Investigation of the Scope of Heterogeneous and Homogeneous Procedures for Preparing Magnesium Chelates of Porphyrins, Hydroporphyrins, and Phthalocyanines

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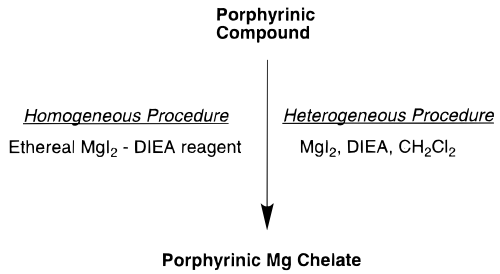
A simple method has been developed for metalation of porphyrinic compounds under homogeneous conditions at room temperature using a stable ethereal solution of MgI_2 and *N,N*-diisopropylethylamine. A previously developed heterogeneous procedure employs a mixture of a magnesium halide and a nonnucleophilic amine in a noncoordinating solvent at room temperature. The scope of the heterogeneous and homogeneous magnesium insertion procedures has been investigated across a family of 19 porphyrinic compounds, including synthetic porphyrins, synthetic or naturally occurring chlorins, and organic-soluble phthalocyanines. The rate of magnesium insertion increased in the series phthalocyanines < chlorins < porphyrins, which parallels the basicity of the ligands. Though phthalocyanines have the smallest core size, the magnesium phthalocyanines were far more stable than magnesium porphyrins to acid-induced demetalation. The heterogeneous method is broadly applicable to porphyrins, chlorins, and phthalocyanines. The homogeneous method is generally slower than the heterogeneous method, though both afford rapid metalation of most porphyrins, including electron-deficient, peripherally coordinating, or facially encumbered *meso*-substituted tetraarylporphyrins, and the β-substituted octaethylporphyrin. Chlorin e_6 trimethyl ester and methyl pyropheophorbide a were metalated cleanly under homogeneous but not heterogeneous conditions, while pheophytin a failed with both methods. The homogeneous method failed altogether with phthalocyanines. Several methods in magnesium chemistry have been developed that augment these procedures, including a mild synthesis of tetraphenylchlorin and a streamlined separation of porphyrin, chlorin, and bacteriochlorins based on selective formation of the magnesium chelates. Collectively, these methods should broaden the scope of model systems based on magnesium chelates of porphyrinic compounds.

Introduction

Chlorophylls and bacteriochlorophylls contain magnesium, and consequently, the study of magnesium-containing porphyrinic compounds has been of longstanding interest. However, the introduction of magnesium into porphyrinic compounds has also been a longstanding problem. Numerous methods have been developed though these generally involve two distinct approaches.[1] One approach employs a magnesium salt (e.g., $MgCl_2$, $Mg(ClO_4)_2$, $Mg(OAc)_2$) in a polar solvent (pyridine, DMF, 1-propanol) at high temperature. The polar solvent is selected to provide mutual solubility of the magnesium halide and the free base porphyrin. A second approach employs hindered Grignard reagents as metalating agents at room temperature, but this approach suffers from the requirements of strict anaerobic conditions and generation of the Grignard reagent immediately prior to use.

Recently we developed a mild, room-temperature procedure for inserting magnesium into tetraarylporphyrins that uses a magnesium halide, a noncoordinating solvent, and a nonnucleophilic amine.[2] This reaction is heterogeneous, abandoning the approach of high mutual solubility of the magnesium reagent and the porphyrin, yet affords rapid metalation. Considerable latitude exists in selecting among magnesium reagents ($MgBr_2$, $MgBr_2{\cdot}O(Et)_2$, MgI_2), solvents (toluene, CH_2Cl_2, $CHCl_3$), and bases (triethylamine, diisopropylethylamine, 2,2,6,6-tetramethylpiperidine) for efficient metalation. The procedure proved successful for tetraphenylporphyrin (TPP) as well as three ortho-substituted tetraarylporphyrins that were examined. The latter are prototypical building blocks in the construction of soluble multi-porphyrin arrays such as light-harvesting arrays,[3] molecular photonic wires,[4] and molecular optoelectronic gates.[5]

Scheme 1. Heterogeneous and Homogeneous Methods for Magnesium Insertion



We wished to explore the application of this heterogeneous magnesium insertion procedure to a wide range of tetrapyrrolic pigments. During the course of this work we discovered homogeneous reaction conditions for performing the magnesium insertion, which is complementary to the heterogeneous method (Scheme 1). In this paper, we describe this homogeneous method in detail. We investigate the scope of the heterogeneous and homogeneous magnesium insertion methods by examining the reaction of 19 porphyrinic compounds. These compounds include seven *meso*-tetraarylporphyrins bearing various substituents (three are from our previous study),[2] the β-substituted octaethylporphyrin (OEP), the porphyrin isomer 2,7,12,17-tetra-

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(1) For a review of magnesium insertion methods, see Table 1 in ref 2.
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n-propylporphycene, six synthetic or naturally occurring hydroporphyrins, and four phthalocyanines. The magnesium hydroporphyrins are important due to their similarity to chlorophylls and bacteriochlorophylls. Magnesium phthalocyanines are of particular interest because of their strong absorbance in the red region of the spectrum and higher fluorescence quantum yield (Φ_f) compared with other metallophthalocyanines.[6−8] Magnesium phthalocyanines are generally prepared by methods that have changed little from Linstead's initial method involving treatment of an *o*-cyanobenzamide or phthalonitrile with Mg metal at high temperature.[9,10] In fact, to our knowledge only seven magnesium phthalocyanines have been prepared.[11−16] Both magnesium hydroporphyrins and magnesium phthalocyanines are of interest as components of light-harvesting arrays, and mild methods are essential for introducing magnesium into soluble derivatives of these pigments that bear sensitive functional groups. As part of this work we needed access to samples of synthetic chlorins, thus we also have developed an improved synthesis and purification of tetraphenylchlorin (TPC) and its magnesium chelate.

Experimental Section

CH_2Cl_2 (Fisher reagent grade) was distilled from K_2CO_3. $CHCl_3$ (99.8%, A.C.S. spectrophotometric grade, stabilized with amylenes) was purchased from Aldrich. Any mention of $CHCl_3$ refers to $CHCl_3$ stabilized with amylenes. Toluene, 1,2-dichlorobenzene, diethyl ether, glacial acetic acid, and trifluoroacetic acid were obtained from Fisher (A.C.S. reagent grade) and were used as received. $MgI_2{\cdot}O(Et)_2$ was obtained from Alfa. All other magnesium reagents were obtained from Aldrich. Magnesium reagents that exist as solid clumps ($MgI_2{\cdot}O(Et)_2$ and $MgBr_2{\cdot}O(Et)_2$) rather than fine powders were pulverized, and the finely pulverized powder was used in all experiments. Since the magnesium reagents hydrate readily in the open air, there was no delay between weighing and use. *N*,*N*-diisopropylethylamine (DIEA), triethylamine (TEA), and 2,2,6,6-tetramethylpiperidine were obtained from Aldrich and were used as received. 5,10,15,20-Tetrakis(pentafluorophenyl)porphyrin, tetra-4-pyridylporphyrin, octaethylporphyrin, tetrakis(4-cumylphenoxy)phthalocyanine, and 1,4,8,11,15,18,22,25-octabutoxyphthalocyanine were purchased from Aldrich. Tetraphenylchlorin, pyropheophorbide a, and chlorin e_6 trimethyl ester were obtained from Porphyrin Products, Inc. (Logan, UT). Pheophytin a was obtained from *Spirulina* blue green algae.[17] All other porphyrins were synthesized by literature methods.[18] All porphyrins used were chlorin-free. 4-(*n*-hexyloxy)phthalonitrile and *tert*-butylphthalonitrile were obtained from TCI America.

Chromatography was performed on alumina (Fisher A-540, 80−200 mesh), grade V alumina, or Baker flash silica gel. Grade V alumina was prepared by adding 15 mL of H_2O to 85 g of alumina (Fisher A-540) with vigorous mechanical stirring. Absorption spectra were collected using HP8451A, HP8452A, and Cary 3 spectrometers. ^{1}H NMR spectra were collected at 300 MHz with an IBM FT-300. Yields were calculated based on the mass of the isolated magnesium porphyrin and were not corrected for any axial ligands or solvent of crystallization. Mass spectra were determined by laser desorption mass spectrometry.

For quantitative reaction monitoring of magnesium insertion or demetalation, samples (∼10 μL) were removed from the reaction mixtures and diluted in 3 mL of CH_2Cl_2/ethanol (3:1). Absorption spectra were collected using an HP8452A spectrometer, and spectra were deconvoluted (HP89532Q) to determine the percent metalation. Yield determinations at the extremes of little reaction or near-total reaction are sensitive to slight baseline shifts and other spectral artifacts; consequently we have stated all high-yielding reactions as >95% and those reactions indicating <1% yield have been reported as 0%. Absorption spectral parameters were taken from the literature for TPP and MgTPP[19] and were determined for tetrakis(4-cumylphenoxy)-phthalocyanine (λ_{abs} CH_2Cl_2/ethanol (3:1) 640, 666, 702 nm, $\epsilon_{702\ nm}$ = 89 300 M^{-1} cm^{-1}) and magnesium tetrakis(4-cumylphenoxy)phthalocyanine (λ_{abs} CH_2Cl_2/ethanol (3:1) 356, 614, 684 nm; $\epsilon_{684\ nm}$ = 172 000 M^{-1} cm^{-1}).

Absorption and emission spectra, including measurements of extinction coefficients and emission quantum yields, were determined at room temperature. Absorption spectra were collected using a Varian Cary 3 with 1 nm band widths and 0.25 nm data intervals. Fluorescence spectra were collected using a Spex Fluoromax with 1 mm slit widths (4.25 nm) and 1 nm data intervals. Emission spectra were obtained with $A_{\lambda max} < 0.1$ and λ_{exc} = 630 nm. Quantum yields were determined by taking the ratio of the integrated corrected emission spectra to that of magnesium tetra-*tert*-butylphthalocyanine in $CHCl_3$ ($\Phi_f = 0.84$).[20]

Heterogeneous Magnesium Insertion Reactions. Mg-**1a**, Mg-**1e**, and Mg-**1f** were prepared previously by the heterogeneous method.[2]

(1) Magnesium Tetrakis(4-carbomethoxyphenyl)porphyrin (Mg-1b). A sample of tetrakis(4-carbomethoxyphenyl)porphyrin (**1b**; 100 mg, 0.118 mmol) in 8 mL of CH_2Cl_2 was treated with MgI_2 (0.33 g, 1.18 mmol) and DIEA (0.41 mL, 2.36 mmol), and the mixture was stirred magnetically at room temperature. After 30 min UV−visible absorption analysis of the reaction mixture showed no product or starting material present. Addition of 1 mL of ethanol resulted in a deeply colored mixture. The absorption spectrum showed only the metalated porphyrin. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (3 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (1:1) gave 92 mg (90% yield): λ_{abs} (CH_2Cl_2/ethanol, 8:1) 428, 526, 566, 606 nm; $C_{52}H_{36}N_4O_8Mg$ calcd mass 868.2, obsd 868.4; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 3.90 (12 H, s, CO_2CH_3), 8.12 (8 H, d, J = 8.1 Hz, *m*-ArH), 8.25 (8 H, d, *o*-ArH), 8.68 (8 H, s, β-pyrrole).

(2) Magnesium Tetra-4-pyridylporphyrin (Mg-1c).[21,22] A sample of tetra-4-pyridylporphyrin (**1c**; 100 mg, 0.161 mmol) in 8 mL of CH_2Cl_2 was treated with MgI_2 (0.45 g, 1.61 mmol) and DIEA (0.56 mL, 3.21 mmol), and the mixture was stirred magnetically at room temperature. After 20 min UV−visible absorption analysis of the reaction mixture showed no product or starting material present. The addition of 1 mL of ethanol resulted in a deeply colored mixture. The absorption spectrum showed only the metalated porphyrin. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness, giving 90 mg (87% yield): λ_{abs} (CH_2Cl_2/ethanol, 8:1) 424, 524, 562, 602 nm; $C_{40}H_{24}N_8Mg$ calcd mass 640.1, obsd 640.9; ^{1}H NMR ($CDCl_3$/

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C_5D_5N, 10:1) δ 8.0 (8 H, d, J = 5.6 Hz, *o*-C_5H_4N), 8.76 (8 H, s, β-pyrrole), 8.89 (8 H, d, *m*-C_5H_4N).

(3) Magnesium Tetrakis(pentafluorophenyl)porphyrin (Mg-1d). A sample of tetrakis(pentafluorophenyl)porphyrin (**1d**; 100 mg, 0.102 mmol) in 8 mL of CH_2Cl_2 was treated with DIEA (0.71 mL, 4.08 mmol) followed by MgI_2 (0.57 g, 2.05 mmol), and the mixture was stirred magnetically at room temperature. After 20 min the reaction was judged to be complete by UV−visible absorption analysis. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (3 × 15 cm) with CH_2Cl_2 eluted residual free base followed by the magnesium porphyrin (83 mg, 81% yield): λ_{abs} (toluene) 366, 404, 424, 558 nm; $C_{44}H_8F_{20}N_4Mg$ calcd mass 996.8, obsd 997.0; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 8.87 (s, β-pyrrole).

(4) Magnesium Tetrakis[2,6-bis(pentafluorobenzyloxy)phenyl]-porphyrin (Mg-1g). A sample of tetrakis[2,6-bis(pentafluorobenzyl-oxy)phenyl] porphyrin (**1g**; 50 mg, 0.023 mmol) in 5 mL of CH_2Cl_2 was treated with MgI_2 (0.12 g, 0.43 mmol) and DIEA (0.15 mL, 0.86 mmol), and the mixture was stirred magnetically at room temperature. After 1 h the reaction was judged to be complete by UV−visible absorption analysis. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (3 × 15 cm) with CH_2Cl_2/ethyl acetate (1:1) first eluted residual free base followed by the magnesium porphyrin (40 mg, 79% yield): λ_{abs} (toluene) 428, 524, 564, 602 nm; $C_{100}H_{36}F_{40}N_4O_8Mg$ calcd mass 2204.1, obsd 2201.5; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 4.50 (16 H, s, OCH_2), 7.02 (8 H, d, J = 8.3 Hz, *m*-ArH), 7.58 (4 H, t, *p*-ArH), 8.46 (8 H, s, β-pyrrole).

(5) Magnesium Octaethylporphyrin (Mg-2).[23] A sample of octaethylporphyrin (**2**; 100 mg, 0.187 mmol) in 8 mL of CH_2Cl_2 was treated with MgI_2 (0.52 g, 1.87 mmol) and DIEA (0.65 mL, 3.73 mmol), and the mixture was stirred magnetically at room temperature. After 20 min the reaction was judged to be complete by UV−visible absorption analysis. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (3 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) gave the magnesium porphyrin (90 mg, 86% yield): λ_{abs} (toluene) 410, 505, 544, 583 nm; $C_{36}H_{44}N_4Mg$ calcd mass 556.3, obsd 556.1; ^{1}H NMR ($CDCl_3$) δ 1.91 (24 H, t, CH_3), 4.12 (16 H, q, CH_2), 10.09 (4 H, *meso* CH).

(6) Magnesium Tetraphenylchlorin (Mg-4).[21,24−26] A sample of tetraphenylchlorin (**4**; 50 mg, 0.081 mmol) in 8 mL of CH_2Cl_2 was treated with MgI_2 (0.45 g, 1.62 mmol) and DIEA (0.56 mL, mmol), and the mixture was stirred magnetically at room temperature. After 1 h the reaction was judged to be complete by UV−visible absorption analysis. The mixture was diluted with 20 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 20 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼1 mL. Column chromatography on grade V alumina (3 × 10 cm) eluting with hexanes gave residual free base and a gradient of CH_2Cl_2/acetone (10:1) gave magnesium tetraphenylchlorin (40 mg, 77% yield): λ_{abs} (toluene) 426, 525, 564, 602, 618 nm; ^{1}H NMR ($CDCl_3$) δ 4.04 (4 H, s, CH_2CH_2), 7.45−8.33 (26 H, m, ArH, β-pyrrole).

(7) Magnesium tetra-*tert*-butylphthalocyanine (Mg-9a).[11,12,20,27] A sample of tetra-*tert*-butylphthalocyanine (**9a**; 76 mg, 0.1 mmol) was dissolved in 15 mL of CH_2Cl_2 in a round-bottom flask. Then MgI_2 (446 mg, 1.6 mmol) followed by DIEA (557 μL, 3.13 mmol) was added, and the mixture was stirred magnetically at room temperature. After 5 h the metalation appeared complete as judged by TLC and absorption spectroscopy. The dark green-blue mixture was diluted with 30 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (2 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) afforded a light yellow band of residual starting material. Elution with CH_2Cl_2/ethyl acetate (1:1) afforded a light blue band of product that was evaporated to dryness. The product was suspended in methanol and vacuum filtered. The filtrate was evaporated to recover the light blue product, which was then suspended in methanol once again and vacuum filtered. The combination of the two filtrations afforded 52 mg (68% yield): λ_{abs} (CH_2Cl_2/ethanol, 3:1) 614, 682 nm; $\epsilon_{682\ nm}$ = 221 000 M^{-1} cm^{-1}; λ_{em} ($CHCl_3$) 693, 757 nm; $C_{48}H_{46}N_8Mg$ calcd mass 761.3, obsd 761.0; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 1.7 (36 H, s, $C(CH_3)_3$), 8.13−8.16 (12 H, m, ArH).

(8) Magnesium Tetra-*n*-hexoxyphthalocyanine (Mg-9b). A sample of tetra-*n*-hexoxyphthalocyanine (**9b**; 75.0 mg, 0.08 mmol) was dissolved in 15 mL of CH_2Cl_2 in a round-bottom flask. Then MgI_2 (445 mg, 1.6 mmol) followed by DIEA (557 mL, 3.13 mmol) was added, and the mixture was stirred magnetically at room temperature. After 4 h the metalation was complete as judged by TLC and absorption spectroscopy. The dark green-blue mixture was diluted with 30 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 25 mL), dried (Na_2SO_4), filtered, and concentrated to ∼3 mL. Column chromatography on alumina (2 × 10 cm) eluting with CH_2Cl_2/ethyl acetate (5:1) afforded a light yellow band of residual free base phthalocyanine. Elution with CH_2Cl_2/ethyl acetate (1:10) afforded a light green band of product that was evaporated to dryness. The product was suspended in methanol and vacuum filtered, affording 56.7 mg (74% yield): λ_{abs} (CH_2Cl_2/ethanol, 3:1) 354, 616, 684 nm; $\epsilon_{684\ nm}$ = 119 000 M^{-1} cm^{-1}; $C_{56}H_{64}N_8O_4Mg$ calcd mass 937.5, obsd 937.5; λ_{em} ($CHCl_3$) 699, 764 nm; Φ_f = 0.62; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 1.01 (12 H, br s, CH_3), 1.48 (24 H, br s, $(CH_2)_3$), 2.0 (8 H, br s, CH_2), 4.25 (8 H, br, OCH_2), 7.17−7.45 (6 H, br, ArH), 8.28−8.93 (6 H, br, ArH).

(9) Magnesium Tetrakis(4-cumylphenoxy)phthalocyanine (Mg-9c).[16] A sample of tetrakis(4-cumylphenoxy)phthalocyanine (**9c**; 500 mg, 0.363 mmol) was dissolved in 50 mL of CH_2Cl_2 in a round-bottom flask. Then MgI_2 (2.05 g, 7.37 mmol) followed by DIEA (2.57 mL, 14.75 mmol) was added, and the mixture was stirred magnetically at room temperature. After 4 h the metalation appeared complete as judged by TLC and absorption spectroscopy. The blue-green mixture was diluted with 100 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 50 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼10 mL. Column chromatography on alumina (4 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) afforded a light green band of residual free-base phthalocyanine. Elution with a gradient of CH_2Cl_2/ethyl acetate (1:1) to ethyl acetate/methanol (10:1) afforded a blue band of product that was evaporated to dryness. The product was suspended in methanol and vacuum filtered, affording 497 mg (98% yield): λ_{abs} (CH_2Cl_2/ethanol, 3:1) 356, 614, 684 nm; $\epsilon_{684\ nm}$ = 172 000 M^{-1} cm^{-1}; λ_{em} ($CHCl_3$) 696, 761 nm; Φ_f = 0.68; $C_{92}H_{72}N_8O_4Mg$, calcd mass 1377.9, obsd 1378.4; ^{1}H NMR ($CDCl_3$/C_5D_5N, 10:1) δ 1.7 (24 H, s, CH_3), 7.17−7.26 (48 H, m, ArH).

(10) Magnesium 1,4,8,11,15,18,22,25-Octabutoxyphthalocyanine (Mg-9d). The commercial sample of octabutoxyphthalocyanine (**9d**, dye content 85%) was chromatographed on grade V alumina (2 × 10 cm) with CH_2Cl_2/ethyl acetate (10:1), yielding a light red band, and subsequent elution with CH_2Cl_2/ethyl acetate (1:1) yielded the purified phthalocyanine as a green band. A sample of purified octabutoxy-phthalocyanine (**9d**; 52 mg, 0.048 mmol) was dissolved in 6 mL of CH_2Cl_2 in a round-bottom flask. Then MgI_2 (534.6 mg, 1.92 mmol) followed by DIEA (668 μL, 6.78 mmol) was added, and the mixture was stirred magnetically at room temperature. After 8 h the metalation was complete as judged by TLC and absorption spectroscopy. The dark brown mixture was diluted with 30 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on grade V alumina (2 × 10 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) afforded a green band of residual starting material. Elution with CH_2Cl_2/ethyl acetate (1:1) afforded a red band. Elution with CH_2Cl_2/ethyl acetate (1:10) gave a brown band. Elution with CH_2Cl_2/methanol (10:1) gave a green-brown band of product that was evaporated to dryness. The

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product was suspended in water and vacuum filtered, affording 1.5 mg (3% yield): λ_{abs} (toluene) 740, 800 nm; λ_{abs} (pyridine) 740, weak shoulder at 820 nm; $C_{64}H_{80}N_8O_8Mg$ calcd mass 1112.5 obsd 1114.9. ^{1}H NMR ($CDCl_3/C_5D_5N$, 10:1) δ 1.02 (24 H, t, CH_3), 1.55 (16 H, m, CH_2), 2.18 (16 H, m, CH_2), 4.80 (16 H, t, OCH_2), 7.45 (8 H, s, ArH).

Homogeneous Magnesium Insertion Reactions. Preparation of "Ethereal MgI_2−DIEA" Reagent. Diethyl ether (25 mL of 99% anhydrous A.C.S. reagent grade; used as received) was placed in a 50 mL one-neck round-bottom flask equipped with a magnetic stir bar and fitted for gentle purging with nitrogen or argon. Then MgI_2 (500 mg, 1.79 mmol; used as received) was added, which dissolved with stirring at room temperature. Then DIEA (0.62 mL, 3.58 mmol; used as received) was added, which resulted in the immediate separation of a small amount of a more dense, faint yellow oil. Stirring was continued under argon for 20 min. Stirring was discontinued, whereupon the oil layer separated to the bottom of the flask. The top ethereal layer constitutes the ethereal MgI_2−DIEA reagent. The flask (containing both layers) was capped off with a rubber septum and stored at 4 °C. Upon cooling, the lower oil layer often crystallizes but melts on warming to room temperature. Aliquots of the upper ethereal layer can be removed by Pasteur pipet on the open benchtop as required, taking care not to remove any of the lower oil layer (the lower oil layer alone is inactive in magnesium insertions). The atmosphere was purged with argon before storing the flask again. The upper ethereal layer remained active after 2 weeks on storing at 4 °C; with time the lower oil layer became darker in color but the upper ethereal layer remained colorless.

(1) Magnesium Tetraphenylporphyrin (Mg-1a).[2] A solution of TPP (**1a**; 50 mg, 0.08 mmol) in 2 mL of CH_2Cl_2 was treated with 8 mL of the ethereal MgI_2−DIEA reagent and the solution was stirred for 30 min, at which time metalation appeared complete by UV−visible absorption spectroscopy. Workup by extraction and chromatography[2] afforded 46 mg (90% yield). Spectral data were identical to the product from the heterogeneous procedure.

Survey reactions of porphyrins **1b**−**g** were performed at the 10 mg scale. The reactions of **1c** and **1d** failed, **1e**−**g** succeeded and remained homogeneous, and **1b** succeeded in spite of limited solubility. The latter is given as an example:

(2) Magnesium Tetrakis[4-(methoxycarbonyl)phenyl]porphyrin (Mg-1b). Tetrakis[4-(methoxycarbonyl)phenyl]porphyrin (**1b**; 10 mg, 0.011 mmol) was treated with 3 mL of the ethereal MgI_2−DIEA reagent, and the reaction mixture was stirred for 24 h. A homogeneous solution was never obtained. Removal of a sample of the solid porphyrin and UV−visible absorption spectral analysis showed that metalation had occurred. The product coated the sides of the reaction flask. A small amount of ethanol was added followed by CH_2Cl_2 to dissolve the precipitate. Subsequent chromatographic workup as described in the heterogeneous procedure afforded 9 mg (90% yield). Spectral data were identical to the product from the heterogeneous procedure.

(3) Magnesium Octaethylporphyrin (Mg-2). To a solution of OEP (**2**; 50 mg, 0.0935 mmol) in 2 mL of CH_2Cl_2 was added 8 mL of the ethereal MgI_2−DIEA reagent, and the solution was stirred for 30 min at which time metalation appeared complete by UV−visible absorption spectroscopy. Chromatographic workup as described in the heterogeneous procedure afforded 44 mg (84% yield). Spectral data were identical to the product from the heterogeneous procedure.

(4) Magnesium Tetraphenylchlorin (Mg-4). To a solution of TPC (**4**; 5 mg, 0.0081 mmol) in 0.5 mL of CH_2Cl_2 was added 3 mL of the ethereal MgI_2−DIEA reagent, and the reaction mixture was stirred for 24 h at which time metalation appeared to be ∼90% complete by absorption spectroscopy. TLC analysis (grade V alumina, CH_2Cl_2/acetone, 9:1) showed starting material, product, and one other faint spot running above the product. Chromatographic workup afforded 3 mg (60% yield). Spectral data were identical to the product from the heterogeneous procedure.

(5) Magnesium Methyl Pyropheophorbide a (Mg-6b).[28] To a solution of methyl pyropheophorbide a (**6b**; 10 mg, 0.018 mmol) in 0.25 mL of CH_2Cl_2 was added 3 mL of the ethereal MgI_2−DIEA reagent, and the reaction mixture was stirred for 1 h at which time a dark green oil had separated from the solution. The reaction mixture was diluted with 10 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 5 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼1 mL. Column chromatography on alumina (3 × 5 cm) eluting with CH_2Cl_2/methanol (10:1) gave Mg-**6b** (7 mg, 70% yield): λ_{abs} (ether) 426, 578, 620, 660 nm; $C_{34}H_{34}N_4O_3Mg$ calcd mass 570.24, obsd 570.63.

(6) Magnesium Chlorin e_6 Trimethyl Ester (Mg-7).[28] To a solution of chlorin e_6 trimethyl ester (**7**; 10 mg, 0.014 mmol) in 0.25 mL of CH_2Cl_2 was added 3 mL of the ethereal MgI_2−DIEA reagent, and the reaction mixture was stirred for 1 h at which time a dark green oil had separated from the solution. The reaction mixture was diluted with 10 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 5 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼1 mL. UV−visible absorption spectroscopy showed the product Mg-**7** (one spot by TLC on alumina (CH_2Cl_2/methanol, 10:1)). Column chromatography on alumina (3 × 5 cm) eluting with CH_2Cl_2/methanol (10:1) gave 8 mg of product (80% yield): λ_{abs} (ether) 414, 524, 600, 642 nm; $C_{37}H_{40}N_4O_6Mg$ calcd mass 660.27, obsd 660.69.

***(7)* Attempted Reconstitution of Chlorophyll *a*.** Pheophytin a (**8**; 0.005 g) was treated with 3 mL of the ethereal MgI_2−DIEA reagent, and the mixture was stirred for 2 h. A green oil separated from the solution and coated the walls of the flask. The reaction mixture was diluted with 20 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 5 mL), dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness. TLC analysis (alumina, CH_2Cl_2/acetone) showed at least five new more polar products. The reaction mixture was worked up and chromatographed (alumina, CH_2Cl_2/acetone), and the more polar products were isolated as a mixture. Absorption spectral analysis (diethyl ether) of this mixture of new products showed a broad long-wavelength band (λ_{max} 654 nm), in contrast with pheophytin a (λ_{max} 668 nm) or chlorophyll a (λ_{max} 658 nm), indicating predominantly metalated products. This reaction mixture has not been characterized further.

Hydroporphyrin Chemistry. (1) Isolation of MgTPC by Diimide Reduction of TPP and the Heterogeneous Magnesium Insertion Method. A solution of TPP (100 mg, 0.16 mmol) and triisopropylbenzenesulfonyl hydrazide[29] (0.096 g, 0.32 mmol) in 10 mL of dry THF was heated at reflux under argon. After 3 h a solution of triisopropylbenzenesulfonyl hydrazide (0.096 g, 0.32 mmol) in 2 mL of THF was added, and heating was continued for a further 3 h. UV−visible analysis showed the reaction mixture to comprise ∼40% TPC.[30] The cooled reaction mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% NaOH (2 × 25 mL), and dried over Na_2SO_4. Removal of the solvent by rotary evaporation gave a solid which was dried under high vacuum for 2 h. This solid was dissolved in 10 mL of CH_2Cl_2, treated with MgI_2 (0.89 g, 3.2 mmol) and DIEA (1.1 mL, 6.4 mmol), and stirred for 2 h at room temperature. The mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness. Column chromatography on grade V alumina (4 × 20 cm) packed with hexanes gave the following fractions: (i) Hexanes gave a mixture of the nonmetalated species TPC and TPBC. (ii) A slow gradient of 100% hexanes to 100% CH_2Cl_2 eluted MgTPP. (iii) A gradient of CH_2Cl_2 to acetone brought off further trace amounts of MgTPP. (iv) Elution with acetone/methanol (90:10) gave MgTPC (26 mg, 25% yield).

(2) Isolation of MgTPC by Diimide Reduction of TPP and the Homogeneous Magnesium Insertion Method. Samples of TPP (100 mg, 0.16 mmol) and triisopropylbenzenesulfonyl hydrazide[29] (0.143 g, 0.24 mmol) in 10 mL of dry THF were heated under reflux under argon. After 3 h a solution of triisopropylbenzenesulfonyl hydrazide (0.048 g, 0.16 mmol) in 2 mL of THF was added, and heating was continued for a further 3 h. UV−visible analysis showed the reaction mixture to comprise ∼40% TPP, 55% TPC, and 5% TPBC.[30] The cooled reaction mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% NaOH (2 × 25 mL), and dried over Na_2SO_4. Removal of the solvent by rotary evaporation gave a solid which was dried under high vacuum for 2 h. The solid was dissolved in 2 mL of CH_2Cl_2 and treated

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with 12 mL of ethereal MgI_2−DIEA reagent (∼7-fold molar excess based on the amount of TPP present in the mixture) and stirred at room temperature for 1 h. The solution was diluted with 25 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (2 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness. Column chromatography on grade V alumina (4 × 20 cm) packed with hexanes gave the following fractions: (i) Hexanes/CH_2Cl_2 (10:1) eluted TPC (0.05 g, 50% yield; 90% pure) and then CH_2Cl_2 (100%) eluted MgTPP.

(3) Isolation of MgTPC via Diimide Reduction of MgTPP. MgTPP (100 mg, 0.157 mmol) and triisopropylbenzenesulfonyl hydrazide[29] (0.23 g, 0.77 mmol) in 10 mL of dry THF were heated under reflux under argon. Additional samples of triisopropylbenzenesulfonyl hydrazide (0.096 g, 0.32 mmol) in 2 mL of THF were added after 3 h and after 6 h. The mixture was heated for a total of 9 h. (If a sample of the reaction mixture was removed and diluted in toluene for UV−visible analysis, the conversion of MgTPC to $(MgTPC)^{\bullet+}$ in the cuvette was complete within 1 h, by analogy with the spectral changes observed for conversion of ZnTPC to its radical cation[31]) The cooled reaction mixture was added immediately into a separatory funnel containing 25 mL of CH_2Cl_2 and 25 mL of 5% NaOH, washed with a further portion of base, dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness. Column chromatography on grade V alumina (4 × 20 cm) packed with hexanes gave the following fractions: (i) Hexanes gave a mixture of the nonmetalated species TPC and TPiBC; (ii) a slow solvent gradient of 100% hexanes to 100% CH_2Cl_2 eluted MgTPP. A gradient of CH_2Cl_2 to acetone brought off further trace amounts of MgTPP. Elution with acetone/methanol (90:10) gave MgTPC (15 mg, 15%).

(4) Synthesis of TPBC by Diimide Reduction of TPP.[30,32] A solution of TPP (100 mg, 0.16 mmol) and triisopropylbenzenesulfonyl hydrazide (0.19g, 0.64 mmol) in 10 mL of dry THF was heated under reflux under argon. After 3 and 6 h a solution of triisopropylbenzenesulfonyl hydrazide (0.096g, 0.32 mmol) in 2 mL of THF was added, and heating was continued for a total of 9 h. The cooled reaction mixture was diluted with 25 mL of CH_2Cl_2, washed with 5% NaOH (2 × 25 mL), dried (Na_2SO_4), and filtered. Evaporation of the filtrate to dryness gave a brown solid which was further dried under high vacuum (85 mg, 85%). λ_{abs} (toluene) 356, 368, 378, 522, 742 nm.

Phthalocyanine Chemistry. (1) Tetra-*tert*-butylphthalocyanine (9a).[11] Following a slight modification of the method of Tomoda et al.,[33] a solution of 4-*tert*-butylphthalonitrile (1.0 g, 1.4 mmol) in 15 mL of refluxing pentanol in a 50 mL round-bottom flask was treated with 1.2 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 8 mmol) and heating was continued. After 24 h the reaction was complete as judged by TLC and UV−visible absorption spectroscopy. The dark green-blue mixture was evaporated to dryness and vacuum desiccated for 1 h. The residue was then washed with several portions of methanol, filtering the washings through a Buchner funnel to isolate the product, until the washings became colorless. The filtered material was dissolved in CH_2Cl_2, and the solution was concentrated to 6−7 mL. Column chromatography on alumina (4 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) afforded a light green-blue band that was evaporated to dryness. The product was suspended in methanol and vacuum filtered, affording 644 mg (64% yield): λ_{abs} (CH_2Cl_2/ethanol; 3:1) 602, 642, 662, 698 nm; $\epsilon_{698\ nm} = 134\ 000\ M^{-1}\ cm^{-1}$; $C_{48}H_{48}N_8$ calcd mass 737.0, obsd 737.8. ^1H NMR ($CDCl_3$) δ 9.25−8.90 (8 H, m, ArH), 8.20−8.14 (4 H, m, ArH), 1.89, 1.88, 1.86 (36 H, s, $C(CH_3)_3$), −1.9−2.0 (2 H, br s, NH).

(2) Tetra-*n*-hexoxyphthalocyanine (9b). Following a slight modification of the method of Tomoda et al.,[33] a solution of 4-*n*-hexoxyphthalonitrile (1.0 g, 1.1 mmol) in 15 mL of refluxing pentanol in a 50 mL round-bottom flask was treated with 0.95 mL of DBU (6 mmol) and heating was continued. After 24 h the reaction was complete as judged by TLC and UV−visible absorption spectroscopy. The dark green mixture was evaporated to dryness and vacuum desiccated for 1 h. The residue was washed with several portions of methanol, filtering the washings through a Buchner funnel to isolate the product, until the washings became colorless. The filtered material was dissolved in CH_2Cl_2, and the solution was concentrated to ∼5 mL. Column chromatography on alumina (4 × 15 cm) eluting with CH_2Cl_2/ethyl acetate (10:1) afforded a light green band that was evaporated to dryness. The product was suspended in methanol and vacuum filtered, affording 740 mg (72% yield): λ_{abs} (CH_2Cl_2/ethanol; 3:1) 642, 668, 704 nm; $\epsilon_{704\ nm} = 81\ 300\ M^{-1}\ cm^{-1}$; $C_{56}H_{66}N_8O_4$ calcd mass 915.2, obsd 914.4; ^1H NMR ($CDCl_3$) δ 7.76−7.25 (6 H, m, ArH), 6.93−6.54 (6 H, m, ArH), 3.82 (8 H, m, OCH_2), 1.91 (8 H, br s, CH_2), 1.56 (24 H, br s, $(CH_2)_3$), 1.1 (12 H, br s, CH_3), −5.4, −5.5, −5.6, −5.8 (2 H, singlets in ratio of 1:2:4:1, NH).

(3) Direct Synthesis of Magnesium Phthalocyanines: Magnesium Tetra-*n*-hexoxyphthalocyanine (Mg-9b). A sample of 4-(*n*-hexoxy)-phthalonitrile (212 mg, 0.9 mmol) in a 5 mL round-bottom flask was treated with $MgBr_2$ (83 mg, 0.45 mmol) and 2,2,6,6-tetramethylpiperidine (140 μL, 0.83 mmol). The faint yellow mixture was heated to 135 °C. The mixture turned deep red after 15−30 min and dark green after several hours. After 24 h the reaction was complete as judged by TLC and absorption spectroscopy. The dark green mixture was diluted with 15 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was concentrated to ∼3 mL. Column chromatography on alumina (2 × 15 cm) eluting with (CH_2Cl_2/ethyl acetate, 10:1) afforded a light green-blue band comprised of residual free base phthalocyanine. Elution with CH_2Cl_2/ethyl acetate (1:1) afforded a light green band of product that was evaporated to dryness. The green product was then suspended in methanol and vacuum filtered affording 65 mg (30% yield) of the magnesium phthalocyanine. This product gave analytical data identical to that prepared from the heterogeneous insertion reaction (vide supra).

(4) Demetalation of Magnesium Phthalocyanines: Tetra-*tert*-butylphthalocyanine (9a). A sample of Mg-**9a** (10.9 mg, 0.01 mmol) dissolved in 2 mL of CH_2Cl_2 was treated with a 1 mL solution of TFA/H_2O (1:1, v/v), and the solution was stirred for 30 min at room temperature. The dark green-blue mixture was diluted with 10 mL of CH_2Cl_2, washed with 5% $NaHCO_3$ (3 × 25 mL), dried (Na_2SO_4), and filtered; the filtrate was evaporated to dryness. The blue product was suspended in methanol and vacuum filtered, affording 6.4 mg (60% yield) of the free base phthalocyanine: λ_{abs} (CH_2Cl_2/ethanol, 3:1) 602, 642, 662, 698 nm; $\epsilon_{698\ nm} = 134\ 000\ M^{-1}\ cm^{-1}$; $C_{48}H_{48}N_8$ calcd mass 737.0, obsd 737.8.

Results

A. Heterogeneous Reaction Conditions for Magnesium Insertion. (1) Porphyrins. The heterogeneous magnesium insertion method involves a slurry of the magnesium halide in a solution of the porphyrin and base (Scheme 1). Various combinations of magnesium reagents ($MgBr_2$, $MgBr_2{\cdot}O(Et)_2$, MgI_2), solvents (toluene, CH_2Cl_2, $CHCl_3$), and bases (triethylamine, diisopropylethylamine, 2,2,6,6-tetramethylpiperidine) at room temperature gave metalation of **1a**; however MgI_2 and DIEA in CH_2Cl_2 provided a very efficient combination. These conditions give quantitative metalation of **1a** (2 mM) within 5 min and are applicable to ortho-substituted tetraarylporphyrins.[2]

We examined the heterogeneous magnesium insertion procedure with a wider range of porphyrinic derivatives (Chart 1) to determine the scope of its applicability. Porphyrins (5−20 mM) in CH_2Cl_2 were treated with MgI_2 (10 molar excess) and DIEA (20 molar excess) at room temperature. Samples were removed periodically for analysis by absorption spectroscopy or by TLC. The reaction mixtures were worked up by washing with aqueous $NaHCO_3$ followed by chromatography on alumina to remove traces of free base starting material. In the case of porphyrins **1a**, **1d**, and **2**, the metalation was complete within 20 min. With the peripherally coordinating porphyrins (ester, **1b**; pyridyl, **1c**), extensive precipitates formed and spectral analysis of the reaction mixtures after 20 min showed neither starting material nor product. The addition of a small amount of ethanol disrupted the aggregates, and analysis of each of the reaction mixtures then showed metalated porphyrin only. The

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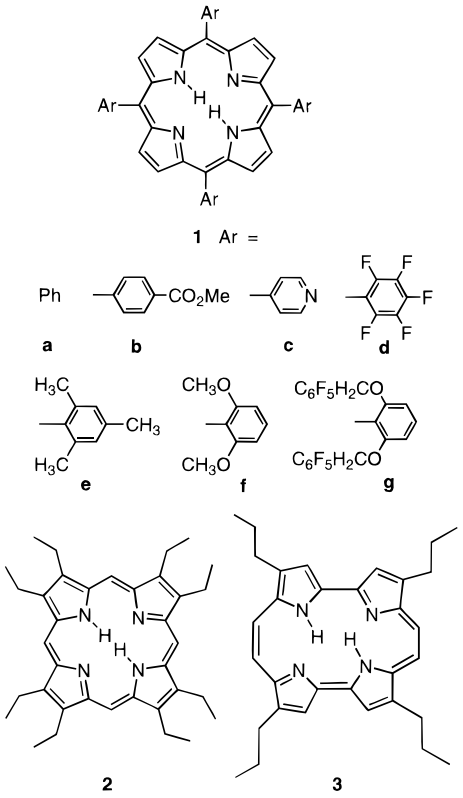
(32) Dorough, G. D.; Miller, J. R. *J. Am. Chem. Soc.* **1952**, *74*, 6106−6108.
(33) Tomoda, H.; Saito, S.; Ogawa, S.; Shiraishi, S. *Chem. Lett.* **1980**, 1277−1280.

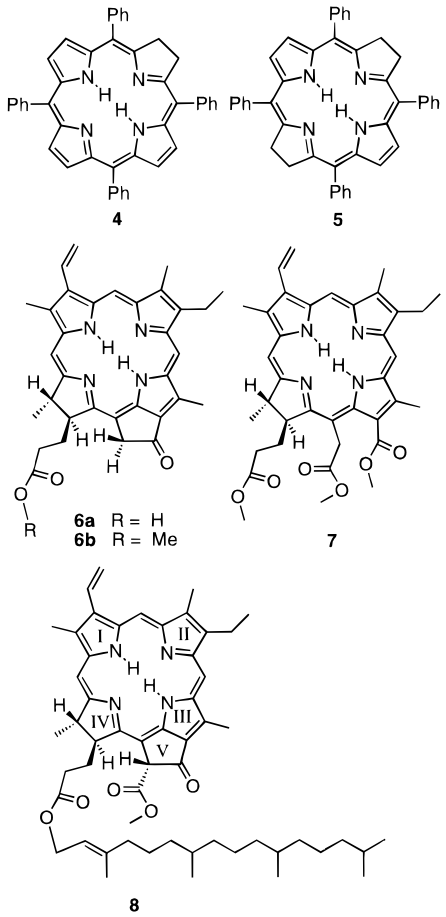
Chart 1. Free Base Porphyrins



facially encumbered porphyrins **1e** and **1f** have been metalated using these conditions,[2] and the very bulky porphyrin **1g** was successfully metalated in 1 h. The first limitation of the heterogeneous reaction conditions that we encountered occurred with 2,7,12,17-tetra-*n*-propylporphycene (**3**),[34] which could not be forced to form a magnesium chelate even with larger amounts of MgI_2 (20 molar excess) and DIEA (40 molar excess) and prolonged stirring at room temperature (1 week), or at reflux in CH_2Cl_2 for 24 h. The porphycene remained in solution throughout the attempted reaction. Thus, these conditions for magnesium insertion are suitable for peripherally coordinating (**1b**, **1c**), electron-deficient (**1d**), or facially encumbered (**1e**−**g**) tetraarylporphyrins, and the β-substituted OEP (**2**), but not porphycene **3**.

(2) Hydroporphyrins. We investigated the applicability of the heterogeneous procedure with several hydroporphyrins including tetraphenylchlorin (TPC, **4**), tetraphenylbacteriochlorin (TPBC, **5**), pyropheophorbide a (**6a**), chlorin e_6 trimethyl ester (**7**), and pheophytin a (**8**) (Chart 2). The same conditions employed above were successful for the dihydroporphyrin **4**, but larger excesses of MgI_2 and DIEA were employed as the reaction was slower compared with TPP. One unknown impurity was observed in the TPC reaction, but this could be removed by chromatography. Attempts to insert magnesium into tetrahydroporphyrin **5** did not yield any MgTPBC. Instead the only product observed was MgTPC even if the reaction was carried out under an atmosphere of nitrogen. The order of metalation/oxidation in the conversion of TPBC to MgTPC is not known; however the extremely facile oxidation of metallohydroporphyrins by trace amounts of oxygen or other oxidants

Chart 2. Free Base Hydroporphyrins



has been reported.[35] MgTPBC has been prepared by treatment of TPBC with ethyl magnesium iodide.[32]

The reconstitution of chlorophylls from their pheophytins would be a superb application of a magnesium insertion method. Pheophytin a (**8**) was treated with MgI_2 and DIEA in CH_2Cl_2 at room temperature. After stirring the reaction mixture for a period of time, absorption spectral analysis showed neither the free base nor chlorophyll a. When the reaction mixture was worked up by washing with aqueous $NaHCO_3$, the free base **8** was regenerated and no chlorophyll a was obtained. We attribute the failure of this reaction to complexation of the β-keto ester moiety on ring V of pheophytin a with a magnesium species, thus forming an insoluble complex. The precipitated material is then not accessible for magnesium insertion at the core of the macrocycle. The addition of water regenerated the free base by disrupting the peripheral coordination complex. Thus, our goal of applying this heterogeneous magnesium insertion method for the reconstitution of chlorophyll a was not realized. The less complex derivatives of pheophytin a, including **6a**, **6b**, and **7**, each also gave a similar negative result. These pheophytins contain two (**6a**, **6b**) or three (**7**) carbonyl groups, and we also attribute the failed metalations of these compounds to complexation-induced insolubility.

(3) Phthalocyanines. Magnesium phthalocyanines are of interest as components of light-harvesting arrays because of their strong absorbance in the red region of the spectrum and high fluorescence quantum yield. For incorporation into light-harvesting arrays, it is essential that the phthalocyanine have high organic solubility. We chose the known compounds tetra-*tert*-butylphthalocyanine (**9a**) and tetrakis(4-cumylphenoxy)-phthalocyanine (**9c**) as models for optimizing conditions for magnesium insertion into phthalocyanines (Chart 3). The effects

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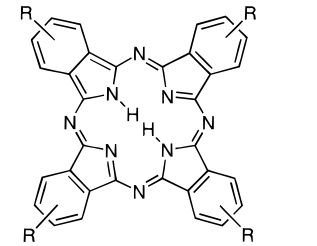
(35) Lahiri, G. K.; Summers, J. S.; Stolzenberg, A. M. *Inorg. Chem.* **1991**, *30*, 5049−5052.

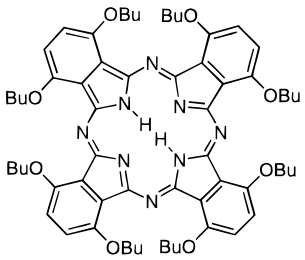
Table 1. Reaction Conditions Yielding Magnesium Tetrakis(4-cumylphenoxy)phthalocyanine (Mg-**9c**)[a]

			% yield of magnesium tetrakis(4-cumylphenoxy)phthalocyanine			
time (h)	solvent	base	$MgBr_2$	$MgBr_2{\cdot}O(Et)_2$	$MgI_2{\cdot}O(Et)_2$	MgI_2
	CH_2Cl_2	tetramethylpiperidine[b]				
2			0	1.4	6	53
4			0	3	12	87
	CH_2Cl_2	DIEA				
2			-	0	14	67
4			-	0	14	91
	CH_2Cl_2	TEA				
2			-	0	5.5	7.6
4			-	1	6	10
	$CHCl_3$	tetramethylpiperidine[b]				
2			0	0	6	2.2
4			0	0	7	10
	toluene	tetramethylpiperidine[b]				
2			0	0	0	0
4			0	0	3	41

[a] Reactions were performed using 5 mM tetrakis(4-cumylphenoxy)phthalocyanine (**9c**), 20 molar excess of magnesium reagent, and 200 mM amine base at room temperature in 6 mL of solvent in 20 mL scintillation vials. Yields were determined by absorption spectral analysis based on spectral characteristics of authentic samples. [b] 2,2,6,6-Tetramethylpiperidine.

Chart 3. Free Base Phthalocyanines





9d

of magnesium reagent, solvent, and base on the rate of magnesium insertion into **9c** (5 mM) are listed in Table 1. The efficiency toward metalation progressed in the series $MgBr_2$ < $MgBr_2{\cdot}O(Et)_2$ < $MgI_2{\cdot}O(Et)_2$ < MgI_2. No metalation was achieved with $MgBr_2$ and <5% yield was observed with $MgBr_2{\cdot}O(Et)_2$ with any of the combinations of base and solvent. The best combination of reagents was provided by MgI_2 in CH_2Cl_2 with 2,2,6,6-tetramethylpiperidine or DIEA. The concentration of the phthalocyanine solution is an important parameter that affects the rate of reaction. The reaction of 2 mM **9a** with MgI_2 (40 equiv) and DIEA (160 mM) in CH_2Cl_2 took 16 h to reach completion. In contrast, the reaction of 5 mM **9a** with MgI_2 (20 equiv), DIEA (200 mM), and CH_2Cl_2 took only 5 h and utilized only half the molar excess of MgI_2 and DIEA.

These conditions of MgI_2 and DIEA in CH_2Cl_2 were applied to four phthalocyanines (5−8 mM) at the 50−500 mg scale, affording yields of 68% (Mg-**9a**), 74% (Mg-**9b**), and 98% (Mg-**9c**), but only 3% isolated yield with the octabutoxyphthalocyanine **9d**. The latter exhibited nearly complete metalation by TLC and absorption spectroscopy but proved rather insoluble and was difficult to purify.

B. Homogeneous Reaction Conditions for Magnesium Insertion. Encouraged by our success with the heterogeneous method but not satisfied with our failures, we sought to develop a method by which the metal insertion could be achieved under homogeneous conditions. It was the apparent desire for high solubility of both porphyrin and magnesium halide that led to the use of strongly coordinating solvents (DMF, pyridine, 1-propanol) in the early methods, consequently necessitating high reaction temperatures due to the formation of stable octahedral magnesium complexes. A method that achieves mutual solubility of the magnesium reagent and the porphyrinic compound without forming stable octahedral magnesium complexes would be attractive in many respects. Potential applications of a robust, homogeneous magnesium insertion method include metalations where the heterogeneous method fails, experiments to probe the mechanism of magnesium insertion, incorporation of magnesium isotopes, and competition experiments among various porphyrinic compounds to assess relative insertion rates and binding affinities for magnesium.

In order to achieve mutual solubility but not at the expense of forming inactive complexes of magnesium, we chose diethyl ether as a solvent having intermediate coordination strength. Evans and Rowley showed that $MgBr_2$ forms mono-, di-, and triethereal complexes, with the triethereal complex being insoluble in diethyl ether.[36] We found that a homogeneous solution of MgI_2 (0.5 g, 0.075 M) in 25 mL of diethyl ether could be readily prepared at room temperature. Treating this solution with 2 molar equiv of DIEA (0.62 mL) resulted in phase separation, yielding an upper ethereal layer (>95% by volume) and a more dense faint yellow oil (<5% by volume). The oil could be crystallized on cooling. Addition of aliquots of the upper ethereal layer (taking care not to include any of the lower oil layer) to a solution of TPP in a minimal amount of CH_2Cl_2 cleanly afforded MgTPP in 20 min in a homogeneous solution. We refer to the upper ethereal layer as the ethereal MgI_2−DIEA reagent, and its use constitutes the homogeneous magnesium insertion method (Scheme 1). The flask containing both layers is conveniently stored, and samples of the ethereal MgI_2−DIEA reagent (upper layer) can be drawn for up to 2 weeks without loss of activity.

(36) Evans, W. V.; Rowley, H. H. *J. Am. Chem. Soc.* **1930**, *52*, 3523−3534. Rowley, H. H. *J. Am. Chem. Soc.* **1936**, *58*, 1337−1341. Rowley, H. H. *J. Am. Chem. Soc.* **1937**, *59*, 621−625.

Attempts to use the lower oil in magnesium insertions by adding this oil to a solution of TPP in CH_2Cl_2 and diethyl ether (same solvent composition as above) yielded a green solution with no magnesium insertion. The formation of a green solution occurs when a magnesium halide such as MgI_2 is used in the absence of a base. These results suggest that the lower oil is an etherate of MgI_2 lacking sufficient base for metalation. Conversely, the upper ethereal layer must contain most or all of the DIEA, which would be in large excess relative to the porphyrin and to the MgI_2.

In order to quantitate the composition of the upper ethereal and lower oil layers, a 25 mL solution was prepared (0.50 g of MgI_2, 0.62 mL of DIEA) and the layers were separated by decanting. Solvent was removed from each layer under vacuum and then the material from each layer was heated under vacuum (120 °C) for 5 h, affording a waxy yellow solid from each layer. In three trials the upper layer constituted 0.25 ± 0.01 g and the lower layer constituted 0.27 ± 0.02 g, consistent with nearly complete removal of all of the ether and amine, leaving only MgI_2. These results indicate that the concentration of MgI_2 in the upper layer is approximately half that of the original ethereal solution (0.075 M) prior to adding DIEA; in other words the [MgI_2] in the ethereal MgI_2−DIEA reagent is ∼0.04 M.

In order to assess the amount of the ethereal MgI_2−DIEA reagent required for effective metalation, we performed the following experiments: (i) A 10 mg sample of TPP (0.016 mmol) in ∼0.5 mL of CH_2Cl_2 or in solid form was treated with 3 mL of the ethereal MgI_2−DIEA reagent (0.12 mmol MgI_2), affording complete metalation in 15 or 30 min, respectively. (ii) A solution of TPP (10 mg, 0.016 mmol) in ∼0.5 mL CH_2Cl_2 was added to the entire biphasic solution of MgI_2 (0.080 or 0.032 mmol) and DIEA (1.28 mmol) in 3 mL of ether. With 5 equiv of MgI_2 per porphyrin, quantitative metalation occurred in 30 min, but with 2 equiv of MgI_2 only ∼50% metalation was achieved in 30 min. In the following synthetic applications, we generally have used 3 mL of the ethereal MgI_2−DIEA reagent (0.12 mmol of MgI_2)/0.01 mmol of porphyrin dissolved in a minimal amount of CH_2Cl_2, a 12-fold excess. This ratio is comparable to that used in the heterogeneous reactions.

(1) Porphyrins. The scope of this homogeneous magnesium insertion procedure was investigated with the porphyrins listed in Chart 1. Rapid metalation was observed for TPP and OEP. **1b** was poorly soluble but metalated successfully over 24 h. The pyridyl porphyrin **1c** and pentafluorophenyl porphyrin **1d**, used as solids or as concentrated solutions in CH_2Cl_2, were completely insoluble upon exposure to the ethereal MgI_2−DIEA reagent and failed to metalate. The facially encumbered porphyrins **1e**−**g** also were metalated, albeit more slowly, taking 12−24 h for completion. Thus this homogeneous method was successful for all porphyrins in Chart 1 with the exception of those porphyrins that precipitated in the reaction medium. The porphycene derivative (**3**) failed to yield any metalated product, the same result observed with the heterogeneous procedure.

(2) Hydroporphyrins. Our next objective was to establish the viability of the homogeneous procedure with chlorins, the dihydroporphyrins central to photosynthesis. We hoped that the homogeneous solution of MgI_2−DIEA would be the answer to the shortcomings observed in the heterogeneous procedure with the more complex dihydroporphyrin derivatives. The metalation of TPC by the heterogeneous method yielded MgTPC but also formed an impurity which could be removed by chromatography.[2] Under homogeneous conditions, the reaction was cleaner and had less of the impurity, but formation of MgTPC was appreciably slower with only ∼90% conversion after 24 h. In contrast, the heterogeneous metalation affords MgTPC within 30 min. Application of the homogeneous magnesium insertion procedure to TPBC afforded MgTPC, the same result obtained with the heterogeneous procedure.

We next examined the naturally occurring hydroporphyrins and their derivatives. The pheophytin a derivative, **7**, was effectively metalated with the homogeneous method in 1 h in high yield. In contrast, all attempts to achieve metalation using the heterogeneous method had failed. **6a** failed to metalate under homogeneous conditions. Absorption spectral analysis of the reaction mixture showed broadened absorption bands of the free base starting material. We attribute the failure of the metalation to coordination of the magnesium halide with the peripheral carboxylic acid. Methylation of the carboxylic acid with diazomethane gave **6b**, which did metalate readily under homogeneous conditions, but which had failed under heterogeneous conditions. **8** was treated with the ethereal MgI_2−DIEA reagent, affording a green oil coating the walls of the flask. TLC analysis following workup showed at least five new more polar products. Absorption spectral analysis of the mixture of new products showed a broad long-wavelength band (λ_{max} 654 nm) which is more blue-shifted than either pheophytin a (λ_{max} 668 nm) or an authentic sample of chlorophyll a (λ_{max} 658 nm). This reaction mixture has not been characterized further. In summary, a variety of hydroporphyrins can be metalated with magnesium under the homogeneous conditions, but neither the homogeneous nor the heterogeneous method is suited for reconstituting chlorophyll a.

(3) Phthalocyanines. The phthalocyanines examined (**9a**−**d**) were soluble in the reaction solvents composed of the ethereal MgI_2−DIEA reagent in CH_2Cl_2 as well as in diethyl ether alone. However, in each case with **9a**−**d**, the homogeneous magnesium insertion method failed even on prolonged stirring (24 h) at room temperature. We attribute the failure of these reactions to the low reactivity of the phthalocyanines.

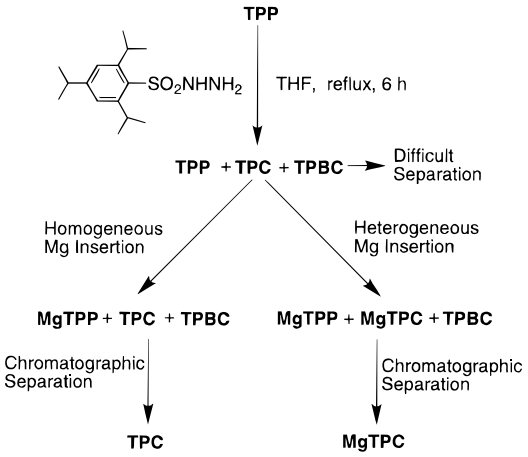
C. Improved Synthesis and Purification of Tetraphenylchlorin. TPC (**4**) is typically prepared by reduction of TPP followed by chromatography of the resulting mixture of TPP, TPC, and TPBC. We have investigated milder reduction conditions and have exploited the selectivity of the magnesium insertion reactions in order to achieve a simpler separation scheme. Together these two methods yield a streamlined procedure for isolating TPC or MgTPC from TPP.

Whitlock et al. performed the diimide reduction of TPP in pyridine at 105 °C with potassium carbonate and with *p*-toluenesulfonyl hydrazide as the diimide source.[30] We wished to avoid such high temperatures and basic conditions. 2,4,6-Triisopropylbenzenesulfonyl hydrazide has been shown to be an effective source of diimide for the reduction of a range of organic compounds in refluxing THF without the requirement for a base.[29] Treatment of TPP in refluxing THF with a 4 molar excess of triisopropylbenzenesulfonyl hydrazide (in two portions over 6 h) gave a mixture of approximately 45% TPP, 50% TPC, and 5% TPBC. Addition of further portions of hydrazide (8 molar excess over 9 h) led to complete reduction of TPP and the formation of larger quantities of TPBC (86%). Higher yields of TPC could possibly be achieved by using longer reaction times and greater excesses of hydrazide, followed by selective oxidation of TPBC to TPC with *o*-chloranil.[30]

The isolation of TPC from mixtures of TPP, TPC, and TPBC involves protracted chromatography,[37] extraction of the porphyrins from benzene with phosphoric acid solutions of various concentration,[30] or the selective formation of ZnTPP with free base TPC remaining unreacted, followed by chromatographic

(37) Ball, R. H.; Dorough, G. D.; Calvin, M. *J. Am. Chem. Soc.* **1946**, *68*, 2278−2281.

Scheme 2. Streamlined Procedures for Isolating Chlorins (TPC or MgTPC)



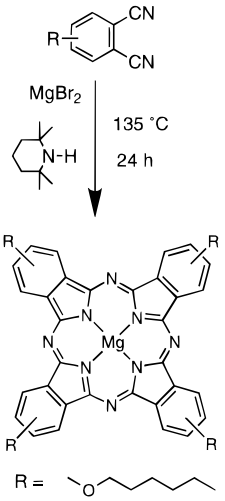
separation on talc.[24] Our aim was to exploit magnesium insertions to effect a more facile separation. Three methods were explored:

(i) Heterogeneous magnesium insertion conditions were applied to the mixture of porphyrin, chlorin, and bacteriochlorin (utilizing MgI_2, DIEA, and CH_2Cl_2). TPP and TPC were converted to MgTPP and MgTPC, respectively, while TPBC remained unmetalated. Separation by chromatography on grade V alumina afforded MgTPC in 25% yield (Scheme 2).

(ii) Homogeneous magnesium insertion conditions were applied to the mixture of porphyrin, chlorin, and bacteriochlorin (using the ethereal MgI_2−DIEA reagent). The relative rates of metalation for TPP (20 min) and TPC (24 h) under homogeneous conditions can be exploited as a separation scheme. Treatment of the porphyrin/hydroporphyrin mixture with the ethereal MgI_2−DIEA reagent (∼7-fold molar excess based on the amount of TPP present) converted TPP to MgTPP in 1 h, with TPC and TPBC remaining in the free base form. Chromatographic workup on grade V alumina with hexanes/CH_2Cl_2 (10:1) eluted the free base species (TPC, TPBC, and residual TPP) first, and any metalated species remained at the origin. This resulted in an overall 50% isolated yield of TPC (90% pure with the remainder due mainly to TPP). To obtain a sample of TPC free of TPBC, the selective oxidation of TPBC to TPC with *o*-chloranil could be employed prior to metalation.[30] Given the simplicity of the separation of TPC from MgTPP and the respectable overall yield, this is the method of choice for obtaining the chlorin product (Scheme 2).

(iii) Taking advantage of the mild reduction conditions, we decided to reverse the order of metal insertion/reduction by performing the direct reduction of MgTPP. Treatment of MgTPP with 2,4,6-triisopropylbenzenesulfonyl hydrazide in refluxing THF for 9 h afforded a mixture of MgTPP and MgTPC, with trace amounts of other pigments. No significant demetalation occurred. However, as samples were removed from the reaction mixture for analysis and exposed to air, $(MgTPC)^{\bullet+}$ formed rapidly in the absorption spectral cuvette, with complete conversion within 1 h without alteration of MgTPP (MgTPC has lower oxidation potential than MgTPP).[26,38] Such facile oxidation of MgTPC did not occur in procedures i and ii. This oxidation could be avoided at the preparative level by cooling the reaction mixture under argon with immediate workup, but after column chromatography the overall yield of MgTPC was only 15%. Treatment of MgTPP with excess hydrazide for periods longer than 9 h yields further

Scheme 3. Direct Synthesis of Magnesium Tetra-*n*-hexoxyphthalocyanine



conversion as well as another product which is provisionally assigned to the magnesium isobacteriochlorin (MgTPiBC), by analogy with the results observed by Whitlock et al. for reduction of ZnTPP.[30] However, any MgTPiBC or MgTPBC that is formed is readily oxidized upon workup and is not isolated.

D. Properties and Reactions of Magnesium Phthalocyanines. (1) Solubility. High solubility in organic solvents is a prerequisite for incorporating the magnesium-containing pigments in covalent arrays. The *tert*-butyl- and cumylphenoxy-substituted magnesium phthalocyanines are soluble in organic solvents such as CH_2Cl_2, $CHCl_3$, toluene, and ethyl acetate. Mg-**9b** was insoluble in most organic solvents tested (acetone, CH_2Cl_2, $CHCl_3$, toluene, ethyl acetate, tetrahydrofuran, dimethyl sulfoxide, dimethylformamide, pyridine, and methanolic solutions of tetrahydrofuran or CH_2Cl_2), although modest solubility was obtained in 1,2-dichlorobenzene. We attribute the insolubility to ligation of the alkoxy oxygen of one phthalocyanine to the magnesium of another phthalocyanine. The cumylphenoxy-substituted magnesium phthalocyanine Mg-**9c** does not undergo the same process, indicating the steric bulk of the cumylphenoxy functional group prevents ligation of oxygen with magnesium. Mg-**9a** has no coordinating functional group to ligate with magnesium and thus is soluble in most organic solvents.

(2) Direct Synthesis of Magnesium Phthalocyanines. Numerous procedures for preparing magnesium phthalocyanines employ reactions with phthalocyanine precursors and magnesium metal at high temperatures.[9−16] Tomoda et al. reported a method using phthalonitrile and $MgCl_2$ in 1-pentanol at reflux, affording magnesium phthalocyanine in 53% yield, though the synthesis of more elaborate phthalocyanines was not demonstrated.[39] We attempted to directly synthesize the magnesium phthalocyanines from the corresponding phthalonitriles using the same principles of the heterogeneous magnesium insertion procedure (the use of a noncoordinating solvent, a nonnucleophilic base, and a magnesium halide). A mixture of 4-(*n*-hexoxy)phthalonitrile, $MgBr_2$, and 2,2,6,6-tetramethylpiperidine was heated at 135°C in the absence of a solvent for 24 h, affording magnesium tetra-*n*-hexoxyphthalocyanine in 30% yield (Scheme 3). Replacing DIEA with 2,2,6,6-tetramethylpiperidine, or with toluene as a solvent and with DIEA or 2,2,6,6-tetramethylpiperidine, gave <5% yield in each case. These

(38) Carnieri, N.; Harriman, A. *Inorg. Chim. Acta* **1982**, *62*, 103−107.

(39) Tomoda, H.; Saito, S.; Shiraishi, S. *Chem. Lett.* **1983**, 313−316.

results do not appear to be superior to those obtained using Tomoda's method.[39]

(3) Demetalation of Magnesium Phthalocyanines. In order to complement the preparation of magnesium phthalocyanines, we devised a mild method to demetalate the magnesium phthalocyanines. A solution of H_2O/trifluoroacetic acid (TFA, 1:1 v/v) was added to an equal volume of Mg-**9a** in CH_2Cl_2. This biphasic solution was stirred at room temperature. Demetalation was complete within 30 min and the free base phthalocyanine **9a** was isolated in high yield. The demetalated phthalocyanine had analytical properties identical to an authentic sample. This demetalation procedure is milder than Linstead's involving concentrated H_2SO_4 at -3 °C.[9]

(4) Spectral Properties of Magnesium Phthalocyanines. The free base and magnesium phthalocyanines have strong absorption in the ultraviolet and the red regions of the spectrum. In addition, the fluorescence quantum yields are very high. **9a**, for example, has $\epsilon_{696\ nm} = 174\ 000\ M^{-1}\ cm^{-1}$ (heptane), while Mg-**9a** is shifted hypsochromically ($\epsilon_{678\ nm} = 214\ 000\ M^{-1}\ cm^{-1}$ in isopentyl alcohol).[12] Magnesium tetra-*tert*-butylphthalocyanine fluoresces ($\lambda_{max} = 691$ nm) strongly with quantum yield[20] of 0.84 and lifetime[27] of 5.7 ns (benzene). We find that magnesium tetrakis(4-cumylphenoxy)phthalocyanine has similar absorption features, with $\epsilon_{678\ nm} = 172\ 000\ M^{-1}\ cm^{-1}$ (CH_2Cl_2/ethanol, 3:1). The integrated fluorescence quantum yields (Φ_f) of the other magnesium phthalocyanines in $CHCl_3$ at room temperature are 0.62 (Mg-**9b**) and 0.68 (Mg-**9c**). However, Mg-**9d** aggregated in nonpolar solvents (toluene, $CHCl_3$), giving absorption peaks at 740 and 800 nm and a strongly quenched fluorescence spectrum. In pyridine the peak at 800 nm largely disappeared. In contrast to the high fluorescence quantum yields of Mg-**9a**−**c**, the related zinc tetra-*n*-butoxyphthalocyanine exhibited $\Phi_f = 0.42$, illustrating the diminished heavy atom effect in magnesium phthalocyanines.[40] These spectral features make organic-soluble magnesium phthalocyanines Mg-**9a** and Mg-**9c** excellent candidates as absorbers in light-harvesting arrays or as emitters in molecular photonic wires.

E. Comparative Stability of Magnesium Chelates of Porphyrinic Compounds. The well-known lability of magnesium porphyrins to weak acids, as well as the harsh acidic conditions employed by Linstead for demetalating magnesium phthalocyanine,[9] prompted us to assess the relative stability of the magnesium chelates to acid-induced demetalation. Treatment of a CH_2Cl_2 solution of the magnesium chelate (~1 mM) at room temperature with silica gel (2% w/v) gave steady demetalation of MgTPP (32% demetalation at 1 h; 88% at 6 h) but no detectable demetalation of Mg-**9c** after 24 h. Similar treatment of a CH_2Cl_2 solution with acetic acid (10% v/v) gave >95% demetalation of MgTPP in 15 min, while again there was no detectable demetalation of Mg-**9c** after 24 h. These results show that the magnesium phthalocyanine is much more stable than the magnesium porphyrin toward acid-induced demetalation. Exposure of the magnesium phthalocyanine in CH_2Cl_2 to an aqueous solution of trifluoroacetic acid at room temperature gave efficient demetalation (vide supra).

Discussion

A. Comparison of Heterogeneous and Homogeneous Magnesium Insertion Procedures. The magnesium insertion as portrayed by eq 1 appears simple in principle, but in practice its subtle complexities become apparent. Factors that play crucial roles include the nature of the tetrapyrrolic species, magnesium source, base, and solvent.

$$H_2\text{-porphyrin} + MgX_2 \rightarrow \text{Mg-porphyrin} + 2HX \quad (1)$$

Many older methods for magnesium insertion employ a polar solvent with a magnesium salt, thus ensuring complete solubility of both the porphyrin and the magnesium reagent. However, all conditions that employ strongly coordinating solvents also require high temperatures for metalation. Magnesium has a strong affinity for oxygen and a weaker affinity for nitrogen, forming octahedral complexes with both types of ligands. Indeed, although $MgBr_2$ and MgI_2 each show the octahedral CdI_2 type structure,[41] upon dissolution in polar solvents, both yield octahedral complexes by coordination of oxygenic or nitrogenous ligands about the magnesium without sharing of the halides between adjacent magnesium atoms.[42] In polar solvents, the success of the metalation reaction requires forcing conditions to disrupt the stable coordination complex of magnesium with solvent.

The heterogeneous method (e.g., a slurry of MgI_2 with DIEA in CH_2Cl_2) abandons the requirement of mutual solubility of the magnesium halide and the porphyrin but avoids forming relatively inactive coordination complexes of magnesium with solvent or base. The amine serves to neutralize the hydrogen halide generated in the reaction, thereby preventing the reverse acid-promoted demetalation reaction,[43] and perhaps facilitates deprotonation of the free base porphyrin. The amine may complex with magnesium, but these interactions are weak[44] and are insignificant under the reaction conditions. The heterogeneous method is widely applicable to different porphyrinic derivatives (Table 2). No order-of-addition effects (MgI_2, DIEA) were observed in achieving porphyrin metalation. The reaction workup procedure involves washing the reaction mixture with aqueous $NaHCO_3$ followed by column chromatography on alumina to remove any residual free base compound. The order of reactivity among the compounds studied was phthalocyanines < chlorins < porphyrins.

The homogeneous procedure (a solution of MgI_2 and DIEA in diethyl ether) uses a weakly coordinating solvent to solubilize MgI_2 but is not strongly coordinating enough to form unreactive complexes with magnesium. These reaction conditions give a cleaner procedure by avoiding insoluble slurries of magnesium halide and are less forcing than the heterogeneous conditions. Indeed, the less reactive porphyrinic derivatives (TPC and the facially encumbered porphyrins) react much slower under these conditions, and the phthalocyanines, which were the slowest to react by the heterogeneous procedure, do not react at all by the homogeneous method. The absence of large insoluble quantities of magnesium halide allows the more complex macrocycles such as **7** and **6b** to be metalated which otherwise fail under heterogeneous conditions due to complexation-induced insolubility.

The structure of magnesium halides dissolved in ether has been studied intensively because of their relevance to the nature

(40) Kobayashi, N.; Sasaki, N.; Higashi, Y.; Osa, T. *Inorg. Chem.* **1995**, *34*, 1636−1637.

(41) Wells, A. F. *Structural Inorganic Chemistry*, 5th ed.; Oxford University Press: Oxford, England, 1986; p 413.

(42) $MgBr_2(pyridine)_6$,[a] $MgBr_2(THF)_4$,[b] $MgBr_2(THF)_4(H_2O)_2$,[c] $MgBr_2(CH_3OH)_6$,[d] and $MgI_2(CH_3OH)_6$.[e] (a) Halut-Desportes, S. *Acta Crystallogr.* **1977**, *B33*, 599−601. (b) Schröder, F.; Spandau, H. *Naturwissenschaften* **1966**, *53*, 360. Perucaud, M.-C.; Le Bihan, M.-T. *Acta Crystallogr.* **1968**, *B24*, 1502−1505. (c) Sarma, R.; Ramirez, F.; McKeever, B.; Chaw, Y. F.; Marecek, J. F.; Nierman, D.; McCaffrey, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 5289−5295. (d) Brusset, H.; Halut-Desportes, S.; Privat, C.; Jouan, M. *Bull. Soc. Chim. Fr.* **1968**, 4794−4798. (e) Halut-Desportes, S.; Philoche-Levisalles, M. *Comp. Rend. C* **1976**, *283*, 393−395.

(43) Snellgrove, R.; Plane, R. A. *J. Am. Chem. Soc.* **1968**, *90*, 3185−3194.

(44) Banerjee, A. K.; Sinha, S. K.; Ghosh, M. K.; Roy, S. K. *J. Ind. Chem. Soc.* **1985**, *62*, 269−271.

Table 2. Scope of Heterogeneous and Homogeneous Magnesium Insertion Methods[a]

	free base compound	heterogeneous	homogeneous
	Porphyrins[b]		
1a	C_6H_5	+	+
1b	4-CH_3O_2C-C_6H_4	+	+
1c	4-C_5H_4N	+	−
1d	C_6F_5	+	−
1e	2,4,6-$(CH_3)_3C_6H_2$	+	+
1f	2,6-$(CH_3O)_2C_6H_3$	+	+
1g	2,6-$(C_6F_5CH_2O)_2C_6H_3$	+	+
2	octaethylporphyrin	+	+
3	2,7,12,17-tetra-*n*-propylporphycene	−	−
	Chlorins		
4	TPC	+	+
5	TPBC[c]	−	−
6a	pyropheophorbide a	−	−
6b	methyl pyropheophorbide a	−	+
7	chlorin e_6 trimethyl ester	−	+
8	pheophytin a	−	−
	Phthalocyanines (Pc)		
9a	(*tert*-butyl)$_4$Pc	+	−
9b	(*n*-hexoxy)$_4$Pc	+	−
9c	(4-cumylphenoxy)$_4$Pc	+	−
9d	(*n*-butoxy)$_8$Pc	+	−

[a] The + or − sign indicates whether the magnesium chelate was isolated or not. [b] *meso* substituent for **1a**−**g**. [c] Metalation occurred but the product isolated was MgTPC.

of Grignard reagents. MgI_2 (or $MgBr_2$) is essentially monomeric in a dilute solution of diethyl ether (<0.08 M) but forms dimeric and higher-order complexes at concentrations of ≥0.28 M.[45] Wellmar and Persson found that, at higher concentration, MgI_2 in diethyl ether (in the absence of any amine) yields two liquid layers; the upper layer consists of 0.2 M MgI_2 while the lower layer is yellowish, viscous, crystallizes below 30 °C, and consists of 2.5 M MgI_2 and 5.45 M diethyl ether.[46] Large-angle X-ray scattering of the lower layer at 44 °C did not coincide with a single structure. This solution is regarded as an "ionic melt", ionic because of insolubility in ether and a melt because with only two molecules of Et_2O per (Mg^{2+}, $2I^-$) there is no free solvent.[46] Though the phase separation observed with MgI_2 in diethyl ether resembles that in forming the ethereal MgI_2−DIEA reagent, in the former both the upper and lower layers are highly concentrated. In contrast, the ethereal MgI_2−DIEA reagent is dilute (∼0.04 M MgI_2) and thus the magnesium presumably is monomeric. The coordination number of the magnesium ion is not known under these conditions; however, magnesium is likely not octahedral. Though most complexes of magnesium with coordinating solvents are octahedral, the crystal structure of $MgBr_2{\cdot}2O(Et)_2$ is not octahedral, showing independent molecules with a tetracoordinated magnesium ion at the center of a distorted tetrahedron.[47] In contrast to the dilute upper ethereal layer (MgI_2−DIEA reagent), the lower oil is highly concentrated and may consist of $MgI_2{\cdot}2O(Et)_2$, by analogy with the results of Wellmar and Persson,[46] or $MgI_2{\cdot}3O(Et)_2$, by analogy with the related results of Rowley and Evans with $MgBr_2{\cdot}3O(Et)_2$;[36] however, the presence of some amine in the lower oil cannot be ruled out.

We find the ethereal MgI_2−DIEA reagent to be very robust. It is known that the maximum concentration of MgI_2 dissolved in diethyl ether depends on the purity of the diethyl ether.[48] Water-saturated diethyl ether dissolved 0.4 M MgI_2 while freshly distilled diethyl ether (from Na) dissolved 0.2 M MgI_2. We prepare the ethereal MgI_2−DIEA reagent with reagent grade diethyl ether (without further distillation) and DIEA (as obtained commercially) in a flask under argon on the benchtop and flush the atmosphere of the flask with argon prior to storage. In general we store the biphasic solution in a capped round-bottom flask in the refrigerator and draw reagent as needed from the upper layer in order to perform metalations. This may ensure a saturated solution of reagent in the upper layer. We have prepared the ethereal MgI_2−DIEA reagent at least 20 times in this manner and have obtained consistent metalation results.

B. Intrinsic Reactivity of Porphyrinic Compounds. Four main findings bear on the issue of relative reactivity of various porphyrin compounds toward magnesium insertion. First, the reactivity increases in the series phthalocyanines < chlorins < porphyrins. Second, the porphyrin isomer porphycene did not metalate under any conditions. Third, the more elaborate chlorins (**6b**, **7**) succeed with homogeneous but not heterogeneous metalation conditions. Fourth and conversely, phthalocyanines succeed with heterogeneous but not homogeneous metalation conditions.

Factors governing the ability of cyclic tetrapyrrole derivatives to chelate magnesium include differences in basicity of the pyrrolic nitrogen atoms, differences in core size, differences in flexibility of the ligand, and the presence of peripheral substituents on the porphyrinic species. Basicity, core size, and flexibility are intrinsic properties of the macrocycle, while substituents can alter the metalation process by complexation with magnesium or by causing insolubility in the reaction medium. We first consider intrinsic features of the macrocycles affecting magnesium insertion.

(1) Basicity. The basicity of the porphyrinic derivative plays a central role in the rate of metal insertion. The following acid-base dissociations can occur in the inner core of porphyrinic (P) compounds, where H_2P is the free base compound:

$$H_4P^{2+} \rightarrow H_3P^{1+} + H^+ \qquad (K_4)$$

$$H_3P^{1+} \rightarrow H_2P + H^+ \qquad (K_3)$$

$$H_2P \rightarrow H_1P^{1-} + H^+ \qquad (K_2)$$

$$H_1P^{1-} \rightarrow P^{2-} + H^+ \qquad (K_1)$$

The basicity of the parent free base porphyrinic system often is assessed by the values of K_4 and K_3 determined by acid titrations. A less frequent measurement involves determination of K_2 by basic titration of the free base compound, thereby determining the stability of the monoanion of the porphyrinic compound.

Porphyrins exhibit coalescence of K_3 and K_4 at pH ∼2, indicating two nitrogens of similar basicity in the molecule.[49,50] Chlorins, in contrast, exhibit one protonation (K_3) at pH ∼2 and a second (K_4) at pH ∼−1, indicating the presence of one nitrogen comparably basic to that of a porphyrin and one nitrogen ∼1000 times less basic. Thus porphyrins are more basic than chlorins. Phthalocyanines can undergo two protonations at the inner nitrogens as well as four additional protonations at the peripheral nitrogen atoms. Consequently, the best means of assessing basicity of phthalocyanines involves acid dissociation of the free base compound (K_2). Tetra-*tert*-

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butylphthalocyanine has pK_2 = 10,[51] phthalocyanine sulfonic acid has pK_2 = 10.7,[52] while tetraphenylporphyrin has pK_2 = 21.[53] The electron-withdrawing effect of the four *meso* nitrogens in phthalocyanines renders the inner hydrogens in phthalocyanines 10 orders of magnitude more acidic than porphyrins (K_2), and therefore free base phthalocyanines also are expected to be less basic than the porphyrins (K_3, K_4). Though all values of K_1-K_4 are not available for the three types of porphyrinic compounds, the values that are available indicate the basicity increases in order of phthalocyanines < chlorins < porphyrins.

The reactivity trend observed with magnesium insertion parallels the basicity of the macrocycles (phthalocyanines < chlorins < porphyrins). The rate of metal insertion for a range of metals also follows the series TPBC < TPC < TPP.[35] We believe that basicity of the macrocycle is the major determinant of the rate of formation of the magnesium chelate.

Hambright has studied rates and equilibria of metalation as a function of basicity of water-soluble porphyrins at room temperature.[54] These studies show that the rate of metalation (with cadmium or zinc) increases slightly with increasing basicity of the ligand, while the rate of hydrolysis increases by several orders of magnitude with increasing basicity. Thus in aqueous solution the less basic porphyrin forms the more stable metal chelate. Corwin et al. performed a variety of equilibration experiments among magnesium chelates under protic or aprotic conditions.[55,56] In competition and exchange experiments among dipyrromethenes and magnesium dipyrromethenes in boiling anhydrous 4-methyl-1,3-dioxane (bp 114 °C), magnesium was bound more tightly by the more basic dipyrromethene.[55] When a chlorin and porphyrin competed under the same conditions for the magnesium in a magnesium dipyrromethene, the chlorin bound magnesium first but ultimately the more stable magnesium porphyrin was formed.[55] Equilibration studies in phenol at 100 °C of a magnesium and free base pair drawn from a set of chlorins and porphyrins indicated the magnesium porphyrins were more stable than the corresponding magnesium chlorins. However, among porphyrins (or chlorins) with varying basicity, the less basic porphyrin (or chlorin) formed the more stable magnesium chelate.[56] The diverse conditions of these studies make direct comparison difficult. We find that under the homogeneous or heterogeneous conditions the rate of magnesium insertion increased with increasing basicity of the ligand (phthalocyanines < chlorins < porphyrins). We also find that the magnesium porphyrin undergoes more rapid demetalation than the magnesium phthalocyanine under acidic conditions. Our data concern rates of magnesium insertion (and demetalation) and are done under conditions that presumably are irreversible and, therefore, do not necessarily reflect thermodynamic stability of the magnesium chelates.

(2) Core Size. The core size, defined by the $N_{pyrrole}$ to Ct (middle of the central cavity) distance, increases in the series phthalocyanines < porphyrins $\lesssim$ chlorins. Core size is important because the ionic radius of the magnesium (0.72 Å)[57] is sufficiently large that the magnesium ion does not fit exactly into the porphyrinic core. In magnesium chelates of porphyrinic compounds, the magnesium often rests out-of-plane in a square-pyramidal geometry,[58,59] though with appropriate ligands sometimes forms an in-plane octahedral complex.[60] Thus one would expect that porphyrinic macrocycles with larger cores would better accommodate magnesium.

For free base hydroporphyrins the core size is slightly larger than for the porphyrin,[61] however, upon metalation the core size can vary depending on the central metal and the number and type of axial ligands.[62] Given the small differences in core size between porphyrins and chlorins, and the ability of these macrocycles to adapt to the size of the metal, the ostensible differences in core size are arguably not a critical factor in determining their magnesium insertion rates.

The core size of phthalocyanine (Ct−N radius of 1.92 Å) is 0.14 Å smaller than that of TPP (Ct−N radius of 2.05−2.06 Å) due to the replacement of the *meso* bridging carbons with nitrogens.[63] One crystal structure of magnesium phthalocyanine shows the 5-coordinate magnesium resting 0.496 Å out of the plane of the phthalocyanine.[64] A very early preliminary study of magnesium phthalocyanine suggested an octahedral geometry, implying an in-plane magnesium, but no reliable phthalocyanine structure showing this geometry has been determined.[65] Thus, whether the phthalocyanine has sufficient flexibility to accommodate an in-plane magnesium remains unknown. The contraction in core size has a dramatic effect on the ability of phthalocyanines to chelate magnesium, though the origin of the effect is not due solely to available space for the metal in the core. The decreased dimensions of the central core in phthalocyanines gives rise to internal hydrogen bonding of one NH group to the adjacent pyrrole nitrogen. This internal hydrogen bonding can present a significant kinetic barrier to metalation in phthalocyanines.[51] However, use of a solvent such as pyridine to disrupt the internal hydrogen bonds gives significant rate accelerations with a variety of metals, including rates of insertion that are faster than for porphyrins.[51] The greater acidity of the phthalocyanine inner protons leads to deprotonation in basic solvents, generating a structure more resembling the transition state for metalation, hence the very fast rates. In our homogeneous or heterogeneous conditions, the absence of an agent that disrupts this internal hydrogen bond results in a very slow reaction. Thus, the slow rate observed with phthalocyanines may not be due to the available space in the core per se but rather to the stable internal hydrogen bonding which is a consequence of the contracted core.

The core of tetrapropylporphycene (**3**), although not symmetrical (N_{pyr}−Ct, 1.920 and 1.933 Å), is smaller than porphy-

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rins and is comparable to that of phthalocyanines. **3** exhibits a strong N−H···N hydrogen bond which inhibits insertion for a variety of metals.[34] The failure of magnesium insertion under relatively mild, weakly or noncoordinating conditions (compared with pyridine) may be due to the inability to overcome strong internal H-bonding in this macrocycle. However, phthalocyanines also have internal H-bonds and can be metalated with magnesium under the heterogeneous reaction conditions, while porphycene did not metalate under any conditions we examined. The asymmetrical shape of the porphycene core may also be a critical factor in determining the metalation rate.

(3) Flexibility. The flexibility of the macrocycle is one additional factor that can influence core size and metalation. Structural data for hydroporphyrin systems indicates that the reduced rings have increased flexibility[66] which can adjust to accommodate the relatively larger magnesium ionic radius, while a molecular mechanics calculation argues that porphyrins and chlorins have similar flexibilities.[67] Regardless, because chlorins have slightly larger cores than porphyrins, and hydroporphyrins have at least as much flexibility as porphyrins, ring flexibility cannot explain the observation that chlorins metalate more slowly than porphyrins. To our knowledge, data are not available about flexibility of phthalocyanines.

In summary, we attribute the observed rates of metalation (phthalocyanines < chlorins < porphyrins) largely to a basicity effect. The slightly larger core size of the chlorin compared with the porphyrin appears insignificant in affecting the ease of metalation. The much slower rate of metalation of phthalocyanines is attributed to both the weaker basicity and the strong internal H-bonding in phthalocyanines. The hydrogen bonding in phthalocyanines is not disrupted easily under the heterogeneous or homogeneous reaction conditions.

C. Effects of Substituents. The types of substituents carried by porphyrinic compounds are important as some substituents can interfere with the metalation reaction. Some substituents cause insolubility in the reaction solvent while others can complex with the magnesium reagent and cause precipitation, thereby terminating metalation.

Porphyrin **1g** bears eight pentafluorobenzyloxy substituents in the ortho positions; however, metalation proceeded smoothly with both the heterogeneous (1 h) and homogeneous (24 h) procedures. Apparently the faces of these types of ortho-substituted porphyrins are less encumbered than might otherwise appear. A similar porphyrin bearing eight benzyloxy substituents in the ortho positions underwent zinc insertion under homogeneous conditions only 5 times slower than TPP.[68]

Porphyrins bearing peripheral groups that can coordinate with magnesium often precipitate under the reaction conditions. The porphyrins bearing ester (**1b**) or pyridyl (**1c**) groups precipitated in the heterogeneous procedure, but the addition of ethanol upon workup disrupted the aggregates and in each case the magnesium porphyrin was obtained. In the homogeneous procedure, both compounds again precipitated but upon similar workup Mg-**1b** was obtained while the free base **1c** remained unchanged. Aggregation in these types of compounds presumably involves intermolecular coordination of oxygen or nitrogen of the peripheral substituent to the magnesium of another porphyrin, an aggregation phenomenon well-known with chlorophylls, particularly in some light-harvesting arrays, where the ester functionality on the fifth ring coordinates to the magnesium of another chlorophyll unit.[69] **6a** failed to metalate via either homogeneous or heterogeneous procedures, forming precipitates in both cases. Methylation of the carboxylic acid substituent, forming **6b**, led to successful metalation via the homogeneous procedure. A special case is provided by **1d**, which metalated under the heterogeneous conditions but precipitated upon exposure to the ethereal MgI_2−DIEA reagent in the homogeneous conditions. This porphyrin lacks coordinating groups, and failure here is attributed to solubility rather than complexation problems.

In the case of **8** the β-ketoester group on ring V has the ability to chelate magnesium thereby binding it externally to pheophytin a. Such peripheral complexes with the β-ketoester moiety on ring V of pheophytin a have been studied in saturated $MgClO_4$/pyridine solutions and have been shown to prevent magnesium insertion into the core.[70] Triethylamine is a strong enough base to cause rapid epimerization,[71] and the ability of the enolizable β-ketoester to coordinate with magnesium is enhanced in the presence of bases, as in the homogeneous or heterogeneous reaction conditions. With compounds having similar structures as pheophytin a but lacking the β-ketoester functionality (**6b**, **7**), magnesium insertion occurred under homogeneous conditions. The Eschenmoser hindered Grignard reagent[72] successfully introduces magnesium into a variety of pheophytins and bacteriopheophytins.[73] In the biosynthesis of chlorophyll a, magnesium insertion occurs in protoporphyrin IX, long before the construction of ring V and conversion to the hydroporphyrin.[74] The homogeneous magnesium insertion method should be applicable to those chlorophyll derivatives that lack the enolizable β-ketoester function of ring V.

The organic-soluble phthalocyanines **9a**−**d** can be converted to their magnesium chelates by the heterogeneous but not the homogeneous method. The magnesium phthalocyanines with hydrocarbon (**9a**) or bulky aryloxy (**9c**) substituents are soluble in a variety of organic solvents, but the alkoxy-substituted magnesium phthalocyanines **9b** and **9d** have poor solubility. The ability to prepare magnesium phthalocyanines under mild conditions should facilitate the synthesis of a wide variety of magnesium phthalocyanine derivatives bearing sensitive substituents. Indeed, to our knowledge only a handful of magnesium phthalocyanines have been made previously, including the parent magnesium phthalocyanine and magnesium phthalocyanines bearing *tert*-butyl, 4-cumylphenoxy, phenyl, methoxy, nitro, or 3-nitro-5-*tert*-butyl groups.[9−16] These have been prepared by direct condensation methods employing a magnesium reagent (often Mg metal) and a phthalonitrile, phthalimide, or *o*-cyanobenzamide derivative or, alternatively, by treatment of the free base with a magnesium salt in refluxing quinoline[9] or with a magnesium viologen at reflux.[75] The mild conditions associated with the route demonstrated here should allow the synthesis of magnesium phthalocyanines that subsequently can be incorporated into multipigment light-harvesting arrays and related molecular photonic devices.

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Outlook

Magnesium insertion can be accomplished with a diverse group of porphyrins, chlorins, and phthalocyanines, as long as substituents causing solubility problems are not present. Significant compounds that failed to undergo magnesium insertion by either of these methods include tetraphenylbacteriochlorin and pheophytin a. Further work is required to investigate magnesium insertion into bacteriochlorins as well as macrocycles containing an enolizable β-ketoester group. The rate of magnesium insertion increases in the series phthalocyanines < chlorins < porphyrins. Though core size has been viewed as a key factor affecting metalation reactions, under both the homogeneous and heterogeneous conditions the rate of metalation increases with the basicity of the ligand, not with core size. Comparison of a magnesium phthalocyanine and a magnesium porphyrin toward acid-induced demetalation showed the former was far more stable in spite of its smaller core size, indicating the importance of basicity rather than core size in determining stability of magnesium chelates.

The homogeneous magnesium insertion method complements the heterogeneous method. Each provides a gentle means for inserting magnesium into porphyrinic ligands. The heterogeneous reaction is faster and succeeds with porphyrins, chlorins, and phthalocyanines, while the homogeneous method succeeds only with porphyrins and chlorins. The homogeneous method opens the door to a range of physical studies, such as characterizing the kinetics of magnesium incorporation with ligands of different structure. Though these types of investigations could be performed with other more vigorous magnesium insertion methods, or under heterogeneous conditions, the homogeneous conditions at room temperature are ideal for working with diverse porphyrinic pigments in dilute solution where problems of aggregation largely can be avoided. The ease of implementation and robustness of both the homogeneous and heterogeneous methods should make the magnesium chelates of a wide variety of porphyrinic compounds readily available, including as building blocks for incorporation in molecular photonic devices.

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