Porphyrinoids

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One-Pot Synthesis of Indene-Expanded Porphyrins**

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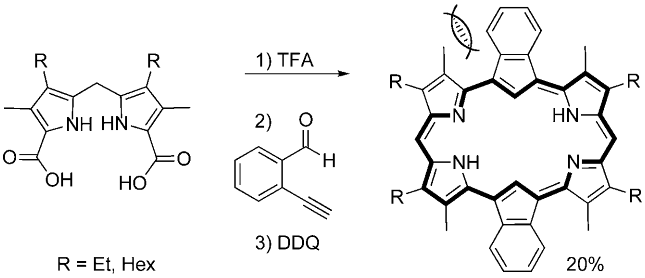
Our research group reports the [2+2] acid-catalyzed condensation of β-alkyl-substituted dipyrromethanes with 2-ethynylbenzaldehyde provides a convenient route to new indene-expanded porphyrins in 20% yield (Scheme 1). These aromatic porphyrinoids may be formulated as [22]dibenzo-dicarba-hexaphyrin(1.0.0.1.0.0) species, but will be referred to herein as "E.P." for simplicity.



Scheme 1. Synthesis of [22]dibenzo-dicarba-hexaphyrin(1.0.0.1.0.0). DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, TFA = trifluoroacetic acid.

In early studies, expanded porphyrins were synthesized to probe the nature and limits of classical "[4n+2]" Hückel aromaticity,[1] while more recently, they have provided insights into Möbius aromaticity.[2,3] Syntheses of expanded porphyrins have generated species with desirable spectroscopic properties leading to potential applications in cation and anion complexation and as near infra-red chromophores in biomedicine.[4] As a result of this research, expanded porphyrins currently represent a growing class of structurally diverse pigments.[5] Yet while fundamental and applied interest in these porphyrinoids has gained momentum, their synthesis has remained challenging.

By using a synthetic protocol for classical porphyrin synthesis, we executed the sequential, one-pot decarboxylation, condensation, and oxidation reactions of dipyrromethane-dicarboxylate with 2-ethynyl-benzaldehyde under acidic conditions (TFA). However, an unexpected in situ annulation occurred in which the aldehydes and alkynes cyclized to give the indene-expanded structure shown in Scheme 1. Presumably, the indene fragments described here are formed subsequent to a typical aldehyde/α-pyrrole condensation step. Thereafter, a 5-*endo*-dig cyclization involving the terminal alkyne group and the aldehyde carbon atom could generate the indene components of the E.P. species. An alternative explanation for formation of the indene unit is a process akin to Overman's nucleophile-promoted iminium ion alkyne cyclization.[6] The indene-expanded porphyrin is a structural cycloisomer of the anticipated classical porphyrin, which was only present in trace quantities in the crude product, under the conditions described here. Although analysis by UV/Vis and NMR spectroscopy suggests that the reaction had not produced a conventional porphyrin, initial structural identification of the product proved challenging because E.P. and the anticipated *trans*-meso-(2-ethynyl-phenyl)-porphyrin have exactly the same mass and are similarly symmetrical.

As β-Me,hexyl-substituted E.P. defied all crystallization efforts, β-Me,Et-substittued E.P. was prepared and successfully crystallized by diffusion of MeOH into a solution of β-Me,Et-substituent E.P. in $CHCl_3$.[7] Single-crystal X-ray analysis revealed an expanded porphyrin in which indene units bridge two dipyrromethane components. In the free-base form, these indene units are canted out of the median macrocyclic plane by approximately 24–30° as steric interactions with neighboring methyl groups preclude macrocyclic planarity (Scheme 1). Hence, E.P. may form a bowl-shaped *syn* conformer (Figure 1 a) or a chair-shaped *anti* conformer. In a second crystal structure (CH_2Cl_2/MeOH),[8] both the *syn*- and *anti*-canted conformers are present in the unit cell, thus suggesting negligible differences in the energies of the two conformations. The ^{1}H NMR spectrum of E.P. implies D_{2d} symmetry from room temperature to $-60\,^\circ C$, thus supporting the notion of facile conformational fluxionality of the indene components in solution. The effect of a diamagnetic ring current causes the internal C–H bond to resonate at $\delta = -4.5$ ppm (confirmed by an HMQC experiment) and the meso-like protons to resonate at $\delta = 9.5$ ppm. The internal NH protons for the free-base species seem to undergo rapid intermolecular exchange and were only observed as a broad resonance at $\delta = 0.44$ ppm in [D$_8$]toluene under stringently anhydrous conditions. The UV/Vis spectrum of the free-base E.P. displays a broad Soret-like band (Figure 2) with a maximum at 543 nm ($1.18\times10^5\,M^{-1}$) in $CHCl_3$.

One may draw comparisons between our E.P. and many other expanded porphyrins in the literature dating back over four decades. Franck's bisvinylogous porphyrins[9] and LeGoff's platyrin[10] bear the nearest resemblance to our E.P. as

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CCDC 755001–7055005 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via < url href = “http://www.ccdc.cam.ac.uk/cgi-bin/catreq.cgi” >.

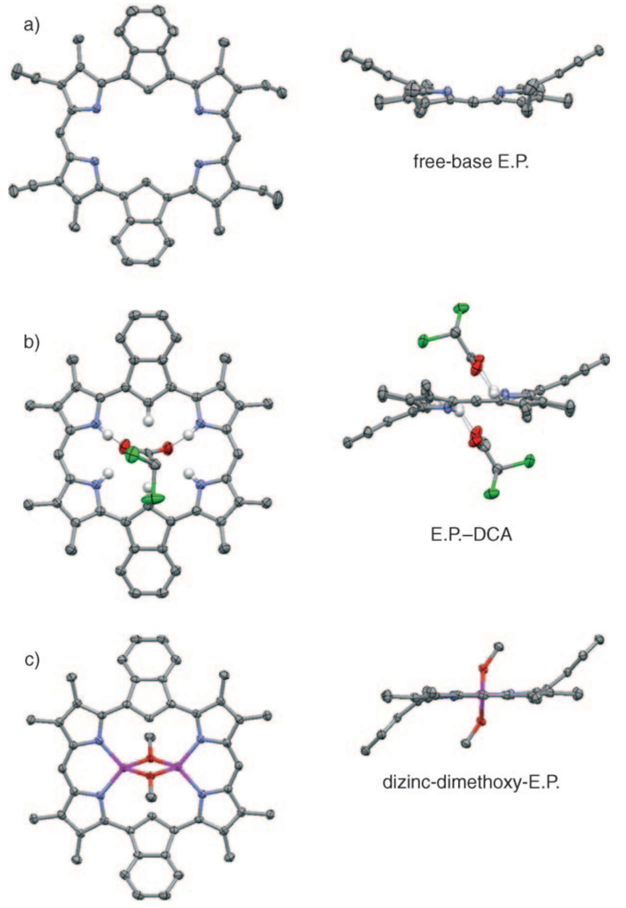

Figure 1. X-ray structures with thermal ellipsoids scaled at the 50% probability level. Omissions for clarity include 1) all solvent molecules, 2) one DCA unit in the top view of b), and 3) truncated hexyl chains in b) and c). N blue, Cl green, Zn magenta, O red.

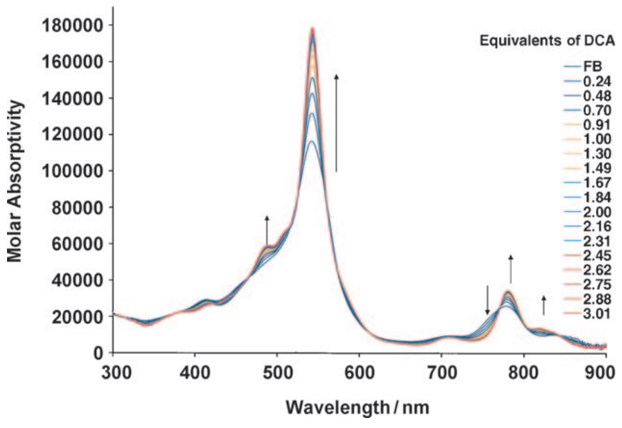

Figure 2. Titration of DCA into E.P. under concentration-constant conditions for E.P. FB = free base.

[22]porphyrin(3.1.3.1) species. Nevertheless, the Soret-like band of our E.P. (Figure 2) is 60–80 nm red-shifted from the corresponding absorbance bands in bisvinylogous porphyrin[9] and platyrin.[10] Also, E.P. possesses a nonplanar shape as a result of its particular structure and peripheral functionalization. One may also consider our E.P. as an aromatic, carba-amethyrin. The 24π non-aromatic amethyrin[11] shares very similar cavity dimensions and overall topology with E.P., and the dizinc amethyrin crystal structure displays the same coplanar dizinc coordination as our dizinc E.P. structure (Figure 1c). The Lash research group has also made numerous contributions concerning syntheses and properties of indene-containing expanded porphyrins[12] and carba-porphyrins[13] over many years.[14] However, there are comparatively few accounts describing ring-fused aryl moieties at the edges of expanded porphyrins (as opposed to at the corners). Several non-aromatic expanded porphyrins featuring edge-aryl moieties[15] have been reported, but our system is aromatic and exhibits a diamagnetic ring current. In the context of the many related porphyrins in the literature, E.P. stands out because of its unique combination of symmetry, topology, aromaticity and ease of preparation. If elaborated further, the use of *ortho*-ethynyl aryl aldehydes in pyrrolic condensations would provide a valuable new route to expanded porphyrins with size-adjustable aromatic surfaces.

Given this new expanded porphyrin, we embarked on understanding its rudimentary chemistry, including its protonation and metalation characteristics. Dichloroacetic acid (DCA) served as a diagnostic reporter acid for protonation studies by ^{1}H NMR spectroscopy because the chemical shift of the β proton of DCA can betray its proximity to the shielding cone of the porphyrinoid ring current. Upon addition of DCA to E.P. (in $CDCl_3$), the meso and internal C−H bond resonances became further deshielded ($\Delta\delta = 1.4$ ppm) and shielded ($\Delta\delta = -1.7$ ppm), respectively. A sharp new resonance integrating to four protons and assigned as the four core NH protons of the E.P. dication also appeared at $\delta = -1.5$ ppm. Furthermore, the β proton of dichloroacetate resonates at $\delta = 4.6$ ppm, compared to $\delta = 6$ ppm in the absence of E.P. ($\Delta\delta = -1.4$ ppm). These observations point to ion-pairing of dichloroacetate and protonated E.P. in solution. Such coordination of DCA to E.P. would place the dichloroacetate in the shielding cone of the porphyrinoid ring current, thereby lowering the chemical shift of the β-proton resonance.[16] Ion-pairing may also limit the amplitude of fluctuation of the indene units, thereby on average placing the internal protons in the most shielded regions of the porphyrin annulus. Single-crystal X-ray analysis of the E.P.–DCA assembly revealed ditopic hydrogen bonding between dichloroacetate and the protonated porphyrinoid (Figure 1b)—the NH groups are tipped out of the plane of the porphyrinoid toward the oxygen atoms of the dichloroacetates on each face. A crystal structure for the HSO_4Me salt also displayed ditopic hydrogen bonding of the anion to protonated E.P. In the DCA[17] and HSO_4Me[18] salt structures, the angle of indene inclination is lowered to 22.03(4)° and 19.15(6)°, respectively, compared to a minimum inclination of 24.17(5)° as seen in free-base structures. These characteristics of the solid-state protonated E.P.–acid assemblies correlate well with ^{1}H NMR spectroscopic evidence for ion-paired assemblies in solution.

Unlike classical porphyrins, which necessarily distort dramatically upon protonation and consequently undergo significant absorbance shifts in their electronic spectra, protonation of E.P. and subsequent ion-pairing seems to exert a negligible structural influence on the macrocycle, as no shift of the Soret-like band is observed upon addition of DCA (Figure 2). Instead, the protonation chemistry of E.P. resembles that described for bisvinylogous porphyrins.[19] That is, the absorbance intensity of E.P. simply increases (from $1.18\times10^{5}\,\text{M}^{-1}$ to $1.79\times10^{5}\,\text{M}^{-1}$ at 543 nm) upon protonation with DCA. With regard to the related bisvinylogous porphyrins, Franck and Nonn[19] have previously attributed this increased absorptivity to increased symmetry in the system with all four nitrogen atoms being protonated.

In spite of expectations for diverse metalation and coordination properties, reports of metallo-expanded porphyrins are only recently becoming evident.[3,20] Nevertheless, the wide cavity of the E.P. core merited investigation as a host for homo and hetero bimetalation. Titration of $Zn(OAc)_2$ ([D$_4$]MeOH) into E.P. ($CDCl_3$) followed by ^{1}H NMR spectroscopy demonstrated sequential mono and dimetalation (Figure 3). At low ratios of Zn/E.P. a new set of resonances appear in addition to the free-base resonances. The splitting pattern of the new set of peaks resembles those of free-base E.P. except that one axis of molecular symmetry has been removed resulting in a pair of meso-like resonances, a pair of inner-C–H bond resonances, etc. (Figure 3b). Further addition of $Zn(OAc)_2$ led to the disappearance of the free-base resonances altogether and concomitant appearance of a second new set of resonances with a restoration of symmetry. As a result, a spectrum similar in appearance to that of the original free-base analogue, but with resonances at different chemical shifts (Figure 3c) is observed for dizinc E.P. An excess of added $Zn(OAc)_2$ simply increased the proportion of the dimetalated system relative to the monometalated analogue (Figure 3d). The monozinc E.P. may be quantitatively prepared by addition of one equivalent of $Zn(OAc)_2$ to the free-base E.P. in $CHCl_3$/MeOH (10:1), and subsequent solvent removal. This species proved stable in $CHCl_3$ but was demetalated by repeated washing with water, thus indicating lability of a single zinc cation. The dizinc E.P. species was generated in quantitative yield by addition of excess $Zn(OAc)_2$ in MeOH to E.P. in $CHCl_3$ at room temperature and subsequent aqueous workup. Crystallization by diffusion of MeOH into a solution of dizinc E.P. in toluene provided crystals suitable for X-ray analysis (Figure 1c).[21] The resulting structure revealed that dizinc E.P. recruits two ancillary methoxy ligands from the solution, which coordinate in a μ-oxo fashion to the two zinc atoms, one on each face of E.P. The tetrapyrrollic portion of the E.P. skeleton is planar, and the two zinc ions are accommodated in a coplanar fashion with an internuclear distance of only 2.835 Å. The indene residues cant out of the macrocyclic plane by 40.09(4)°—more than in any of the other crystal structures obtained to date.

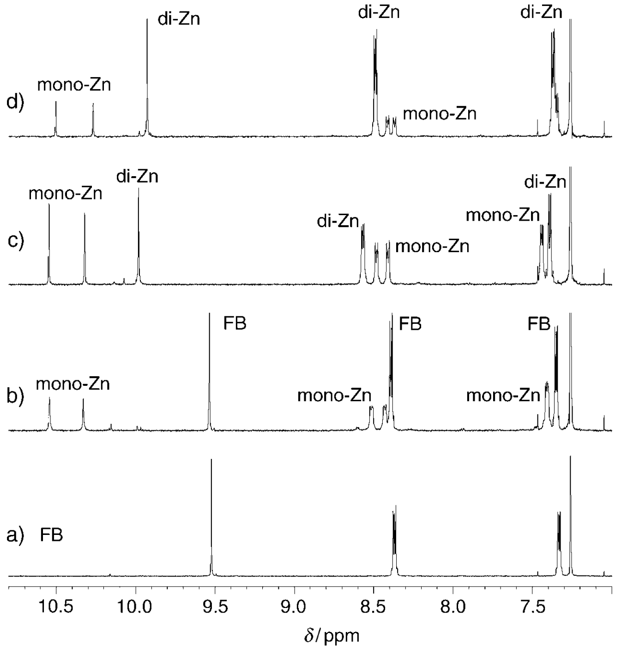

Figure 3. Selected ^{1}H NMR spectra of the zinc acetate titration into E.P. Meso and aromatic regions shown; a) 0 equiv, b) 0.5 equiv, c) 1.5 equiv, and d) 4.0 equiv of $Zn(OAc)_2$.

In conclusion, an in situ annulation reaction during a [2+2] aldehyde-dipyrromethane condensation affords new, ring-fused aromatic expanded porphyrins in an unprecedented one-pot reaction sequence. The availability of this facile route to edge-aryl moieties in expanded porphyrins creates new possibilities in porphyrinoid design. Solution and solid state structures of the free base, protonated, and dizinc analogues of this expanded porphyrin have been described. Metalation with excess zinc acetate proceeds with rapid kinetics at room temperature to quantitatively afford the stable dimetalated species, while stoichiometric addition of zinc afforded the monozinc species. In view of these findings, the potential for the preparation of heterobimetallic structures is currently under investigation.

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[8] Crystal data for β-Me,Et-substituted E.P. crystallized from CH_2Cl_2/MeOH by vapor diffusion, CCDC 755004: $3\,C_{48}H_{46}N_4 \cdot 4\,CH_2Cl_2$, $M = 2376.37$, monoclinic, space group Cc, $a = 26.9352(3)$, $b = 15.9265(2)$, $c = 29.0183(4)$ Å, $\alpha = 90$, $\beta = 102.773(1)$, $\gamma = 90°$, $V = 12140.3(3)$ Å^3, $\rho_{calcd} = 1.300\,g\,cm^{-1}$, $T = 180(2)$ K, $Z = 4$, 35429 reflections measured, 13591 unique, ($R_{int} = 0.0396$), $R_1 = 0.1397$ ($I > 2\sigma((I)$), wR_2 (all data) $= 0.4353$, (isotropic displacement parameters for all but the Cl atoms).

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[17] Crystal data for β-Me,hexyl-substituted E.P.·2 DCA crystallized from $CHCl_3$/MeOH by vapor diffusion, CCDC 755005: $C_{64}H_{84}N_4 \cdot 2\,C_2H_2O_2Cl_2$, $M = 161.18$, monoclinic, space group $P21/c$, $a = 12.1274(4)$, $b = 16.0077(6)$, $c = 16.1414(6)$ Å, $\alpha = 90$, $\beta = 101.079(2)$, $\gamma = 90°$, $V = 3075.16(19)$ Å^3, $\rho_{calcd} = 1.254\,g\,cm^{-1}$, $T = 180(2)$ K, $Z = 2$, 24301 reflections measured, 5360 unique, ($R_{int} = 0.045$), $R_1 = 0.0508$ ($I > 2\sigma((I)$), wR_2 (all data) $= 0.1301$.

[18] Crystal data for β-Me,hexyl-substituted E.P. $\cdot 2\,HSO_4Me$ crystallized from $CHCl_3$/MeOH by vapor diffusion, CCDC 755003: $C_{48}H_{46}N_4 \cdot 2\,HSO_4CH_3 \cdot 4\,CHCl_3$, $M = 1380.56$, triclinic, space group $P\bar{1}$, $a = 10.858(2)$, $b = 11.2797(2)$, $c = 13.6255(3)$ Å, $\alpha = 69.613(1)$, $\beta = 89.266(1)$, $\gamma = 86.659(1)°$, $V = 1561.6(3)$ Å^3, $\rho_{calcd} = 1.468\,g\,cm^{-1}$, $T = 180(2)$ K, $Z = 1$, 20007 reflections measured, 9017 unique, ($R_{int} = 0.0370$), $R_1 = 0.0811$ ($I > 2\sigma((I)$), wR_2 (all data) $= 0.2165$.

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[21] Crystal data for β-Me,hexyl-substituted E.P. ·2Zn(OMe) crystallized from toluene/MeOH by vapor diffusion, CCDC 755001: $C_{64}H_{82}N_4Zn_2 \cdot 2\,CH_3O \cdot 4\,C_7H_7$, $M = 1278.36$, monoclinic, space group $P21/c$, $a = 18.4909(3)$, $b = 18.0211(4)$, $c = 10.3245(2)$ Å, $\alpha = 90$, $\beta = 96.412(2)$, $\gamma = 90°$, $V = 341887(11)$ Å^3, $\rho_{calcd} = 1.242\,g\,cm^{-1}$, $T = 180(2)$ K, $Z = 2$, 24061 reflections measured, 7798 unique, ($R_{int} = 0.0433$), $R_1 = 0.0430$ ($I > 2\sigma((I)$), wR_2 (all data) $= 0.1026$.