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Syntheses of normal, expanded, strapped and N-confused calixbenzophyrins from a single starting material†

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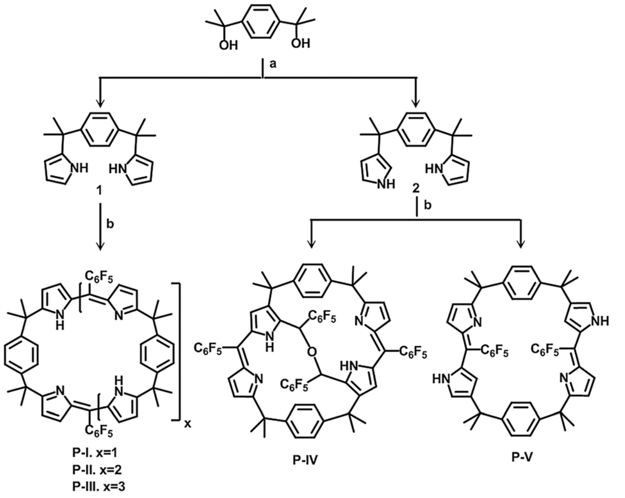
The syntheses and spectral and structural characterization of hitherto unknown *p*-benzene incorporated normal, expanded, strapped and N-confused calixbenzophyrins are achieved; altogether five new macrocycles from a single starting material are reported. The binding studies of the strapped macrocycle revealed that the molecule is selective towards Fe(III) ions.

Pyrrolic macrocyclic systems have attracted growing interest due to their diverse application in the areas of anion binding, cation coordination, conducting polymers, liquid crystals, and nonlinear optics.[1] Among these, the chemistry of porphyrinogens especially calixphyrins have received renewed interest since they offer promising perspectives in the field of substrate recognition.[2] A large number of structurally diverse calixphyrins have been reported in the literature which include normal, expanded, N-confused, three dimensional and core modified macrocycles with unexpected coordination properties.[3]

Strapped macrocycles have been identified as one of the more attractive hosts because of the presence of diametrical bridging that provides a convenient means of introducing functionalized groups at or near the binding domain. Such type of porphyrins and calixpyrroles are well established in the literature.[4] However, the corresponding calixphyrins are still unknown. In the context of ongoing attempts to develop the chemistry of calixphyrins, we report the synthesis of four different classes of *p*-benzene based calixphyrins such as normal, expanded, strapped and N-confused derivatives from a single starting material. Among these, the strapped derivative represents a new class of calixbenzophyrins bearing a strap with an ether linkage on one side of the molecule which is hitherto unknown in calixphyrin chemistry. The formation of normal and strapped calixbenzophyrins was confirmed by single crystal X-ray diffraction analysis. Further, the strapped calixbenzophyrin binds selectively to Fe(III) ions.



Scheme 1 Syntheses of calix[*n*]-*p*-benzo[*m*]phyrins. (a) BF_3OEt_2, pyrrole; (b) CH_2Cl_2, C_6F_5CHO, TFA, DDQ.

The syntheses of calixbenzophyrins are outlined in Scheme 1. The precursors for the target macrocycles were obtained by the acid catalysed condensation of 1,4-bis(1,1-dimethylhydroxy methyl)benzene with pyrrole.[2c] The reaction afforded two types of precursors, α,α′ substituted bispyrrolylphenyl derivative, **1**, and N-confused α,β′ substituted bispyrrolylphenyl derivative, **2** in 32% and 20% yields (Fig. S1 and S2, ESI†). Both of the precursors led to the formation of entirely different classes of calixphyrins, when condensation with pentafluorobenzaldehyde in dichloromethane in the presence of trifluoroacetic acid (TFA) was followed by oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Precursor **1** afforded the formation of normal and expanded calix[*n*]-*p*-benzo[*m*]phyrins (*n* = 2,3,4; *m* = 4,6,8)

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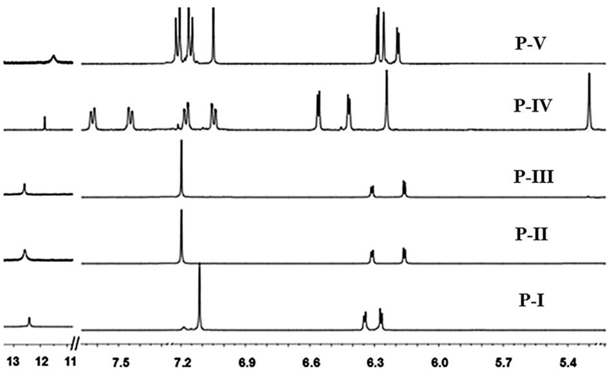

Fig. 1 ^{1}H NMR spectra of **P-I** to **P-V**. The signals correspond to the protons of the *meso* groups and solvent peaks are omitted for clarity.

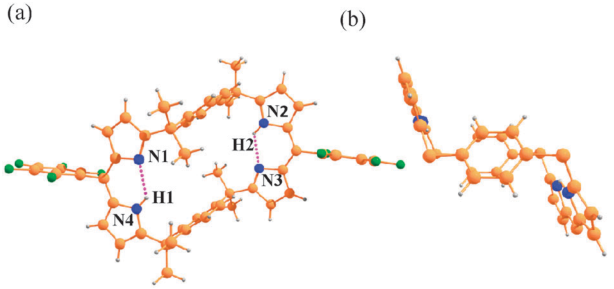

Fig. 2 Single crystal X-ray structure of **P-I**. (a) Top view and (b) side view. In the side view the *meso* groups are omitted for clarity.

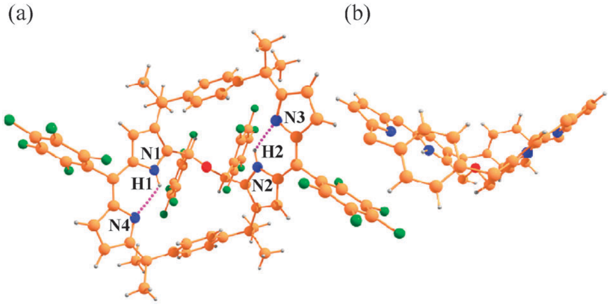

Fig. 3 Single crystal X-ray structure of **P-IV**. (a) Top view and (b) side view. In the side view the *meso* groups are omitted for clarity.

in 20% (**P-I**), 10% (**P-II**), and 5% (**P-III**) yields, respectively, while **2** resulted in the generation of strapped and N-confused calixbenzophyrins in 20% (**P-IV**) and 10% (**P-V**) yields.

All of the macrocycles were characterized using various spectroscopic techniques such as FAB-MS (Fig. S3–S7, ESI†) and ^{1}H NMR spectral studies (Fig. S8–S12, ESI†), and the structure of **P-I** and **P-IV** was unambiguously determined through single-crystal X-ray diffraction analysis. The exact composition of the macrocycles **P-I** to **P-V** was established from FAB mass spectra which showed molecular ion signals at *m*/*z* 936.66, 1404.55, 1874.19, 1311.54 and 937.79, respectively. In the ^{1}H NMR spectrum of **P-I** to **P-III**, NH protons resonated as a broad singlet at 12.5 ppm suggesting the intramolecular hydrogen bonding interaction between the amine and imine pyrrolic NHs (Fig. 1). The *p*-phenyl protons resonated as a singlet at 7.12 ppm indicating the similar chemical environment in the benzene protons, whereas pyrrolic β-CH protons resonated as two doublets at 6.11 and 6.35 ppm respectively.

In the ^{1}H NMR spectrum of **P-IV**, *p*-phenyl –CH protons resonated as four doublets from 7.63 to 7.04 ppm, which suggests that all of the four phenyl protons are in different chemical environments. There are two types of pyrrolic β-CH protons, where the two doublets at 6.56–6.41 ppm correspond to normal pyrrolic β-CH protons, while the strapped pyrrolic β-CH protons resonated as a singlet at 6.24 ppm, which is confirmed from ^{1}H–^{1}H COSY spectral analysis (Fig. S13, ESI†). The –CH protons which are close to the oxygen atom in the strap appeared as a singlet at 5.29 ppm. On the other hand, there are two kinds of pyrrolic moieties present in **P-V**, normal and N-confused. The normal pyrrolic β-CH protons resonated as two doublets at 6.29 and 6.18 ppm whereas the confused pyrrolic α and β-CH protons appeared as two singlets at 7.05 and 6.25 ppm, respectively, which were further confirmed by ^{1}H–^{1}H COSY spectral analysis (Fig. S14, ESI†). The *p*-phenyl –CH protons resonated as double doublets at 7.23–7.15 ppm. Finally the NH protons of the strapped and N-confused calixbenzophyrins appeared as singlets at 12.00 ppm.

The single crystal X-ray structure of **P-I** is shown in Fig. 2 where the macrocycle crystallizes in the triclinic crystal system. As predicted from the NMR analysis, the dipyrrin unit contains both the amine and imine pyrrole nitrogens which are involved in intramolecular hydrogen bonding interactions with the distance and angle of N2–H2···N3 and N4–H1···N1 being 2.10 Å and 129° respectively. The dipyrrin units are perpendicular to the *meso*-pentafluorophenyl unit as well as the *p*-phenyl rings and adopt a chair-like conformation (Fig. 2b). The crystal analysis of **P-I** shows two types of 1-D arrays formed from the intermolecular C–H···F interactions between (i) pyrrolic β-CH (C26–H26) and F atom (F4) and (ii) the *meso*-methyl C–H (C22–H22) units and fluorine (F5) of the neighbouring pentafluorophenyl group with the distances and angles of C26–H26···F4 and C22–H22···F5 being 2.58, 2.59 Å and 150°, 154° respectively (Fig. S16, ESI†). These two 1-D arrays combined together to generate a 2-D supramolecular assembly in the solid state (Fig. S17, ESI†).

The single crystal X-ray structure of **P-IV** is shown in Fig. 3 where the structure crystallizes in a monoclinic crystal system. As observed from the spectral analysis, in addition to the *p*-phenyl rings in the macrocyclic framework, the dipyrrin moieties contain both the normal and confused pyrrole rings. The α-position of the confused pyrrole units are connected by a strap with an ether linkage containing two pentafluorophenyl units in it. Both the pyrrole units are involved in intramolecular hydrogen bonding interactions with the distances and angles of N1–H1···N4: 2.15 Å, 127° and N2–H2···N3: 2.20 Å and 122° respectively (Fig. 3a). The pentafluorophenyl rings which are in the strap are pointing downwards, whereas in the *meso*-positions they are in a side on manner and are perpendicular to the mean dipyrrin plane and adopt a bowl-like conformation (Fig. 3b and Fig. S19, ESI†). The crystal packing revealed the presence of intermolecular interactions through C–H···F hydrogen bonding, F···F and C–F···π interactions which leads to the formation of two self-assembled dimers (Fig. S19, ESI†)

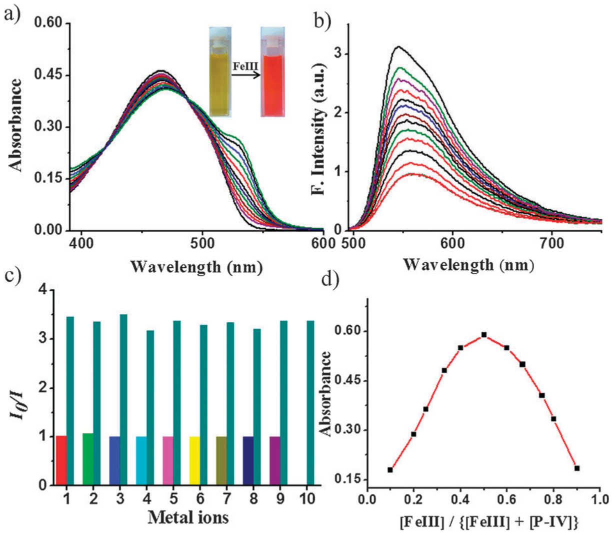

Fig. 4 (a) The absorption and (b) emission changes in **P-IV** (15 μM) upon titration with Fe(III) ions. Inset of (a) shows the color change of **P-IV** upon addition of Fe(III) ions under visible light. (c) Metal ion selectivity of **P-IV** (8.7 μM) in the presence of 10 equivalents of various metal ions. (1) Cu(II); (2) Cd(II); (3) Ca(II); (4) K(I); (5) Li(I); (6) Ni(II); (7) Pb(II); (8) Hg(II); (9) Zn(II); and (10) Fe(III). The small, coloured bars represent the changes in the emission intensity of a solution of **P-IV** with the cation of interest. The cyan bars show the fluorescence change that occurs upon addition of 10 equivalents of Fe(III) to the solution containing **P-IV** and the respective cation. (d) Jobs plot indicating 1 : 1 stoichiometry.

and two 1-D arrays (Fig. S20, ESI†). The two self-assembled dimers are generated by the combination of (i) F···F and C–H···π interaction with the distances of F7···F13 and C41–H41···Py(π) being 2.09 Å and 2.87 Å and (ii) two C–H···F and one C–F···π_F interactions with the distances and angles of C53–H53···F10, C40–H40···F2 and C9–F9···π_F being 2.51 Å, 2.40 Å, 3.17 Å and 164°, 175° respectively. The two 1-D arrays are formed through F···F interactions between (i) F3 and F7 and (ii) F8 and F18 with the distances of 2.86 and 2.74 Å, respectively, which are well within the Van der Waals radii (Fig. S20, ESI†). The dimers and 1-D arrays combined together to generate a two-dimensional grid (Fig. S21, ESI†).

P-IV reported here offers a potential advantage as it possesses additional oxygen atoms in the strap that facilitates the receptor property of the macrocycle. All the spectroscopic measurements were carried out in 5% aqueous acetonitrile solution. **P-IV** was treated with ten equivalents of various biologically important metal ions, such as Cu(II), Cd(II), Ca(II), K(I), Li(I), Ni(II), Pb(II), Hg(II), Zn(II) and Fe(III), to test the sensing ability. Among the tested metal ions, only Fe(III) exhibited effective changes in the absorption and emission spectra. To have a quantitative picture, various equivalents of Fe(III) ions were gradually added to the **P-IV** solution. Upon increasing the Fe(III) ion concentration, in the absorption spectral analysis, the band at 450 nm decreases gradually and a new band appears at 530 nm with the isosbestic point at 490 nm (Fig. 4a). The color of the ligand changes from yellow in the uncoordinated state to red in the Fe(III)-bound form (Fig. 4a, inset). Similarly, in the emission spectral analysis, the band at 550 nm gradually quenches (Fig. 4b). Also, the competitive-recognition studies reveal that **P-IV** selectively binds to Fe(III) ions even in the presence of other metal ions (Fig. 4c). The changes in the emission-spectral data indicate a 1 : 1 binding mode with an association constant of 2.8×10^3 M^{-1} (Fig. 4d and Fig. S23, ESI†). The reversibility of the binding mode was examined by the addition of EDTA (Fig. S24, ESI†). To understand the role of the oxygen atom in the strap, the binding ability of **P-I** and **P-V** was evaluated with Fe(III), Hg(II) and Cu(II) under similar conditions of **P-IV**, which revealed that **P-I** and **P-V** have no selectivity towards these metal ions as compared to **P-IV** (Fig. S25 and S26, ESI†).

In summary, we have demonstrated the synthesis and spectral and structural characterization of four different classes of calixphyrins, normal, expanded, strapped and N-confused calixbenzophyrins, from a single starting material. The reported strapped calixbenzophyrin is the first of its kind in the calixphyrin area with a strap in it. Furthermore, the single-crystal X-ray analysis of normal and strapped calixbenzophyrins reveals the presence of both inter- and intramolecular hydrogen bonding interactions including C–H···F, F···F, C–H···π and C–F···π_F interactions and generates two-dimensional supramolecular assemblies. Strapped calixbenzophyrin binds selectively to Fe(III) ions over the biologically important different metal ions. Studies on the receptor properties of other macrocycles are currently underway in our laboratory.

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