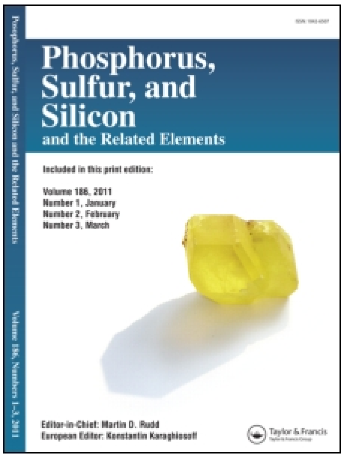

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1,2,4,5-TETRAMERCAPTOBENZENE. A Facile Route to the Benzo[1,2-d: 4,5-d']bis[1,3]dithiole Ring System

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1,2,4,5-TETRAMERCAPTOBENZENE

A Facile Route to the Benzo[1,2-d: 4,5-d']bis[1,3]dithiole Ring System

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The dissolving metal reduction of 1,2,4,5-tetrakis(ethylthio)benzene (**2**) with alkali metals in various solvents was investigated. Reduction of **2** with lithium in *n*-propylamine solvent gave 1,2,4,5-Tetramercaptobenzene (**1**) in high yield. The acid catalysed reaction of **1** with aldehydes and ketones gave the benzo-[1,2-d: 4,5-d']bis[1,3]dithiole ring system.

During the course of our work, we had wished to investigate the properties of the benzo[1,2-d: 4,5-d']bis[1,3]dithiole ring system, which a thorough literature search shows is unreported in the literature. The synthesis of the benzo[1,3]dithiole ring system from 1,2-dimercaptobenzene and an aldehyde or ketone has been well documented.[1,2] The analogous reaction with 1,2,4,5-tetramercaptobenzene (**1**) appeared to be a viable route to the bis[1,3]dithiole system.

The reaction of polyhalogenated benzenes with alkylmercaptide anions to give poly(alkylthio)benzene and their subsequent reduction to polymercaptobenzenes has received renewed interest in the recent literature. Prior procedures utilized the reaction of copper (I) alkylmercaptide with chloro- or bromobenzenes in a mixture of quinoline and pyridine as solvent[3–5] followed by sodium in ammonia reduction[6] to the corresponding mercaptobenzene. The use of the aprotic dipolar solvent *N,N*-dimethylacetamide (DMAC) for the nucleophilic substitution of aryl halides by thiolate anions has been reported by J. R. Campbell.[7] Recently, the use of hexamethylphosphoric triamide (HMPT) has been advocated as the solvent of choice for the nucleophilic substitution of activated[8] and unactivated[9,10] aryl halides by alkylmercaptide anions.

The reduction of **2** with sodium in ammonia[11] or **3** with sodium in HMPT[12,13] has been reported to give **1**.

We report in this paper a reinvestigation of the sodium in ammonia reduction of **2**. It is shown that lithium in *n*-propylamine reduces **2** to **1** in high yield avoiding the use of the potentially carcinogenic HMPT.[14] This in turn allowed the convenient synthesis of the heretofor unknown benzo[1,2-d: 4,5-d']bis[1,3]dithiole ring system:

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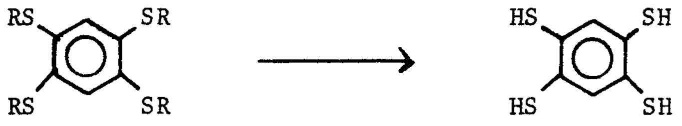


2 R = ethyl

3 R = 2-propyl

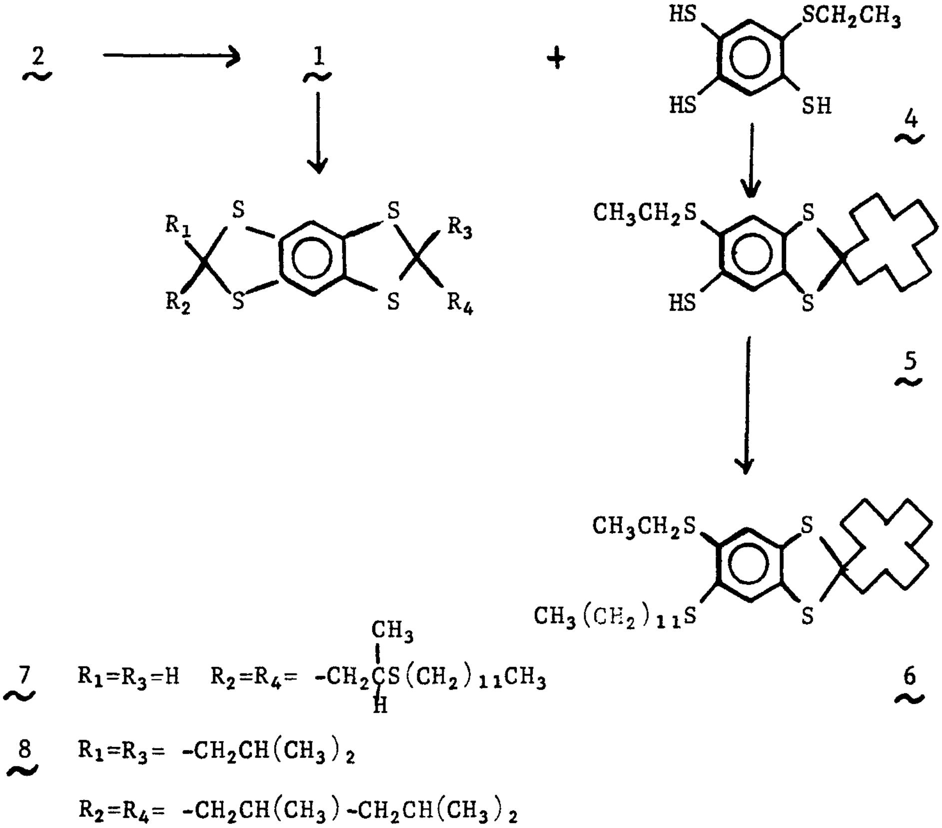
1

SCHEME 1

RESULTS AND DISCUSSION

Compound **2** was synthesized from 1,2,4,5-tetrachlorobenzene and sodium ethylmercaptide in DMAC solvent, albeit at lower yield than obtained by Tiecco *et al.*[10] using HMPT as solvent.

The reduction of **2** with sodium in ammonia according to the procedure of Reifschneider[11] gave a product which consisted of a 90:10 molar ratio of **4**:**1** by ^1H NMR spectral analysis.



7 $R_1=R_3=H \quad R_2=R_4= -CH_2\overset{CH_3}{\underset{H}{C}}S(CH_2)_{11}CH_3$

8 $R_1=R_3= -CH_2CH(CH_3)_2$

$R_2=R_4= -CH_2CH(CH_3)-CH_2CH(CH_3)_2$

SCHEME 2

Compound **4** was isolated by distillation of the crude reaction residue and identified by its ^{1}H NMR spectrum. Further proof of structure was provided by condensation of **4** with cyclododecanone using tetrafluoroboric acid catalysis to give **5**, which was characterized by its ^{1}H NMR and IR spectrum (SH stretch 2550 cm^{-1}). Conversion of **5** to **6** was accomplished by treatment with *n*-butyl lithium followed by addition of *n*-dodecyl bromide. Satisfactory elemental analysis and spectral data were obtained for **6**.

Dilution of reactant concentration lead to an increased yield of **1** (Table I).

The precipitation of **4** from the reaction medium was the apparent cause of incomplete reduction. The use of tetrahydrofuran (THF) cosolvent was without avail, although providing a convenient route to the partially reduced **4**.

Aromatic hydrocarbons are reduced by lithium metal in low-molecular-weight amines.[15] Truce *et al.* reported the alkali metal reduction of alkylthiobenzenes to mercaptobenzenes in methylamine solvent.[16,17] We found that the reduction of **2** with lithium metal in *n*-propylamine solvent proceeded smoothly to give **1** in high yield. Examination of the ^{1}H NMR spectrum of the crude reaction product showed that **4** was now a minor product. The use of *n*-propylamine as solvent was found to provide an alternative to the lower-boiling amines[16,17] and troublesome HMPT.[13]

As anticipated, the tetrafluoroboric acid catalyzed condensation of **1** with two moles of 3-dodecylthiobutyraldehyde[18] or 2,6,8-trimethyl-4-nonanone[19] gave the bis-[1,3]dithioles **7** and **8** as isomer mixtures respectively. Compounds **7** and **8** were fully characterized by their spectral and elemental analysis.

EXPERIMENTAL

All melting points were determined in open capillary tubes on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared Spectra (1% solution—potassium bromide cells) were recorded on a Perkin-Elmer 710 spectrophotometer. Proton NMR spectra were taken on a Varian XL-100 (100 MHz) instrument. Mass spectra were determined on an AEI (KRATOS) MS 902. Reagents were purchased from Aldrich Chemical Company.

1,2,4,5-Tetrakis(ethylthio)benzene (2). In a flame-dried flask under a dry nitrogen atmosphere, a stirred solution of 30.5 g (1.3 mol) of sodium metal in 500 ml ethyl alcohol was treated with 93.0 g (1.5 mol) ethanethiol at 0–5°C. After the addition was complete, the reaction was refluxed one hour and then treated with a solution of 64.8 g (0.3 mol) of 1,2,4,5-tetrachlorobenzene in 300 ml DMAC. Volatiles were slowly removed by distillation and the reaction temperature was held at 160–165°C for 18 hours. The reaction was cooled, poured onto 900 ml ice-water, and the resultant mixture extracted twice with diethyl ether. The combined ether extracts were washed with brine, dried over anhydrous sodium sulfate, and the solvent removed *in vacuo*. The residue was recrystallized from acetone-methyl alcohol followed by 2-propyl alcohol to give 33 g (35%) of white crystals, mp 65–67°C (lit.[10] 65–67°C); NMR (deuteriochloroform): δ 1.36 (triplet, methyl, 12H), 2.96 (quartet, methylene, 8H), 7.22 (singlet, aromatic, 2H). Anal. Calcd. for $C_{14}H_{22}S_4$: C, 52.78; H, 6.96; S, 40.26. Found: C, 52.99; H, 6.63; S, 40.00.

1,2,4,5-Tetramercaptobenzene (1). In a flame-dried flask under a dry nitrogen atmosphere, one liter

TABLE I

Dissolving Metal Reduction of **2**

Exp. #	Metal	Conc. **2** (M)	Reaction Solvent	Product Ratio **1**:**4**[a]
1	Na	0.21	NH_3	10:90
2	Na	0.10	NH_3	40:60
3	Na	0.03	NH_3	75:25
4	Na	0.21	NH_3-THF	5:95
5	Li	0.10	*n*-$C_3H_7NH_2$	90:10

[a] By ^{1}H NMR spectral integration.

of *n*-propylamine (dried over potassium hydroxide) was stirred with 5.2 g (0.75 mol) of lithium metal until a blue color persisted. The resultant suspension was treated with 30 g (0.094 mol) of **2** with strict exclusion of oxygen and stirred for 19 hours. An additional 0.2 g (0.03 mol) of lithium metal was added and the reaction mixture heated to gentle reflux for one-half hour producing a persistent green color. The reaction mixture was cooled with an ice bath, treated with 10 g anhydrous ammonium chloride, concentrated *in vacuo*, acidified with 6N HCl to pH 1, and extracted well with chloroform. The combined chloroform extracts were washed with brine, dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was triturated with diethyl ether and the resultant solid sublimed (120°C @ 0.05 mm Hg) to give 8.7 g (45%) of a white crystalline solid, mp 137–142°C (lit.[13] 139–141°C); NMR (deuteriochloroform): δ 3.64 (exchangeable singlet, thiol, 4H), 7.36 (singlet, aromatic, 2H); Mass Spec. m/e (Rel. Int.): 206 (100). Anal. Calcd. for $C_6H_6S_4$: SH, 64.10. Found (iodine-thiosulfate titration): SH, 63.74.

2,4,5-Trimercapto-Ethylthiobenzene (4). In a flame-dried flask under a dry nitrogen atmosphere, a stirred suspension of 20.0 g (0.063 mol) of **2** in 300 ml of anhydrous liquid ammonia was treated with 10.1 g (0.44 mol) of sodium metal at −33°C. At the end of the additon a dark blue color was allowed to persist for 20 minutes, then quenched with 20.0 g anhydrous ammonium chloride, and the ammonia was allowed to evaporate. The residue was treated with 150 ml water, washed with 50 ml diethyl ether (discarded), cooled, acidified with 6N HCl to pH 1, and the heterogeneous mixture extracted twice with ether. The combined ether extracts were washed with brine, dried over anhydrous sodium sulfate, concentrated *in vacuo*, and distilled at reduced pressure to give 10.6 gram (72%) of a clear white liquid, bp 145–150°C (0.01 mm Hg); IR (CCl_4): 2550 cm^{-1}, 2600 cm^{-1} (SH); NMR (deuteriochloroform): δ 1.26 (triplet, methyl, 3H), 2.85 (quartet, methylene, 2H), 3.75 (exchangeable singlet, thiol, 2H), 4.26 (exchangeable singlet, thiol, 1H), 7.46 (complex, aromatic, 2H). Anal. Calcd. for $C_8H_{10}S_4$: SH, 42.3: Found (iodine-thiosulfate titration): SH, 42.1.

5-Dodecylthio-6-ethylthio-spiro[1,3-benzodithiole-2,1′-cyclododecane] (6). In a flask under a nitrogen atmosphere, a stirred solution of 3.0 g (0.013 mol) of **4** and 5.3 g (0.03) of cyclododecanone in 50 ml toluene was treated with 2 ml of tetrafluoroboric acid-diethyl ether complex, stirred 18 hours, warmed to 70°C for three hours, and poured onto 100 ml cold aqueous sodium bicarbonate solution. The mixture extracted twice with diethyl ether, the combined extracts washed with brine, concentrated in vacuo, and purified by flash chromatography[20] to give 5.2 g (76%) of **5** as an oil; IR (CCl_4): 2550 cm^{-1} (SH); NMR (deuteriochloroform): δ 1.28 (triplet, methyl, 3H), 1.39 (b. singlet, 18H), 2.15 (complex, 4H), 2.80 (quartet, methylene, 2H), 4.26 (exchangeable singlet, thiol, 1H), 7.18 (complex, aromatic, 2H).

In a flame dried flask under a dry nitrogen atmosphere, a solution of 4.7 g (0.012 mole) of **5** in 30 ml dry THF was treated with 7.4 ml 1.6 M *n*-butyllithium in hexane at −78°C. After the addition was complete, 3.2 g (0.012 mol) of *n*-dodecyl bromide was added, the reaction warmed to r.t., stirred for 18 hours, cooled, and treated with 15 ml saturated ammonium chloride solution. The mixture extracted twice with diethyl ether, the combined extracts washed with brine, dried over anhydrous sodium sulfate, concentrated *in vacuo*, and the residue recrystallized from 2-propyl alcohol to give 4.8 g (71%) of a white solid, mp 67–70°C; NMR (deuteriochloroform) δ 0.91 (triplet, methyl, 3H), 1.31 (complex, 41H), 2.19 (complex, 4H), 2.84 (overlapping quartet and triplet, methylene, 4H), 7.09 (singlet, aromatic, 2H). Anal. Calcd. for $C_{32}H_{54}S_4$: C, 67.78; H, 9.60; S, 22.62. Found: C, 67.52; H, 9.51; S, 22.65.

2,6-Dihydro-2,6-bis(2-methyl-2-dodecylthioethyl)-benzo[1,2-d: 4,5-d′]bis[1,3]dithiole (7). Under a dry nitrogen atmosphere, a stirred solution of 3.0 g (0.014 mol) of **1** and 7.9 g (0.029 mol) of 3-dodecylthiobutyraldehyde in 100 ml toluene was treated with 2 ml tetrafluoroboric acid-diethylether complex, warmed to 50°C for 2 hours, cooled, and poured onto 150 ml cold 2N sodium hydroxide solution. The layers were separated, the aqueous layer extracted with diethyl ether, the combined organic layers washed sequentially with 5% aqueous acetic acid, saturated sodium bicarbonate and brine, and dried over anhydrous sodium sulfate. Concentration in vacuo and flash chromatography[20] afforded 4.5 g (43%) of an off-white low-melting wax; NMR (deuteriochloroform): δ 0.87 (triplet, 6H), 1.29 (complex, 46H), 2.05 (complex, 4H), 2.49 (triplet, 4H), 2.89 (complex, 2H), 5.06 (complex, methine, 2H), 7.02 (singlet, aromatic, 2H). Anal. Calcd. for $C_{38}H_{66}S_6$: C, 63.80; H, 9.30; S, 26.90. Found: C, 63.99, H, 9.23, S, 27.30.

2,6-Bis(2-methylpropyl)-2,6-bis(2,4-dimethylpentyl)-benzo[1,2-d: 4,5-d′]bis[1,3]dithiole (8). By the procedure of compound **7**, compound **8** was prepared from 3.2 g (0.020 mol) of **1**, 7.0 g (0.038 mol) of 2,6,8-trimethyl-4-nonanone, and 2 ml tetrafluoroboric acid-diethyl ether complex. Chromatography gave 1.6 g of a colorless liquid; NMR (deuteriochloroform): δ 0.091 (complex, 40H), 1.93 (complex, 8H), 6.89 (singlet, aromatic, 2H). Anal Calcd. for $C_{30}H_{50}S_4$: S, 23.80. Found S, 23.89.

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