



# Synthesis of $\beta$ -di and tribromoporphyrins and the crystal structures of antipodal tri-substituted Zn(II)-porphyrins

P. Bhyrappa\*, V. Velkannan

Department of Chemistry, Indian Institute of Technology Madras, Chennai 600 036, India

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## ABSTRACT

Bromination of *meso*-tetraphenylporphyrin,  $H_2TPP$  with controlled amounts of *N*-bromosuccinimide at ambient conditions in  $CHCl_3$  produced  $\beta$ -dibromo and tribromotetraphenylporphyrins. The regiochemistry of the  $ZnTPPR_3$  ( $R = Br, Ph$ ) complexes indicate the antipodal substitution at the  $\beta$ -pyrrole positions.

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## 1. Introduction

Functionalised porphyrins and metalloporphyrins have been widely employed as models of tetrapyrrole pigments of nature.<sup>1</sup> Besides, these substituted porphyrins exhibit unique physicochemical properties.<sup>2</sup> Synthesis of  $\beta$ -pyrrole-substituted porphyrins is of growing interest since the substituents are in direct conjugation with the  $\pi$ -system which can alter the properties of the macrocycle dramatically. The preparation of partial  $\beta$ -pyrrole brominated tetraphenylporphyrin leads to mixture of products.<sup>3</sup> In a previous report, the regiochemistry of the  $H_2TPPBr_n$  ( $n = 2-4$ ) was suggested based on the  $18-\pi$  electron delocalisation pathway.<sup>4a</sup> Use of such porphyrins as precursor<sup>4</sup> resulted in a symmetric  $\beta$ -pyrrole mixed substituted tetraphenylporphyrins with interesting electrochemical redox and stereochemical properties.<sup>5</sup> 2,3-dibromo-tetraphenylporphyrin was prepared by bromination reaction of  $H_2TPP(\beta-NO_2)$  derivative followed by denitration.<sup>6</sup> However, the synthesis and regiochemistry of the dibromo and tribromoporphyrins remain largely unexamined. Synthesis of partially brominated  $H_2TPP$  provides an easy entry into various asymmetrically substituted porphyrins or materials, which are otherwise synthetically difficult.<sup>4a,5-8</sup> Furthermore, asymmetrically substituted porphyrins are potentially useful in non-linear optical applications.<sup>9</sup>

In this Letter, the synthesis of 2,12/2,3/2,13-dibromo-5,10,15,20-tetraphenylporphyrin and 2,3,12-tribromo-5,10,15,20-tetraphenylporphyrins are reported (Fig. 1). Suzuki cross-coupling reaction of  $H_2TPPBr_3$  has been examined and the crystal structures of the antipodal-substituted  $ZnTPPR_3$  ( $R = Br, Ph$ ) complexes are explored.

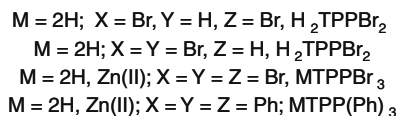
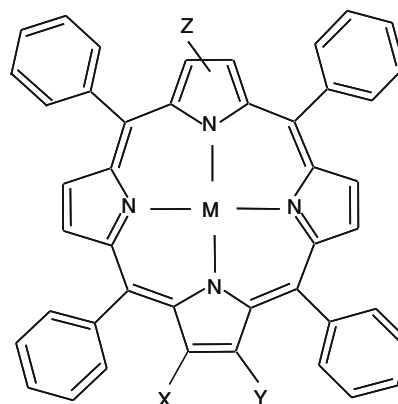


Figure 1. Molecular structure of  $\beta$ -di and tri-substituted porphyrins.

## 2. Results and discussion

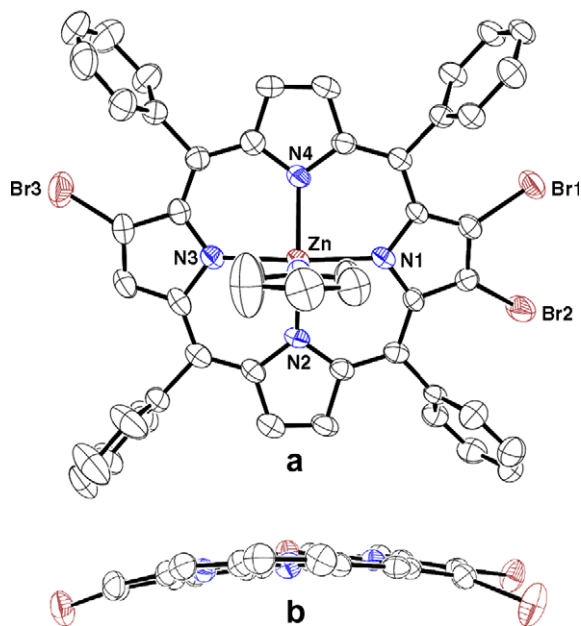
$\beta$ -Dibromo- and tribromo- $H_2TPP$  derivatives were synthesised at room temperature by bromination reaction of free-base *meso*-tetraphenylporphyrin using 2.8 equiv of *N*-bromosuccinimide.<sup>10</sup> Refluxing of the reaction mixture resulted in the formation of small amounts of tetrabromo- $H_2TPP$ . Attempted selective synthesis of  $H_2TPPBr_2$  or  $H_2TPPBr_3$  by controlling the concentration of *N*-bromosuccinimide was unsuccessful. Under optimised reaction conditions, at room temperature, the reaction showed essentially two products,  $\beta$ -dibromo- and tribromo-5,10,15,20-tetraphenylporphyrins. These porphyrins were separated by silica gel column

\* Corresponding author.

E-mail address: pbhyrappa@hotmail.com (P. Bhyrappa).

chromatography using 35% CHCl<sub>3</sub> in *n*-hexane solvent mixture. H<sub>2</sub>TPPBr<sub>2</sub> and H<sub>2</sub>TPPBr<sub>3</sub> were isolated as first and second fraction with the yield of 30% and 40%, respectively. Synthesised porphyrins were characterised by electronic absorption, <sup>1</sup>H NMR, mass spectroscopy, and elemental analysis.<sup>10</sup> Electronic absorption spectrum of the H<sub>2</sub>TPPBr<sub>*n*</sub> (*n* = 2 and 3) revealed red-shifts of the visible absorption bands relative to H<sub>2</sub>TPP and are consistent with the literature values.<sup>3</sup> However, H<sub>2</sub>TPPBr<sub>2</sub> mixture indicates blue shifted absorption in contrast to reported 2,3-dibromo-H<sub>2</sub>TPP.<sup>6</sup> Interestingly, <sup>1</sup>H NMR of H<sub>2</sub>TPPBr<sub>2</sub> mixture showed an intense peak at –2.94 ppm with moderately intense peak at –2.83 ppm and two very weakly intense peaks at –2.65 and –2.78 ppm for the core imino protons. It was reported previously that 2,3-dibromo-H<sub>2</sub>TPP isomer showed a singlet for the imino-proton at –2.83 ppm.<sup>6</sup> The presence of an intense imino proton resonance signal centred at –2.94 ppm suggests the presence of a major isomer as 2,12 (or 2,13) and minor component as 2,3-dibromoporphyrin under the above reaction conditions. As proposed earlier, the suggested regiochemistry of the dibromo-H<sub>2</sub>TPP was 2,3 or 2,12, or 2,13-dibromo-tetraphenylporphyrins.<sup>4a</sup> Moreover, the *meso*-phenyl (*o*-H's, 8.07–8.18 ppm; *m*- and *p*-H's, 7.71–7.79 ppm) and β-pyrrole protons (8.72–8.89 ppm) signals showed complex multiplets. The formation of the dibromo-H<sub>2</sub>TPP was evidenced from the analytical and mass spectroscopy data. The separation of the individual isomers was unsuccessful on the silica gel column chromatography using CHCl<sub>3</sub>/hexane solvent mixture.

<sup>1</sup>H NMR spectrum of H<sub>2</sub>TPPBr<sub>3</sub> in CDCl<sub>3</sub> features two singlets for imino protons and the number of proton resonances arising from β-pyrrole and *meso*-phenyl groups indicates the antipodal substitution of the bromo atoms at the pyrrole positions. The integrated intensity of the resonances is consistent with the proposed structure. Considering the 18-electron cyclic polyene model, the tri-bromination is anticipated at the antipodal β-pyrroles. In an effort to elucidate the regiochemistry, the crystal structure of the ZnTPPBr<sub>3</sub> was examined.<sup>11,12</sup> The ORTEP diagram of the ZnTPPBr<sub>3</sub>(Py)·(C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub>) complex is shown in Figure 2. The three bromine atoms showed disorder over four antipodal β-pyrrole

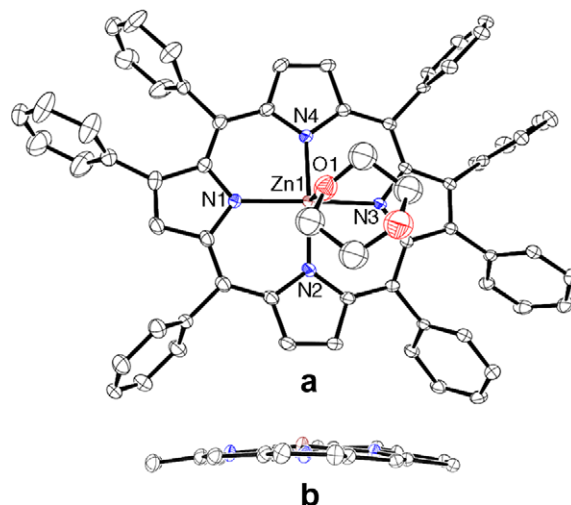


**Figure 2.** ORTEP diagram of the ZnTPPBr<sub>3</sub>(Py)·C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub> complex. The minor disordered bromine atom is not shown for clarity. (a), Top view; (b), side view. 1,2-dichloroethane solvate is not shown for clarity. For the side view, hydrogens, *meso*-phenyls and axial pyridine are omitted. Thermal ellipsoids are shown at 40% probability level.

positions with the occupancies of 0.92, 0.76, 0.80, and 0.52 for Br1, Br2, Br3, and Br4, respectively. Zn(II) ion shows square pyramidal geometry with axially coordinated pyridine solvate. The brominated pyrroles exhibited average Zn–N bond distance of 2.115(5) Å while the other unsubstituted pyrroles showed Zn–N = 2.038(6) Å. This is perhaps due to decreased electron density on the nitrogens induced by the electron-withdrawing bromine atoms. Zn(II) ion is situated 0.382(4) Å above the equatorial four nitrogen plane and the axially coordinated pyridine is almost planar with a Zn1–N5 bond distance of 2.156(5) Å.<sup>13</sup> The macrocyclic ring is nearly planar within 0.191(4) Å. *meso*-Phenyl groups are oriented perpendicular to the porphyrin mean plane with an average dihedral angle of 73.5(2)°.

Suzuki-cross coupling of the H<sub>2</sub>TPPBr<sub>3</sub> with phenyl boronic acid was performed using reported procedure<sup>5</sup> and H<sub>2</sub>TPP(Ph)<sub>3</sub> was isolated in 80% yield. Its Zn(II)-complex was prepared using literature method.<sup>5</sup> The synthesised compounds were characterised by conventional spectroscopic methods.<sup>14</sup> Electronic absorption spectrum of the MTPP(Ph)<sub>3</sub> (M = 2H, Zn(II)) reveal blue shifted absorption of the spectral bands (3–10 nm) relative to the corresponding MTPP(Ph)<sub>4</sub> (M = 2H, Zn(II)) complexes.<sup>5</sup> <sup>1</sup>H NMR of the H<sub>2</sub>TPP(Ph)<sub>3</sub> shows resonances arising from β-pyrrole, *meso*-phenyl, and imino protons. The imino-protons appear as a singlet at –2.23 ppm. <sup>1</sup>H NMR of the ZnTPP(Ph)<sub>3</sub> complex revealed the absence of core imino protons while the phenyl and β-pyrrole protons are down-fielded marginally (0.1–0.25 ppm) and the integrated intensity of the resonances are consistent with the expected structure.<sup>14</sup>

To examine the distribution of the phenyl groups at the β-pyrrole positions, crystal structure of the ZnTPP(Ph)<sub>3</sub> was examined.<sup>15</sup> The ORTEP diagram of the ZnTPP(Ph)<sub>3</sub>(dioxane) complex is shown in Figure 3. The Zn(II) ion is situated above (0.280(3) Å) the equatorial four nitrogen plane with axially coordinated dioxane as the fifth ligand. In the equatorial plane, the mean Zn–N bond distance is 2.099(3) Å along the substituted pyrrole direction and it is longer than the other unsubstituted pyrrole direction 2.015(3) Å. The axially coordinated 1,4-dioxane shows two disordered positions with Zn1–O1 distance of 2.273(4) Å. The macrocyclic ring shows near planarity within 0.142(3) Å from the mean plane of the 24-atom core. The average dihedral angle formed by the β-pyrrole phenyls (77.4(1)°) is slightly higher than that of *meso*-phenyl groups (75.9(2)°). Both the ZnTPPBr<sub>3</sub>(Py)·(C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub>) and ZnTPP(Ph)<sub>3</sub>(diox-



**Figure 3.** Crystal structure of the ZnTPP(Ph)<sub>3</sub>(dioxane) complex. (a), Top view, hydrogens and the minor disordered part of the dioxane is not shown for clarity. (b), side view, hydrogens, phenyls and 1,4-dioxane are omitted. Thermal ellipsoids are shown at 40% probability level.

ane) complexes exhibited gentle non-planarity of the porphyrin rings when compared to five-coordinated ZnTPPBr<sub>4</sub>(MeOH)·DMF structure.<sup>16</sup> The decreased non-planarity in ZnTPPBr<sub>3</sub> (R = Br, Ph) structures is perhaps due to less steric crowding at the periphery of the porphyrin.

### 3. Conclusions

In summary, room temperature syntheses of free-base β-dibromo and tribromotetraphenylporphyrins have been reported. Crystal structures of the ZnTPPBr<sub>3</sub> (R = Ph, Br) complexes reveal antipodal β-pyrrole distribution of the substituents. Synthesis and properties of asymmetrically dodeca-substituted porphyrins and their metal complexes are in progress.

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- (a) General procedure for the synthesis and purification of H<sub>2</sub>TPPBr<sub>n</sub> (n = 2, 3) derivatives is as follows: To a stirred solution of H<sub>2</sub>TPP<sup>10b</sup> (0.25 g, 0.406 mmol) in CHCl<sub>3</sub> (50 ml), freshly recrystallised NBS (0.202 g, 1.138 mmol) in 20 ml of CHCl<sub>3</sub> was added dropwise over a period of 30 min. Then the reaction mixture was allowed to stir for a further period of 24 h at room temperature. At the end of this period, the reaction mixture was rotary-evaporated to dryness and the purple coloured residue was washed with methanol twice (25 ml × 2) and it was dried at 85 °C for 8 h. The residue was re-dissolved in minimum amount of CHCl<sub>3</sub> and pre-adsorbed on silica gel (100–200 mesh). The slurry was subjected for rotary evaporation to remove CHCl<sub>3</sub> to get the dry silica gel powder. The dry silica gel powder was chromatographed on to silica gel column using 35% CHCl<sub>3</sub> in hexane as the eluent. H<sub>2</sub>TPPBr<sub>2</sub> mixture and H<sub>2</sub>TPPBr<sub>3</sub> were collected as first and second fractions, respectively. The samples were dried at 85 °C under vacuum (8 mbar) for 8 h and the yield of the H<sub>2</sub>TPPBr<sub>2</sub> and H<sub>2</sub>TPPBr<sub>3</sub> were found to be 0.095 (30%) and 0.139 (40%), respectively. **H<sub>2</sub>TPPBr<sub>2</sub>**: UV-visible spectrum in CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>max</sub>, nm (log ε): 423 (5.46), 520 (4.27), 553 (3.57), 595 (3.74), 651 (3.74). <sup>1</sup>H NMR (400 MHz) in CDCl<sub>3</sub>: δ = 8.86 (m, β-pyrrole-H), 8.83 (m, β-pyrrole-H), 8.76 (m, β-pyrrole-H), 8.17 (m, meso-o-phenyl-H), 8.08 (m, meso-o-phenyl-H), 7.75 (m, meso-m and p-phenyl-H), -2.65 (s, imino-NH), -2.78 (s, imino-NH), -2.83 (s, imino-NH), -2.94 (s, imino-NH). ESI-MS (m/z): Found 773 (Calcd, 772.54). Elemental Anal. Calcd for C<sub>44</sub>H<sub>28</sub>N<sub>4</sub>Br<sub>2</sub>: C, 68.41; H, 3.65; N, 7.25. Found: C, 68.23; H, 3.78; N, 7.18. **H<sub>2</sub>TPPBr<sub>3</sub>**: UV-visible in CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>max</sub>, nm (log ε): 428 (5.44), 525 (4.27), 602 (3.57), 663 (3.75); <sup>1</sup>H NMR (400 MHz) in CDCl<sub>3</sub>: δ = 8.86 (d, J = 5.2 Hz, 1H, β-pyrrole-H), 8.79 (m, 2H, β-pyrrole-H), 8.74 (s, 1H, β-pyrrole-H), 8.71 (d, J = 5.2 Hz, 1H, β-pyrrole-H), 8.19 (m, 2H, meso-o-phenyl-H), 8.14 (m, 4H, meso-o-phenyl-H), 8.10 (m, 2H, meso-o-phenyl-H), 7.78 (m, 12H, meso-m and p-phenyl-H), -2.86 (s, 1H, imino-NH), -2.99 (s, 1H, imino-NH). ESI-MS (m/z): 853 (Calcd, 851.44). Elemental Anal. Calcd for C<sub>44</sub>H<sub>27</sub>N<sub>4</sub>Br<sub>3</sub>: C, 62.07; H, 3.20; N, 6.58. Found: C, 62.13; H, 3.48; N, 6.39. **ZnTPPBr<sub>3</sub>**: UV-visible spectrum in CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>max</sub>, nm (log ε): 427 (5.59), 520 (sh), 556 (4.30), 593 (3.93). <sup>1</sup>H NMR (400 MHz) in CDCl<sub>3</sub>: δ = 8.99 (s, 1H, β-pyrrole-H), 8.79 (d, 4H, β-pyrrole-H), 8.09 (m, 8H, meso-o-phenyl-H), 7.73 (m, 12H, meso-m and p-phenyl-H). MALDI-MS (m/z): 914.39 (914); (b) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.
- The crystals of ZnTPPBr<sub>3</sub>(Py)·(C<sub>2</sub>H<sub>4</sub>Cl<sub>2</sub>) were grown by diffusing vapours of hexane to the Zn(II)-porphyrin solution in dichloroethane containing a few drops of pyridine over a period of five-days at room temperature. Crystal data: C<sub>51</sub>H<sub>33</sub>Br<sub>3</sub>N<sub>5</sub>Cl<sub>2</sub>Zn, M.W. = 1091.82, triclinic, P1. Cell dimensions: a = 9.9381(3) Å, b = 13.5657(4) Å, c = 18.2548(6) Å; α = 100.989(2)°, β = 96.752(2)°, γ = 91.808(2)°. v = 2395.50(13) Å<sup>3</sup>, Z = 2. T = 293 K. D<sub>calcd</sub>. = 1.514 g/cm<sup>-3</sup>. Data/restraints/parameters 8240/10/561. Final R indices [I > 2σ(I)], R<sub>1</sub> = 0.0711, wR<sub>2</sub> = 0.2236. Crystallographic data excluding structure factors have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 737940. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ, UK [Direct line: +44 1223 762910, fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
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- H<sub>2</sub>TPP(Ph)<sub>3</sub>**: UV-visible absorption spectrum in CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>max</sub>, nm (log ε): 429 (5.42), 525 (4.19), 561 (3.85), 598 (3.75), 662 (3.45). <sup>1</sup>H NMR (400 MHz) in CDCl<sub>3</sub>: δ = 8.69 (s, 1H, β-pyrrole-H), 8.66 (d, J = 4.8 Hz, 1H, β-pyrrole-H), 8.51 (d, J = 4.8 Hz, 2H, β-pyrrole-H), 8.41 (d, J = 4.8 Hz, 1H, β-pyrrole-H), 8.25 (m, 2H, meso-o-phenyl-H), 7.94 (d, J = 6.8 Hz, 2H, meso-o-phenyl-H), 7.82 (d, J = 7.2 Hz, 4H, meso-o-phenyl-H), 7.73 (m, 3H, meso-m and p-phenyl-H), 7.36 (m, 2H, meso-m-phenyl-H), 7.20 (m, 12H, meso and β-phenyl-H), 6.94 (d, J = 7.2 Hz, 4H, β-o-phenyl-H), 6.87 (m, 6H, β-m & p-phenyl-H), -2.23 (s, 2H, -NH). ESI-MS (m/z): found 843.0 (Calcd, 843.05). **ZnTPP(Ph)<sub>3</sub>**: UV-visible spectrum in CH<sub>2</sub>Cl<sub>2</sub>, λ<sub>max</sub>, nm (log ε): 428 (5.53), 555 (4.62), 590 (sh). <sup>1</sup>H NMR (400 MHz) in CDCl<sub>3</sub>: δ = 8.82 (m, 2H, β-pyrrole-H), 8.67 (d, J = 4.8 Hz, 1H, β-pyrrole-H), 8.63 (d, J = 4.4 Hz, 1H, β-pyrrole-H), 8.54 (d, J = 4.8 Hz, 1H, β-pyrrole-H), 8.22 (m, 2H, meso-o-phenyl-H), 7.88 (m, 2H, meso-o-phenyl-H), 7.77 (m, 4H, meso-o-phenyl-H), 7.71 (m, 3H, meso-m and p-phenyl-H), 7.36 (m, 2H, meso-m-phenyl-H), 7.18 (m, 12H, meso and β-phenyl-H), 6.98 (m, 4H, β-o-phenyl-H), 6.87 (m, 6H, β-m and p-phenyl-H). MALDI-MS (m/z): 905.5 (906.41).
- Crystals of the ZnTPP(Ph)<sub>3</sub>(dioxane) complex was grown by diffusing hexane to the porphyrin in 1,4-dioxane over a period of five days. Crystal data: C<sub>66</sub>H<sub>48</sub>N<sub>4</sub>O<sub>2</sub>Zn, M.W. = 994.47, triclinic, P1. Unit cell: a = 11.3557(2) Å, b = 13.3857(3) Å, c = 16.5454(4) Å, α = 81.490(10)°, β = 86.604(1)°, γ = 80.007(1)°; v = 2448.09(9) Å<sup>3</sup>, Z = 2. T = 173 K. Data/restraints/parameters 8562/14/645 with Final R indices [I > 2σ(I)] R<sub>1</sub> = 0.0637, wR<sub>2</sub> = 0.1738. Crystallographic data excluding structure factors have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 737941. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ, UK [Direct line: +44 1223 762910, fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
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