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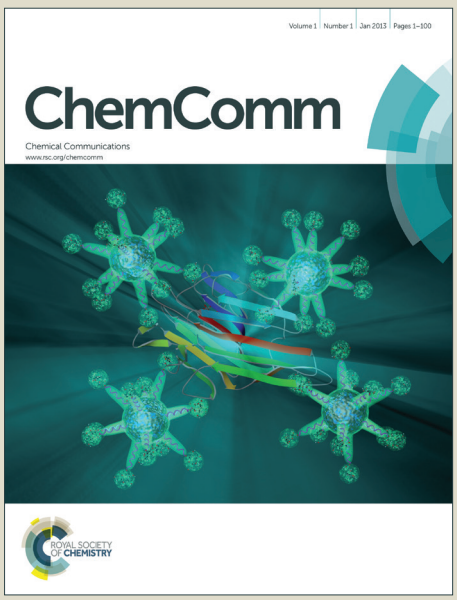

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Unprecedented non-aromatic, confomationally locked dibenzohexaphyrin analogs carrying multiple *meso*-exocyclic double bonds

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Acid-catalysed, '3+3' condensation of *m*-bispyrryl benzene derivatives with acetone afforded new non-aromatic macrocycles that can be converted to *meso*-alkylidenyl dibenzohexaphyrins by DDQ oxidation carrying four exocyclic double bonds at *meso*-positions.

The chemistry of the expanded porphyrins has been one of the important topics in conjunction with in-depth understanding of the macroaromaticity and their unique spectroscopic properties. One of the most interesting aspects of expanded porphyrins are their topological features.[1] So called, 'figure-eight' conformation of octaphyrin inherently induce chirality of the systems and often shows intriguing aspects of the aromaticity of the system.[2-3] The expanded porphyrins display unique structural features and often show considerably red-shifted absorption maximum relative to those of classical porphyrins. However, until recently, not much attention has been given to similar non-aromatic porphyrin congeners. One of the most recent progresses in this line of porphyrin modification are '*meso*-alkylidenyl porphyrins' that stand for the porphyrin analogues bearing exocyclic double bonds at *meso*-positions (Figure 1). The structures of the *meso*-alkylidenyl porphyrins are unique in terms of their tautomerization properties, protonation selectivity and spectroscopic properties. These porphyrins do not exhibit normal porphyrin-like macro-aromatic properties due to the disruption of the full conjugation pathway and inherent non-planar structure. The presence of the tautomerizable core N-H group did not exhibit any aromatic character. We have recently reported several analogous systems bearing diethyl malonylidene groups at *meso*-positions and their unusual tautomerization properties.[4-5]

As part of the continuing efforts to understand the interplay between the electronic features of the porphyrins and aromaticity, we have been interested in the development of new *meso*-alkylidenyl porphyrin analogues, we herein report the synthesis, structural characterization and some chemical properties of new expanded *meso*-alkylidenyl porphyrins, *meso*-alkylidenyl-di(*m*-benzi)-hexaphyrin analogues. The synthesis are based on the recent report for the synthesis and properties of the non-aromatic, *meso*-alkylidenyl-(*m*-benzi)porphyrins, *meso*-alkylidenyl-(*p*-benzi) porphyrins and *meso*-alkylidenyl-(*m*-benzi)pentaphyrins.[6-7]

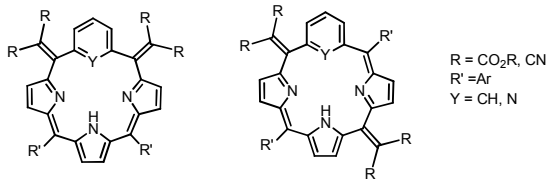


Figure 1. Schematic representation of a *meso*-alkylidenyl porphyrin.

The observations made in these studies indicated that all the porphyrinoids are non-aromatic and do not exhibit any porphyrin-like, global-aromatic character. Instead, all the porphyrins possess severely disrupted pi-systems with limited conjugation of double bonds. These unusual properties have inspired us to further explore the chemistry of the macrocycles. Thus, we designed and synthesized the hexaphyrin analogues carrying multiple exocyclic double bonds at *meso*-positions. Synthesized compounds were highly symmetric and achiral

The synthesis of the hexaphyrin analogs (**2**) and (**4**) were accomplished by typical '3+3' type condensation. Tetraethyl-2,2'-((1R,1'S)-1,3-phenylenebis((1*H*-pyrrol-2-yl)methylene))dimalonate (**1**) or tetraethyl 2,2'-((1S,1'R)-pyridine-2,6-diylbis((1*H*-pyrrol-2-yl)methylene))dimalonate (**3**), which were synthesized by the reported method.[7,8] The *meso*-configuration of the starting material (**1**) was confirmed by single crystal X-ray diffraction analysis as shown in Figure 2. The solid state structure also clearly indicates that the compound (**1**) adopt an anti-conformation at least in solid state.

Since the stereochemistry of the starting material (**1**) has been confirmed, we attempted an acid-catalyzed condensation with acetone. As shown in Scheme 1, compound (**1**) or (**3**) and acetone were dissolved in methylene chloride followed by treatment with catalytic amount of trifluoroacetic acid. Subsequent workup and column chromatographic separation afforded the macrocycles (**2**) and (**4**) in 16 % and 12 % yield, respectively.

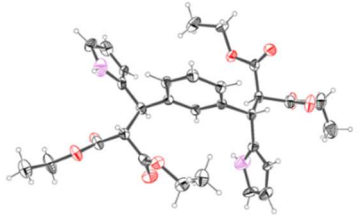
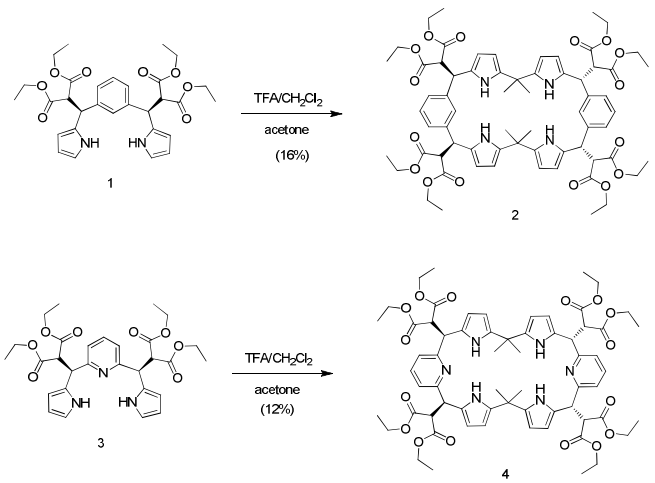
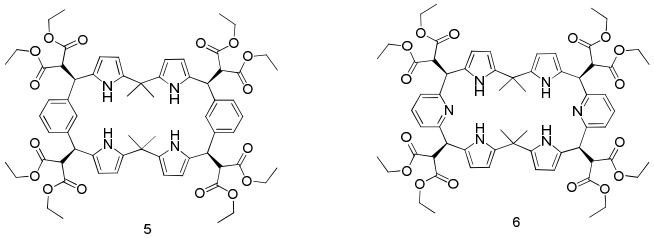


Figure 2. The solid state structure of compound **1** clearly showing the (*S, R*) configuration of the two benzylic positions. The displacement ellipsoids have been scaled to 15% probability level.

The condensation reaction proceeded by stereospecific manner resulting corresponding *meso*-compound (**2**) or (**4**) in which two sets of diethyl malonate groups on the benzylic positions are on the opposite side of the macrocyclic plane (*vide infra*). No evidences were found for the formation of corresponding diastereomeric compound (**5**) or (**6**). Proton NMR spectrum of the product (**2**) revealed the symmetric nature of the compound. The formation of the single stereoisomer indicates that the compound (**2**) and (**4**) are confomationally rigid and adopt the optimal geometry for reducing steric congestion. Only single signal for the pyrrole N-Hs appeared at δ 10.30 ppm. The *meso*-protons and α-protons of the malonyl group were appeared as doublets of doublet at δ 4.2 and δ 4.4 ppm, respectively.



Scheme 1. Synthesis of target macrocycles.



Single crystal X-ray diffraction analysis of the macrocycle (**4**)[9] revealed the severely puckered geometry of the structure and two diethyl malonyl groups on the benzylic position are clearly pointing upward and the other two are pointing downward way (Figure 3). Two pyrrole rings and one pyridine ring (east half) adopt cone-type conformation and the other (west half) pointed the opposite direction.

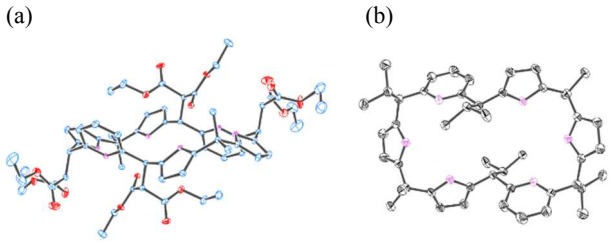
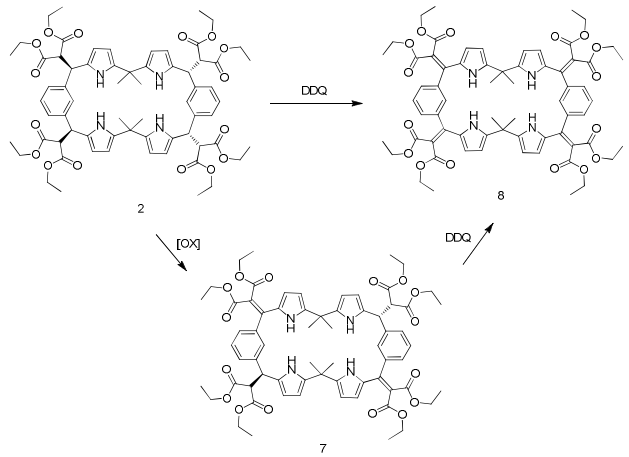


Figure 3. (a) Single crystal X-ray structures of compound **4**. The hydrogen atoms have been removed for clarity. (b) The core structure of **4**. The diethyl malonate groups are removed for clarity. The displacement ellipsoids have been scaled to 15% probability level.

Compound (**2**) is rather unstable and is partially oxidized during growth of the crystal in dichloromethane solution. Indeed, the single crystal X-ray analysis revealed that the correct structure was compound (**7**) other than compound (**2**), which must be formed by partial oxidation of compound (**2**) during crystal growing period. The structure is shown in the Figure 4. Careful analysis of the structure revealed heavily puckered geometry. The two exocyclic double bonds at *meso*-positions are pointing opposite direction each other and the exocyclic double bonds are almost perpendicular to the imaginary macrocyclic plane. This geometric adaptation is attributed to the minimization of torsional strain around the double bonds. The other two diethyl malonyl groups also pointed opposite direction each other. Two pyrrole rings and one pyridine ring (east half) adopt cone-type conformation and the other (west half) pointed the opposite direction.



Scheme 2 Oxidation of macrocycle **2**.

Separate treatment of compound (**2**) with DDQ resulted in quantitative formation of the fully oxidized compound (**8**). The proton NMR spectrum revealed that the signal of the pyrrole N-Hs appeared at δ 10.1 ppm in compound (**2**) is shifted to δ 11.9 ppm. This observation indicate the presence of the intramolecular hydrogen bond between pyrrole N-Hs and carbonyl groups. Careful analysis of the crystal structure also revealed that the compound (**7**) has different conformation from that of compound (**4**), which adopts a cone-conformation. On the other hand, the compound (**7**) adopts a partial cone conformation.

(a) (b)

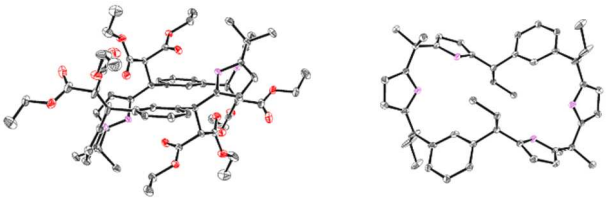


Figure 4. (a) Single crystal X-ray structures of **7**, a partially oxidized form of compound **2**. The hydrogen atoms have been removed for clarity. (b) The core structure of 7. The diethyl malonate groups are removed for clarity. The displacement ellipsoids have been scaled to 20 % probability level.

The absorption spectra taken in $CHCl_3$ indicate that free base **8** contains two absorption maxima, consisting Soret-like banc at 395 nm ($\varepsilon = 6.5 \times 10^4$) and relatively smaller absorption band at 258 nm. The fact that acid titration do not show any appreciable changes in absorption band, indicates that compound **8** possess severe steric congestion between the diethyl molonate groups resulting no-interaction of exocyclic double bonds with rest of the conjugated system (Figure 5).

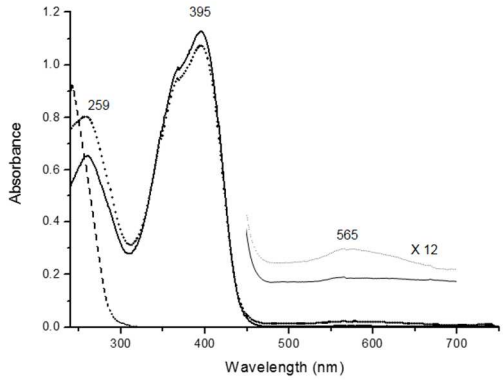


Figure 5. UV-vis absorption spectra of compound **8** (solid), after addition of excess TFA (10 equiv) (dot) and **2** (dashed) measured in $CHCl_3$ ([**8**] = [**2**] =1.70 x 10^{-5} M).

The non-aromatic porphyrin analogs reported here are optically inactive in spite of the presence of multiple stereogenic centers. However, most compounds obviously adopt chiral conformation at least in solid state.

In conclusion, we have synthesized new *meso*-non-aromatic expanded porphyrins displaying unique structural features. *meso*-Bis(diethylmalonyl-pyrryl)benzene (**1**) or *meso*-bis(diethylmalonyl-pyrryl)benzene (**2**) reacted with acetone to yield macrocyclic *meso*-compound (**2**) or (**4**), which can be easily oxidized by DDQ to yield non-aromatic version of the *meso*-alkylidenyl hexaphyrins. Currently, extensive studies along with these lines are under investigation.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Synthetic details of all the compounds, spectroscopic data and single crystal X-ray data are available from the Cambridge Crystallographic Data Centre by quoting the CCDC number 957472 (compound **4**) & 957473 (compound **7**). See DOI: 10.1039/b000000x/

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8. Typical synthesis: Compound **5** (0.11 g, 0.20 mmol) and acetone (2.5 mL, 34.0 mmol) were dissolved in CH_2Cl_2 (33 mL) and then TFA (0.08 mL, 1.06 mmol) was added. The whole mixture was stirred for 3 hr at room temperature. Then Aqueous NaOH (0.1 N, 30 mL) was added to quench the reaction and extracted with CH_2Cl_2 (50 mL × 3). The organic layer was dried (anhydrous Na_2SO_4) and the solvent was removed in vaccuo. The residual solid was purified by column chromatography on silica ($CHCl_3$/EtOAc = 19/1) to afford pure product **4**. Yield: 0.014 g (12%); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.99 (br s, 4H), 7.49 (t, J = 7.76 Hz, 2H), 7.03 (d, J = 7.76 Hz, 4H), 5.68 (br s, 4H), 5.37 (br s, 4H), 4.65 (d, J = 11.53 Hz, 4H), 4.47 (d, J = 11.53 Hz, 4H), 4.05-3.85 (m, 16H), 1.43 (br s, 12H), 1.02-0.95 (m, 24H); MALDI-TOF MS Calcd. for $C_{64}H_{78}N_6O_{16}$ exact mass 1186.55, Found 1187.55.
9. X-ray data of a crystal **4** having dimension of 0.2 x 0.03 x 0.03 mm were collected on a Nonius CAD4 mach 3 diffractometer equipped with graphite-monochromated M_oK_α radiation (λ=0.71073 A^o) at room temperature. The unit cell was determined to be monoclinic, P21/n (No. 14), jZ=2, a=12.3538(10), b=13.2468(11), c=19.3848(16) A^o, β=93.400(14), V=3166.7(5) A^{o3}, ρ_{calc}=1.239 gcm^{-3} on the basis of 25 reflections. A total of 15747 reflections were measured, 5469 unique (R_{int}=0.0540). The structure was refined data F_2 to R_w=0.1512, R=0.0649 (5469 reflections with $F_o>4\sigma F_o$), and G_oF=1.125 for 433 refined parameters. The data collected by using the ω-2θ scan technique in the range 2.14<θ<26.29^o. No absorption corrections were applied. The structure was solved by direct method and refined by full matrix least square calculation with SHELXL-97. Anisotropic thermal parameters were used for all non-hydrogen atoms.

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