21 was reduced from 3 to 1.5, the yield of **22** dropped from 64 to 40% (and to 35% at 60 °C). When the proportion was increased to 6, the yield was 20%. Generation of the somewhat unstable sulfinic acid in situ from three proportions of the salt with equivalent concentrated HCl, with reaction at 60 °C, gave **22** in 35% yield.

(b) Preparation of 23 from 22. Solutions were prepared by adding 0.90 mL of 1 N NaOH (0.9 mmol), and then 5 mL of EtOH, to 0.31 g (0.90 mmol) of **22** and also to 0.11 g (0.89 mmol) of α-toluenethiol (**19**). The solution of the resulting thiolate of **19** then was added to that (cloudy) of **22**. The solution, which then became clear, was stirred at ~25 °C for 2 h more and then was acidified with 10% aqueous HCl to pH 1. When the cloudy solution was kept at ~0 °C for 2 h, 0.12 g of the disulfide **23** precipitated: yield 43%; mp 152–153 °C. The melting point, mixture melting point, TLC, IR spectrum, and NMR spectrum were identical with those of **23** prepared from **18**.

Disproportionation. Aqueous solutions (having the millimolarity parenthetically stated) of **3** (38 mM), **5** (174 mM), **7** (62 mM), and **23** (6 mM) were stirred and heated under reflux in the dark (foil wrapped) at 100 ± 0.1 °C in an oil bath. Minute portions of the solutions were removed periodically and spotted on 3 × 10 cm glass slides coated with Brinkmann silica gel G, eluted (EtOH for **3**, EtOH–H_2O for **5**, MeOH for **7**, $CHCl_3$ for **23**), and subsequently developed in I_2 vapor. The "onset" of disproportionation (Table I) was taken as the time when a single spot in each case, corresponding to the unsymmetrical disulfide initially, first gave rise to three spots; the two new spots corresponded to the two symmetrical counterparts, which were run simultaneously on the plate, as was the original disulfide. "No further change" (Table I) was taken as the time when the two new spots and the initial spot no longer appeared to change in intensity or area. For study of the free base of **17**, a solution of 10 mg of **17** in 2 mL of CH_2Cl_2 was shaken with saturated aqueous $NaHCO_3$, washed with H_2O, and dried ($MgSO_4$). TLC (benzene) on one portion of the solution kept at ~25 °C in the dark still showed only one spot after 72 h. Another portion kept in ambient light at ~25 °C first showed spots corresponding to **14** and di-*tert*-butyl disulfide after ~12 h and no apparent further change in these three spots after ~15 h.

Registry No. D-**1**, 52-67-5; **2**, 38695-52-2; D-**3**, 70527-76-3; **4**, 10027-70-0; D-**5**, 70561-52-3; **6**, 18321-15-8; D-**7**, 70527-77-4; **8**, 605-65-2; **9**, 67101-61-5; **10**, 70527-78-5; **11**, 26555-40-8; **12**, 70527-79-6; D,L-**13**, 59-53-0; **14**, 70527-80-9; **14** 2HI, 70527-81-0; **15** picrate, 70527-82-1; D,L-**16**, 70527-83-2; **17**, 70527-84-3; **17** free base, 70527-87-6; D,L-**18**, 67776-06-1; **19**, 100-53-8; **21**, 536-57-2; D,L-**22**, 70527-85-4; D,L-**23**, 70527-86-5; (chlorocarbonyl)sulfenyl chloride, 24768-49-8; 2-methyl-2-propanethiol, 75-66-1; sodium *p*-toluenesulfinate, 824-79-3; trichloromethanesulfenyl chloride, 25004-95-9.

A Macrocyclic Tetradisulfide from Tetrafluoro-1,4-benzenedithiol

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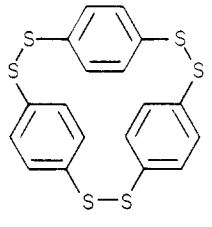
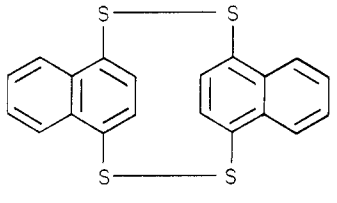
Received February 27, 1979

A macrocyclic tetradisulfide (**4**) has been obtained in 95% yield by the oxidation of tetrafluoro-1,4-benzenedithiol with dimethyl sulfoxide. The compound forms complexes with *N,N'*-dimethyldihydrophenazine and 1,3-diphenylisobenzofuran. Conformational changes take place in solution with changes in temperature.

Oxidation of aromatic 1,4-dithiols has been the subject of a number of studies. 1,4-Benzenedithiol is reported to give polymeric disulfides.[2-4] However, by carrying out the oxidation with iodine at high dilution, Wong and Marvel obtained the three-unit macrocycle **1** in 30% yield.[5]

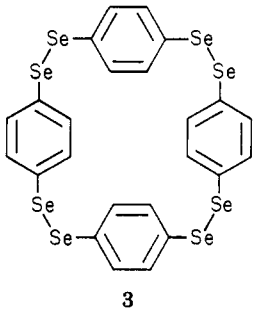


1

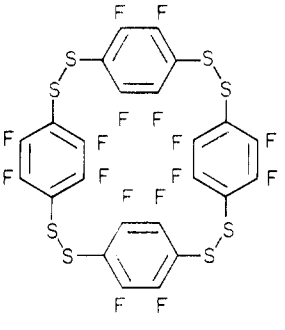


2

Marschalk recorded the formation of **2**, supported by molecular weight data, in unspecified yield from oxidation of 1,4-naphthalenedithiol with alkaline ferricyanide.[6] Air oxidation of 1,4-benzenediselenol gives the four-unit macrocycle **3** quantitatively.[7]



3



4

Synthesis and Properties of 4. In the present work, tetrafluoro-1,4-benzenedithiol has been oxidized with dimethyl sulfoxide.[8] When the dithiol is placed in dimethyl sulfoxide, it quickly dissolves with formation of a deep orange solution, the solution becomes warm, and the crystalline, four-unit macrocycle **4** soon precipitates in 95% yield while the color fades. This facile synthesis of **4** is a peculiarity of tetrafluoro-1,4-benzenedithiol, as 1,4-benzenedithiol, 2,5-dimethoxy-1,4-benzenedithiol, and tetramethyl-1,4-benzenedithiol formed polymers under the

(1) Contribution No. 2645.
(2) Leuckart, R. *J. Prakt. Chem.* **1890**, *41* (2), 179.
(3) Zincke, T.; Frohneburg, W. *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 2727.
(4) Parekh, V. C.; Guha, P. C. *J. Indian Chem. Soc.* **1934**, *11*, 95. The authors formulation of their product as a two-unit macrocycle is unjustified. It has the properties of a polymer.
(5) Wong, D. T.; Marvel, C. S. *J. Polym. Sci.* **1976**, *14*, 1637.
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(8) Studies of the oxidation of thiols with sulfoxides: (a) Yiannios, C. H.; Karabinos, J. V. *J. Org. Chem.*, **1963** *28*, 3246. (b) Wallace, T. J. *Ibid.* **1964**, *86*, 2018. (c) Wallace, T. J.; Mahon, J. J. *J. Am. Chem. Soc.* **1964**, *86*, 4099; *J. Org. Chem.* **1965**, *30*, 1502. (d) Lowe, O. G. *Ibid.* **1975**, *40*, 2096. (e) Tanikaga, R.; Tanaka, K.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1978**, 865.

0022-3263/79/1944-2629$01.00/0

same conditions. Tetrachloro-1,4-benzenedithiol gave a crystalline oxidation product, but determination of its molecular weight was precluded by its great insolubility and nonvolatility.

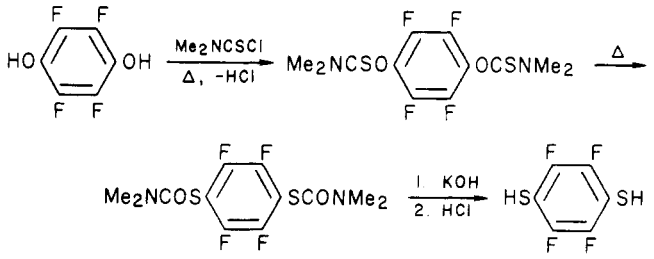
The tetrameric formula for 4 is shown by ebullioscopic molecular weight determinations in benzene and in chloroform and by mass spectrometry which reveals strong peaks corresponding to one, two, three, and four units of $C_6F_4S_2$. A Raman spectrum peak at 485 cm^{-1} is ascribed to the disulfide link. Crystals from chloroform are highly ordered and tetragonal by X-ray inspection. Differential thermal analysis shows a melting endotherm at 268 °C. Heating was continued to look for an endotherm which would signal depolymerization, but none was observed. Instead, an exothermic decomposition set in around 320 °C.

The freshly prepared, deep orange solution of tetrafluoro-1,4-benzenedithiol in dimethyl sulfoxide has absorption peaks at 413 nm (ϵ 6530) and 320 nm (ϵ 13350). The nature of the colored complex has not been established, but some negative evidence has been collected. On the basis of kinetic studies of the oxidation of thiols by sulfoxides, Wallace[8b,c] has postulated that an intermediate adduct, formulated as $R_2S(OH)SR'$, is formed, but such a structure does not explain the color. The orange solution does not give an ESR signal which is evidence against a free radical. The oxidation was carried out in the presence of 2,3-dimethylbutadiene in an attempt to trap the dithioquinone, if formed, but no adduct was produced. Only 4 was formed.

Complexing Ability of 4. Compound 4 exhibits complexing properties. When it is prepared in dimethyl sulfoxide in the presence of *N,N'*-dimethyldihydrophenazine, a 1:1, black, nonconducting, charge-transfer complex is formed. Preparation in the presence of 1,3-diphenylisobenzofuran gives an unusual reddish orange complex containing 1 mol of 4 to 4 mol of 1,3-diphenylisobenzofuran. The complexes can also be prepared starting with 4 and the complexing agent. Extraction of the complexes with hot cyclohexane removes the complexing agents and leaves 4. With benzene, 4 forms a solvate that effloresces in air.

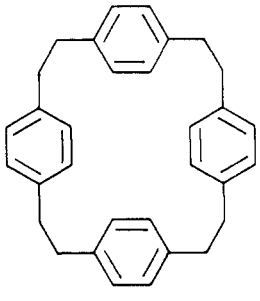
Conformational Changes of 4. When a model of 4 is examined, four possible conformations become apparent—ones where the pairs of disulfide links attached to a benzene ring are all cis, all trans, alternating cis and trans, and cis-cis-trans-trans. Within these skeletal conformations, further conformations are possible if the phenylene groups are not free to rotate. Examination of the compound by fluorine NMR (Varian XL-100 instrument) in solution in chlorobenzene from −65 to +140 °C shows that reversible conformation changes do take place. At 26 °C, broadened peaks of equal area are present at −128.8 and −132.7 ppm, and a minor peak having about 15% of the area of either of the major peaks is present at −129.9 ppm, referenced to CCl_3F. A fourth absorption occurs as a shoulder on the high-field side of the −128.8-ppm peak. These minor peaks are present whether 4 is prepared by using dimethyl sulfoxide or bromine as the oxidant or whether 4 is recrystallized from chloroform or benzene. The peaks also rise from 4 purified by chromatography over silica followed by recrystallization from chloroform. Thus, the minor peaks are concluded not to arise from impurities. At 55 °C all the NMR peaks have disappeared, and as the temperature is raised, a single peak forms at −131.2 ppm. As the temperature is lowered from +26 to −65 °C, the NMR peaks sharpen but the width and shape suggest that F–F coupling is present, though

Scheme I



the coupling constant is not determinable from the spectra. This indication of coupling shows some restriction of rotation of the phenylene rings at the low temperature. The energy barrier for the conformational change, calculated from the coalescence temperature of the two major peaks, is 18 ± 2 kcal/mol. The two major peaks possibly result from two different sets of pairs of fluorine atoms which could arise from either the all-cis or the all-trans conformation.

A similar conformational situation could be expected for 5.[9] However, for this molecule in carbon disulfide at



5

temperatures down to −111 °C, the aromatic protons were reported to show only small line broadening, "which indicated that motions of benzene rings were not remarkedly restricted". The singlet for the ethylene protons changed to an AB quartet, attributed to axial–equatorial exchange.

The reported[5] mass spectral molecular weight of 1 has been confirmed by ebullioscopic measurement in benzene. The rigidity of a model of this compound suggests that conformational changes are unlikely to take place. In chloroform the compound shows an NMR singlet at 7.2 ppm which is unchanged at −70 °C.

Synthesis of the Dithiols. The reported synthesis of tetrafluoro-1,4-benzenedithiol in 24% yield from sulfur and 1,4-dilithiotetrafluorobenzene[10] could not be repeated. The compound was readily prepared by a simplification of the thiocarbamate method.[11] No base is required for the esterification, and the thiono ester is obtained directly (see Scheme I).

Tetrachloro-1,4-benzenedithiol was made by the same method.

Experimental Section

The ^1H NMR spectra were determined in Varian A-60 and XL-100 instruments, using Me_4Si as an internal reference. The ^{19}F NMR spectra were measured in a Varian XL-100 instrument, using trichlorofluoromethane as internal reference. All downfield values are recorded as positive. A Perkin-Elmer Model 21 spectrometer was used for IR spectra. Melting and boiling points are uncorrected.

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(10) Mobbs, R. W. *Chem. Ind. (London)* **1965**, 1562.
(11) (a) Kwart, H.; Evans, E. R. *J. Org. Chem.* **1966**, *31*, 410. (b) Newman, M. S.; Karnes, H. A. *Ibid.* **1966**, *31*, 3980.

Dimethylthiocarbamoyl chloride should be handled with appropriate care since dimethylcarbamoyl chloride is a cancer suspect agent.

Tetrafluoro-*p*-phenylene *O,O'*-Bis(dimethylthiocarbamate). Tetrafluorohydroquinone[12] (45.5 g, 0.25 mol) and 76 g (0.62 mol) of dimethylthiocarbamoyl chloride[13] were heated in a flask in an oil bath at 140–150 °C for 1 h. The mixture liquefied, hydrogen chloride was evolved, and the product then crystallized. The product was cooled and washed with methanol to give 77.5 g (87%) of the diester. Recrystallization from benzene gave 75 g (84%) in three crops: mp 191–192 °C; ^{1}H NMR ($CDCl_3$) 3.37 (s), 3.46 (s) ppm.

Anal. Calcd for $C_{12}H_{12}F_4N_2O_2S_2$: C, 40.45; H, 3.39; N, 7.86. Found: C, 40.55; H, 3.47; N, 7.97.

Tetrafluoro-*p*-phenylene *S,S'*-Bis(dimethylthiocarbamate). The thiono diester (88 g) of the preceding section and 70 mL of diphenyl ether were heated together in a flask in an oil bath at 190–195 °C for 45 min under nitrogen. The mixture was cooled and then filtered, and the solid was rinsed with methanol to give 73 g (83%) of rearranged ester. Recrystallization from benzene (decolorizing charcoal) gave 70.3 g (74%) in two crops: mp 238–239 °C; ^{1}H NMR ($CDCl_3$) 3.13 (s) ppm. The rearrangement can be followed by NMR as esters of the type $Me_2NC(=S)OR$ show two singlets for Me_2 whereas esters of the type $Me_2NC(=O)SR$ show one.

Tetrafluoro-1,4-benzenedithiol. The above rearranged diester (35.6 g, 0.1 mol) was added to 59 g (0.9 mol) of 85% potassium hydroxide dissolved in 35 mL of water and 170 mL of methanol, and the mixture was refluxed for 1 h. The solution was diluted to 900 mL with water, and 110 mL of hydrochloric acid was added. The precipitated dithiol was filtered off and air-dried (21.3 g). Recrystallization from pentane gave 16.2 g (75%) of the dithiol in two crops: mp 70.5–71.5 °C (lit.[10] mp 70–72 °C); ^{1}H NMR ($CDCl_3$) 3.66 (s, SH) ppm.

Oxidation of Tetrafluoro-1,4-benzenedithiol. Tetrafluoro-1,4-benzenedithiol (6 g) was added to 24 mL of dimethyl sulfoxide. The solution became deep orange and warm. Crystals of the macrocycle soon separated and the color faded with formation of the product. After 1 h the product was filtered off and washed with acetone; yield 5.71 g (95%). Recrystallization from chloroform gave 5.30 g (89%) in two crops of pale yellow 5,6,11,12,17,18,23,24,25,26,27,28,29,30,31,32-hexadecafluoro-2,3,8,9,14,15,20,21-octathiapentacyclo[20.2.2.2^{4,7}.2^{10,13}.2^{16,19}]dotriaconta-4,6,10,12,16,18,22,24,25,27,29,31-dodecaene (4), mp 266–267 °C. Solubility in boiling chloroform is about 5%.

Anal. Calcd for $C_{24}F_{16}S_8$: C, 33.96; S, 30.23; mol wt 848.76. Found: C, 34.08; S, 30.12; mol wt (ebullioscopic) 859 (C_6H_6), 863 ($CHCl_3$). Spectral data: mass spectrum (direct introduction at 275–325 °C) *m/e* 848, 636, 424, 212 (strong peaks); IR 1618, 1471 (aromatic C=C), 1252 (aromatic CF) cm^{-1}, simple spectrum suggesting a symmetrical molecule; Raman 1615 (aromatic C=C), 485 (SS) cm^{-1}; UV 255 (ϵ 46 800 aromatic), 308 (ϵ 19 100) nm.

Complexes of 4. (a) With *N,N'*-Dimethyldihydrophenazine. *N,N'*-Dimethyldihydrophenazine (1.05 g, 5 mmol) was dissolved in 50 mL of dimethyl sulfoxide, and 1.07 g (5 mmol) of tetrafluoro-1,4-benzenedithiol was added. The solution became orange and then turned dark, and black crystals began to separate. After 63 h the crystals were filtered off and washed with ether: yield 1.06 g (80%); mp 186–189 °C.

Anal. Calcd for $C_{24}F_{16}S_8{\cdot}C_{14}H_{14}N_2$ ($C_{38}H_{14}F_{16}N_2S_8$): C, 43.09; H, 1.33; N, 2.65; F, 28.75. Found: C, 42.71; H, 1.37; N, 2.73; F, 28.60.

The complex can be made starting from **4** and *N,N'*-dimethyldihydrophenazine, but the above procedure is better.

Compaction resistivity of the complex is 10^{10} Ω cm.

(b) With 1,3-Diphenylisobenzofuran. 1,3-Diphenylisobenzofuran (2.02 g, 7.5 mmol) was dissolved in 60 mL of dimethyl sulfoxide, and 1.07 g (5 mmol) of tetrafluoro-1,4-benzenedithiol was added. The solution became red. After 16 h the reddish orange crystals that formed were filtered off, washed first with dimethyl sulfoxide and then with water, and air-dried to give 2.11 g (87.5%) of the complex: mp 163.5–164.5 °C, unchanged after recrystallization from chloroform containing 1,3-diphenylisobenzofuran; ^{1}H NMR ($CDCl_3$) same as for 1,3-diphenylisobenzofuran; ^{19}F NMR same as for **4**.

Anal. Calcd for $C_{24}F_{16}S_8{\cdot}4C_{20}H_{14}O$ ($C_{104}H_{56}F_{16}O_4S_8$): C, 64.72; H, 2.92; S, 13.29. Found: C, 64.02; H, 3.00; S, 13.57.

The complex can also be prepared in chloroform from **4** and 1,3-diphenylisobenzofuran.

Tetrachloro-*p*-phenylene *O,O'*-Bis(dimethylthiocarbamate). This diester was prepared at 125 °C as described for the tetrafluoro analogue. The methanol-washed product was slurried with 5% sodium hydroxide solution, filtered, and washed with water followed by acetone to give a 63% yield. Recrystallization from chlorobenzene left a 55% yield: NMR ($CDCl_3$) 3.40 (s), 3.47 (s) ppm; IR 2959 (CH), 1550 (S=CN) cm^{-1}. When the compound was placed in a bath at 242 °C, it melted, rearranged, and then solidified. Slow heating to 250 °C caused no melting.

Anal. Calcd for $C_{12}H_{12}Cl_4N_2O_2S_2$: C, 34.14; H, 2.87; N, 6.64. Found: C, 34.25; H, 2.87; N, 6.59.

Tetrachloro-*p*-phenylene *S,S'*-Bis(dimethylthiocarbamate). The above diester (38 g) and 50 mL of diphenyl ether were heated under reflux, using an oil bath at 240 °C, for 0.5 h after reflux started. The mixture was cooled and then filtered, and the product was washed with acetone to give 34.5 g (91%) of the rearranged diester: mp 282.5–283.5 °C from dimethylformamide; NMR ($CDCl_3$) 3.08 (s) ppm; IR 2950 (CH), 1675 (C=O) cm^{-1}.

Anal. Calcd for $C_{12}H_{12}Cl_4N_2O_2S_2$: C, 34.14; H, 2.87; N, 6.64. Found: C, 34.20; H, 2.93; N, 6.60.

Tetrachloro-1,4-benzenedithiol. The rearranged diester (72 g, 0.17 mol) was refluxed with 100 g (1.52 mol) of 85% potassium hydroxide in 60 mL of water, 300 mL of methanol, and 300 mL of pyridine for 2 h. The solution was poured into 2400 mL of water and ice, and 800 mL of hydrochloric acid was added (foaming). The precipitated dithiol was filtered off, washed with water, and air-dried. Recrystallization from chloroform gave 34 g (72%) of the dithiol: mp 261–262 °C; NMR ($CDCl_3$) 3.09 (s) ppm.

Anal. Calcd for $C_6H_2Cl_4S_2$: C, 25.74; H, 0.72; S, 22.90. Found: C, 25.40; H, 0.78; S, 23.01.

Oxidation of Tetrachloro-1,4-benzenedithiol. One gram of tetrachloro-1,4-benzenedithiol was heated with 5 mL of dimethyl sulfoxide on a steam bath for 30 min. The dimethyl sulfoxide assumed a light orange color, and the needles of dithiol, largely undissolved, were gradually replaced by dense, yellow, granular crystals. The mixture was cooled and then filtered, and the crystals were washed with dimethyl sulfoxide and with chloroform to give 0.97 g of product, mp 335–337.5 °C. The compound is insoluble in organic solvents except for slight solubility in boiling dimethyl sulfoxide. Nothing was extracted by 5% KOH solution. The infrared spectrum is simple, indicative of a symmetrical molecule, and has a weak band at 1511 cm^{-1} for a highly substituted aromatic structure; Raman 485 cm^{-1} (vs, SS), 1505 (C=C) cm^{-1}, no indication of SH. The molecular weight was not established because of the nonvolatility and insolubility of the product.

Anal. Calcd for $(C_6Cl_4S_2)_n$: C, 25.93; Cl, 51.02; S, 23.08. Found: C, 26.07; Cl, 51.24; S, 23.25.

Tetramethyl-*p*-phenylene *O,O'*-Bis(dimethylthiocarbamate). A mixture of 3.32 g (0.02 mol) of tetramethylhydroquinone,[14] from the reduction of duroquinone,[13] 15 mL of quinoline, and 7.40 g (0.06 mol) of dimethylthiocarbamoyl chloride was heated at 200 °C for 45 min. The cooled mixture was treated with 10% HCl to dissolve the quinoline, and the ester was filtered off and washed with water; yield 6.76 g (99.5%). Recrystallization from acetone left 5.97 g (92%): mp 270–272 °C (lit.[11b] mp 235–236 °C); NMR ($CDCl_3$) 2.07 (s, ring CH_3), 3.35 (s), 3.47 (s) ppm.

Anal. Calcd for $C_{16}H_{24}N_2O_2S_2$: C, 56.44; H, 7.10; N, 8.23. Found: C, 56.66; H, 6.97; N, 8.22.

Tetramethyl-*p*-phenylene *S,S'*-Bis(dimethylthiocarbamate). The *O,O'*-diester was heated in a bath at 280 °C for 15 min under nitrogen. Longer heating results in decomposition. Recrystallization from chloroform provided an 87% yield of rearranged diester in three crops: mp 253–256 °C (lit.[11b] mp

(12) PCR, Inc.
(13) Aldrich Chemical Co.

(14) Conant, J. B.; Fieser, L. F. *J. Am. Chem. Soc.* **1923**, *45*, 2194. Smith, L. I.; Dobrovolny, F. J. *ibid.* **1926**, *48*, 1420.

247–248 °C); NMR ($CDCl_3$) 2.38 (s, ring CH_3), 2.98 (s) ppm.

Tetramethyl-1,4-benzenedithiol. The above *S,S'*-diester (11 g, 0.032 mol) was refluxed with 60 mL of pyridine, 11 mL of water, 60 mL of methanol, and 20 g (0.3 mol) of potassium hydroxide for 6.5 h under nitrogen with stirring. The volume was then reduced under nitrogen, the solution was diluted with water, and hydrochloric acid was added until precipitation of the dithiol was complete. The dithiol was filtered off, air-dried, and recrystallized from dichloromethane to give 5.8 g (91%) in two crops: mp 195–198.5 °C; NMR ($CDCl_3$) 2.37 (s, CH_3), 3.12 (s, SH) ppm; NMR (C_6D_6) 2.17 (s, CH_3) 2.84 (s, SH) ppm.

Anal. Calcd for $C_{10}H_{14}S_2$: C, 60.56; H, 7.11; S, 32.33. Found: C, 60.88; H, 7.25; S, 32.50.

2,5-Dimethoxy-1,4-benzenedithiol. 2,5-Dimethoxy-1,4-benzenedisulfonyl chloride[15] (40 g, 0.12 mol), 650 mL of ethanol, 200 g (2.9 mol) of 95% zinc dust, and 240 mL (2.86 mol) of hydrochloric acid were stirred and refluxed for 30 min. The mixture was poured into 2 L of water, and the product and excess zinc were filtered off. The air-dried mixture was extracted with cyclohexane, and the dithiol was crystallized from the cyclohexane to give 16.5 g (68%), mp 124–126 °C (lit.[16] mp 122 °C, prepared by another route).

1,4-Benzenedithiol. This dithiol was prepared by the hydrolysis of *p*-phenylene *S,S'*-bis(dimethylthiocarbamate)[11b] as described for the tetrafluoro derivative.

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Registry No. 4, 70470-78-9; **4** *N,N*-dimethyldihydrophenazine complex (1:1), 70470-79-0; **4** 1,3-diphenylisobenzofuran complex (1:4), 70470-80-3; tetrafluoro-*p*-phenylene *O,O'*-bis(dimethylthiocarbamate), 70470-81-4; tetrafluorohydroquinone, 771-63-1; dimethylthiocarbamoyl chloride, 16420-13-6; tetrafluoro-*p*-phenylene *S,S'*-bis(dimethylthiocarbamate), 70470-82-5; tetrafluoro-1,4-benzenedithiol, 3467-78-5; *N,N'*-dimethyldihydrophenazine, 15546-75-5; 1,3-diphenylisobenzofuran, 5471-63-6; tetrachloro-*p*-phenylene *O,O'*-bis(dimethylthiocarbamate), 70470-83-6; tetrachlorohydroquinone, 87-87-6; tetrachloro-*p*-phenylene *S,S'*-bis(dimethylthiocarbamate), 70470-84-7; tetrachloro-1,4-benzenedithiol, 67341-48-4; tetramethyl-*p*-phenylene *O,O'*-bis(dimethylthiocarbamate), 13522-73-1; tetramethylhydroquinone, 527-18-4; tetramethyl-*p*-phenylene *S,S'*-bis(dimethylthiocarbamate), 13512-07-7; tetramethyl-1,4-benzenedithiol, 70470-85-8; 2,5-dimethoxy-1,4-benzenedithiol, 30079-16-4; 2,5-dimethoxy-1,4-benzenedisulfonyl chloride, 19116-92-8; 1,4-benzenedithiol, 624-39-5; *p*-phenylene-*S,S'*-bis(dimethylthiocarbamate), 13512-06-6; 2,3,5,6-tetrachloro-1,4-benzenedithiol homopolymer, 70470-87-0; poly[dithio(2,3,5,6-tetrachloro-1,4-phenylene)], 70470-88-1.

Oxidative Cyclization of 3-(Amino)thioethers to Form S-Substituted Isothiazolidinium Salts[1]

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The reaction in which methionine is cyclized to form dehydromethionine (*S*-methylisothiazolidinium-3-carboxylate) by iodinic oxidation at neutral pH[3] has now been shown to be a general one for compounds possessing an amine group γ to a thioether function. Thus, the reaction provides a convenient route to the preparation of N-protonated, cyclic sulfilimines. The S-substituted isothiazolidinium salts from ethionine, *S*-phenylhomocysteine, *S*-benzylhomocysteine, and 3-(methylthio)propylamine were prepared and characterized by elemental analyses and NMR spectra. Cyclization of L-methionine was shown to produce a mixture of diastereomers which are chiral at positions 1 (sulfur) and 3. Evidence was obtained that hydrolysis of each diastereomer to form the sulfoxide proceeds with inversion of configuration. Oxidative cyclization of 3-(amino)thioethers was found to also be induced by a variety of *N*-halo derivatives and by lead tetraacetate.

Substances containing an isothiazolidine ring unsubstituted at sulfur are unknown, presumably because of their instability. The only previous example of an S-substituted isothiazolidine is dehydromethionine (*S*-methylisothiazolidinium-3-carboxylate) which was isolated by Lavine as a stable intermediate on the pathway to sulfoxide when methionine was oxidized by iodine in neutral solution.[2-4] Lavine's proposed structure for dehydromethionine was confirmed by X-ray diffraction.[5] Additional studies of dehydromethionine have been concerned with reversibility of the formation reaction and hydrolysis to the sulfoxide[6] and with reduction by thiols to form methionine.[7] Evidence has also been presented that a sulfurane intermediate is on the pathway to dehydromethionine when methionine is oxidized by iodine.[8]

In this paper, we report our findings regarding the scope of the reaction resulting in formation of S-substituted isothiazolidinium salts. We find that iodine and several *N*-halo derivatives will induce ring closure of substances containing a 3-(amino)thioether moiety. Many of the substances cyclized by us are amino acid derivatives and the carboxyl group neither prevents nor interferes with the cyclization reaction. Ring closure introduces a chiral center at sulfur and the mixture of diastereomers resulting from L- and/or D-amino acids is separated by chromatography.

The S-substituted isothiazolidinium salts may be viewed as the conjugate acids of cyclic sulfilimines. The sulfilimine class has been the subject of a recent review[9] and in

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