Facile Synthesis of β-Derivatized Porphyrins—Structural Characterization of a $\beta-\beta$-Bis-Porphyrin[**]

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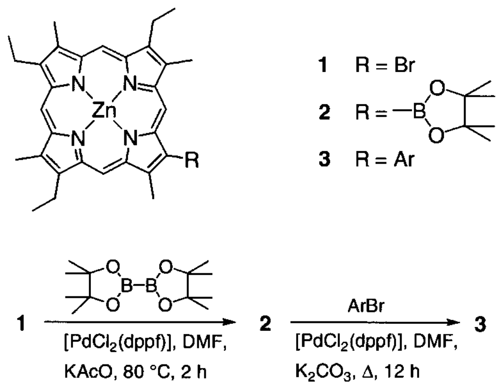
Linked porphyrin complexes have been a popular structural motif for studies of electron and energy transfer. The ability to tune the electronic properties of porphyrins by their catenation is central to controlling the efficiencies and rates of these transfers,[1–6] engendering applications in areas ranging from the design of "molecular wires" and optoelectronic materials to the development of biomimetic models of photosynthetic reaction centers and light-harvesting antenna complexes.[7–12] Modification of porphyrins is more common at the *meso*-position than at the β-position, which confronts more lengthy syntheses and lower product yields. This is especially true for bis-porphyrins where several new emerging methodologies for direct *meso* coupling[13–16] contrast a limited set of approaches for the synthesis of $\beta-\beta$ linked bis-porphyrins.[16b, 17] Porphyrin coupling chemistry has changed in recent years with the emergence of metal-catalyzed cross-coupling methods, which have been employed to link bis-porphyrins via phenyl and ethynyl spacers at *meso*–*meso*-, *meso*–β- and $\beta-\beta$-positions.[7, 8] The direct coupling of porphyrins by such methods, however, has not yet been achieved. We now show the utility of metal-mediated cross-coupling for the general synthesis of β-derivatized porphyrins, including the preparation and first structural characterization of a bis-porphyrin unit directly linked at the β-position.

Scheme 1 shows the strategy developed for the direct $\beta-\beta$ coupling of the porphyrin rings. Air- and water-stable **2** was isolated in 76% yield by applying the method of Miyaura et al.[18] to couple the pinacol diboronate with bromoporphyrin **1**.[19] Porphyrin **2** can also be prepared according to Masuda's method where the pinacol borane is the transmetalating reagent.[20, 21] The same boronate has recently been applied to synthesize porphyrins derivatized at the *meso*-position[22] in yields similar to that reported here for β-derivatization. Cross-coupling **1** and **2** under typical Suzuki reaction conditions affords the previously reported bis-porphyrin **3a**,[17, 23] but prepared here more conveniently and in higher yield (62%).



a: Ar = (7,12,17-triethyl-3,8,13,18-tetramethylporphyrinato)zinc(II);
b: Ar = Ph; **c:** Ar = p-CH$_3$Ph; **d:** Ar = 9-Anthryl; **e:** Ar = p-OHCPh

Scheme 1. Synthesis of **3a–e**.

The crystal structure of the porphyrin dimer **3a**[24] (Figure 1) is unique inasmuch as no porphyrin system directly linked by a carbon–carbon bond at the β-position of the rings has been heretofore structurally characterized. Connection at the less sterically encumbered β-position results in a dihedral angle (51.7°) (defined by four $N_{pyrrolyl}$ atoms of each porphyrin) between the two porphyrin macrocyles that is considerably smaller than that observed between the phenyl and porphyrin rings in tetraphenylporphyrin (TPP),[25] other crystallographically characterized TPP type compounds[26, 27] and, most pertinently, than two porphyrins directly linked by a C–C bond at their *meso*-positions (dihedral angle of 65 to 84°).[14] The unique bridging C2–C2′ bond (1.46 Å) is also shorter than the C–C bond of the *meso*–*meso* coupled bis-porphyrin ($d = 1.51$ Å) and the sp^3–sp^3 distance of a recently reported $\beta-\beta$ linked bis-chlorin ($d = 1.61$ Å), which is typical of a single bond.[28] These bond length comparisons suggest greater electronic conjugation between two porphyrin macrocycles when linked at their β-positions.

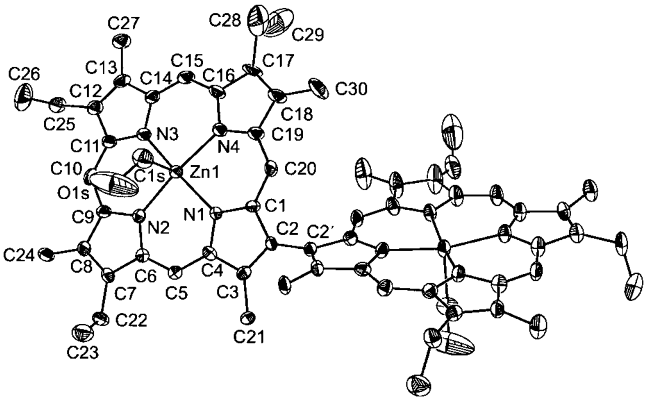


Figure 1. ORTEP representation of **3a** with hydrogen atoms omitted for clarity. Thermal ellipsoids are drawn at the 30% probability level.

Figure 2a compares the electronic absorption spectra of the monomeric subunit (zinc(II) etio-I porphyrin) and **3a**. The

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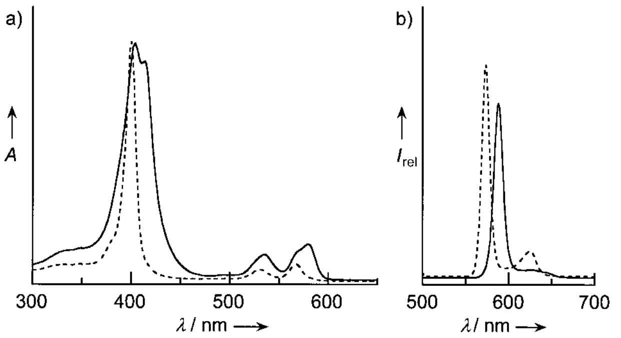

Figure 2. a) Absorption and b) emission spectra of **3a** (——) and zinc(II) etio-I porphyrin (monomer) (– – –) in CH_2Cl_2 at 22 °C.

Soret (B) and Q band absorptions are clearly perturbed upon β-catenation of the monomer subunits. The B band maximum of **3a** is red-shifted relative to that of the monomer. A concomitant broadening and splitting of the B band is indicative of exciton splitting within the bis-porphyrin superstructure.[29] A similar splitting is also reflected in the Q band absorptions to lower energy. The difference in energy (ΔE) of 539 cm^{-1} between the two maxima of the split B band (and an analogous $\Delta E = 395\ cm^{-1}$ for the split Q band) is smaller than that of bis-porphyrins connected by a C–C bond at the *meso*–β- ($\Delta E = 1265\ cm^{-1}$) and *meso*–*meso*- ($\Delta E = 2100\ cm^{-1}$) positions.[16]

The crystal structure of **3a** provides critical insight into the trend in ΔE for the three cases. Exciton splittings arise from allowed transitions (B_y and B_x) resulting from the constructive vector sum of transition dipole moments of coplanar bis-porphyrin subunits in a parallel (μ_y) and in-line (μ_x) disposition. For the case of the *meso*–*meso* bis-porphyrin system, the in-line transition dipoles are always aligned[14] and only the parallel transition moment varies with rotation about the connecting C–C bond. Conversely, the crystal structure of the β–β linked bis-porphyrin **3a** shows that the μ_x and μ_y transition dipole moments assume an oblique angle due to the fanning of the two porphyrin subunits from each other. In the situation of oblique transition dipoles, the exciton splitting energy will be attenuated owing to the angular dependence of the transition moment. Although the orientation of the porphyrin rings in a *meso*–β system has not been crystallographically determined,[16b] the observation that the exciton splitting energy lies between the β–β and *meso*–*meso* bis-porphyrin systems suggests that the two porphyrins are also obliquely disposed but to a lesser degree than observed for **3a**.

Excitation into the absorption manifold of **3a** results in the intense luminescence bands characteristic of $Q(0,0)$ and $Q(0,1)$ transitions (Figure 2b). As with the absorption profile, the emission bands are red-shifted with respect to monomer emission and a splitting of the lowest energy emission band is clearly evident ($\Delta E = 345\ cm^{-1}$). The luminescence red shift, consistent with increased conjugation of the bis-porphyrin pair, is reflected in a slightly shorter lifetime than that of the monomer ($\tau_{obs}(\mathbf{3a}) = 1.55(1)$ ns and τ_{obs}(zinc(II) etio-I porphyrin) = 1.61(1) ns).

The β-derivatized boronate **2** is a general building block for modification of porphyrins at the β-position. Cross coupling between **2** and various aryl halides was carried out in DMF in the presence of a catalytic amount (5–10 mol%) of $[PdCl_2(dppf)]$ (dppf = 1,1′-bis(diphenylphosphanyl)ferrocene) and 10 equivalents of aqueous K_2CO_3 at 80 °C under an inert atmosphere to give the corresponding β-substituted porphyrins in high yields.[30] Reaction of bromobenzene and *p*-bromotoluene with **2** affords the phenyl and tolyl β-derivatized porphyrins **3b** and **3c**, respectively, in yields that are similar to that obtained for the coupling between **1** and phenyl boronic acid or *p*-tolyl boronic acid. Although molecules such as anthryl porphyrin **3d** may be synthesized by reacting water-sensitive dichlorozinc anthracene reagents with **1**,[31] the air and water stability of **2** makes the approach reported here superior for preparing this type of compound in high yields. Furthermore, **2** reacts smoothly with aryl halides bearing electrophilic functional groups; coupling of **2** with 4-bromobenzaldehyde leads to the formation of **3e** with the reactive aldehyde group remaining intact, thus demonstrating the suitability of **2** for a wide range of substrates. Along these lines, utilization of β-boronate **2** as a coupling precursor provides a general alternative to recent methods relying on arylboronic acids[32] and boronates,[9] with the advantage that it is more tolerant to base-sensitive functional groups.

A structurally characterized *meso*–*meso*, *meso*–β, β–β bis-porphyrin series provides a solid foundation from which to interpret trends in the observed electronic spectra of directly coupled porphyrins. The ability to differentially perturb electronic structure by the site of substitution about the porphyrin periphery has important reactivity issues. As we have recently shown, substituents at the β-position that are in direct electronic communication with the porphyrin ring can profoundly influence the rates of electron transfer.[33] In view of the rich chemistry of boronic acid esters and borates,[34] further application of **2** will undoubtedly provide unique porphyrin architectures that will further advance our understanding of the spectroscopic and the electron/energy transfer properties of catenated porphyrin supermolecules.

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[21] **2**: 76% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 401, 533, 574$ nm; ^1H NMR (300 Hz, $CDCl_3$, 25 °C): $\delta = 1.78$ (s, 12H; CH_3), 1.80 (m, 9H; CH_3), 3.44, 3.50, 3.64, 3.96 (s, 3H each; CH_3), 3.98 (m, 6H; CH_2), 9.60, 9.64, 9.90, 10.76 (s, 1H each; *meso*-H); FAB HRMS for $C_{36}H_{43}BN_4O_2Zn$: calcd: 638.27712; found: 638.27705.

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[23] **3a**: 62% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 403, 415, 534, 579$ nm; ^1H (300 Hz, $CDCl_3$, 25 °C): $\delta = 1.74$ (t, $^3J(H,H) = 7.2$ Hz, 6H; CH_3), 1.90 (t, $^3J(H,H) = 7.2$ Hz, 6H; CH_3), 2.02 (t, $^3J(H,H) = 7.2$ Hz, 6H; CH_3), 2.88, 3.65, 3.74, 3.92 (s, 6H each; CH_3), 4.20 (m, 12H; CH_2), 10.06, 10.14, 10.22, 10.50 (s, 2H each; *meso*-H); FAB HRMS for $C_{60}H_{62}N_8Zn_2$: calcd: 1022.36804; found: 1022.36765; elemental analysis (%) for $C_{60}H_{62}N_8Zn$: calcd: C 70.24, H 6.09, N 10.92; found: C 70.32, H 6.12, N 11.03.

[24] Crystallographic data: $C_{63}H_{74}N_8O_3Zn_2$ from CH_3OH/CH_2Cl_2, $M_r = 1122.04$, monoclinic, space group $C2/c$, $a = 14.58560(10)$, $b = 21.5321(3)$, $c = 19.6353(3)$ Å, $\beta = 104.5520(10)°$, $V = 5968.81(13)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.249$ g cm^{-3}, $F(000) = 2368$, $\lambda(Mo_{K\alpha}) = 0.7107$ Å, crystal dimensions $0.5 \times 0.25 \times 0.10$ mm^3. A total of 8840 reflections were collected at −90 °C using a Siemens diffractometer equipped with a CCD detector in the θ range of 1.72 to 20.00°, of which 2788 were unique ($R_{int} = 0.0570$). The structure was solved by the Patterson heavy atom method in conjunction with standard difference Fourier techniques. Hydrogen atoms were placed in calculated positions using a standard riding model and were refined isotropically. A methanol solvent molecule was found to be disordered and was modeled by standard procedures. The largest peak and hole in the difference map were 0.957 and −0.424 e Å^{-3}, respectively. The least-squares refinement converged normally giving residuals of $R = 0.0749$ and $wR^2 = 0.1983$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133672. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[29] Standard exciton considerations predict that B_y should blue-shift and B_x should red-shift about the unperturbed B band. In **3a**, both transitions red-shift relative to the B band of the monomer. The same situation occurs for the *meso*–β and the *meso*–*meso* bis-porphyrins of ref. [16b)]. These red shifts indicate that the exciton coupling in porphyrins linked by a single bond is augmented by other factors; one likely factor is electronic coupling between porphyrin subunits across the C−C bond.

[30] **3b–e**: **3b**, 91% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 402, 530, 570$ nm; ^1H NMR (300 Hz, $CDCl_3$, 25 °C): $\delta = 1.73$ (m, 9H; CH_3), 3.39, 3.41, 3.50, 3.64 (s, 3H each; CH_3), 3.86 (m, 6H; CH_2), 7.70–8.22 (m, 5H; Ar−H), 9.41, 9.53, 9.74, 9.84 (s, 1H each; *meso*-H); FAB HRMS for $C_{36}H_{36}N_4Zn$: calcd: 588.2223; found: 588.2230. **3c**, 93% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 402, 533, 569$ nm; ^1H NMR (300 Hz, $CDCl_3$, 25 °C): $\delta = 1.75$ (m, 9H; CH_3), 2.72 (s, 3H; CH_3), 3.39 (s, 6H; CH_3), 3.44, 3.66 (s, 3H each; CH_3), 3.86 (m, 6H; CH_2), 7.68, 8.08 (dd, $^3J(H,H) = 14.5$ Hz, 2H; Ar−H), 9.40, 9.50, 9.73, 9.84 (s, 1H each; *meso*-H); FAB HRMS for $C_{37}H_{36}N_4OZn$: calcd: 602.23879; found: 602.23908. **3d**, 88% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 404, 534, 570$ nm; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 1.74$ (t, $^3J(H,H) = 7.5$ Hz, 3H; CH_3), 1.85 (t, $^3J(H,H) = 7.3$ Hz, 3H; CH_3), 1.92 (t, $^3J(H,H) = 7.5$ Hz, 3H; CH_3), 3.07, 3.41, 3.56, 3.65 (s, 3H each; CH_3), 4.08 (m, 6H; CH_2), 7.17 (m, 2H; Ar−H), 7.53 (m, 2H; Ar−H), 7.81 (d, $^3J(H,H) = 8.8$ Hz, 2H; Ar−H), 8.30 (d, $^3J(H,H) = 8.9$ Hz, 2H; Ar−H), 8.86 (s, 1H; Ar−H), 9.48, 10.00, 10.06, 10.34 (s, 1H each, *meso*-H); FAB HRMS for $C_{44}H_{40}N_4Zn$: calcd: 688.25444; found: 688.25432. **3e**, 82% yield. UV/Vis (CH_2Cl_2): $\lambda_{max} = 406, 533, 574$ nm; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 1.72$ (m, 9H; CH_3), 3.36 (s, 3H; CH_3), 3.40 (s, 6H; CH_3), 3.59 (s, 3H; CH_3), 3.84 (m, 6H; CH_2), 8.34 (dd, $^3J(H,H) = 14.9$ Hz, 2H; Ar−H), 9.43, 9.50 (s, 1H each; *meso*-H), 9.62 (s, 2H; *meso*-H), 10.35 (s, 1H; CHO); FAB HRMS for $C_{37}H_{36}N_4OZn$: calcd: 616.21806; found: 616.21786.

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One-Pot Synthesis of Antigen-Bearing, Lysine-Based Cluster Mannosides Using Two Orthogonal Chemoselective Ligation Reactions[**]

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Dendritic cells (DCs) are well-recognized for playing a crucial role in the control of immunity. These professional antigen-presenting cells act both as initiators and modulators

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