Regioselective Synthesis of Antipodal β-Tetrabrominated *meso*-Tetraarylporphyrins

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A series of *meso*-tetraarylporphyrins bearing electron-donor or electron-withdrawing substituents at the *meso*-phenyl groups were examined for antipodal β-pyrrole tetrabromination using different brominating agents. Porphyrins bearing electron-donor substituents undergo bromination at moderate temperatures with *N*-bromosuccinimide as the brominating agent while the electron-deficient porphyrins require liq. Br_2 at room temperature. The brominated porphyrins were isolated in moderate to very good yields. Synthesized compounds were characterized by electronic absorption, ^{1}H NMR, and mass spectroscopic methods. Regioselectivity of an electron-deficient porphyrin, 2,3,12,13-tetrabromo-5,10,15,20-tetrakis(4-methoxycarbonylphenyl)porphyrin was examined by single-crystal X-ray structure analysis and showed antipodal β-pyrrole bromo substitution.

The past two decades have witnessed numerous reports on the synthesis and exploration of the properties of highly substituted porphyrins.[1] Notably, perhalogenated high-valent metalloporphyrins have been employed in oxidative transformation of organic substrates in the presence of strong oxygen donors to mimic cytochrome P_{450} like activity.[2–5] These halogenated porphyrins exhibited greater catalytic robustness in the presence of strong oxygen donors. Perhaloporphyrins exhibit dramatic changes in the optical spectral, electrochemical redox, and stereochemical properties which make these porphyrins unique.[6] Furthermore, perhalogenated porphyrins exhibit facile metallation reactions.[7] Partially brominated or perbrominated porphyrins have been employed as useful precursors in the synthesis of other functionalized porphyrins that are synthetically difficult.[8] Mixed substituted porphyrins reported by Senge et al.[9] and others[8f] indicated the variation in nonplanar conformation of the macrocycle. Earlier, the synthesis of antipodal β-tetrabrominated tetraphenylporphyrin, H_2TPPBr_4 using *N*-bromosuccinimide as the brominating agent was reported.[10] Regioselective synthesis of such antipodal tetrabromo-*meso*-tetraarylporphyrins is largely unknown.

Herein, we report the regioselective synthesis of various tetrabrominated tetraarylporphyrins, $H_2TArPBr_4$s (Figure 1) bearing varying *meso*-aryl groups at room and slightly higher temperatures. These porphyrins were prepared in moderate to very good yields. Crystal structure of the tetrabrominated electron-deficient tetraarylporphyrin showed substitution of the bromo groups at the β-pyrrole antipodal positions.

Experimental

Solvents employed in this study were of analytical grade and distilled prior to use.[11] 1,1,2,2-Tetrachloroethane, CH_2Cl_2, and $CHCl_3$ purchased from Rankem (India) were distilled before use. Benzyltrimethylammonium tribromide, and liq. Br_2 procured from Sigma-Aldrich (India) were used as received. *N*-bromosuccinimide, NBS was recrystallized from hot water prior to use. Pyridinium bromochromate was prepared using a literature method.[12] All the aryl-aldehydes procured from Sigma-Aldrich (India) were used as received. Pyridine and pyrrole purchased from SRL chemicals (India) were distilled before use.[11] Aluminum sheets coated with silica gel thin layer chromatography plates procured from Merck (Germany) were used as received. Silica gel (100–200 mesh) for column chromatography procured from Rankem (India) was used as received. Various tetraarylporphyrins (H_2TArPs) and their mixed *meso*-aryl-substituted porphyrins have been prepared using literature procedures.[13]

Instrumentation. Optical absorption spectra of the brominated porphyrins were recorded on a JASCO V550 model UV–visible absorption spectrophotometer using 10-mm path length cells in CH_2Cl_2 at 298 K. ^{1}H NMR spectra of the porphyrins were recorded on a Bruker 400 MHz Avance spectrometer in $CDCl_3$ at 298 K. Mass spectral measurements of the samples were carried out using electro-spray ionization (ESI) mass spectrometer model Micromass Q-TOF micro™ in 10% formic acid in methanol/$CHCl_3$ medium under positive ion mode.

Crystal structure data of $H_2T(4\text{-}CO_2CH_3Ph)P\cdot 2(CHCl_3)$ complex was collected on a Bruker AXS (Kappa Apex2) CCD diffractometer at 173 K. Monoclinic, space group, $C2/c$, $a = 37.2210(14)$ Å, $b = 7.1903(2)$ Å, $c = 24.5806(10)$ Å, $\beta = 123.207(4)^\circ$, $\alpha = \gamma = 90.00^\circ$, $V = 5504.2(3)$ Å^3, $Z = 4$. $d_{calcd} = 1.691$ g m^{-3}, Mo Kα = 0.71073 Å, $\theta_{max} = 25^\circ$, $R = 0.0747$, $wR = 0.2127$ for 4852 unique reflections, refinements on F^2. SIR92 (WINGX) program was used to solve the structure by direct methods. Structure refinement was performed using SHELXS-97 and SHELXL-97 software.[14] The crystallographic information file for $H_2T(4\text{-}CO_2CH_3Ph)PBr_4\cdot 2(CHCl_3)$ (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 657108. Copies of the data can be obtained, free of charge, on application to CCDC, 12, Union Road, Cambridge, CB2 1EZ, UK (Fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

β-Tetrabromination of Electron-Rich Tetraarylporphyrins.

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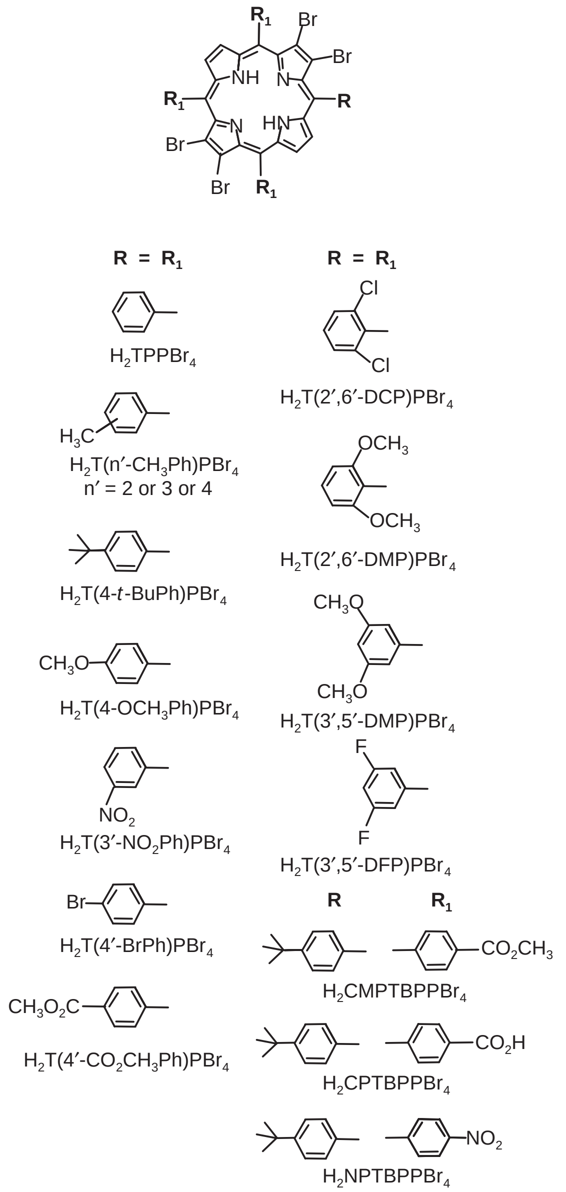

Figure 1. Chemical structures of tetrabrominated *meso*-tetraarylporphyrins.

Typical bromination procedure for some electron-rich tetraarylporphyrins is as follows: To a stirred solution of $H_2T(3\text{-}CH_3Ph)P$ (0.2 g, 0.3 mmol) in 120 mL of freshly distilled $CHCl_3$, freshly recrystallized NBS[8] (0.38 g, 1.78 mmol) in $CHCl_3$ (20 mL) was added dropwise over a period of 30 min. Then, the reaction mixture was allowed to stir vigorously for 24 h. At the end of this period, the solvent was rotary evaporated to dryness under vacuum. The resulting residue was redissolved in minimum amount of $CHCl_3$ and chromatographed on a silica gel column using $CHCl_3$ as the eluant. The fast moving fraction was collected and rotary evaporated to dryness, recrystallised from $CHCl_3/CH_3OH$ (1:3, v/v) mixture and dried under vacuum (3 mbar) at 90 °C for 6 h. Yield of the product was found to be 0.21 g (70%). With similar concentration of NBS, $H_2T(3\text{-}CH_3Ph)P$ in refluxing $CHCl_3$ for 4 h yielded $H_2T(3\text{-}CH_3Ph)PBr_4$. Then, the $CHCl_3$ was rotary evaporated to dryness and the residue was washed with CH_3OH (10 mL). Then, the reaction mixture was processed as described above. Yield of the product was found to be 0.162 g (55%). Some electron-rich or mixed substituted tetraarylporphyrins can be brominated using the above procedure.

$H_2T(3\text{-}CH_3Ph)PBr_4$: UV–vis ($CH_2Cl_2$) λ_{max}, nm (log ε) 437 (5.46), 535 (4.25), 616 (3.59), 684 (3.97). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 4H, β-pyrrole-H), 7.99 (brs, 8H, *o*-Ar-H), 7.64 (m, 8H, *m*- and *p*-Ar-H), 2.66 (s, 12H, –CH_3), −2.85 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 989 (calcd, 986.44). Elemental analysis calcd for $C_{48}H_{34}N_4Br_4$: C, 58.45; H, 3.47; N, 5.68%. Found: C, 57.98; H, 3.30; N, 5.45%.

$H_2T(2\text{-}CH_3Ph)PBr_4$: UV–vis ($CH_2Cl_2$) λ_{max}, nm (log ε) 430 (5.17), 526 (4.04), 604 (3.51), 660 (3.60). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (m, 4H, β-pyrrole-H), 7.84 (m, 4H, *o*-Ar-H), 7.70 (t, $J = 7.1$ Hz, 4H, *p*-Ar-H), 7.55 (m, 8H, *m*-Ar-H), 2.02 (m, 12H, –CH_3), −3.0 (d, $J = 17.2$ Hz, 2H, imino-H). ESI-MS (*m*/*z*): Found: 987.0 (calcd, 986.44). Elemental analysis calcd for $C_{48}H_{34}N_4Br_4$: C, 58.45; H, 3.47; N, 5.68%. Found: C, 58.29; H, 3.55; N, 5.36%.

$H_2T(4\text{-}t\text{-}BuPh)PBr_4$: UV–vis ($CH_2Cl_2$) λ_{max}, nm (log ε) 440 (5.45), 538 (4.21), 618 (3.29), 691 (4.02). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 4H, β-pyrrole-H), 8.11 (d, $J = 8.4$ Hz, 8H, *o*-Ar-H), 7.79 (d, $J = 8.4$ Hz, 8H, *m*-Ar-H), 1.59 (s, 36H, *t*-butyl-H), −2.72 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 1155 (calcd, 1154.76).

$H_2T(4\text{-}CH_3Ph)PBr_4$: UV–vis ($CH_2Cl_2$) λ_{max}, nm (log ε) 441 (100), 539 (7.5), 617 (sh), 688 (5.5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 4H, β-pyrrole-H), 8.06 (d, $J = 8.0$ Hz, 8H, *o*-Ar-H), 7.58 (d, $J = 8.0$ Hz, 8H, *m*-Ar-H), 2.70 (s, 12H, –CH_3), −2.78 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 987 (calcd, 986.44).

$H_2T(4\text{-}OCH_3Ph)PBr_4$: UV–vis ($CH_2Cl_2$) λ_{max}, nm (log ε) 446 (5.37), 543 (4.12), 590 (3.82), 700 (3.97). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 4H, β-pyrrole-H), 8.09 (d, $J = 8.4$ Hz, 8H, *o*-Ar-H), 7.32 (d, $J = 8.4$ Hz, 8H, *m*-Ar-H), 4.09 (s, 12H, –OCH_3), −2.71 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 1051.0 (calcd, 1050.44). Elemental analysis calcd for $C_{48}H_{34}N_4O_4Br_4$: C, 54.88; H, 3.26; N, 5.33%. Found: C, 54.65; H, 3.10; N, 5.40%.

$H_2NPTBPPBr_4$: UV–vis (CH_2Cl_2) λ_{max}, nm (log ε) 441 (5.44), 538 (4.26), 613 (sh), 689 (4.04). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, $J = 5.2$ Hz, 1H, β-pyrrole-H), 8.76 (q, $J = 4$ Hz, 2H, β-pyrrole-H), 8.65 (d, $J = 8.56$ Hz, 2H, *o*-Ar(3-NO_2)-H), 8.56 (d, $J = 5.2$ Hz, 1H, β-pyrrole-H), 8.40 (d, $J = 8.71$ Hz, 2H, *m*-Ar(3-NO_2)-H), 8.10 (t, $J = 7.12$ Hz, 6H, *o*-Ar(4-*t*-butyl)-H), 7.80 (d, $J = 7.68$ Hz, 6H, *m*-Ar(4-*t*-butyl)-H), 1.59 (s, 27H, *t*-butyl-H), −2.73 (d, $J = 12.3$ Hz, 2H, imino-NH). MALDI-TOF-MS (*m*/*z*): Found: 1143.69 (calcd, 1143.65). Elemental analysis calcd for $C_{56}H_{49}N_5O_2Br_4$: C, 58.81; H, 4.32; N, 6.12%. Found: C, 59.05; H, 4.12; N, 6.01%.

$H_2CMPTBPPBr_4$: UV–vis (CH_2Cl_2) λ_{max}, nm (log ε) 442 (5.37), 539 (4.33), 610 (sh), 687 (4.15). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (m, 4H, β-pyrrole-H), 8.46 (d, $J = 7.2$ Hz, 2H, *o*-Ar(4-CO_2CH_3)), 8.30 (d, $J = 7.0$ Hz, 2H, *m*-Ar(4-CO_2CH_3)), 8.10 (m, 6H, *o*-Ar(4-*t*-butyl)-H), 7.80 (d, $J = 7.0$ Hz, 6H, *m*-Ar(4-*t*-butyl)-H), 4.11 (s, 3H, CO_2CH_3), 1.61 (s, 27H, *t*-butyl-H), −2.73 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 1157.0 (calcd, 1156.69). Elemental analysis calcd for $C_{58}H_{52}N_4O_2Br_4$: C, 60.23; H, 4.53; N, 4.84%. Found: C, 60.11; H, 4.21; N, 4.62%.

$H_2T(4\text{-}BrPh)PBr_n$. Bromination of $H_2T(4\text{-}BrPh)P$ (0.1 g, 0.10 mmol) was carried out with NBS (0.11 g, 0.60 mmol) in TCE (30 mL) at 90 °C for 24 h. At the end of this period, the solvent was rotary evaporated, the residue washed with methanol and recrystallized from $CH_3OH/CHCl_3$ (3:1, v/v) solvent mixture. The product on silica gel TLC in $CHCl_3$/hexane (2:3, v/v) mixture shows two spots. UV–vis ($CHCl_3$) λ_{max}, nm (relative intensity) 437 (100), 532 (15), 606 (sh), 677 (9). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.67 (m, 4H, β-pyrrole-H), 8.02 (m, 8H, *o*-Ar-H), 7.92 (m, 8H, *m*-Ar-H), −2.80 (m, 2H, imino-NH).

H$_2$T(2,6- or 3,5-DMP)PBr$_n$. Bromination of H$_2$T(2,6- or 3,5-DMP)P derivatives were performed with 6–12 molar equiv of NBS in 1,1,2,2-tetrachloroethane at (110–120 °C) for 24 h. The reaction mixture was rotary evaporated and washed with CH$_3$OH and air dried. The product was chromatographed on a basic alumina column using CHCl$_3$ as the eluant. UV–visible and ^{1}H NMR data of the product is listed below for the reaction with 12 molar equiv of NBS.

H$_2$T(2,6-DMP)PBr$_n$: The product on silica gel TLC in CHCl$_3$ exhibits three spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 429 (100), 521 (13), 598 (7), 655 (6.5). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.78 (m, 4H, β-pyrrole-H), 7.97 (m, 4H, *m*-Ar-H), 6.99 (m, 4H, *p*-Ar-H), 3.57 (m, 12H, OCH$_3$), 3.07 (m, 12H, OCH$_3$), −2.86 (m, 2H, imino-NH).

H$_2$T(3,5-DMP)PBr$_n$: The product on silica gel TLC in acetone/CHCl$_3$ (1:1, v/v), two spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 433 (100), 527 (13), 603 (7), 659 (6). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.69 (m, 4H, β-pyrrole-H), 7.22 (m, 2H, *o*-Ar-H), 7.01 (m, 2H, *p*-Ar-H), 6.95 (d, $J = 2.3$ Hz, 2H, *p*-Ar-H), 4.14 (m, 16H, OCH$_3$), 3.92 (m, 8H, OCH$_3$), −3.05 (m, 2H, imino-NH).

***β*-Tetrabromination of Electron-Deficient Tetraarylporphyrins.** To a stirred solution of H$_2$T(4-CO$_2$CH$_3$Ph)P (0.20 g, 0.24 mmol), liq. Br$_2$ (0.36 mL, 7.1 mmol) (Caution: Liq. Br$_2$ is corrosive and harmful) in 30 mL was added dropwise over a period of 30 min and the reaction mixture was stirred for a further period of 4 h. At the end of this period, pyridine (0.6 mL) in 5 mL of CHCl$_3$ was added dropwise and the solution was allowed to stir for 15 h. To the reaction mixture, aqueous sodium disulfite (20%) 100 mL was added and the solution was stirred for 30 min. The organic layer was dried over anhydrous Na$_2$SO$_4$, concentrated to small volume and separated on a silica gel column using 1% acetone in CHCl$_3$ as the eluant. The yield of the product, H$_2$T(4-CO$_2$MePh)PBr$_4$ was found to be 0.137 g (50%). Similarly, H$_2$T(3-NO$_2$Ph)PBr$_4$ and H$_2$T(3,5-DFPh)PBr$_4$ were prepared using the above procedure.

H$_2$T(4-CO$_2$CH$_3$Ph)PBr$_4$: UV–vis (CH$_2$Cl$_2$) λ_{max}, nm (log ε) 437 (5.35), 533 (4.19), 606 (3.63), 683 (3.79). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.65 (s, 4H, β-pyrrole-H), 8.45 (d, $J = 8.4$ Hz, 8H, *o*-Ar-H), 8.24 (d, $J = 8.4$ Hz, 8H, *m*-Ar-H), 4.11 (s, 12H, –CO$_2$CH$_3$), −2.85 (s, 2H, imino-H). ESI-MS (*m*/*z*): Found: 1163 (calcd, 1162.48). Elemental analysis calcd for $C_{48}H_{34}N_4O_8Br_4$: C, 51.73; H, 3.08; N, 5.03%. Found: C, 51.90; H, 3.25; N, 5.23%.

H$_2$T(3-NO$_2$Ph)PBr$_4$: UV–vis (CH$_2$Cl$_2$) λ_{max}, nm (log ε) 437 (5.34), 532 (4.21), 610 (3.64), 675 (3.71). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.05 (brs, 4H, β-pyrrole-H), 8.71 (m, 8H, *o*-Ar-H), 8.56 (m, 4H, *m*-Ar-H), 8.02 (m, 4H, *p*-Ar-H), −2.85 (s, 2H, imino-NH). ESI-MS (*m*/*z*): Found: 1111 (calcd, 1110.32). Elemental analysis calcd for $C_{44}H_{22}N_8O_8Br_4$: C, 47.60; H, 2.00; N, 10.09%. Found: C, 47.51; H, 2.31; N, 9.96%.

H$_2$T(3,5-DFP)PBr$_4$: UV–vis (CH$_2$Cl$_2$) λ_{max}, nm (log ε) 436 (5.21), 533 (4.20), 609 (3.71), 676 (3.72). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.78 (s, 4H, β-pyrrole-H), 7.71 (dd, $J = 7.2$, 2.0 Hz, 8H, *o*-Ar-H), 7.32 (m, 4H, *p*-Ar-H), −3.03 (s, 2H, imino-NH). ESI-MS (*m*/*z*): Found: 1077 (calcd, 1074.26). Elemental analysis calcd for $C_{44}H_{18}N_4Br_4F_8$: C, 49.20; H, 1.69; N, 5.22%. Found: C, 48.95; H, 1.42; N, 5.10%.

H$_2$T(2,6-DCP)PBr$_n$. Bromination of H$_2$T(2,6-DCP)P with 30 molar equiv of liq. Br$_2$. The reaction was performed as described above. The product on silica gel TLC in CHCl$_3$/hexane (3:7, v/v) solvent mixture shows four spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 427 (100), 530 (17), 608 (13), 665 (18). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.71 (m, 5H, β-pyrrole-H), 7.76 (m, 12H, *m*- and *p*-Ar-H), −2.61 (m, 2H, imino-NH).

H$_2$T(4-BrPh)PBr$_n$. Bromination of H$_2$T(4-BrPh)P with 30 molar equiv of liq. Br$_2$. The reaction was carried out as described above. The product on silica gel TLC in CHCl$_3$/hexane (3:7, v/v) mixture exhibits three spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 445 (100), 536 (9), 611 (5), 686 (6). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.61 (m, 3H, β-pyrrole-H), 8.04 (m, 8H, *o*-Ar-H), 7.99 (m, 8H, *m*-Ar-H), −2.90 (m, 2H, imino-NH).

Bromination of H$_2$TPP with Benzyltrimethylammonium Tribromide. The tetrabromination of H$_2$TPP (0.1 g, 0.16 mmol) with benzyltrimethylammonium tribromide (0.38 g, 0.98 mmol, 6 molar equiv) was carried out in CHCl$_3$/CH$_3$OH (95:5, v/v) mixture (60 mL) in presence of CaCO$_3$ (0.1 g) either stirring at room temperature or under refluxed conditions for 48 h.[15] The progress of the reaction was monitored by UV–visible and TLC. At the end of 48 h, the product was evaporated to dryness. Then, it was washed with CH$_3$OH and the filtrate was dried at 60 °C under vacuum to obtain purple-colored residue. The product on silica gel TLC in CHCl$_3$/hexane (1:2, v/v) mixture shows three spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 425 (100), 521 (7), 598 (5), 653 (3). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.80 (m, 6H, β-pyrrole-H), 8.14 (m, 8H, *o*-phenyl-H), 7.61 (m, 12H, *m*- and *p*-phenyl-H), −2.86 (m, 2H, imino-NH).

Bromination of H$_2$TPP with Pyridinium Bromochromate. H$_2$TPP (0.10 g, 0.16 mmol) was dissolved in 60 mL of CHCl$_3$, to this solution, pyridinium bromochromate (0.253 g, 1.0 mmol) was dissoved in 15 mL of CHCl$_3$/CH$_3$OH (1:1, v/v) mixture and added dropwise for a period of 10 min. The reaction mixture was stirred for 24 h and was washed with (100 mL × 2) water. Then, the organic layer was separated, washed with dilute HCl (100 mL × 2) followed by aqueous NaHCO$_3$ (10%) and dried over anhydrous Na$_2$SO$_4$. The product on silica gel TLC in CHCl$_3$/hexane (2:3, v/v) mixture exhibits two spots. UV–vis (CHCl$_3$) λ_{max}, nm (relative intensity) 426 (100), 523 (9), 598 (4), 658 (4). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.79 (m, 6H, β-pyrrole-H), 8.17 (m, 8H, *o*-phenyl-H), 7.77 (m, 12H, *m*- and *p*-phenyl-H), −2.90 (m, 2H, imino-NH).

Preparation of H$_2$CPTBPPBr$_4$ Derivative. This was achieved by de-esterification of H$_2$CMPTBPPBr$_4$ derivative using a reported procedure.[16] Yield of the product was found to be 75%.

H$_2$CPTBPPBr$_4$: UV–vis (CH$_2$Cl$_2$) λ_{max}, nm (log ε) 441 (5.25), 539 (4.02), 611 (sh), 687 (3.82). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.82 (d, $J = 5.04$ Hz, 1H, β-pyrrole-H), 8.77 (m, 2H, β-pyrrole-H), 8.64 (d, $J = 5.0$ Hz, 1H, β-pyrrole-H), 8.55 (d, $J = 8.1$ Hz, 2H, *o*-Ar(4-CO$_2$H)-H), 8.35 (d, $J = 8.1$ Hz, 2H, *m*-Ar(4-CO$_2$H)-H), 8.12 (m, 6H, *o*-Ar(4-*t*-butyl)-H), 7.81 (d, $J = 8.1$ Hz, 6H, *m*-Ar(4-*t*-butyl)-H), 1.61 (s, 12H, *t*-butyl-H), −2.71 (brs, 2H, imino-NH). ESI-MS (*m*/*z*): Found: 1143 (calcd, 1142.67). Elemental analysis calcd for $C_{57}H_{50}N_4O_2Br_4$: C, 59.91; H, 4.41; N, 4.90%. Found: C, 60.0; H, 4.18; N, 4.79%.

Results and Discussion

Precursor tetraarylporphyrins, H$_2$TArPs were prepared using reported procedures.[13] The choice of the free base porphyrins over metal complexes of the TArPs is to induce regioselectivity at the antipodal β-pyrrole positions.[10c] Unlike metalloporphyrins,[17] free-base porphyrins retain 18-electron cyclic polyene

Table 1. Synthesis of Tetrabrominated Tetraarylporphyrins in $CHCl_3$

Entry	Porphyrin	Brominating agent	Yield/%[a)]	
			Room temp	Reflux
1	H_2TPPBr_4	NBS	70	66
2	$H_2T(4\text{-}CH_3Ph)PBr_4$	NBS	65	60
3	$H_2T(3\text{-}CH_3Ph)PBr_4$	NBS	70	55
4	$H_2T(2\text{-}CH_3Ph)PBr_4$	NBS	—	25[b)]
5	$H_2T(4\text{-}t\text{-}ButylPh)PBr_4$	NBS (5 mol. amt.)	70	50
6	$H_2T(4\text{-}OCH_3Ph)PBr_4$	NBS (4.5 mol. amt.)	72	48
7	$H_2CMPTBPPBr_4$	NBS	77	68
8	$H_2NPTBPPBr_4$	NBS	80	55
9	$H_2T(3\text{-}NO_2Ph)PBr_4$	Liq. Br_2	55	—
10	$H_2T(4\text{-}CO_2CH_3Ph)PBr_4$	Liq. Br_2	50	—
11	$H_2T(3,5\text{-}DFPh)PBr_4$	Liq. Br_2	46	—
12	$H_2T(2,6\text{-}DMP)PBr_n$	NBS (12 mol. amt.)	—	—[c)]
13	$H_2T(3,5\text{-}DMP)PBr_n$	NBS (12 mol. amt.)	—	—[c)]
14	$H_2T(2,6\text{-}DCP)PBr_n$	Liq. Br_2	—[d)]	—
15	$H_2T(4\text{-}BrPh)PBr_n$	Liq. Br_2	—[d)]	—

a) In $CHCl_3$. b) At 80 °C in TCE. c) Mixture of products in TCE at 110–120 °C. d) Mixture of brominated products.

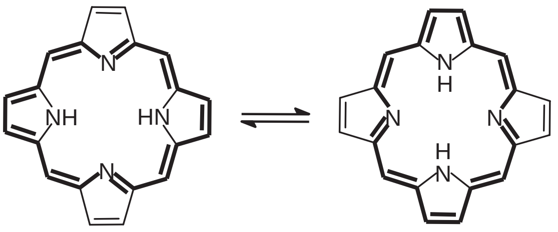

Figure 2. Tautomers of porphine showing isolated antipodal β-pyrrole double bonds. 18π electron delocalization pathway is shown in heavy line.

which isolate the two double bonds at the antipodal 2,3,-12,13-positions of the β-pyrrole carbons (Figure 2) and are susceptible to electrophilic substitution reactions.[10b] In this article, we have examined the effect of *meso*-aryl substituents on the antipodal tetrabromination of the H_2TArPs bearing various groups on the *meso*-aryl rings. Generally, electron donor *meso*-aryl substituents produce cathodic shift and electron-withdrawing substituents produce anodic shift of their redox potentials.[18]

Synthesis of brominated tetraarylporphyrins was carried out at room temperature to identify the feasibility of the reaction as well as to improve the yield of the tetrabrominated porphyrins. Earlier report on the synthesis of H_2TPPBr_4 in refluxing $CHCl_3$ with 6 molar equiv of *N*-bromosuccinimide, NBS showed 65% yield.[10d] At room temperature, with 4.5-to-6 molar equiv of NBS over a period of 24 h in $CHCl_3$ or CH_2Cl_2 produced electron-rich tetrabrominated arylporphyrins (Table 1) in higher yields (65–80%). Among the porphyrins, $H_2T(4\text{-}OCH_3Ph)P$ showed higher reactivity with NBS even at room temperature and the yield of the tetrabrominated product increases with decrease in amount of the brominating agent up until 4.5 molar. Interestingly, $H_2T(2\text{-}CH_3Ph)P$ in $CHCl_3$ or CH_2Cl_2 with 6 molar equiv of NBS fails to show completion of the bromination at ambient conditions while at 80 °C in 1,1,2,2-tetrachloroethane, TCE produced tetrabrominated product in 25% yield.

Mixed *meso*-aryl-substituted porphyrins, $H_2NPTBPP$ and $H_2CMPTBPP$ exhibited facile bromination with NBS in $CHCl_3$ medium to generate very good yields of the corresponding antipodal tetrabrominated products (Table 1). However, electron-deficient porphyrins, H_2TArPs [$H_2T(4\text{-}CO_2CH_3Ph)P$, $H_2T(3\text{-}NO_2Ph)P$, $H_2T(3,5\text{-}DFP)P$, and $H_2T(4\text{-}BrPh)P$] fail to undergo regioselective tetrabromination with 6 molar equiv of NBS even under reflux conditions in $CHCl_3$ or in TCE at high temperatures upto a period of 24 h and yielded a mixture of products.

Tetrabromination of electron-rich tetraarylporphyrins with liq. Br_2 exhibited considerable degradation of the porphyrin. This is may be attributed to the ease of oxidation of the porphyrin ring by the liq. Br_2 since the first one electron oxidation potentials are shifted cathodic[19] relative to the Br_2 oxidation potential[19] (+1.08 V). Regioselective tetrabromination of electron-deficient H_2TArP derivatives was achieved using 30 molar equiv of liq. Br_2 at room temperature with moderate to good yields (Table 1). The stability of the substituted H_2TArPs bearing electron-withdrawing groups is perhaps due to the anodic shift in first one electron oxidation potential of porphyrin π-system (>1.10 V)[19] relative to oxidation potential of Br_2 (1.08 V). An increase in concentration of the liq. Br_2 (>30 molar equiv) lead to decrease in yield of the brominated porphyrin and also formation of higher brominated products.

Other highly substituted tetraarylporphyrins [$H_2T(2,6\text{-}$ or $3,5\text{-}DMP)P$ and $H_2T(2,6\text{-}DCP)$] showed a mixture of brominated products with 6–12 molar equiv of NBS in TCE at 110–120 °C. Further, $H_2T(4\text{-}BrPh)P$ derivative with liq. Br_2 (30 molar equiv) in $CHCl_3$ yielded mixture of products. This was evidenced from the TLC, UV–visible, and ^1H NMR data. The lower red-shift and the higher brominated products in the $H_2T(2,6\text{-}$ or $3,5\text{-}DMP)P$ indicates the possible bromination at the *meso*-aryl as well as at the β-pyrrole positions. Such higher bromination of the $H_2T(2,6\text{-}$ or $3,5\text{-}DMP)P$ derivatives is perhaps due to the electron-rich nature of the *meso*-aryl groups. The electron-deficient $H_2T(2,6\text{-}DCP)P$ with NBS or in liq. Br_2 (30 molar equiv) generated mixtures of products and it

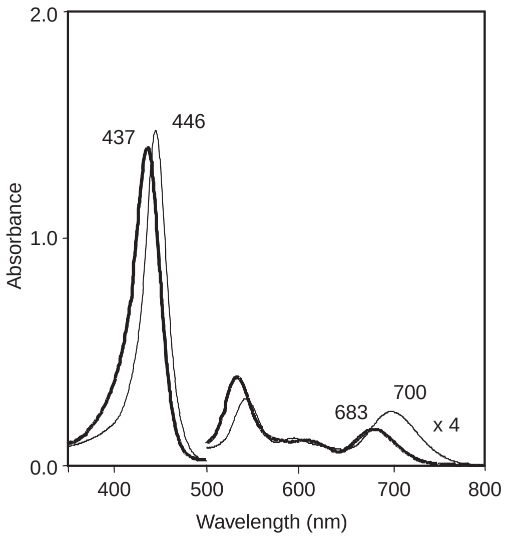

Figure 3. Optical absorption spectra of $H_2T(4\text{-}CO_2\text{-}CH_3Ph)PBr_4$ (heavy line) and $H_2T(4\text{-}OCH_3Ph)PBr_4$ (thin line) in CH_2Cl_2 at 298 K. The concentrations of the porphyrins were 5 µM. Q bands are magnified by four times for clarity.

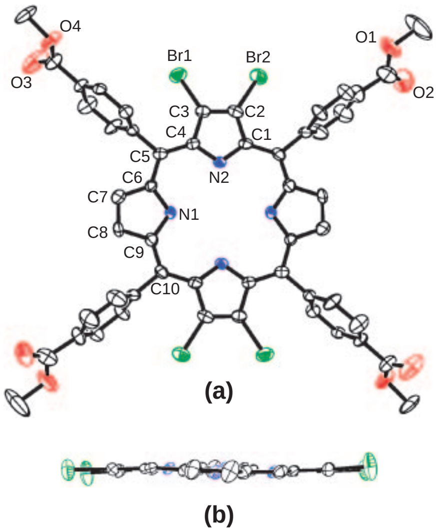

Figure 4. ORTEP of $H_2T(4\text{-}CO_2MePh)PBr_4 \cdot 2(CHCl_3)$ complex at 40% probability level. (a), Top view; (b), side view. The hydrogens, *meso*-phenyl, and $CHCl_3$ groups are not shown for clarity.

is possibly due to steric and/or electronic factors. A previous report on the bromination of CuT(3,5-DMP)P with liq. Br_2 showed the formation of 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetrakis(2,6-dibromo-3,5-dimethoxyphenyl)porphinatocopper(II) complex.[20]

Tetrabromination reaction of H_2TPP was also performed with other brominating agents such as benzyltrimethylammonium tribromide (BTMAT) and pyridinium bromochromate (PBC). The tetrabromination of H_2TPP with 6 molar equiv of BTMAT in $CHCl_3/CH_3OH$ in the presence of $CaCO_3$ powder at room temperature for 48 h and also under reflux conditions yielded partially brominated products, H_2TPPBr_n ($n = 1$–3). Similar product distribution was observed for the reaction of H_2TPP with PBC (6 molar equiv) in $CHCl_3/CH_3OH$. This was evidenced from the less red-shifted absorption (B and Q bands) and the multiplicity of the β-pyrrole proton NMR resonances of the H_2TPPBr_n products (see the Experimental Section).

Among the tetrabromoporphyrin derivatives, $H_2T(4\text{-}CH_3Ph)PBr_4$ showed very poor solubility in different organic solvents including CH_2Cl_2, $CHCl_3$, DMF, and DMSO etc. All the synthesized $H_2TArPBr_4$s were characterized by electronic absorption, ^{1}H NMR and mass spectroscopic methods. Tetrabrominated tetraarylporphyrins showed characteristic red-shifted electronic absorption spectral features. Typical absorption spectra of $H_2T(4\text{-}OCH_3Ph)PBr_4$ and $H_2T(4\text{-}CO_2CH_3Ph)PBr_4$ in CH_2Cl_2 are shown in Figure 3. Of the synthesized derivatives, $H_2T(4\text{-}OCH_3Ph)PBr_4$ exhibited the most red-shifted absorption, which is possibly due to the conjugative effect of the 4-methoxyphenyl groups with the porphyrin π-system. In general, these porphyrins feature a "B" and three visible, Q bands in contrast to a "B" and four "Q" bands observed for the H_2TArP derivatives. $H_2TArPBr_4$ derivatives showed approximately 20–30 nm red shift of the "B" relative to their unsubstituted tetraarylporphyrins. However, the long wavelength, Q(0,0) band was red shifted by ≈20–55 nm. Molar absorption coefficients of these derivatives are comparable to the reported values of H_2TPPBr_4 derivative.[10,21]

The ^{1}H NMR spectra of $H_2TArPBr_4$ derivatives exhibited resonances arising from β-pyrrole, *meso*-aryl, and imino protons. In general, β-pyrrole protons were up-fielded by 0.30–0.40 ppm while the *meso*-aryl protons and imino hydrogens are marginally down-fielded relative to their corresponding ^{1}H NMR spectra of the unbrominated H_2TArPs in $CDCl_3$ at 298 K. The mixed substituted tetrabrominated tetraarylporphyrins [$H_2NPTBPP$, $H_2CMPTBPPBr_4$, and $H_2CPTBPPBr_4$] and $H_2T(2\text{-}CH_3Ph)PBr_4$ showed multiplets for the β-pyrrole protons due to the asymmetric nature of the porphyrin. The imino hydrogen resonances are not significantly affected relative to their corresponding unsubstituted porphyrin resonances. Furthermore, the integrated intensity of the proton resonances of the aryl rings correlates with the β-pyrrole proton resonances and they are consistent with the proposed structures. The electrospray ionization mass spectroscopic analysis of the brominated porphyrins in $CH_3OH/CHCl_3$ solvent medium in formic acid showed a cluster of peaks to the main peak and it is due to the presence of bromine atoms. The observed mass spectral data is in good agreement with the calculated values.

To examine the regioselectivity of the bromo groups at the pyrrole positions, the crystal structure of the $H_2(4\text{-}CO_2CH_3Ph)PBr_4$ complex was examined. The crystals of $H_2T(4\text{-}CO_2MePh)PBr_4 \cdot 2(CHCl_3)$ complex were grown by vapor diffusion of methanol to a solution of the porphyrin in $CHCl_3$ over a period of four days. The ORTEP of the porphyrin is shown in Figure 4. The structure shows four bromo substituents at the antipodal β-pyrrole positions with nearly planar geometry of the 24-atom macrocyclic ring (within ±0.10 Å) and the two-bromo groups on the same pyrrole unit are up and down by 0.145 Å. This is reflected from the side on view of the complex (Figure 4b). Previous report on the H_2TPPBr_4 showed nearly planar geometry of the macrocycle.[22] In the present structure, the opposite nitrogens of the pyrrole rings with bromo groups are separated by 4.250 Å while the imino nitrogens of the other two pyrrole rings are at 4.095 Å away. These distances are marginally higher than those reported for H_2TPP structure[23] (4.06 and 4.20 Å) and similar to that reported for H_2TPPBr_4 (4.21(2) and 4.10(2) Å). This is possibly due to the steric and electronic factors induced by the bromo groups at the pyrrole rings of the macrocycle.[24] The *para*-methyl ester groups of the phenyl groups are not completely coplanar with the aryl ring. The average C_β–C_β bond length for the bromo-substituted pyrroles is 1.347(4) Å and for the other pyrroles is 1.366(3) Å and are similar to that reported for H_2TPPBr_4. Phenyl rings makes an average dihedral angle of 81.80(2)° with respect to the 24 atom core which is considerably higher than that found in the H_2TPP structure (72°).

Conclusion

In summary, the present work reports the regioselective β-tetrabromination of tetraarylporphyrins with varying substituents at ambient to mild reaction temperatures. The regioselective tetrabromination of electron-rich H_2TArPs was achieved using *N*-bromosuccinimide while electron-deficient H_2TArPs undergo bromination under liq. Br_2. The stability of the electron-deficient porphyrins in the presence of liq. Br_2 is perhaps responsible for the regioselective bromination of these systems. The tetrabrominated products were isolated in moderate to very good yields. The crystal structure of the electron-deficient $H_2T(4\text{-}CO_2CH_3Ph)PBr_4$ derivative was examined and it showed tetrabromination at the antipodal β-pyrrole positions.

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Supporting Information

^{1}H NMR and mass spectra of β-tetrabrominated tetraarylporphyrins. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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