C, 58.83; H, 6.87; N, 10.17; S, 12.25. Bulb-to-bulb distillation [ca. 115 °C (0.01 mmHg)] was possible only with small quantities, even then some decomposition was observed.

***N*-Tosylmethyl-*N'*-*tert*-butylurea.** A solution of **3b** (1.00 g, 3.3 mmol) in a mixture of EtOH (10 mL) and H_2O (10 mL) was refluxed for 0.5 h. Upon addition of more H_2O a precipitate of *N*-(tosylmethyl)-*N'*-*tert*-butylurea was formed: 90% yield; mp 139–140 °C (from EtOH–H_2O). Anal. Calcd for $C_{13}H_{20}N_2O_3S$: C, 54.98; H, 7.10; N, 9.86; S, 11.59. Found: C, 55.23; H, 7.99; N, 9.48; S, 11.63.

***N*-(Tosylmethyl)carbodiimides 3c–e** were prepared similarly to **3b** from the corresponding thioureas[20] **9c–e** (10 mmol) and yellow HgO (2–3 equiv) in acetone or CH_2Cl_2. The resulting crude oils (Table I) could not be purified by column chromatography or distillation without decomposition.

5-Phenyl-2-[(triphenylmethyl)amino]oxazole (10a). By Phase-Transfer Catalysis. To a solution of carbodiimide **3a** (2.00 g, 4.4 mmol), benzaldehyde (0.47 g, 4.4 mmol), and *n*-Bu_4NBr (1.5 g, 4.4 mmol) in CH_2Cl_2 (30 mL) was added 30% (w/w) aqueous NaOH (5 mL). After the mixture was stirred for 1 h at room temperature, H_2O (100 mL) and CH_2Cl_2 (50 mL) were added. The organic layer was washed with water (3 × 50 mL), dried (Na_2SO_4), and concentrated under vacuum. The resulting oil was stirred with MeOH (10 mL) to give solid **10a**: 1.40 g (78%); mp 214–215 °C. Crystallization from CH_2Cl_2–MeOH gave an analytically pure sample with the same melting point: IR (KBr) 1610 (C=N), 3300 cm^{-1} (NH); ^1H NMR ($CDCl_3$) δ 6.30 (s, 1), 6.7–7.5 (m, 20), 7.9 (br s, 1). Anal. Calcd for $C_{28}H_{22}N_2O$: C, 83.58; H, 5.57. Found: C, 82.81; H, 5.55.

By Using NaH in DME. A solution of carbodiimide **3a** (2.00 g, 4.4 mmol) and benzaldehyde (0.50 g, 4.5 mmol) in dry DME (25 mL) was cooled with ice. NaH (0.3 g, 50% dispersion in mineral oil, ca. 6 mmol) was added, and the mixture was stirred for 20 h, while the ice bath was allowed to reach room temperature. The suspension was poured in water (100 mL). Extraction (CH_2Cl_2), washing with water (50 mL), drying (Na_2SO_4), and concentration as above gave **10a**: 1.30 g (73%); mp 213–215 °C; IR and ^1H NMR spectra identical with those of the product from the PTC reaction.

5-Phenyl-2-(*tert*-butylamino)oxazole (10b) was prepared by phase-transfer catalysis by stirring a mixture of carbodiimide **3b** (0.266 g, 1.0 mmol), benzaldehyde (0.106 g, 1.0 mmol), and *n*-Bu_4NBr (0.322 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) and 50% aqueous NaOH (5 mL) for 1 h at room temperature. After addition of water (25 mL) and CH_2Cl_2 (10 mL) and separation, the water layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were concentrated. For removal of *n*-Bu_4NBr, ether (15 mL) and water (10 mL) were added to the residue. After separation, the water layer was extracted with ether (10 mL), and the combined ether layers were washed with saturated NaCl solution (5 mL) and dried ($MgSO_4$). The solvent was removed, and the residue was crystallized once from CH_2Cl_2–pentane to give 0.172 g (80%) of **10b**: mp 124–125 °C; IR (Nujol) 1635 (C=N), 3420 cm^{-1} (NH); ^1H NMR ($CDCl_3$) δ 1.45 (s, 9), 5.3 (br s, 1), 6.95 (s, 1), 7.3 (m, 5). Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.96. Found: C, 72.20; H, 7.46; N, 12.92.

Oxazoles 10c–e,g were prepared by the PTC method analogously to **10a**, and **10f,h** were prepared analogously to **10b**.[20]

Typical Procedure for Detritylation: 2-Amino-5-phenyloxazole (11a). To a suspension of oxazole **10a** (1.50 g, 3.7 mmol) in MeOH (20 mL) was added concentrated, aqueous HCl (0.7 mL, 8.4 mmol). The mixture was refluxed for 0.5 h. After cooling, the mixture was added to 1 N aqueous NaOH (30 mL), and the precipitate was collected, washed with EtOH and with Et_2O, and crystallized from acetone to give 0.5 g (84%) of **11a**, mp 215–216 °C (lit.[13] mp 216 °C).

Acknowledgment. This work was supported (in part) by the Netherlands Foundation for Chemical Research (SON) with a fellowship to S.P.J.M.v.N.

Registry No. 3a, 76757-96-5; **3b**, 76757-97-6; **3c**, 76757-98-7; **3d**, 76757-99-8; **3e**, 76758-00-4; **8a**, 76758-01-5; **8b**, 7204-48-0; **8c**, 103-85-5; **8d**, 5055-72-1; **8e**, 598-52-7; **9a**, 76758-02-6; **9b**, 76758-03-7; **9c**, 76758-04-8; **9d**, 76758-05-9; **9e**, 76758-06-0; **10a**, 76758-07-1; **10b**, 76758-08-2; **10c**, 76758-09-3; **10d**, 76758-10-6; **10e**, 76758-11-7; **10f**, 76758-12-8; **10g**, 76758-13-9; **10h**, 76758-14-0; **11a**, 6826-24-0; **11b**, 13576-56-2; **11c**, 6825-91-8; **11d**, 13576-51-7; triphenylmethyl chloride, 76-83-5; thiourea, 62-56-6; triphenylmethanol, 76-84-6; *N*-(tosylmethyl)-*N'*-(triphenylmethyl)urea, 76758-15-1; *N*-tosylmethyl-*N'*-*tert*-butylurea, 76758-16-2; benzaldehyde, 100-52-7; *p*-nitrobenzaldehyde, 555-16-8; *p*-methoxybenzaldehyde, 123-11-5; *p*-chlorobenzaldehyde, 104-88-1.

Supplementary Material Available: Spectral (^1H NMR and IR) and analytical data are available of compounds **9c–e**, **10c–h**, and **11n–d** (3 pages). Ordering information is given on any current masthead page.

(20) Supplementary material available.

Studies toward Cyclic Trisulfides. Trisulfide Polymers and Sulfur Extrusion[1]

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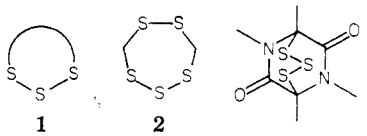
Attempts were directed toward the synthesis of a variety of cyclic trisulfides, particularly by the reaction of *N,N'*-dibenzimidazolyl sulfide with dithiols. Only one monomeric cyclic trisulfide was prepared by this method; other cases yielded either mixtures of oligomers characterized as low molecular weight (<5000) polymers or as products which spontaneously extruded sulfur to give the cyclic disulfides. We conclude that only where osmometric molecular weights or X-ray structures have been determined are monomeric cyclic trisulfides unambiguously defined.

Cyclic trisulfides (**1**) are a class of compounds of which only a few examples have been found in nature. The antibiotic compound lenthionine (**2**) has been isolated from both the edible mushroom Shiitake (*Lentinus edodes*)[2] and the red alga *Chondria californica*.[3] The bicyclic epitrithiodioxopiperazine unit **3** is a structural feature of a



1 2 3

(1) Organic Sulfur Chemistry. 40. For part 39, see: Harpp, D. N.; Steliou, K.; Cheer, C. *Chem. Commun.* **1980**, 825.

(2) (a) Morita, K.; Kobayashi, S. *Tetrahedron Lett.* **1966**, 573. (b) Morita, K.; Kobayashi, S. *Chem. Pharm. Bull.* **1967**, *15*, 988.

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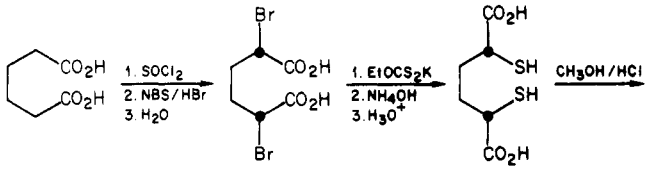
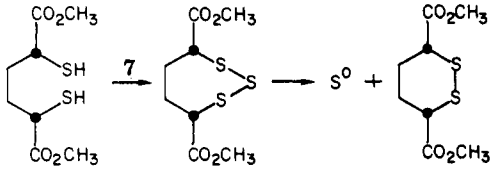
Scheme I



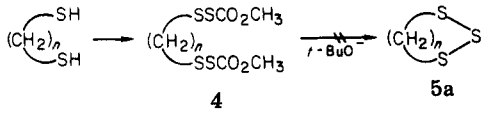
meso



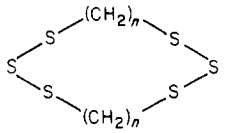
13 12 14

number of fungal metabolites.[4-8] X-ray crystal structure determinations of two cyclic trisulfides have been recently reported[9,10] while conformational aspects of this class have been investigated.[11]

The syntheses of several cyclic trisulfides have been reported;[12] however, there appears to be no general, successful approach to this type of compound. Efforts in our laboratory toward cyclic trisulfides by *tert*-butoxide-induced cyclization of disulfenyl thiocarbonates **4** were reported recently.[13] This technique provided in all cases (**4**, n = 2–10) mixtures of oligomers from which no monomeric species (**5a**) could be isolated. Interestingly, for **4** (n = 6–8, 10), crystalline dimeric bis(trisulfides) **5b** were



4 5a

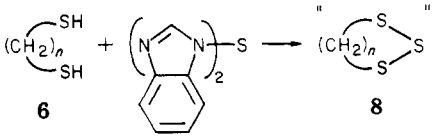


5b

obtained in moderate yield. Our research in the chemistry of azole sulfur-transfer reagents[14] included the attempted syntheses of small cyclic trisulfides **5a** (n = 2–4). Treatment of the dithiol precursors with a diazolyl sulfide provided white, clean, insoluble polymeric material for **5** (n = 2), a solid monomer/polymer mixture for **5** (n = 3), and a crystalline low molecular weight polymer (found mol wt 1390) for **5** (n = 4). We now report our further studies toward the synthesis of cyclic trisulfides.

Results and Discussion

Although the reaction of dithiols with azole sulfur-transfer reagents was unsuccessful in the preparation of monomeric **5a** for n = 2–4,[14] it was of interest to apply this method toward the unknown trisulfides **5a** (n = 5, 6, 8). Treatment of dithiols **6** (n = 5, 6, 8) with *N,N'*-dibenzimidazolyl sulfide (**7**)[14] afforded materials **8** which displayed the appropriate spectral and physical properties expected of the cyclic trisulfides **5a**. However, these properties were also comparable with those of the polymeric and/or dimeric products obtained by the disulfenyl thiocarbonate method.[13] For example, analysis of product **8** (n = 6; mp 35–37 °C) was nearly identical[15] with that of the corresponding dimer[13] **5b** (n = 6; mp 75–77 °C). Only ^{13}C NMR spectroscopy and osmometric molecular weight[16] determinations conclusively demonstrated a difference between these two materials. Thus **8** (n = 6) was characterized as a low molecular weight polymer (found mol wt 4241; calcd for monomer, 180). ^{13}C NMR spectroscopy was sensitive to the structural differences of polymer **8** (n = 6) and dimer **5b** (n = 6) but could not be used a priori to characterize them.[18] Products **8** (n = 5, 8) were similarly concluded to be low molecular weight polymers.



6 7 8

In contrast to the above results, the known momeric cyclic trisulfide **9** was prepared in 85% yield by reaction of **7** with the corresponding dithiol, compared to the re-

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(4) Hodges, R.; Shannon, J. S. *Aust. J. Chem.* **1966**, *19*, 1059.
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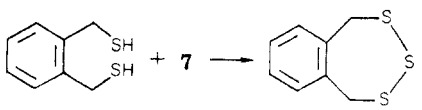
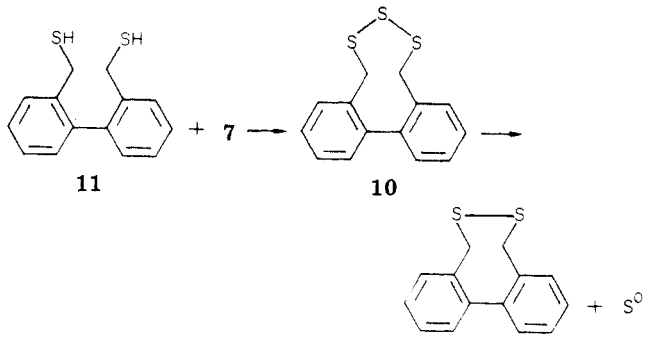
(12) For a concise literature survey, see ref 6 and 7 cited in ref 13. In addition, the following should be noted: Fedoseeva, V. N.; Petrun'kin, V. E. *Ukr. Khim. Zh. (Ukr. Ed.)* **1967**, *33*, 596; *Chem. Abstr.* **1967**, *67*, 90729; Tokunaga, H.; Akiba, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 506; Adesogan, E. K.; *Chem. Commun.* **1974**, 906; Japanese Patent, 78 142 529; *Chem. Abstr.* **1979**, *90*, 116456r; Rasheed, K.; Warkentin, J. D. *J. Org. Chem.* **1980**, *45*, 4806; Yamazaki, N.; Nakahama, S.; Yamaguchi, K.; Yamaguchi, T. *Chem. Lett.* **1980**, 1355.
(13) Harpp, D. N.; Granata, A. *J. Org. Chem.* **1979**, *44*, 4144.
(14) Harpp, D. N.; Steliou, K.; Chan, T. H. *J. Am. Chem. Soc.* **1978**, *100*, 1222.
(15) GC, TLC, and ^{1}H NMR, IR, and mass spectra were identical for **8** (n = 6) and **5b** (n = 6). The Rast[16a] molecular weight for **8** (n = 6) was 190 (calcd for monomer 180); the Rast molecular weight for **5b** (n = 6) was 205; however, the osmometric[16] molecular weight found for **5b** (n = 6) was 360 (calcd for dimer 360).[13] The mixture melting point of these two products was 73.5–75 °C. When **8** (n = 6) was melted, cooled, and then remelted, its melting point increased from 35–37 °C to 68–70 °C. Both compounds exhibited intense bands in the Raman spectra at 490 cm^{-1} indicative of the S–S–S stretch,[17] with only minor spectral differences. Raman bands associated with di- and tetrasulfides[17] were absent; thus both **8** (n = 6) and **5b** (n = 6) have trisulfide structures rather than averaged trisulfides (i.e., di- plus tetrasulfides).
(16) (a) Pasto, D. J.; Johnson, C. R. "Organic Structure Determination"; Prentice-Hall: Toronto, Canada, 1969; p 74. (b) Billmeyer, F. W., Jr. "Textbook of Polymer Science", 2nd ed.; Wiley-Interscience: New York, 1971; p 67.
(17) (a) Feher, F.; Krause, G.; Vogelbruch, K. *Chem. Ber.* **1957**, *90*, 1570. (b) Van Wart, H. E.; Scheraga, H. A. *J. Phys. Chem.* **1976**, *80*, 1812. (c) Catchpaugh, B.; Butler, I. S., unpublished results. (d) Colthup, N. B.; Daly, L. H.; Wiberley, S. E. "Introduction to Infrared and Raman Spectroscopy", 2nd ed.; Academic Press: New York, 1975. (e) Freeman, S. K. "Application of Lasar Raman Spectroscopy"; Wiley-Interscience: New York, 1974; Chapter 8.
(18) For polymer **8** (n = 6): ^{13}C NMR ($CDCl_3$) 38.76, 28.65, 28.03 ppm (sharp peaks). For dimer **5b** (n = 6): ^{13}C NMR ($CDCl_3$) 40.29, 29.03, 27.80 ppm (sharp peaks).[13] These minor differences were confirmed by the ^{13}C NMR spectrum of a mixture of the two samples (six peaks). Other than the ^{13}C NMR spectrum reported for a bridged bicyclic trisulfide,[19] cyclic trisulfides are apparently not included in the ^{13}C NMR literature of sulfur-containing heterocycles.[20]
(19) Fritz, H.; Weis, C. D. *Tetrahedron Lett.* **1974**, 1659.
(20) Block, E.; Bazzi, A. A.; Lambert, J. B.; Wharry, S. M.; Andersen, K. K.; Dittmer, D. C.; Patwardham, B. H.; Smith, D. J. H. *J. Org. Chem.* **1980**, *45*, 4807, and references cited therein.



9

ported 48% yield by the use of Na_2S.[21] The ^1H NMR of **9** shows an equilibrium between the predominant chair conformer (AB quartet at δ 4.4 for $ArCH_2$) and the boat conformer (singlet at δ 4.0 for $ArCH_2$), as reported previously.[11b,22,23,26]

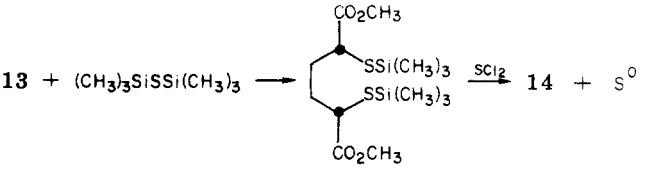
It was felt that trisulfide **10** would be an interesting target, as hindered rotation about the phenyl–phenyl bond would induce magnetic nonequivalence in the benzylic protons.[28] Treatment of dithiol **11** with reagent **7** yielded



11 **10**

what appeared to be crude **10**, as a sticky oil;[26] however, crystallization attempts failed. Chromatography on silica gel provided elemental sulfur and a white solid which was concluded (^1H NMR and C, H, and S analysis) to be a 45:55 trisulfide–disulfide mixture. Presumably, trisulfide **10** had decomposed to the disulfide by elimination of a sulfur atom.[29] Other examples of sulfur atom ejection under "mild" conditions are known in the literature.[31]

For a study of the stereochemical consequences of the desulfurization of trisulfides by tertiary phosphorus compounds,[32] we required a cyclic trisulfide having substituents at the two α-carbons. *cis*-4,7-Bis(carbomethoxy)-1,2,3-trithiepane (**12**, Scheme I) was particularly desirable, as the corresponding *cis*- and *trans*-disulfides can be desulfurized by tris(diethylamino)phosphine to the trans and cis cyclic sulfides, respectively.[33] Thus adipic acid was α-halogenated[34] to give a diastereomeric mixture of α,α'-dibromoadipic acid. Crystallization afforded the meso acid, which was converted in two steps to dimethyl *meso*-α,α'-dimercaptoadipate (**13**) by standard procedures. Earlier attempts to prepare **12** from **13** by the action of sulfur dichloride or by the Bunte salt method[21] had failed.[35] It was now hoped that reaction of **13** with reagent **7** might provide access to **12**. However, this technique afforded instead a good yield of the corresponding *cis*-dithiane **14** plus elemental sulfur, with no evidence of the desired trisulfide **12**. Access to trisulfide **12** via the corresponding tetrasulfide or dithiosulfite [RS(S=O)SR][36] was also considered; however, reaction of **13** with *N,N'*-dibenzimidazolyl disulfide[14] or sulfoxide[39] also afforded disulfide **14** plus elemental sulfur.[40] As a final approach to **12**, dithiol **13** was disilylated by treatment with hexamethyldisilathiane[25] and then reacted with sulfur dichloride; the product obtained was again *cis*-disulfide **14**.



As several synthetic routes directed toward **12** yielded in every case the disulfide **14** plus elemental sulfur, it is probable that **12** was indeed formed but rapidly extruded a sulfur atom to give **14**. If so, this represents another example of "spontaneous" desulfurization.[31] That the *meso*-dithiane **14** is formed rather than a mixture of diastereomers implies that the central sulfur atom is being expelled.

Another attractive α,α'-disubstituted cyclic trisulfide target was *cis*-4,7-dimethyl-1,2,3-trithiepane (**15**). Both

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(22) Kabuss, S.; Lüttringhaus, A.; Friebolin, H.; Mecke, R. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1966**, *21B*, 320.
(23) For comparison, the corresponding cyclic sulfide[24] was prepared in 96% yield by reaction of α,α'-dibromo-*o*-xylene with hexamethyldisilathiane[25] (160 °C, 48 h): ^1H NMR ($CDCl_3$) δ 7.0 (s, 4 H), 4.1 (s, 4 H).
(24) Cava, M. P.; Deana, A. A. *J. Am. Chem. Soc.* **1959**, *81*, 4266.
(25) Harpp, D. N.; Steliou, K. *Synthesis* **1976**, 721.
(26) Although cyclic tetrasulfides are known,[5c,27] the tetrasulfide analogue of this trisulfide could not be obtained by reaction of the appropriate dithiol with *N,N'*-dibenzimidazolyl disulfide;[14] the product appeared to be a mixture of polysulfides and polymer.
(27) (a) Krespan, C. G.; Brasen, W. R. *J. Org. Chem.* **1962**, *27*, 3995. (b) Ariyan, Z. S.; Martin, R. L. *Chem. Commun.* **1969**, 847. (c) Murdock, K. C. *J. Med. Chem.* **1974**, *17*, 827. (d) Bottino, F.; Foti, S.; Pappalardo, S.; Bresciani-Pahor, N. *Tetrahedron Lett.* **1979**, 1171.
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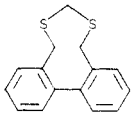
(29) Interestingly, the structurally similar 1,5-dihydro-2,4-dibenzodithionin was stable at room temperature.



This compound was synthesized in 90% yield by reaction of the potassium salt of dithiol **11** with methylene iodide in methanol (similar to the procedure for another compound[30]): mp 67–70 °C; ^1H NMR ($CDCl_3$) δ 8.7–7.1 (m, 8 H), 3.80–3.25 (AB-pattern, J_{AB} = 14 Hz, 4 H), 3.6 (s, 2 H); ^{13}C NMR ($CDCl_3$) 140.57, 138.09, 129.51, 128.59, 127.94, 127.08, 40.77, 35.80 ppm (from Me_4Si); mass spectrum, *m/e* (relative intensity) 258 (66, M^+), 212 (45), 211 (66), 197 (32), 179 (100), 178 (61), 166 (29), 165 (56).
(30) Harpp, D. N.; Steliou, K.; Friedlander, B. T. *Org. Prep. Proced. Int.* **1978**, *10*, 133.
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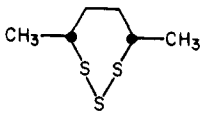
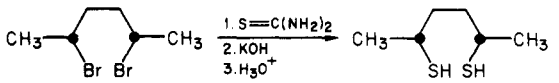
(32) (a) Harpp, D. N.; Ash, D. K.; Smith, R. A. *J. Org. Chem.* **1980**, *45*, 5155. (b) Harpp, D. N.; Smith, R. A., manuscript in preparation.
(33) Harpp, D. N.; Gleason, J. G. *J. Am. Chem. Soc.* **1971**, *93*, 2437.
(34) Harpp, D. N.; Bao, L. Q.; Black, C. J.; Gleason, J. G.; Smith, R. A. *J. Org. Chem.* **1975**, *40*, 3420.
(35) (a) Reaction of **13** with SCl_2 gave an oil which appeared to have the corresponding cyclic disulfide as its major component by GC and mass spectral analysis.[35b] The Bunte salt method[21] applied to **13** yielded an uncharacterizable oil.[35b] (b) Ash, D. K. Ph.D. Thesis, McGill University, 1973.
(36) Aryl and alkyl dithiosulfites are known to decompose thermally to give equal amounts of di- and trisulfides.[37] Alternatively, the 2-oxide of **14** could presumably be deoxygenated to **14** by triphenylphosphine.[38]
(37) (a) Akiyama, F. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1046. (b) Field, L.; Lacefield, W. B. *J. Org. Chem.* **1966**, *31*, 3555.
(38) (a) Hayashi, S.; Furukawa, M.; Yamamoto, J.; Hamamura, K. *Chem. Pharm. Bull.* **1967**, *15*, 1310. (b) Harpp, D. N.; Gleason, J. G.; Ash, D. K. *J. Org. Chem.* **1971**, *36*, 322.
(39) (a) Harpp, D. N.; Steliou, K., unpublished results. (b) A report of the reaction of diazolyl sulfoxides, including dibenzimidazolyl sulfoxide, with thiols [$2(>N)_2S{=}O + 4RSH \rightarrow RSSSR + RSSR$] has recently appeared: Ogata, M.; Matsumoto, H.; Shimizu, S. *Heterocycles* **1980**, *14*, 955. A mechanism was given which provides an alternative to ours[40] for the reaction with dithiol **13**. (c) For additional information on diazolyl sulfoxides, see Ogata, M.; Matsumoto, H. *Synth. Commun.* **1980**, *10*, 733, and Walter, W.; Radke, M. *Liebigs Ann. Chem.* **1979**, 1756.
(40) Sulfur formed in the second case might be due to a decomposition of trisulfide **14** formed,[36] or alternatively by a disproportionation of eliminated sulfur monoxide.[34]



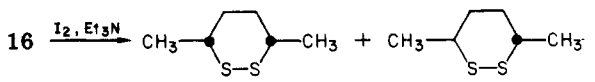
15

the corresponding *cis*- and *trans*-disulfides are known,[41] and Eliel and co-workers[41a] have shown that the *trans*-disulfide is desulfurized by $(Et_2N)_3P$ to the corresponding cis cyclic sulfide. The trisulfide (diastereomeric mixture of **15**) has been reported by Cairns and co-workers as a product (25%) from the reaction of acetonylacetone with hydrogen sulfide under pressure (7500–8500 atm, 80 °C, 15 h).[42] Thus, by reaction of thiourea with crystalline *meso*-2,5-dibromohexane was prepared 2,5-hexanedithiol (**16**). Analysis of **16** indicated a purity of >99.7%.



meso 16

However, oxidation of **16** gave the dithiane which was clearly a mixture of cis (**17a**) and trans (**17b**) isomers in

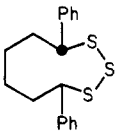


17a 17b

a ratio of ca. 3:1 (GC, NMR). It is quite unlikely that these reaction conditions would cause any isomerization at the α-carbons; therefore, the dithiol **16** obtained was evidently a ca. 3:1 meso/*dl* mixture of diastereomers which could *not* be differentiated by our GC analysis.

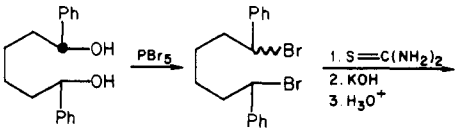
Dithiol **16** was then treated with reagent **7** in the hope of obtaining trisulfide **15** (**16** + **7** $\rightarrow$ **15**). The product obtained showed no evidence of eliminated elemental sulfur (TLC); however, GC and gas chromatography/mass spectroscopy indicated four distinct components: 10% of ca. 3:1 *cis*-/*trans*-dithianes **17a** and **17b**, 85% trithiepane **15**, and 5% of the corresponding cyclic tetrasulfide. Attempted distillation of this material in vacuo afforded no product distillate but rather polymerized the product to an insoluble, sticky, rubbery gel. A series of osmometric molecular weight determinations showed that the viscous oil which was first isolated was a low molecular weight polymer (found mol wt ca. 530; calcd for monomer, 180). This could be "purified" by filtration through silica gel to give a free-flowing oil of reduced molecular weight (found mol wt ca. 275). Heating neat at 50 °C for 5 h did not significantly affect the molecular weight or viscosity of this "purified" material; however, prolonged storage (70 days) at room temperature significantly increased the viscosity while the molecular weight increased by only a few percent. In contrast, reaction of dithiol **16** with sulfur dichloride afforded a viscous oil having an osmometric molecular weight of 1900.

As a final attempt toward the synthesis of a cyclic trisulfide substituted at the two α-carbons, 4,9-diphenyl-1,2,3-trithionane (**18**) was chosen as a target compound.

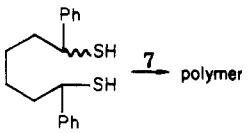


18

Treatment of the racemic diastereomer of 1,6-diphenyl-1,6-hexanediol (**19**) with phosphorus pentabromide afforded the dibromide **20** in good yield.[43] From the crude



19 20



21

product oil (presumably a mixture of meso and *dl* diastereomers) could be isolated a crystalline dibromide diastereomer. Reaction of this compound with thiourea provided the dithiol **21** (after chromatography) in low yield as an impure oil. Treatment of this impure dithiol **21** with reagent **7** gave a viscous oil which had not eliminated elemental sulfur. However, the product was concluded to be a mixture of oligomers of **18**. Attempts to isolate monomer **18** from this mixture failed, and the synthesis of this cylic trisulfide was thus abandoned.

In summary, in contrast to the efficient use of the azole sulfur transfer reagent for the preparation of linear trisulfides, only the known[21] monomeric cyclic trisulfide **9** could be obtained by reaction of the dithiol with this reagent. All other attempts to prepare monomeric cyclic trisulfides with this reagent or by other techniques failed, yielding either a mixture of oligomers (low molecular weight polymer) or a product which extruded a sulfur atom to afford the corresponding cyclic disulfide. Our results lead us to conclude that the criteria generally used in the literature[12] (solubility and ^1H NMR and mass spectra) for characterization of cyclic trisulfides were *not* found to be

(41) (a) Eliel, E. L.; Hutchins, R. O.; Mebane, R.; Willer, R. L. *J. Org. Chem.* **1976**, *41*, 1052. (b) Isenberg, N.; Herbrandson, H. F. *Tetrahedron* **1965**, *21*, 1067. (c) Dodson, R. M.; Nelson, V. C. *J. Org. Chem.* **1968**, *33*, 3966.

(42) Cairns, T. L.; Evans, G. L.; Larchar, A. W.; McKusick, B. C. *J. Am. Chem. Soc.* **1952**, *74*, 3982. It should be noted that the boiling point and n_D value of the disulfide component from this reaction do not compare well with those of dithiane obtained by classical means[41b] and that analyses of both the disulfide and trisulfide are not within acceptable error limits.

(43) Attempted tosylation of **19** by the standard procedure and workup[44] afforded no product;[45] attempted mesylation of **19** afforded no dimesylate, but rather an 18–25% yield of 1,6-dichloro-1,6-diphenylhexane (see Experimental Section).[47] This dichloro compound could also be obtained quantitatively by treatment of **19** with $SOCl_2$ (see Experimental Section). However, treatment of this dichloro compound with thiourea in ethanol afforded no significant amount of dithiol **21**; the major product was 1,6-diphenyl-6-ethoxy-1-hexanethiol (see Experimental Section); the ethoxy moiety apparently formed by solvolysis.

(44) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 1180.

(45) Difficulty in the preparation of benzylic tosylates has been noted: ref 44, p 1079. The lack of any other material isolated by the ether extraction is likely due to the formation of pyridinium tosylate salts[46] (soluble in aqueous pyridine).

(46) (a) Edgell, W. F.; Parts, L. *J. Am. Chem. Soc.* **1955**, *77*, 4899. (b) Goerdeler, J. *Method. Chim.* **1975**, *6*, 625. (c) March, J. "Advanced Organic Chemistry—Reactions, Mechanisms, and Structure", 2nd ed.; McGraw-Hill: New York, 1977; pp 272, 377, 378.

(47) The formation of alkyl chlorides by reaction of alcohols with sulfonyl chlorides is not normally observed in the presence of base.[48] However, the proposed formation of a pyridinium sulfonate salt to account for the low yield of organic material from this reaction[45] is consistent with the formation of some dichloro compound by a similar attack of chloride ion at the benzylic carbon atom.[48,49]

(48) Martin, D. In "Preparative Organic Chemistry"; Hilgetag, G., Martini, A., Eds.; Wiley-Interscience: New York, 1972; p 678.

(49) Reference 46c, p 392.

reliable in this investigation; even ^{13}C NMR and Raman spectroscopy did not help to characterize the trisulfide products obtained as monomeric, dimeric, or polymeric substances. We now conclude that in the literature of cyclic trisulfides[12] (including crystalline compounds), only where osmometric molecular weights[21] or X-ray structures[9,10] have been determined are monomeric cyclic trisulfides unambiguously defined.

Experimental Section

Unless stated otherwise, chemical reagents were used directly as obtained from commerical sources. Melting points were obtained on a Gallenkamp block apparatus and are uncorrected. Boiling points are also uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 257 grating spectrophotometer, calibrated with the 1602-cm^{-1} band of a polystyrene film. Raman spectra were recorded by using a Jarrel-Ash 25-300 Raman spectrophotometer using a coherent radiation Model 52 argon ion laser operating on the 514.5-nm plasma line; calibration was done by using a standard neon lamp. Proton magnetic resonance spectra were measured with a Varian Associates T-60 spectrophotometer, while ^{13}C decoupled spectra were recorded on a Bruker WH-90 equipped with Fourier transform. Mass spectra were obtained on an AEI-MS-902 or LKB 9000 mass spectrometer using a direct-insertion probe, while gas chromatography/mass spectral analyses were performed by using a Hewlett-Packard 5984A system. Gas chromatographic analyses were obtained by using a Hewlett-Packard F&M Model 5751A research chromatograph equipped with a Perkin-Elmer Model 194B printing integrator. High-pressure liquid chromatographic analyses were performed on a Waters Associates high-speed chromatograph equipped with a Model 6000A pump, a U6K loop injector, and Schoeffel SF770 variable-wavelength ultraviolet and Waters R401 refractive index detectors. Thin-layer chromatographic analyses were performed on E. Merck silica gel 60 F-254 sheets (catalogue no. 5775) having a fluorescent indicator; column chromatography was accomplished with E. Merck silica gel 60 (catalogue no. 7734). Elemental analyses were performed by the microanalysis department of the H. C. Ørsted Institute of the University of Copenhagen, Denmark, or by Galbraith Laboratories.

Osmometric molecular weight determinations of compound **15** oligomeric products were obtained in CCl_4 at 40.6 °C by using a Hitachi Perkin-Elmer Model 115 molecular weight apparatus calibrated with benzil; molecular weights of authentic samples of PhSSPh, $(PhCH_2S)_2S$, and $(n\text{-}PrS)_2S$ were measured and were accurate to within 4%. Osmometric molecular weight determinations of compound **8** oligomeric products were kindly carried out by Dr. Hector Séguin of the National Research Council.

Synthesis of Trisulfides 8. A solution of dithiol **6** (20 mmol) in benzene (40 mL) was added dropwise to a suspension of reagent **7**[14] (20 mmol) in benzene (60 mL) under a dry nitrogen atmosphere over a 3-h period with stirring. Upon complete addition, the mixture was stirred for an additional 3 h and then filtered to remove benzimidazole. The filtrate was concentrated under reduced pressure, and the residue obtained was chromatographed on silica gel by using benzene as eluant. This afforded a nearly quantitative yield of material which was essentially identical (^1H NMR, IR, and mass spectra) with the corresponding polymeric and/or dimeric products obtained by the disulfenyl thiocarbonate method.[13] Thus, **8** (n = 5) was obtained as an oil: ^{13}C NMR ($CDCl_3$) 38.58, 28.30, 27.26 ppm (sharp peaks). Product **8** (n = 6) was a solid: mp 35–37 °C; ^{13}C NMR ($CDCl_3$) 38.76, 28.65, 28.03 ppm (sharp peaks); mol wt (Rast method[16a]) found 189, 192 (calcd for monomer, 180); osmometric molecular weight[16] found 4241. Product **8** (n = 8) was a viscous colorless oil: ^{13}C NMR ($CDCl_3$) 38.69, 28.84, 28.62, 28.26 ppm (sharp peaks); osmometric molecular weight found 4793 (calcd for monomer, 208).

α,α′-Dimercapto-o-xylene. Thiourea (42 g, 0.56 mol) and α,α′-dibromo-o-xylene (66 g, 0.25 mol) were stirred in 95% ethanol at reflux for 24 h. After the mixture cooled to room temperature, the solvent was evaporated at reduced pressure, and an aqueous solution of the residue was made alkaline and then acidified to pH 4. Extraction with CH_2Cl_2 (3 × 200 mL), drying ($MgSO_4$), and evaporation of the solvent afforded a white solid residue (34.0 g) which was recrystallized from hexanes to yield 33 g (78%) of α,α′-dimercapto-o-xylene as colorless crystals, mp 46–48 °C (lit.[50a] mp 45–46 °C, lit.[50b] mp 44 °C).

1,5-Dihydro-2,3,4-benzotrithiepin (9). A solution of α,α′-dimercapto-o-xylene (1.7 g, 10 mmol) in benzene (50 mL) was added dropwise to a suspension of reagent **7** (2.7 g, 10 mmol) in benzene (100 mL) over a 1-h period with stirring. The mixture was then stirred overnight, filtered to remove benzimidazole (2.5 g), and evaporated under reduced pressure to yield a yellow residue. This was crystallized from chloroform to afford 1.7 g (85%) of cyclic trisulfide **9** as colorless plates: mp 98–101 °C (lit.[21] mp 101–102 °C); ^1H NMR ($CDCl_3$) δ 7.0 (s, 4 H), 4.4 (AB pattern, Δδ = 0.7 ppm, J = 15 Hz, 2.9 H), 4.0 (s, 1.1 H).

2,2-Bis(bromomethyl)biphenyl. To a 2-L, three-necked flask equipped with a mechanical stirrer, a pressure-equilibrated dropping funnel, a thermometer, and an inlet for dry nitrogen were added 2,2-bis(hydroxymethyl)biphenyl[14] (53 g) and dry tetrahydrofuran (100 mL). After the mixture was cooled in an ice–salt bath to 0–5 °C, phosphorus tribromide (125 g) was added dropwise with vigorous mixing at such a rate that the reaction temperature was kept at 0–5 °C. Following this, an additional amount of the diol (53 g), PBr_3 (125 g), diol (53 g), and PBr_3 (250 g) were introduced successively to the reaction flask in a similar manner [total diol, 159 g (0.75 mol); total PBr_3, 500 g (1.85 mol)]. The resulting reaction solution was then heated at reflux overnight (16 h), cooled to 0 °C, and diluted with anhydrous diethyl ether (700 mL) whereupon a milky precipitate formed. Water (400 mL) was cautiously and slowly added with vigorous stirring at 0 °C to destroy excess PBr_3, and additional water (500 mL) caused the separation of aqueous and organic phases and the formation of a precipitate. Filtration and washing with Et_2O afforded 75 g of a white crystalline solid. The aqueous layer was separated from the filtrate, and the organic phase was washed with 20% aqueous Na_2CO_3 (3 × 150 mL) and water (2 × 150 mL), dried ($MgSO_4$), and cooled (−20 °C) overnight to effect crystallization. The crystals (165 g) were collected and combined with the first batch for a total yield of 240 g (94%) of 2,2-bis(bromomethyl)biphenyl, mp 87–90 °C (lit.[51] mp 91–93 °C).

2,2′-Bis(dimercaptomethyl)biphenyl (11). This dithiol was prepared from the corresponding dibromide (above) in a manner analogous to the synthesis of α,α′-dimercapto-o-xylene described above. The dithiol **11** was obtained in 95% yield as a light yellow oil [lit.[28a] bp 156–157 °C (0.3 mm)] not requiring further purification.

1,5-Dihydro-2,3,4-dibenzotrithionin (10). A solution of dithiol **11** (3.7 g, 15 mmol) in benzene (200 mL) was added dropwise to a suspension of reagent **7** (4.0 g, 15 mmol) in benzene (100 mL) over a 1-h period with stirring. The resulting mixture was stirred overnight, filtered to remove benzimidazole (3.6 g), and evaporated under reduced pressure to afford 4.5 g of a light yellow sticky residue which could not be induced to crystallize. Chromatography over silica gel using benzene as eluant provided elemental sulfur plus 3.9 g of a white solid, mp 132–140 °C. ^1H NMR analysis of the product at various intervals before and after chromatography, compared with the ^1H NMR of an authentic sample of the corresponding disulfide[28a] and of a mixture of the product and disulfide, indicated the trisulfide **10** was spontaneously decomposing to the corresponding disulfide. By subtraction of the disulfide spectrum, the spectrum of cyclic trisulfide **10** was concluded to be as follows: ^1H NMR ($CDCl_3$) δ 7.4–7.0 (m, 8 H), 3.8 (AB pattern, Δδ = 0.2 ppm, J = 12 Hz, 4 H). Anal. Calcd for a 45/55 ratio of $C_{14}H_{12}S_3/C_{14}H_{12}S_2$: C, 65.23; H, 4.68; S, 30.08. Found for the chromatographed product: C, 65.20; H, 5.13; S, 29.45. Pure trisulfide **10** could not be isolated from the trisulfide–disulfide mixture by either recrystallization or chromatography.

***meso*-α,α′-Dibromoadipic Acid.** The *N*-bromosuccinimide method[34] of α-bromination was utilized. Thus a mixture of 73.0 g (0.50 mol) of adipic acid and 144 mL (2.0 mol) of thionyl chloride was heated at reflux (85 °C bath). After 1.25 h, the resulting solution was cooled to room temperature, and 213.6 g (1.20 mol) of *N*-bromosuccinimide, 10 drops of concentrated (48%) hydro-

(50) Kötz, A. *Chem. Ber.* **1900**, *33*, 729. (b) Mayerle, J. J.; Denmark, S. E.; DePamphilis, B. V.; Ibers, J. A.; Holm, R. H. *J. Am. Chem. Soc.* **1975**, *97*, 1032.
(51) Hall, D. M.; Lesslie, M. S.; Turner, E. E. *J. Chem. Soc.* **1950**, 711.

bromic acid, and 400 mL of CCl_4 were added. After being heated at reflux (80 °C bath) for 2.0 h, the mixture was cooled to 0 °C, the succinimide was removed by filtration, and the filtrate was evaporated under reduced pressure to give a pale orange, clear liquid. To this residue was then added 250 mL of water, and the mixture was heated at 85 °C for 15 min. The resulting solution was cooled to yield 79.6 g of precipitate which was recrystallized from water to give 35.2 g (23%) of crystals of *meso*-α,α'-dibromoadipic acid, mp 184–187 °C (lit.[52] mp 192–193 °C).

***meso*-α,α'-Dimercaptoadipic Acid.** By use of the procedure of Fredga,[53] the sodium salt of 29.6 g (97.5 mmol) of *meso*-α,α'-dibromoadipic acid was treated with 32.6 g (0.20 mol) of ethylxanthic acid potassium salt. Hydrolysis of the resulting xanthate ester with concentrated NH_4OH afforded, after workup, 8.7 g (42%) of *meso*-α,α'-dimercaptoadipic acid, mp 180–184 °C (H_2O) (lit.[53] mp 188 °C).

Dimethyl *meso*-α,α'-Dimercaptoadipate (13). A suspension of 8.0 g (38 mmol) of *meso*-α,α'-dimercaptoadipic acid in 500 mL of methanol was stirred at 0 °C as anhydrous hydrogen chloride gas was bubbled through for 1 h, during which time all of the diacid dissolved. The methanol was then removed under reduced pressure, 100 mL of diethyl ether was added, and the solution was dried ($MgSO_4$) and evaporated to give 9.1 g of a yellow oil. The oil was treated with activated charcoal in 500 mL of boiling hexanes, filtered, and allowed to cool slowly to −20 °C to yield 6.9 g (76%) of the diester **13** as colorless plates: mp 40–41 °C (lit.[35b] mp 40.5–44.5 °C); NMR (CCl_4) δ 3.75 (s, 6 H), 3.45–3.05 (m, 2 H), 2.0 (d, 2 H), 2.1–1.7 (m, 4 H).

Attempted Synthesis of *cis*-4,7-Bis(carbomethoxy)-1,2,3-trithiepane (12). A solution of 1.0 g (4.2 mmol) of dithiol **13** in 50 mL of benzene or carbon tetrachloride was added dropwise over an ca. 4-h period to a mixture of 1.23 g (4.6 mmol) of reagent **7** in 50 mL of the same solvent stirred at room temperature. Analysis of the reaction mixture by TLC, GC, and NMR indicated complete conversion to the dithiane **14**. TLC (C_6H_6) also indicated the presence of elemental sulfur. The reaction mixture was filtered to remove benzimidazole and unreacted reagent **7**, and the residue obtained upon evaporation of the solvent was chromatographed over 20 g of silica gel with petroleum ether as eluant. Initial fractions contained 47 mg (36%) of elemental sulfur, mp and mmp 111–117 °C. Elution with benzene gave a 70–80% yield of crude *cis*-3,6-bis(carbomethoxy)-1,2-dithiane (**14**) as an oil which crystallized on standing; mp 61–65 °C. This material was identical with the unchromatographed product by TLC, GC, and NMR, and was >95% pure **14** by analytical liquid chromatography (Porasil C18 column, 1:3 THF–H_2O at 1.0 mL/min). Recrystallization from petroleum ether–benzene gave 578 mg (58%) of product [mp 71.5–73 °C (lit.[33] mp 72–76 °C)] identical in all respects (NMR, IR, and mass spectra) with authentic dithiane.[33] Anal. Calcd for $C_8H_{12}O_4S_2$: C, 40.66; H, 5.13. Found: C, 41.28; H, 5.44. Further elution of the column with $CHCl_3$ and CH_3OH gave a viscous oil (130 mg) which was similar to dithiane **14** (NMR, TLC, GC) and which was concluded to be a mixture of higher oligomers.

The reaction of dithiol **13** with *N,N'*-dibenzimidazolyl disulfide[14] was similar in procedure, analysis, and workup to the reaction of **13** with **7** described above. Thus was obtained a 55% yield of elemental sulfur and a 73% yield of dithiane **14**.

The procedure, analysis, and workup of the reaction of dithiol **13** with *N,N'*-dibenzimidazolyl sulfoxide[39] was also similar to that of the reaction of **13** with **7**.

Attempted Synthesis of Trisulfide 12 via a Disilylated Intermediate. A mixture of 1.0 g (4.2 mmol) of dithiol **13** and 785 mg (4.4 mmol) of hexamethyldisilathiane[25] in 2 mL of CCl_4 was stirred for 5 h. After evaporation of the volatiles, the disilylated dithiol was dissolved in 100 mL of CCl_4, and a solution of 460 mg (4.5 mmol) of purified[14] sulfur dichloride in 100 mL of CCl_4 was added over a 2.5-h period, followed by stirring at room temperature. Monitoring of the reaction by NMR spectroscopy indicated the formation of chlorotrimethylsilane. After 23 h, an additional ca. 0.8 mL of SCl_2 was added to the reaction solution, and after an additional 3 h, complete conversion of $RSSi(CH_3)_3$ to $ClSi(CH_3)_3$ was confirmed by ^1H NMR analysis. Analysis of the reaction mixture by TLC (C_6H_6) indicated the presence of elemental sulfur and dithiane **14**. Evaporation of volatiles under reduced pressure followed by column chromatography (35 g of silica gel, petroleum ether eluant) yielded 71 mg (53%) of elemental sulfur. Elution with benzene afforded 106 mg of a mixture of sulfur and dithiane **14** (TLC) and 294 mg (30%) of a colorless oil (pure dithiane **14** by GC, Apiezon L, 200 °C) which crystallized on standing. Recrystallization from petroleum ether–benzene gave 103 mg (10%) of colorless crystals [mp 68–69.5 °C (lit.[33] mp 72–76 °C)] identical with dithiane **14** (IR, NMR).

***meso*-2,5-Dibromohexane.** The procedure was based on that of Kornblum and Eicher[54] and afforded an 86% yield of a clear slightly yellow liquid. Cooling on dry ice initiated crystallization of the *meso* dibromide, which was recrystallized (four crops) from methanol to afford 104.7 g (43%) of *meso*-2,5-dibromohexane, mp 38–39 °C (lit.[54] mp 39 °C). The mother liquors were distilled under reduced pressure to yield 86.0 g (35%) of a colorless liquid [bp 97–99 °C (26–27 mm) [lit.[54] bp 87–89 °C (12–13 mm)]] which was ca. 90% *dl*-2,5-dibromohexane by GC (10% Carbowax 20M, 75 °C). Under these GC conditions partial separation of the two diastereomers was achieved, and the crystalline material was confirmed to be homogeneous by this technique. No chromatographic separation of diastereomers was achieved by GC on 10% Apiezon L.

***meso*-2,5-Hexanedithiol (16).** A mixture of 73.2 g (0.30 mol) of *meso*-2,5-dibromohexane, 68.5 g (0.90 mol) of thiourea, and 60 mL of water was heated at reflux (120 °C bath) for 9 h. A solution of 87.3 g (1.56 mol) of KOH in 160 mL of water was then added, and the resulting mixture refluxed under nitrogen for 6 h. After cooling to room temperature, the mixture was acidified with dilute H_2SO_4 and extracted three times with $CHCl_3$. The organic phases were combined, dried ($MgSO_4$), concentrated, and distilled to yield 35.4 g (79%) of a clear colorless liquid, bp 52–52.5 °C (2.4 mm) [lit.[41a] bp 76–78 °C (5 mm)]. ^1H NMR and IR analyses were in accord with the dithiol structure, as was the very strong unpleasant odor. This liquid was homogeneous by GC analysis on a 6-ft 10% Apiezon L column (programmed 100–150 °C at 15 °C/min) and was >99.7% pure by GC analysis on a 6-ft 10% Carbowax 20M column at 90 °C. However, it was concluded to be a mixture of 73% *meso*- and 27% *dl*-2,5-hexanedithiol on the basis of the oxidation products (vide infra).

3,6-Dimethyl-1,2-dithiane (17a,b). To a stirred solution of 1.5 g (10 mmol) of the dithiol **16** in 150 mL of $CHCl_3$ was added 2.12 g (21 mmol) of Et_3N. A saturated $CHCl_3$ solution of iodine was then added dropwise with stirring at room temperature until a slight excess of I_2 was evidenced by its color. The solution was washed with aqueous $Na_2S_2O_3$ and dilute HCl, dried ($MgSO_4$), and evaporated under reduced pressure to yield 1.4 g (95%) of a clear nearly colorless liquid. GC analysis (6-ft column, 10% Carbowax 20M at 85 °C; 12-ft column, 20% Carbowax 20M, programmed 100–200 °C at 20 °C/min; 6-ft column, 10% SE-30, programmed 50–250 °C at 20 °C/min) indicated two close components in a ratio of 27:73, with the larger peak having the longer retention time. ^1H NMR analysis compared with that in the literature[41b] confirmed this to be an ca. 3:1 mixture of *cis*- and *trans*-3,6-dimethyl-1,2-dithiane.

Reaction of Dithiol 16 with Reagent 7. The following procedure is representative. To 5.85 g (22 mmol) of reagent **7** stirred at room temperature in 200 mL of benzene or carbon tetrachloride was added dropwise a solution of 3.00 g (20 mmol) of dithiol **16** in 100 mL of the same solvent over a 2–3-h period. After complete addition a lead acetate test for thiol was negative. TLC indicated the absence of dithiol and elemental sulfur but revealed more than five product components. Concentration under reduced pressure and filtration gave a quantitative yield of trisulfide oligomers as a viscous insoluble oil, osmometric molecular weight (CCl_4) found 530 (calcd for monomer, 180). GC analysis (6-ft column, 10% Carbowax 20M, programmed 75–200 °C at 20 °C/min, or 10% SE-30, programmed 50–250 °C at 20 °C/min) indicated ca. 10% 3:1 *cis*- and *trans*-dithianes **17a** and **17b**, ca. 85% trithiepane **15**, and ca. 5% 5,8-dimethyl-1,2,3,4-tetrathiocane. Gas chromatographic/mass spectroscopic analysis confirmed this: mass spectrum (for **17a,b**), *m/e* (relative intensity)

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148 (65, M^+), 83 (36), 64 (16), 59 (16), 55 (100), 41 (44), 39 (20); for trithiepane **15**, *m/e* 180 (48, M^+), 148 (28), 115 (43), 101 (19), 83 (30), 55 (100), 41 (59); for tetrathiocane, *m/e* 212 (16, M^+), 180 (5), 148 (51), 83 (43), 55 (100), 41 (51).

An attempted distillation gave 250 mg (7%) of colorless liquid: bp 65–70 °C (0.75 mm) [lit.[42] bp 54 °C (0.5 mm)?]; ca. 40% dithiane and 60% trithiepane by GC analysis. The pot residue from the distillation was a clear, brown, sticky gel, insoluble in common organic solvents.

In a number of experiments the crude viscous oil product obtained after filtration was filtered through ca. 10 g of silica gel (CCl_4 eluant) to give a 53–75% yield of colorless free-flowing oil, soluble in benzene, THF, and acetone. (Further elution with benzene gave a dark, yellow, viscous oil which was not characterized.) NMR and GC analyses of this silica gel purified oil were similar to those of the crude product: IR (neat) 2940, 2900, 2840, 1040, 1370, 1260, 790, 770 cm^{-1}. Anal. Calcd for $C_6H_{12}S_3$: C, 39.95; H, 6.71; S, 53.34. Found: C, 39.57; H, 7.45; S, 52.60. Osmometric weight determinations (CCl_4) for various samples of this SiO_2-purified product were 266–290. One sample had n^{20}_D 1.6148 (lit.[42] n^{25}_D 1.5639?). An attempted short-path distillation of silica gel purified product at 0.05 mm gave no distillate up to a bath temperature of 150 °C; the pot residue was a clear, sticky gel, insoluble in organic solvents.

Reaction of Dithiol 16 with Sulfur Dichloride. A solution of 1.5 g (10 mmol) of dithiol **16** in 100 mL of anhydrous diethyl ether was added dropwise over a 1.5-h period to a stirring solution of 1.03 g (10 mmol) of freshly purified[14] SCl_2 in 100 mL of anhydrous diethyl ether. After complete addition, GC analysis was similar to that of the reaction of **16** with **7**. TLC (hexanes) indicated more than eight components. The reaction solution was evaporated under reduced pressure or washed twice with water and twice with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and then evaporated under reduced pressure to quantitatively give a very viscous, nearly colorless oil which was insoluble in most solvents. ^1H NMR (CCl_4) spectroscopy showed broad signals, different from those of the product from **16** plus **7**. The osmometric molecular weight (CCl_4) was found to be 1900 (calcd for monomer, 180).

***dl*-1,6-Diphenyl-1,6-hexanediol (19).** From hexanedioic acid was prepared 1,4-dibenzoylbutane, as in the literature.[55] Reduction of this diketone with $LiAlH_4$ in the usual way afforded the crude diol in ca. 80% overall yield from hexanedioic acid. This crude diol was fractionally recrystallized from ether–ethanol to give one fraction (28%) of the meso diastereomer of **19** as colorless needles [mp 125–127 °C (lit.[56] mp 127 °C for the meso diol)] and another fraction (10%) of *dl* diol **19** as granular crystals (mp 127–129 °C), which was recrystallized from methanol; mp 133–134 °C (lit.[56] mp 132–134 °C for the *dl* diol). The remaining diol was a mixture of diastereomers, mp 119–123 °C.

Preparation of 1,6-Dichloro-1,6-diphenylhexane.[43] Method A. To a solution of 5.4 g (20 mmol) of diol **19** in 75 mL of distilled pyridine stirred at 0 °C was gradually added 9.2 g (80 mmol) of methanesulfonyl chloride. After 24 h at 5 °C, the dark orange solution and crystals were poured with stirring into 400 mL of ice–water followed by extraction with ether (3 × 125 mL). The ethereal portions were combined, washed with cold 1:1 hydrochloric acid (3 × 50 mL) and cold H_2O (50 mL), dried (K_2CO_3–Na_2SO_4), and evaporated under reduced pressure to give 1.11–1.54 g (18–25%) of a yellow liquid, identified as 1,6-dichloro-1,6-diphenylhexane.[47] This oil was homogeneous by TLC ($CHCl_3$) but decomposed in the gas chromatograph (five peaks) and also decomposed extensively on attempted purification over silica gel (NMR analysis). The crude oil obtained from the extraction gave a strongly positive Beilstein test for halogens,[57] a mass spectrum with no M^+ at *m/e* 306, and a correct elemental analysis: NMR (CCl_4) δ 7.3 (s, 10 H), 4.7 (t, *J* = 7 Hz, 2 H), 2.3–1.7 (m, 4 H), 1.7–1.1 (m, 4 H); IR (neat) 3020, 2930, 2850, 1600, 1495, 1455, 1250, 1030, 910, 790, 765, 700 cm^{-1}; mass spectrum, *m/e* (relative intensity) 273 (2), 272 (6), 271 (6), 270 (17), 235 (18), 131 (52), 125 (29), 117 (51), 104 (29), 91 (100). Anal. Calcd for $C_{18}H_{20}Cl_2$: C, 70.36; H, 6.56; Cl, 23.08. Found: C, 70.49; H, 6.75; Cl, 23.08.

Method B. To 5.4 g (20 mmol) of the diol **19** was added 7 mL (ca. 100 mmol) of thionyl chloride with stirring. Vigorous bubbling ensued during the exothermic reaction. The mixture was stirred 2 h at room temperature and heated at reflux (bath temperature ca. 80 °C) for 0.5 h. Excess thionyl chloride was removed under reduced pressure to quantitatively afford an oil (homogeneous by TLC (C_6H_6), positive Beilstein test for halogens[57]) which was identical with authentic 1,6-dichloro-1,6-diphenylhexane obtained above.

Reaction of 1,6-Dichloro-1,6-diphenylhexane with Thiourea.[43] The dichloro compound obtained above (1.5 g, 4.9 mmol) and thiourea (3.0 g, 40 mmol) in 100 mL of 95% ethanol were mixed with stirring at 0 °C, and the mixture was then refrigerated (5 °C) for 10 h. The mixture was then refluxed 3 h, a solution of 2.4 g (60 mmol) of NaOH in 50 mL of H_2O was added, and the mixture was refluxed an additional 2 h. The mixture was acidified with dilute H_2SO_4 and extracted with benzene (2 × 300 mL). The benzene phases were combined, washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and saturated aqueous NaCl (50 mL), dried (K_2CO_3–$MgSO_4$), and evaporated to give 1.5 g of yellow liquid. This liquid contained two main components: a 1:3 mixture of the starting dichloro compound and one major product by TLC and NMR analysis. There was no significant SH band at 2600–2550 cm^{-1} in the IR spectrum. Trituration of this liquid provided an almost homogeneous (TLC) sample of the major product as an oil, identified as 1,6-diphenyl-6-ethoxy-1-hexanethiol: NMR ($CDCl_3$) δ 7.1 (s, 10 H), 4.0 (m, 2 H), 3.2 (q, *J* = 7 Hz, 2 H), 2.1–1.0 (m, 12 H), with δ 1.7 (d, *J* = 5 Hz, SH), 1.1 (t, *J* = 7 Hz); IR (neat) 2920, 2850, 2550 (SH, vw), 1600, 1495, 1455, 1100, 765, 705 cm^{-1}; mass spectrum, *m/e* (relative intensity) 314 (6, M^+), 268 (98, M^+ – EtOH)), 244 (53), 186 (42), 135 (100, $PhCH{=}OEt^+$), 130 (40), 91 (29). This compound decomposed in the GC (many peaks) as confirmed by gas chromatographic/mass analysis of the major peaks.

1,6-Dibromo-1,6-diphenylhexane (20). To a solution of 11.9 g (44 mmol) of PBr_3 in 12 mL of CH_2Cl_2 stirred at 0 °C was added dropwise over a 20-min period a solution of 7.2 g (45 mmol) of bromine in 8 mL of CH_2Cl_2. A bright yellow precipitate (PBr_5) was formed during the addition.

To the resulting mixture stirred at 0 °C was slowly added portionwise over a 15-min period 5.4 g (20 mmol) of diol **19**. An additional 25 mL of CH_2Cl_2 was added, and the orange mixture was stirred at 0 °C for 1 h and then 21 h at room temperature. After the reaction mixture was cooled to 0 °C, 40 mL of ice–water was added, and the mixture was stirred 1 h at room temperature. The organic layer was separated and washed successively with 40 mL of H_2O, 40 mL of saturated $NaHCO_3$, and 40 mL of saturated NaCl, dried ($MgSO_4$), treated with decolorizing charcoal, and evaporated under reduced pressure to give a mixture of yellow oil and crystals which gave a positive Beilstein test for halogens.[57] This oil was homogeneous by TLC (CH_2Cl_2) but decomposed in the gas chromatograph (many peaks). Recrystallization from ethanol–petroleum ether afforded 1.92 g (24%) of colorless needles of 1,6-dibromo-1,6-diphenylhexane (**20**), mp 80–82 °C. These crystals gave a positive Beilstein test[57] and were identical (TLC, GC, NMR) with the crude product and to the 4.2 g (53%) of mother liquor (an oil): NMR (CCl_4) δ 7.3 (s, 10 H), 4.8 (t, *J* = 7 Hz, 2 H), 2.4–1.7 (m, 4 H), 1.7–1.2 (m, 4 H); IR (KBr) 2900, 1490, 1450, 1215, 895, 835, 765, 735, 695 cm^{-1}; mass spectrum, *m/e* 398, 396, and 394 (M^+ cluster, ratio 1:2:1), 317 and 315 (M^+ – Br cluster, ratio 1:1), 235, 171, 169, 157, 143, 131, 129, 117, 115, 104, 91.

The use of commercially available PBr_5 afforded a 39% yield of crystalline material plus a 55% yield of oil (mother liquor, dibromo compound **20**).

1,6-Diphenyl-1,6-hexanedithiol (21). A mixture of 1.10 g (2.78 mmol) of crystalline dibromo compound **20**, 0.43 g (5.6 mmol) of thiourea, and 3 mL of ethanol was heated at reflux (85 °C bath) for 6 h, at which time all the dibromo compound was consumed (TLC, C_6H_6). A solution of 0.3 g (7.5 mmol) of NaOH in 3 mL of water was added, and the mixture was refluxed 2 h and then stirred overnight at room temperature. Acidification with dilute H_2SO_4 was followed by concentration under reduced pressure. Diethyl ether (ca. 75 mL) was added, and the organic layer was separated and washed with 10 mL of H_2O, 10 mL of saturated

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$NaHCO_3$, 5 mL of H_2O, and 5 mL of saturated NaCl, dried (Na_2SO_4), and evaporated to yield 820 mg of nearly colorless oil. TLC (C_6H_6) and NMR analyses indicated a complex mixture of compounds. IR (neat) spectroscopy revealed a weak but significant SH band at 2560 cm^{-1}. The oil was chromatographed over 15 g of silica gel with benzene as eluant to give (a) 300 mg (36%) of 1,6-diphenyl-1,6-hexanedithiol (**21**) as an oil [ca. 70% pure by TLC and NMR; NMR (CCl_4) δ 7.2 (s), 3.8 (m, CHSH), 3.3–2.9 (m, impurity), 2.0–0.9 (m), with 1.7 (d, J = 5 Hz, SH)] and (b) fractions containing mixtures of **21** and 1,6-diphenyl-6-ethoxy-1-hexanethiol (TLC and NMR as above). The impure dithiol (fraction a) could not be crystallized, and it decomposed in the gas chromatograph.

Attempted Synthesis of 4,9-Diphenyl-1,2,3-trithionane (18). To 146 mg (0.55 mmol) of reagent **7** stirred at room temperature in 100 mL of CCl_4 was added dropwise over a 5-h period a solution of 151 mg (0.50 mmol) of the impure dithiol **21** (obtained above) in 100 mL of CCl_4. TLC (C_6H_6, hexanes) 2.5 h after complete addition indicated the absence of elemental sulfur and dithiol **21**. The reaction mixture, after being allowed to stand overnight, was concentrated under reduced pressure to a 5-mL volume, filtered, and evaporated to give a viscous oil. IR and NMR spectroscopy indicated no significant amount of thiol: NMR (CCl_4) δ 7.1 (br s, 6.3 H), 4.2–3.6 (br t?, 1 H), 3.4–3.0 (br, 0.4 H), 2.3–1.5, 1.5–0.9 (br, 5.5 H); IR (neat) 3010, 2900, 2840, 1600, 1585, 1490, 1450, 1070, 1030, 790, 760, 700 cm^{-1}. Crystallization attempts failed. TLC (8:2 hexanes–$CHCl_3$) indicated several components, possibly a mixture of oligomers. Column chromatography over 20 g of silica gel (8:2 hexanes–$CHCl_3$ eluant) yielded only a few milligrams of each of the first 4 or 5 components, which were not characterized.

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Registry No. 6 (n = 5), 928-98-3; **6** (n = 6), 1191-43-1; **6** (n = 8), 1191-62-4; **7**, 65952-73-0; **8** (n = 5), 76583-30-7; **8** (n = 6), 76583-31-8; **8** (n = 8), 76583-32-9; **9**, 3354-86-7; **10**, 76583-65-8; **11**, 17749-54-1; **13**, 76583-66-9; **14**, 76599-27-4; **15**, 76583-67-0; **16** (meso), 53585-65-2; **16** (*dl*), 53585-66-3; **17a**, 2506-33-4; **17b**, 57819-14-4; **19** (meso), 39997-18-7; **19** (*dl*), 39997-17-6; **20**, 76583-68-1; **21**, 76583-69-2; thiourea, 62-56-6; α,α'-dibromo-*o*-xylene, 91-13-4; α,α'-dimercapto-*o*-xylene, 41383-84-0; 2,2′-bis(bromomethyl)biphenyl, 38274-14-5; 2,2′-bis(hydroxymethyl)biphenyl, 3594-90-9; *meso*-α,α'-dibromoadipic acid, 3425-65-8; *meso*-α,α'-dimercaptoadipic acid, 35605-89-1; *meso*-2,5-dibromohexane, 54462-67-8; 5,8-dimethyl-1,2,3,4-tetrathiocane, 76583-70-5; 1,4-dibenzoylbutane, 3375-38-0; 1,6-dichloro-1,6-diphenylhexane, 58819-38-8; 1,6-diphenyl-6-ethoxy-1-hexanethiol, 76583-71-6; hexanedioic acid, 124-04-9.

Synthesis of 2,2-Dichloro-1,3-diarylaziridines by Reduction of Trichloroacetophenone Imines

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2,2-Dichloro-1,3-diarylaziridines, usually obtained by addition of dichlorocarbene to benzylideneanilines, were synthesized by reaction of *N*-aryl-α,α,α-trichloroacetophenone imines with lithium aluminium hydride in ether.

Introduction

Since the first preparation of a 2,2-dichloroaziridine by Fields and Sandri in 1959,[2] several methods have been developed for the synthesis of the title compounds. The most stable members of this series are 2,2-dichloro-1,3-diarylaziridines and are generally accessible by reaction of substituted benzylideneanilines with dichlorocarbene, the latter being generated by a variety of methods.[2-7] Another method involves the base-induced ring closure of α-aryl-β,β,β-trichloroalkylanilines[8,9] and *N*-(trichloroethyl)benzamides.[10] The latter methods are the only two examples hitherto of a dichloroaziridine synthesis in which the final carbon skeleton is already present in the starting materials. We would like to report another example of the synthesis of 2,2-dichloro-1,3-diarylaziridines in which the products result from an intramolecular displacement reaction.

Table I. Synthesis of 1-Aryl-2,2-dichloro-3-phenylaziridines 5[a]

compd	R	% yield[b]	mp, °C	lit. mp, °C	reacn conditions[c]
5a	H	66	99	99–100[d] 98–99[e]	Δ, 1 h
5b	*p*-Me	81	70	70–71[d]	Δ, 15 min
5c	*m*-Me	64	59		Δ, 20 min
5d	*p*-OMe	71	93	92–93[d]	30 min at room temp, Δ, 2 min

[a] Compounds 5 gave satisfactory N analyses. [b] Isolated yield, starting from ketimines 2 (two steps). [c] Reflux period for the reaction of α,α,α-trichloro ketimines 3 with 8 equiv of lithium aluminium hydride in ether. [d] Reference 20. [e] Reference 2.

Results

Recently, the reaction of mixed metal hydrides with α-halogenated imino compounds was developed as a method for the synthesis of aziridines.[11-14] When the reaction

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