ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 9358–9360

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COMMUNICATION

Host–guest interactions in acid–porphyrin complexes†

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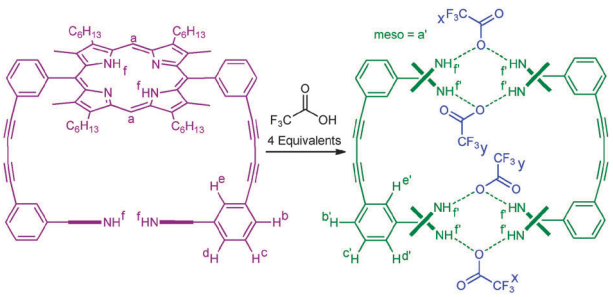
Received 22nd May 2012, Accepted 30th July 2012
DOI: 10.1039/c2cc33668e

In this report we use the weak interactions of acid–porphyrin complexes to selectively bind competing acids to the faces of a rigid cyclic porphyrin dimer, and characterise the resulting interactions by NMR spectroscopy and nano-electrospray ionisation spectrometry.

This report addresses the protonation of a freebase cyclic porphyrin butadiyne linked dimer (**1**) used previously as a potential 'catalytic host' (Scheme 1).[1] Metallation with zinc allowed Sanders and co-workers to accelerate Diels–Alder and acyl transfer reactions within the cavities of the conformationally restricted cyclic dimer and related trimer 'hosts'.[2] In more recent work, the oxophilic nature of Sn(IV) porphyrins was used to direct carboxylic acids, with varying structural and electronic properties, to the two faces ('interior' and 'exterior') of the cyclic butadiyne porphyrin dimers and trimers.[3] Mizuno and Aida have also been able to show that their *p*-xylylene linked cyclic porphyrin dimer enhances circular dichroism activity.[4] We have found that, in the absence of metals, **1** also presents an 'interior' and an 'exterior' face for selective recognition of fluorinated acids.



Scheme 1 Representation of the conversion of the freebase dimer **1** to the bis acid–porphyrin dimer complex with TFA (**1**·**TFA$_4$**).

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† Electronic supplementary information (ESI) available: General experimental information, synthetic procedures and additional figures and spectra. See DOI: 10.1039/c2cc33668e
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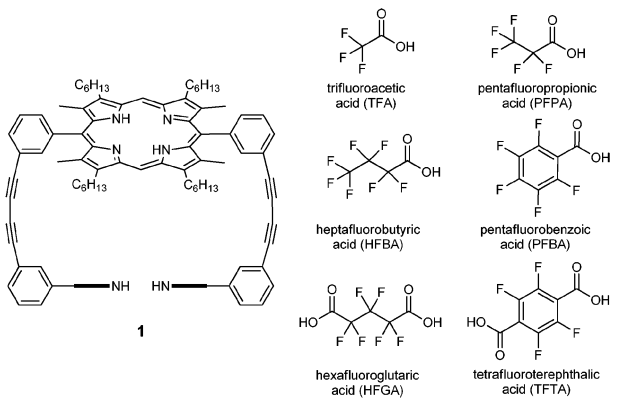


Fig. 1 Dimer **1** with a schematic representation of the lower porphyrin viewed side-on with hexyl and methyl groups omitted for clarity. The distance between the two porphyrin planes is 11.5 Å (Fig. S1, ESI†). Also shown are the six fluorinated acids used in this investigation.

The experiments outlined below focus on the site specific protonation of the freebase form of the cyclic porphyrin host. Since realising of the potential of acid–porphyrin complexes for molecular assembly, our interest has been directed towards exploiting the acid–porphyrin binding motif for cavity specific recognition.[5]

A selection of fluorinated mono- and diacids has been added to **1**, and the resulting assemblies have been characterised using ^{1}H and ^{19}F NMR spectroscopy, and nano-electrospray ionisation spectrometry. Six fluorinated acids (four mono and two di-acids) were chosen for this study (Fig. 1). Trifluoroacetic acid was chosen as the 'standard' acid because it readily protonates the porphyrin and can be easily accommodated inside the cavity of the host. Pentafluoropropionic (PFPA) and heptafluorobutyric (HFBA) acids offer longer alkyl chains with accompanying steric demands and a corresponding degree of flexibility, while pentafluorobenzoic acid (PFBA) provided contrasting rigidity in the form of the aromatic ring. Two dicarboxylic acids, hexafluoroglutaric acid (HFGA) and tetrafluoroterephthalic acid (TFTA), were chosen for their ability to bind cooperatively inside the cavity of **1**.

Protonation of **1** (in *d*-chloroform) with TFA gave a statistical mixture of assemblies (as evident from the ^{1}H NMR data outlined below) before the stoichiometry reached 4 : 1 (acid : dimer) (Scheme 1). The protonation of one porphyrin of the dimer occurred independently of the second, and reflected all the characteristic features of the comparable protonation of a

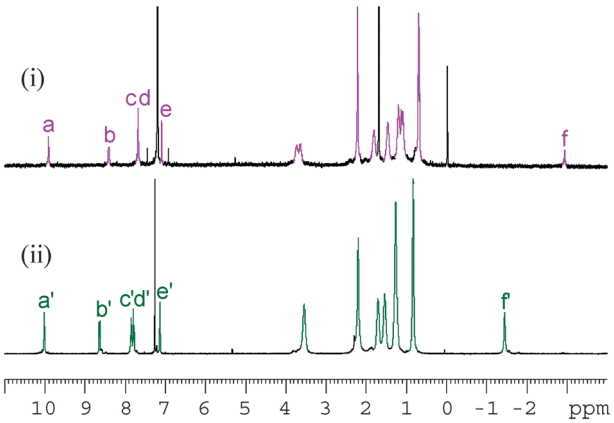


Fig. 2 ^{1}H NMR spectra (400 MHz, *d*-chloroform, 253 K) of (i) **1**, and (ii) **1** with 4.0 equivalents of TFA (**1·TFA$_4$**). The labels of the resonances match the proton environments in Scheme 1.

porphyrin monomer – change in colour from purple to green; distortion of the porphyrin plane to accommodate the four protons within the core of the heterocycle; and stabilisation of the resulting charge by the 'complexation' of the anion of the protonating acid.

Prior to addition of TFA to **1**, the ^{1}H NMR spectrum (Fig. 2(i), acquired at 253 K to minimise any exchange effects) exhibited diagnostic resonances for the symmetrical cyclic dimer with a characteristic core NH signal (f, −2.85 ppm). Only one species was evident after TFA was added to achieve a 4 : 1 stoichiometry of TFA : **1** (see also Fig. S2, ESI†), as characterised by the single *meso* proton peak (a′, 10.01 ppm) and the single core NH peak (f′, −1.43 ppm) (Fig. 2(ii)). Integration of the peaks with respect to each other indicated the formation of the bis acid–porphyrin dimer (**1·TFA$_4$**). It was not possible by ^{1}H NMR spectroscopy to discriminate between the core NH protons directed inside and those directed outside the distorted dimer cavity, all of which were observed as a broad signal.

The ^{19}F NMR spectrum, recorded after the addition of four equivalents of TFA at 253 K (Fig. S3, ESI†), did however identify only two signals (−78.7 and −79.5 ppm) in a ratio of 1 : 1, neither of which corresponded to free TFA in solution (−75.8 ppm), but both of which coalesced to a peak at −78.8 ppm at room temperature. The low temperature resonances were assigned to the trifluoroacetate anions bound to the '*exterior*' and '*interior*' faces of the dimer, respectively, as the anion inside the cavity would be influenced by the additive shielding effect of the adjacent porphyrin and appear at the lower (more shielded) chemical shift.

Titrations involving the incrementally longer alkyl fluorinated acids, PFPA and HFBA, exhibited similar features by ^{1}H NMR spectroscopy described for TFA (Fig. S4 and S5, ESI†), whereby the bis acid–porphyrin dimers were generated and identified upon addition of four equivalents of acid, and for fewer than four equivalents of acid a statistical mixture of complexes was identified. Analysis of the ^{19}F NMR spectra of the respective acid–porphyrin dimer complexes (Fig. S6–S8, ESI†) suggested that the degree of shielding (displacement from 'free' chemical shift) experienced by each of the acid resonances, and the resolution of the respective signals, was dependent on the

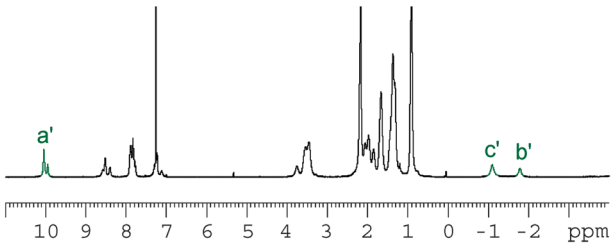
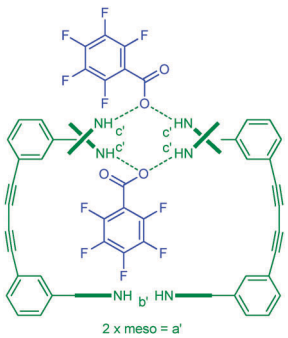


Fig. 3 ^{1}H NMR spectrum (400 MHz, *d*-chloroform, 223 K) of the porphyrin dimer **1** with 4.0 equivalents of PFBA.

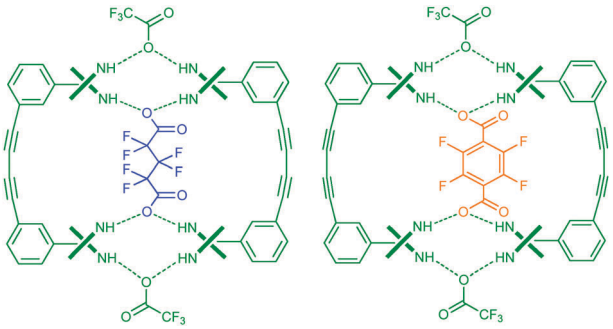
acid size (TFA > PFPA > HFBA). This behaviour may be the result of the increased lability (exchange) of the larger anions as a result of their greater steric 'repulsion' within the restricted dimer cavity, or the re-adjustment of the geometry to accommodate the larger anion.

The ^{1}H NMR spectrum (Fig. 3) of the dimer system after the addition of four equivalents of PFBA (see also Fig. S9, ESI†) exhibited more peaks than observed previously with the less 'bulky' acids at the same stoichiometry. Multiple *meso* CH (a′) and core NH (b′ and c′) signals suggested the presence of multiple species in solution. However, the relative intensities and chemical shifts indicated that the appearance of the spectrum was the result of a single unsymmetrical species, with the two core NH signals (b′ and c′, in a ratio of 1 : 2) assigned according to Scheme 2, with the freebase NH resonance (b′) shifted downfield as a result of the close proximity to the fluoroaromatic anion. Protonation of **1** with the bulky anion of pentafluorobenzoic acid (PFBA) allowed only one of the two porphyrins of **1** to generate an acid–porphyrin complex despite the presence of four equivalents of PFBA. Protonation and subsequent complexation at the inner face of the cavity by PFBA blocked any further access to the dimer core and, as a result, inhibited protonation and complexation of the second porphyrin altogether.

The integrity of **1·PFBA$_2$** (Scheme 2) was confirmed by ^{19}F NMR spectroscopy in which a set of resonances was recorded at approximately −144 (*ortho*), −159 (*meta*) and −163 (*para*) ppm, as compared to −136, −144 and −159 ppm, respectively, for the corresponding resonances of the 'free' acid (Fig. S10(i), ESI†). The formation of **1·PFBA$_2$** provides an interesting contrast to the observations reported when two equivalents of a series of aromatic carboxylic acids were added to the di-tin metallated analogue of **1**.[3] Tin porphyrins form



Scheme 2 Schematic representation of the unsymmetrical acid–porphyrin dimer **1·PFBA$_2$**. Only two acid molecules participate in complexation with the host.



Scheme 3 Two schematic representations of the **1·HFGA–TFA$_2$** (left) and **1·TFTA–TFA$_2$** (right) porphyrin dimer complexes.

strong bonds with the carboxylates of the acids, and stacking interactions operate in the cavity between two neighbouring aromatic groups bound to the two 'interior' faces of the porphyrins. In the protonation mechanism[5] the plane of one porphyrin must distort in order to accommodate the extra protons, and the additional distance required to form the (weak) interaction with the carboxylate anion creates a micro-environment that inhibits protonation with the second porphyrin of the dimer.

The monometallation of **1** can be achieved by adding less than one equivalent of a zinc salt but this typically leads to a mixture of the freebase, mono-zinc, and di-zinc dimers which are extremely difficult to separate chromatographically. In our previous work[5] we identified the significance of the role of the anion in the zinc metallation of porphyrins. The **1·PFBA$_2$** system offered the opportunity to investigate the potential for selectively mono-metallating the dimer by directing the metallation using the PFBA to 'activate' a single porphyrin core (Fig. S11 and S12, ESI†). Unfortunately, the lability of the acid–porphyrin complex resulted in scrambling of the Zn metallation that ultimately led to the same unsatisfactory mixture of products according to our NMR spectroscopy.

In order to establish the competitive binding preference of a mixture of acids, **1** was challenged with a 1 : 1 mixture of TFA and PFBA. Only a mixture of complexes was identified in solution, with no preference for the acids for the 'interior' or 'exterior' faces of the host (Fig. S13, ESI†).

In contrast, mixtures of TFA and dicarboxylic acids such as HFGA or TFTA did show site-specific preference, and the complexes (Scheme 3) were characterised by ^{1}H (Fig. S14 and S15, ESI†) and ^{19}F NMR spectroscopy. For example, a single peak (indicative of symmetry) was identified for the TFTA ligand of the **1·TFTA–TFA$_2$** complex at −148.6 ppm in the ^{19}F NMR spectrum (Fig. S16, ESI†), compared to the chemical shift of 'free' acid at −141.3 ppm. One single TFA resonance was observed at −78.2 ppm. The chemical shift implies that the anions were bound to the 'exterior' faces of the complex whilst the absence of a second resonance at 253 K (Fig. S3, ESI†) suggests one chemical environment and assembly symmetry. Similar structural features were identified for **1·HFGA–TFA$_2$**. The length of the dicarboxylic acids was such that protonation at one of the 'interior' faces preorganised the protonation of the second 'interior' face (especially in the case of the more rigid TFTA) such that the intramolecular cooperativity led to cavity-specific recognition of the dicarboxylic acids. This left the smaller mono-functional TFA to satisfy the requirement for protonation and anion complexation at the 'exterior' faces.

Further characterisation of the acid–porphyrin host–guest complexes was provided by nano-ESI mass spectrometry. Two peaks were recorded for **1** at 902 and 1803 m/z for the 2+ and 1+ charge states (Fig. S17, ESI†). Peaks corresponding to the freebase dimer **1** were again recorded in the presence of TFA together with additional signals (Fig. S18, ESI†). In this case, no signals were observed for the **1·TFA$_4$** complex unlike the assemblies characterised by NMR spectroscopy (Fig. 2). However, under the same conditions, the MS results of the dimer with HFGA and TFTA (with TFA to cap the 'exterior' faces) were able to support the NMR characterisation. The spectrum of the acid–porphyrin dimer with HFGA (**1·HFGA**) was dominated by a peak at 1022 m/z, assigned to the 2+ charge state of the complex (Fig. S19, ESI†). The equivalent experiment with TFTA generated a spectrum for **1·TFTA** also dominated by the diprotonated state of the host–guest complex at 1021 m/z (Fig. S20, ESI†). These two results with the diacids are consistent with the structures shown in Scheme 3 in the absence of the exterior bound TFA molecules.

In conclusion, we have exploited the restricted cavity of the freebase porphyrin dimer **1** and its unique capacity for protonation and anion complexation to selectively accommodate diacid guests into the core whilst using NMR spectroscopy together with the diamagnetic ring currents of the porphyrins to better understand the complexation behaviour of (fluorinated) acids. The use of nano-ESI mass spectrometry (not previously reported for comparable complexes) provided an additional technique for characterisation of more elaborate complexes using these 'weak' interactions. The lability of the complexation has directed us to explore the cavity of analogous cyclic hosts as potential 'reaction centres'.

We thank the EPSRC for financial support (studentship for MJW).

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