



## The First Preparation of Crown Ether-Annulated Porphyrin

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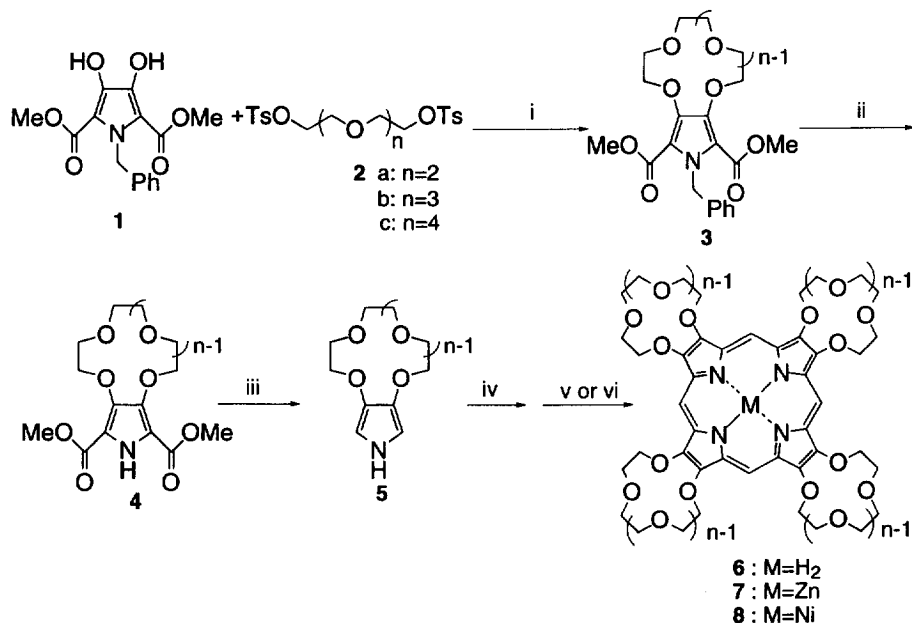
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**Abstract:** Pyrroles fused with crown ethers are prepared by the reaction of 3,4-dihydroxy pyrrole **1** and polyethylene glycol ditosylate **2** in the presence of cesium fluoride using a convenient high dilution method. These pyrroles can be converted into the corresponding porphyrins with four crown ether moieties, which are expected to form ion channels. Copyright © 1996 Elsevier Science Ltd

As a number of natural systems have two or more active sites, di- and polytopic receptors have been synthesized and the chemical and physical properties of such poly-macrocyclic ligands capable of complexation with two or more metal ions have been widely studied. The well-known examples are the crown ether-capped metalloporphyrins.<sup>1</sup> This system could be a model for the metalloproteins such as hemoprotein; thus, many "crowned" porphyrins and crown-fenced porphyrins<sup>2</sup> have been reported. On the other hand, crown ether-substituted phthalocyanines also were investigated as they serve as synthetic models for ion channels and the novel mesomorphic forms of these compounds.<sup>3</sup> To the best of our knowledge, however, compounds which have crown ether units at the porphyrin periphery are unknown. In this paper we report on the synthesis of novel porphyrins containing four crown ether moieties which are on the same plane of the porphyrins.

Crown ether-annulated pyrroles **3** were prepared by condensation of *N*-benzyl-2,5-dicarbomethoxy-3,4-dihydroxy pyrrole **1**<sup>4</sup> and polyethylene glycol ditosylate **2** in the presence of cesium fluoride using a convenient high dilution method. The high dilution conditions were accomplished as follows: A Dean-Stark trap was filled with a solution of **1** (4.5 g, 15 mmol) and tetraethylene glycol ditosylate **2b** (6.0 g, 12 mmol) in DMF (45 ml) and fitted into the top of a flask containing a suspension of cesium fluoride (9.1 g, 60 mmol) in acetonitrile (450 ml). When the suspension was refluxed, the mixture of **1** and **2** ran over the brim of the trap and a small amount flowed down into the flask.

The debenzylation of these pyrroles **3** was performed at 50 °C in the presence of Pd(OH)<sub>2</sub>/C and hydrogen at a pressure of 10 atm. The ester function of the pyrroles **4** could be readily removed by heating at 190 °C with KOH in ethylene glycol to afford  $\alpha$ -free pyrroles **5** in good yields, which were precursors for symmetrical porphyrins fused with crown ethers **6**. Porphyrins **6** were obtained by the reaction of **5** with paraformaldehyde under an acid catalysis, followed by oxidation with *p*-chloranil. Then, the reaction mixture was evaporated under vacuo and the residue was subsequently converted to a Zn-complex by treatment with zinc (II) acetate in chloroform. The reaction conditions are given in the Scheme and the yields are listed in the Table.



**Scheme. Reagents and Conditions :** (i) CsF, CH<sub>3</sub>CN, DMF, (ii) Pd(OH)<sub>2</sub>/C, H<sub>2</sub>(10 atm), AcOH, (iii) KOH, HOCH<sub>2</sub>CH<sub>2</sub>OH, 190°C, (iv) (CH<sub>2</sub>O)<sub>n</sub>, *p*-TsOH, chloranil, (v) (CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>Zn, chloroform, (vi) (CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>Ni, chloroform

The compounds **7** were diagnosed by <sup>1</sup>H NMR, <sup>13</sup>C NMR, ms and UV-vis spectra except for the compound **7c**; because of its very small quantity, **7c** was confirmed only by the UV-vis spectrum.<sup>5</sup>

Treatment of the free-base porphyrin **6a** with nickel (II) acetate instead of zinc (II) acetate gave the nickel porphyrin **8**.

These novel porphyrins complexed with transition metals and alkali or alkaline-earth metals could be captured at the crown moieties. Thus, these crown-annulated porphyrins are expected to show metastable mesophases like the crowned phthalocyanines and are able to form ion channels.

The chemical and physical properties of these porphyrins are under investigation.

**Table.** Yields of Pyrroles and Porphyrins

Run	n	Yield/%				
		3	4	5	7	8
a	2	46	72	80	6	5
b	3	40	96	85	6	—
c	4	51	86	71	trace	—

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5. Selected spectroscopic and analytical data for compound **3a** (n=2);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.78 (10H, brs), 3.84-3.87 (4H, m), 4.19-4.21 (4H, m), 6.00 (2H, s), 6.96 (2H, d, *J* 7.81) and 7.15-7.24 (3H, m);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  48.3, 51.1, 69.5, 70.1, 74.7, 116.2, 125.5, 126.4, 127.8, 138.4, 142.6 and 160.0; *m/z* (EI) 419 ( $\text{M}^+$ , 100), 331 (8), ; (Found: C, 59.99; H, 6.06; N, 3.27.  $\text{C}_{21}\text{H}_{25}\text{NO}_8$  requires C, 60.13; H, 6.01; N, 3.34 %); compound **4a** (n=2);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.78 (4H, s), 3.85 (4H, t, *J* 3.90), 3.89 (6H, s), 4.28 (4H, t, *J* 3.91) and 8.96 (1H, brs);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  51.7, 69.9, 70.5, 74.9, 113.3, 142.0 and 159.8; *m/z* (EI) 329 ( $\text{M}^+$ , 54.6), 241 (25.7) and 209 (100); (Found: C, 50.57; H, 5.82; N, 4.24.  $\text{C}_{14}\text{H}_{19}\text{NO}_8$  requires C, 51.06; H, 5.82; N, 4.25 %); compound **7a** (n=2);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.57 (16H, s), 3.94 (16H, s), 4.92 (16H, s) and 10.00 (4H, s);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  70.8, 71.4, 75.3, 95.5, 140.6 and 145.3; UV/nm  $\lambda_{\text{max}}$  398.0, 531.0 and 570.0; compound **3b** (n=3);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.74 (8H, s), 3.79 (6H, s), 3.89 (4H, t, *J* 4.89), 4.23 (4H, t, *J* 4.88), 5.98 (2H, s), 6.92 (2H, d, *J* 7.81) and 7.17-7.26 (3H, m);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  48.6, 51.4, 70.1, 70.4, 70.8, 74.3, 116.2, 125.6, 126.6, 128.1, 138.7, 142.6 and 160.4; *m/z* (EI) 463 ( $\text{M}^+$ , 100); (Found: C, 59.48; H, 6.35; N, 3.11.  $\text{C}_{23}\text{H}_{29}\text{NO}_9$  requires C, 59.60; H, 6.31; N, 3.02 %); compound **4b** (n=3);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.73 (8H, s), 3.86-3.92 (10H, m), 4.33 (4H, t, *J* 4.85) and 9.14 (1H, brs);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  51.1, 69.6, 70.1, 70.2, 73.7, 112.6, 141.0 and 159.4; *m/z* (EI) 373 ( $\text{M}^+$ , 20.1), 285 (11.7), 241 (33.9) and 209 (100); (Found: C, 51.29; H, 6.26; N, 3.78.  $\text{C}_{16}\text{H}_{23}\text{NO}_9$  requires C, 51.47; H, 6.21; N, 3.75 %); compound **7b** (n=3);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.71 (16H, s), 3.79 (16H, s), 4.19 (16H, s), 5.12 (16H, s) and 10.06 (4H, s);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  70.4, 70.9, 74.7, 95.2, 140.4 and 143.9; *m/z* (FAB $^+$ ) 1132 ( $\text{M}^+$ ); UV/nm  $\lambda_{\text{max}}$  398.5, 532.5 and 573.0; (Found: C, 55.30; H, 6.06; N, 4.91.  $\text{C}_{52}\text{H}_{68}\text{N}_4\text{O}_{20}\text{Zn}$  requires C, 55.0; H, 6.04; N, 4.94 %); compound **3c** (n=4);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.69 (4H, s), 3.74 (8H, s), 3.79 (6H, s), 3.86 (4H, t, *J* 4.88), 4.24 (4H, t, *J* 4.88), 5.98 (2H, s), 6.91 (2H, d, *J* 7.32) and 7.17-7.25 (3H, m);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  48.8, 51.6, 70.2, 70.67, 70.69, 70.9, 74.3, 116.4, 125.8, 126.8, 128.3, 138.9, 142.5 and 160.6; *m/z* (EI) 507 ( $\text{M}^+$ , 100), 419 (19.4), 375 (17.4) and 331 (53.2); compound **4c** (n=4);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.68 (4H, s), 3.73 (8H, s), 3.88 (10H, s), 4.32 (4H, brs) and 9.02 (1H, brs);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  51.7, 69.9, 70.3, 70.4, 70.6, 73.8, 112.9, 141.2 and 159.8; *m/z* (EI) 417 ( $\text{M}^+$ , 16.7), 329 (9), 285 (10.8), 241 (47.7) and 209 (100); compound **7c** (n=4); UV/nm  $\lambda_{\text{max}}$  402.0, 536.0 and 575.0.

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