Notiz / Note

Synthesis and X-Ray Structures of New Macrocyclic Thioethers

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4,6:12,14-Di(1,3-adamantano)-1,9-dithiacyclohexadecane (**1**), 4,6:12,14:20,22-tri(1,3-adamantano)-1,9,17-trithiacyclotetracosane (**2**), and 5,7:14,16-di(1,3-adamantano)-1,2,10,11-tetrathiacyclooctadecane (**3**) have been obtained by intermolecular cyclization of 1,3-bis(2-bromoethyl)adamantane (**4**) with thioacetamide using a high-dilution technique. The reaction is concentration-dependent. The crystal structures of **1**, **2**, and **3** have been determined by single-crystal X-ray diffraction.

Compounds containing a sulfide linkage have found widespread applications as substrates in synthesis[1] and as ligands of defined shape and defined bonding properties for complexing metal ions[2] or as compounds useful for the examination of sulfur-sulfur bonding and electronic properties of these molecules[3].

The first macrocyclic thioethers containing a polycyclic cage system as a building block have been published recently[4,5]. It has been found that the polycyclic unit, as the cubyl group, may be viewed as a low-molecular weight-concentrated lipophilic center which fixes the ionophore in the membrane. This is especially true in the case of macrocyclic polyethers containing two or more such units[5].

In this paper we report on the synthesis of new macrocyclic thioethers **1** and **2** which contain a 1,3-bridged adamantanediyl system as a rigid lipophilic component. Macrocyclic tetrasulfide **3** has also been prepared.

Synthesis of Macrocyclic Thioethers

The synthesis of **1**–**3** has been achieved by intermolecular cyclization of 1,3-bis(2-bromoethyl)adamantane (**4**) with thioacetamide using a high-dilution technique[6]. The reaction, as depicted in Scheme 1, is concentration-dependent. It proceeds smoothly in a 10^{-3} M solution to give **1** and **2** in a ratio of 3:1 and in 52% overall yield.

However, in more concentrated solution (10^{-1} M) the noncyclic dimer is the major product, while in the 10^{-4} M solution besides **1**, **2**, and traces of unreacted starting material **3** is formed in 3% yield.

All three compounds are colorless crystalline, stable to air and insoluble in polar organic solvents. However, the solubility is very high in CH_2Cl_2 and $CHCl_3$. Analytical and spectroscopic data are summarized in the experimental section.

Crystal and Molecular Structures of 1 and 3

The molecular structures of **1** and **3** have been determined by X-ray diffraction methods (Figures 1 and 2). The crystal of **2** is sensitive to X-ray radiation, and intensity data are of poor quality. The molecular structure of **2** has been confirmed by X-ray structure analysis (Figure 3), but the refinement has not been successful due to unresolved disordered solvent molecules.

The macrocyclic thioether molecule **1** has molecular symmetry 222 although this is not imposed crystallographically. The adamantane units show the expected geometry. Two S atoms in **1** are oriented away from the center of the macrocyclic cavity, and they are exodentate with respect to the macrocyclic ring. In the $-SCH_2CH_2-$ portion of the molecule the C–S bonds approximately adopt a *gauche* orientation whereas C–C bonds assume an *anti* orientation. The structure of the macrocyclic ring can be easily described in terms of the structure of tetrathia-12-crown-4 thioether, 12S4[7], where two adamantane units are replaced by two sulfur atoms. In this case we would obtain a structure with a square projection like 12S4 and with torsional angles almost identical with that of 12S4. The S–C bond lengths range from 1.812(4) to 1.815(4) Å while the C–C bond lengths in the macrocyclic ring range from 1.522(5) to 1.547(5) Å. The average C–C bond length in the highly symmetric adamantane units is 1.535(5) Å, and the average C–C–C angle is 109.5(3)° being the largest [111.9(3)°] at the site of its fusion with the macrocyclic ring. The nonbonding S···S distance is 8.389(1) Å. In the crystal lattice molecules translated along the *c* axes with their 16-membered ring cavities form the infinite channels.

The 18-membered macrocyclic ring in compound **3** (Figure 2) has a crystallographic center of inversion. Two disulfide groups are oriented exodentate relative to the ring. The S–S bond length in the disulfide group is 2.0320(9) Å. S–C bond lengths are 1.816(2) and 1.823(2) Å. The C–C bond

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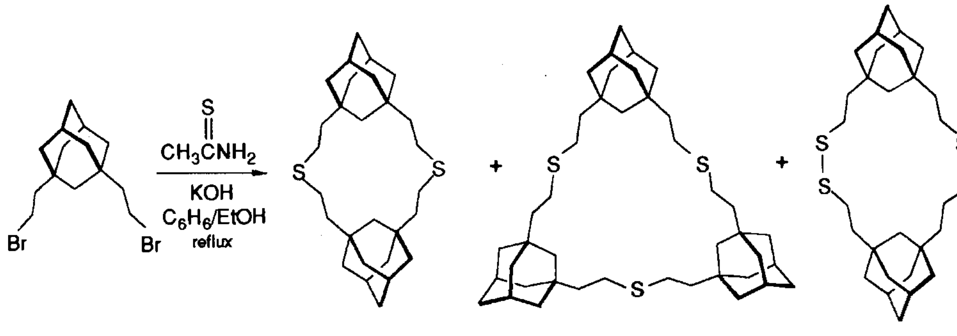
Scheme 1



4 **1** **2** **3**

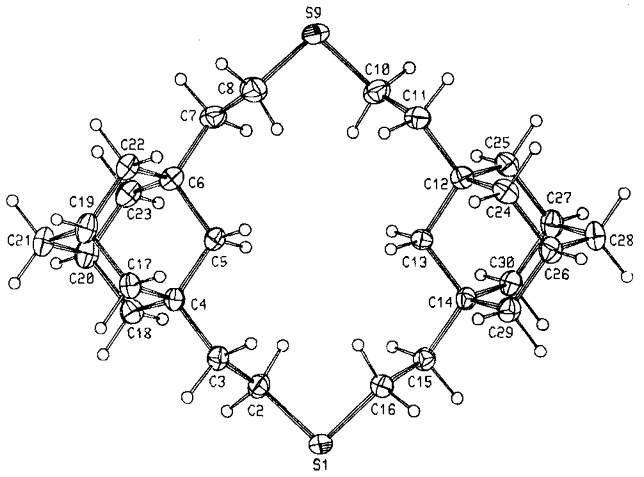


Figure 1. Molecular structure of **1** with atomic numbering. – Selected bond lengths [Å] and angles [°]: S1–C2 1.815(4), C2–C3 1.532(5), C3–C4 1.536(5), C4–C5 1.537(4), C5–C6 1.547(5), C6–C7 1.538(6), C7–C8 1.531(5), C8–S9 1.812(4), S9–C10 1.813(4), C10–C11 1.522(5), C11–C12 1.539(5), C12–C13 1.540(4), C13–C14 1.543(4), C14–C15 1.533(5), C15–C16 1.529(6), C16–S1 1.814(4); C2–S1–C16 99.3(2), S1–C2–C3 112.8(3), C2–C3–C4 116.4(3), C3–C4–C5 111.3(3), C4–C5–C6 111.9(3), C5–C6–C7 110.9(3), C6–C7–C8 116.0(3), C7–C8–C9 112.8(3), C8–S9–C10 99.4(2), S9–C10–C11 112.9(3), C10–C11–C12 115.8(3), C11–C12–C13 111.1(3), C12–C13–C14 111.9(3), C13–C14–C15 111.0(3), C14–C15–C16 116.1(3), C15–C16–S1 113.2(3)

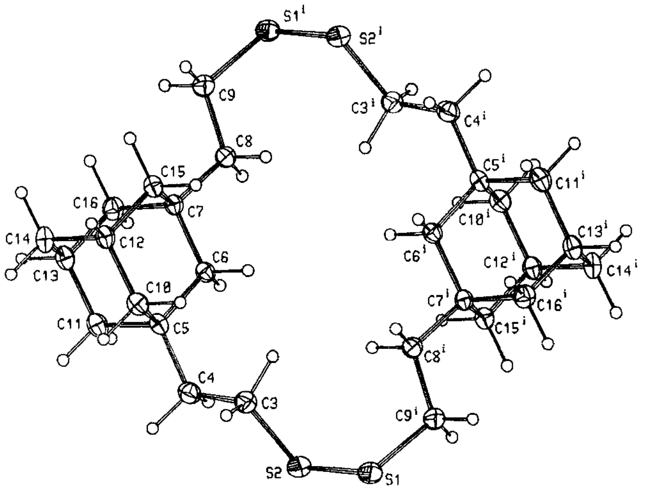


Figure 2. Molecular structure of **3** with atomic numbering. – Selected bond lengths [Å] and angles [°]: S1–S2 2.0320(9), S2–C3 1.816(2), C3–C4 1.528(3), C4–C5 1.536(2), C5–C6 1.533(1), C6–C7 1.542(1), C7–C8 1.538(1), C8–C9 1.522(2), C9–S1^i 1.823(2); S2–S1–C9^i 104.8(1), S1–S2–C3 104.0(1), S2–C3–C4 109.0(1), C3–C4–C5 114.3(2), C4–C5–C6 111.3(1), C5–C6–C7 112.3(1), C6–C7–C8 107.1(1), C7–C8–C9 116.2(1), C8–C9–S1^i 114.1(1). Symmetry code: (*i*) *x*, 1 – *y*, 1 – *z*

lengths in the macrocyclic ring range from 1.522(2) to 1.542(1) Å. The average C–C bond in the adamantane unit is 1.535(2) Å, and the average C–C–C angle is 109.7(1)° being the largest [112.32(9)°] at the site of its fusion with the macrocyclic ring. In the crystal lattice the molecules of **3** translated along the *a* axis form channels passing through the macrocyclic cavities.

These macrocyclic thioether ligands may serve as potential extraction agents for soft- and heavy-metal ions and as precursors for the preparation of macrocyclic hydrocarbons with spherical molecular frameworks.

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Experimental

The experiments were carried out under dry nitrogen. Solvents were dried and distilled before use. – NMR: Jeol 90Q and Varian

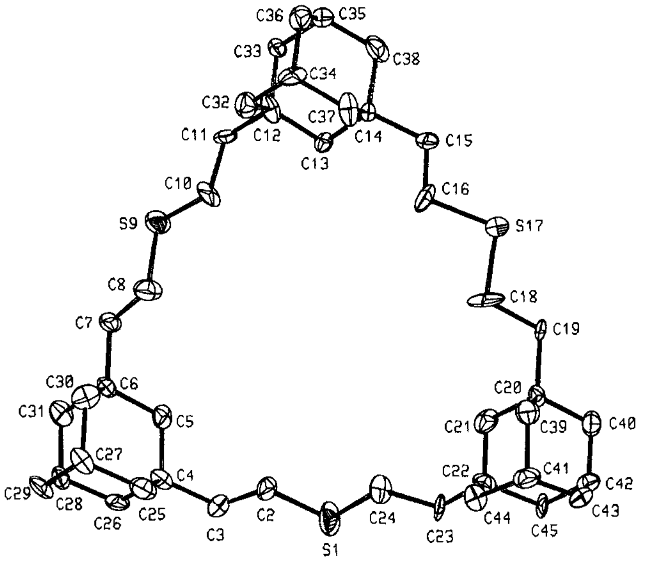

Figure 3. ORTEP plot of **2** showing the labeling of the non-H atoms. Thermal ellipsoids are shown at 30% probability level

Gemini-300 spectrometers. – MS: EXTREL FTMS 2001. – IR: Perkin Elmer 297.

1,3-Bis(2-bromoethyl)adamantane (**4**): A stirred solution of 1,3-bis(2-hydroxyethyl)adamantane[8] (1.5 g, 6.7 mmol) in 63% aqueous hydrogen bromide (15 ml) was treated at room temp. with concd. sulfuric acid (7 ml). The mixture was warmed to 80–90°C, and stirring was continued overnight. After cooling to ambient temp. the reaction mixture was extracted with ether (3 × 30 ml). The combined etheral extracts were washed with a saturated aqueous $NaHCO_3$ solution and dried with $MgSO_4$. Evaporation of the solvent afforded 2.23 g (95%) of dibromide **4** with a purity higher than 98% (GLC, DB-210, 180°C), m.p. 45–47°C. – IR (KBr): $\tilde{\nu}$ = 2970–2840 cm^{-1} (CH), 660 (CBr). – ^{1}H NMR ($CDCl_3$): δ = 3.41–3.36 (t, 4H, CH_2Br), 2.04 (m, 2H, CH), 1.77–1.71 (t, 4H), 1.58 (m, 2H), 1.54–1.35 (m, 8H), 1.26 (s, 2H). – ^{13}C NMR ($CDCl_3$): δ = 47.23 (t, 2 C), 46.39 (t, 1 C), 41.00 (t, 4 C), 35.82 (t, 1C), 34.17 (s, 2 C), 28.32 (t, 2 C), 28.26 (d, 2 C). – HRMS $C_{14}H_{22}Br_2$: calcd. 350.0062, found 350.0076. – $C_{14}H_{22}Br_2$ (350.15): calcd. C 48.02, H 6.33; found C 47.99, H 6.28.

Cyclization of **4**: A solution of **4** (0.70 g, 2.17 mmol) and thioacetamide (0.16 g, 2.17 mmol) in 100 ml of ethanol/benzene (1:1) and a solution of KOH (0.3 g, 4.9 mmol) in 100 ml of ethanol/water (20:1) were added simultaneously during 20 h to 600 ml of anhydrous ethanol. This mixture was refluxed for 4 d. The solvent was removed by distillation and the residual solid chromatographed over silica gel using 20 → 40% of CH_2Cl_2 in pentane as eluent. Thus 0.164 g (34%) of **1** and 0.083 g (17%) of **2** were obtained. The analytical samples of **1** and **2** were isolated by crystallization from CH_2Cl_2 and $CH_3OH/CHCl_3$ (1:1), respectively. In the experiment carried out in more diluted solution, 3% of **3** was isolated. A sample of **3** was crystallized from $CHCl_3$ solution.

4,6:12,14-Di(1,3-adamantano)-1,9-dithiacyclohexadecane (**1**): M.p. 270–272°C. – IR (KBr): $\tilde{\nu}$ = 2950 cm^{-1} (m), 2910 (s), 2850 (s), 1445 (m), 1345 (w), 765 (w). – ^{1}H NMR ($CDCl_3$): δ = 2.37–2.21 (m, 8H), 1.99 (m, 4H), 1.61 (m, 4H), 1.47–1.43 (m, 8H), 1.42–1.34 (m, 16H), 1.23 (s, 4H). – ^{13}C NMR ($CDCl_3$): δ = 45.73 (t, 4 C), 44.11 (t, 2 C), 42.09 (t, 8 C), 36.51 (t, 2 C), 33.17 (s, 4 C), 28.73 (d, 4 C), 23.89 (t, 4 C). – HRMS: $C_{28}H_{44}S_2$: calcd. 444.2879, found 444.2883. – $C_{28}H_{44}S_2$ (444.8): calcd. C 75.61, H 9.97; found C 75.45, H 9.71.

4,6:12,14:20,22-Tri(1,3-adamantano)-1,9,17-trithiacyclotetracosane (**2**): M.p. 240–242°C. – IR (KBr): $\tilde{\nu}$ = 2900 cm^{-1} (s), 2840 (s), 1450 (m), 1360 (w), 730 (w). – ^{1}H NMR ($CDCl_3$): δ = 2.54–2.41 (m, 12H), 2.03 (m, 6H), 1.57 (m, 6H), 1.50–1.42 (m, 24H), 1.40–1.34 (m, 12H), 1.25 (s, 6H). – ^{13}C NMR ($CDCl_3$): δ = 45.65 (t, 3 C), 43.82 (t, 6 C), 42.01 (t, 12 C), 36.58 (t, 3 C), 33.43 (s, 6 C), 28.94 (d, 6 C), 26.13 (t, 6 C). – $C_{42}H_{66}S_3$ (667.1): calcd. C 75.61, H 9.97; found C 75.58, H 9.94.

5,7:14,16-Di(1,3-adamantano)-1,2,10,11-tetrathiacyclooctadecane (**3**): M.p. 262–264°C. – IR (KBr): $\tilde{\nu}$ = 2920 cm^{-1} (s), 2840 (s), 1450 (m), 1360 (w), 830 (w). – ^{1}H NMR ($CDCl_3$): δ = 2.72–2.59 (m, 8H), 2.04 (m, 4H), 1.59 (m, 4H), 1.52–1.45 (m, 8H), 1.43–1.35 (m, 16H), 1.26 (s, 4H). – ^{13}C NMR ($CDCl_3$): δ = 45.71 (t, 2 C), 42.28 (t, 4 C), 41.99 (t, 8 C), 36.40 (t, 2 C), 33.47 (s, 4 C), 31.89 (t, 4 C), 28.95 (d, 4 C). – MS (70 eV), *m/z* (%): 509 (23) [M$^+$], 508 (34), 507 (100), 287 (5), 286 (6), 285 (32), 255 (7), 254 (12), 253 (64). – $C_{28}H_{44}S_4$ (508.9): calcd. C 66.08, H 8.72; found C 66.13, H 8.65.

Crystal Structure Determination[9]: Data were collected on an Enraf-Nonius CAD4 diffractometer using graphite-monochromatized Cu (for **3**) and Mo (for **1**) radiations in the $\omega/2\Theta$ mode. Lorentz and polarization effects were corrected by using the Nonius SDP package. The structures were solved by direct methods using SHELX86 and refined anisotropically by the full-matrix least-squares method using SHELX76. H atoms were included in geometrically idealized positions (C–H 1.08 Å).

Crystal Data of **1**: $C_{28}H_{44}S_2$, $M_r = 444.79$, triclinic, $a = 9.76(2)$, $b = 9.78(2)$, $c = 13.13(2)$ Å, $\alpha = 100.03(9)$, $\beta = 93.9(1)$, $\gamma = 97.6(1)°$, $V = 1218(3)$ Å^3, space group $P\bar{1}$, $Z = 2$, $D_c = 1.21$ Mg m^{-3}, $\mu(\text{Mo-}K_\alpha) = 0.221$ mm^{-1}. 4643 reflections in the range $2.5 < \Theta < 70°$ as $0 < h < 11$, $-11 < k < 11$, $-15 < l < 15$ were recorded. Out of 3627 independent reflections 2597 having $I > 2.5\sigma(I)$ were used for calculations. The final $R = 0.049$ and $R_w = 0.059$ $\{w = 1/[\sigma^2(F_o) + |g|(F_o)^2]\}$.

Crystal Data of **2**: $C_{42}H_{66}S_3$ + unresolved solvent, monoclinic, $a = 25.862(3)$, $b = 16.889(2)$, $c = 21.153(3)$ Å, $\beta = 111.90(1)°$, $V = 8573(2)$ Å^3, space group $C2/c$, $Z = 8$.

Crystal Data of **3**: $C_{28}H_{44}S_4$, $M_r = 508.92$, triclinic, $a = 6.418(4)$, $b = 10.06(1)$, $c = 10.94(1)$ Å, $\alpha = 108.47(5)$, $\beta = 94.88(5)$, $\gamma = 92.56(5)°$, $V = 666(1)$ Å^3, space group $P\bar{1}$, $Z = 1$, $D_c = 1.27$ Mg m^{-3}, $\mu(\text{Cu-}K_\alpha) = 3.32$ mm^{-1}. 2766 reflections in the range $2.5° < \Theta < 25.0°$ as $0 < h < 7$, $-12 < k < 12$, $-13 < l < 13$ were recorded. Out of 2487 independent reflections 2361 having $I > 4\sigma(I)$ were used for calculations. The final $R = 0.047$ and $R_w = 0.062$ $\{w = 1/[\sigma^2(F_o) + |g|(F_o)^2]\}$.

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[25/94]