

Synthesis and X-ray structure of a three dimensional calixpyrarin

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The synthesis of an unprecedented pyrrole-containing, cryptand-like system with sp^2 hybridized apical bridging carbon atoms is reported.

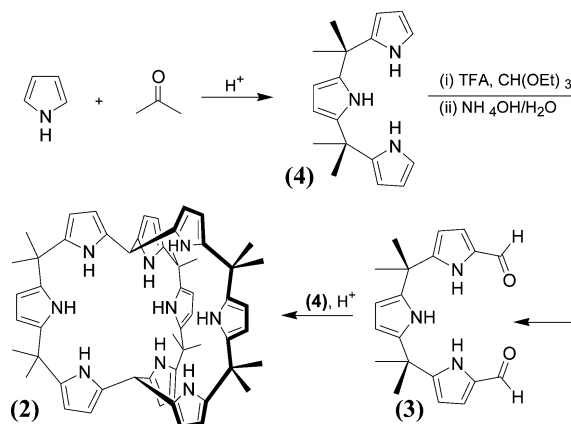
Since their introduction by Simmons and Park¹ and independently and more forcefully by Lehn and co-workers,² three dimensional molecular receptor systems have proved a source of inspiration for chemists, attracting attention not only for their wide-ranging utility in the fields of molecular recognition, catalysis and transport, but also for their inherent synthetic challenge and aesthetic beauty.³ In the course of our on-going studies of pyrrole-containing receptors (especially calix[*n*]pyrroles⁴ and calix[*n*]pyrins⁵), we have been keen for some time to design and synthesize related bicyclic or “cryptand-like” systems. In the context of this work, we recently reported the synthesis, solid state structure, and anion binding properties of the bicyclic[3,3,3]nonapyrrole (**2**)⁶ (Scheme 1), the first cryptand-like calixpyrrole analogue constructed uniquely from pyrrole moieties and bridging carbon atoms. We now wish to report a new, oxidized form of this system.[†]

Compound **2** was synthesized from an acid catalysed condensation of tripyrrane (**4**) and its diformyl analogue (**3**) in 15% yield. It was found to adopt an *in-in* configuration wherein both *meso*-like bridging carbon atoms are pointing in toward the center of the molecule. Although we have been able to synthesize, isolate and study this intriguing three dimensional system, it was found to be moderately unstable when exposed to air and light as evidenced by the fact that it undergoes a color change, from colorless to light red in a matter of hours when left unprotected on the bench top.

Owing to its strained structure and to the light red color emerging with time when dichloromethane solutions of (**2**) were allowed to stand in the presence of air or light, we made the assumption that the primary decomposition product could involve a single, well-defined molecular species containing sp^2 , as opposed to sp^3 , hybridized carbon atoms at the bridgehead positions. Such a derivative would represent the calix[*n*]pyrin analogue of the original calix[*n*]pyrrole bicycle. Calix[*n*]pyrins are hybrid molecules that lie at the structural crossroads

between porphyrins and calixpyrroles and which bear analogy to both the porphyrins and calixpyrroles since they contain a mixture of sp^2 and sp^3 hybridized *meso*-like bridging carbon atoms.^{7,8} This leads to conjugation pathways that are longer than those found in calix[*n*]pyrroles but are still interrupted relative to the pathways present in porphyrins, phthalocyanines, expanded porphyrins, and many other oligopyrrolic systems. In the case of simple macrocyclic species, this combination of sp^2 and sp^3 hybridized *meso*-like bridging carbon atoms leads to novel structural features and interesting anion and cation recognition properties.⁵ An appreciation that this could prove true in the case of a bicyclic system provided the incentive to try isolating the red decomposition product(s) produced from (**2**).

Initial attempts to isolate one or more well-defined by-products from dichloromethane solutions of (**2**) kept in the air for several days proved unsuccessful. Appreciating, however, that the coloration of the solution could arise from at least a partial, oxygen-induced, oxidation of the cryptand-like calixpyrrole, we considered the use of oxidizing agents to promote this reaction. In accord with such thinking, it was found that the addition of two equivalents of 5,6-dichloro-2,3-dicyano-*p*-benzoquinone (DDQ) to (**2**), dissolved in dichloromethane, induced a quick color change from colorless to bright red, producing a solution with a UV-vis absorption maximum at 474 nm. Removal of the dichloromethane under reduced pressure, followed by purification by column chromatography over neutral alumina using 1% methanol in dichloromethane as the eluent, yielded a red solid, the UV-vis spectral characteristics of which turned out to be generally comparable to those of partially oxidized calix[*n*]pyrin-type macrocycles. In particular, this species was characterized by the absence of aromaticity-induced “porphyrin-like” features (*e.g.*, strong Soret and weaker accompanying Q-like bands) in its UV-vis spectrum (recorded in CH_2Cl_2).⁹ Rather, it displayed only moderately intense ($\epsilon < 10^5 \text{ l mol}^{-1} \text{ cm}^{-1}$) absorption bands between 400 and 500 nm at $\lambda_{\text{max}} = 421, 474 \text{ nm}$, respectively (Fig. 1). These asymmetric spectroscopic features contrast, however, with the sole broad absorption centered at 449 nm observed for calix[6]pyrin-(1.1.1.1.1), a possible monocyclic analogue that was prepared and characterized recently.⁸



Scheme 1 Synthetic route corresponding to the synthesis of (**2**).⁶

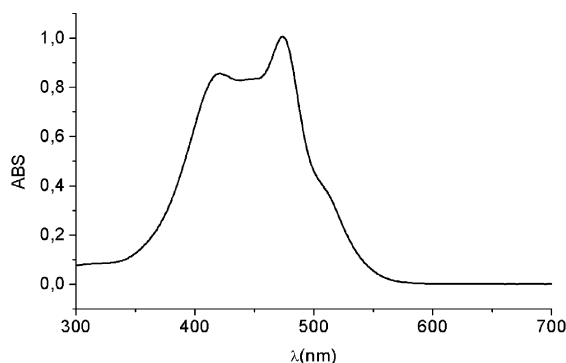
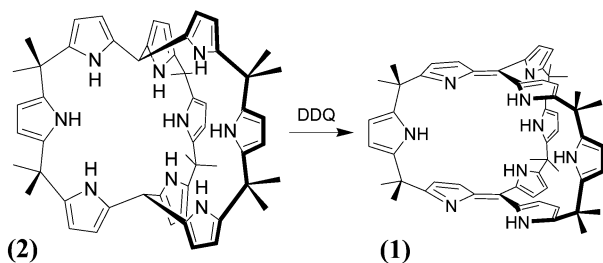


Fig. 1 UV-Vis spectrum of (**1**) recorded in CH_2Cl_2 (RT, 1.17×10^{-5} M).



Scheme 2 Schematic representation of the chemically induced oxidation of (2) leading to the calix[*n*]phyrin-like cryptand (1).

The ^1H NMR spectral characteristics of the oxidized product produced from (2), recorded in deuterated chloroform, were consistent with a non-symmetric species, *i.e.* six signals observed between 5.5 and 7 ppm that are attributed to six non-equivalent β -pyrrolic protons; this compares to the three signals observed in the same region for the highly symmetric species (2). The ^1H NMR spectrum of the oxidized product also revealed the presence of four, as opposed to two, NH signals, which were found to be non-equivalent. As importantly, it provided no evidence for the presence of bridging CH hydrogen atoms, the corresponding signals for which were observed at *ca.* 4.7 ppm in the spectrum of (2). This is consistent with the proposal that these protons (two NH and two CH) were removed, as expected, during the oxidation process. Further support for this latter critical conclusion came from mass spectrometric analysis (CI) of this oxidized product; it revealed a molecular weight of 861 (*m/z*), corresponding to a 4 amu reduction in molecular mass as compared to the molecular weight of the starting compound (2). Taken together, therefore, the spectroscopic and mass spectrometric data are considered consistent with the oxidized product produced from (2) being the three-dimensional, cryptand-like derivative (1) (Scheme 2).

The structure of (1), which to the best of our knowledge is unprecedented in the oligopyrrolic literature, was further confirmed by an X-ray diffraction analysis performed on a single crystal obtained by slow evaporation of a solution of (1) in a mixture of ethanol and ethyl acetate. The resulting Ortep views (Fig. 2) revealed the presence of solvent molecules, as

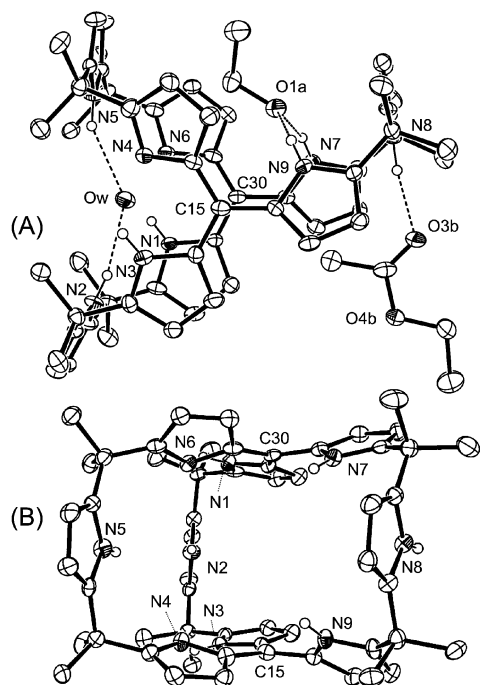


Fig. 2 Top (A) and side (B) Ortep views of (1) showing partial atom labeling scheme. For reasons of clarity, the bound solvent molecules have been omitted on the side view (B).

well as two water molecules bound to the cryptand through a combined total of five N–H...O hydrogen bonding interactions. In contrast to what was observed in the solid state structure of (2), where the two bridging CH hydrogen atoms point inward, thus closing up the inner core, the two sp^2 hybridized bridging carbon atoms of (1) serve to establish a more open cavity that allows for the partial “inside binding” of water and, potentially, other substrate molecules ($d(\text{C}15\text{--C}30) \approx 5.7$ and 4.3 \AA for (1) and (2), respectively).

Two stacked dipyrromethene subunits, to which the visible features of (1) are ascribed, are also evident in the structure, as inferred from the absence of hydrogen atoms on either the N4 and N6 nitrogen atoms, as well as from the bond length differences measured for C15–C16, C15–C14 and C15–C44 (1.40, 1.44 and 1.44 \AA , respectively). The rather complex UV-vis features of (1), as compared to those of the topologically related calix[6]phyrin-(1.1.1.1.1.1)⁸ that also contains two similar dipyrromethene chromophores, reflects most probably the strained and hence less-symmetrical nature of the unprecedented bicyclic structure. To the extent such a supposition is true, the X-ray diffraction analysis provides important support for both the proposed novel calix[*n*]phyrin-like three-dimensional structure and a rationale for the unusual UV-vis spectroscopic features. The X-ray structure, in revealing the presence of a bound water molecule, also supplies an important “hint” that systems such as (1) could have a role to play in the area of substrate-specific molecular recognition. Research efforts devoted to exploring this latter possibility are currently in progress.

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Notes and references

† *Spectroscopic data for 1*: (60% yield) HRMS (CI): $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{56}\text{H}_{62}\text{N}_9$: 860.5128; found: 860.5126; ^1H NMR (CDCl_3 , 250 MHz, 293 K) δ 1.62 (s, 12H, Me), 1.63 (s, 12H, Me), 1.78 (s, 12H, Me), 5.90 (d, $J = 2.5 \text{ Hz}$, 4H), 5.99 (d, $J = 2.5 \text{ Hz}$, 2H), 6.01 (d, $J = 4.1 \text{ Hz}$, 4H), 6.17 (d, $J = 3.5 \text{ Hz}$, 2H), 6.42 (d, $J = 3.5 \text{ Hz}$, 2H), 6.54 (d, $J = 4.1 \text{ Hz}$, 4H), 7.43 (br s, 1H, –NH–), 8.49 (br s, 2H, –NH–), 9.41 (br s, 2H, –NH–), 11.95 (br s, 2H, –NH–); $\lambda_{\text{max}}/\text{nm}$ (CH_2Cl_2) (e) 421 (80,736), 474 (85,665), 505 (sh).

Crystallographic summary for $(\text{C}_{56}\text{H}_{61}\text{N}_9)\text{--C}_2\text{H}_6\text{O--C}_4\text{H}_8\text{O}_2\text{--H}_2\text{O}$, **1**, triclinic, *Pc* (no. 7), $Z' = 2$, $a = 10.3046(2)$, $b = 20.6383(3)$, $c = 26.6070(7) \text{ \AA}$, $\beta = 93.783(1)^\circ$, $V = 5646.2(2) \text{ \AA}^3$, $\rho_{\text{calc}} = 1.19 \text{ g cm}^{-3}$, $F(000) = 2176$. A total of 24408 reflections were measured on a Nonus Kappa CCD using graphite monochromatized MoK α radiation ($\lambda = 0.71073 \text{ \AA}$) at -120°C . The structure was refined on F2 to an $R_w = 0.189$, with a conventional $R = 0.0824$ (12171 reflections with $F_o > 4[\sigma(F_o)]$), and a goodness of fit = 1.04 for 1366 refined parameters. The two unique macrocyclic complexes are observed that are related by a pseudo inversion center at 0.17, 0.26, 0.52. Transformation of the origin to this pseudo center results in a space group that is nearly *P21/c*. Refinement of the model in the centrosymmetric space group *P21/c* yields an $R_w = 0.403$, with a conventional $R = 0.171$. CCDC 205549. See <http://www.rsc.org/suppdata/cc/b3/b302508j/> for crystallographic data in .cif or other electronic format.

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