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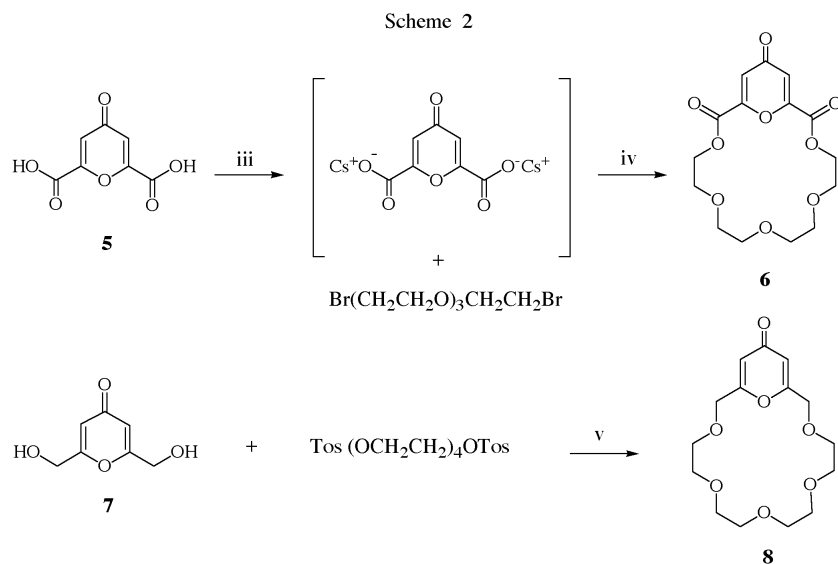
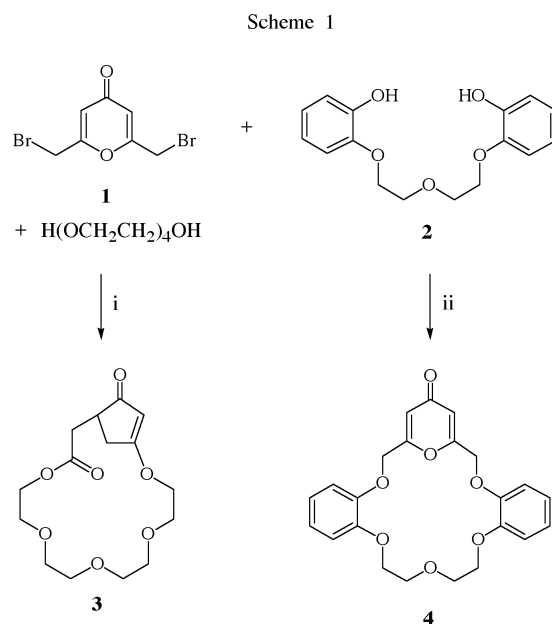
Dedicated to the memory of Raymond N. Castle

The preparation of novel crown type compounds **6** and **8** with a 4-pyrone unit is described.

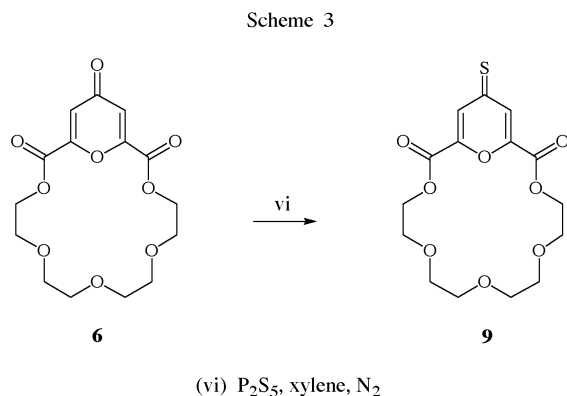
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Macrocyclic compounds containing heterocycles have been the subject of much interest in the field of host-guest chemistry because of their different complexation properties as compared to normal macrocyclic compounds according to the specific coordination properties of heteroatoms. Although many macrocyclic compounds containing heterocycles, such as pyridine [1] and furan [2] have been synthesized and studied, the 4-pyrone ring as a subunit of a macrocyclic compound like **4** (Scheme 1) has been reported for only a few cases [3-5]. As an extension of our studies of the synthesis of new polyethers including the 4-pyrone subunit, we report herein the synthesis of crown compounds **6** and **8**.

Attempts to obtain **8** starting from **1** were unsuccessful. In fact, contrary to all expectations, the reaction of **1** with tetraethylene glycol (TEG) under various conditions afforded the polyether **3** after ring transformation of the 4-pyrone subunit, due to the highly reactive starting compound **1** with five electrophilic centers (Scheme 1) [6]. Thus, an alternative route was utilized for the preparation of compounds **6** and **8**. In these cases 4-pyrones **5** and **7** [6] served as nucleophiles and the corresponding TEG derivatives functioned as electrophiles. The crown ester **6** has been prepared using the bis-cesium salt of chelidonic



acid, which was used in the reaction with dibromo trioxaundecane without further characterisation. Pieper and Kellogg have shown that Cs^+ plays an important role for the formation of the macrocycle **6** (Scheme 2) [4,7]. The conversion of **6** into **8** via thionoesters and subsequent desulfurization was not performed because **6** is only transformed into **9** by reacting with P_2S_5 (Scheme 3) [8].



The formation of **8** was of interest in the light of the first simple prototype 18-crown-6 compound with 4-pyrone subunit. The reaction of the diol **7** with TEG-ditosylate was carried out in refluxing acetonitrile/acetone (2:1) using cesium carbonate as the base and the templating reagent and afforded the crown **8** in 10 % yield (Scheme 2). The unchanged compounds **7** and TEG-ditosylate were also detected by tlc in the reaction mixture and other long-chain ethers may be formed, for example derived from **7** and TEG-ditosylate by the intermolecular version of the Williamson synthesis. High dilution conditions have been used to reduce polycondensation. Because **7** is only partially soluble in acetonitrile/acetone (2:1) at lower temperatures, the resulting suspension must be stirred in the dropping funnel. Studies on those applications of **6** and **8** in the field of crown compounds are now in progress.

EXPERIMENTAL

General Methods.

The melting points are uncorrected. The infrared spectra were obtained using dispersions in KBr and the ^1H -nmr spectra on a Perkin-Elmer-spectralphotometer 297 were recorded on a 400 MHz Bruker AVANCE DPX spectrometer. Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS). EI mass spectra were obtained at 70 eV on a CH-7A-Varian MAT spectrometer. The FAB-spectrum was recorded at 80 eV on a CH-5-DF-MAT-Varian spectrometer. Silica gel 60 (Merck, 230-400 mesh) and silica gel plates (Merck 60, F254) were used for flash chromatography and tlc.

3,6,9,12,15,21-Hexaoxabicyclo[15.3.1]hencosa-17,20-diene-2,16,19-trione (**6**).

To a stirred solution of compound **5** (1.0 g, 5.43 mmoles) dissolved in 20 mL ethanol and 5 mL water was added 20% aqueous cesium carbonate solution to pH 7. After 1 hour of reaction at room temperature, the solvents were concentrated *in vacuo* and the residue obtained was extracted with 50 mL dimethylformamide. To the resulting solution 1,11-dibromo-3,6,9-trioxaundecane (1.9 g, 5.94 mmoles) was added and the mixture was stirred at 100 °C for 24 hours. After removal of the solvent *in vacuo*, the resulting residue was diluted with 50 mL of water, extracted with ethyl acetate (3 x 60 mL) and worked up in the usual manner. The oily residue was purified by flash chromatography on a short column of silica gel (60 g) eluting with ethyl acetate. The solvent was evaporated under reduced pressure to give a colourless solid which was recrystallized from ethyl acetate/*n*-hexane (1:1). Yield: 0.56 g (30%), mp 131 °C (Lit. [5]: 174.4-176.1 °C); ir (potassium bromide): ν 3057, 2943, 1736, 1726, 1666 cm^{-1} ; ^1H -nmr (deuteriochloroform): δ 3.71 (s, 8H), 3.84-3.86 (m, 4H), 4.54-4.56 (m, 4H), 7.22 (s, 2H) ppm; ms (FAB pos.) 343 ($[\text{M}+\text{H}]^+$, 100%).

Anal. Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_9$ (342.3): C, 52.63 H, 5.30. Found: C, 52.59 H 5.42.

3,6,9,12,15,21-Hexaoxabicyclo[15.3.1]hencosa-17,20-diene-19-one (**8**).

A solution of tetraethylene glycol ditosylate (9.6 g, 19.1 mmoles) in 50 mL acetonitrile/acetone (2:1) and a stirred suspension of compound **7** (3.12 g, 19.9 mmoles) in 50 mL acetonitrile/acetone (2:1) were simultaneously added to refluxing acetonitrile/acetone (2:1) (250 mL) and cesium carbonate (13.0 g, 39.9 mmoles). The reaction mixture was heated for an additional 24 hours under reflux and filtered. The solvent was removed *in vacuo*. The oily product was purified by flash chromatography using dichloromethane/methanol (9:1) as the eluent. This yielded the macrocycle **8** as a white solid after trituration of the resulting oily residue with ethyl acetate. Yield: 0.63 g (10 %), mp 113-114 °C; ir (potassium bromide): ν 3050, 2901, 1668, 1621 cm^{-1} ; ^1H -nmr (dimethylsulfoxide- d_6): δ 3.50 (s, 8H), 3.56 (m, 4H), 3.61 (m, 4H), 4.41 (s, 4H), 6.28 (s, 2H) ppm; ms 314 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_7$ (314.3): C, 57.32 H, 7.05. Found: C, 57.19 H 6.88.

3,6,9,12,15,21-Hexaoxabicyclo[15.3.1]hencosa-17,20-diene-19-thioxo-2,6-dione (**9**).

To a stirred solution of compound **6** (0.2 g, 0.58 mmoles) in 5 mL xylene was added slowly phosphorous pentasulfide (0.26 g, 1.17 mmoles) and the resulting mixture was then heated at 100 °C for 4 hours, filtered, and evaporated. The residue was chromatographed with ethyl acetate and, after evaporation of the solvent, the residue was recrystallized from ethyl acetate to give green crystals of **9**. Yield: 0.1 g (48 %), mp 252 °C (Z); ir (potassium bromide): ν 3077, 2895, 1726, 1628, 1326 cm^{-1} ; ^1H -nmr (deuteriochloroform): δ 3.72 (s, 8H), 3.83-3.85 (m, 4H), 4.85 (m, 4H), 7.84 (s, 2H) ppm; ms 358 (M^+ , 100%).

Anal. Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_8\text{S}$ (358.4): C, 50.27 H, 5.06. Found: C, 50.21 H 4.97.

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