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Synthesis, Complexation, and Supramolecular Assembly of 21,30-Dithia-17,25-dimethyl-1,4,7,10,13-pentaoxa[13.3.3](1,2,6)cyclophane[†]

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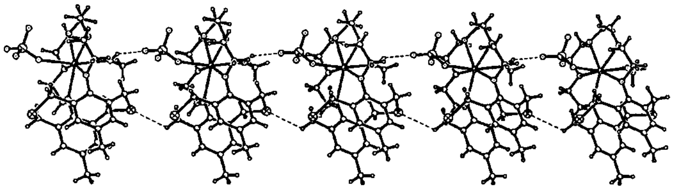
ABSTRACT



A crownophane consisting of a dithia[3.3]metacyclophane moiety was synthesized by employing a high dilution method. The crystal structure and complexation behavior of this crownophane was studied. A hydrogen-bonded linear supramolecular assembly using anion–Na$^+$–crownophane–solvent as a synthon was observed in the solid state. This supramolecular assembly was also stabilized via an intermolecular S···H–C interaction.

Crownophanes exhibit interesting properties due to the presence of both rigid and flexible moieties in one molecule.[1] The crown component of a crownophane is conformationally mobile and can bind cations similar to classical crown ethers. Nishimura reported that a cyclobutane-modified crownophane showed excellent selectivity for the Li$^+$ ion.[2] In another example, a crownophane prepared by a tandem Claisen rearrangement could capture a water molecule via multiple hydrogen bonds.[3] Dithia[3.3]metacyclophane is an important member of the cyclophane family as it can undergo interesting aromatic ring-tilting and bridge-flipping processes.[4−6] If it is incorporated into a crownophane, the cavity size of the crown moiety may be to some extent varied by the tilting of the two aromatic rings, while the mobility of the thia-bridges may also have an effect on its complexation behavior. This paper thus describes the preparation, complexation behavior, and molecular structure of a dithia[3.3]metacyclophane-based crownophane.

The synthetic pathway leading to **3** is shown in Scheme 1.[7] Tetrol **2a** was prepared by the reaction of **1** with tetraethylene glycol dibromide in dry acetone in the presence of anhydrous potassium carbonate. Conversion of **2a** to

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[†] Taken in part from the Ph.D. Dissertation of J. Xu.

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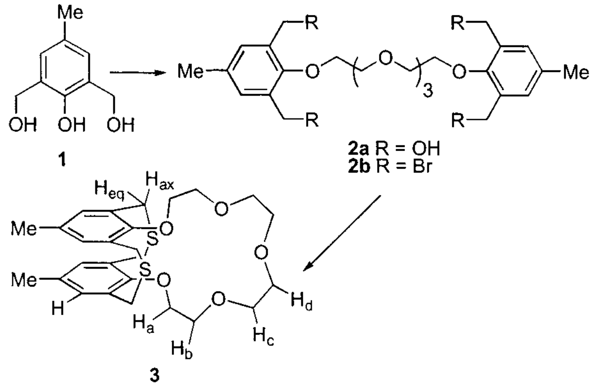
Scheme 1. Synthesis of Crownophane **3**[a]



[a] **1→2a**: $Br(CH_2CH_2O)_3CH_2CH_2Br$, K_2CO_3, acetone, reflux. **2a→2b**: PBr_3, 1,4-dioxane, 0−10°C. **2b→3**: $Na_2S\cdot9H_2O$, ethanol/benzene, high dilution condition.

tetrabromide **2b** was achieved in a high yield using phosphorus tribromide in dry dioxane at 0−10 °C. The compound **2b** underwent an intramolecular coupling reaction with $Na_2S\cdot9H_2O$ under high dilution conditions[8] in a mixture of 95% ethanol and benzene to afford the corresponding crownophane.

The single-crystal structure of **3** was determined by X-ray crystallography, and its ORTEP drawing is shown in Figure 1a. In **3**, both thia-bridges adopt a *pseudochair* conformation. The aromatic rings do not significantly deviate from planarity but form a small inter-ring angle of 13.4°. The distance between the centers of the two aromatic rings is 3.454 Å, and on this basis alone there is no clear indication of any significant transannular $\pi-\pi$ interaction. The average diameter of the cavity formed by the polyether oxygen atoms is 1.89 Å, which is very similar to the diameter of a Na^+ ion (1.90 Å). The complexation behavior of **3** was examined, and the logarithm of association constant[9] (log K_{ass}) was determined to be 4.63, 3.96, 2.91, and 2.81 for Na^+, K^+, Rb^+, and Cs^+, respectively. The order of log K_{ass} is $Na^+ > K^+ > Rb^+ > Cs^+$, which is as expected largely dependent on the cavity size of the crown moiety. As the crown unit in **3** structurally resembles that of 15-crown-5, a comparison of their selectivity is of interest. The selectivity of Na^+/K^+, Na^+/Rb^+, and Na^+/Cs^+ significantly increases from 1.3, 1.7, and 6.0 for 15-crown-5[9] to 4.7, 52, and 67 for **3**, respectively. This result is in fact consistent with the size-match principle. Studies on the complexes of monothia-18-crown-6 with NaSCN, KSCN, and RbSCN indicate that the sulfur atom interacts only weakly with K^+ and Rb^+, and there is no coordination at all with Na^+.[10] In our work, **3** may adopt several possible conformations (**3a−d**) in solution as shown in Figure 2. The bridging sulfur atoms may serve as donors in the complexation with cations or exhibit relatively weak interactions with a cation if **3** adopts the *pseudochair−pseudoboat* conformation (**3c** and **3d**). This, however, is considered unlikely because the electrostatic repulsion between sulfur and phenolic oxygen atoms will compel crownophane **3** to adopt the *pseudochair−pseudochair* conformation (**3a** and **3b**), thus resulting in no favorable

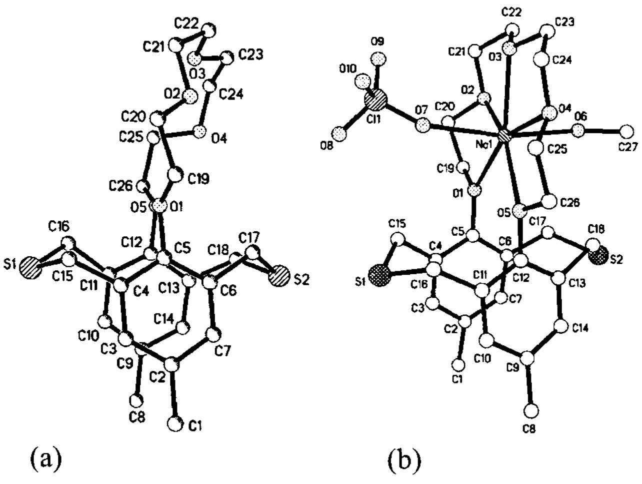


Figure 1. ORTEP drawings of (a) **3** and (b) $\mathbf{3}\cdot NaClO_4\cdot CH_3OH$.

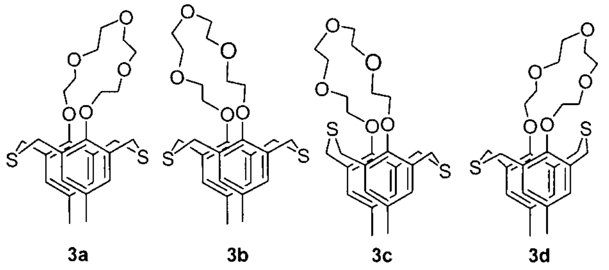


Figure 2. Possible conformations of **3** in solution.

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(7) **1,11-Bis(4-methyl-2,6-dihydoxymethylphenoxyl)-3,6,9-trioxaundecane 2a:** (65%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 6H, CH_3), 3.26 (t, 4H, J = 5.7 Hz, −OH), 3.70−3.76 (m, 8H, $-OCH_2CH_2O-$), 3.78−3.83 (m, 4H, $ArOCH_2CH_2O-$), 4.07−4.10 (m, 4H, $ArOCH_2CH_2O-$), 4.63 (d, 8H, J = 5.7 Hz, $-CH_2OH$), 7.06 (s, 4H, Ar−H); MS (EI) (m/z) 458 ($M^+ - 2H_2O$, 1), 440 ($M^+ - 3H_2O$, 5). Anal. Calcd for $C_{26}H_{38}O_9$: C, 63.14; H, 7.74. Found: C, 63.31; H, 7.90. **1,11-Bis(4-methyl-2,6-dibromomethylphenoxyl)-3,6,9-trioxaundecane 2b:** (75%) as a white solid; mp 95−96.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.28 (s, 6H, $-CH_3$) 3.79 (s, 8H, $-OCH_2CH_2O-$), 3.88−3.92 (m, 4H, $ArOCH_2CH_2O-$), 4.24−4.27 (m, 4H, $ArOCH_2CH_2O-$), 4.60 (s, 8H, $-CH_2Br$), 7.16 (s, 4H, Ar−H); MS (EI) (m/z) 742 (M^+, 0.4), 744 ($M^+ + 2$, 1.0), 746 ($M^+ + 4$, 1.6), 748 ($M^+ + 6$, 1.2), 750 ($M^+ + 8$, 0.2). Anal. Calcd for $C_{26}H_{34}Br_4O_5$: C, 41.85; H, 4.59. Found: C, 41.90; H, 4.90. **21,30-Dithia-17,25-dimethyl-1,4,7,10,13-pentaoxa[13.3.3](1,2,6)cyclophane 3:** (60%) as colorless crystals; mp 194−196 °C; ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 6H, CH_3), 3.27 (d, 4H, J = 14.6 Hz, $-CH_2SCH_2-$), 3.60−3.63 (m, 4H, $-OCH_2CH_2O-$), 3.83−3.86 (m, 8H, $-OCH_2CH_2O-$), 3.66−3.91 (m, 4H, $ArOCH_2CH_2O-$), 4.50 (d, 4H, J = 14.6 Hz, $-CH_2SCH_2-$), 6.80 (s, 4H, Ar−H); ^{13}C NMR ($CDCl_3$) δ 153.67, 133.09, 130.44, 129.87, 74.29, 71.49, 70.87, 70.64, 30.04, 20.61; MS (EI) (m/z) 490 (M^+, 63). Anal. Calcd for $C_{26}H_{34}O_5S_2$: C, 63.64; H, 6.98; S, 13.07. Found: C, 63.20; H, 7.10; S, 12.93.

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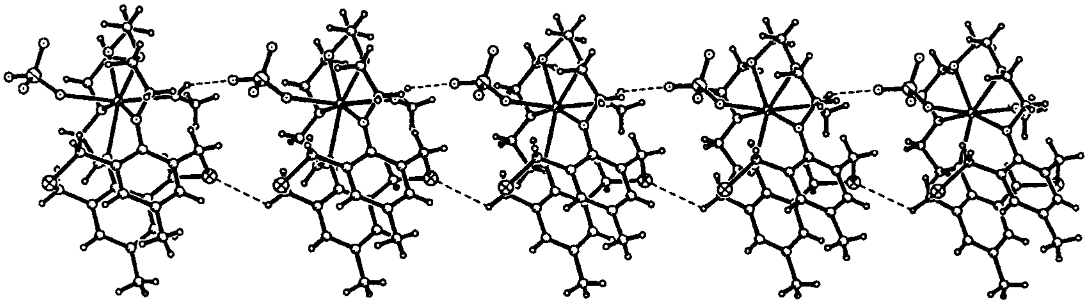

Figure 3. Supramolecular assembly of **3**·$NaClO_4$·CH_3OH. Dashed-lines represent hydrogen bonds and S···H−C interactions.

interaction between any sulfur atom and the metal ion. In fact, an estimation derived from AM1 calculations[11] indicates that conformer **3a** (or **3b**) is significantly more stable than conformer **3c** (or **3d**) by 7.2 kcal/mol, an energy difference sufficient to push the equilibrium almost completely to favor conformer **3a** (or **3b**).

Single crystals of complex **3**·Na^+ suitable for an X-ray crystallographic study[12] were obtained from a methanol solution of **3** and an equimolar amount of $NaClO_4$ upon slow evaporation. The crystals were found to contain a stoichiometric amount of methanol. The ORTEP drawing of the complex **3**·$NaClO_4$·CH_3OH is shown in Figure 1b. The crown ether unit and the coordinated Na^+ ion lie approximately in a plane (mean deviation = 0.109 Å), while methanol and the perchlorate anion are located on opposite sides of the plane. The Na^+ ion is exactly “nesting” in the cavity of the crown ether somewhat resembling the position of K^+ ion in the 18-crown-6·K^+ complex.[13] The Na^+−O distances found experimentally for **3**·$NaClO_4$·CH_3OH are comparable to the reported values in Na^+ complexes of crown ether.[14] The thia-bridges in **3**·$NaClO_4$·CH_3OH adopt a *pseudochair*−*pseudochair* conformation similar to that in the free ligand. There is, however, a significant decrease in the inter-ring angle of the two benzene rings going from 13.4° in **3** to 10.6° in **3**·$NaClO_4$·CH_3OH. This in turn results in an increase of 12% in the distance (3.329 Å) between the two phenolic oxygen atoms (O1 and O5) in **3**·$NaClO_4$·CH_3OH relative to that of the free ligand (2.984 Å). This O1−O5 distance is in fact considerably longer than the other adjacent O−O distances (2.738−2.803 Å) in **3**·$NaClO_4$·CH_3OH. In contrast, the O1−O5 distance (2.984 Å) is very similar to other adjacent O−O distances (2.845−3.030 Å) in uncomplexed **3**. This clearly illustrates the function of the tilting of the aromatic rings in the dithiametacyclophane in allowing a variation of the cavity size. Besides the size-match factor to control the selectivity, the orientation of donor atoms also plays an important role in metal ion recognition.[15] The relatively longer O1−O5 distance compared with other adjacent O−O distances in **3**·$NaClO_4$·CH_3OH probably allows **3** to behave more like a unique “16-crown-5”. The latter exhibits optimal donor atom orientation and correspondingly higher selectivity for Na^+ ion than 15-crown-5,[10] which is a typical example of noncomplementary ether oxygen.[16] This again reveals that the conformational adjustment (ring-tilting) in the cyclophane component in **3** was to a certain extent contributing to a higher selectivity for the Na^+ ion.

Another interesting feature in the crystals of **3**·$NaClO_4$·CH_3OH is that hydrogen bonding is observed between the hydrogen atom of coordinated methanol and one of the oxygen atoms of the perchlorate anion. This results in a linear one-dimensional hydrogen-bonded polymer (Figure 3) in its crystalline state. The distance of O···H is 2.191 Å and the O−H···O angle is 147.1°. Another interesting observation is that one of the bridging sulfur atoms in each crownophane is in close proximity to one of the benzylic protons of an adjacent crownophane (distance of S···H = 2.829 Å; angle of S···H−C = 117.5°). This S···H distance is less than the sum of their van der Waals radii (3.05 Å),[17] and this kind of S···H−C interaction may assist in holding the host−guest moieties to form the infinite supramolecular assembly. The field of inclusion chemistry describes the phenomena where solvent and other species are incorporated into vacant space within the crystalline lattice of the molecule to be crystallized.

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(11) Spartan 5.1.3 Unix software. http://www.wavefun.com.

(12) Crystal structures were solved by direct methods with any remaining non-hydrogen atoms located from different Fourier maps. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions with fixed isotropic thermal parameters. Refinements were made by full-matrix least-squares methods, and final refinements were made on F^2 using a weighting scheme of the form $w = 1/[\sigma^2(F_0^2 + (\mathrm{a}P)^2 + \mathrm{b}P)$ where $P = [\max.(F_0^2) + 2(F_c^2)]/3$. **Crystal data for 3:** $C_{26}H_{34}O_5S_2$, M = 490.65, triclinic, space group $P\bar{1}$, $a = 9.1151(1)$ Å, $b = 10.0902$ (3) Å, $c = 13.9221(4)$ Å, $\alpha = 89.227$ (1)°, $\beta = 85.947$ (1)°, $\gamma = 83.901$ (2)°, $V = 1270.01$ (5) Å^3, $Z = 2$, $D_{\mathrm{calcd}} = 1.283$ M/gm^3, μ(Mo Kα) = 0.244 mm^{-1}, $F(000) = 524$, 6338 reflections collected, 4196 independent reflections ($R_{\mathrm{int}} = 0.0389$), GOF = 1.000, $R_1 = 0.0715$, w$R_2 = 0.1689$, for $I > 2\sigma(I)$, $R_1 = 0.11207$, w$R_2 = 0.1889$ for all data. **Crystal data for 3·$NaClO_4$·CH_3OH:** $C_{27}H_{38}ClNaO_{10}S_2$, M = 645.13, monoclinic, space group $P2_1/c$, $a = 20.1695$ (6) Å, $b = 9.2913$ (3) Å, $c = 16.3782$ (5) Å, $\alpha = 90°$, $\beta = 90.883$ (1)°, $\gamma = 90°$, $V = 3073.03$ (16) Å^3, $Z = 4$, $D_{\mathrm{calcd}} = 1.394$ M/gm^3, μ(Mo Kα) = 0.328 mm^{-1}, $F(000) = 1360$, 18 621 reflections collected, 7457 independent reflections (R_{int} =0.0334), GOF = 1.068, $R_1 = 0.0639$, w$R_2 = 0.1482$, for $I > 2\sigma(I)$, $R_1 = 0.1037$, w$R_2 = 0.1652$ for all data.

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Studies[18] of crown ether/metal salt mixtures, for example, have resulted in a range of hydrogen-bonded crystalline arrays involving water/oxonium ions as the hydrogen bond donor and the crown ether as a hydrogen bond acceptor. To the best of our knowledge, however, there is no previous report of a crystalline array of crownophane/metal salt/solvent mixture derived from hydrogen bonding through the anion and the solvent molecule. In this respect, the hydrogen-bonded supramolecular polymer formed by **3**·$NaClO_4$·CH_3OH is likely to be the first such example.

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Supporting Information Available: Crystallographic data of **3** and **3**·$NaClO_4$·CH_3OH (in CIF format). This material is available free of charge via the Internet at http://pubs.acs.org.

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