Facile Elaboration of Porphyrins via Metal-Mediated Cross-Coupling

Stephen G. DiMagno, Victor S.-Y. Lin, and Michael J. Therien*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323

Received June 7, 1993•

Metal-mediated cross-coupling methodologies have been successfully employed to porphyrinic systems, providing a powerful, versatile, and general synthetic approach for the fabrication of elaborated porphyrin structures. A large number of coupling reactions have been carried out at two halogenated porphyrin templates, [2-bromo-5,10,15,20-tetraphenylporphinato]zinc and [5,15-dibromo-10,20-diphenylporphinato]zinc, generating a variety of porphyrins, 10 of which are novel: [2-*n*-butyl-5,-10,15,20-tetraphenylporphinato]zinc(II), [2-(2,5-dimethoxyphenyl)-5,10,15,20-tetraphenylporphinato]-zinc(II), [2-(9-anthracenyl)-5,10,15,20-tetraphenylporphinato]zinc(II), [2-vinyl-5,10,15,20-tetraphenyl-porphinato]zinc(II), [2,5,10,15,20-pentaphenylporphinato]zinc(II), [2-isobutyl-5,10,15,20-tetraphe-nylporphinato]zinc(II), [2-(pentafluorophenyl)-5,10,15,20-tetraphenylporphinato]zinc(II), [5,15-bis-[[2-(4′-methyl-2′-pyridyl)-4-pyridyl]methyl]-10,20-diphenylporphinato]zinc(II), [5,15-dimethyl-10,20-diphenylporphinato]zinc(II), [5,15-divinyl-10,20-diphenylporphinato]zinc(II), [5,15-bis(2,5-dimethoxy-phenyl)-10,20-diphenylporphinato]zinc(II), and [5,15-bis(pentafluorophenyl)-10,20-diphenylpor-phinato]zinc(II). The structures of [2,5,10,15,20-pentaphenylporphinato]zinc(II) and 5,15-bis-(pentafluorophenyl)-10,20-diphenylporphyrin have been determined; X-ray data are as follows: $P2_1/n$ with a = 21.425(4) Å, b = 9.718(1) Å, c = 24.905(2) Å, β = 110.83(1)°, V = 4846(3) Å^3, d_{calc} = 1.260 g cm^{-3}, and Z = 4 for the former; and $P2_1/c$ with a = 15.223(2) Å, b = 10.162(1) Å, c = 12.375(2) Å, β = 112.75(2)°, V = 1765.6(9) Å^3, d_{calc} = 1.495 g cm^{-3}, and Z = 2 for the latter. This study demonstrates that cross-coupling reactions at the porphyrin periphery are seemingly not subject to the steric or electronic constraints that often limit the scope of these reactions in simple aryl and vinyl systems.

Introduction

Porphyrin synthesis impacts a large and continually growing number of research endeavors in physical, biological, organic, and inorganic chemistry. Aside from a few notable exceptions,[1-3] porphyrin synthetic schemes are generally plagued by low yields and difficult separation of reactants from products. These limitations are particularly troublesome given that much of the cutting edge research in porphyrin chemistry depends critically on the synthesis of exotic porphyrins that are elaborated in either the β- or *meso*-positions or both. For example, porphyrin-containing donor–spacer–acceptor compounds,[4-15] porphyrins designed to bind to electrodes and surfaces,[16-18] a variety of porphyrinic arrays[19,20] and materials,[21-28] porphyrin-derived multielectron reduction[29,30] and selec-

• Abstract published in *Advance ACS Abstracts*, September 15, 1993.

(1) *Porphyrins and Metalloporphyrins*, Smith, K. D., Ed.; Elsevier: New York, 1975.

(2) (a) Kim, J. B.; Adler, A. D.; Longo, F. R. In *The Porphyrins*, Dolphin, D., Ed.; Academic Press: London, 1978; Vol. I. (b) Paine, J. B. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: London, 1978; Vol. I.

(3) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827–836.

(4) Bergkamp, M. A.; Dalton, J.; Netzel, T. L. *J. Am. Chem. Soc.* **1982**, *104*, 253–259.

(5) (a) Wasielewski, M. R.; Niemczyk, M. P. *J. Am. Chem. Soc.* **1984**, *106*, 5043–5045. (b) Wasielewski, M. R.; Niemczyk, M. P.; Svec, W. A.; Pewitt, E. B. *J. Am. Chem. Soc.* **1985**, *107*, 1080–1082. (c) Wasielewski, M. R.; Niemczyk, M. P.; Johnson, D. G.; Svec, W. A.; Minsek, D. W. *Tetrahedron* **1989**, *45*, 4785–4806. (d) Wasielewski, M. R.; Johnson, D. G.; Neimczyk, M. P.; Gaines, G. L., III; O'Neil, M. P.; Svec, W. A. *J. Am. Chem. Soc.* **1990**, *112*, 6482–6488. (e) O'Neil, M. P.; Niemczyk, M. P.; Svec, W. A.; Gosztola, D.; Gaines, G. L., III; Wasielewski, M. R. *Science (Washington, DC)* **1992**, *257*, 63–65.

(6) (a) Bolton, J. R.; Ho, T.-F.; Liauw, S.; Siemiarczuk, A.; Wan, C. S.; Weedon, A. C. *J. Chem. Soc., Chem. Commun.* **1985**, 559–560. (b) Bolton, J. R.; Liu, J. *J. Phys. Chem.* **1992**, *96*, 1718–1725.

(7) Joran, A. D.; Leland, P. M.; Felker, A. H.; Zewail, A. H.; Hopfield, J. J.; Dervan, P. B. *Nature (London)* **1987**, *327*, 508–511.

(8) (a) McLenden, G. *Acc. Chem. Res.* **1988**, *21*, 160–167. (b) Helms, A.; Heiler, D.; McLendon, G. *J. Am. Chem. Soc.* **1991**, *113*, 4325–4327. (c) Helms, A.; Heiler, D.; McLendon, G. *J. Am. Chem. Soc.* **1992**, *114*, 6227–6238.

(9) (a) Sessler, J. L.; Johnson, M. R.; Lin, T.-Y. *Tetrahedron* **1989**, *45*, 4767–4784. (b) Sessler, J. L.; Capuano, V. L. *Agnew. Chem., Int. Ed. Engl.* **1990**, *29*, 1134–1137. (c) Rodriguez, J.; Kirmaier, D.; Johnson, M. R.; Friesner, R. A.; Holten, D.; Sessler, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 1652–1659.

(10) Sakata, Y.; Nakashima, S.; Goto, Y.; Tatemitsu, H.; MIsumi, S.; Asahi, T.; Hagihara, M.; Nishikawa, S.; Okada, T.; Mataga, N. *J. Am. Chem. Soc.* **1989**, *111*, 4958–4959.

(11) Osuka, A.; Maruyama, K.; Mataga, N.; Asahi, T.; yamazaki, I.; Tamai, N. *J. Am. Chem. Soc.* **1990**, *112*, 4958–4959.

(12) Knapp, S.; Muali Dhar, T. G.; Albaneze, J.; Gentemann, S.; Potenza, J. A.; Holten, D.; Schugar, H. J. *J. Am. Chem. Soc.* **1991**, *113*, 4010–4013.

(13) Lendzian, F.; Schlûpmann, J.; von Gersdorff, J.; Möbius, K.; Kurreck, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1461–1463.

(14) Gust, D.; Moore, T. A.; Moore, A. L.; Gao, F.; Luttrull, D.; DeGraziano, J. M.; Ma, X. C.; Makings, L. R.; Lee, S.-J.; Trier, T. T.; Bittersmann, E.; Seely, G. R.; Woodward, S.; Benasson, R. V.; Rougée, M.; De Schryver, F. C.; Van der Auweraer, M. *J. Chem. Soc.* **1991**, *113*, 3638–3649.

(15) Kamioka, K.; Cormier, R. A.; Lutton, T. W.; Connolly, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 4414–4415.

(16) Yoneyama, M.; Fujii, A.; Maeda, S.; Murayama, T. *Chem. Lett.* **1991**, 929–932.

(17) Bedioui, F.; Granados, S. G.; Devynck, J. *New J. Chem.* **1991**, *15*, 939–941.

(18) Luttrull, D. K.; Graham, J.; DeRose, J. A.; Gust, D.; Moore, T. A.; Lindsay, S. M. *Langmuir* **1992**, *8*, 765–768.

(19) (a) Nagata, T.; Osuka, A.; Maruyama, K. *J. Am. Chem. Soc.* **1990**, *112*, 3054–3059. (b) Osuka, A.; Nakajima, S.; Maruyama, K.; Mataga, N.; Asahi, T. *Chem. Lett.* **1991**, 1003–1006. (c) Osuka, A.; Maruyama, K.; Mataga, N.; Asahi, T.; Yamazaki, I.; Tamai, N.; Nishimura, Y. *Chem. Phys. Lett.* **1991**, *181*, 413–418.

(20) Anderson, H. L.; Sanders, J. K. M. *Angew. Chem., Int. Ed. Eng.* **1991**, *29*, 1400–1402.

(21) Kamogawa, H.; Miyama, S.; Minoura, S. *Macromolecules* **1989**, *22*, 2123–2126.

(22) Gregg, B. A.; Fox, M. A.; Bard, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 3024–3029.

(23) Kojima, T.; Urata, Y.; Yonekura, H. *J. Polym. Sci., Part C: Polym. Lett.* **1990**, *28*, 129–132.

(24) Ishikawa, Y.; Kunitake, T. *J. Am. Chem. Soc.* **1991**, *113*, 621–630.

0022-3263/93/1958-5983$04.00/0

tive oxidation[31-36] catalysts, and porphyrin species suitable for incorporation into supramolecular systems[37,38] as well as a number of porphyrin-based pharmaceuticals[39] and imaging agents[40] all require the fabrication of porphyrins with peripheral substituents that confer unusual (or secondary) reactivity, electronic features, steric constraints, or binding properties.

We have recently demonstrated[41] the utility of metal-mediated cross-coupling[42] for carbon–carbon bond-forming reactions involving porphyrins.[43] This new approach to porphyrin synthesis provides several important advantages to the fabrication of elaborated porphyrins, namely: (1) catalytic, quantitative conversion of reactants to products, (2) facile reaction conditions, (3) straightforward purification and isolation of products, (4) decoupling of porphyrin ring cyclization chemistry from porphyrin derivatization, and (5) its potential to be generally suitable for the construction of a wide range of porphyrinic compounds.[4-40] Here we report the first in a series of full accounts[44] of this work that describe the scope of this chemistry and demonstrate the remarkable latitude this methodological approach provides to tune both the steric and electronic properties at the porphyrin periphery.

Experimental Section

Materials. All manipulations were carried out under nitrogen previously passed through an O_2 scrubbing tower (Schweizerhall R3-11 catalyst) and a drying tower (Linde 3-Å molecular sieves) unless otherwise stated. Air-sensitive solids were handled in a Braun 150-M glovebox. Standard Schlenk techniques were employed to manipulate air-sensitive solutions. All solvents utilized in this work were obtained from Fisher Scientific (HPLC Grade). Tetrahydrofuran (THF), diethyl ether, and toluene were predried over 4-Å molecular sieves and then distilled from Na/benzophenone under N_2. Methylene chloride and pyridine were distilled under N_2 from calcium hydride and barium oxide, respectively. All NMR solvents were treated similarly but distilled under vacuum. Benzaldehyde was distilled under vacuum and stored under N_2. Trifluoroacetic acid, bromopentafluorobenzene, 1,4-dimethoxybenzene, 4,4′-dimethyl-2,2′-bipyridine, 9-bromoanthracene, and tributyltin chloride were used as received. Organolithium and Grignard reagents were titrated before use. $ZnCl_2$ was dried by heating under vacuum and stored under N_2. The catalyst $Pd[(PPh)_3]_4$ (Strem) was used as received while $Pd(dppf)Cl_2$ was synthesized[45] from $PdCl_2$ (Aldrich) and 1,1′-bis(diphenylphosphinoferrocene) (dppf) (Aldrich). 2,2-Dipyrrylmethane was prepared according to the published procedure[46] and stored under an inert atmosphere at −40 °C. Chemical shifts for ^1H NMR spectra are relative to residual protium in the deuterated solvents ($CDCl_3$, δ = 7.24 ppm; THF, δ = 3.58 ppm). Chemical shifts for ^{13}C NMR spectra are relative to deuteriochloroform solvent ($CDCl_3$, δ = 77.00 ppm). Carbon assignments were made on the basis of DEPT experiments; the number of attached protons is found in parentheses following the chemical shift value. Chromatographic purification (Silica Gel 60, 230–400 mesh, EM Science) of all newly synthesized elaborated porphyrins was accomplished on the bench top. Elemental analyses were performed either at the Microanalytical Laboratory in the Department of Chemistry (University of Pennsylvania) or at Robertson Microlit Laboratories (Madison, NJ).

Instrumentation. Electronic spectra were recorded on an OLIS UV/vis/NIR spectrophotometry system that is based on the optics of a Carey 14 spectrophotometer. The purity of the halogenated porphyrin precursors was verified by analytical HPLC (8-μm silica) utilizing a Rainin gradient system.

5,15-Diphenylporphyrin.[47] A flame-dried 1000-mL flask equipped with a magnetic stirring bar was charged with 2,2′-dipyrrylmethane (458 mg, 3.1 mmol), benzaldehyde (315 μL, 3.1 mmol), and 600 mL of freshly distilled methylene chloride. The solution was degassed with a stream of dry nitrogen for 10 min. Trifluoroacetic acid (150 μL, 1.95 mmol) was added via syringe, the flask was shielded from light with aluminum foil, and the solution was stirred for 3 h at room temperature. The reaction was quenched by the addition of DDQ (900 mg, 3.96 mmol), and the solution was stirred for an additional 30 min. The mixture was neutralized with 3 mL of triethylamine and poured directly on top of a silica gel column (20 × 2 cm) packed in hexane. The product was eluted in 700 mL of CH_2Cl_2. The solvent was evaporated leaving purple crystals that were washed once with hexane, filtered, and dried. This compound (518 mg, 1.12 mmol, 72.2%) was sufficiently pure for further reactions.

5,15-Dibromo-10,20-diphenylporphyrin. 5,15-Diphenylporphyrin (518 mg, 1.12 mmol) was dissolved in 250 mL of chloroform and cooled to 0 °C. Pyridine (1.0 mL) was added to act as an acid scavenger. *N*-Bromosuccinimide (400 mg, 2.2 mmol) was added directly to the flask, and the reaction was followed by TLC (50% CH_2Cl_2/hexanes eluant). After 10 min, the reaction reached completion and was quenched with 20 mL of acetone. The solvents were evaporated, and the product was washed with several portions of methanol and pumped dry to yield 587 mg (0.94 mmol, 85%) of a reddish purple solid. The compound was sufficiently pure to carry through to the next reaction at this point. An analytical sample was recrystallized from toluene. ^1H NMR (250 MHz, $CDCl_3$): δ 9.59 (d, 4 H, J = 4.9), 8.81 (d, 4 H, J = 4.8), 8.14 (dd, 4 H, J = 7.6, 1.8), 7.78 (m, 6 H), −2.77 (s, 2 H). Vis ($CHCl_3$): 421 (5.55), 489 (3.63), 521 (4.20), 556 (4.04), 601 (3.71), 658 (3.73). Anal. Calcd for $C_{32}H_{20}N_4Br_2$: C, 61.96; H, 3.25; N, 9.03. Found: C, 62.19; H, 2.97; N, 8.78.

[5,15-Dibromo-10,20-diphenylporphinato]zinc(II). 5,15-Dibromo-10,20-diphenylporphyrin (587 mg, 0.94 mmol) was

(25) Fleischer, E. B.; Shachter, A. M. *J. Heterocycl. Chem.* **1991**, *28*, 1693–1699.
(26) Traylor, T. G.; Byun, Y. S.; Traylor, P. S.; Battioni, P.; Mansuy, D. *J. Am. Chem. Soc.* **1991**, *113*, 7821–7823.
(27) Scamporrino, E.; Vitalini, D. *Macromolecules* **1992**, *25*, 1625–1632.
(28) Suslick, K. S.; Chen, C.-T.; Meredith, G. R.; Cheng, L.-T. *J. Am. Chem. Soc.* **1992**, *114*, 6928–6930.
(29) (a) Durand, R. R.; Bencosme, C. S.; Collman, J. P.; Anson, F. C. *J. Am. Chem. Soc.* **1983**, *105*, 2710–2718. (b) Collman, J. P.; Hutchinson, J. E.; Lopez, M. A.; Guilard, R.; Reed, R. A. *J. Am. Chem. Soc.* **1991**, *113*, 2794–2796. (c) Mest, Y. L.; L'Her, M.; Hendricks, N. H.; Kim, K.; Collman, J. P. *Inorg. Chem.* **1992**, *31*, 835–847.
(30) Chang, C. K.; Abdalmuhdi, I. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 164–165.
(31) (a) Traylor, P. S.; Dolphin, D.; Traylor, T. G. *J. Chem. Soc., Chem. Commun.* **1984**, 279–280. (b) Traylor, T. G.; Hill, K. W.; Fann, W. P.; Tsuchiya, S.; Dunlap, B. E. *J. Am. Chem. Soc.* **1992**, *114*, 1308–1312.
(32) Ellis, P. E., Jr.; Lyons, J. E. *Coord. Chem. Rev.* **1990**, *105*, 181–193.
(33) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791–5796.
(34) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, R. *J. Chem. Soc., Chem. Commun.* **1985**, 155–156.
(35) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991**, *113*, 6865–6872.
(36) Konishi, K.; Oda, K.-I.; Nishida, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1992**, *114*, 1313–1317.
(37) Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435–461 and references therein.
(38) A number of examples are discussed in: Lehn, J. M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89–112.
(39) *Photodynamic Therapy of Neoplastic Disease*; Kessel, D., Ed.; CRC Press: Boca Raton, FL, 1990, Vol. I, II.
(40) Lauffer, R. B. *Chem. Rev.* **1987**, *87*, 901–927.
(41) DiMagno, S. G.; Lin, V. S.-Y.; Therien, M. J. *J. Am. Chem. Soc.* **1993**, *115*, 2513–2515.
(42) (a) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669–679. (b) Negishi, E.-I.; Luo, F. T.; Frisbee, R.; Matsushita, H. *Heterocycles* **1982**, *18*, 117–122. (c) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151. (d) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508–524.
(43) Heck- and Stille-type reactions have also been utilized to vinylate 2,4-bis(chloromercurio)- and 2,4-dibromodeutieroporphyrin IX dimethyl ester to protoporphyrin IX. See: Minnetian, O. M.; Morris, I. K.; Snow, K. M.; Smith, K. M. *J. Org. Chem.* **1989**, *54*, 5567–5574.
(44) Lin, V. S.-Y.; DiMagno, S. G.; Therien, M. J. Manuscript in preparation.
(45) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158–163.
(46) Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. *Aust. J. Chem.* **1969**, *22*, 229–238.
(47) Manka, J. S.; Lawrence, D. S. *Tetrahedron Lett.* **1989**, *30*, 7341–7344.

suspended in 30 mL of DMF containing 500 mg of $ZnCl_2$. The mixture was heated at reflux for 2 h and poured into distilled water. The precipitated purple solid was filtered through a fine fritted disk, washed with water, methanol, and acetone, and dried in vacuo to yield 610 mg, 0.89 mmol, 95% of a reddish purple solid. The compound was recrystallized from THF/heptane to yield large purple crystals of [5,15-dibromo-10,20-diphenylporphinato]zinc(II), 564 mg, 0.82 mmol, 88%. ^{1}H NMR (250 MHz, THF-d_8): δ 9.59 (d, 4 H, J = 4.8), 8.81 (d, 4 H, J = 4.8), 8.07 (d, 4 H, J = 6.5), 7.70 (m, 6 H). Vis (THF): 428 (5.50), 526 (3.53), 541 (3.66), 564 (4.17), 606 (3.95).

General Procedure for the Preparation of 2-Substituted 5,10,15,20-Tetraphenylporphyrins. The organotin or organozinc chloride reagent (syntheses described below) was transferred to a Schlenk-style storage tube containing [2-bromo-5,10,15,20-tetraphenylporphinato]zinc (0.10 mmol) and 3 mg of the palladium catalyst. The total solvent volume was adjusted to 40 mL. For the fabrication of 2-*n*-butyl-, 2-(2,5-dimethoxyphenyl)-, 2-(9-anthracenyl)-, and 2-vinyl-substituted [5,10,15,-20-tetraphenylporphinato]zinc complexes, the catalyst $Pd(PPh_3)_4$ was used. For $Pd(PPh_3)_4$-catalyzed reactions, the general procedure consisted of heating the catalyst, [2-bromotetraphenylporphinato]zinc, and the organometallic reagent at 60 °C in the sealed Schlenk tube. The course of the reaction was monitored by TLC. Regardless of the organometallic reagent used, it was found that 12 h was required to completely consume the starting material, [2-bromotetraphenylporphinato]zinc. The mixture was then quenched with water, extracted with chloroform, dried over $CaCl_2$, and evaporated. For the fabrication of [2-(pentafluorophenyl)-5,10,15,20-tetraphenylporphinato]zinc(II), the catalyst Pd(dppf) was used; the reaction was carried out at room temperature and complete within 1 h. Details for the isolation of each compound are given below.

[2-*n*-Butyl-5,10,15,20-tetraphenylporphinato]zinc(II).[49d] *n*-Butyllithium was added to a solution of $ZnCl_2$ (160 mg, 1.17 mmol) in 20 mL of THF to yield the organozinc chloride reagent. Upon conclusion of the coupling reaction, the product was purified by column chromatography on silica gel using 1:1 CH_2Cl_2:hexane. A single red band was isolated, and the solvent was evaporated. Isolated yield = 62.5 mg (92%, based on 70 mg of the porphyrin starting material). Characterization data have been previously reported.[41]

[2-(2,5-Dimethoxyphenyl)-5,10,15,20-tetraphenylporphinato]zinc(II). (2,5-Dimethoxyphenyl)lithium was prepared from 1,4-dimethoxybenzene (138 mg, 1 mmol) and *tert*-butyllithium (1 mmol) in ether at −78 °C. The organolithium reagent was added to a solution of $ZnCl_2$ (160 mg, 1.17 mmol) in 20 mL of THF to yield the organozinc chloride reagent. Upon conclusion of the coupling reaction, excess dimethoxybenzene was removed from the crude reaction mixture by sublimation. The product was purified by column chromatography on silica gel using 1:9 THF:hexane. Isolated yield = 147 mg (91%, based on 150 mg of the porphyrin starting material). Characterization data have been previously reported.[41]

[2-(9-Anthracenyl)-5,10,15,20-tetraphenylporphinato]zinc(II). An oven-dried 50-mL Schlenk tube equipped with a magnetic stirring bar was charged with 9-bromoanthracene (257 mg, 1 mmol) and 20 mL of freshly distilled di-*n*-butyl ether. The solution was stirred under N_2 for 10 min and cooled to −78 °C. *tert*-Butyllithium in hexane (0.76 mL, 1 mmol) was added by syringe. The mixture was stirred for 30 min. A solution of 1.5 mmol of zinc chloride in 20 mL of THF was introduced by syringe, and the solution was warmed to room temperature, yielding the organozinc chloride reagent. At the reaction endpoint, the crude product was purified by column chromatography on silica gel using 1:9 THF:hexane solution as eluant. The red band was collected and evaporated. Isolated yield = 65 mg (88%, based on 64 mg of the porphyrin starting material). Selected characterization data are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.06 (s, 1H), 9.00 (s, 2 H), 8.96 (d, 1 H, J = 4.6), 8.94 (d, 1 H, J = 4.6), 8.78 (d, 1 H, J = 4.7), 8.48 (d, 1 H, J = 4.7), 8.27 (s, 2 H), 8.27 (m, 4 H), 8.22 (d, 2 H, J = 6.9), 8.18 (dd, 2 H, J = 7.7, 1.6), 7.92 (d, 2 H, J = 8.6), 7.75 (m, 6 H), 7.65 (m, 3 H), 7.58 (d, 2 H, J = 8.9), 7.35 (dd, 2 H, J = 8.5, 6.5), 7.18 (d, 2 H, J = 7.9), 7.07 (dd, 2 H, J = 8.9, 6.4), 6.59 (t, 1 H, J = 7.6), 6.25 (t, 2 H, J = 7.7). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.31, 150.51, 150.39, 150.36, 150.29, 150.23, 149.67, 149.50, 142.81, 142.78, 142.73, 139.68, 136.84, 134.55, 134.47, 134.42, 134.35, 132.53, 132.24, 132.14, 132.08, 131.99, 131.62, 131.37, 131.30, 128.06, 127.75, 127.53, 127.40, 126.59, 126.53, 126.35, 124.75, 124.61, 123.51, 122.33, 121.50, 121.11, 120.82. An analytical sample was demetalated with HCl. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.94 (s, 1 H), 8.88 (m, 4 H), 8.68 (d, 1 H, J = 4.9), 8.39 (d, 1 H, J = 4.8), 8.22 (m, 7 H), 7.95 (d, 2 H, J = 8.5), 7.72 (m, 6 H), 7.62 (m, 3 H), 7.58 (d, 2 H, J = 8.9), 7.38 (t, 2 H, J = 7.4), 7.17 (d, 2 H, J = 7.1), 7.10 (dd, 2 H, J = 8.8, 6.5), 6.61 (t, 1 H, J = 7.5), 6.28 (t, 2 H, J = 7.7), −2.54 (s, 2 H). Anal. Calcd for $C_{58}H_{38}N_4$: C, 88.07; H, 4.85; N, 7.08. Found: C, 87.95; H, 4.76; N, 7.29.

[2,5,10,15,20-Pentaphenylporphinato]zinc(II). An oven-dried 50-mL Schlenk tube equipped with a magnetic stirring bar was charged with zinc chloride (200 mg, 1.5 mmol) and 20 mL of freshly distilled THF. The solution was stirred under N_2 for 10 min. A solution of phenyllithium in cyclohexane/diethyl ether (70/30) (1 mmol) was added by syringe, and transmetalation occurred within 10 min. Upon completion of the coupling reaction, the crude mixture was purified by column chromatography on silica gel using 1:1 toluene:hexane. The reddish purple band was isolated and evaporated. Isolated yield = 62 mg (89%, based on 70 mg of the porphyrin starting material). Selected characterization data are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.96 (m, 4 H), 8.89 (s, 1 H), 8.88 (d, 1 H, J = 5.6), 8.81 (d, 1 H, J = 4.6), 8.26 (m, 6 H), 7.91 (d, 2 H, J = 6.8), 7.76 (m, 9 H), 7.39 (dd, 2 H, J = 7.4, 1.8), 7.28 (t, 1 H, J = 7.4), 7.22 (m, 2 H), 7.15 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.23, 150.38, 150.25, 150.18, 150.14, 150.06, 147.79, 147.23, 146.58, 143.20, 143.10, 143.06, 143.03, 141.57, 139.78, 135.68, 135.31, 134.49, 134.43, 132.51, 131.96, 131.87, 131.82, 131.75, 131.26, 130.28, 127.35, 127.11, 127.02, 126.47, 126.43, 126.40, 125.75, 125.38, 122.22, 121.24, 120.90, 120.73, 120.34. Vis ($CHCl_3$): 424 (5.32), 551 (4.08), 594 (3.52). FAB MS: 691 (calcd 691).

[2-Vinyl-5,10,15,20-tetraphenylporphinato]zinc(II).[48] An oven-dried 50-mL Schlenk tube equipped with a magnetic stirring bar was charged with zinc chloride (204 mg, 1.5 mmol) and 20 mL of freshly distilled THF. The solution was stirred under N_2 for 10 min. Vinylmagnesium bromide in hexane (0.134 mL, 1 mmol) was added to the solution by syringe, and transmetalation occurred within 10 min. Upon completion of the coupling reaction, the crude reaction mixture was purified by column chromatography on silica gel using 1:1 toluene:hexane. The reddish purple band was isolated and evaporated. Isolated yield = 55 mg (85%, based on 70 mg of the porphyrin starting material). Selected characterization data are as follows. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.97 (s, 1 H), 8.90 (m, 4 H), 8.87 (d, 1 H, J = 4.7), 8.79 (d, 1 H, J = 4.7), 8.20 (m, 6 H), 8.06 (d, 2 H, J = 6.6), 7.74 (m, 12 H), 6.39 (dd, 1 H, J = 17.0, 9.1), 5.83 (dd, 1 H, J = 17.1, 2.0), 5.01 (dd, 1 H, J = 10.7, 2.0). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.90, 150.46, 150.25, 150.05, 148.55, 146.84, 144.58, 142.99, 142.78, 134.40, 133.86, 133.17, 132.32, 132.00, 131.47, 130.84, 127.93, 127.47, 126.76, 126.53, 121.39, 121.29, 120.90, 120.44, 115.18. Vis ($CHCl_3$): 426 (5.53), 517 (3.68), 555 (4.22), 595 (3.68). An analytical sample was demetalated with HCl. Anal. Calcd for $C_{46}H_{32}N_4$: C, 86.22; H, 5.03; N, 8.74. Found: C, 86.54; H, 5.09; N, 8.45.

[2-(Pentafluorophenyl)-5,10,15,20-tetraphenylporphinato]zinc(II). An oven-dried 50-mL three-neck round bottom flask equipped with a magnetic stirring bar was charged with Mg (25 mg, 1 mmol) and 20 mL of freshly distilled THF. Pentafluorobromobenzene (0.125 mL, 1 mmol) was added to the solution. The solution was stirred for 2 min, cooled to 0 °C, and stirred for another 3 h. A solution of zinc chloride (165 mg, 1.2 mmol) in 20 mL of THF was added, and the solution was brought to room temperature, yielding the organozinc chloride reagent. Upon completion of the reaction, the crude product was purified by column chromatography on silica gel using 1:9 THF:hexane.

(48) Callot, H. J. *Tetrahedron* **1973**, *29*, 899–901.

(49) (a) Samuels, E.; Shuttleworth, R.; Stevens, T. S. *J. Chem. Soc. C* **1968**, 145–147. (b) Callot, H. J. *Bull. Soc. Chim. Fr.* **1974**, 1492. 2-Bromoporphyrin and 2-nitroporphyrin have been utilized previously for several direct substitution reactions. Direct substitution reactions involving porphyrin substrates are neither general nor efficient; see: (c) Callot, H. J. *Tetrahedron Lett.* **1973**, *50*, 4987–4990. (d) Crossley, M. J.; Harding, M. M.; Sternhall, S. *J. Am. Chem. Soc.* **1986**, *108*, 3608–13.

Isolated yield = 49 mg (87%, based on 50 mg of the porphyrin starting material). ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.93 (m, 4 H), 8.92 (s, 1 H), 8.86 (d, 1 H, J = 4.6), 8.72 (d, 1 H, J = 4.6), 8.20 (m, 6 H), 8.01 (d, 2 H, J = 7.0), 7.74 (m, 9 H), 7.43 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.82, 150.14, 147.43, 145.57, 144.44, 142.52, 141.06, 138.11, 136.43, 134.41, 133.82, 132.66, 132.39, 131.93, 128.09, 127.95, 127.61, 126.59, 125.79, 121.57, 121.57, 121.45, 120.99, 114.77, 99.23. Vis ($CHCl_3$): 424 (5.62), 554 (4.31), 596 (3.57). An analytical sample was demetalated with HCl. FAB MS: 781 (calcd 781).

General Conditions for the Preparation of 5,15-Disubstituted 10,20-Diphenylporphyrins. A 1-mmol solution of the organotin or organozinc chloride reagent (see below) was transferred to a Schlenk-style storage tube containing [5,15-dibromo-10,20-diphenylporphinato]zinc(II) (0.10 mmol) and 3 mg of the palladium catalyst. The total reaction volume was 40 mL. For the syntheses of 5,15-divinyl-, 5,15-dimethyl-, and 5,15-(4,4′-dimethyl-2,2′-dipyridyl)-substituted [10,20-diphenylporphinato]-zinc complexes, $Pd(PPh_3)_4$ was utilized as the catalyst. For the $Pd(PPh_3)_4$-catalyzed reactions, the general procedure consisted of heating the reaction mixture to 60 °C in the Schlenk tube. The course of the reaction was monitored by TLC. Irrespective of the organometallic reagent, it was found that 48 h was required to completely consume the starting material [5,15-dibromo-10,-20-diphenylporphinato]zinc(II). At the endpoint, the reaction was quenched with water, extracted with chloroform, dried over $CaCl_2$, and evaporated. For the dimethoxyphenyl and pentafluorophenyl coupling reactions to the [5,15-dibromo-10,20-diphenylporphinato]zinc(II) template, Pd(dppf) was used as the catalyst; the reactions were carried out at room temperature and completed within 12 h. Details for the isolated of each compound are given below.

[5,15-Bis[[2-(4′-methyl-2′-pyridyl)-4-pyridyl]methyl]-10,-20-diphenylporphinato]zinc(II). A −78 °C solution of 4,4-dimethyl-2,2′-bipyridine (1.0 mmol) in 15 mL of THF was treated with a THF solution of LDA (0.95 mmol) and stirred for 2 h. Tributyltin chloride (1.05 mmol) was added, and the mixture was heated at reflux for 1 h. The resulting organotin reagent was used without further purification.

After completion of the metal-mediated cross-coupling reaction, excess 4,4′-dimethyl-2,2′-bipyridyl was removed from the crude reaction mixture by sublimation and chromatography was carried out on silica gel with a mixture of $CHCl_3$, acetone, and triethylamine. The porphyrin was eluted in one broad band. The 75 mg of product obtained from this procedure (88%, based on 70 mg of the porphyrin starting material) was contaminated with a small amount (0.2 equiv per equiv of porphyrin) of coordinated triphenylphosphine, as determined by integration of the ^{1}H NMR spectrum. This sample was demetalated with concentrated HCl and purified by chromatography using chloroform/acetone/triethylamine to give the purified demetalated porphyrin in an overall yield of 81%. Characterization data have been previously reported.[41]

[5,15-Divinyl-10,20-diphenylporphinato]zinc(II). The vinyl source was tri-*n*-butylvinyltin. At the reaction endpoint, the crude product was absorbed on silica gel and loaded onto a column packed in hexane. Elution was carried out with hexane utilizing a CH_2Cl_2 gradient (0–50%). A small quantity of uncharacterized purple material led the main fraction. The main band was evaporated to yield 54 mg of pure [5,15-divinyl-10,20-diphenylporphinato]zinc (91%, based on 70 mg of the porphyrin starting material). An analytical sample was rechromatographed. Selected characterization data have been previously reported.[41]

[5,15-Dimethyl-10,20-diphenylporphinato]zinc(II). Methylzinc chloride was prepared from methyllithium and anhydrous zinc chloride in THF. Upon completion of the cross-coupling reaction, the crude solid was dissolved in THF/heptane, poured onto 10 g of silica gel, and evaporated to dryness. This silica gel was loaded onto a column packed in 50% CH_2Cl_2/hexane. A single band was eluted (50% CH_2Cl_2/hexane) to yield 50 mg of pure [5,15-dimethyl-10,20-diphenylporphinato]zinc(II), (88%, based on 70 mg of the porphyrin starting material). An analytical sample was recrystallized from THF/heptane by slow evaporation under N_2. Selected characterization data are as follows. ^{1}H NMR (500 MHz, 3:1 $CDCl_3$, THF-d_8): δ 9.34 (d, 4 H, J = 4.6), 8.71 (d, 4 H, J = 4.6), 8.02 (dd, 4 H, J = 7.5, 1.4), 7.57 (m, 6 H), 4.51 (s, 6 H). ^{13}C NMR (125 MHz, 3:1 $CDCl_3$, THF-d_8): δ 150.07 (0), 148.88 (0), 143.34 (0), 134.18 (1), 131.42 (1), 128.09 (1), 126.73 (1), 125.88 (1), 119.29 (0), 113.74 (0), 20.81 (3). Vis (THF): 424 (5.58), 522 (3.40), 559 (4.12), 605 (3.88). Anal. Calcd for $C_{34}H_{24}N_4Zn$: C, 73.72; H, 4.37; N, 10.11. Found: C, 73.43; H, 4.09; N, 10.09.

[5,15-Bis(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]zinc(II). (2,5-Dimethoxyphenyl)lithium was prepared from 1,4-dimethoxybenzene and *tert*-butyllithium in 10 mL of diethyl ether at −78 °C. The organolithium reagent was added to a solution of $ZnCl_2$ in 10 mL of THF to yield the organozinc chloride reagent. Approximately half of the solvent was removed under vacuum. This reagent was used immediately. At the completion of the reaction, two highly fluorescent spots were visible by TLC. Excess dimethoxybenzene was removed from the reaction mixture by sublimation, and the crude product was chromatographed on silica gel using $CHCl_3$ as eluant. The solvent was evaporated to give a 90% yield of two isomeric porphyrins. Further chromatography allowed the two isomers to be separated. The first band off the column proved to be the C_{2h} isomer of [5,15-bis-(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]zinc. This band was evaporated giving 34 mg (42% yield, based on 70 mg of [5,-15-dibromo-10,20-diphenylporphinato]zinc) of C_{2h}-[5,15-bis(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]zinc(II).

[5,15-Bis(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]-zinc(II)—C_{2h} Isomer. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.91 (s, 8 H), 8.22 (d, 4 H, J = 6.5), 7.75 (m, 6 H), 7.59 (d, 2 H, J = 2.2), 7.26 (br s, 4 H), 3.86 (s, 6 H), 3.54 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.10 (0), 152.30 (0), 150.13 (0), 143.00 (0), 134.10 (1), 132.62 (0), 132.00 (1), 131.44 (1), 127.35 (1), 126.44 (1), 121.34 (1), 120.69 (0), 116.59 (0), 114.76 (1), 112.13 (1), 56.70 (3), 55.95 (3). Vis ($CHCl_3$): 424 (5.64), 551 (4.34), 584 (3.43).

The C_{2v} isomer that followed trailed the C_{2h} isomer off the column. The solvent was evaporated leaving 31 mg of pure [5,-15-bis(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]zinc (38%). This compound is much more soluble in chloroform than the C_{2h} isomer. The assignment of stereochemistry was made from the NMR data.

[5,15-Bis(2,5-dimethoxyphenyl)-10,20-diphenylporphinato]-zinc(II)—C_{2v} Isomer. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.90 (s, 8 H), 8.21 (d, 2 H, J = 7.9), 8.19 (d, 2 H, J = 6.5), 7.73 (m, 6 H), 7.58 (s, 2 H), 7.24 (br s, 4 H), 3.84 (s, 6 H), 3.53 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.14 (0), 152.31 (0), 150.15 (0), 142.94 (0), 134.40 (1), 132.66 (0), 132.02 (1), 131.48 (1), 127.37 (1), 126.46 (1), 126.44 (1), 121.30 (1), 120.72 (0), 116.69 (0), 114.73 (1), 112.28 (1), 56.75 (3), 55.92 (3). A demetalated sample was analyzed. Anal. Calcd for $C_{48}H_{38}N_4O_4$: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.64; H, 5.13; N, 7.51.

The C_{2v} and C_{2h} isomers slowly interconvert over the course of several days in solution at room temperature.

[5,15-Bis(pentafluorophenyl)-10,20-diphenylporphinato]-zinc(II). An oven-dried 50-mL three-neck round-bottom flask equipped with a magnetic stirring bar was charged with Mg (50 mg, 2 mmol) and 20 mL of freshly distilled THF. Pentafluorobromobenzene (0.125 mL, 1 mmol) was added to the solution. The solution was stirred for 5 min, cooled to 0 °C, and stirred for 3 h. Zinc chloride (165 mg, 1.2 mmol) in 20 mL of THF was added, and the solution was warmed to room temperature and stirred for 5 min. At the reaction endpoint, the crude product was chromatographed on silica gel using 1:10 THF:hexane as eluant. A single red band was collected and evaporated, leaving 97 mg of pure product (93%, based on 83 mg of the porphyrin starting material). ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.01 (d, 4 H, J = 4.6), 8.87 (d, 4 H, J = 4.7), 8.18 (dd, 4 H, J = 7.4, 1.3), 7.77 (m, 6 H). The sample was demetalated with HCl in chloroform. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (d, 4 H, J = 4.7), 8.79 (d, 4 H, J = 4.7), 8.20 (dd, 4 H, J = 7.8, 1.4), 7.80 (m, 6 H), −2.83 (s, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.60 (dd, $J_{(C-F)}$ = 245, 10), 142.00 (d, $J_{(C-F)}$ = 254), 141.22 (0), 137.55 (dt, $J_{(C-F)}$ = 250, 16), 134.57 (1), 132.70 (1, br), 129.48 (1, br), 128.16 (1), 126.90 (1), 121.48 (0), 116.47 (td, $J_{(C-F)}$ = 20, 4), 102.13 (0). FAB MS: 795 (calcd 795).

Table I. Summary of Structure Determination of [2,5,10,15,20-Pentaphenylporphinato]zinc(II) and 5,15-Bis(pentafluorophenyl)-10,20-diphenylporphyrin

formula	$ZnC_{55}H_{37}N_5 \cdot C_6H_{14}$	$C_{44}H_{20}F_{10}N_4$
formula weight	919.49	794.66
crystal class	monoclinic	monoclinic
space group	$P2_1/n$ (No. 14)	$P2_1/c$ (No. 14)
Z	4	2
cell constants		
a	21.425(4) Å	15.223(2) Å
b	9.718(1) Å	10.162(1) Å
c	24.905(2) Å	12.375(2) Å
β	110.83(1)°	112.75(2)°
V	4846(3) Å^3	1765.6(9) Å^3
μ	10.28 cm^{-1}	10.66 cm^{-1}
D_{calc}	1.260 g cm^{-3}	1.495 g cm^{-3}
$F(000)$	1928	804
radiation	Cu Kα (λ = 1.54184 Å)	Cu Kα (λ = 1.54184 Å)
θ range	2.0–65.0°	2.0–65.0°
scan mode	ω-2θ	ω-2θ
h, k, l collected	±25, ±11, ±29	±17, ±11, ±14
no. reflectns measurd	9002	4042
no. unique reflectns	8238	2994
no. reflectns used in refinemnt	5589 ($F^2 > 3.0\sigma$)	2564 ($F^2 \geq 3.0\sigma$)
no. parameters	604	307
data/parameter ratio	9.3	8.4
R_1	0.054	0.050
R_2	0.071	0.073
GOF	1.948	2.541

X-ray Crystallography.[50] The crystal structures for 5,15-bis(pentafluorophenyl)-10,20-diphenylporphyrin and [2,5,10,15,-20-pentaphenylporphinato]zinc(II) were solved by direct methods (SIR88).[51] Table I contains details of the crystal and data collection parameters. The structures were determined by Dr. Patrick Carroll at the Chemistry Department's X-ray facility at the University of Pennsylvania.

5,15-Bis(pentafluorophenyl)-10,20-diphenylporphyrin. Crystallization was induced by layering pentane onto a chloroform solution of the compound and storing the mixture at 0 °C under N_2 for 2 weeks, yielding rectangular purple plates. The crystal dimensions were 0.05 × 0.42 × 0.55 mm^3. 5,15-Bis(pentafluorophenyl)-10,20-diphenylporphyrin crystallizes in the monoclinic space group $P2_1/c$ (systematic absences $0k0$, k = odd and $h0l$, l = odd) with a = 15.223(2) Å, b = 10.162(1) Å, c = 12.375(2) Å, β = 112.75(2)°, V = 1765.6(9) Å^3, Z = 2, and d_{calc} = 1.495 g cm^{-3}. The cell constants were determined from a least-squares fit of the setting angles for 25 accurately centered reflections. X-ray intensity data were collected on an Enraf-Nonius CAD4 diffractometer employing graphite-monochromated Cu Kα radiation (λ = 1.5418 Å) and using the ω–2θ scan technique. A total of 4042 reflections were measured over the ranges: $4 \leq 2\theta \leq 130°$, $-17 \leq h \leq 17$, $-11 \leq k \leq 1$, and $-1 \leq l \leq 14$. Three standard reflections measured every 3500 s of X-ray exposure showed an intensity decay of less than 1% over the course of the data collection.

The intensity data were corrected for Lorentz and polarization effects but not for absorption effects. Of the reflections measured, a total of 2564 unique reflections with $F^2 > 3\sigma(F^2)$ were used during subsequent structure refinement. Refinement was by full-matrix least-squares techniques based on F to minimize the quantity $S_w(|F_o|-|F_d|)^2$ with $w = 1/\sigma^2(F)$. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined isotropically. During the latter stages of refinement, it became apparent from the difference maps that the hydrogen on the pyrrole nitrogen was disordered between two possible locations. It was bonded to N1 in approximately $^2/_3$ of the molecules and to N2 in $^1/_3$ of the molecules. Refinement converged to R_1 = 0.050 and R_2 = 0.073.

[2,5,10,15,20-Pentaphenylporphyrinato]zinc(II). The compound was repurified by column chromatography on silica gel using pyridine as the eluent; crystallization was induced by layering hexane onto a methylene chloride solution of the compound and storing the mixture at 0 °C under N_2 for 6 weeks, yielding rectangular purple plates. The crystal dimensions were 0.15 × 1.28 × 0.35 mm^3. [2,5,10,15,20-Pentaphenylporphyrinato]-zinc(II) crystallizes in the monoclinic space group $P2_1/n$ (systematic absences $0k0$; k = odd and $h0l$; $h + l$ = odd) with a = 21.425(4) Å, b = 9.718(2) Å, c = 24.905(2) Å, β = 110.83(1)°, V = 4846(3) Å^3, Z = 4, and d_{calc} = 1.260 g cm^{-3}. The cell constants were determined from a least-squares fit of the setting angles for 25 accurately centered reflections. A total of 9002 reflections were measured over the ranges: $4 \leq 2\theta \leq 130°$, $-25 \leq h \leq 25$, $0 \leq k \leq 11$, $0 \leq l \leq 29$. Three standard reflections measured every 3500 s of X-ray exposure showed an intensity decay of 5.2% over the course of the data collection. A linear decay correction was applied.

The intensity data were corrected for Lorentz and polarization effects, and an empirical absorption correction was applied (minimum transmission 90.46%, maximum 99.97%, mean 95.59%). Of the reflections measured, a total of 5589 unique reflections with $F^2 > 3\sigma(F^2)$ were used during subsequent structure refinement. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included as constant contributions to the structure factors and were not refined. Refinement converged to R_1 = 0.054 and R_2 = 0.071.

Results and Discussion

Two readily synthesized halogenated porphyrins 2-bromotetraphenylporphyrin (BTPP) and 5,15-dibromo-10,-20-diphenylporphyrin (DBDPP) were chosen to explore the applicability of metal-mediated cross-coupling methodology to porphyrin synthetic schemes. The first (BTPP), the most readily available porphyrin bearing a single halogen in the β-position,[49] is synthesized by the reaction of 1 equiv of *N*-bromosuccinimide (NBS) with tetraphenylporphyrin in chloroform.[52] The second porphyrin template, the previously unreported DBDPP, is readily prepared in high yield by simple extensions of literature methods.[53] Under conditions similar to those reported for exclusive *meso* halogenation of porphine, treatment of a chloroform solution of 5,15-diphenylporphyrin at 0 °C with 2 equiv of NBS gave the desired *meso*-dibromoporphyrin in high yield with no trace of substitution at other positions. These two halogenated porphyrins serve as templates in our studies for the fabrication of unsymmetrical porphyrins (2-substituted tetraphenylporphyrins) as well as symmetrically *meso*-substituted porphyrins (5,-15-disubstituted 10,20-diphenylporphyrins). Additionally, these halogenated porphyrin templates provide two systems that allow us to probe in a preliminary fashion the importance of substrate steric and electronic features upon coupling reactivity. Results obtained with other halogenated porphyrin substrates will be reported separately.

Since free base porphyrins are generally not stable in the presence of strong Lewis bases,[54] these studies necessitated the use of metalated porphyrin templates. Several considerations dictated the choice of the central metal atom for the coupling reactions; key factors included the ease of metal insertion and removal and the stability of both the porphyrin reactant and the porphyrin product to reasonably reducing reaction conditions. Ideally, the

(50) The atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Date Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ UK.

(51) Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Polidori, G.; Spagna, R.; Viterbo, D. *J. Appl. Crystallogr.* **1989**, *72*, 389–93.

(52) We have found that even when less that 1 equiv of *N*-bromosuccinamide is used in the reaction, traces of dibrominated porphyrins (two isomers) are always present. The resulting mixture may be purified by flash chromatography. Analytical HPLC was used to insure that the monobromotetraphenylporphyrin used in this study was >99% pure.

(53) Nudy, L. R.; Hutchinson, H. G.; Schieber, C.; Longo, F. R. *Tetrahedron* **1984**, *40*, 2359–2363 and references therein.

(54) A notable exception is the preparation of dilithium salts of porphrins via reaction with $LiN(SiMe_3)_2$. See: Arnold, J. *J. Chem. Soc., Chem. Commun.* **1990**, 976–978 and references therein.

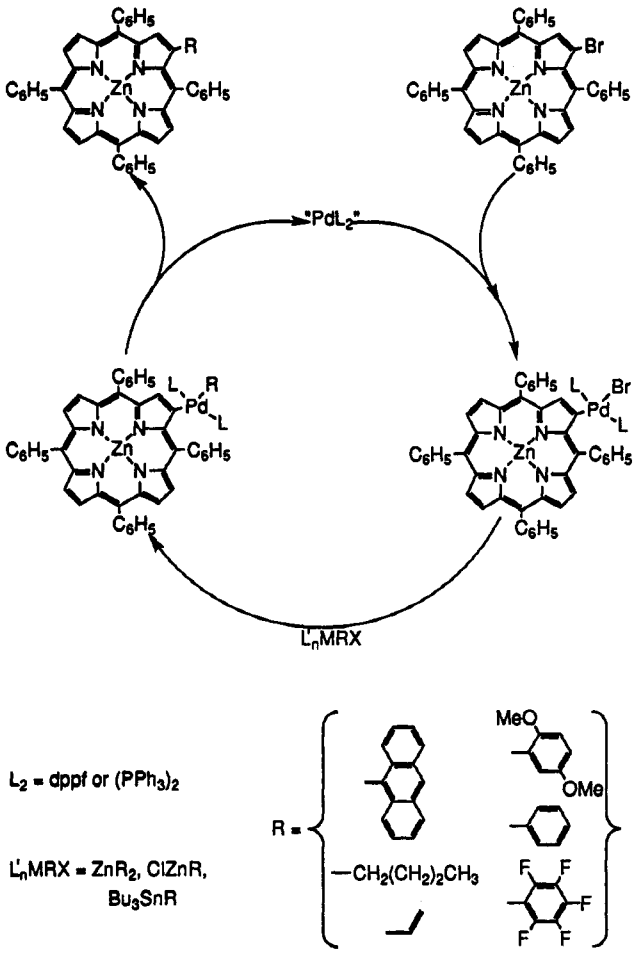
metalated porphyrin product should be robust with respect to common chromatographic media (silica and alumina) as well as inert to oxygen to allow chromatography on the bench top. Our work indicates that Zn(II) fulfills all of these criteria satisfactorily; it, in fact, has been used in the bulk of our studies, though successful coupling reactions have been carried out with a number of other central metal ions.[55]

The choice of organometallic reagents employed in this study was governed by their ability to reduce the brominated porphyrin substrates. Organolithium and Grignard reagents readily reduce the [bromoporphinato]zinc(II) species to their respective porphyrin radical anions, and metal-mediated cross-coupling reactions were not successful under our reaction conditions. This study utilizes organozinc chloride and organotributyltin reagents exclusively in cross-coupling reactions with the brominated porphyrin starting materials. Work completed to date, however, indicates that a variety of metallo–organic species are suitable for cross-coupling chemistry with haloporphyrin templates, provided they meet the key criterion of being incapable of participating in outer-sphere electron transfer with either the reactant or the product.

The reaction conditions were dependent upon the choice of catalyst used. For reactions run in the presence of catalytic quantities of $Pd(PPh_3)_4$, THF solutions were maintained at 60 °C for 12 h and 48 h to obtain complete conversion of [2-bromo-5,10,15,20-tetraphenylporphinato]-zinc (BTPP-Zn) and [5,15-dibromo-10,20-diphenylporphinato]zinc (DBDPP-Zn), respectively, to their corresponding substituted derivatives. Reactions run in the presence of Pd(dppf) required much milder conditions; conversion to products was achieved within 1 h at room temperature for BTPP-Zn and within 12 h at room temperature for DBDPP-Zn. Since cross-coupling reactions at the β-position of [tetraphenylporphinato]zinc involve steric interactions not present in metal-mediated couplings at the *meso*-positions of [diphenylporphinato]-zinc, substrate electronic features appear to be the key in determining the reactivity of the halogenated porphyrin template. This agrees well with related experimental evidence, namely, that (i) the Pd-catalyzed cross-couplings involving simple aromatic halides are accelerated by substrate electron-withdrawing groups[9-12,56,57] and (ii) the porphyrin methine carbons are more electron-rich than pyrrolic ones.[53,58] Our studies to date, however, can not rule out the possible electronic interaction of the 20-phenyl group with the Pd center in cross-coupling reactions at the porphyrin 2-position.

Scheme I outlines the proposed oxidative addition–transmetalation–reductive elimination reaction sequence for Pd-catalyzed cross-coupling to a halogenated prophyrin substrate and inventories a wide variety of alkyl, vinyl, and aryl moieties coupled to BTPP-Zn. Monitoring the time course of each reaction by TLC revealed two key features of the cross-coupling reactions: (1) the complete conversion of reactants to products took place for each organometallic reagent and (2) the reaction time depended only on the catalyst used (the nature of the Sn or Zn reagent appeared to have little effect). The reaction appears

Scheme I



unimpeded by seemingly demanding steric constraints. Fairly bulky groups such as 9-anthracenyl or 2,5-dimethoxyphenyl react on time scales comparable to those of vinyl or *n*-butyl. The coupling is also remarkably forgiving in terms of the basicity of the organometallic reagent. Electron-deficient groups such as pentafluorophenyl are coupled onto the porphyrin with ease. These results indicate that a wide variety of steric and electronic modulations are possible at the porphyrin periphery.

While 2-alkyl- and 2-vinyl-substituted tetraphenylporphyrins have easily interpretable ^1H and ^{13}C NMR spectra, magnetic perturbations and rotational effects cause 2-aryl-substituted tetraphenylporphyrins to have relative complex ^1H NMR spectra. Figure 1 shows the 500-MHz ^1H NMR spectrum of [2-(2,5-dimethoxyphenyl)-5,10,15,20-tetraphenylporphinato]zinc(II) along with the aromatic region chemical shift assignments. A prominent feature of this spectrum is the broadening of the signals H_α, H_β, and H_γ. The fixed dimethoxyphenyl ring sufficiently changes the magnetic environment above and below the porphyrin ring so that slow rotation of the phenyl rings is observed. The large upfield shifts observed for the resonances from H_2 to H_6 are due to the mutual shielding of the two stacked aryl groups at the 2- and 20-positions of the porphyrin ring. We believe that the exchange broadening of these signals indicates a slow, windshield-wiper interconversion of the two conformers. Variable-temperature ^1H NMR experiments confirmed that the broadening arises from a dynamic process.

A more dramatic example of shielding due to neighboring aromatic groups on porphyrins is shown in the 500-MHz

(55) DeRege, P. J. F.; Therien, M. J. Unpublished results.
(56) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998.
(57) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158–163.
(58) Gouterman, M. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: London, 1978; Vol. III, pp 1–165.

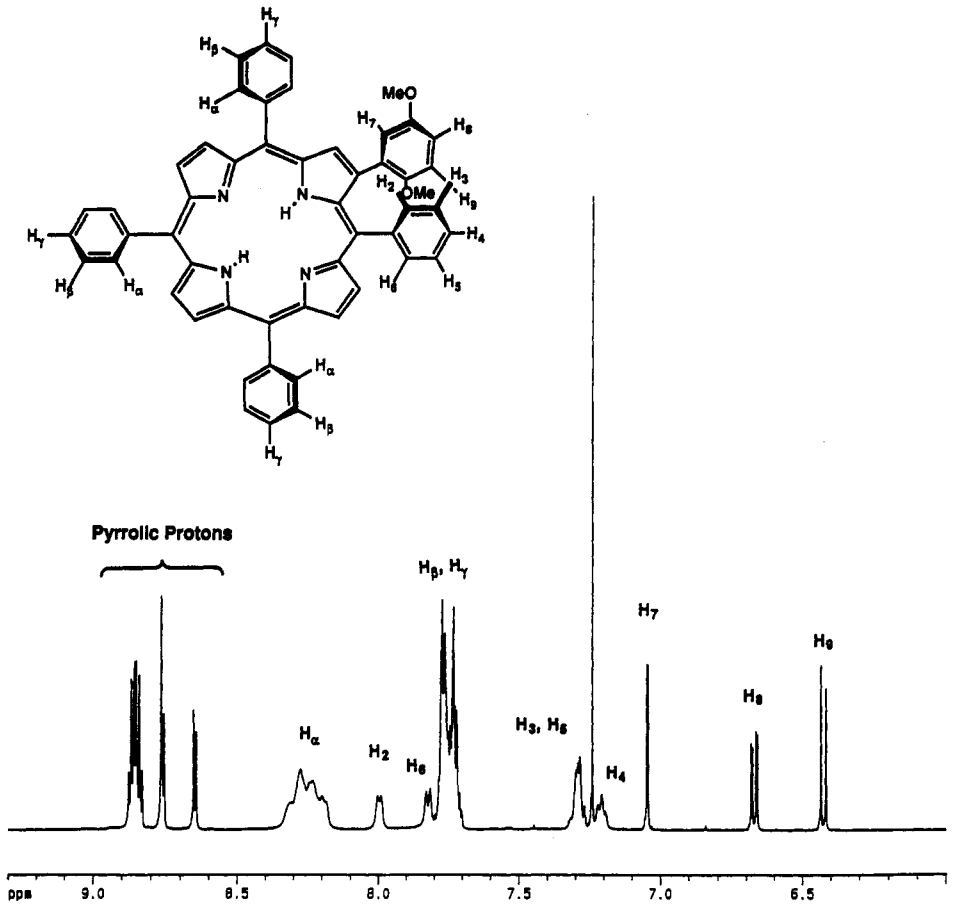


Figure 1. ^{1}H NMR spectrum of 2-(2,5-dimethoxyphenyl)-5,10,15,20-tetraphenylporphyrin.

homonuclear COSY spectrum of 2-(9-anthracenyl)-5,10,-15,20-tetraphenylporphyrin (Figure 2). The more pronounced upfield shifts in this case (compared to those 2-(2,5-dimethoxyphenyl)-5,10,15,20-tetraphenylporphyrin or 2,5,10,15,20-pentaphenylporphyrin) result from the larger aromatic residue at the 2-position. The assignment for reasonances due to the anthracene moiety can be made easily from the spectrum. The buried singlet from the proton at the anthracene 10-position is visible at 8.27 ppm, and the remaining anthracenyl signals fall at 7.97, 7.62, 7.39, and 7.11 ppm. The pyrrolic protons are visible between 8.4 and 9.0 ppm.

Few, if any, pentasubstituted porphyrins have been studied crystallographically.[59] An X-ray crystallographic structure was determined for one of these 2-substituted tetraphenylporphyrins; Figure 3 shows an ORTEP view of the pyridine adduct of [2,5,10,15,20-pentaphenylporphinato]zinc(II). Table II lists selected bond lengths and angles. This structure shows that the Zn atom is displaced 0.346 Å from the plane of the nitrogens, with an average $Zn-N_{por}$ bond distance of 2.073(1) Å and a $Zn-N_{py}$ bond distance of 2.164(3) Å. These values are similar to those found in X-ray structures of analogous Zn porphyrins.[60]

The distance between the center of the β-phenyl ring (tilted 75.28° with respect to the porphyrin plane) and the center of the 20-phenyl group (tilted 74.38° with respect to the porphyrin plane) is 3.639 Å. A close examination of the structural data shows that the 2- and 20-phenyl rings are nested (staggered) with respect to each other. This arrangement minimizes the strain expected from close approach of the phenyl quaternary carbon atoms ($C_{21}-C_{45}$ distance = 3.07 Å).

Catalytic conversion fo DBDPP-Zn to 5,15-disubstituted [10,20-diphenylporphinato)zinc complexes provides a facile route to a wide range of symmetrically *meso*-substituted porphyrins (Scheme II). In common with reactions carried out with MBTPP-Zn, these syntheses can be accomplished with a wide range of organometallic reagents; in fact, this methodology allows fabrication of a seemingly limitless number of porphyrins elaborated in the *meso*-position bearing reactive organic moieties, ligands for metal binding, sterically demanding structures, or unusual electron-donating or electron-withdrawing groups. Furthermore, the linear, difunctional nature of DBDPP coupled with its amenability to large-scale synthesis makes it an ideal synthon for the preparation of porphyrinic arrays and polymers. As observed with cross-couplings at the porphyrin β-position, quantitative reactant-to-product conversions generally allowed for isolation of the materials depicted in Scheme II in excess of 90% yield.

The use of DBDPP-Zn greatly simplifies the preparation of *anti*-substituted diarylporphyrins. Such compounds are typically difficult to obtain from aldehydes and monopyrroles, particularly when aldehydes of differing reactivities are used. As a case in point, pyridine-4-

(59) The Cambridge Crystallographic Data Base shows no examples of such structures.

(60) (a) Cullen, D. L.; Meyer, E. F., Jr. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1976**, *32*, 2259–2269. (b) Hatano, K.; Kawasaki, K.; Munakata, S.; Iitaka, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1985–1992. (c) Barkigia, K. M.; Berber, M. D.; Fajer, J.; Medforth, C. J.; Renner, M. W.; Smith, K. M. *J. Am. Chem. Soc.* **1990**, *112*, 8851–8857. (d) Bobrik, M. A.; Walker, F. A. *Inorg. Chem.* **1980**, *19*, 3383–3390. (e) Collins, D. M.; Hoard, J. L. *J. Am. Chem. Soc.* **1970**, *92*, 3761–3771. (f) Bonnett, R.; Hursthouse, M. B.; Malik, K. M. A.; Mateen, B. *J. Chem. Soc., Perkin Trans. 2* **1977**, 2072–2076.

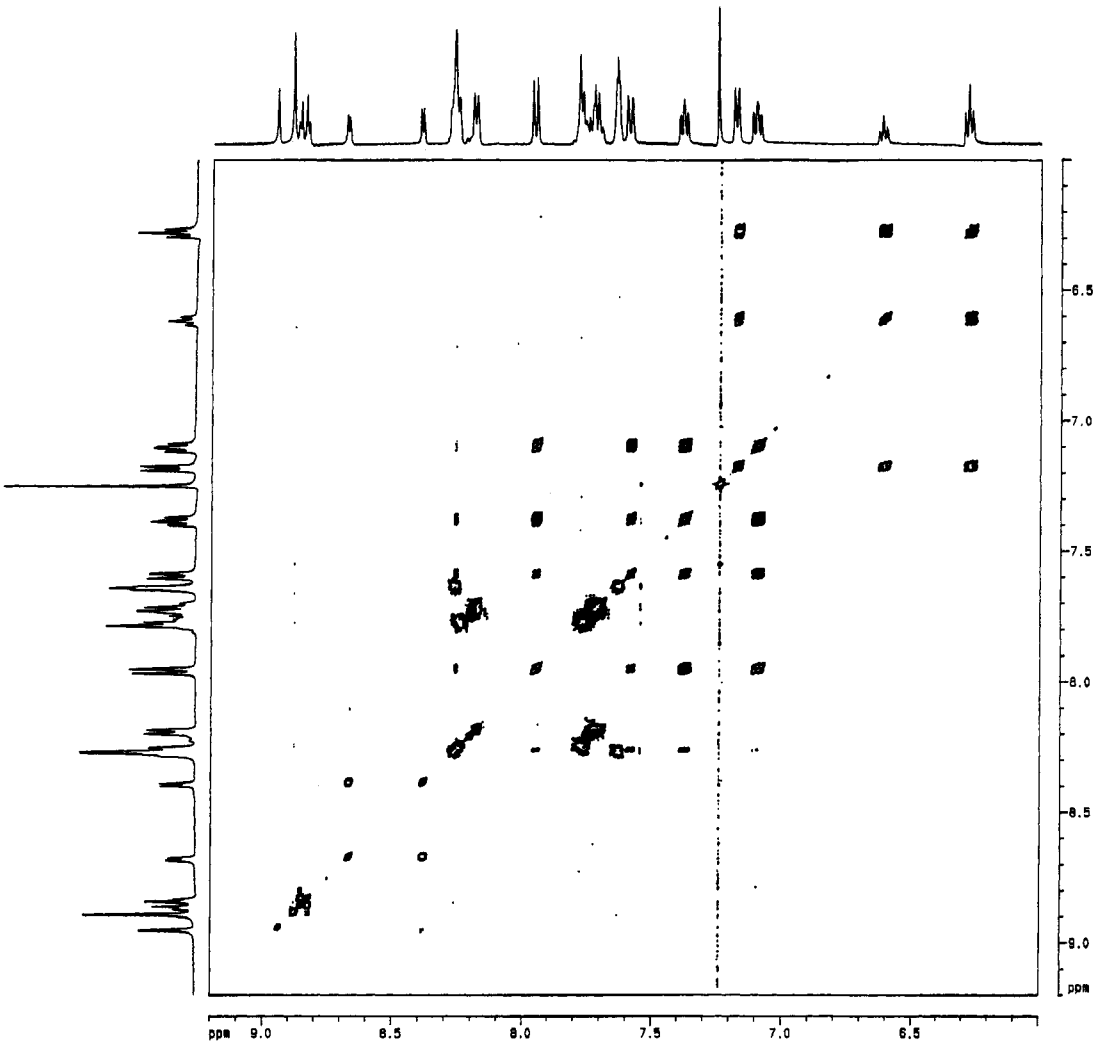


Figure 2. 500-MHz homonuclear COSY spectrum of 2-(9-anthracenyl)-5,10,15,20-tetraphenylporphyrin.

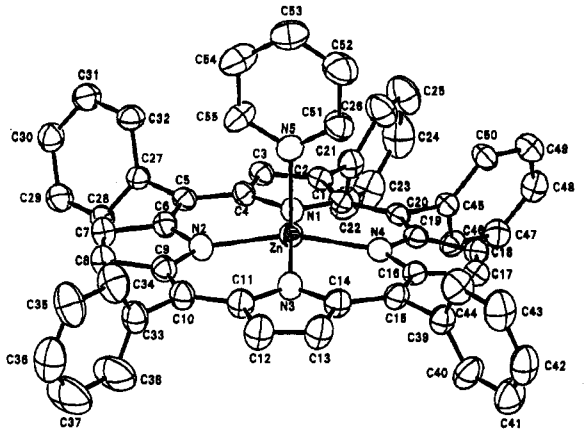


Figure 3. ORTEP view of [2,5,10,15,20-pentaphenylporphinato]-zinc(II) with thermal ellipsoids at 30% probability.

Table II. Selected Bond Distances and Angles

bond	distance, Å	angle	angle, deg
[2,5,10,15,20-Pentaphenylporphyrinato]zinc(II)			
$Zn-N_1$	2.088(3)	$C_2-C_1-C_{20}$	127.7(3)
$Zn-N_4$	2.061(2)	$C_8-C_9-C_{10}$	125.3(4)
$Zn-N_5$	2.164(3)	$C_1-C_2-C_{21}$	133.2(3)
N_1-C_1	1.389(5)	$C_3-C_2-C_{21}$	120.7(3)
C_1-C_2	1.460(5)	$C_1-C_{20}-C_{45}$	118.7(3)
C_2-C_3	1.342(4)	$C_{33}-C_{10}-C_{11}$	117.2(4)
C_1-C_{20}	1.401(4)	$C_{33}-C_{10}-C_9$	117.0(3)
C_2-C_{21}	1.483(6)	$C_{11}-C_{12}-C_{13}$	108.3(4)
$C_{20}-C_{45}$	1.503(5)	$C_{19}-C_{20}-C_{45}$	115.4(3)
5,15-Bis(pentafluorophenyl)-10,20-diphenylporphyrin			
N_2-C_1	1.372(2)	$C_2-C_1-N_2$	109.7(1)
C_1-C_2	1.449(2)	$C_1-C_2-C_3$	107.1(2)
C_2-C_3	1.341(2)	$C_3-C_4-C_5$	124.8(1)
C_4-C_5	1.395(3)	$C_4-C_5-C_{17}$	117.6(2)
C_5-C_{17}	1.493(2)		

carboxaldehyde and benzaldehyde react under Alder–Longo conditions[61] to yield a mixture of six porphyrin products, and the *syn* isomer predominates over the *anti* isomer for the diphenyldipyridylporphyrins. *Anti*-substituted porphyrins can be fabricated from appropriately substituted dipyrryl synthons;[62] a particularly elegant example of such a synthesis is Casiraghi's[63] recent report of a porphyrin bearing *anti*-substituted sugar residues.

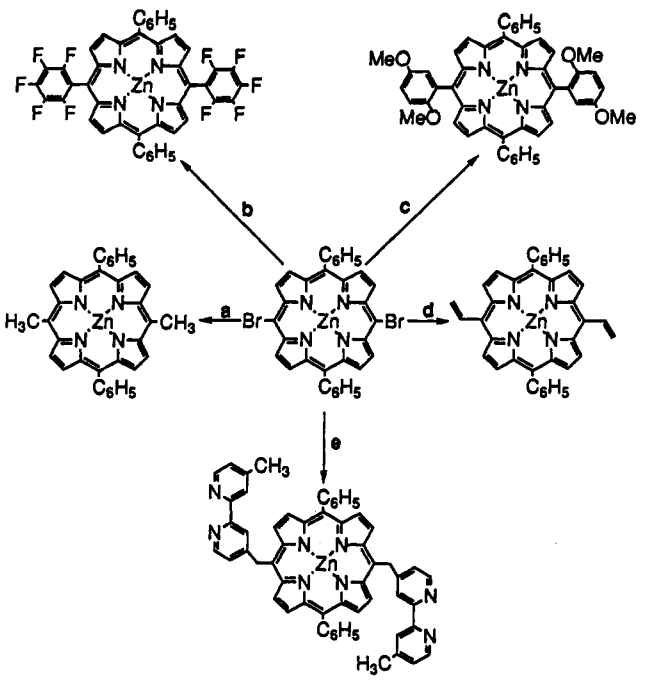
The diverse, new porphyrinic compounds shown in Scheme II demonstrate the power of this approach for the fabrication of *anti*-substituted diarylporphyrins. Successful couplings carried out with alkyl, aryl, vinyl, and

(61) Sari, M. A.; Battioni, J. P.; Dupré, D.; Mansuy, D.; Le Pecq, J. B. *Biochemistry* **1990**, *29*, 4205–4215.

(62) Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1993**, 243–245.

(63) Casiraghi, G.; Cornia, M.; Rassu, G.; Del Sante, C.; Spanu, P. *Tetrahedron* **1992**, *48*, 5619–5628.

Scheme II[a]



[a] (a) MeZnCl, PdL_2 = $Pd(PPh_3)_2$; (b) C_6F_5ZnCl, PdL_2 = Pd(dppf); (c) 2,5-$(OMe)_2C_6H_3ZnCl$, PdL_2 = Pd(dppf); (d) $Bu_3Sn(CH{=}CH_2)$, PdL_2 = $Pd(PPh_3)_2$; (e) $Bu_3Sn[(4\text{-}CH_2)\text{-}4'\text{-}CH_3\text{-bpy})]$, PdL_2 = $Pd(PPh_3)_2$.

benzylic organometallic reagents yield novel porphyrins; these compounds would be challenging target molecules if standard porphyrin synthetic approaches were used in which pyrrole was utilized as a starting material. For example, although porphyrins with *meso*-methyl substituents are known, standard porphyrin syntheses utilizing acetaldehyde generally give abysmal yields of *meso*-methylated porphyrins.[64] As noted for the literature preparation of di-*meso*-pyridyl-di-*meso*-phenylporphyrins, straightforward synthesis and isolation of 5,15-bis(2,5-dimethoxyphenyl)-10,20-diphenylporphyrin via Adler–Longo or Lindsey methods would be difficult due to the disparate reactivities of 2,5-dimethoxybenzaldehyde and benzaldehyde. The successful fabrication of 5,15-bis-(pentafluorophenyl)-10,20-diphenylporphyrin represents a more extreme example of this method's ability to sidestep the problems that arise during a typical mixed aldehyde–porphyrin synthesis.

Also of key significance is the methodological circumvention of keto–enol equilibria, which for some aldehyde substrates may significantly affect the yield in more traditional porphyrin syntheses. For example, it is likely that the fabrication of 5,15-bis[[2-(4'-methyl-2'-pyridyl)-4-pyridyl]methyl]-10,20-diphenylporphyrin would be much less efficient under conditions of high temperature[2] or acid catalysis[3] due to extensive keto–enol equilibria of the 2-arylacetaldehyde synthon. The benefits of avoiding acrolein for similar reasons as a starting material in a di-*meso*-vinyl-substituted porphyrin synthesis have already been noted.[41]

The ability of append electron-deficient perfluoroaryl groups to preformed porphyrin templates is exceptionally noteworthy. There are several examples of stoichiometric carbon–carbon coupling of (perfluoroaryl)Cu(I) species to

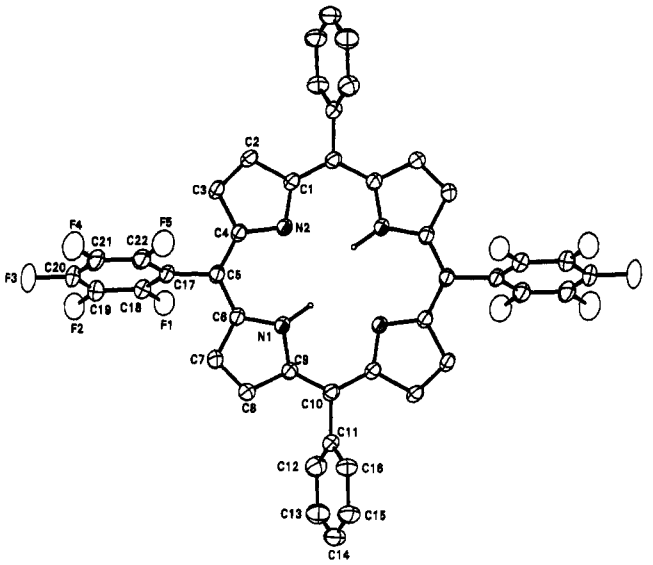


Figure 4. ORTEP view of 5,15-bis(pentafluorophenyl)-10,20-diphenylporphyrin with thermal ellipsoids at 30% probability.

aryl halides,[65,66] but there is a conspicuous absence in the literature of Pd- or Ni-catalyzed couplings involving perfluoroaromatic organometallic reagents with halogenated aromatic systems.[67,68] The X-ray crystal structure determination of 5,15-bis(pentafluorophenyl)-10,20-diphenylporphyrin is shown in Figure 4. Table II lists selected bond lengths and angles. This structure has many features in common to those reported for [5,10,15,20-tetrakis-(pentafluorophenyl)porphinato]cobalt(II).[69] The porphyrin ring is relatively flat, with the largest deviation from planarity being 0.062 Å for N1, similar to the 0.05-Å distortion in the [perfluorophenylporphinato]cobalt complex. The planes of the phenyl and pentafluorophenyl rings are tilted 67.57° and 68.09°, respectively, relative to the porphyrin plane. These values are slightly smaller than the 75.6° value for the dihedral angles observed in [tetrakis(pentafluorophenyl)porphinato]cobalt(II). Since the porphyrin ring is planar and the minor reductions in the dihedral angle of the *meso*-aromatic rings with respect to the porphyrin plane would not give rise to appreciable electronic delocalization, we attribute these differences in the present structure to crystal packing forces.

A number of attempts were made to use this methodology to cross-couple secondary and tertiary alkylzinc reagents to the porphyrin 2-position. It is well known that transmetalated 2° and 3° carbon centers in the coordination sphere of $Pd^{II}(aryl)(PR_3)_2$ complexes are subject to carbon skeleton rearrangements as well as to

(64) McGhee, E. M.; Godfrey, M. R.; Hoffman, B. M.; Ibers, J. A. *Inorg. Chem.* **1991**, *30*, 803–808.

(65) House, H. O.; Fischer, W. F., Jr.; Gall, M.; McLaughlin, T. E.; Peet, N. P. *J. Org. Chem.* **1971**, *36*, 3429–3437.

(66) (a) Reike, R. D.; Rhyne, L. D. *J. Org. Chem.* **1979**, *44*, 3445–3446. (b) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280–5282. (c) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 4482–4488.

(67) There are a few examples of Pd-catalyzed cross-coupling of pentafluorophenyl moieties to vinyl groups. The unusual stability of the transmetalated $(C_6F_5)Pd^{II}(vinyl)L_2$ species in these reactions has been duly noted. See (a) Numata, S.; Okawara, R.; Kurosawa, H. *Inorg. Chem.* **1977**, *16*, 1737–1741. (b) Kurosawa, H.; Urabe, A.; Miki, K.; Kasai, N. *Organometallics* **1986**, *5*, 2002–2008. (c) Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333–6340.

(68) Acetylenes have been cross-coupled to polyfluorphenyl bromides. See: Neenan, T. X.; Whitesides, G. M. *J. Org. Chem.* **1988**, *53*, 2489–2496.

(69) Kadish, K. M.; Araullo-McAdams, C.; Han, B. C.; Franzen, M. M. *J. Am. Chem. Soc.* **1990**, *112*, 8364–8368.

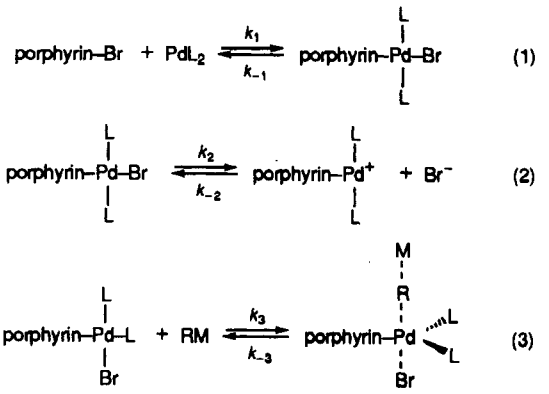
Table III. Pd(dppf)-Catalyzed Cross-Coupling of Butylzinc Chlorides to BTPP[a]

organozinc chloride	isolated yield, %[b]				
	n-BuTPP	*s*-BuTPP	*i*-BuTPP	*t*-BuTPP	TPP
n-BuZnCl	93				0
s-BuZnCl	68	0			12
t-BuZnCl	0		30	0	50

[a] Reaction conditions: 100 mg of BTPP, 3 mg of catalyst, 40 mL of THF, room temperature, reaction time = 1 h. [b] Reaction products identified by ^{1}H NMR spectroscopy.

arene reduction via β-hydride elimination.[42] Pd(dppf) was chosen for this study since it is known to be the most effective catalyst at suppressing these undesired side reactions as well as maximizing the desired reductive elimination reaction with transmetalated, branched hydrocarbon moieties in cross-coupling reactions involving substituted arylhalides.[57] While *n*-butylzinc chloride gave a quantitative yield of the desired porphyrin, *sec*-butylzinc chloride gave a 5:1 mixture of 2-*n*-butyltetraphenylporphyrin and the reduced porphyrin TPP. Similarly, the Pd-catalyzed reaction of BTPP-Zn with *tert*-butylzinc chloride gave a 1.5:1 mixture of the reduction product and the butyl group isomerization product 2-isobutyltetraphenylporphyrin. These results are summarized in Table III and markedly contrast similar reactions in simple aromatic systems in which Pd(dppf) cross-couples 2° carbon centers to the arene periphery without appreciable alkyl group rearrangement or aryl halide reduction.[57] The reason for this difference in reactivity is not yet obvious. Since it is generally assumed that catalysis mediated by Pd(dppf) must either retard β-hydride elimination or accelerate reductive elimination from the diorganopalladium intermediate relative to those by other $Pd(PR_3)_2$ catalysts, it may indeed be the case that electronic or steric perturbations in the porphyrinic transmetalated intermediate (TPP-Pd^{II}-R) relative to those in a typical arene-based transmetalated intermediate (Ar-Pd^{II}-R) favor an elongated reductive elimination time scale. Steric constraints introduced by the phenyl group neighboring the porphyrin β-carbon may partly account for this difference in reactivity; further studies will be needed to elucidate the factors that contribute to the enhanced production of reduced porphyrin and isomerized alkyl groups in cross-coupling reactions involving BTPP. Pd-catalyzed coupling of 2° and 3° carbon centers to the sterically unencumbered porphyrin 5- and 15-positions of DBDPP may proceed with suppressed β-hydride elimination.

Because the time required for reactant to product conversion depends only on the choice of catalyst and halogenated porphyrin template (as judged qualitatively by monitoring the time course of cross-coupling reactions at the porphyrin periphery by TLC), one of two hypotheses regarding the nature of the rate-determining step in the catalytic cycle can be made at this time: either oxidative addition is rate-limiting (eq 1) or rate-limiting loss of halide from the porphyrin-Pd-L_2Br intermediate is required for transmetalation to occur (eq 2). Although transmetalation is generally believed to be rate-determining in the oxidative addition–transmetalation–reductive elimination catalytic cycle,[42,57,70-72] cases in which the rate of oxidative addition



determines the overall rate are not without precedent.[56] Since porphyrins are more readily reduced and have a smaller HOMO–LUMO gap than simple haloaromatics, it would not be surprising if the oxidative addition product (porphyrin-Pd-L_2Br) was relatively stable in the presence of excess organozinc or organotin reagents. Extensive electronic delocalization provided by the porphyrin may disfavor the classic S_E2 mechanism (eq 3) for transmetalation by making the Pd center less electrophilic. Loss of halide may thus be necessary for the porphyrin intermediate formed via oxidative addition to advance through the catalytic cycle. As is the case for both vinylic and aromatic substrates, use of a different halogenated porphyrin template and/or organometallic reagents may result in other steps of the catalytic cycle (such as transmetalation or reductive elimination) to be rate-limiting.

On a final note, we wish to emphasize that it is rather unusual for organometallic moieties that vary significantly in either their steric or their electronic nature to function equally well in metal-mediated cross-coupling reactions at a single halo vinyl or aryl species,[42,56,70-72] especially when both the catalyst used and the reaction conditions remain invariant throughout the series of couplings. Since these reactions at porphyrins are exceptionally clean and occur over time periods amenable to convenient kinetic analysis, a combination of mechanistic studies and electronic structure calculations may prove illuminating.

Summary and Conclusions

Utilizing metal-mediated cross-coupling methodology along with simple halogenated porphyrin substrates accords multiple synthetic advantages to porphyrin fabrication. (1) Catalytic, quantative conversion of reactants to products allows highly efficient derivatization of the porphyrin periphery. (2) Facile reaction conditions permit the incorporation of organic groups sensitive to heat and acid. (3) Decoupling of porphyrin ring cyclization chemistry from the elaboration of the porphyrin periphery provides a methodological approach to facilitate syntheses of target porphyrin molecules that are not amenable to fabrication by typical condensation reactions. The insensitivity of Pd-catalyzed cross-coupling at porphyrin templates to both steric and electronic properties of the organometallic reagent opens up a number of intriguing possibilities; for example, fabrication of porphyrins possessing (i) polymerizable organic moieties, (ii) groups that confer unusual optical properties, or (iii) substituents that limit the closest bimolecular approach of reactive por-

(70) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.
(71) Negishi, E.-I.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukado, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393–2401.
(72) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595.

phyrin metal centers represents only a small subset of potential arenas in which to exploit this chemistry. (4) Fast purification and isolation of products are possible since generally only one porphyrin species is present at the reaction endpoint. This feature naturally endows the ability to quickly synthesize families of related molecules from the parent brominated porphyrin template, a particularly useful capability when a large number of similar complexes are required for mechanistic studies or when optimization of particular structural or electronic features is desired; for example, tuning the affinity (or stereoselectivity) of a substrate binding site at the porphyrin or the reactivity of a porphyrin-based catalyst should both become less cumbersome endeavors. The large number of available halogenated porphyrins[32,43,49,53,72-75] underscores the potential for this methodological approach.

Acknowledgment. M.J.T. thanks the Searle Scholars and Beckman Young Investigator Programs for generous financial support.

(73) (a) Traylor, T. G.; Tsuchiya, S. *Inorg. Chem.* **1987**, *26*, 1338–1339. (b) Hoffman, P.; Labat, G.; Robert, A.; Meunier, B.; *Tetrahedron Lett.* **1990**, *31*, 1991–1994. (c) Wijesekera, T.; Matsumoto, A.; Dolphin, D.; Lexa, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1028–1030. (d) Gonsalves, A. M.; Johnstone, R. A. W.; Pereira, M. M.; Shaw, J.; Sobral, A. J. F. *Tetrahedron Lett.* **1991**, *32*, 1355–1358. (e) Mandon, D.; Ochsenbein, P.; Fischer, J.; Weiss, R.; Jayaraj, K.; Austin, R. N.; Gold, A.; White, P. S.; Brigaud, O.; Battioni, P.; Mansuy, D. *Inorg. Chem.* **1992**, *31*, 2044–2049.

(74) Bonnett, R.; Campion-Smith, I. H.; Kozyrev, A. N.; Mironov, A. F. *J. Chem. Res. Synop.* **1990**, 138–139.

(75) Ali, H.; vanLier, J. E. *Tetrahedron Lett.* **1991**, *32*, 5015–5018.