This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
β-Tetrachlorotetramethoxyporphycenes: positional effect of substituents on structure and photophysical properties†

Anup Rana a and Pradeepa K. Panda a

We report the regiospecific synthesis of first chloro substituted porphycenes as two positional isomers of β-tetrachlorotetramethoxyporphycene. The positional effect of the substituents on these isomers could be clearly distinguished in their structure and photophysical properties.

Porphycene reported by Vogel is the first constitutional aromatic isomer of porphyrin. Its unique intense absorption in red region compared to latter, make it one among the best choices of photosensitizer for photodynamic therapy (PDT). Further, porphycenes have also been explored for their potential application in the field of protein mimicry, catalysis, material chemistry, nonlinear optical studies and most recently for dye sensitized solar cell application. Owing to its rectangular coordination core, porphycene displays strong NH...N hydrogen bonding. Therefore, NH-tautomerism, double hydrogen transfer study and excited state photodynamics of this macrocycle are of great fundamental interest. Recently, we found fusion of β-β' bipyrrolic positions of porphycene led to unprecedented square type metallo-complexes, along with very interesting laser intensity dependent multiphoton absorption.

Very recently, Hayashi and coworkers demonstrated formation of unusual cis-tautomer of meso dibenzo-fused porphycene. In spite of many interesting attributes, the studies on porphycene is quite limited due to difficulty associated with the synthesis of the building blocks e.g. bipyrrrole dialdehydes or bispyrrrollethane. In this regard, recently we found octamethoxyporphycene displayed very good lipophilicity and also hydrophilicity, with its Pd(II)-complex producing singlet oxygen efficiently (φ; 0.73). On the other hand, very recently we noticed replacement of electron donating methoxy moieties led to intense large red shifted absorption with unique coalesced Q-bands displaying strong enhancement in two photon absorption cross-sections. It is well known that properties of porphycene are sensitive to the type of substituent and their positions. However, to the best of our knowledge, the positional effect of substituents in porphycene chemistry is yet to be investigated.

The unexpected synthesis of 3-chloro-4-methoxypyrrole-2-aldehyde helped us to explore the synthesis of two positional isomers of first chloro-substituted porphycenes, namely β-tetrachlorotetramethoxyporphycenes 1a and 1b along with their metallo-derivatives, to study the positional effect of substituents in their structure, electrochemical and photophysical properties along with the singlet oxygen generation ability (φ). As 5 could be synthesized in good yield and we found Ullmann coupling of its iodo derivative did not yield the desired bipyrrrole dialdehyde (Scheme S1 in ESI†), therefore we decided to explore alternative oxidative coupling approach and towards this, the aldehyde group has to be protected as it is sensitive to the reaction condition. In order to synthesize the other isomeric porphycene 1b, 4-chloro-3-methoxypyrrole-2-aldehyde emerged as the desired precursor. Towards this we employed 5 as the starting material (Scheme 1). The aldehyde group of 5 was converted to oxime, followed by dehydration with phthalic anhydride under reflux condition to obtain the desired 3-chloro-4-methoxypyrrole-2-nitrile 7 in 84% overall yield. The Vilsmeier-Haack formylation of 7 afforded the aldehyde 8 in 73% yield, whose structure was further confirmed by single crystal XRD (Fig. S23 in ESI†). Subsequent hydrolysis of 8 with aqueous NaOH under reflux condition led
to the formation of carboxylic acid 9 in 83% yield. However, our repeated effort towards deprotection of 9 under all standard conditions failed. Therefore, we employed decarboxylative iodination of 9 with KI/NaHCO₃ to form the iodo-derivative 10 in 87% yield, followed by de-iodination using catalytic amount of Pd/C with activated Zn, led to the formation of desired α-free pyrrole aldehyde 6 in 90% yield, whose structure was further confirmed by XRD analysis (Fig. S23 in ESI†).

With both the pyrrolic precursors in hand, we proceed to perform oxidative coupling to synthesize the bipyrrole dialdehydes (Scheme 1). Towards this the aldehyde group of 5, and 6 was protected to obtain the corresponding cyanoacrylate pyroles 11a and 11b by Knoevenagel condensation, with ethyl cyanocacetate in 94 and 97% yields, respectively. Scholl oxidation of 11a and 11b with FeCl₃ using TFA as solvent, led to the formation of corresponding bipyrroles,11 and without further characterization, the cyanoacrylates groups were deprotected by refluxing in 3M aqueous NaOH to afford the desired bipyrrole dialdehydes 12a and 12b in 39 and 15% yields, respectively in two steps. Interestingly, our previously developed oxidative coupling method using PIFA and BF₃·OEt₂ on 11a, followed by deprotection as mentioned above provided the desired 12a in comparable yield (34%).12 However, synthesis of 12b under identical condition resulted in failure, indicating probably PIFA is not sufficiently strong to activate α-position of pyrrole 11b, due to the presence of deactivating chloro group at the adjacent β-position.12 Further, the structure of 12a was confirmed by single crystal XRD technique (Fig. S23 in ESI†) and very interestingly, it exists in the unusual cis conformation. Finally, McMurry coupling of 12a and 12b with Zn/TiCl₄/CuCl under reflux condition provided the desired porphycenes 1a and 1b in 28 and 22% yields, respectively. Both the freebase porphycenes were further converted to their corresponding Zn(II) and Pd(II) complexes. All the compounds were well characterized by standard spectroscopic techniques.

The ¹H NMR spectra of freebase porphycenes 1a and 1b display very marginal difference in meso proton resonances occurring at 9.80 and 9.65 ppm, whereas significant upfield shift could be noticed in imino proton resonances for 1b (0.16 ppm) compared to that of 1a (0.98 ppm). This may be attributed to the greater non-bonding interactions between four bulky chloro substituents at 3,6- and 13,16- positions in 1b compared to O’s of methoxy substituents in 1a, decreasing the N-H...N hydrogen bonding in case of the former. This could be further confirmed by comparison of ¹H NMR spectrum of analogous porphycene 2 imino protons with that of 1a (0.36 vs 0.98 ppm), where the marginal down field shift in case of latter could be attributed to the four electron withdrawing chloro groups.6

The UV-Vis spectrum of 1a in CHCl₃ consists of split Soret bands at 376 and 384 nm, along with three Q-type bands at 565, 608 and 647 nm, whereas that of 1b displays Soret band at 385 nm and Q-type bands at 572, 625 and 646 nm (Fig. 1 and Table S1 in ESI†). The lowest energy band is 17 nm red shifted, respectively for 1a and 1b compared to octamethoxy analogue 2,6 indicating electron deficient nature of these porphycenes. Further, between them, while there is hardly any change in the absorption of the Soret band, the lowest energy band for 1b is 17 nm red shifted compare to 1a and this may be attributed to the greater non-bonding interaction between relatively bulky chloro groups at 3,6- and 13,16- positions. This clearly reflects the positional effect of substituents in the two porphycene isomers, which is more evident in their Q-bands than Soret bands, as substituents are expected to perturb only the frontier orbitals significantly. Further, Zn(II) and Pd(II) complexes of 1a and 1b consist of red shifted Soret band at 389-391 nm and blue shifted Q-bands at 606-638 nm compared to corresponding freebase porphycenes. Notably, here also the positional effect of substituents could be clearly observed in these isomers with lowest energy bands of complexes of 1b are red shifted compared to that of 1a. Interestingly, both the metallo-derivatives of 1b consist of split Q-bands, a trend also observed for complexes of octaethyl analogue 3,13 whereas, the split Soret bands observed in freebase porphycene 1a, merged into one upon complexion with metal ions. The above trend clearly indicates, while 1a behaves more like the octamethoxyporphycene 2, its isomer 1b resembles with the octaethyl analogue 3. Unlike the porphycene 2, which is non-fluorescent in nature (ϕᵣ < 10⁻⁴), the freebase porphycenes 1a and 1b are weakly emissive (ϕᵣ for 1a and 1b: 0.0007) with emission maxima at 655 and 676 nm, respectively (Fig. 1 and Table S1 in ESI†). Complexation with Zn(II) led to substantial enhancement in emission for both Zn1a and Zn1b (ϕᵣ for Zn1a, 0.17 and Zn1b, 0.16) with emission maxima at 645 and 654 nm, respectively. More strikingly, replacement of four

---

Scheme 1 Synthesis of β-tetrachlorotetramethoxytporphycenes

---

Fig. 1 UV-Vis (solid line) and fluorescence (dot dash line) spectra of 1a and 1b along with their Zn(II) and Pd(II) complexes in CHCl₃ at 25 °C.
methoxy group of Zn2 ($\phi_F$ 0.025),6 with chloro groups (Zn1a and Zn1b) resulted in large enhancement of their fluorescence, indicating electron donating methoxy groups probably act as quencher of fluorescence through enhanced intramolecular charge transfer (ICT).21 This is again reflected in the relatively longer fluorescence lifetime observed for Zn1a ($\tau_F$ 2.9 ns) than Zn1b ($\tau_F$ 2.2 ns) (Fig. S31 in ESI†) and the chloromethoxy-porphycene complexes displaying much longer singlet lifetime compared to octamethoxy analogue Zn2 ($\tau_F$ 0.6 ns).6

The crystal structures of 1a and 1b along with their axially pyridine (Py) ligated Zn(II)-complexes i.e. Zn1a.Py and Zn1b.Py were characterized by XRD techniques (Fig. 2). The molecular structures of 1a and 1b display planar configuration (maximum displacement of N from mean plane drawn through macrocyclic core: 0.053 and 0.032 Å for 1a and 1b, respectively). As per our anticipation the presence of relatively smaller chloro groups at 3,6- and 13,16- positions in 1b, didn’t exert any distortion on macrocyclic core owing to lesser nonbonding interaction, unlike that reported for the tetrabromoporphycene.4 Also, crystal packing structures of 1a and 1b (Fig. S24 in ESI†) display strong face to face π-π stacking interaction with inter-planar distance of 3.42 and 3.49 Å, and corresponding centroid-centroid distance of 3.95 and 4.13 Å, respectively. A closer look at the packing diagrams of both the porphycenes reveal when the methoxy substituents are at the inner β-positions (1a), the π-π stacking interaction is enhanced owing to interaction between the alternate methoxy O of one macrocycle and the methoxy H of the neighbouring macrocycle in the stack, with chloro groups not involved in further interactions (Fig. S25 in ESI†). On the other hand, when the methoxy substituents are at the outer β-positions (1b), the π-π stacking interaction is slightly reduced, as owing to its unique structure, alternate chloro groups of each porphycene could come in close contact with two methoxy Hs of porphycene molecule in the neighbouring stack, further each methoxy O while interacts with the methoxy H of the macrocycle in the same stack, in addition also interact with that of the macrocycle in another neighboring stack (Fig. S26 in ESI†). In analogy to other octasubstituted porphycenes, 1a and 1b retain square type core (N1-N2: 2.78 Å, N2-N3: 2.715 Å and N1-N2: 2.727 Å, N2-N3: 2.761 Å for 1a and 1b, respectively). Surprisingly, the core of 1a is comparatively more rectangular in nature than 1b and in case of the latter unexpectedly the core has undergone slight expansion in N2-N3 distance, with concomitant contraction in N1-N2 distance. This could be explained by relatively stronger in-plane nonbonding repulsion of chloro groups at 3,6- and 13,16- positions in 1b. This is further supported by comparatively upfield shift of imino protons in ‘H NMR resulting from relatively weak N-H·N H-bonding interaction for 1b. Thus we can conclude that the distinct substitution effects on absorption and emission properties of 1a and 1b arise from the in plane non-bonding interaction at 3,6- and 13,16-positions and the resultant change in core size.

The Zn1a.Py and Zn1b.Py complexes display typical rectangular core (Fig. 2). The axial coordination with pyridine led to Zn ion residing above the plane of the macrocycle in both cases. Interestingly, the axial ligation of Zn with pyridine, led to elevation of Zn along with substantial deformation of core of the macrocycle in case of Zn1a.Py to result in a cone shape formation, but in contrast, for Zn1b.Py only elevation of Zn is observed but core of macrocycle remains almost planar and this is further reflected in the degree of displacements of B-C’s from mean plane drawn through four imino nitrogens with the maximum displacement observed is 0.72 and 0.17 Å, respectively. Also, displacement of imino Ns from the mean plane drawn through macrocycle is 0.22 and 0.04 Å, respectively for Zn1a.Py and Zn1b.Py indicating a relatively more planar core for latter. Again a closer inspection of the packing diagram of both the complexes divulge in case of Zn1b.Py, there is weak π-π stacking interaction between two porphycene moieties (inter-planar distance 3.49 Å and centroid to centroid distance 6.89 Å), whereas in case of Zn1a.Py, very interestingly the axially ligated pyridine moiety from a neighbouring porphycene unit slips into the two porphycene moieties involved in π-π stacking interaction (Fig. S27-28 in ESI†). As a result the pyridine moiety has better stacking with one of the two porphycene units, while reducing the interaction between the latter. The combined effect possibly resulted in the large out of plane distortion in Zn1a.Py complex. These attributes clearly demonstrate further the positional effect of substituents, even in case of the metallo-porphycenes.

The NIR singlet oxygen luminescent spectra (emission maxima ~1278 nm) of all porphycenes in aerated toluene were measured in order to evaluate their singlet oxygen generation ability. Unlike 4,14 freebase porphycenes 1a and 1b could not able to produce singlet oxygen, indicating probably chloro groups can’t effectively enhance triplet population, a key requirement for singlet oxygen generation. However, upon complexation we could observe effective singlet oxygen generation, with quantum yield ($\phi_A$) for Zn1a and Zn1b, 0.73 and 0.57, respectively and that for Pd1a and Pd1b, 0.86 and 0.83, respectively (Fig. S30 in ESI†). There is a substantial enhancement in singlet oxygen quantum yield by replacing four methoxy groups of analogous metal complexes of 2 ($\phi_A$ for Zn2 and Pd2 0.12 and 0.73, respectively) with chloro groups. This clearly indicates the electron donating methoxy groups act as triplet state quencher through effective ICT character and possibly more efficiently at the outer β-positions, and the presence of electron withdrawing chloro groups, probably counter the ICT process, thereby enhancing the fluorescence, singlet state lifetime and also the singlet oxygen generation ability compared to octamethoxy-porphycenes.6

The electrochemical properties of porphycene 1a, 1b and their Zn(II) complexes were characterized by cyclic

![Fig. 2 Molecular structures of (a) 1a (above front and below side view) (d) 1b (above front and below side view), (b) Zn1a.Py front view, (c) Zn1a.Py side view, (e) Zn1b.Py front view and (f) Zn1b.Py side view, scaled in 35% probability level. Pyridine from all front views (for Zn(II) complexes), and chloro and methoxy groups from all side views are removed for clarity. Color code: C, grey; N, blue; O, red; Cl, yellow green; H, white; Zn, pink.](image-url)
voltagemetry (CV) and differential pulse voltammetry (DPV) in CH2Cl2 (Fig. S32 in ESI† and Table 1) and that of the Pd(II) complexes couldn’t be performed due to their poor solubility. These porphycenes and their Zn(II) complexes display typical two reversible and/or quasi reversible one electron reduction and two one electron oxidation potentials. Introduction of four chloro groups by replacing methoxy groups of 2 leads to more positively shifted oxidation and reduction potentials. The first reduction potential is 0.51 and 0.55 V more positive and similarly first oxidation potential is 0.37 and 0.38 V more positive, respectively for 1a and 1b compare to octamethoxy analogue 2, confirming the relatively more electron deficient nature of both the macrocycles. Also, the more positive change in redox potential compared to oxidation potential proves that LUMO is more stabilized compare to HOMO upon introduction of four chloro groups. Surprisingly, the positional effect of substituents on the redox potentials of these porphycenes is found to be minimal, in particular for the first oxidation and reduction potentials. Further, all Zn(II) complexes (Zn1a and Zn1b) show more positive redox potential and oxidation potentials compared to analogous Zn2. The experimental HOMO-LUMO gap (ΔE measured from CV) for porphycene 1a and 1b found to be 1.75 and 1.72 V, respectively, which is 0.14 and 0.17 V lower compared to 2. The marginal difference in ΔE between the two isomers is again reflected in the computationally obtained data by single point calculation of crystal structures of 1a and 1b by using B3LYP (6-31+G) method (Fig. S37 in ESI†). This may be attributed to cancellation of the electronic effect of the substituents owing to their symmetrically opposite disposition at the macrocycle periphery (dipole moment obtained from DFT study is zero for both 1a and 1b).

In conclusion, we have synthesized the first chloro substituted porphycynes, namely β-tetrachlorotetramethoxy-porphycenes as two positional isomers, regiospecifically. The oxidative coupling of protected pyrrole aldehyde enables us to synthesize bipyrole dialdehyde in three steps from pyrrole aldehyde and this strategy helps avoid unstable α-free bipyrole intermediate. This protocol can also be used for regioselective synthesis of porphycene isomers. Further, the positional effects of substituents in porphycene is investigated for the first time and owing to the presence of two α-α’ fused bipyrorolic units, the substituents exert significant positional effect on structure and photophysical properties of these porphycenes, including their metallo-derivatives. In addition, all the metalloporphycenes effectively generate singlet oxygen and therefore may find applicability as efficient photosensitizers for PDT along with photo inactivation of bacteria and viruses, and for photoxidation.

This work is supported by DST, India (SR/S1/IC-56/2012 to P.K.P). A.R. thanks CSIR, India for senior research fellowship and DRDO, India for financial assistance. The authors also thank Mr. Navendu Mondol and Mr. B. Satish Kumar, School of Chemistry, University of Hyderabad for the fluorescence lifetime and DFT studies, respectively.

### Notes and references


