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meso-Alkylidenyl dibenzihexaphyrins: Synthesis and protonation studies

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The synthesis and characterization of the alkylidenyl-dibenzihexaphyrins bearing four indanedionyl groups at the *meso*-positions linked *via* four *meso*-exocyclic double bonds is reported. Treatment with trifluoroacetic acid at 50 °C leads to C(α)-protonation of the two indanedionyl groups resulting increased macrocyclic conjugation with dramatic red shifted absorption spectra.

Core modified porphyrins, such as carbaporphyrinoids and their metal complexes,[1-7] pyridine containing porphyrinoids,[8] their thiophene or furan-containing congeners,[9] and the recently introduced *meso*-alkylidenyl porphyrins, have attracted attention in part because they are helping to advance our understanding of the photophysical and spectroscopic properties of both natural tetrapyrrole systems and their synthetic analogues. Core modified porphyrinoids that display protean features, such as responding to changes in the environment, are particularly interesting in this regard. Within this subset, we have focused on *meso*-alkylidenyl porphyrin analogues. Many of these systems do not display classic porphyrin-like global aromatic properties in their native states due to their non-planar nature and the presence disrupted macrocyclic conjugation pathways. However, the presence of a tautomerizable functional group can allow switching to forms that display conjugated features.[10] This type of tautomeric switching can give rise to dramatic changes in the overall system electronics and photophysical features. Previously, we reported unusual N-H vs C-H tautomerism effects in *meso*-alkylidenyl porphyrins.[11-19] In those instances, the N-H tautomer bearing two exocyclic *meso*-double bonds proved to be more stable than the corresponding C-H tautomer lacking the *meso*-exocyclic double bonds. Recent efforts in the expanded porphyrin area have been focused on exploring factors that may modulate the electronic states and redox potentials of various analogues.[20] Tautomerization of *meso*-alkylidenyl-bearing analogues could provide one means of advancing these efforts. Recently, we reported the synthesis and spectroscopic properties of *meso*-alkylidenyl-porphyrinoids, including *meso*-alkylidenyl-thia(*m*-benzi)-porphyrins and *meso*-alkylidenyl-thia(*p*-benzi)porphyrins, containing stable *meso*-exocyclic C-C double bonds at multiple *meso*-positions.[21-22] Here we report the synthesis, characterization, and structural features of a larger set of analogues, namely the core-modified expanded dibenzihexaphyrins **5** and **6**. These systems possess four *meso*-indanedionyl groups linked *via* exocyclic double bonds. They thus constitute to our knowledge the first examples of *meso*-alkylidenyl expanded porphyrins bearing four *meso*-exocyclic double bonds. As detailed below, compounds **5** and **6** differ from their smaller porphyrin congeners in terms of their structure and protonation patterns. As formed, these porphyrinoids are devoid of porphyrin-like global aromatic character, a feature ascribed in part to the non-planarity of the systems resulting from the presence of multiple large substituents at the *meso*-positions, as well as the presence of the exocyclic double bonds. Protonation does not engender conversion to a highly conjugated aromatic form. Rather, it leads to C-protonation of two of the *meso*-alkylidenyl groups α to the corresponding *meso* carbon bridges and an increase in macrocycle conjugation. In the case of **5**, stereoselective *meso*-dihydroxylation was also observed when the compound was allowed to sit in strongly acidic aqueous media for an extended period; this treatment results in formation of a rigid chiral barrel-shaped macrocycle, i.e., **8**.

The synthesis of **5** and **6** is summarized in Scheme 1. Briefly, *meta*- or *para*-phthalaldehyde was condensed with 1,3-indanedione under Knoevenagel-type condensation conditions to afford intermediates **1** or **2**,[23] respectively, in moderate yield (ESI†). Subsequent reaction of either **1** or **2** with pyrrole yielded the corresponding tripyrranes **3** and **4**. Reaction of **3** or

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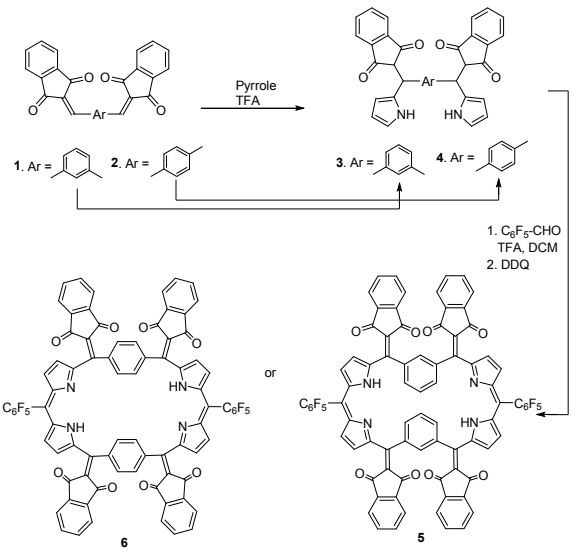
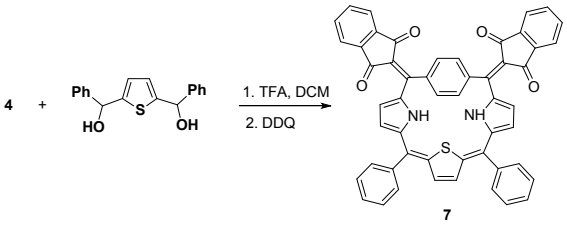
4 with pentafluorobenzaldehyde in the presence of an acid catalyst followed by DDQ oxidation afforded macrocycles **5** and **6** in 6% and 15% yields, respectively.

Initially, we expected that the reaction of **3** or **4** with pentafluorobenzaldehyde would produce the partially endocyclic keto tautomers **5a** and **6a** or the enol tautomer **5b** and **6b** (ESI†). However, full characterization of the products (*vide infra*) revealed that products **5** and **6**, which bear four exocyclic double bonds at the *meso* positions, were actually formed. The spectral data proved consistent with the structures proposed for **5** and **6**. For instance, the pyrrole NH signals appeared at 14.27 and 14.45 ppm in the case of **5** and **6**, respectively (ESI†). These large downfield shifts in the NH signals lead us to suggest that two sets of pyrrole rings are inverted to form strong intramolecular hydrogen bonds with the carbonyl groups of an adjacent indanedione moiety.



Scheme 1. Synthesis of dibenzihexaphyrins **5** and **6**



Scheme 2. Synthesis of *p*-benziporphyrin **7**

As part of the present synthetic effort, we also explored whether the tripyrrane precursor could be utilized to synthesize analogous heteroporphyrins. However, it was found that condensation of tripyrrane **4** with 2,5-bis-thiophenedimethanol followed by DDQ oxidation afforded only the thia(*p*-benzi)porphyrin **7** (Scheme 2). In this case pyrrole NH signals appeared at 8.50 ppm corresponding to the typical N-H chemical shifts in simple pyrrole derivatives.

Further support for the structure of compound **6** came from a single crystal X-ray diffraction analysis.‡ As shown in Fig. 1, macrocycle **6** adopts a heavily puckered geometry, at least in the solid state. Consistent with the inferences drawn from the ^{1}H NMR spectral analysis, it was found that two pyrrole subunits are inverted and, based on the metric parameters, are engaged in strong intramolecular hydrogen bonding interactions involving one of the carbonyl moieties of a indanedione substituent of **6**. All four *meso*-indanedionyl groups reside essentially within the same plane as one of the pyrroles to which they are linked. The average C-C bond distance of the four *meso*-exocyclic bonds is 1.36 Å, would be expected given the proposed double bond character of the four linking exocyclic bonds.

A single crystal X-ray structural analysis of compound **7** revealed that the benzene moiety lies almost perpendicular to the N-S-N plane, an observation ascribed to the steric congestion in the core (ESI†). The dihedral angle between the *meso*-phenyl group and the rest of the pi-system is 52.7°. The C(1)-C(2) distance is 1.499 Å, a value that is consistent with the absence of appreciable macrocyclic conjugation. On the other hand, the C(15)-C(16) distance is 1.36 Å, which we take as an indication of local conjugation within structure **7**. Finally, double bond character for both *meso*-exocyclic bonds is inferred from the average C-C bond distance of 1.39 Å.

The diprotonated form of **6** was also subject to single crystal X-ray diffraction structural analysis. A conformation similar to that of the corresponding free base is seen, as shown in Fig. 1. Efforts to obtain diffraction grade single crystals of **5** proved unsuccessful. On the other hand, when crystal growth conditions consisting of wet CH_2Cl_2/TFA/CH_3CN were used, a stereo-selectively dihydroxylated compound **8** was obtained (Fig. 2). The resulting X-ray diffraction structure revealed unique features. All four indanedionyl groups were found to be hydrogen bonded to pyrrole N-H protons, while the four pyrrole rings were found to adopt a 1,2-alternate conformation (Fig. 2). The combined effect is to make the structure rigid. The two phenyl groups are locked into planar conformations that mirror one another. The two *meso*-hydroxyl groups that presumably insert during the course of the crystallization process are oriented in a relative *trans* configuration. Consideration of the packing diagram reveals that one of the indandionyl groups inserts into, and occupies, the cavity.

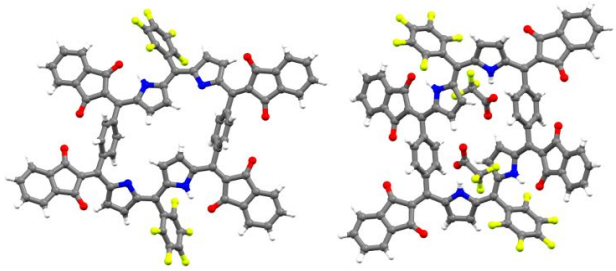


Fig. 1 Single crystal X-ray structures of compound **6** (left), **6**•2TFA (right). Note the puckered geometry and the intramolecular hydrogen bond between the inverted pyrrole NH proton and the carbonyl group of an indanedione moiety in the case of **6**.

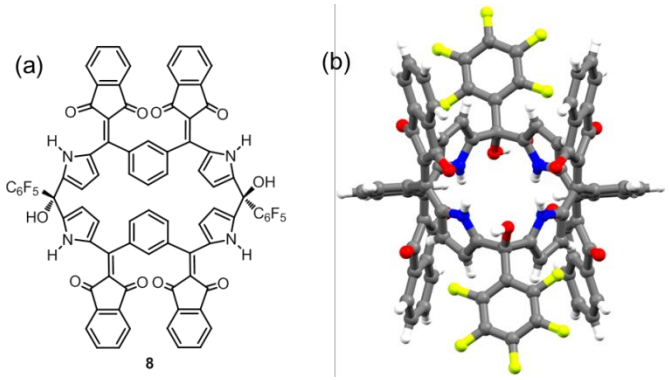


Fig. 2 Chemical structure of (a) **8** and (b) single crystal X-ray diffraction structure of **8**. Note the 1,2-alternate conformation of the pyrroles and an orientation consistent with the presence of strong intramolecular hydrogen bond between the pyrrole N-H protons and the carbonyl groups.

In order to study the tautomeric behaviour of compounds **5** and **6**, solutions of compounds **5** and **6** were titrated independently with trifluoroacetic acid (TFA) in CH_2Cl_2. Dramatic changes in the associated absorption spectra were seen. As shown in Fig. 3, the wavelength maximum of the Soret-like bands of the free base (568 nm and 570 nm for **5** and **6**, respectively) were shifted to longer wavelengths (to 607 nm and 616 nm for **5** and **6**, respectively) with a single isosbestic point being observed in both cases. These bathochromic shifts were attributed to an equilibrium involving *meso*-protonation and formation of the corresponding endocyclic tautomers **9** and **10** as shown in Fig. 4.

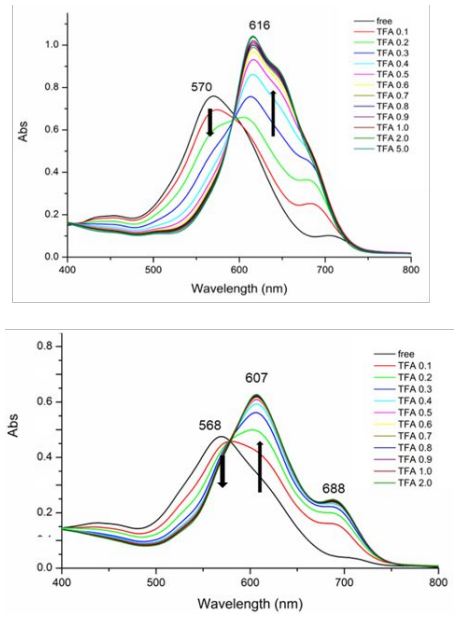


Fig. 3 UV-vis spectral changes seen when compound **5** (bottom) and **6** (top) are titrated with TFA (up to 2 to 5 equivalents, respectively) in CH_2Cl_2. [**5**] = [**6**] = 4.31 X 10^{-6} M.

In order to see the anion binding property of the macrocycle **5** and **6**, ^{1}H NMR and UV-vis spectral changes were monitored by addition of tetrabutylammonium fluoride in $CDCl_3$ and DCM. However, Immediate deprotonation of pyrrole N-Hs and peak broadening in proton NMR were observed. Resulting delocalized anionic species displayed dramatic red-shifted absorption spectra (ESI†).

In an effort to characterize products **9** and **10** produced through α-protonation, ^{1}H NMR spectral titrations were carried out. When **5** and **6** were treated with TFA in $CDCl_3$ at room temperature, the resulting spectral changes could not be interpreted readily. When similar titrations were carried out at 50 °C changes consistent with α-protonation (i.e., *C*-protonation) were observed (ESI†), although the possibility of *N*-protonation could not be unambiguously ruled out. A new signal appearing at 4.72 ppm in ^{1}H NMR upon incremental addition of TFA clearly indicated the α-protonation. Notably, such tautomerization process is not observed upon acid (TFA) titration in dimethylsulfoxide, whereas noticeable UV-vis spectral changes in acetonitrile and dichloromethane were seen at room temperature but different absorption pattern with those of high temperature (ESI†).

That the α-diprotonated tautomeric forms **9** and **10** are favoured relative to *N*-protonation under the solution phase conditions used for the ^{1}H NMR and UV-vis spectroscopic analyses is rationalized in terms of steric strain release and formation of products characterized by a higher level of cross conjugation than those produced by *N*-protonation. Nevertheless, the greater degree of basicity expected for a pyrrolidine nitrogen leads us to predict that a different outcome might be anticipated under conditions where the thermodynamic factors favouring product formation are slightly modified.

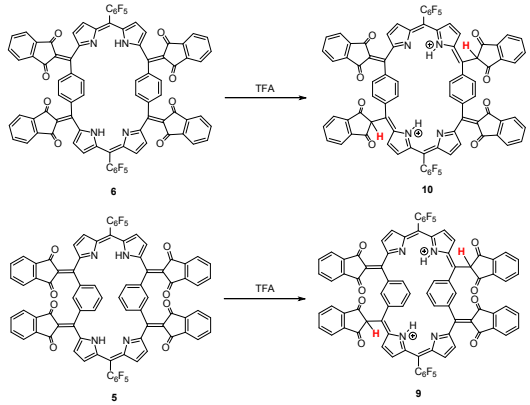


Fig. 4 Proposed equilibria involving the N-diprotonated forms of compounds **5** and **6** and the corresponding C-diprotonated isomers, **9** and **10**. The diprotonated species were obtained by treating compounds **5** and **6** with trifluoroacetic acid (TFA).

Consistent with the proposition that different products, namely the *N*-diprotonated forms of **5** and **6** vs isomeric C-protonated structures **9** and **10** could be supported under different protonation conditions is the finding that the solid state structure of the diprotonated form of **6**, as determined by single crystal X-ray diffraction analysis, is consistent with *N*-protonation. This difference in solution and solid state results, as well as the temperature-dependent nature of the ^{1}H NMR spectroscopic studies, leads us to suggest that temperature

dependent switching of protonation sites occurs in the case of hexaphyrins **5** and **6** and that the position of the equilibrium might be further perturbed through other modifications to the reaction conditions.

In summary, we have shown that the hitherto unknown *meso*-alkylidenyl-dibenzihexaphyrins bearing four 1,3-indanedionyl group at *meso*-positions, macrocycles **5** and **6**, as well as a hydrated analogues (e.g., **8**) can be readily prepared. Spectroscopic analyses and solid state structural studies provide support for the suggestion that the free base forms **5** and **6** possess four exocyclic double bonds and lack global aromatic character, a finding ascribed in part to their severely distorted geometries.[13] Treatment of **5** and **6** with TFA leads to *C*-protonation at the α-positions of two of the alkylidenyl double bonds under most conditions of solution phase conditions, including those associated with ^{1}H NMR spectroscopic analysis in $CDCl_3$ at 50 °C. However, the corresponding *N*-diprotonated species appeared favoured in the solid state. We believe that compounds such as those reported in this study have a role to play in understanding the interplay between structural and electronic effects in larger analogues of porphyrins and related tetrapyrrolic pigments. In this context non-centrosymmetric derivatives are likely to be of particular interest. Efforts to generate such species are underway.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

‡ Details of the crystal structures may be obtained from the Cambridge Crystallographic Data Centre by making reference to CCDC numbers 1921508-1921511.

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Graphical abstract