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Our aim to enlarge the ring of the crown type compound **1**, using the two component dilution principle, leads to hitherto unknown macrocycles **6** and **7**.

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The synthesis is described according to Yamamoto *et al.* as follows [1]: The crown type compound **1** which is synthesized from 2,6-bis(bromomoethyl)-4-pyrone and 1,5-bis(hydroxyphenoxy)-3-oxapentane [2], was treated with phosphorous pentasulfide in benzene followed by an excess of methyl iodide to afford the corresponding pyrylium compound **3**. This salt was hydrolyzed with potassium carbonate in aqueous methanol solution to give the ring-opened diketone **4**. This diketone was without isolation desulfurized with Raney nickel in ethanol followed by aqueous titanium trichloride to provide the macrocyclus **5** and the diastereomeric diol **6**. Compound **5** could not be isolated because a transformation to the cyclohexanone compound **7** takes place on account of an excess of potassium carbonate.

Compound **6** is obtained as a 1:1 mixture of diastereomers as can be seen from the ^{13}C nmr spectrum, in which all signals are split into two lines. Interestingly, the ^1H nmr spectrum displays two signals for the OH protons at 2.87 and 3.12 ppm; one signal belonging to one diastereomer and the other to the second diastereomer.

The constitution follows from DEPT-135 °C ^{13}C nmr spectrum. To determine the con-figuration at the cyclohexanone ring of compound **7**, several NOE experiments were performed. Irradiation of H_C causes signal enhancement of both H_D and H_B , but not H_A . Therefore, H_C must be equatorial. Irradiation of H_D results in signal enhancement of H_C and H_B , but not of H_A . The OH group is also equatorial. These results are only in accord with the depicted conformation, thus the compound **7** has the *cis*-configuration (O-Ar and OH_D on the same side).

EXPERIMENTAL

Melting points were determined on a Linström apparatus and are uncorrected. The uv spectrum was obtained on a HP 8451A Diode Array Spectrophotometer. The ir spectra were recorded on a Perkin-Elmer 297 spectrometer. The ^1H nmr and the ^{13}C nmr spectra were recorded on a Bruker AC 300 and a Bruker AVANCE CPX 400 spectrometer respectively. Mass spectra were

obtained on a Finnigan MAT Bremen CH-7A spectrometer and Finnigan MAT Bremen CH-5DF. FAB spectra were determined on a CH-5-DF-MAT-Varian (80 eV). Elemental analyses were performed by the Institut für Pharmazie Analytical Service Laboratory.

2,9,12,15,22-Pentaoxa[2.7]-*o*-cyclo[2]-(2,6)-pyranophan-28-thione (**2**).

To crown type compound **1** [1] (2 g, 4.873 mmoles) in dry benzene (100 ml) phosphorous pentasulfide (1.12 g, 5.06 mmoles) was added, and the mixture was heated to reflux for 1 hour. After cooling the mixture was filtered and the solution was removed by evaporation at room temperature. The residue was purified by column chromatography (silica gel, ethyl acetate). Pure fractions were combined and concentrated. Red crystals were obtained from ethyl acetate/n-hexane, yield 1.5 g (72%), mp 162 °C; ir (potassium bromide): ν 1648, 1256 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.93-3.95 (m, 4H), 4.19-4.21 (m, 4H), 4.92 (s, 4H), 6.92-7.05 (m, 8H), 7.30 (s, 2H); ^1H nmr (deuterioacetonitrile): δ 3.86-3.87 (m, 4H), 4.13-4.14 (m, 4H), 4.87 (s, 4H), 6.95-7.05 (m, 8H), 7.30 (s, 2H); EI-*ms*: *m/z* 426 (M^+).

Anal. Calcd. for $\text{C}_{23}\text{H}_{22}\text{O}_6\text{S}$ (426.49): C, 64.77; H, 5.20. Found: C, 64.63; H, 5.34.

2,9,12,15,22-Pentaoxa[2.7]-*o*-cyclo-[2]-28-methylthio-(2,6)-pyrylophanium Iodide (**3**).

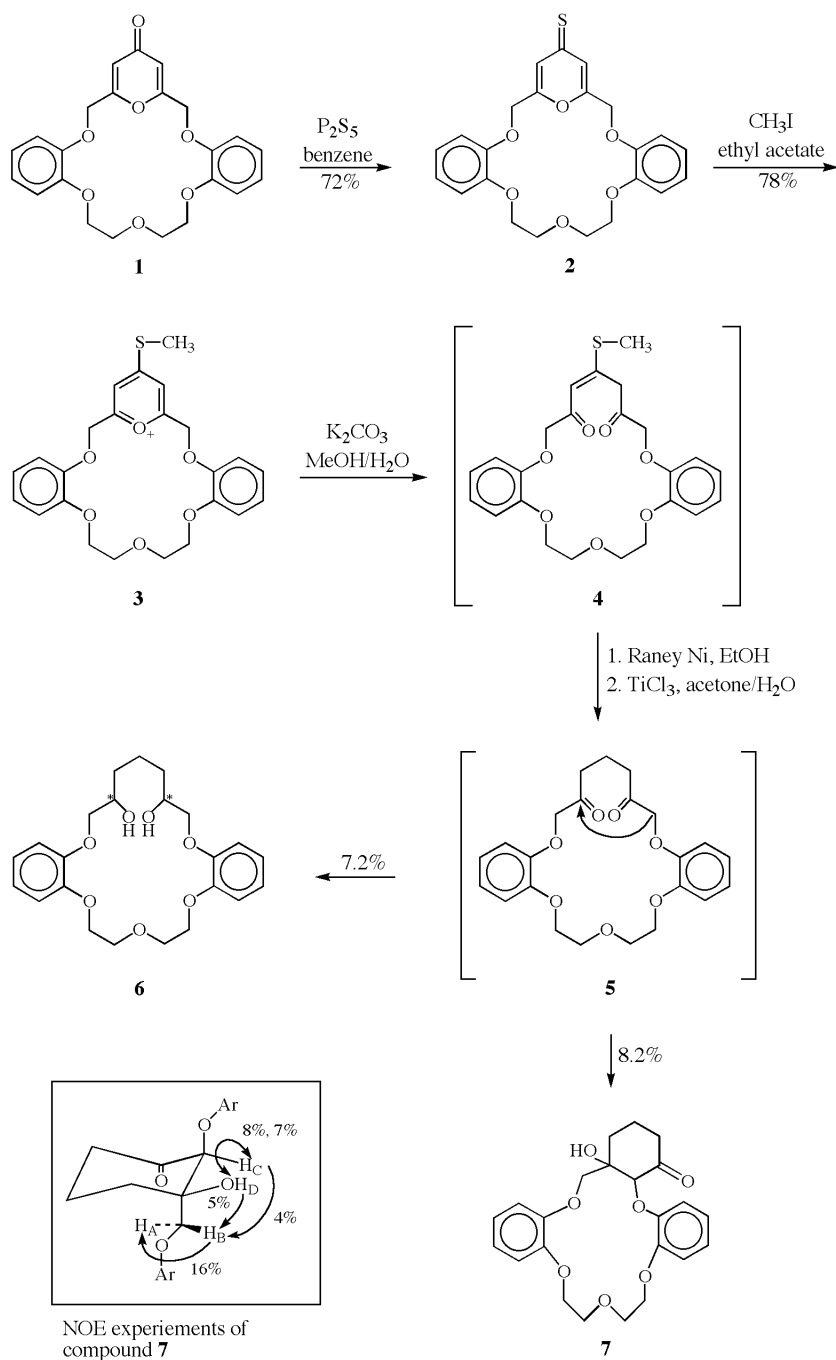
An excess of methyl iodide (2 ml, 32.06 mmoles) was added to a mixture of **2** (1.5 g, 3.527 mmoles) in dry ethyl acetate (70 ml) and heated to reflux for 90 minutes. The mixture was filtered and the solvent was evaporated at room temperature to give 1.66 g (83%) of a red solid, which was diluted with acetonitrile (5 ml) and filtered again. The red crystals were dried at 70 °C for 24 hours. Yield 1.56 g (78%), mp 122 °C; ir (potassium bromide): ν 1633, 1254 cm^{-1} ; uv (dichloromethane): 328 nm; ^1H nmr (deuterioacetonitrile): δ 2.87 (s, 3H), 3.69-3.71 (m, 4H), 4.10-4.12 (m, 4H), 5.31 (s, 4H), 6.94-7.17 (m, 8H), 8.00 (s, 2H).

Anal. Calcd. for $\text{C}_{24}\text{H}_{25}\text{IO}_6\text{S}\cdot 2\text{H}_2\text{O}$ (604.46): C, 47.69; H, 4.84. Found: C, 47.94; H, 4.64.

4,8-Dihydroxy-2,10,17,20,23-pentaoxa[9.7]-*o*-cyclophane (**6**) (mixture of diastereomers), and 17-Hydroxy[0 17,22][7.9]-*o*-cyclophan-21-one (**7**).

A mixture of **3** (1.5 g, 2.64 mmoles), potassium carbonate (411 mg, 2.98 mmoles) and aqueous methanol (20 ml, 50%) was stirred first at 0 °C for 30 minutes and then 1 hour at room

Scheme



temperature. The mixture was concentrated, then dissolved in water (20 ml) and extracted with three 25 ml portions of benzene. The benzene solution was dried over sodium sulfate, filtered and concentrated to give a yellow oil (**4**).

A solution of this yellow oil in dry ethanol (20 ml) was heated to reflux for 3 hours with an excess of Raney nickel. The solid was filtered and washed with ethanol (20 ml). After evaporation of the solvent the yellow oil was added to a

solution of aqueous titanium trichloride (2 ml, 20%) in acetone (5 ml) and stirred for 1 hour at room temperature. The reaction mixture was poured into brine (20 ml) and extracted with three 30 ml portions of benzene. The organic layer was dried over sodium sulfate, filtered and evaporated at room temperature to give a brown oil. This oil was chromatographed (silica gel, ethyl acetate) and white crystals of **6** and **7** were obtained from ethyl acetate/*n*-hexane.

Compound **6** was obtained in 7.2% yield (80 mg), mp 169-171 °C; ir (potassium bromide): ν 3427, 1593, 1507 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.67-1.85 (m, 6H), 2.87 and 3.12 (both: d, $J = 5.5$ Hz, 2H, OH, D_2O exchangeable), 3.92-4.02 (m, 10H), 4.14-4.23 (m, 4H), 6.89-6.98 (m, 8H); ^{13}C nmr (deuteriochloroform): δ 21.1, 21.9, 32.0, 32.3, 69.5, 69.6, 69.7, 70.0, 70.4, 70.5, 73.7, 73.8, 115.0, 115.1, 116.2, 116.4, 121.7, 121.8, 122.5, 122.6, 149.0, 149.1, 149.6, 149.7; FAB-ms: m/z 419 (MH^+).

Anal. Calcd. for $\text{C}_{23}\text{H}_{30}\text{O}_7$ (418.49): C, 66.01; H, 7.23. Found: C, 65.85; H, 7.16.

Compound **7** was obtained in 8.2% yield (90 mg), mp 177 °C; ir (potassium bromide): ν 3478, 1595, 1500 cm^{-1} ; ^1H nmr ($\text{DMSO}-d_6$): δ 1.83-1.85 (m, 1H), 1.93-2.01 (m, 2H), 2.15-2.26 (m, 2H), 2.61-2.67 (m, 1H), 3.78-3.87 (m, 4H), 3.98 (d, $J = 10.6$ Hz, 1H, H_A), 4.07-4.16 (m, 4H), 4.27 (s, 1H, H_C), 4.38

(d, $J = 10.6$ Hz, 1H, H_B), 5.18 (s, 1H, OH, D_2O exchangeable), 6.76-6.85 (m, 3H), 6.91-7.04 (m, 5H); ^{13}C nmr (deuteriochloroform) with DEPT-135 °C-Data: δ 20.7, 30.1, 39.5, 66.9, 68.0, 69.3, 69.6, 74.8, 78.3, 90.7, 113.1, 113.7, 120.1, 121.2, 121.6, 121.8, 124.0, 124.4, 148.2, 148.4, 150.1, 151.2, 207.4; FAB-ms: m/z 415 (MH^+).

Anal. Calcd. for $\text{C}_{23}\text{H}_{26}\text{O}_7$ (414.45): C, 66.65; H, 6.32. Found: C, 66.42; H, 6.25.

REFERENCES AND NOTES

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