Trans-Disubstituted Tetraarylporphyrin as a Precursor to Larger Molecular Architectures: An Application of MacDonald "2 + 2" Porphyrin Synthesis in Aqueous Anionic Surfactant

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Introduction

Tetraarylporphyrins have been employed as building blocks for making various assemblies that are of interest to materials scientists and bioinorganic chemists. These assemblies include multiporphyrin arrays[1] and porphyrins with appended axial ligands or steric constraints for controlling the axial ligation.[2] Although most of the *meso*-substituted porphyrins used for these purposes have four identical aryl substituents, less symmetric porphyrins are expected to make more varied structures possible. Specifically, *trans*-*meso*-A_2B_2 porphyrins may be employed to make assemblies that are difficult to make from the conventional *meso*-A_4 porphyrins. First, *trans*-*meso*-A_2B_2 porphyrins may be used to make one-dimensional structures and therefore may be employed to make molecular wires,[3] transmembrane artificial proton pumps,[4] and nonbranching squares.[5] Second, assemblies made from *trans*-*meso*-A_2B_2 porphyrins offer better control of *both* axial ligation sites.[6,7]

Unfortunately, the development of such porphyrin assemblies has been hampered by the difficulty of preparing isomerically pure *trans*-*meso*-A_2B_2 porphyrins, by either chromatographic separation or rational synthesis. Traditionally, low-symmetry tetraarylporphyrins have been prepared by reaction of pyrrole with two different arenecarbaldehydes, followed by chromatographic isolation of the desired species. Porphyrins with *meso*-AB_3 structure are easy to isolate using this method.[8,9] However, *meso*-A_2B_2 porphyrins are usually found to elute simultaneously as *trans*- and *cis*-isomers, thus precluding the preparation of isomerically pure *meso*-A_2B_2 porphyins. The only exceptions are porphyrins that are substituted by either aminophenyl[10,11] or pyridyl groups.[12] If one desires a *trans*-*meso*-A_2B_2 porphyrin that is functionalized with hydroxy groups, a rational synthesis is required. For such a synthesis to be successful, the scrambling must be avoided because chromatographic separation cannot be relied upon to purify an isomerically impure *meso*-A_2B_2 porphyrin.

For the rational synthesis of *trans*-*meso*-A_2B_2 tetraarylporphyrins, the most obvious strategy is to react a *meso*-aryldipyrromethane with a different arenecarbaldehyde. This strategy was first successfully explored by Lee and Lindsey.[13] The method they developed has been widely used, but it has the disadvantage of causing considerable scrambling if one of the aryls has an electron-donating substituent.[6,14,15] Although some other synthetic methods have been developed to minimize scrambling,[6,16] development of other methods is warranted because of the importance of *trans*-*meso*-A_2B_2 tetraarylporphyrins in various potential applications. In this paper we present a novel synthetic method in which the suppression of scrambling is achieved by the use of sodium dodecyl sulfate micelles. This reaction condition was first used by Bonar-Law for synthesis of *meso*-A_4 tetraarylporphyrins.[17] The utility of our method as a step for constructing a large porphyrin assembly is demonstrated here by the attachment of bulky hydrotris(3,5-dimethylpyrazolyl)boratooxomolybdenum(V) groups onto the periphery of two phenyls that are mutually *trans*. The porphyrin systems containing only one such bulky groups have been suggested by Enemark and co-workers[18,19] to be potential spectroscopic mimics of sulfite oxidase. Our aim, however, is larger than just to make a protein mimic. Rather, it is to explore the feasibility of this synthetic method for the construction of larger porphyrin assemblies. We report herein the synthesis and characterization of 5,15-di-*p*-tolyl-10,20-bis[2,3-[((hydrotris(3,5-dimethylpyrazolyl)borato)oxomolybdenio)dioxy]phenyl]porphyrin[20] (**1**), with 5,15-di-*p*-tolyl-10,20-bis(2,3-dimethoxyphenyl)porphyrin (**2**) as the most important precursor.

Results and Discussion

2,3-Dimethoxyphenyldipyrromethane (**3**) was synthesized in 57% yield by following the procedure of Lee and Lindsey.[13] Attempts to react this dipyrromethane with *p*-tolualdehyde using the condition of Lee and Lindsey[13] resulted in extensive scrambling.[14] The "2 + 2" reaction was later carried out in acidified aqueous sodium dodecyl sulfate using 1000 mg of **3**. The subsequent oxidation by tetrachloroquinone (TCQ) produced **2** in 16% yield (230 mg) with no observable scrambling. (When the reaction was scaled down to one-tenth, 25% yield was obtained. Since the quantity of surfactant was much smaller, the extraction of the product from the precipitated surfactant

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(1) Wojaczynski, J.; Latos-Grazynski, L. *Coord. Chem. Rev.* **2000**, *204*, 113−171 and references therein.
(2) Morgan, B.; Dolphin, D. *Struct. Bonding* **1987**, *64*, 115−203 and references therein.
(3) Wagner, R. W.; Lindsey, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 9759−9760.
(4) Steinberg-Yfrach, G.; Liddell, P. A.; Hung, S.-C.; Moore, A. L.; Gust, D.; Moore, T. A. *Nature* **1997**, *385*, 239−241.
(5) Drain, C. M.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 2313−2315.
(6) Setsune, J.; Hashimoto, M.; Shiozawa, K.; Hayakawa, J.; Ochi, T.; Masuda, R. *Tetrahedron* **1998**, *54*, 1407−1424.
(7) Walker, F. A.; Reis, D.; Balke, V. L. *J. Am. Chem. Soc.* **1984**, *106*, 6888−6898.
(8) Little, R. G.; Anton, J. A.; Loach, P. A.; Ibers, J. A. *J. Heterocycl. Chem.* **1975**, *17*, 343−349.
(9) Koerner, R.; Wright, J. L.; Nesset, M. J. M.; Ding, X. D.; Aubrecht, K.; Watson, R.; Barber, R. A.; Tipton, A. R.; Norvell, C. J.; Skidmore, K.; Mink, L. M.; Simonis, U.; Walker, F. A. *Inorg. Chem.* **1998**, *37*, 733−745.
(10) Collman, J. P.; Elliot, C. M.; Halbert, T. R.; Tovrog, B. S. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 18−22.
(11) Walker, F. A.; Balke, V. L.; McDermott, G. A. *Inorg. Chem.* **1982**, *21*, 3342−3348.
(12) Fleischer, E. B.; Shachter, A. M. *Inorg. Chem.* **1991**, *30*, 3763−3769.
(13) Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427−11440.
(14) Littler, B. J.; Ciringh, Y.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 2864−2872.
(15) Wilson, G. S.; Anderson, H. L. *Synlett* **1996**, 1039−1040.
(16) Rao, P. D.; Littler, B. J.; Geier, G. R.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 1084−1092.
(17) Bonar-Law, R. P. *J. Org. Chem.* **1996**, *61*, 3623−3634.
(18) Basu, P.; Raitsimring, A. M.; LaBarre, M. J.; Dhawan, I. K.; Weibrecht, J. L.; Enemark, J. H. *J. Am. Chem. Soc.* **1994**, *116*, 7166−7176.
(19) Basu, P.; Shokhirev, N. V.; Enemark, J. H.; Walker, F. A. *J. Am. Chem. Soc.* **1995**, *117*, 9042−9055.
(20) The nomenclature was adapted from: Basu, P.; Raitsimring, A. M.; Enemark, J. H.; Walker, F. A. *Inorg. Chem.* **1997**, *36*, 1088−1094.

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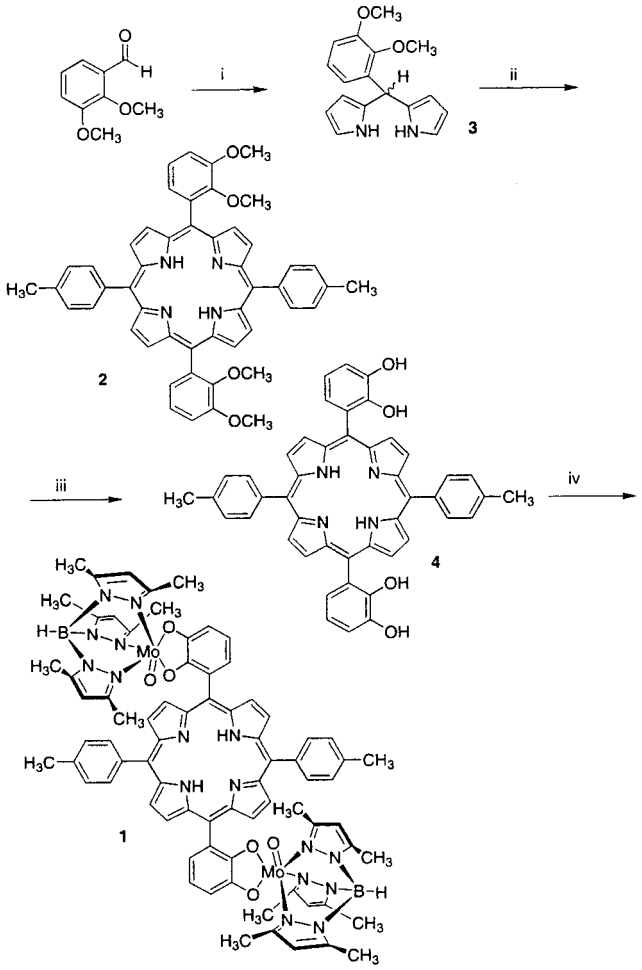
Scheme 1. Reagents, Conditions, and Percent Yields[a]



[a] (i) Pyrrole/CF_3COOH, room temperature, 2 h; 57%. (ii) Sodium dodecyl sulfate (0.5 M)/H_2O/HCl, room temperature, 4 h; then TCQ/THF, 12 h; 16−25%. (iii) BBr_3/CH_2Cl_2, −78 °C → room temperature, 12 h; 75%. (iv) $HB(3,5\text{-}Me_2Pyz)_3OMo(OCH_2CH_2O)$ (**5**)/toluene, 60 °C, 3 days; 12%.

was easier, and this resulted in the higher yield.) The proof that the product consisted only of the *trans*-isomer instead of the *cis* or a *trans*−*cis* mixture was provided by the ^{1}H NMR spectrum, in which the signal from the β-pyrrole protons appeared as two clean peaks at 8.92 and 8.99 ppm that were mutually spin-coupled ($J = 5$ Hz) (Figure 1). (The *cis*-isomer would have given rise to *four* β-pyrrole peaks, two singlets and two mutually coupled doublets.) During the reaction, the acidity was kept relatively low (30 mM HCl was added, about one-fourth of the concentration used by Bonar-Law[17]) in order to minimize the scrambling.[6,14] It is also likely that the micelles play a role in suppressing the scrambling by acting as thermodynamic traps for the porphyrinogen[17] and/or separators between the acid catalyst and the lipophilic product.[17,21,22]

The demethylation of **2** by BBr_3 produced the corresponding bis(dihydroxyphenyl)porphyrin **4** in 75% yield. Although porphyrin catechols are susceptible to oxidative degradation,[23] this problem was minimized by performing all the purification steps under strongly acidic conditions, thereby keeping the catechol

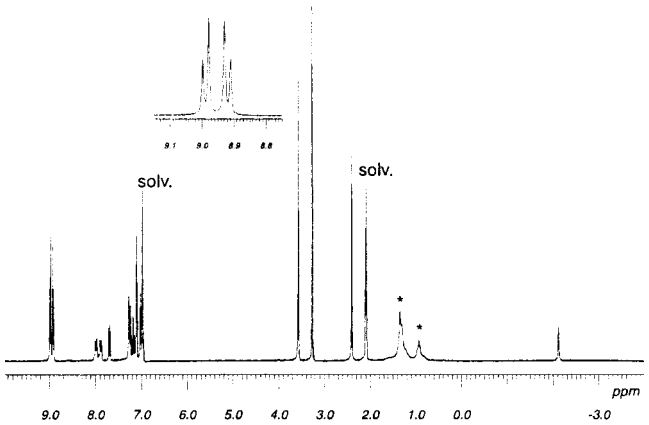


Figure 1. ^{1}H NMR spectra of **2** ($\alpha\alpha$ atropisomer) in toluene-d_8. (Impurities denoted by *.) See the Experimental Section for the peak assignment. Inset: expanded plot of the β-pyrrole region. The presence of two peaks that are coupled to each other is consistent with *trans*-substitution.

side group less susceptible to oxidation to the corresponding *o*-quinone,[24] and also diminishing the photosensitization of oxygen by the porphyrin.[25] The acidic condition also kept the porphyrin catechol **4** from binding too tightly to the silica gel chromatographic matrix. Complex **1** was synthesized from the porphyrin **4** and $HB(3,5\text{-}Me_2Pyz)_3OMo^V(OCH_2CH_2O)$[26] (**5**) in 12% yield. Only one band was found during silica gel column chromatography. The identity of the product was confirmed by FAB-MS (positive ion detection) (Figure 2). The lack of *m*/*z* peaks between the matrix and the parent peak regions indicates the robustness of **1**. Although the mass spectrum does not give any information on the atropisomers present, the product is expected to consist almost completely of the $\alpha\beta$ atropisomer because of the steric interaction between the two tris(dimethylpyrazolyl)borate groups during the formation. The EPR spectrum (X-band) of **1** was taken on a glassy, frozen 1 mM solution of **1** in 1:1 DMF/CH_2Cl_2. The spectrum ($g = 1.973, 1.968, 1.923$) is similar to that of $HB(Me_2Pyz)_3OMo^V(o\text{-}O_2C_6H_4)$.[26] It is very close to axial, because of the *fac*-arrangement of the three N and three O atoms.[18]

In summary, we have demonstrated the following. (1) Applying Bonar-Law's method to the "2 + 2" procedure results in an efficient and regiospecific synthesis of the *trans*-disubstituted tetraarylporphyrin **2**. (2) A large porphyrin-based structure such as the bis(oxomolybdenum(V)) complex **1** may be synthesized from a *trans*-*meso*-A_2B_2 tetraarylporphyrin synthesized by our method. Future directions could include application of the present method to the synthesis of the *cis*-substituted isomer[27−30] and usage of *trans*-bis(hydroxyphenyl)-diarylporphyrins in making other large structures of interest to bio-inspired chemistry and materials science.[1−5]

(21) Fendler, J. H.; Fendler, E. J. *Catalysis in Micellar and Macromolecular Systems*; Academic Press: New York, 1975 and references therein.
(22) Evans, C. A.; Bolton, J. R. *Photochem. Photobiol.* **1979**, *30*, 697−707.
(23) Speck, M.; Kurreck, H.; Senge, M. O. *Eur. J. Org. Chem.* **2000**, 2303−2314.
(24) Hudnall, P. M. In *Ullmann's Encyclopedia of Industrial Chemistry*, 5th ed.; Elvers, B., Hawkins, S., Ravenscroft, M., Schulz, G., Eds.; VCH: Weinheim, Germany, 1989; Vol. A13, pp 499−505.
(25) Chirvony, V. S.; Van Hoek, A.; Galievsky, V. A.; Sazanovich, I. V.; Schaafsma, T. J.; Holten, D. *J. Phys. Chem. B* **2000**, *104*, 9909−9917.
(26) Cleland, W. E., Jr.; Barnhart, K. M.; Yamanouchi, K.; Collison, D.; Mabbs, F. E.; Ortega, R. B.; Enemark, J. H. *Inorg. Chem.* **1987**, *26*, 1017−1025.
(27) Lee, C.-H.; Li, F.; Iwamoto, K.; Dadok, J.; Bothner-By, A. A.; Lindsey, J. S. *Tetrahedron* **1995**, *51*, 11645−11672.
(28) Heo, P.-H.; Lee, C.-H. *Bull. Korean Chem. Soc.* **1996**, *17*, 515−520.
(29) Brückner, C.; Sternberg, E. D.; Boyle, R. W.; Dolphin, D. *J. Chem. Soc., Chem. Commun.* **1997**, 1689−1690.
(30) Littler, B. J.; Miller, M. A.; Hung, C.-H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391−1396.

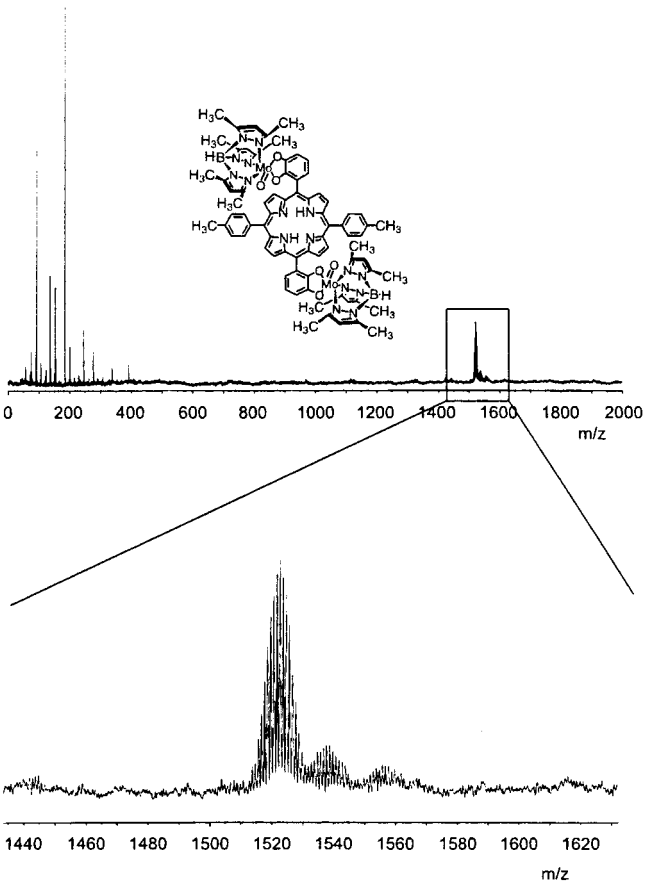


Figure 2. FAB(+)-MS of **1** (top, $m/z = 0-2000$; bottom, enlarged region of the signal from **1**, centered around $m/z = 1522$.) The peak pattern reflects the isotopic distribution of two molybdenums. The signals centered at $m/z = 1538$ and 1554 are caused by the addition of one and two oxygen atoms, respectively, to **1**. A similar peak pattern for oxygenated species (M + 16 and M + 32) is observed in the FAB(+)-MS of the Mo(V) complex **5**.

Experimental Section

Reagents, Materials, and Physical Measurements. Methylene chloride, toluene, pyrrole, and *p*-tolualdehyde were purified using standard methods.[31] Triethylamine was passed through a silica gel column before use. $HB(3,5\text{-}Me_2Pyz)_3OMo^{V}(OCH_2CH_2O)$ (**5**) was synthesized using the procedure of Cleland et al.[26] The other reagents were used as received. All reactions were done under a nitrogen or argon atmosphere and with magnetic stirring. Silica gel used in the preparations was J.T. Baker 60−200 mesh. TLC plates were J.T. Baker Silica Gel IB2. 1-D NMR spectra were recorded with a Bruker AM 250 MHz spectrometer. 2-D NMR spectra were recorded with a Varian Unity 300 MHz spectrometer. EPR spectra were recorded with a Bruker ESP-300E spectrometer equipped with an Oxford CF935 cryostat. Fast-atom bombardment mass spectra (FAB-MS) were recorded by the Mass Spectrometer Facility (Department of Chemistry, University of Arizona) with a JEOL HX-110A spectrometer; for the matrix, glycerol/*m*-nitrobenzyl alcohol was used.

2,3-Dimethoxyphenyldipyrromethane (3). Pyrrole (50 mL, 48 g, 0.72 mol) and 2,3-dimethoxybenzaldehyde (1.706 g, 10.27 mmol) were reacted, and the product was isolated using the procedure of Lee and Lindsey.[13] The resulting solid was recrystallized from MeOH/H_2O. Yield: 1.555 g (54%). ^{1}H NMR ($CDCl_3$): δ 8.33 (s, 2H, pyrrole NH), 6.98 (t, $J = 8$ Hz, 1H, phenyl 5-H), 6.83 (d, $J = 8$ Hz, 1H, phenyl 4-H), 6.78 (d, $J = 8$ Hz, 1H, phenyl 6-H), 6.65 (m, 2H, pyrrole(1,9)-H), 6.13 (m, 2H, pyrrole(2,8)-H), 5.92 (m, 2H, pyrrole(3,7)-H), 5.69 (s, 1H, *meso*-H), 3.86 (s, 3H, 3-OCH_3), 3.49 (s, 3H, 2-OCH_3). ^{13}C NMR ($CDCl_3$): δ 152.9 (phenyl 2-C), 146.1 (phenyl 3-C), 136.6 (phenyl 1-C), 132.5 (pyrrole(4,6)-C), 124.2 (phenyl 5-C), 121.5 (phenyl 6-C), 116.7 (pyrrole (1,9)-C), 111.1 (phenyl 4-C), 108.1 (pyrrole (2,8)-C), 106.7 (pyrrole (3,7)-C), 60.3 (3-OCH_3), 55.6 (2-OCH_3), 39.3 (*meso*-C). FAB(+)-MS: calcd (M + 1), 283.14; found, 283.14.

5,15-Di-*p*-tolyl-10,20-bis(2,3-dimethoxyphenyl)porphyrin (2). In a 200 mL Schlenk flask containing 18 g of sodium dodecyl sulfate and 100 mL of H_2O, *p*-tolualdehyde (47 μL, 0.399 mmol) was first added, and then **3** (100 mg, 0.354 mmol). After 1 h, 250 μL of 12 M HCl was added, producing a concentration of HCl of 30 mM. The reaction was monitored using two methods: UV/visible spectroscopy for monitoring the yield of the porphyrin[17] and TLC for monitoring the possible rearrangement products.[32] After the reaction was complete (4 h), 220 mg (0.895 mmol) of tetrachloroquinone (TCQ) was added. After the oxidation was complete (overnight), the surfactant and the porphyrin were precipitated using a mixture of 0.5 g of KOH, 1 g of pH 7 phosphate buffer powder ($Na_2HPO_4 + KH_2PO_4$), and 1 g of KCl in 20 mL of H_2O and 50 mL of toluene. The precipitate was extracted with toluene. The organic layer was washed with H_2O and then dried. The resulting solid was chromatographed on a silica gel column (4 × 20 cm). The $\alpha\beta$ (CH_2Cl_2) and $\alpha\alpha$ (100:1 CH_2Cl_2/EtOAc) atropisomers were recovered. The total yield of the *trans*-disubstituted porphyrins was 34 mg (25%). In another preparation, the entire reaction was scaled up so that 1002 mg (3.55 mmol) of **3** was used. The yield of the porphyrin in this preparation was 230 mg (16%). The $\alpha\alpha$ atropisomer is readily soluble in CH_2Cl_2, $CHCl_3$, DMF, and toluene. The solubility of the $\alpha\beta$ atropisomer is considerably lower than that of the $\alpha\alpha$ atropisomer. ^{1}H NMR ($\alpha\alpha$ in toluene-d_8): δ 8.99 (d, $J = 5$ Hz, 4H, β-pyrrole H), 8.92 (d, $J = 5$ Hz, 4H, β-pyrrole H), 7.98 (d, $J = 8$ Hz, 2H, MePh *o*-H), 7.88 (d, $J = 8$ Hz, 2H, MePh *o*-H), 7.69 (d, $J = 7$ Hz, 2H, $(MeO)_2$Ph *o*-H), 7.26 (d, $J = 8$ Hz, 4H, MePh *m*-H), 7.19 (t, $J = 8$ Hz, 2H, $(MeO)_2$Ph *m*-H), 3.58 (s, 6H, $(MeO)_2$Ph *m*-OMe), 3.27 (s, 6H, $(MeO)_2$Ph *o*-OMe), 2.41 (s, 6H, *p*-Me), −2.13 (s, 2H, pyrrole NH). (In the spectrum of the $\alpha\beta$ atropisomer, only one signal from MePh *o*-H is observed at δ 7.94 (d, $J = 8$ Hz, 4H). Also, the signal from $(MeO)_2$Ph *o*-OMe shifts to δ 3.25.) FAB(+)-MS: calcd (M + 1), 763.32; found, 763.33.

5,15-Di-*p*-tolyl-10,20-bis(2,3-dihydroxyphenyl)porphyrin (4). A 100 mL Schlenk flask containing 1 mL (3 g, 10 mmol) of BBr_3 and 3 mL of CH_2Cl_2 was placed in a dry ice bath. In a 100 mL Schlenk flask, **2** (52 mg, 0.068 mmol, mixture of the two atropisomers) and freshly distilled CH_2Cl_2 (3 mL) were stirred and transferred into the BBr_3/CH_2Cl_2 mixture. The resulting solution was stirred in the dry ice bath for 2 h and then at room temperature overnight. The flask was then placed in an ice−water bath, and 20 mL of H_2O was added slowly. The mixture was washed three times with 50 mL of 0.1 M HCl. The solvent was then removed from the organic layer. The remaining green solid was chromatographed through a 4 × 30 cm column of silica gel that had been acidified with 1% v/w trifluoroacetic acid. (If the matrix is not acidified, the porphyrin adsorbs tightly and becomes difficult to elute.) The desired product was eluted with 1:1 CH_2Cl_2/EtOAc. The solvent was then removed. The protonated porphyrin was redissolved in 50 mL of CH_2Cl_2, neutralized three times with 40 mL of pH 7 buffer (0.1 M Na_2HPO_4/KH_2PO_4), and washed three times with 40 mL of H_2O. The solvent was removed, and the resulting purple amorphous solid was washed with pentane and then dried (36 mg, 75%). The product was highly soluble in acetone, soluble in MeOH, EtOAc, and DMF, and moderately soluble in CH_2Cl_2. ^{1}H NMR ($\alpha\alpha-\alpha\beta$ mixture in acetone-d_6): δ 8.92 (d, $J = 5$ Hz, 4H, pyrrole β-H), 8.85 (d, $J = 5$ Hz, 4H, pyrrole β-H), 8.49 (s, 1H, $(HO)_2$Ph *o*-OH), 8.39 (s, 1H, $(HO)_2$Ph *o*-OH), 8.11 (d, $J = 8$ Hz, 4H, MePh *o*-H), 7.64 (s, 2H, $(HO)_2$Ph *m*-OH), 7.63 (d, $J = 8$ Hz, 4H, MePh *m*-H), 7.48 (m, 2H, $(HO)_2$Ph *o*-H), 7.34 (m, 2H, $(HO)_2$Ph *p*-H), 7.12 (m, 2H, $(HO)_2$Ph *m*-H), 2.69 (s, 6H, MePh *p*-CH_3), −2.75 (s, 2H, pyrrole NH). (The peaks from the hydroxide and amine protons disappear upon addition of CD_3OD.) FAB(+)-MS: calcd (M + 1), 707.27; found, 707.26.

(31) Perrin, D. D.; Perrin, D. R.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon Press: Oxford, U.K., 1980.

(32) When the mixture is spotted on a J.T. Baker Silica Gel IB2 plate and eluted with Et_2O, the disubstituted porphyrin appears at $R_f = 0.6$; the mono- and trisubstituted porphyrins appear close to the disubstituted porphyrin, but they do separate clearly ($\Delta R_f \approx 0.03$).

5,15-Di-*p*-tolyl-10,20-bis[2,3-[((hydrotris(3,5-dimethylpyrazolyl)-borato)oxomolybdenio)dioxy]phenyl]porphyrin (1). A 100 mL Schlenk flask containing 173 mg (0.245 mmol) of **4**, 493 mg (1.053 mmol) of **5**, and 50 mL of toluene was placed in an oil bath at room temperature, and the bath was slowly warmed to 63 °C. The reaction was monitored by TLC. After the reaction was complete (3 days), the reaction mixture was cooled to room temperature and dried. The resulting solid was chromatographed first on a short column (4 × 2 cm) and then a long column (4 × 20 cm) of silica gel. The impurities were eluted with toluene, and then the desired product was eluted with CH_2Cl_2. The product was recrystallized from CH_2Cl_2/MeOH. Yield: 45 mg (12%). FAB(+)-MS: calcd (M + 1, tallest peak of the isotopic mixture), 1522.44; found, 1522.44. EPR (X-band, 1:1 CH_2Cl_2/DMF, 77 K): g = 1.973, 1.968, 1.923.

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Supporting Information Available: Spectral data from 1- and 2-D NMR and EPR spectroscopies. This material is available free of charge via the Internet at http://pubs.acs.org.

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