HETEROCYCLES, Vol 16, No 10, 1981

SYNTHESIS OF NEW MACROCYCLIC POLYTHIAETHER

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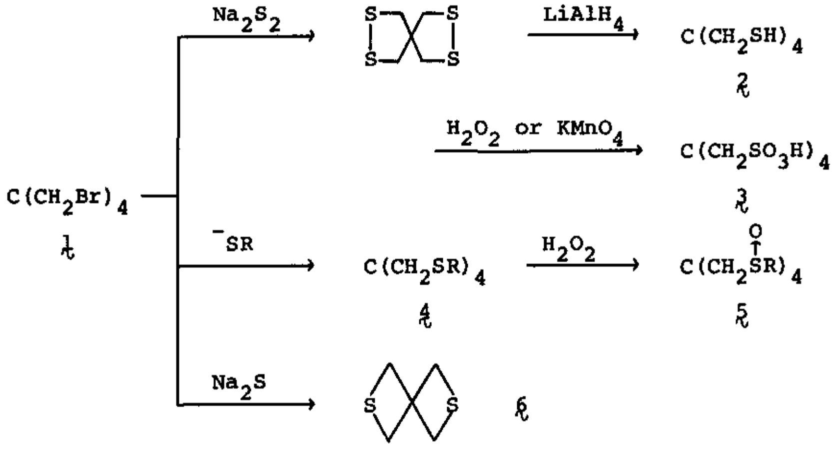
Abstract — Synthesis of a new macrocyclic polythiaether (**12**) which is easily obtained in a good yield via 2,6-dithia-4-spiroheptane (**6**) is described. Several reactions of pentaerythrityl bromide (**1**) with nucleophiles and a few ring opening reactions of **6** with methyl iodide are also described.

Recently, preparation and properties of numerous macrocyclic polyethers have been reported,[1] whereas, only a few macrocyclic polythiaethers[2] and mixed aza- or/and oxa-thia macrocyclic and macrobicyclic polyethers containing four or more sulfur atoms in the macrocyclic rings have been known. These macrocyclic polythiaethers are known to coordinate rather selectively with heavy metals such as copper and mercury.[3]

However, syntheses of these macrocyclic polythiaethers are not easy while the yields are generally poor and hence a simple and improved method to prepare macrocyclic polythiaethers in good yields has been desired. This communication describes a facile synthesis of a new macrocyclic polythiaether (**12**) starting from 2,6-dithia-4-spiroheptane (**6**), and also a few reactions of 2,6-dithia-4-spiroheptane (**6**) with some nucleophiles.

Pentaerythrityl bromide (**1**), prepared by treating pentaerythritol with phosphorus tribromide,[4] having a neopentyl type carbon skeleton, was found to be very unreactive in the reaction with such nucleophiles as amine, phosphine, and cyanide anion due to the steric hindrance around the reaction center. However, the reactions of **1** with sulfur nucleophiles such as Na_2S_2, and Na_2S, and ^-SR proceeded smoothly (Scheme I). For example, the reaction of **1** with Na_2S_2 gave 2,3,7,8-tetrathia-5-spirononane which was then treated with $LiAlH_4$ to afford



Scheme I

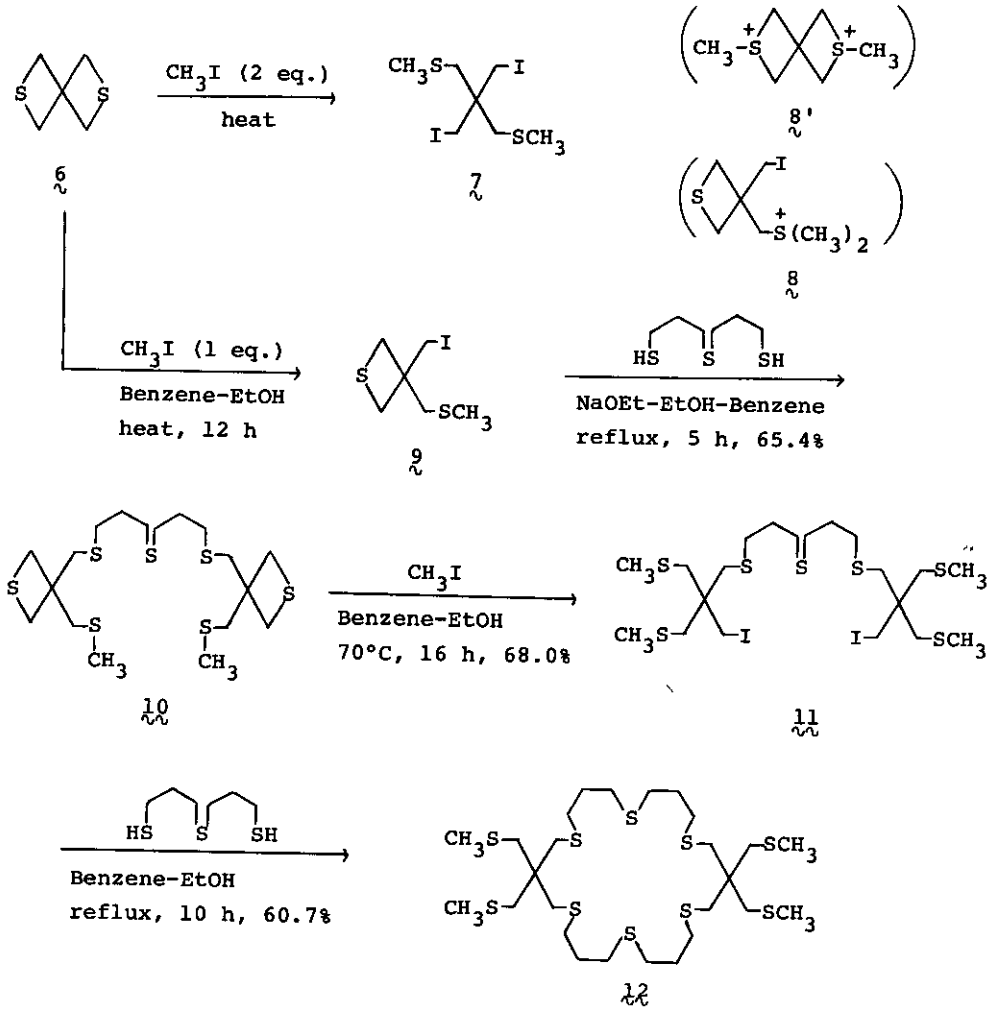
tetrakis(mercaptomethyl)methane (2) nearly quantitatively. Tetrakissulfonic acid (3) was prepared quantitatively by oxidation of 2 with hydrogen peroxide or potassium permanganate. The reactions of pentaerythrityl bromide with several sodium alkyl mercaptides also gave the corresponding tetrakissulfides (4) nearly quantitatively. The sulfides (4) were also readily oxidized to give the corresponding *tetrakissulfoxides (5) or sulfones. When 1 was allowed to react with* Na_2S in aqueous ethanol solution, an interesting key intermediate, 2,6-dithia-4-spiroheptane (6), bp 70-72°C/1.0 Torr, was obtained in 51.1% yield.[5]

6: NMR ($CDCl_3$) δ 3.28 (s, 8H, $-C\underline{H}_2S$). New macrocyclic polythiaether (12) was prepared via 9 starting from the compound 6 as illustrated in Scheme II. Treatment of 2,6-dithia-4-spiroheptane (6) with 2 Mol. equiv. of methyl iodide afforded unexpectedly the ring opened product 7 but did not give such a sulfonium salt, 8 or 8'. 7: bp 135°C/1.0 Torr; NMR ($CDCl_3$) δ 2.28 (s, 6H, $-SC\underline{H}_3$), 2.85 (s, 4H, $-C\underline{H}_2S$), 3.47 (s, 4H, $-C\underline{H}_2I$). Meanwhile, when an equimolar mixture of 6 and methyl iodide was heated in a sealed tube at 80°C for 12h and then the product was distilled, the compound 9 was obtained in 62.8% yield.

9: bp 110-113°C/1.0 Torr; NMR ($CDCl_3$) δ 2.28 (s, 3H, $-SC\underline{H}_3$), 3.05 (s, 6H, $-C\underline{H}_2S$), 3.69 (s, 2H, $-C\underline{H}_2I$).

The synthesis of macrocyclic polythiaether (12) was carried out by the *following Scheme II, starting with 9 via formations of a few stable intermediates* 10 and 11, which were prepared in the following reactions.

10: A mixture of 0.304 g (13.2 mmole) of sodium ethoxide, 1.0 g (5.5 mmole)



Scheme II

of 1,7-dimercapto-4-thiaheptane, and 2.74 g (10 mmole) of 9 in 40 ml of fifty-fifty mixture of benzene and ethanol, was refluxed under nitrogen for 5 h, then the solvent was evaporated under vacuum and the residue was extracted with benzene. The residue was chromatographed [silica gel, benzene-chloroform (1:1)] affording 1.55 g (65.4%) of 10.

10: NMR ($CDCl_3$) δ 1.88 (m, 4H, $-CH_2C\underline{H}_2CH_2-$), 2.19 (s, 6H, $-SC\underline{H}_3$), 2.65 (m, 8H, $-SC\underline{H}_2-$), 3.05 (m, 16H, $-SC\underline{H}_2CC\underline{H}_2S-$).

11: A mixture of 0.47 g (1 mmole) of 10 and 0.28 g (2 mmole) of methyl iodide in 20 ml of benzene-ethanol was heated in a sealed tube at 70°C for 18 h and then the solvent was removed under reduced pressure. The residue was purified by column chromatography [silica gel, benzene] to afford **11**, 0.51 g (68.0%). **11**: NMR ($CDCl_3$) δ 1.89 (m, 4H, $-CH_2C\underline{H}_2CH_2-$), 2.28 (s, 12H, $-SC\underline{H}_3$), 2.78 (m, 20H, $-C\underline{H}_2SC\underline{H}_2-$ and $-C\underline{H}_2SCH_3$), 3.48 (s, 4H, $-C\underline{H}_2I$).

12: To a stirred refluxing mixture of **11** (0.156 g, 0.2 mmole) in benzene (30 ml) and sodium (0.021 g, 0.9 mmole) in ethanol (30 ml) was added dropwise 1,7-dimercapto-4-thiaheptane within 2 h under a nitrogen atmosphere and the mixture was refluxed further for 10 h. After evaporation of the solvent, the residue was extracted with chloroform. The compound was chromatographed on silica gel [hexane -ethyl acetate (9:1) as eluant] to give 0.082 g of **12** (60.7%). **12**: NMR ($CDCl_3$) δ 1.99 (m, 8H, $-CH_2C\underline{H}_2CH_2-$), 2.28 (s, 12H, $-SC\underline{H}_3$), 2.83 (m, 32H, $-C\underline{H}_2SC\underline{H}_2-$ and $-C\underline{H}_2SCH_3$). Anal. Calcd for $C_{26}H_{52}S_{10}$: C, 45.56; H, 7.64. Found: C, 45.00; H, 7.26.

The spectral data supported well the assigned structure for **10**, **11**, and **12**. Thus, the new macrocyclic polythiaether **12** was obtained in a good yield by these simple procedures.

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Received, 29th June, 1981