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The First "Crowned" Expanded Porphyrin

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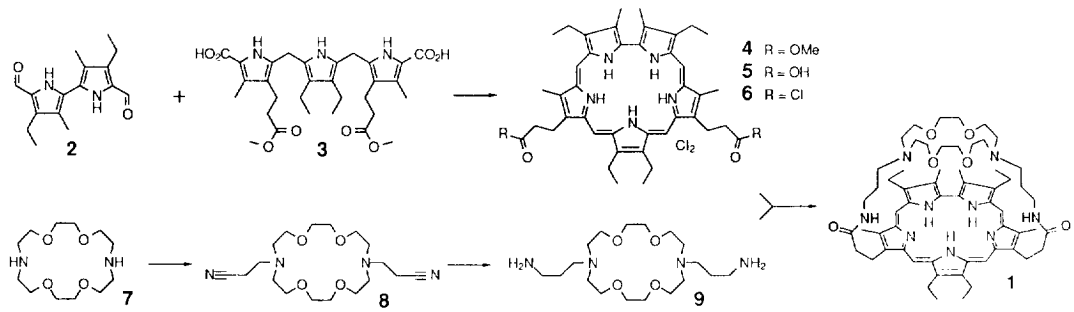
Abstract: The synthesis of a cyclophane containing both a crown ether and an expanded porphyrin, sapphyrin, is described. This system acts as a receptor for the concurrent complexation of both anionic and cationic substrates.

A large number of natural systems have two active sites held in close proximity.[1] This has prompted substantial interest in the chemistry of ditopic receptors,[2] including synthetic analogs containing both a crown ether and a porphyrin.[3] A ditopic ligand capable of holding two cations and/or anions in constrained positions simultaneously would be an important 'next step' model, especially in light of the cation/anion channels in living cells.[4] We wish to report here the synthesis of such a novel ligand, the 'crown sapphyrin' **1**. This system allows for the simultaneous coordination of both cationic and anionic substrates.

The structure of crown sapphyrin **1** bears close analogy to several previously reported capped porphyrins.[5,6] This analogy might be expected to hold in terms of synthesis as well. At present, two generally applicable routes to capped porphyrins are known. The first begins with the porphyrin precursors built onto the ends of the cap with the porphyrin ring then being prepared *vis* an intramolecular cyclization.[5] The second relies on porphyrin systems bearing side chain functional groups and condensation with another bifunctional molecule as the means of forming the capped macrocycle.[6] This latter strategy was considered preferable for **1** since an efficient route to disubstituted sapphyrins was recently developed in our laboratory.[7]



Briefly, the route, as shown above, starts with an oxidative condensation of a bipyrrole, **2**,[8] and a tripyrrane, **3**,[9] followed by acid- or base-mediated hydrolysis of the resulting diester dihydrochloride sapphyrin **4**, to the diacid sapphyrin **5**.[7] (The basic hydrolysis is faster, but gives a lower yield.) This diacid

5 is activated with oxalyl chloride. Good yields are obtained for all of these steps. The crown ether bifunctional cap **9** was synthesized according to a modification of an existing procedure.[3a] The cyanoethyl side chains were introduced to the diaza-18-crown-6,[10] **7**, by prolonged heating in acrylonitrile. Hydrogenation of **8** afforded the *bis*-aminopropyl derivative, **9**. The coupling of the two bifunctional molecules is affected under high dilution conditions. The sapphyrin diacid chloride **6** in a minimum amount of dry dichloromethane is slowly dripped into a larger dichloromethane solution of the dried *bis*-aminopropyl crown ether **9** containing triethylamine. The crown sapphyrin **1** hydrochloride is then isolated by column chromatography (silica gel; methanol in chloroform gradient as eluent) in 23% yield.

Spectroscopic data support the indicated structure. In the ^{1}H NMR spectrum ($CDCl_3$), the crown ether methylene protons resonate in a multiplet at *ca.* δ 3.75, whereas those of the propyl arms appear at δ 1.63, 1.81, and 2.05. (The sapphyrin-derived signals are similar to those of the parent macrocycle.) Also, as might be anticipated, the ^{13}C NMR spectrum ($CDCl_3$) presents 27 well-resolved signals and the mass spectra (CI and FAB) reveal the predicted parent ion peak (1030 amu, free-base form of **1**).

The complexation of ammonium fluoride to the monoprotonated form of **1** (**1**·HCl) was studied by ^{1}H NMR spectroscopy (10% CD_3OD in $CDCl_3$). In accord with the ammonium cation-to-crown binding literature,[3c,11] upfield shifts of the methylene proton resonances (on the order of 0.2 ppm) of the crown ether subunit are observed when NH_4F is added to solutions of **1**·HCl. (Similar shifts were also observed using the control system **7**.) Greatly sharpened and slightly displaced sapphyrin proton resonances are also observed in the course of this addition. Further, as expected,[12] the sapphyrin Soret band is seen to undergo a *ca.* 10 nm blue-shift when these same initial and final NMR samples are studied by UV/visible spectroscopy. Taken together, these changes are consistent with those expected for the concurrent complexation of an ammonium cation *and* a fluoride anion into the crown and sapphyrin subunits, respectively, of **1**·HCl. Thus, this system acts as a ditopic receptor for the simultaneous binding of both cationic and anionic substrates. Supporting this conclusion are the results of preliminary mass spectrometric studies: Upon the addition of the appropriate salts, signals corresponding to [**1**·2H + $Mg(SO_4)_2$], [**1**·4HN_3], and [**1**·4H + $Fe(CN)_6$] are seen.

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