6), 2.42 (t, 2), 1.92–1.20 (m, 6)	(D_2O) 180.51, 63.30, 40.74, 37.81, 36.38, 30.61, 29.63, 23.78	
13	*p*-$CH_3C_6H_4$	3	85	50 (40)[g]	50 (6%)[g] 100 (<120)[g]	50 (50)[e] 100 (100)[e]	1500, 1405, 1390, 1320, 1260, 1130, 1090, 1050, 1020, 1000, 980, 975, 810, 770, 740, 700	(CD_3OD) 7.40–7.00 (m, 4), 2.80 (t, 2), 2.40–1.88 (m, 7)	(CD_3OD) 138.39, 135.33, 130.67, 129.72, 61.79, 39.47, 23.19, 21.00	
14		4	60	50 (25)[g]	50 (3)[g] 100 (<120)[g]	50 (20)[e] 100 (80)[e]				13
15		5	63	50 (300)[g]	50 (20)[g] 100 (<120)[g]	50 (15)[e] 100 (40)[e]	1490, 1300, 1110, 1040, 1010, 990, 970, 800, 720	(CD_3OD) 7.40–7.00 (m, 4), 2.68 (t, 2), 2.36–2.04 (m, 5), 1.80–1.20 (m, 6)	(CD_3OD) 138.39, 135.46, 130.72, 129.58, 63.14, 39.74, 29.66, 29.12, 23.21, 21.00	
16	C_6H_5	3	86	*h*	*h*	*h*	1575, 1470, 1430, 1400, 1005, 980, 970, 960, 860, 820, 730, 685	(CD_3OD) 7.56–7.12 (m, 5), 2.82 (t, 2), 2.32 (t, 2), 2.12–1.80 (m, 2)	(CD_3OD) 138.71, 130.00, 128.88, 127.96, 61.70, 39.49, 23.19	
17		5	74	*h*	*h*	*h*	1580, 1440, 1220, 1000, 740, 690	(CD_3OD) 7.52–7.00 (m, 5), 2.68 (t, 2), 2.20 (t, 2), 1.80–1.20 (m, 6)	(CD_3OD) 138.88, 130.04, 128.69, 127.93, 63.09, 39.79, 29.71, 29.12, 23.16	
18	2,4,6-$(CH_3O)_3C_6H_2$	4	78	50 (20–25)[g] 100 (300)[g]		*i*	1600, 1460, 1420, 1340, 1230, 1210, 1160, 1130, 1090, 1000, 960, 820, 740	(CD_3OD) 6.19 (s, 2 H), 3.82 (2 s, 9 H), 2.75 (t, 2 H), 2.25 (t, 2 H), 1.73 (m, 4 H)	(CD_3OD) 164.58, 163.69, 106.53, 92.53, 63.03, 56.69, 56.02, 39.47, 30.01, 22.75	
19	$H_2N(CH_2)_2$ (with H for Na)[j]	4	53	(<1.5 h)[k]				(D_2O) 3.42 (t, 2), 3.14 (t, 2), 2.84 (t, 2), 2.42 (t, 2), 2.04–1.44 (m, 4)	(D_2O) 62.17, 40.01, 39.55, 36.16, 29.61, 22.40	14

[a] Satisfactory analytical data (±0.4% for C, H, and S) were reported for all new compounds (no "previous report") listed in Table I, as well as for **19**, except for compound **12**·0.4H_2O (calcd for H, 5.24; found 4.66). [b] Disproportionation percent, calculated as described in the Experimental Section, observed at the time shown in parentheses. [c] Included only when not previously reported. Other values were consistent with all earlier reports. [d] negligible. [e] By NMR in D_2O or CD_3OD; only very rough estimates could be made for **10–12**. [f] By TLC. [g] By isolation (see Figure 1). [h] Much like the tolyl series, **13–15**, so not done quantitatively. See text. [i] In MeOH, trace of precipitate in 180 min. [j] Compound **19** seems best represented as $H_3N^+(CH_2)_2SS(CH_2)_4SO_2^-$. [k] Lack of cleanly separated NMR peaks precluded calculation of percent disproportionation, but a considerable amount of **20** formed in 1.5 h at ca. 25 °C in ambient light.

I, since one would expect a much more difficult cyclization for $n = 5$ (in **15**) than for $n = 3$ or 4 (**13**, **14**). In contrast, the greater similarity of results under UV light (followed by NMR) indicates that the light-induced reactions have a large homolytic component, where intermolecular reactions minimize the importance of chain length. We have commented before on the fact that unsymmetrical disulfides can disproportionate by either heterolytic or homolytic paths depending on the circumstances (cf. ref 1b and citations therein). Aqueous solutions of **16** and **17**, like those of **13**–**15**, became turbid in a few minutes, much more rapidly with **16** than **17**. The phenyl disulfides will be of interest in antiradiation studies as reference points between the active tolyl series and the virtually inactive chloro series.[15] The radioprotective activity of **14**[15] led to the synthesis of **18** with still more electron-donating substituents. Although an aqueous solution of **18** became turbid in seconds, the longer term resistance to disproportionation, reflected in Figure 1, was much like that of the *p*-tolyl counterpart, **14**; a log plot of the results from **18** in Figure 1 was kinetically inconclusive.

We reported the aminoethyl compound **19** some years ago (Table I).[14] In connection with present interests, we reexamined **19** and were startled by a mass spectrometric peak at twice the molecular weight of **19** (along with the peak expected for **19**). To allay concern that the **19** reported earlier had not been in fact a mixture of disproportionation products that would produce the salt **20** (eq 2), a number of experiments were done. Our conclusion

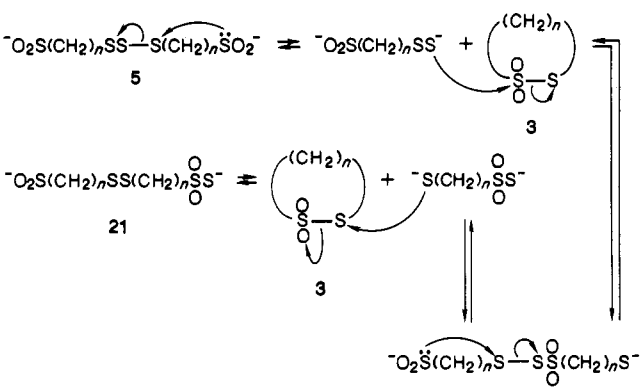
$$\underset{\mathbf{19}}{2H_3N^+(CH_2)_2SS(CH_2)_4SO_2^-} \rightleftharpoons \underset{\mathbf{20}}{[H_3N^+(CH_2)_2S]_2{\cdot}[^-O_2S(CH_2)_4S]_2} \quad (2)$$

was that the report of **19** as a pure compound was correct but that disproportionation in water occurs rather readily to produce **20** (presumably water used in preparing the MS sample led to the MS result). The evidence was the following:[2] (1) The change of the NMR spectrum of **19** in D_2O during 1.5 h at ambient conditions to a new NMR spectrum, A, was consistent with approach to an equilibrium mixture containing **20** (which has a distinguishably different NMR spectrum from **19**). (2) Amino disulfides such as the free base of **19** disproportionate very rapidly.[16] When **19** was treated with an equimolar amount of NaOD, heated 10 min at 100 °C, and reacidified with DCl equivalent to the NaOD, essentially spectrum A resulted (hence, as in (1), pure **19** had disproportionated). (3) A mixture of the two disulfides that would produce **20** (**7**, with $n = 4$; $[ClH_3N(CH_2)_2S]_2$) equilibrated in D_2O in 70 min at ca. 25 °C to give essentially spectrum A; also, treatment of a mixture of these two disulfides with NaOD/HCl as in (2) gave spectrum A. (4) A mixture of the two disulfides mentioned and **20** (molar proportions 1:1:2) gave a spectrum different from that of **19** and quite similar to spectrum A.

Trisulfides (5). The tetramethylene trisulfide **5** ($n = 4$) was prepared as usual (Scheme I),[17] and **5** with $n = 3$ and 5 were obtained similarly (yields 73–85% after precipitation).

The stabilities of the trisulfides to heat and light were of much interest. As mentioned, thermally induced changes of disulfides such as **1** often have contrasted with changes caused by UV, no doubt as a reflection of heterolysis vs homolysis. Thermal stabilities of the trisulfides were followed with NMR spectra while solutions were heated at 68 °C in the dark. After 18 h, **5** ($n = 5$) had rearranged completely to a compound that to our astonishment proved to be the disulfide monosulfinate monothiosulfonate **21** ($n = 5$). This type of rearrangement appears to be totally novel. Scheme II shows one of several mechanisms that can be written for the rearrangement. NMR afforded part of the evidence for the structure of **21** ($n = 5$), based on models described below.[2] Thus the peak for CH_2SSSCH_2 (δ 2.93, t, 4 H) disappeared, as did that for one of the two CH_2SO_2Na groups (δ 2.32, t, 4 H to 2 H). Meanwhile, the peak for CH_2SSCH_2 of **2** ($n = 5$) appeared (δ 2.73, 4 H, t), along with a peak for one CH_2SO_2SNa (δ 3.30, t, 2 H). The trisulfides **5** ($n = 4$) and **5** ($n = 3$) showed similar changes at 68 °C but with complete conversion at 80 and 40 min, respectively, in contrast to 18 h for **5** ($n = 5$). ^1H NMR, ^{13}C NMR, and IR spectra were consistent with structure **21** ($n = 4$) for the rearrangement product of **5** ($n = 4$); IR absorption persisted at 980 cm^{-1} (SO_2Na), but strong new bands appeared at 1180 and 1070 cm^{-1} (SO_2SNa; vide infra). At 68 °C in the dark, the relative stabilities are **5** ($n = 5$) $\gg$ **5** ($n = 4$) > **5** ($n = 3$). The same order was observed at ca. 25 °C in the dark: **5** ($n = 5$) showed no change in 2 h, **5** ($n = 4$) was 40% converted to **21** ($n = 4$) in 2 h, and **5** ($n = 3$) was 50% converted in 2 h to **21** ($n = 3$).

Scheme II



Assignment of the peak at δ 3.30 to CH_2SO_2SNa was based on sodium methanethiosulfonate (**23**), which was synthesized by heating the sulfinate **22** with sulfur (eq 3).[18] The NMR peak at δ 2.30 for **22** shifted to 3.30 for **23**; **23** no longer showed the IR band at ca. 1000 cm^{-1} characteristic of SO_2Na and, instead, showed strong bands at 1200 and 1090 cm^{-1}, which were attributed to SO_2S (vide infra); it is noteworthy that one molar proportion of sulfur dissolved after only 10 min of reflux, to give **23**, since for an arenesulfinate we have used ca. 3 days.[1b]

$$\underset{\mathbf{22}}{CH_3SO_2Na} \xrightarrow{S,\ H_2O,\ \Delta} \underset{\mathbf{23}}{CH_3SO_2SNa} \xrightarrow{PhCH_2Br} \underset{\mathbf{24}}{CH_3SO_2SCH_2Ph} \quad (3)$$

$$3\ \mathbf{24} + 4OH^- \rightarrow \underset{\mathbf{25}}{(PhCH_2S)_2} + 3\underset{\mathbf{22}}{CH_3SO_2^-} + PhCH_2SO_2^- + 2H_2O \quad (4)$$

(15) For example, **14** led to 80% survival of mice at a dose ip of 63 mg/kg.[3b] The best survival for the *p*-chloro analogue was 10% at 75 mg/kg (unpublished data kindly provided by J. J. Clement of A. D. Little, Inc., and supplied through the Walter Reed Army Institute of Research).

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

(17) Field, L.; Khim, Y. H. *J. Med. Chem.* **1972**, *15*, 312.

(18) Alkanethiosulfonates usually have been synthesized from sulfonyl chlorides, but our procedure from the alkanesulfinate salt is not completely novel since sodium β-aminoethanethiosulfonate has been synthesized from the sulfinic acid and sulfur in a two-phase alkaline system: Westley, J.; Heyse, D. *J. Biol. Chem.* **1971**, *246*, 1468.

In order to provide confirmation of structure for **21** (n = 4), the thiosulfonate **23** was used as a model and was benzylated to give **24**. With the presumption that the stoichiometry for the reaction of **24** with alkali should resemble that stated by Kice and Rogers for $ArSO_2SAr$,[19] eq 4 may apply; on this basis, the yield of benzyl disulfide from the model **23** was 50%. When **21** (n = 4) was benzylated in the same way (eq 5), the IR spectrum of **26** met

$$\mathbf{5}\ (n=4) \xrightarrow{\Delta,\ H_2O} \mathbf{21}\ (n=4) \xrightarrow{PhCH_2Br} PhCH_2S(O)_2(CH_2)_4SS(CH_2)_4S(O)_2SCH_2Ph \xrightarrow{OH^-,\ \Delta} \mathbf{25} \quad (5)$$

$$\mathbf{26}$$

expectation, and reaction with alkali as with **24** gave benzyl disulfide (**25**) in a yield of 28% from **21** (n = 4). Since the stoichiometry of eq 4 and 5 is uncertain, however, the yields of "50%" and "28%" are meant only by their similarity to establish the presence of the SO_2S linkage in **21**, rather than to be rigorously correct.

We reported previously that compounds of structure **27**, where n was 4 or more, showed strong IR absorption at ca. 1230–1120 and 1080–1025.[5] When these absorptions were proved not to result from a sulfonate function, they were attributed to the polysulfide bis(alkanesulfinate) structure **27**. However, the strong IR absorptions that

$$\underset{\mathbf{27}}{NaO_2S(CH_2)_4S_n(CH_2)_4SO_2Na}$$

$$\underset{\mathbf{28}}{NaO_2S(CH_2)_4S_4(CH_2)_4SO_2SNa} \qquad \underset{\mathbf{29}}{[NaSSO_2(CH_2)_4S]_2S_n}$$

now appear to be characteristic for SO_2S at 1220–1170 and 1100–1070 for **21** (n = 4), **23**, and **29** (n = 0) (vide infra) now make it seem extremely likely that the bands attributed to **27** resulted from presence of a significant amount of SO_2SNa function(s) in the **27**.[20] Hence, for example, the compound earlier reported to be **27** with an average n = 4.9 probably contained significant amounts of **28** and/or **29** (n = 1), together with the product originally reported to be **27** (n = 4.9).

Under UV light, **5** (n = 3,4) did not react significantly more rapidly than when heated, but **5** (n = 5) (despite the difference thermally) with light evidently becomes as sensitive as **5** with n = 3 or 4. The products were the same as those that resulted with heating (congruent NMR spectra). The half-survival time was ca. 35–70 min for all three trisulfides under UV, and rearrangement for all three was complete within ca. 140–280 min. The more rapid thermal rearrangement of **5** (n = 3, 4) than of **5** (n = 5) is consistent with the *intra*molecular mechanism of Scheme II, since all three trisulfides should behave quite similarly if *inter*molecular reactions were involved. It also is consistent with the heterolytic neighboring-group mechanism of Scheme II, since involvement of the seven-membered ring of **5** (n = 5) should be much less favorable than for the five- and six-membered rings. In contrast, with behavior reminiscent of the disulfides (**1**), under UV light the dominant mechanism evidently shifts from *intra*molecular heterolysis to *inter*molecular homolysis, since all three disulfides behave similarly.

The facile incorporation of sulfur into SO_2Na groups led to interest in such reactions of **7** (n = 4). When one molar proportion of **7** (n = 4) was heated with seven of sulfur, ca. three molar proportions of sulfur dissolved (eq 6).

$$\underset{\mathbf{7}\ (n=4)}{[NaO_2S(CH_2)_4S]_2} \xrightarrow{S,\ H_2O,\ \Delta} [C_8H_{16}Na_2O_4S_7] \xrightarrow[-1S]{\Delta,\ H_2O} \underset{\mathbf{29}\ (n=0)}{[NaSS(O)_2(CH_2)_4S]_2S_n} \quad (6)$$

Undissolved sulfur was removed, and the solution was heated until precipitation of sulfur ceased. The product (**29**, n = 0) had IR spectra and elemental analyses consistent with the conversion of both SO_2^- groups to SO_2S^-. However, TLC showed three spots, and ^1H NMR spectra indicated ca. 55% of the disulfide bisthiosulfonate (**29**, n = 0), with possibly 25% of the corresponding trisulfide (**29**, n = 1) and 20% of still higher sulfides (**29**, n > 1); ^{13}C spectra were consistent.

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-FX-90Q (90 mHz), an IBM NR/300 (300 MHz), or a Bruker AM-400-NB (400 MHz) instrument, with TMS as an internal standard, except with DSS [$Me_3Si(CH_2)_3SO_3Na$] in D_2O; in the stability studies with trisulfides to avoid contamination by DSS, DOH was used as a standard for δ (ca. 4.65 ppm), so that such values of δ may be less reproducible. ^{13}C NMR spectra were obtained at 22.5 MHz with the JEOL-FX-90Q spectrometer or at 100 MHz with the Bruker AM-400-NB; the standards were DSS for D_2O or the solvent peak for CD_3OD and $CDCl_3$. Mass spectra (FAB) were obtained with a VG 70-250 GC–MS instrument (having extended geometry and equipped with a VG 11/250 data system and capability for fast atom bombardment) by Prof. B. J. Sweetman (Department of Pharmacology; funds provided by the NIH, Division of Research Resources Grant RR01688). IR spectra were obtained with a Perkin-Elmer Model 727 spectrometer; all were obtained with Nujol mulls. Spectral data given have not been reported previously. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN; most of the sulfinate salts were isolated as hydrates, but, unlike our frequent experiences, drying gave anhydrous products except for **5** (n = 3)·H_2O, **12**·0.4H_2O, **17**·0.35H_2O, and **29** (n = 0)·0.5H_2O.

Solvents were removed with a rotary-flask evaporator (aspirator) and then an oil pump. TLC usually was performed on Eastman Chromagram plates (catalog no. 13181) or Whatman K5F silica gel plates, with visualization by UV or I_2 vapor, except that the salts **10–12** were done with Whatman KC18F C_{18} reversed-phase plates and 5% H_2O/MeCN. Flash chromatography was performed essentially as described,[21] with use of Baker 7024 silica gel (40 μm).

Starting Materials.[2] **1,2-Dithiolane 1,1-dioxide (3, n = 3)** was prepared by the method of Harpp, Gleason, and Ash;[7] typical yield after flash chromatography (silica gel, Et_2O), 31%: mp ca. 20 °C (lit.[7] mp 24.5–26 °C); IR and ^1H NMR spectra were consistent with **3** (n = 3);[6,7] ^{13}C NMR ($CDCl_3$) δ 58.17, 36.69, 24.87. We found that crude **3** (n = 3) should be chromatographed immediately after preparation to obviate polymerization; pure **3** (n = 3) is stable for at least a month at −20 °C. **1,2-Dithiane 1,1-dioxide (3, n = 4)** usually was prepared by the same procedure;[7] typical yield after recrystallization from Et_2O (or CCl_4), 31%: the ^1H NMR and IR were consistent;[6,7] ^{13}C NMR ($CDCl_3$) δ 59.8, 35.3, 26.3, 25.2; mp 53–55 °C (lit.[6] mp 54.5–55 °C). **1,2-Dithiepane 1,1-Dioxide (3, n = 5).** Essentially as reported,[6,10] 1,2-dithiepane (**9**, n = 5) was prepared by adding 1,5-pentanedithiol (5.00 g, 36.7 mmol) in Et_2O (200 mL) to $FeCl_3$·6 H_2O (39.8 g, 147 mmol) in AcOH (36 mL)–Et_2O (280 mL) under reflux during 5 days; as before,[6] recommended precautions of using quartzware and excluding light[10] were unnecessary; yield of **9**, n = 5, 3.69 g (75%): n^{23}_D 1.5725 (lit.[6] n^{25}_D 1.5710); ^1H NMR ($CDCl_3$) δ 2.83 (t, 4 H), 1.62–2.16 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 39.3, 30.1, 26.1; IR consistent.[6] The dithiepane (**9**, n = 5) was converted to 1,2-dithiepane 1,1-dioxide (**3**, n = 5) by adding a solution of sodium perborate ($NaBO_3$·4H_2O; 2.28 g, 14.8 mmol) in AcOH (30 mL, warmed to dissolve the perborate, then cooled) dropwise to a

(19) Kice, J. L.; Rogers, T. E. *J. Am. Chem. Soc.* **1974**, *96*, 8009

(20) Mintel and Westley state that 1063 cm^{-1} is the "fundamental S–O stretching mode" and cite 1092 cm^{-1} for CH_3SO_2SNa and 1063 with 1190 (or 1117) cm^{-1} for $C_6H_5SO_2SNa$; Mintel, R.; Westley, J. *J. Biol. Chem.* **1966**, *241*, 3381.

(21) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

solution of 1,2-dithiepane (0.50 g, 3.72 mmol) in AcOH (10 mL) at ca. 20 °C during 1 h. The solution was stirred for 18 h, and the solvent then was removed under reduced pressure. The mixture was added to 35 mL of 2:1 H_2O–saturated aqueous NaCl and extracted with EtOAc (4 × 15 mL). The extract was neutralized with a 1:1 solution of saturated $NaHCO_3$–brine (3 × 20 mL), dried ($MgSO_4$), and concentrated to an oil (0.37 g, 60%), which solidified on standing. Dissolution of the oil in Et_2O (10 mL), filtration through silica gel (0.5 g), and recrystallization from cold Et_2O (Me_2CO–dry ice) gave **3** (n = 5) as a white solid: mp 50–51.5 °C (lit.[6] mp ca. 25 °C); TLC, one spot, R_f 0.69 (Et_2O). A larger scale experiment (2.2 g) led to **3** (n = 5) in a yield of 36: mp 50–51.5 °C (dropped to 47–51 °C after 1 day at −20 °C and **3** (n = 5) then gave two spots in TLC); ^1H NMR ($CDCl_3$) δ 3.24–3.52 (m, 2 H), 2.64–2.96 (m, 2 H), 1.68–2.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 60.21, 28.19, 26.40, 22.23, 17.77; IR consistent.[6] Use of 2.5 equiv of $NaBO_3 \cdot 4H_2O$ instead of 4 equiv led to a 1:1 mixture of 1,2-dithiepane 1-monoxide and 1,1-dioxide (as estimated by IR), and use of 6.0 equiv led to unidentified products with a much lower TLC R_F value.

In the preparation of all three cyclic thiosulfonates (**3**, n = 3–5), EtOAc was superior to CH_2Cl_2 or $CHCl_3$ for isolation from the reaction mixtures. It appeared initially that the thiosulfonates polymerized in CH_2Cl_2 and $CHCl_3$, but it later became clear that the polymers were formed during the oxidations and that they simply are much more soluble in CH_2Cl_2 and $CHCl_3$ than in EtOAc. EtOAc also led to much less trouble with emulsions. All other chemicals were commercial unless otherwise stated.

Reactions of Thiolate Ions (2) with Cyclic Thiosulfonates (3). The general procedure used to prepare **10–18**, much the same as previously,[12] can be illustrated for the new compound sodium 3-(2-carboxyethyldithio)propanesulfinate (**10**); the rationale for using only one molar proportion of NaOMe rather than one each for CO_2H and SH has been explained:[12] A solution of Na (0.713 g, 31.0 mg-atom) in MeOH (20 mL) was added dropwise (10 min) to a solution of 3-mercaptopropionic acid (3.31 g, 31.2 mmol) and 1,2-dithiolane 1,1-dioxide (**3**, n = 3; 4.30 g, 31.2 mmol) in MeOH (50 mL) at ca. 25 °C. The solution was stirred for 5 min, and the salt **10** then was precipitated totally with Et_2O (600 mL). Compound **10** was isolated by centrifugation and dried under reduced pressure to yield 6.55 g (79%) of white **10**. This **10** was dissolved in MeOH (100 mL); 0.70 g was precipitated by Et_2O and removed, and the remainder then was precipitated with Et_2O (600 mL), yield 5.85 g (71%). The properties of **10–19** are given in Table I.

The aminoethyl product (**19**) was prepared essentially as reported,[14] except in MeOH; the change from EtOH led to a yield as an immediate precipitate of 53% instead of 86%, presumably because of greater solubility in MeOH than EtOH (more **19** could be obtained by adding Et_2O). Positive-ion fast atom bombardment mass spectral analysis (FAB-MS) of **19** yielded peaks at m/z 230 (MH^+ for **19**) but also at 153 [MH^+ for $H_3{}^+N(CH_2)_2SS(CH_2)_2NH_2$ and at 459 corresponding to the protonated species **20**·H^+, i.e. $[H_3{}^+N(CH_2)_2S]_2 \cdot HO_2S(CH_2)_4SS(CH_2)_4SO_2^-$.

For the preparation of the 2,4,6-trimethoxythiophenol (**30**) used to prepare the disulfide **18**, a reported method with S_2Cl_2 was used,[22] but with the modification that steam distillation was omitted, and after reduction of the trisulfide of **30**, solvent was removed, the residue was dissolved in Et_2O, and **30** was extracted with 1 N NaOH. The extract was washed with Et_2O and acidified; an unpleasant steam distillation thus was obviated,[22] and the yield of **30** was increased from 52% to 85%: mp 59–60 °C; lit.[22] mp 58–59 °C. The thiol **30** was converted to **18** as usual.

Disodium 3,3′-Trithiobis(propanesulfinate) (5, n = 3). A modification of a reported procedure for **5** (n = 4) was used,[17] with details as follows: A solution of $Na_2S \cdot 9H_2O$ (2.91 g, 12.1 mmol) in MeOH (10 mL) was added dropwise to a solution of 1,2-dithiolane 1,1-dioxide (**3**, n = 3; 3.31 g, 24.0 mmol) in MeOH (20 mL) at ca. 20 °C. After a stirring period of 5 min, the salt **5** (n = 3) was precipitated with Et_2O (600 mL), isolated by centrifugation, and dried at ca. 0.1 Torr. The salt **5** (n = 3) then was dissolved in a minimum of MeOH (30 mL), ca. 10% was precipitated by Et_2O (15 mL) and separated, and the remainder was precipitated by Et_2O (500 mL) to give 3.25 g (73%) of **5** (n = 3) as white solid: TLC (40% MeOH–MeCN), R_f 0.52; IR 1300, 1260, 1240, 1170, 1080–900 (br), 850, 820, 720 cm^{-1}; ^1H NMR (D_2O) δ 3.03 (t, 2), 2.47 (t, 2), 2.08 (m, 2); ^{13}C NMR (D_2O) δ 61.95, 40.12, 24.08. Anal. Calcd for $C_6H_{12}Na_2O_4S_5 \cdot 1.0H_2O$: C, 19.33; H, 3.76; S, 42.99. Found: C, 19.24; H, 3.39; S, 43.02.

Disodium 4,4′-Trithiobis(butanesulfinate) (5, n = 4). The procedure of ref 17 gave **5** (n = 4) in 85% yield; IR and ^1H NMR as reported;[17] ^{13}C NMR (D_2O) δ 62.67, 40.17, 30.20, 22.97.

Disodium 5,5′-Trithiobis(pentanesulfinate) (5, n = 5). Essentially, the procedure of ref 17 gave **5** (n = 5) in a yield of 1.88 g (78%) from $Na_2S \cdot 9H_2O$ (1.42 g, 5.91 mmol) and 1,2-dithiepane 1,1-dioxide (**3**, n = 5; 2.18 g, 13.1 mmol): ^1H NMR (CD_3OD) δ 2.93 (t, 2), 2.32 (t, 2), 1.41–1.97 (m, 6); ^{13}C NMR δ 63.14, 39.52, 29.77, 29.17, 23.27; IR 1410, 1080–900 (s), 720 cm^{-1}. Anal. Calcd for $C_{10}H_{20}Na_2O_4S_5$: C, 29.27; H, 4.88; S, 39.02. Found: C, 29.65; H, 4.58; S, 38.93.

Preparation of Benzyl Disulfide (25) from Sodium Methanethiosulfonate (23) and Benzyl Bromide. A mixture of sodium methanesulfinate [**22**; 1.00 g, 9.8 mmol; ^1H NMR, D_2O, δ 2.30 (s)][23] and sulfur (0.312 g, 9.75 mmol) in MeOH (60 mL) was heated under reflux for 10 min, at which time all of the sulfur had dissolved. Removal of solvent gave **sodium methanethiosulfonate (23)** as a white solid: IR (Nujol) 1320, 1220–1180 (br), 1100–1075 (br), 975, 770 cm^{-1}; ^1H NMR (D_2O) δ 3.30 (s); **23** has been prepared previously by another method,[20] but only the IR (KBr) at 1092 cm^{-1} was reported.[20]

A solution of **23** (0.20 g, 1.49 mmol) and benzyl bromide (0.25 g, 1.46 mmol) in MeOH (10 mL) was heated under reflux for 2.5 h. TLC then showed that the spot for **23** (R_f 0.24, MeCN) had disappeared and that two new spots had formed (R_f 0.48 and 0.83; CH_2Cl_2–hexane, 1:1). Solvent was removed, the mixture was dissolved in CH_2Cl_2 (10 mL), and the NaBr was removed by filtration. Preparative TLC (CH_2Cl_2–hexane, 1:1) separated 0.18 g (61%) of ***S*-benzyl methanethiosulfonate** (**24**; R_f 0.48), which had the expected IR absorption (strong bands at 1320 and 1125 cm^{-1}).

Solid NaOH (0.10 g, 2.5 mmol) then was added to a solution of the **24** in MeOH (5 mL), which then was heated under reflux (10 min). Removal of solvent from the red solution gave 0.06 g (50%, based on **23** and eq 3 and 4) of pink solid, which was washed with pentane (negligible loss) to give dibenzyl disulfide (**25**): mixture mp 69.5–71.5 °C; lit.[24] mp 69–70 °C; IR spectrum identical with that of known **25**.

Preparation of Benzyl Disulfide (25) from the Rearranged Trisulfide (21, n = 4) and Benzyl Bromide. A solution of trisulfide **5** (n = 4) (0.30 g, 0.79 mmol) was heated in H_2O (10 mL) at 70 °C for 3 h, after which lyophilization gave **21** (n = 4): IR 1180 (s), 1100, 1070 (s), 1035, 980 (s), 960, 780, 720 cm^{-1}; ^1H NMR (D_2O) δ 3.34 (t, 2 H), 2.74 (t, 4 H), 2.31 (t, 2 H), 2.00–1.40 (m, 8 H); ^{13}C NMR (D_2O) δ 67.45, 63.14, 40.60, 40.38, 30.58, 29.53, 26.09, 23.30. A solution of **21** (n = 4) (0.15 g, 0.39 mmol) and benzyl bromide (0.14 g, 0.82 mmol) in MeOH (5 mL) then was heated under reflux (4 h). The solvent was removed, CH_2Cl_2 (5 mL) was added, the NaBr was removed by filtration, and solvent was removed to yield **26**; the IR spectrum was consistent (strong bands at 1320 and 1130 cm^{-1}, somewhat higher than for the salt **21** (n = 4), but in good agreement with *S*-benzyl methanethiosulfate (**24**). Solid NaOH (0.018 g, 0.45 mmol) then was added to the **26** obtained, 0.17 g (0.33 mmol) in MeOH (5 mL), which then was stirred for 1 h at ca. 25 °C. The mixture was diluted with brine (15 mL), and an Et_2O extract (3 × 30 mL) was dried ($MgSO_4$) and concentrated to give a clear oil, which showed three spots on TLC (R_f 0.00, 0.22, and 0.41; 10% CH_2Cl_2–hexane). Preparative TLC (10% CH_2Cl_2–hexane) gave **25** [9 mg; 28% yield from **21** (n = 4), based on eq 3 and 4], which was characterized by mixture mp (69–70.5 °C), NMR, and identity of IR spectra.

Reaction of Disodium 4,4′-Dithiobis(butanesulfinate) (27, n = 2) with Sulfur. Disodium 4-mercaptobutanesulfinate (6, n = 4) was prepared, essentially as described,[5] from 1,2-dithiane 1,1-dioxide (**3**, n = 4; 0.60 g, 3.9 mmol) in THF (15 mL) with the

(22) Bottino, F.; Fradullo, R.; Pappalardo, S. *J. Org. Chem.* **1981**, *46*, 2793.

(23) Kindly provided by C. Lee; prepared by the procedure of Field, L.; McFarland, J. W. *J. Am. Chem. Soc.* **1953**, *75*, 5582.

(24) The *Merck Index*; 10th ed.; Windholz, M., Ed.; Merck and Co.: Rahway, NJ, 1983; p 436.

use of sodium (0.15 g, 6.5 mg-atom) in liquid NH_3 (75 mL). The product (**6**, $n = 4$) was dissolved in MeOH (15 mL), a solution of **3** ($n = 4$) (0.65 g, 4.3 mmol) in MeOH (5 mL) was added, and the mixture was stirred for 4 h. The salt then was precipitated by adding Et_2O (300 mL). Redissolution in MeOH (15 mL), partial precipitation with Et_2O (10 mL), and separation of the precipitate, followed by precipitation from the mother liquor with 200 mL of Et_2O, gave 0.69 g (60%) of **disodium 4,4′-dithiobis(butanesulfinate) (27, $n = 2$)**: ^1H NMR (D_2O) δ 2.78 (t, 2), 2.38 (t, 2), 2.04–1.39 (m, 4) (this spectrum was congruent with that of authentic **27** ($n = 2$) prepared by a different method);[17] TLC R_f 0.37 (2:3 MeOH–MeCN).

A mixture of similarly prepared sulfinate (**7**, $n = 4$; 2.44 g, 6.98 mmol) and sulfur (1.57 g, 49.1 mmol) in MeOH (30 mL) then was heated at 68 °C for 24 h. Undissolved sulfur was removed by centrifugation, washed with Me_2CO, and dried to give 0.93 g (29 mmol, 59% recovery) of unreacted sulfur; hence, 0.64 g (20 mmol, 2.9 molar proportions) of sulfur reacted. To obtain a stable product, the MeOH was removed, 30 mL of H_2O was added, and the solution was heated at 68 °C. After 1.5 h, centrifugation gave 0.17 g of sulfur. After 18 h more at 68 °C, 0.03 g more was collected, after which no change occurred during 4 h; the total collected (0.20 g) amounted to 6.3 mmol (0.90 molar proportion). Removal of H_2O from the solution, dissolution in MeOH (10 mL), partial precipitation by Et_2O (10 mL) and discard, and then addition of 200 mL of Et_2O and 200 mL of Me_2CO gave 1.81 g of off-white solid (63% yield, calcd as **29**, $n = 0$): TLC R_f 0.19, 0.33, 0.50 (50% EtOH–CH_2Cl_2); IR 1170, 1070, 770, 720 cm^{-1}; ^1H NMR (D_2O) δ 3.36–3.26 (m, 4), 3.14 (t, 0.2), 3.06 (t, 0.4), 3.00 (t, 1), 2.80 (t, 2.2), 2.06–1.80 (m, 8); ^{13}C NMR (D_2O) δ 67.00, 66.88, 40.25, 40.05, 29.28, 29.06, 25.83, 25.47 (these eight peaks were grouped into four sets of two very close peaks each). Anal. Calcd for $C_8H_{16}Na_2O_4S_6 \cdot 0.5H_2O$: C, 22.69; H, 4.02; S, 45.39. Found: C, 22.60; H, 3.88; S, 45.74.

The crude **29** ($n = 0$) appeared to be a mixture of the disulfide with the corresponding trisulfide (**29**, $n = 1$) and higher sulfides (**29**, $n > 1$) by TLC and NMR,[2] although the elemental analysis is consistent with **29** ($n = 0$)·$0.5H_2O$.

Thermal and Photochemical Stabilities. Experiments with heating were done at ca. 25 or 68 °C with shielding from light. For the carboxy sulfinates **10–12** and trisulfides (**5**, $n = 3$–5), 0.05 M solutions in 0.5 mL of D_2O were followed in NMR tubes; for **10–12**, DSS was the standard and for **5** ($n = 3$–5) the HOD signal set at 4.65 ppm was used as a standard (with the intensity reduced by gated decoupling to increase the signal/noise ratio). For the extractions with **13–15** and **18**, 4 mL of 0.05 M solutions in H_2O at 25 °C (Figure 1) or 68 °C were extracted at the indicated times with 3 mL of Et_2O; the mixtures were centrifuged, and the Et_2O layers were removed, dried ($MgSO_4$), and evaporated; residues were dried (60 °C, 5 min) and weighed [percent disproportionation = 2 (cumulative moles of ArSSAr extracted × 100)/(moles of starting material)]. With **14** and **18** as examples, the identities of di-*p*-tolyl and bis(2,4,6-trimethoxyphenyl) disulfide were established by melting point and mixture melting point.

The experiments under UV were performed by irradiating 0.5 mL of 0.05 M solutions in D_2O in NMR tubes with a 100-W Hanovia lamp 10 cm distant; with the longer irradiations, the temperature rose (briefly) but never above 40 °C. The disulfides **10–12** gave complex mixtures. The identity of di-*p*-tolyl disulfide from **13–15** was established by congruency of the NMR spectrum of a suspension of the authentic disulfide in D_2O with the appropriate parts of the spectra from the experiments.

For calculations from NMR results with **10–15**, percent disproportionation = [(an appropriate integral for product × 100)/(sum of the integrals at the time for the same group in starting materials *and* product, because a little starting material was unchanged)]. For the trisulfides **5** ($n = 3$–5), percent rearrangement = [(integral for $CH_2SO_2S^-$ at the time of interest × 100)/(integral for $CH_2SO_2S^-$ after complete rearrangement)].

Registry No. **3** ($n = 3$), 18321-16-9; **3** ($n = 4$), 18321-15-8; **3** ($n = 5$), 18321-17-0; **5** ($n = 3$), 111848-92-1; **5** ($n = 4$), 56527-86-7; **5** ($n = 5$), 111848-93-2; **6** ($n = 4$), 76832-46-7; **7** ($n = 4$), 34915-82-7; **8** ($n = 5$), 928-98-3; **9** ($n = 5$), 6008-51-1; **10**, 111848-85-2; **12**, 111848-86-3; **13**, 111848-87-4; **14**, 62911-23-3; **15**, 111848-88-5; **16**, 111848-89-6; **17**, 111848-90-9; **18**, 111848-91-0; **19**, 19293-54-0; **20**, 111849-00-4; **21** ($n = 3$), 111848-94-3; **21** ($n = 4$), 111848-95-4; **21** ($n = 5$), 111848-96-5; **22**, 20277-69-4; **23**, 1950-85-2; **24**, 7559-62-8; **25**, 150-60-7; **26**, 111848-97-6; **27** ($n = 2$), 34915-82-7; **29** ($n = 0$), 111848-98-7; **29** ($n = 1$), 111848-99-8; **30**, 77189-99-2; $HS(CH_2)_2CO_2H$, 107-96-0; C_6H_5SH, 108-98-5; $4\text{-}H_3CC_6H_4SH$, 106-45-6; $H_2N(CH_2)_2SH$, 60-23-1; $4,4'\text{-}H_3CC_6H_4S_2C_6H_4CH_3$, 103-19-5; $H_2N(CH_2)_2S_2(CH_2)_2NH_2$, 51-85-4; 1,2-dithiepane 1-monoxide, 111848-84-1; bis(2,4,6-trimethoxyphenyl) disulfide, 80279-40-9.