ABSTRACT

DOĞUTAN, DILEK. New Strategies for the Synthesis of Substituted Magnesium Porphyrins. (Under the direction of Professor Jonathan S. Lindsey).

Porphyrins are valuable compounds for studies in biomimetic and materials chemistry. Efficient routes for the synthesis of porphyrins bearing distinct types and patterns of substituents are essential for such studies and for diverse applications.

A new set of conditions has been developed for the synthesis of a broad class of porphyrins. The conditions entail a metal salt ($MgBr_2$; 3 mol equiv versus the reactant) and a non-coordinating base (DBU; 10 mol equiv versus the reactant) in a non-coordinating solvent (toluene) with heating (conventional or microwave irradiation) in the presence of air.

The reaction of 1-formyldipyrromethane under such basic, Mg-mediated conditions afforded Mg(II)porphine in 30-40% yield. The advantages of the new method include simplicity, high concentration, chromatography-free purification, gram-scale synthesis, and avoidance of the poorly soluble free base porphine. Mg(II)porphine exhibits good solubility in common organic solvents and is a valuable core scaffold for derivatization (Chapter 1).

New methodology is described for the synthesis of porphyrins bearing four (A_4, *cis*-A_2B_2, *cis*-ABC_2, *trans*-A_2B_2) or fewer (A, *cis*-AB, *cis*-A_2, *trans*-A_2) meso-substituents. The rational synthesis of *trans*-A_2B_2- or *trans*-A_2-porphyrins was achieved via condensation of two identical 1-acyldipyrromethanes. The statistical synthesis of various meso-substituted porphyrins was achieved via condensation of two non-identical 1-acyldipyrromethanes. Both routes possess attractive features including (1) no scrambling, (2) good yield (up to 60%) at high concentration (100 mM) for the macrocycle-forming step, (3) reasonable scope (aryl, heteroaryl, alkyl, or no substituent), (4) short reaction time (~2 h) via microwave irradiation, (5) magnesium porphyrins

as the products, which easily undergo demetalation, and (6) facile chromatographic purification. A key advantage of the statistical route is to obtain a *cis*-substituted porphyrin without the corresponding *trans* isomer. In total, 26 1-acyldipyrromethanes and 26 target porphyrins have been prepared, including many with two different pyridyl substituents. One set of amphipathic porphyrins includes *cis*-A_2B_2- or *cis*-A_2BC-porphyrins wherein A = pentyl and B/C = pyridyl (*o*-, *m*-, *p*-). Taken together, the rational and statistical routes enable facile conversion of readily available 1-acyldipyrromethanes to diverse porphyrins bearing 1-4 meso substituents for which access is limited via other methods (Chapter 2).

A new route has been developed for preparing porphyrins bearing up to four different meso-substituents (ABCD-porphyrins). The new strategy relies on two key reactions. One key reaction entails a directed synthesis of a 1-protected 19-acylbilane by acid-catalyzed condensation at high concentration (0.5 M) of a 1-acyldipyrromethane and a 9-protected dipyrromethane-1-carbinol. Three protecting groups were examined, including thiocyanato, ethylthio, and bromo, of which bromo proved most effective. The bilanes were obtained in 72 to 80% yield, fully characterized, and examined by ^{15}N NMR spectroscopy. The second key reaction entails a one-flask transformation of the 1-protected 19-acylbilane under the basic Mg-mediated porphyrin-forming conditions. The target magnesium porphyrin is obtained in 65% yield (Chapter 3).

The new route to bilanes and porphyrins bearing four distinct meso substituents has been studied to elucidate the scope and gain entry to previously inaccessible compounds. In total, 19 new porphyrins having alkyl, aryl, heterocylic or no substituent have been synthesized (Chapter 4). The bilanes were obtained in 35-87% yield, and the target porphyrins in up to 60% yield. Further study of the scope focused on bilanes and porphyrins bearing three heterocyclic substituents (*o*-, *m*-, *p*-pyridyl) or four alkyl groups (ethyl, propyl, butyl, pentyl), in which case

microwave irradiation was used for the porphyrin-forming step. Altogether, 17 bilanes and 19 porphyrins were prepared and characterized.

In summary, the basic Mg-mediated conditions provide facile access to novel substituted porphyrins which should facilitate a wide variety of studies.

New Strategies for the Synthesis of Substituted Magnesium Porphyrins

by
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DEDICATION

I would like to dedicate this work in the loving memory of my father Abdullah Atila Doğutan. Although he is no longer with me physically, he will be forever with me in spirit. Thank you very much for everything that you have done for me. I am deeply sorry for not being with you when you needed me the most. I will always work very hard and make you proud of me. I love you and miss you so very much.

Doktora tezimi sevgili babam Abdullah Atila Doğutan'a ithaf etmek istiyorum. Canim babaciğim bizler ile fiziksel olarak beraber değilsen bile, senin sevgin ve güzel anilarimiz herzaman kalbimde yaşayacak. Bizleri okutmak için annemle beraber yaptiğiniz tüm özveriler için sana ve anneme minettarim. Seni rahatsizliğin süresince ziyaret edemediğim, son gününde yaninda olamadiğim için çok üzgünüm. Şimdiye kadar oldugu gibi bundan sonrada bize öğrettiğin değerlerle yaşayarak benimle gurur duyman için elimden geleni yapacağim. Tekrar görüşünceye kadar seni çok seviyor ve özlüyorum benim canim babaciğim.

BIOGRAPHY

The author, Dilek Doğutan, was born in Istanbul, Turkey. After graduating from Erenköy Kiz Lisesi (High School) in Istanbul, Turkey, Dilek prepared for the competitive examination regulating entry into Middle East Technical University (METU) in Ankara, Turkey. Following the examination, she joined the Department of Chemistry at METU. After graduating from METU, Dilek started working in a pharmaceutical company, Ilsan-Iltas & Hexal, Inc., as a research scientist and worked in both Istanbul, Turkey and Munich, Germany. She applied for graduate schools in the USA and joined the North Carolina State University Department of Chemistry. She began her dissertation under the supervision of Dr. Jonathan S. Lindsey. Dilek was recognized with the Outstanding Graduate Research Accomplishment Award in chemistry in 2005 and 2007 by North Carolina State University Department of Chemistry. Dilek graduated from North Carolina State University in 2008. Upon completion of her Ph.D., she began a postdoctoral position at the Massachusetts Institute of Technology under the direction of Dr. Daniel G. Nocera.

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I would like to thank my family for their continous support. I would not be where I am today without you. I would like to thank my father Abdullah Atila Doğutan and my mother Ayşe Doğutan for all the sacrifices that they have made for me. It was your unconditional love and support which has kept me going all these years. I would like to acknowledge my sisters Necla Doğutan, Meryem Doğutan, Arife Doğutan, and Associate Professor Melek Doğutan Yenidünya for helping me during my education. I truly appreciate everything that you have done for me. I especially thank Associate Professor Melek Doğutan Yenidünya for being a true inspiration to me during my education. I would like to express my special thanks to my brother Mehmet Ali Atalay Doğutan. Finally, I would like to thank my loving husband Halil Kiper. I cannot express

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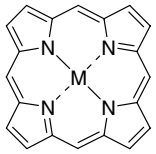
CHAPTER I

A DIRECT SYNTHESIS OF MAGNESIUM PORPHINE VIA 1-FORMYLDIPYRROMETHANE

I.A. Introduction

Porphine (**I-1**, Chart I.1) is the simplest porphyrin and represents the core macrocycle of naturally occurring and synthetic porphyrins. Due to the presence of eight open β-pyrrole sites and four meso sites, porphine is a potential building block for the elaboration of porphyrin derivatives. In this regard, porphine undergoes selective mono-bromination at a α-position to give 2-bromoporphine.[I1] On the other hand, Shi and Wheelhouse showed that the magnesium(II) chelate of porphine (**I-Mg-1**) undergoes tetrabromination to give magnesium(II) *meso*-tetrabromoporphine. Subsequent palladium-coupling reactions afforded tetraaryl A_4-porphyrins, which included target porphyrins that are not easily available by other routes (e.g., with heterocyclic substituents).[I2] Senge has shown that porphine reacts with organolithium reagents to provide meso-substituted A- or *cis*-A_2-porphyrins, which also are difficult to synthesize by other routes.[I3] These reports provide a glimmer of the possible synthetic utility of porphine; however, the practical use of porphine in synthetic chemistry has been thwarted by two vexing and somewhat interrelated limitations: (1) lack of an efficient method of synthesis, and (2) extremely low solubility of the free base porphine (**I-1**).



I-1: M = H,H
I-M-1: M = Mg(II), Zn(II), etc.

Chart I.1. Porphine Structure.

Methods for the synthesis of porphine span the past 70 years [I4-I16] (see the Supporting Information).[I23] The reactants employed include pyrrole and formaldehyde,[I4,I10] pyrrole-2-carboxaldehyde,[I5] *N*,*N*-dimethylaminomethylpyrrole,[I6] and 2-hydroxymethylpyrrole.[I7-I9,I11,I12] The best method to date employs condensation of 2-hydroxymethylpyrrole in an acidified

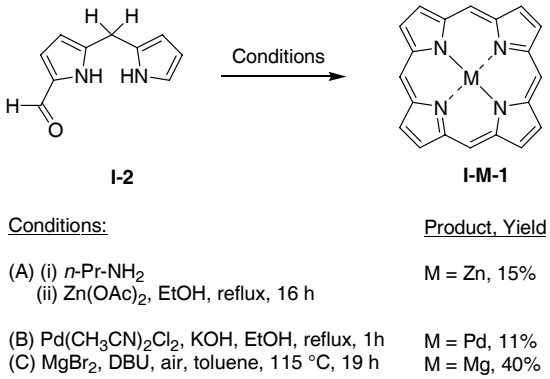
biphasic mixture followed by oxidation with DDQ, which has afforded 30 mg of porphine in 15% yield.[I12] An alternative method entails dealkylation of a tetra-*tert*-butylporphyrin or *meso*-tetrakis(hexyloxycarbonyl)porphyrin in the presence of strong acid, which respectively affords porphine in 64-74%[I14] or 77%[I15] yield; however, this method obviously requires the preparation of the porphyrin precursor. Porphine also can be prepared in 31% yield by the reaction of 5,10,15,17-tetrahydrotripyrrin and 2,5-bis(hydroxymethyl)pyrrole[I13] (or 2-hydroxymethylpyrrole[I16]).

Thus, despite the structural simplicity of porphine, there remains no method of satisfactory yield, scale, and ease of implementation that enables the synthetic utility of porphine to be unlocked. The low yields of macrocycle formation with simple pyrrole compounds are mitigated by the easily available starting materials; however, separation of the poorly soluble porphine from the polymeric material in the crude reaction mixture remains tedious. The use of more elaborate precursors requires more synthetic effort than would seem warranted. Here we report an efficient, concise, and practical method for preparing **I-Mg-1**, which greatly facilitates access to this valuable compound, and from which free base porphine (**I-1**) is readily obtained.

I.B. Results and Discussion

1. Strategy and Survey. Our approach for the synthesis of porphine, which has emerged from our prior studies of routes to *trans*-substituted porphyrins,[I17,I18] focused on methods that afford direct access to the metal chelate. A synthesis that affords direct access to the metalloporphine **I-M-1** would sidestep the difficult purification and handling problems of the poorly soluble free base porphine. In each case, we chose 1-formyldipyrromethane **I-2** as a potentially viable precursor to metal chelates of porphine. The conditions examined are shown

in Scheme I.1.



Scheme I.1. The Conditions Examined for Porphine Synthesis.

2. Formation of Zinc(II)porphine. The reaction of 1,9-diformyldipyrromethane (**I-4**) with *n*-propylamine and subsequent reaction of the bis(imino)dipyrromethane with a dipyrromethane in the presence of $Zn(OAc)_2$ in refluxing ethanol exposed to air affords the zinc(II) complex of the *trans*-AB-porphyrin.[I18] Although application of this method with the unsubstituted dipyrromethane resulted in little or no zinc porphyrin,[I18] we examined the analogous self-condensation with 1-formyldipyrromethane **I-2**. Reaction of **I-2** with excess *n*-propylamine at room temperature afforded quantitatively the corresponding imine. The self-condensation of the latter was carried out in refluxing EtOH containing $Zn(OAc)_2$. Chromatographic workup afforded Zn(II)porphine (**I-Zn-1**) in 15% yield.

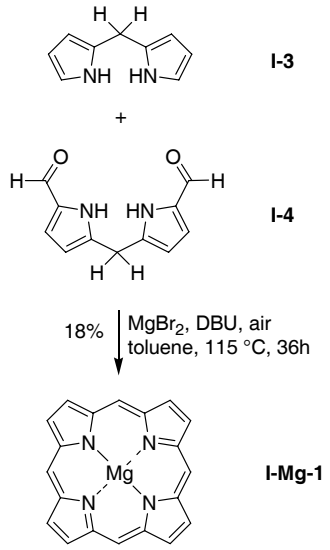
3. Formation of Palladium(II)porphine. The self-condensation of a 1-acyldipyrromethane in refluxing ethanol containing KOH and a palladium reagent affords the corresponding palladium(II) chelate of a *trans*-A_2B_2-porphyrin.[I17] Reaction of **I-2** under such basic, metalating conditions in refluxing ethanol [containing $Pd(CH_3CN)_2Cl_2$ and KOH][I17] afforded palladium(II)porphine (**I-Pd-1**) in 11% yield. Palladium(II)porphine was purified by filtration through a silica pad. **I-Pd-1** and **I-Zn-1** have been prepared via other methods.[I19]

4. Formation of Magnesium(II)porphine. An extensive study was carried out to explore the generality of the basic, metalating conditions [$Pd(CH_3CN)_2Cl_2$ in EtOH containing KOH] for the self-condensation of 1-acylpyrromethanes. The study, which encompassed different metals, solvents, and bases, will be reported elsewhere. One key finding is that a Mg(II) salt (e.g., $MgBr_2$) in the presence of a non-nucleophilic base (e.g., DBU) provides an effective means for the self-condensation of 1-acyldipyrromethanes. The use of $MgBr_2$ and DBU stemmed from our study of magnesium insertion into porphyrins, wherein similar conditions in the absence of any oxygenic ligands afford the magnesium(II)porphyrin.[I20] For the reaction of **I-2**, the formyl group should be activated by coordination to magnesium(II) given the high affinity of magnesium(II) for oxygen. The choice of non-coordinating solvent and non-nucleophilic base avoids competition by the solvent and base versus the 1-formyldipyrromethane in coordination to magnesium.

Thus, the reaction was carried out with a mixture of **I-2** (100 mM) in toluene at 115 °C containing DBU (10 mol equiv vs. **I-2**) and $MgBr_2$ (3 mol equiv) in the presence of air. After 8 h, **I-Mg-1** was present, in part as a precipitate, together with unreacted starting material. After 19 h, TLC analysis of the crude reaction mixture revealed the presence of **I-Mg-1**, polar polymeric material, and no starting material **I-2**. The workup entailed (i) concentration of the reaction mixture, treatment of the resulting residue with THF, and filtration to remove polymeric material and inorganic salts; (ii) washing the filtrate with water to remove DBU; and (iii) crystallization from ethanol/water to afford **I-Mg-1** in 40% yield. Note that **I-Mg-1** was previously prepared by metalation of **I-1**.[I2]

Several related condensations were explored under analogous conditions. The attempted condensation of pyrrole-2-carboxaldehyde, or the condensation of dipyrromethane (**I-3**) and

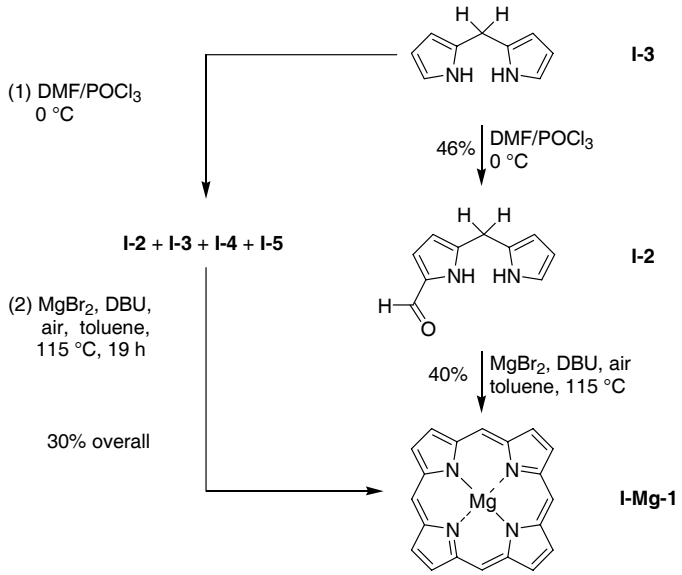
paraformaldehyde, gave no **I-Mg-1**. In contrast, the condensation of dipyrromethane (**I-3**) and 1,9-diformyldipyrromethane (**I-4**) afforded **I-Mg-1** in 18% yield (Scheme I.2).



Scheme I.2. Condensation of Dipyrromethane (**I-3**) and 1,9-Diformyldipyrromethane (**I-4**) to Afford **I-Mg-1**.

5. Scalable Synthesis of I-Mg-1. The reasonable yield and operational simplicity of **I-Mg-1** formation prompted examination of the reaction at multigram scale. We investigated three routes for the multigram synthesis of **I-Mg-1**, each of which employed $MgBr_2$ and DBU in toluene at ~115 °C. In *Method I.I*, the self-condensation of **I-2** (6.97 g) for 19 h afforded **I-Mg-1** (2.68 g, 40% yield) in a single batch process. In *Method I.II*, the self-condensation of **I-2** was carried out using microwave irradiation in an effort to achieve faster reaction. The reaction at 115 °C under otherwise standard conditions (toluene, 100 mM of **I-2**, 3 mol equiv of $MgBr_2$ and 10 mol equiv of DBU) was completed in ~45 min. Subsequent crystallization afforded **I-Mg-1** in 37% yield (0.031 g, 0.50 mmol scale). In both methods, the crude **I-Mg-1** was purified by crystallization (and no chromatography); however, the synthesis of the precursor **I-2** requires chromatography thereby limiting the scale of reaction. We sought to overcome this limitation.

The Vilsmeier formylation[I21] of dipyrromethane (**I-3**)[I22] affords a mixture composed of the target 1-formyldipyrromethane (**I-2**), unreacted **I-3**, 1,9-diformyldipyrromethane (**I-4**), and an unknown byproduct (tentatively assigned as 2-formyldipyrromethane (**I-5**) in a ratio of 24:8:5:1. The mixture typically is chromatographed to isolate pure **I-2**. Given that **I-2** self-condenses to give **I-Mg-1**, and **I-3** + **I-4** react to also give **I-Mg-1**, we examined the porphine-forming reaction with use of the crude Vilsmeier formylation mixture, which contains **I-2**, **I-3**, and **I-4**. Thus, in *Method I.III*, the crude Vilsmeier reaction mixture was concentrated. The resulting mixture (7.34 g) was dissolved in toluene, treated with DBU and $MgBr_2$ (10 and 3 mol equiv vs. the original quantity of **I-3**, respectively), and heated at 115 °C for 19 h whereupon **I-2**, **I-3**, and **I-4** were completely consumed. The chromatography-free purification as described above afforded **I-Mg-1** in 30% yield (1.98 g, 40 mmol scale) (Scheme I.3).



Scheme I.3. The Chromatography-Free Purification of **I-Mg-1**.

The ^{1}H NMR analysis of the crude Vilsmeier reaction mixture (7.34 g) gave a molar composition of **I-2**, **I-3**, **I-4**, **I-5** and DMF = 24:8:5:1:5, corresponding to 25.5 mmol of **I-2**, 8.5 mmol of **I-3**, and 5.3 mmol of **I-4**. The combined reactions of **I-2** → **I-Mg-1** in yield ranging

from 5 – 47% and of **I-3** + **I-4** → **I-Mg-1** in yield ranging from 100 – 0% can account for the observed yield of **I-Mg-1**. It may be coincidental that yields of 40% and 16% for the respective reactions, which are nearly identical to those of the constituent reactions alone, fit the observed data (see Supporting Information[I23]). Regardless of the exact contributions by each reaction, this streamlined, entirely chromatography-free procedure offers a simple and fast method for preparing multigram quantities of **I-Mg-1**.

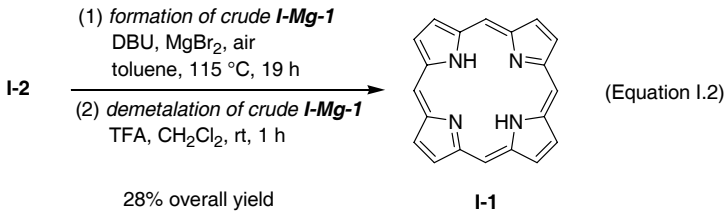
6. Stoichiometry. The overall stoichiometry for the reaction shows the requirement for a base and an oxidant (Equation I.1). The base is required, minimally, to neutralize the two equivalents of HBr liberated upon metal complexation. A $2e^-/2H^+$ oxidant is required to form the unsaturated macrocycle. Oxygen present in air would seem a likely source for the oxidizing equivalents. However, the microwave reaction in a degassed flask gave **I-Mg-1** in 32% spectroscopic yield. An alternative oxidant could be the formyl group of **I-2**, or the imine moiety of DBU. In the latter regard, the reaction with 2,2,6,6-tetramethylpiperidine in place of DBU gave **I-Mg-1** in 4.5% spectroscopic yield. The essential requirement for both $MgBr_2$ and DBU was validated by omission experiments, where the reaction of **I-2** carried out in the absence of either DBU or $MgBr_2$ gave no porphine.

Equation I.1

I-2 + **I-2** + $MgBr_2$ → **I-Mg-1** + 2HBr + $2H_2O$ + $2e^-$ + $2H^+$

7. Synthesis of Porphine I-1. A direct route to **I-1** was examined by demetalation of crude **I-Mg-1** (Equation I.2). Thus, reaction of **I-2** in toluene at 115 °C containing $MgBr_2$ and DBU afforded crude **I-Mg-1**. The reaction mixture was concentrated followed by filtration. Treatment of crude **I-Mg-1** with dilute TFA in CH_2Cl_2 afforded the free base porphine **I-1** in 28% overall yield.

Equation I.2.



(Equation I.2)

I.C. Outlook

One of the intrinsic problems in porphine chemistry is the poor solubility of **I-1** in common organic solvents. Among the various chelates prepared, the general trend in solubility in common organic solvents (CH_2Cl_2, THF, MeOH, diethyl ether, toluene) is as follows: **I-Pd-1** < **I-1** << **I-Zn-1** << **I-Mg-1**. The solubility of **I-Mg-1** in common organic solvents is sufficiently high to perform routine operations (purification, NMR characterization) and reactions at concentrations (1–50 mM) typical of those for porphyrinic compounds. The satisfactory solubility of **I-Mg-1** and its availability in gram quantities without any chromatography makes this simple macrocycle quite attractive for synthetic manipulation. The overall yield of **I-Mg-1** is 17% in a chromatography-free, 3-reaction sequence beginning with pyrrole and paraformaldehyde. In conjunction with the results obtained by Shi and Wheelhouse[I2] (bromination of **I-Mg-1** and subsequent palladium-coupling reactions), the door appears open to the synthesis of porphyrins bearing meso substituents (e.g., ethenyl, ethynyl, heterocyclic, sterically hindered) not easily available by other methods.

I.D. Experimental Section

General. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were collected in THF-d_8 at room temperature unless noted otherwise. Melting points are uncorrected. Silica gel (40 μm average particle size) was used for column chromatography. Anhydrous toluene (Aldrich) was used as received. THF free of BHT (Fisher HPLC grade) was used. The ^{1}H NMR

of the purified fractions THF with BHT revealed presence of the BHT signals on the spectrum. All other chemicals were reagent grade and were used as received. The 1-formyldipyrromethane **I-2**, dipyrromethane **I-3**, and 1,9-diformyldipyrromethane **I-4** are easily detected in TLC upon exposure to Br_2 vapor. Grade V alumina was prepared by adding 15 mL of H_2O (Fisher GC grade) to 85 g of alumina (Fisher A-540) with manual stirring. All absorption spectra were collected in spectroscopic grade toluene at room temperature. Microwave experiments were performed using a commercially available synthesizer.

Porphine (I-1). A sample of DBU (7.5 mL, 50 mmol, 10 mol equiv versus **I-2**) was added dropwise to a suspension of **I-2** (0.871 g, 5.00 mmol, 100 mM) in toluene (50 mL). $MgBr_2$ (2.76 g, 15.0 mmol, 3 mol equiv) was added in a single portion. The reaction mixture was heated at 115 °C with exposure to air for 19 h. On the basis of TLC analysis no starting material was observed. The reaction mixture was concentrated. The resulting residue was twice treated with THF (100 mL), stirred vigorously for 20 min at room temperature, and filtered through a Buchner funnel. The filtrate was concentrated (filtrate 1). The filter cake was mixed with THF (100 mL) and heated to reflux for 1 h to release residual bound **I-Mg-1**. The mixture was filtered through a second Buchner funnel to remove insoluble black material, and the filter cake was washed with THF (5 x 10 mL), affording filtrate 2. Filtrates 1 and 2 were combined, concentrated, and dissolved in diethyl ether (300 mL). The resulting solution was washed (water, brine), dried (Na_2SO_4), and concentrated. The resulting crude product was dissolved in CH_2Cl_2 (100 mL) and treated with TFA (1.93 mL). The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized by addition of TEA (3.5 mL, 25 mmol), washed (water, brine) and concentrated. Crystallization (THF/water 1:2.5) afforded a

shiny brown solid (0.220 g, 28%): ^{1}H NMR (THF-d_8) δ –3.86 to –3.93 (brs, 2H), 9.57 (s, 8H), 10.43 (s, 4H); ^{13}C NMR (THF-d_8) δ 104.8, 132.4, 132.6 (br); LD-MS obsd 309.6; FAB-MS obsd 311.1311, calcd 311.1297 [$(M + H)^+$, M = $C_{20}H_{14}N_4$]; λ_{abs} 396, 490, 564 nm.

1-Formyldipyrromethane (I-2). A sample of DMF (30 mL) was treated with $POCl_3$ (4.50 mL, 49.2 mmol) at 0 °C under argon with stirring for 10 min (Vilsmeier reagent). A solution of **I-3** (5.85 g, 40.0 mmol) in DMF (120 mL) at 0 °C under argon was treated with the freshly prepared Vilsmeier reagent (25 mL, 41 mmol), and the resulting solution was stirred for 1.5 h at 0 °C. The reaction mixture was poured into a mixture of 2 M NaOH (300 mL) and CH_2Cl_2 (200 mL) at 0 °C. The resulting blue reaction mixture was stirred for 20 min at 0 °C. The reaction mixture turned orange-brown. The organic phase was washed (saturated aqueous NH_4Cl (200 mL), water and brine), dried ($NaSO_4$), and concentrated to give a red, oily crude product. The remaining DMF was removed under high vacuum (1 h, 50 °C), resulting in a light-pink solid material. Column chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:1)] gave a yellow solid (3.198 g, 46%). The data (^{1}H NMR, mp, elemental analysis) were consistent with those obtained from samples prepared via earlier routes.[I21]

Method I.I: Synthesis of I-Mg-1 from 1-Formyldipyrromethane. A sample of **I-2** (6.97 g, 40.0 mmol) in a 1000-mL oven-dried round bottom flask was treated with anhydrous toluene (400 mL). The resulting suspension was heated to 80 °C, whereupon DBU (60 mL, 400 mmol, 10 mol equiv) was added dropwise with vigorous stirring over 10 min. The resulting solution was stirred for 5 min, during which the temperature increased from 80 °C to 98 °C and the mixture darkened. $MgBr_2$ (22.1 g, 120 mmol, 3 mol equiv) was added in one portion under vigorous stirring. The reaction flask was attached to a reflux condenser and heated at 115 °C with exposure to air. On the basis of TLC analysis (silica, CH_2Cl_2/ethyl acetate 5:1) and

absorption spectroscopy, porphyrin formation was complete in 19 h. The reaction mixture was concentrated. The resulting residue was treated with THF (2 x 200 mL). The mixture was stirred vigorously for 20 min at room temperature, and then filtered through a Buchner funnel. The filtrate was concentrated (filtrate 1). The filter cake was mixed with THF (200 mL) and heated to reflux for 1 h to release residual bound **I-Mg-1**. The mixture was filtered through a second Buchner funnel to remove insoluble black material, and the filter cake was washed with THF (10 x 10 mL), affording filtrate 2. Filtrates 1 and 2 were combined and concentrated. The resulting crude product was dissolved in diethyl ether (1 L), washed [water (200 mL) and brine (5 x 200 mL); in both cases small amounts of MeOH and Na_2SO_4 were added to facilitate phase separation] and concentrated. Crystallization (ethanol/water 1:3) afforded a purple solid (2.681 g, 40%): mp >370 °C; ^{1}H NMR (THF-d_8) δ 9.47 (s, 8H), 10.26 (s, 4H); ^{13}C NMR δ 105.8, 132.6, 150.0; LD-MS obsd 331.9; FAB-MS obsd 332.0929, calcd 332.0912 ($C_{20}H_{12}N_4Mg$); λ_{abs} 402, 536 nm.

Method I.II. Microwave-Assisted Synthesis of I-Mg-1. A sample of **I-2** (0.087 g, 0.50 mmol) was placed in a 10 mL glass tube containing a magnetic stir bar. Toluene (5 mL) and DBU (0.750 mL, 5.02 mmol) were added. The resulting mixture was stirred for 5 min and treated with $MgBr_2$ (0.276 g, 1.50 mmol). The vessel was sealed with a septum and subjected to microwave irradiation at 300 W. The protocol was as follows: (1) room temperature to 115 °C (irradiation ~30 s), (2) hold at 115 °C (irradiation for 15 min; temperature overshot to 130 °C and then stabilized after 1-2 min), (3) allow to cool to ~60 °C (~3 min), (4) heat to 130 °C (irradiation ~20-30 sec), (5) hold at 115 °C (irradiation for 15 min), and (6) allow to cool to room temperature. The reaction mixture was diluted with THF and filtered. The filter cake was washed with THF (total ~300 mL). The filtrate was concentrated. The residue was dissolved in

diethyl ether (~500 mL) and washed with water (100 mL) and brine (200 mL). The organic phase was concentrated, and the resulting purple solid was crystallized twice from ethanol/water (1:3, 20 mL) to afford purple-violet crystals (31 mg, 37%) with satisfactory characterization data (^{1}H NMR, absorption, LD-MS, FAB-MS) as those for samples prepared via different methods.

Method I.III. Synthesis of I-Mg-1 from Crude 1-Formyldipyrromethane. Vilsmeier formylation of **I-3** (5.85 g, 40.0 mmol) was performed following the above procedure. The resulting crude pink solid (7.34 g) was used without purification. Following Method I.I, the crude product was dissolved in toluene (400 mL) and treated with DBU (60 mL, 400 mmol, 10 mol equiv versus **I-3**) and $MgBr_2$ (22.1 g, 120 mmol, 3 mol equiv versus **I-3**). Crystallization afforded **I-Mg-1** as a purple solid (1.98 g, 30%). The data (^{1}H NMR, ^{13}C NMR, absorption and FAB-MS) were consistent with those obtained from samples prepared via earlier routes.

The contents of this chapter have been published.[I23]

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I.F. Supporting Information for an Efficient Synthesis of Porphine.

1. Results

Table I.S1. Reported Methods for Porphine Synthesis

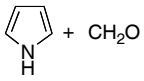
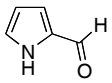
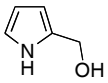
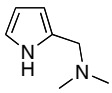
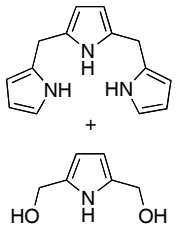
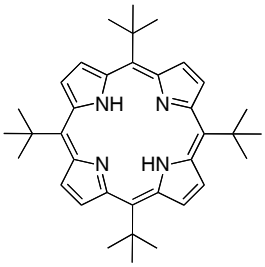
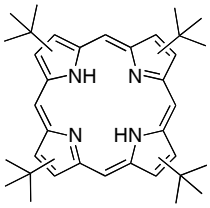
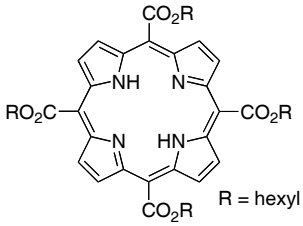
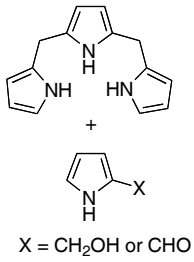
Entry	Starting material	Conditions	Isolated product (mg)	Yield (%)	Ref.
1		pyridine/MeOH sealed tube	~3	~0.02	I4
		propionic acid, pyridine 95 °C	130	0.9	I10
2		HCOOH, reflux	17	0.1	I5
3		H_2O/AcOH $Mg(OAc)_2$ (0.2%) potassium persulfate	0.3	5.33	I7
		DMF, pH = 3.7 145 °C various metal salts	Up to 200	Up to 20.3[b]	I8
		ethylbenzene 100 °C, 11.5 days	NR[a]	18.02	I9
		(1) HCl, H_2O/SDS[c] (2) DDQ	2	2	I11
		(1) 4-methyl-2-pentanone/AcOH/H_2O (2) DDQ	30	15.3	I12
4		(1) EtMgBr, chlorobenzene 180 °C (2) $Cu(OAc)_2$, AcOH	12	3.86	I6

Table I.SI. (continued)

5		(1) BF_3·MeOH (2) *p*-chloranil	NR[a]	31[c]	I13
6		H_2SO_4/1-butanol 90 °C, 15 min	86	74	I14
7		H_2SO_4 200 °C, 15 min	74	64	I14
8		H_2SO_4/H_2O 180 °C, 20-30 min	76	77	I15
9		(1) TFA (2) *p*-chloranil	28	10	I16

[a]Not reported.
[b]This yield is claimed to be non-reproducible; see reference I12.
[c]SDS – sodium dodecyl sulfate.
[d]Yield was determined by absorption spectroscopy.

2. Notes Concerning Porphine Synthesis and Purification.

(1) The order of addition of components is **I-2**, toluene, DBU, and $MgBr_2$. The self-

condensation reaction liberates water. However, it is essential that the reaction be initiated under relatively dry conditions such that the $MgBr_2$ gives a free flowing suspension rather than clumping on the walls of the flask. Accordingly, we have employed an initially dry flask, anhydrous toluene, and vigorous stirring, so that $MgBr_2$ flows freely in a finely divided solid at the outset of the reaction.

(2) It is essential that the starting materials (**I-2**, **I-3**, and **I-4**) be removed completely from the reaction mixture prior to crystallization of **I-Mg-1**. The long heating time (19 h) suffices to diminish the quantity of starting materials such that **I-Mg-1** is readily crystallized.

(3) The crystallization protocol for the purification of **I-Mg-1** is as follows. EtOH (15 mL) was added to the crude product at room temperature under vigorous stirring with a magnetic stir bar. The flask was placed in a water bath (preheated to 85 °C) and fitted with a reflux condenser. The crude mixture was heated to reflux to afford a homogenous solution. Hot EtOH (5 mL) was added to dissolve the remaining solid on the wall of the flask. Water was added dropwise via a Pasteur pipette through the reflux condenser under continued vigorous stirring. After adding 10 mL of water, the mixture was brought to reflux for 5 min. The resulting mixture was monitored for crystals. The water addition step was repeated 5 times (total amount of water = 60 mL). Once crystals were observed, the mixture was treated dropwise with EtOH (1 mL), and removed from the reflux condenser. The flask was allowed to cool to room temperature on the benchtop, sealed with a septum, and kept overnight. The resulting crystals were collected with a Buchner funnel.

3. Evaluation of the Formylation Mixture and Use.

The molar ratio of **I-2**, **I-3**, **I-4**, **I-5**, and DMF in the crude Vilsmeier formylation reaction mixture was determined by analyzing the ^1H NMR spectrum (in $CDCl_3$) of the crude product.

The signals from the *meso* protons of **I-2**, **I-3**, **I-4**, and **I-5** (δ = 4.059, 4.001, 4.128, 3.937) and the methyl protons of DMF (δ = 2.902, 2.973) were integrated. The chemical shifts and integration of each group of protons are given in Figures I.S1 and I.S2.

The relative molar amount of each component of the crude reaction mixture is given by the ^{1}H NMR spectrum. The number of moles of each component (**I-2**, **I-3**, **I-4**, **I-5**, and DMF) in the crude reaction mixture is readily calculated knowing the amount of the crude product (7.34 g) using the following equation.

7.34 g = X[24/43(174.2) + 8/43(146.19) + 5/43(202.21) + 1/43(174.2) + 5/43 (73.09)] (Equation I.S1)

where X is a scaling factor

The value of X is determined to be 0.0457. The actual amount of each component (number of mmol, g) is then calculated as shown in Table I.S2. The number of mmol of **I-2-5** sums to 40.36 mmol, in close agreement with the amount of starting dipyrromethane. The sum of the calculated number of grams of **I-2-5** and DMF sums to 7.327, which also is in close agreement with the amount of isolated crude product. The discrepancies in this calculation likely stem from trace quantities of other materials that may be in the mixture and lack of accuracy of the NMR ratios; however, such discrepancies appear to be very slight at most.

Table I.S2. Analysis of the Crude Reaction Mixture upon Vilsmeier Formylation

Compound	mol ratio	mol weight	mmol	grams
I-2	24	174.2	25.5	4.44
I-3	8	146.19	8.5	1.24
I-4	5	202.21	5.3	1.07
I-5	1	174.2	1.06	0.185
DMF	5	73.09	5.3	0.388

The isolated yield of **I-Mg-1** upon reaction was 1.98 g (5.95 mmol). The contribution of each reaction to the formation of **I-Mg-1** can be explored with the following equation. Given that **I-3** and **I-4** react with each other, in this case **I-4** is the limiting reactant.

5.95 mmol = (12.75 mmol · Y) + (5.3 mmol · Z) (Equation I.S2)

where

100·Y = the % contribution of the self-condensation of **I-2** to the yield of **I-Mg-1**.

100·Z = the % contribution of the condensation of **I-3** and **I-4** to the yield of **I-Mg-1**.

Typical values of Y and Z are listed in Table I.S3. For example, with the reaction of **I-3** + **I- 4** → **I-Mg-1** proceeding in quantitative fashion, the contribution of **I-2** → **I-Mg-1** would only be 5.1%. With no contribution by the reaction of **I-3** + **I-4** → **I-Mg-1**, a yield of 46.7% for **I-2** → **I-Mg-1** would provide for the observed yield.

Table I.S3. Estimated Yield Analysis

Y	Z
0.051	1.0
0.40	0.16
0.45	0.04
0.466	0.0

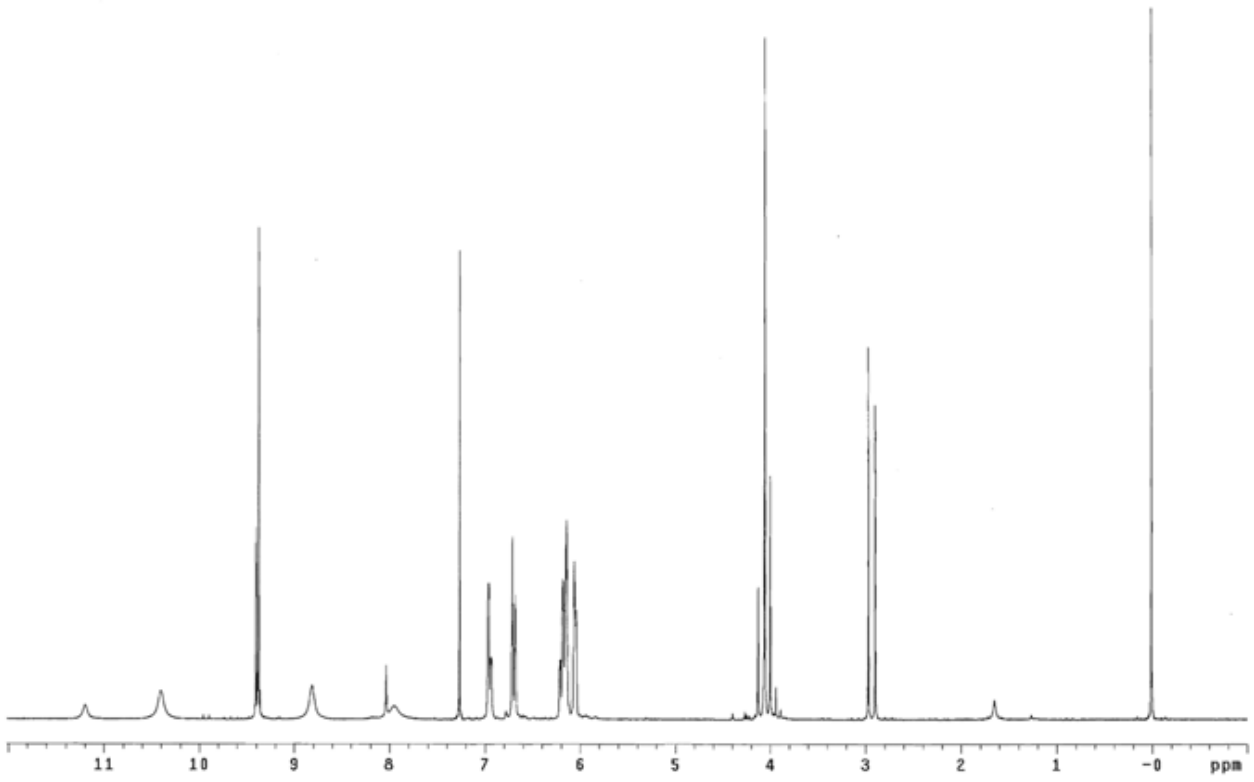


Figure I.S1. ^{1}H NMR Spectrum of the Crude Reaction Mixture upon Vilsmeier Formylation.

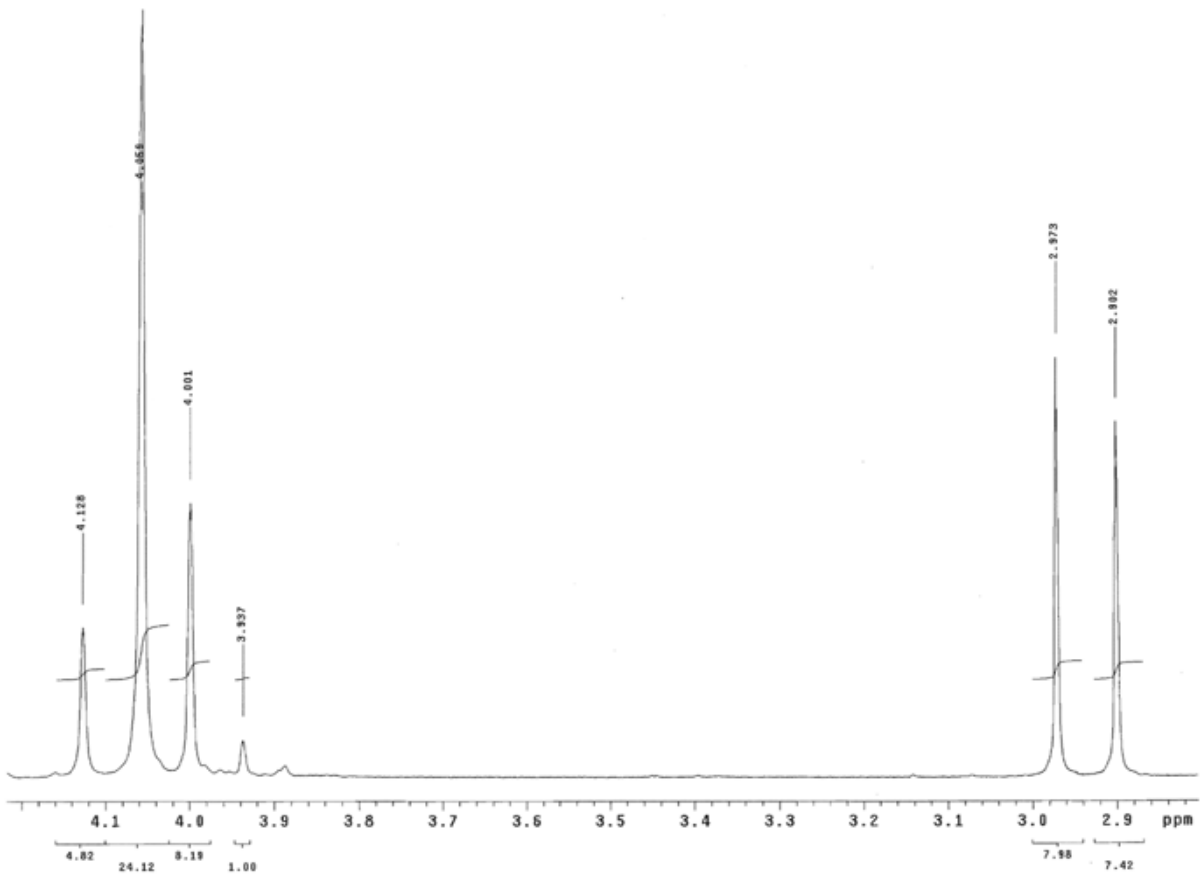


Figure I.S2. Expanded ^{1}H NMR Spectrum of the Crude Reaction Mixture.

4. Experimental Section

Noncommercial compounds. 1-Formyldipyrromethane **I-2**,[I21] dipyrromethane **I-3**,[I22] and 1,9-diformyldipyrromethane **I-4**[I18] were prepared as described in the literature. **I-Zn-1** and **I-Pd-1** were prepared previously via different methods.[I19]

Yield determination. In small-scale reactions, the porphine was purified and isolated by chromatography. Owing to the small quantity of solid porphine, gravimetry was not performed. Instead, the solid sample was dissolved in a known volume of solvent, and the yield was determined by absorption spectrometry, using the molar absorption coefficient of a metalloporphine at the Soret band of 400,000 $M^{-1}cm^{-1}$. This procedure is referred to as the "yield of isolated porphine determined by absorption spectrometry". Several survey reactions were examined by absorption spectroscopy for the yield of **I-Mg-1** without purification. In these latter cases, the reported yield is referred to as the "spectroscopic yield" as has been done previously[IS1] with use of ε_{Soret} = 400,000 $M^{-1}cm^{-1}$.

Zn(II)porphine (I-Zn-1). Following a general procedure for porphyrin formation using 1,9-diformyldipyrromethanes,[I18] a sample of **I-2** (0.871 g, 5.00 mmol) was treated with *n*-propylamine (30 mL). The resulting yellow mixture was stirred at room temperature for 1 h and then concentrated to afford a brown oil, which was used in next step without further purification: ^{1}H NMR δ 0.91 (t, *J* = 7.4 Hz, 3H), 1.60–1.65 (m, 2H), 3.43 (t, *J* = 7.0, 2H), 3.92 (s, 2H), 6.00–6.01 (m, 2H), 6.10–6.11 (m, 1H), 6.39–6.40 (m, 1H), 6.59–6.60 (m, 1H), 7.95 (s, 1H), 8.11–8.38 (brs, 1H). The resulting imine was dissolved in EtOH (250 mL) and treated with $Zn(OAc)_2$ (10.7 g, 50.0 mmol). The mixture was refluxed for 16 h, allowed to cool to room temperature, and concentrated. Column chromatography (silica, CH_2Cl_2) afforded a purple solid (0.087 g, 9%).

Further elution with ethyl acetate provided an additional fraction, which was concentrated, washed with methanol, centrifuged, and decanted. The resulting solid product was chromatographed [silica, CH_2Cl_2/ethyl acetate (5:1)] to provide an additional 0.052 g. Total yield 0.139 g (15%): ^{1}H NMR (THF-d_8) δ 9.55 (s, 8H), 10.35 (s, 4H); ^{13}C NMR δ 105.3, 132.8, 150.6; LD-MS obsd 371.8; FAB-MS obsd 372.0342, calcd 372.0353 ($C_{20}H_{12}N_4Zn$); λ_{abs} 399, 526, 560 nm.

Pd(II)porphine (I-Pd-1). Following a general procedure for porphyrin formation using 1-acyldipyrromethanes,[I17] a sample of **I-2** (0.174 g, 1.00 mmol), KOH (0.281 g, 5.00 mmol) and $Pd(CH_3CN)_2Cl_2$ (0.156 g, 0.600 mmol) was treated with EtOH (10 mL). The resulting suspension was stirred at room temperature for 1 min and then refluxed for 1 h. The reaction mixture was concentrated (but not to dryness given the very poor solubility of the title compound). The concentrated sample was passed over a silica pad and eluted with CH_2Cl_2 (~300 mL) to obtain an orange eluent, which upon concentration afforded an orange solid (0.022 g, 11%): ^{1}H NMR (THF-d_8) δ 9.52 (s, 8H), 10.48 (s, 4H); LD-MS obsd 414.3, calcd 414.01 ($C_{20}H_{12}N_4Pd$); λ_{abs} 393, 503, 535, 589 nm. ^{13}C NMR and FAB-MS spectra were not recorded due to the low solubility of **I-Pd-1**.

Small-scale Preparation of Mg(II)porphine (I-Mg-1) Employing Chromatographic Workup. A suspension of **I-2** (0.174 g, 1.00 mmol) in toluene (10 mL) was treated dropwise with DBU (1.49 mL, 10.0 mmol). The resulting solution was stirred at room temperature for 5 min and treated with a sample of $MgBr_2$ (0.552 g, 3.00 mmol). The resulting suspension was placed in oil bath (preheated to 135 °C) and stirred at 135 °C open to the air for 14 h. The reaction mixture was concentrated under vacuum, dissolved in CH_2Cl_2 and filtered through an alumina column [CH_2Cl_2/ethyl acetate (4:1) → ethyl acetate → CH_2Cl_2/MeOH (5:1)]. Fractions

containing **I-Mg-1** were collected and concentrated. The resulting oily residue was dissolved in CH_2Cl_2. The organic solution was washed with water and brine, dried (K_2CO_3), concentrated and filtered through alumina grade V (CH_2Cl_2) to afford a purple solid (0.067 g, 40%). The data (^{1}H NMR, ^{13}C NMR, absorption spectrum and FAB-MS) were consistent with those obtained from samples prepared via earlier routes.

Synthesis of I-Mg-1 via 1,9-Diformyldipyrromethane. By following the general procedure, a sample of DBU (0.750 mL, 5.02 mmol) was added dropwise to a suspension of **I-3** (0.037 g, 0.25 mmol) and **I-4** (0.051 g, 0.25 mmol) in toluene (5 mL). $MgBr_2$ (0.276 g, 1.50 mmol) was added to the reaction mixture in a single portion. The reaction mixture was heated to 115 °C with exposure to air for 36 h. Column chromatography (alumina, grade V, CH_2Cl_2) afforded **I-Mg-1** as a purple solid (18%, determined by absorption spectrometry on the basis[I19] of ε_{Soret} = 400,000 $M^{-1}cm^{-1}$). The data (^{1}H NMR, ^{13}C NMR, absorption and FAB-MS) were consistent with those obtained from samples prepared via earlier routes.

5. References.

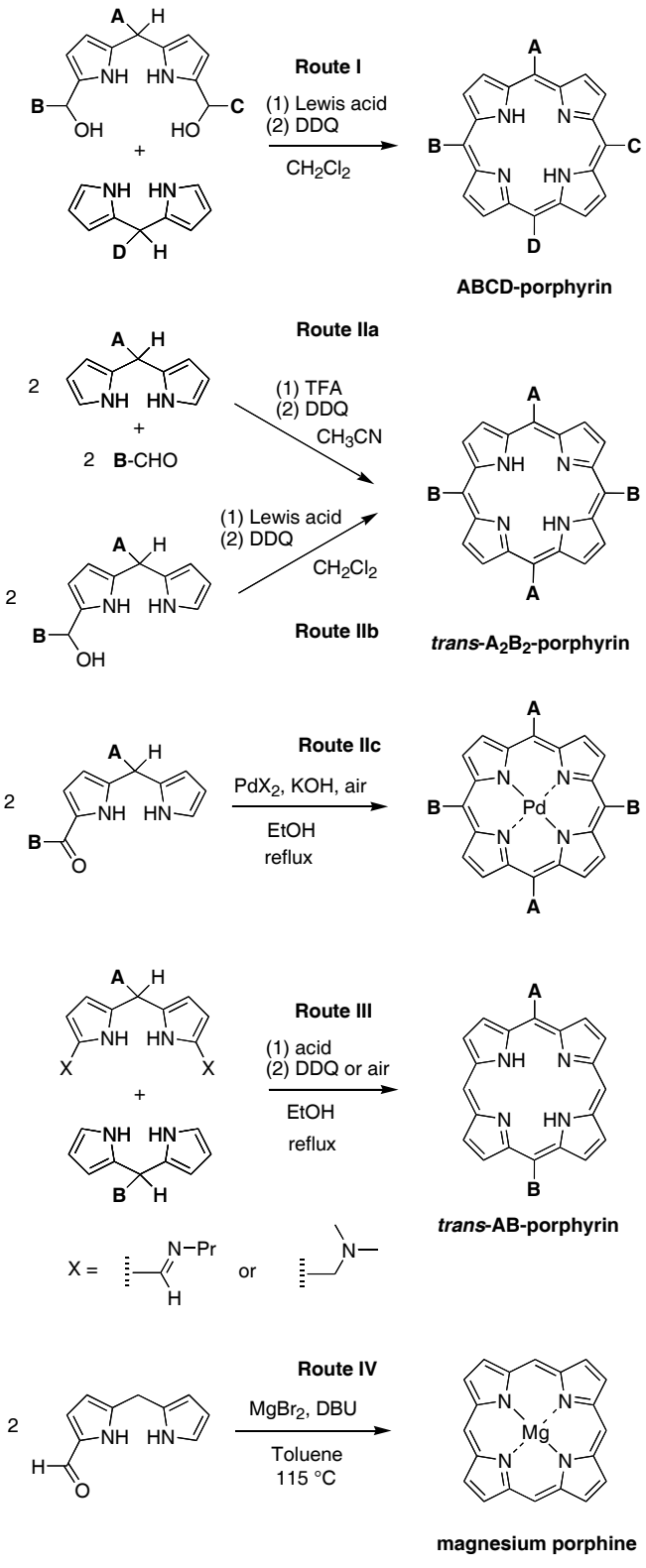
(I-S1) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827–836.

CHAPTER II

RATIONAL OR STATISTICAL ROUTES FROM 1-ACYLDIPYRROMETHANES TO MESO-SUBSTITUTIED PORPHYRINS. DISTINCT PATTERNS, MULTIPLE PYRIDYL SUBSTITUENTS, AND AMPHIPATHIC ARCHITECTURES

II.A. Introduction.

Porphyrins bearing distinct patterns of meso substituents are of interest for a broad range of applications. A number of rational synthetic routes to meso-substituted porphyrins have been developed that rely on dipyrromethane building blocks (Scheme II.1). The routes provide access to ABCD-porphyrins (route I),[II1,II2] *trans*-A_2B_2-porphyrins (route II),[II3-II5] *trans*-AB-porphyrins (route III),[II6,II7] and even porphine (route IV),[II8] which lacks meso substituents altogether. Porphyrins bearing fewer than four meso substituents also can be prepared by route II (*trans*-A_2-porphyrins) and route III (A-porphyrins). Such sparsely substituted porphyrins can be further derivatized at the open meso positions by halogenation followed by palladium-mediated coupling reactions,[II9] or by nucleophilic addition followed by oxidation.[II10]



Scheme II.1. Rational Synthetic Routes to meso-Substituted Porphyrins.

Inspection of routes I-IV might suggest unlimited access to porphyrins bearing any type and pattern of meso-substituents. Setting aside the generic limitation of modest yields that afflict almost all routes in porphyrin chemistry, at least two significant and specific limitations remain in routes I-III. (1) Certain types of substituent patterns, particularly for sparsely substituted porphyrins (e.g., *cis*-A_2, *cis*-AB, and A), remain difficult to access.[II11] Route I, which provides versatile access to porphyrins bearing four distinct substituents (i.e., ABCD-porphyrins), in principle should provide access to porphyrins with fewer numbers of substituents. However, the ABCD synthesis fails in such cases owing to the poor reactivity of primary carbinols in the dipyrromethane-dicarbinol (B, C substituents = H) upon acid-catalyzed condensation with the dipyrromethane.[II12] (2) Certain types of substituents are incorporated with difficulty in most of the routes shown in Scheme II.1, including heterocyclic groups and alkyl groups. In both cases, the conditions for acid-catalyzed condensation (routes I, IIa, IIb, III) are either incompatible with the substituents (heterocyclic groups) or provide poor reactivity (alkyl groups), despite extensive studies of acid catalysis conditions.[II2,II12-II15] The chief problem with many nitrogen heterocycles (e.g., pyridyl) lies in the complexation of the heterocycle with the acid catalyst, resulting in neutralization of the acid and often precipitation of the complex. Some improvement has been achieved by use of modified acid catalysts but the conditions lack generality.[II16-II19] The chief problem with alkyl groups stems from scrambling (i.e., fragmentation and undesired recombination) to give a mixture of porphyrins.[II1,II12,II20]

Heterocyclic and alkyl groups are of interest for biomedical applications and for studies in supramolecular chemistry. In this regard, porphyrins bearing pyridyl groups[II21] have been used for DNA intercalation,[II22-II26] DNA cleavage,[II26,II27] DNA labelling,[II28] telomerase[II29] or acetylcholinesterase[II30] inhibition, prion binding,[II31] superoxide dismutase mimicry,[II32]

photodynamic inactivation,[II33,II34] radiosensitization,[II35] binding to nanoparticles,[II36] and assembly into micelles,[II37] bilayer lipid membranes,[II38] molecular squares,[II39] arrays,[II40] oligomers,[II41,II42] and light-harvesting architectures.[II43] Several examples have been reported where porphyrins bear both pyridyl and alkyl groups.[II23,II24,II44-II52] Most of the porphyrins bearing fewer than four identical pyridyl groups have been formed by statistical reactions, which give multiple products.

The limitations posed by sparsely substituted porphyrin architectures and heterocyclic or alkyl groups often are intertwined: the target porphyrin often contains one or two heterocyclic or alkyl groups as required to achieve the desired polarity and functionality, while sparse substitution is desired to maintain a compact size and low molecular weight. To broaden access to sparsely substituted porphyrins and porphyrins bearing heterocyclic or alkyl groups requires consideration of new routes to porphyrins. Several years ago we found serendipitously that two 1-acyldipyrromethane molecules would condense under basic metal-mediated conditions to give the corresponding *trans*-A_2B_2-porphyrin (route IIc, Scheme II.1).[II5] The conditions employed a palladium reagent and KOH in refluxing ethanol, and afforded the palladium porphyrin. The 1-acyldipyrromethane condensation provided a more concise route to the *trans*-A_2B_2-porphyrin than that of route IIb, which employs the condensation of dipyrromethane-1-carbinol molecules. We were attracted to basic conditions because we felt such conditions would circumvent the twin problems of acidolysis leading to scrambling that occurs with alkyl and other types of groups, and acid-neutralization/complexation that occurs with heterocyclic substituents. However, the formation of the palladium porphyrin represented a limitation in scope given that removal of palladium requires treatment of the porphyrin with strong acid.

To exploit the approach illustrated in route IIc but overcome the fundamental limitations, we embarked on a program to identify conditions that (i) are non-acidic, (ii) use a readily

removable and inexpensive metal, and (iii) provide broad scope. We ultimately found that a non-coordinating solvent and base (e.g., toluene and DBU) with a magnesium halide ($MgBr_2$) support the condensation to give the corresponding magnesium(II) porphyrins. We have already reported the use of these conditions in the synthesis of magnesium porphine (route IV),[II8] and in a quite different route wherein a 1-acylbilane undergoes intramolecular cyclization to give the magnesium porphyrin.[II53] The use of $MgBr_2$ in toluene containing DBU for porphyrin formation has some commonality with conditions used for the insertion of magnesium into free base porphyrins.[II54]

In this chapter we report the development of the basic, magnesium-mediated conditions for condensation of 1-acyldipyrromethanes and the application of these conditions to give diverse meso-substituted porphyrins. The chapter is organized as follows. Part II.I describes the synthesis of 26 1-acyldipyrromethanes with emphasis on a broad survey of functional groups as well as a focus on alkyl and pyridyl substituents. Part II.II summarizes the key conditions for the 1-acyldipyrromethane condensation; extensive studies are contained in the Supporting Information. Part II.III reports the application of the conditions to the synthesis of *trans*-A_2B_2-porphyrins or *trans*-A_2-porphyrins (numbered **II**.**1**). Part II.IV describes the use of statistical reactions wherein two non-identical 1-acyldipyrromethanes undergo condensation, which has been used to gain access to sparsely substituted porphyrins of the type *cis*-A_2, *cis*-AB, and A (numbered **II.2**), and *cis*-ABC_2-porphyrins containing two pentyl groups and two non-identical pyridyl groups (numbered **II.3**). Altogether 26 target porphyrins have been prepared via these routes. Taken together, the approaches described herein support the synthesis of diverse porphyrins bearing substituents (alkyl, aryl, heterocyclic) in a variety of patterns.

II.B. Results and Discussion.

I. Synthesis of 1-Acyldipyrromethanes. 1-Acyldipyrromethanes are typically prepared by formation of a dipyrromethane followed by acylation. In this study, we examined a set of 1-acyldipyrromethanes possessing diverse groups (electron-rich, electron-deficient, heteroaryl, alkyl, bulky, H) at the meso (5-) or 1-positions. Multigram quantities of dipyrromethanes are available by condensation of an aldehyde with excess pyrrole in the presence of acid.[II55] The 14 dipyrromethanes examined herein are shown in Chart II.1. Dipyrromethanes **II-4a**,[II53] **II-4b**,[II2] **II-4c**,[II55] **II-4d**,[II56] **II-4e**,[II48] **II-4f**,[II55] **II-4g**,[II55] **II-4h**,[II57] **II-4i**,[II58] **II-4j**,[II16] **II-4k**,[II16] **II-4l**,[II16] and **II-4n**[II59] are known; however, a more recent procedure (using $InCl_3$)[II55] was used to prepare dipyrromethanes **II-4d** and **II-4e**. The new compound **II-4m** was prepared in 89% yield by condensation of 1-methylsulfonylpyrrole-2-carboxaldehyde[II60] with pyrrole in the presence of $InCl_3$. All of the dipyrromethanes shown in Chart II.1 with the exceptions of **II-4c** and **II-4n** were acylated; the latter were employed in exploration of alternative routes to porphyrins (see the Supporting Information).

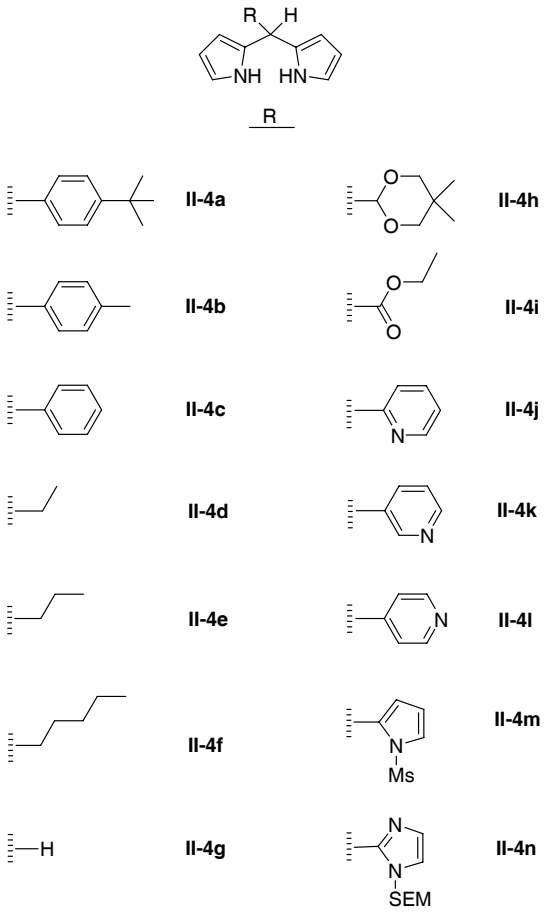


Chart II.1. Examined Dipyrromethanes.

Acylation can be carried out by treatment at –78 °C of the dipyrromethane-Grignard reagent with an *S*-2-pyridyl thioate (Mukaiyama reagent) or acid chloride.[II61] The Mukaiyama reagents (**II-5a-k**) required for the target 1-acyldipyrromethanes were prepared by reaction of the corresponding acid chloride with 2-mercaptopyridine. Mukaiyama reagents **II-5a**,[II53] **II-5b**,[II61] **II-5h**,[II61] and **II-5i**[II61] are known; **II-5c**,[II61] **II-5d**,[II62] **II-5g**,[II12] and **II-5k**[II63] also are known and were prepared according to a new procedure. Formylation can be achieved by treatment of the dipyrromethane-Grignard reagent with phenyl formate,[II64] or by use of the Vilsmeier reagent. The Mukaiyama reagents and other acylating species [acid chloride **II-5l**, phenyl formate (**II-5m**), Vilsmeier reagent (**II-5n**)] are shown in Table II.1.

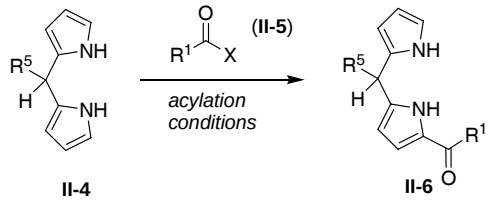


Table II.1. Synthesis of 1-Acyldipyrromethanes[a]

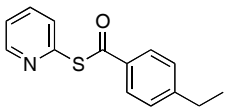
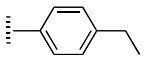
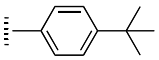
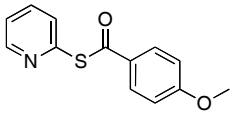
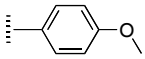
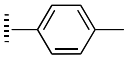
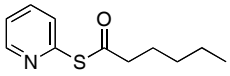
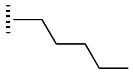
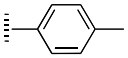
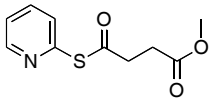
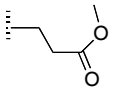
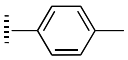
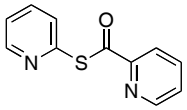
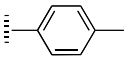
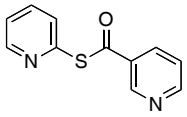
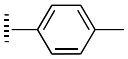
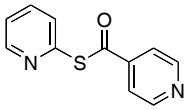
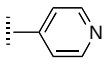
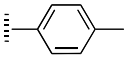
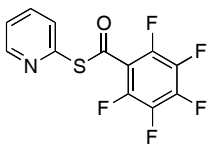
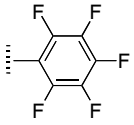
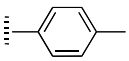
Entry	**II-4**	Acylating reagent		1-Acyldipyrromethane			
		Structure	Cmpd	R^1	R^5	Cmpd	Yield (%)
1	**II-4a**		**II-5a**			**II-6a**	66[b]
2[c]	**II-4b**		**II-5b**			**II-6b**	37
3[c]	**II-4b**		**II-5c**			**II-6c**	22
4	**II-4b**		**II-5d**			**II-6d**	20
5	**II-4b**		**II-5e**			**II-6e**	76
6	**II-4b**		**II-5f**			**II-6f**	61
7	**II-4b**		**II-5g**			**II-6g**	75[d]
8	**II-4b**		**II-5h**			**II-6h**	79

Table II.1. (continued)

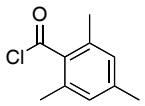
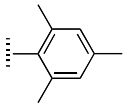
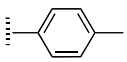
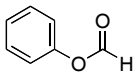
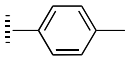
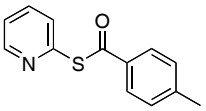
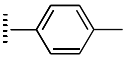
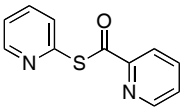
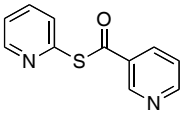
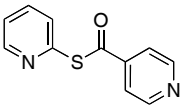
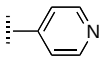
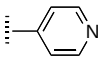
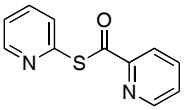
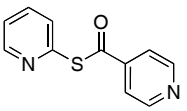
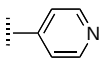
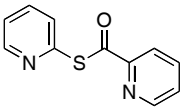
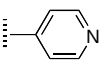
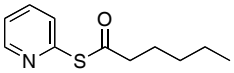
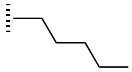
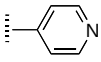
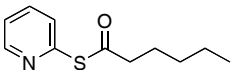
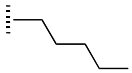
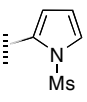
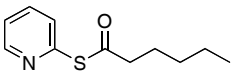
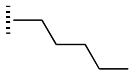
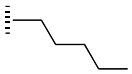
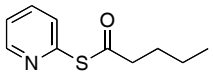
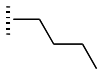
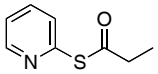
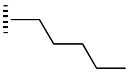
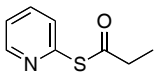
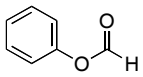
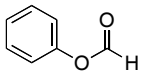
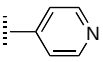
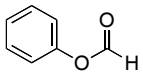
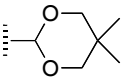
9	**II-4b**		**II-5l**			**II-6i**	27
10	**II-4b**		**II-5m**			**II-6j**	41
11	**II-4g**		**II-5i**			**II-6j′**	62[e]
12	**II-4j**		**II-5e**			**II-6k**	33
13	**II-4k**		**II-5f**			**II-6l**	34
14	**II-4l**		**II-5g**			**II-6m**	60
15	**II-4k**		**II-5e**			**II-6n**	47
16	**II-4k**		**II-5g**			**II-6o**	29
17	**II-4l**		**II-5e**			**II-6p**	51
18	**II-4l**		**II-5c**			**II-6q**	---[f]
19	**II-4m**		**II-5c**			---	---[g]
20	**II-4f**		**II-5c**			**II-6r**	63[h]

Table II.1. (continued)

21	**II-4e**		**II-5j**			**II-6s**	46
22	**II-4f**		**II-5k**			**II-6t**	67
23	**II-4d**		**II-5k**			**II-6u**	81
24	**II-4k**		**II-5m**			**II-6v**	37
25	**II-4l**		**II-5m**			**II-6w**	49
26	**II-4h**		**II-5m**			**II-6x**	65[i]
27	**II-4i**	Vilsmeier reagent	**II-5n**			**II-6y**	58
28	**II-4g**	Vilsmeier reagent	**II-5n**			**II-6z**	46[j]

[a]The acylation reactions were carried out with 5–15 mmol of reactants unless noted otherwise in the experimental section. [b]Reference II53. [c]Yield is given after two steps (boron complexation and decomplexation). [d]Reference II12. [e]Reference II65. [f]Could not be purified. [g]Multiple products on the basis of TLC and ^{1}H NMR analyses. [h]Reference II65. [i]Reference II64 [j]Reference II8.

Five major sets of 1-acyldipyrromethanes were prepared following the benchmark compound (**II-6a**),[II53] which contained *p*-*tert*-butylphenyl at the 5-position and *p*-ethylphenyl at the 1-acyl site. The first set (**II-6b-j**) contained a *p*-tolyl group at the 5-position and diverse groups at the 1-acyl moiety. The second set (**II-6k-p**) contained pyridyl groups at both positions. The third set (**II-6r-u**) contained alkyl groups at both positions. The fourth set (**II-6j**, **II-6v-z**) contained the 1-formyl moiety and diverse 5-substituents. A final type of 1-acyldipyrromethane that we sought contained both alkyl and heterocyclic groups (**II-6q**), but this compound was not

obtained in pure form. Of these 26 1-acyldipyrromethanes (Table II.1), a handful are known compounds (**II6a**,[II53] **II-6g**,[II12] **II-6j′**,[II65] **II-6r**[II65]).

The general procedures for preparing 1-acyldipyrromethanes worked well for most cases, though **II-6d**, **II-6f**, and **II-6k** required additional purification, and the 5-(pyridyl)-containing 1-acyldipyrromethanes gave slightly lower yields. Attempted acylation of 5-(2-pyridyl)dipyrromethane **II-4j** using the *p*-pyridyl-containing Mukaiyama reagent **II-5f** failed (starting material was recovered), whereas acylation of **II-4j** with *o*-pyridyl-containing Mukaiyama reagent **II-5e** provided the 1-acyldipyrromethane **II-6k** in 33% yield. Synthesis of a 1-mesitoyldipyrromethane (**II-6i**) was done by utilizing mesitoyl chloride (entry 9). In several cases (**II-6b** and **II-6c**) a boron complexation strategy[II65] was employed to facilitate purification of the 1-acyldipyrromethane (see Supporting Information). Formylation of 5-(2-pyridyl)dipyrromethane **II-4j** via the Grignard conditions afforded recovered starting material; Vilsmeier conditions ($POCl_3$/DMF) afforded only a trace amount of product. Vilsmeier formylation of dipyrromethane **II-4i** afforded **II-6y** in 58% yield. We note that a number of the 1-acyldipyrromethanes are elaborate compounds containing three or four distinct nitrogenous heterocycles.

II. Conditions for the 1-Acyldipyrromethane Condensation. The development of the conditions for use in the condensation of a 1-acyldipyrromethane entailed an extensive exploration of metal reagents, solvents, bases, concentrations and molar ratios, and reaction duration. The standard procedure that emerged from this study entails reaction of a 1-acyldipyrromethane (100 mM) in the presence of $MgBr_2$ (3.0 mol equiv) and DBU (10.0 mol equiv) in toluene (115 °C) with stirring exposed to air for 12-14 h to give the target *trans*-A_2B_2-porphyrin. Such conditions were tested with substrates that are especially prone to acidolytic

scrambling (e.g., **II-6a**, which bears *p*-*tert*-butylphenyl and *p*-ethylphenyl groups), and no scrambling was detected. The results from this survey are listed in the Supporting Information. Three pertinent points deserve emphasis:

(1) The yield of porphyrin **II-Mg-1a** upon reaction of **II-6a** was 47%, 69% and 65% at 50 mM, 100 mM and 200 mM, respectively, but only 7% in the absence of toluene. The good yield at 200 mM augurs well for scale-up applications.

(2) Among a number of metals examined in place of $MgBr_2$, only $Pd(CH_3CN)_2Cl_2$ afforded a significant amount of the corresponding metalloporphyrin (37% yield).

(3) The rationale for the exposure of the reaction mixture to air stems from the fact that the conversion of two 1-acyldipyrromethane molecules to a molecule of porphyrin requires an oxidant. The balanced reaction is shown in Equation II.1.

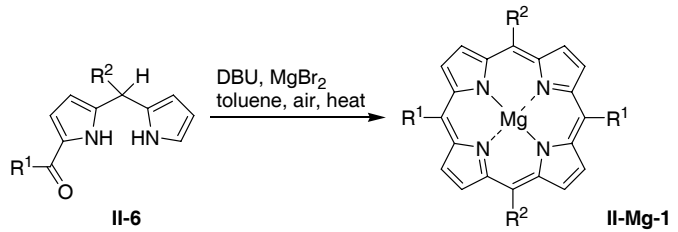
II-6a + **II-6a** + $MgBr_2$ → **II-Mg-1a** + 2HBr + $2H_2O$ + $2e^-$ + $2H^+$ Equation II.1

Oxygen present in air would seem a likely source for the oxidizing equivalents, although prior studies of related reactions, which were quite limited in methods and in range of substrates examined, were not conclusive.[II5,II8,II53]

III. Rational Synthesis of *trans*-A_2B_2-Porphyrins. (1) Conventional Heating. The standard conditions were applied to a wide variety of 1-acyldipyrromethanes to prepare the corresponding *trans*-A_2B_2-porphyrins. Each reaction was carried out with 100 mM 1-acyldipyrromethane and a scale ranging from 0.2 to 3.8 mmol. In each successful porphyrin synthesis, TLC analysis (silica, CH_2Cl_2) of the crude reaction mixture revealed the presence of a trace amount of free base porphyrin (close to the solvent front), the desired magnesium porphyrin, and a trace amount of unreacted 1-acyldipyrromethane. The results are shown in

Table II.2. The reaction of 1-acyldipyrromethane **II-6a**, which was used in all of the studies to develop conditions, gave the highest yield of porphyrin (**II-Mg-1a** in 69% yield: entry 1, Table II.2). Most members of each set of 1-acyldipyrromethanes shown in Table II.1 were examined for conversion to the corresponding *trans*-A_2B_2-porphyrin. The set of 5-*p*-tolyl-1-acyldipyrromethanes (**II-6b-j**) enabled identification of the effects of a particular substituent. In general, 1-acyldipyrromethanes that possess electron-releasing aryl substituents resulted in porphyrins (**II-Mg-1a**, **II-Mg-1b**, **II-Mg-1c**) in relatively high yields. 1-Acyldipyrromethanes bearing a pyridyl substituent (*o*-, *m*-, *p*-) afforded dipyridyl porphyrins **II-Mg-1e**, **II-Mg-1f**, and **II-Mg-1g** in 6%, 43% and 25% yield, respectively, upon use of larger excesses of $MgBr_2$ and DBU. **II-Mg-1f** and **II-Mg-1g** exhibited poor solubility, yet were purified by simply washing the crude reaction mixture with methanol. 1-Formyldipyrromethane **II-6j** gave the corresponding *trans*-A_2-porphyrin **II-Mg-1j** in 39% yield (90% purity owing to the presence of the chlorin analogue).

A sizable number of attempted reactions did not give the corresponding porphyrin. One surprise was the failure of a 1-acyldipyrromethane lacking a meso-substituent (**II-6j′**) given the excellent results with the transposed analogue **II-6j**. The presence of a bulky group (pentafluorophenyl, mesityl) at the 1-position resulted in little (**II-Mg-1h**) or no porphyrin (**II-Mg-1i**). The 1-acyldipyrromethanes bearing two pyridyl groups or two alkyl groups also afforded little or no porphyrin. Further failures include 1-formyldipyrromethanes bearing a pyridyl, acetal, or ester group at the 5-position. These studies indicated only modest scope for macrocycle formation under conventional heating, and prompted a parallel set of studies of the reactions carried out with microwave heating.



II-6 II-Mg-1

Table II.2. *trans*-A_2B_2-Magnesium Porphyrin Synthesis Directly from 1-Acyldipyrromethanes[a]

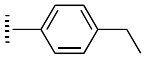
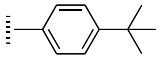
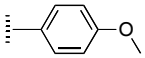
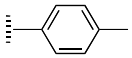
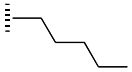
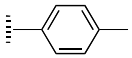
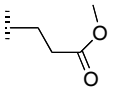
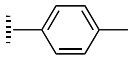
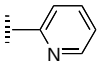
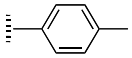
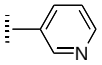
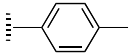
Entry	1-Acyldipyrromethane			Porphyrin Synthesis			Porphyrin type
	Cmpd	R^1 (acyl)	R^2 (meso)	Conventional Heating		Microwave Irradiation	
				Cmpd	Yield (%)	Yield (%)	
1	**II-6a**			**II-Mg-1a**	69	NA[b]	*trans*-A_2B_2
2	**II-6b**			**II-Mg-1b**	46	NA	*trans*-A_2B_2
3	**II-6c**			**II-Mg-1c**	31	NA	*trans*-A_2B_2
4	**II-6d**			**II-Mg-1d**	Trace	NA	*trans*-A_2B_2
5	**II-6e**			**II-Mg-1e**	6[c]	Trace	*trans*-A_2B_2
6	**II-6f**			**II-Mg-1f**	43[d]	NA	*trans*-A_2B_2

Table II.2. (continued)

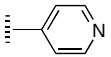
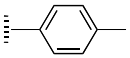
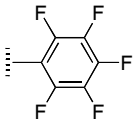
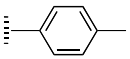
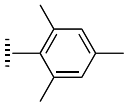
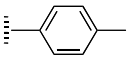
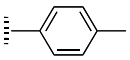
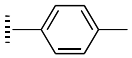
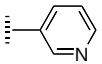
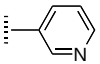
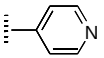
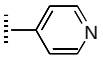
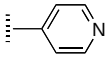
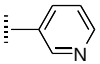
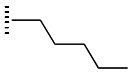
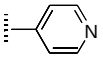
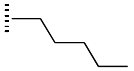
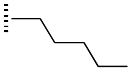
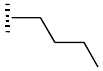
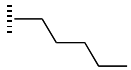
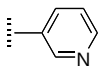
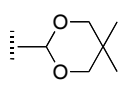
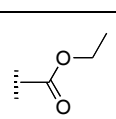
7	**II-6g**			**II-Mg-1g**	25[e]	NA	*trans*-A_2B_2
8	**II-6h**			**II-Mg-1h**	2[f]	1	*trans*-A_2B_2
9	**II-6i**			**II-Mg-1i**	0	0	*trans*-A_2B_2
10	**II-6j**			**II-Mg-1j**	39	19[g]	*trans*-A_2
11	**II-6j′**			**II-Mg-1j**	Trace	0	*trans*-A_2
12	**II-6l**			**II-Mg-1l**	Trace	61	A_4
13	**II-6m**			**II-Mg-1m**	Trace	47	A_4
14	**II-6o**			**II-Mg-1o**	3[f]	21	*trans*-A_2B_2
15	**II-6q**			**II-Mg-1q**	Trace	NA	*trans*-A_2B_2
16	**II-6r**			**II-Mg-1r**	NA	0	A_4
17	**II-6s**			**II-Mg-1s**	NA	0	*trans*-A_2B_2

Table II.2. (continued)

18	**II-6t**			**II-Mg-1t**	0	0	*trans*-A_2B_2
19	**II-6u**			**II-Mg-1u**	NA	0	A_4
20	**II-6v**			**II-Mg-1v**	Trace	4	*trans*-A_2
21	**II-6x**			**II-Mg-1x**	Trace	NA	*trans*-A_2
22	**II-6y**			**II-1y**[g]	0	13	*trans*-A_2
23	**II-6z**			**II-Mg-porphine**	40[h]	37[h]	--

[a]The reactions were carried out with 0.1–2.3 mmol of 1-acyldipyrromethane unless noted otherwise. [b]NA = Not attempted**.** [c]9 equiv of $MgBr_2$, 35 equiv of DBU. [d]3 equiv of $MgBr_2$, 20 equiv of DBU. [e]6 equiv of $MgBr_2$, 10 equiv of DBU. [f]The yield was determined by absorption spectrometry. [g]The free base porphyrin obtained by demetalation. [h]Reference II8.

(2) Microwave Heating. Microwave-assisted organic reactions have become popular for the synthesis of numerous classes of compounds.[II66] We previously found that porphine can be synthesized efficiently under microwave irradition.[II8] Initially, we investigated microwave-assisted reactions under the standard conditions (toluene, 100 mM of the 1-acyldipyrromethane, 3 mol equiv of $MgBr_2$ and 10 mol equiv of DBU) for the trials shown in Table II.2 where poor yields were obtained with conventional heating. The microwave reactions were carried out for ~2 h versus 12-14 h for the conventional reactions. In some cases, no improvement was observed (entries 5, 8-10, and 16-18). On the other hand, a substantial increase in yield was observed in several cases, including *trans*-A_2-porphyrin **II-1y** (A = ethoxycarbonyl) and three porphyrins each bearing four pyridyl groups. The latter include two A_4-porphyrins (tetra-*p*-pyridylporphyrin **II-Mg-1m** and tetra-*m*-pyridylporphyrin **II-Mg-1l**) and a *trans*-A_2B_2-porphyrin bearing two *p*-pyridyl and two *m*-pyridyl groups (**II-Mg-1o**). The porphyrins were obtained in 21-61% yields (Table II.2, entries 12-14). These results indicate the utility of this approach for the synthesis of porphyrins bearing four heterocyclic substituents. Although demonstrated in part by the preparation of A_4-porphyrins, these promising results encouraged further study of the scope of microwave-assisted porphyrin syntheses (vide infra).

IV. Statistical Synthesis of Meso-Substituted Porphyrins from 1-Acyldipyrromethanes. 1. Approach. A time-honored statistical synthesis in porphyrin chemistry entails reaction of two aldehydes (A, B) with pyrrole, affording a mixture of six porphyrins (A_4, A_3B, *trans*-A_2B_2, *cis*-A_2B_2, AB_3, B_4). In such mixtures, the separation of the A_3B-porphyrin is often quite straightforward for those cases where the substituents in aldehydes A and B have different polarity.[II67] However, the separation of *cis*-A_2B_2- and *trans*-A_2B_2-porphyrins is often exceptionally difficult. By contrast, the condensation of two non-identical 1-

acyldipyrromethanes would at most yield only three porphyrins, which presents a more tractable separation problem. Two sets of condensations were examined under microwave irradiation with a particular focus on those substituents that are difficult to introduce via other procedures, particularly heterocyclic moieties, alkyl chains or no substituents.

2. Route to *Cis*-AB-, *Cis*-A_2-, or A-Porphyrins. Reaction of 1-formyldipyrromethane and an AB-substituted 1-acyldipyrromethane is expected to afford a mixture composed of porphine, the *trans*-A_2B_2-porphyrin, and the hybrid *cis*-AB-porphyrin. Note that no *trans*-AB-porphyrin can form, which would complicate separation of the target *cis*-AB-porphyrin. When A = B, the hybrid porphyrin contains the *cis*-A_2 substitution pattern. Access to each of these architectures was explored with 1-acyldipyrromethanes that contained two heterocycles (**II-6k**, **II-6l**, **II-6m**, **II-6n**, **II-6o**, and **II-6p**). Each 1-acyldipyrromethane was condensed with 1-formyldipyrromethane (**II-6z**). As one example, the reaction of 1-acyldipyrromethane **II-6m** (bearing two *p*-pyridyl groups) with 1-formyldipyrromethane followed by treatment with TFA to demetalate the magnesium chelates afforded the three free base porphyrins: *meso*-tetrapyridylporphyrin (**II-1m**, 14%), porphine (16%), and the hybrid *cis*-A_2-porphyrin bearing the two pyridyl units (**II-2c**, 27%). TLC analysis showed the three free base porphyrins to be widely separated. Column chromatographic separation afforded the three porphyrins, which upon washing with hexanes and methanol yielded the pure porphyrin as a purple powder. In this manner, the target *cis*-AB- and *cis*-A_2-porphyrins were obtained in 9-28% yield (Table II.3, entries 1-5), each of which contains two heterocyclic substituents.

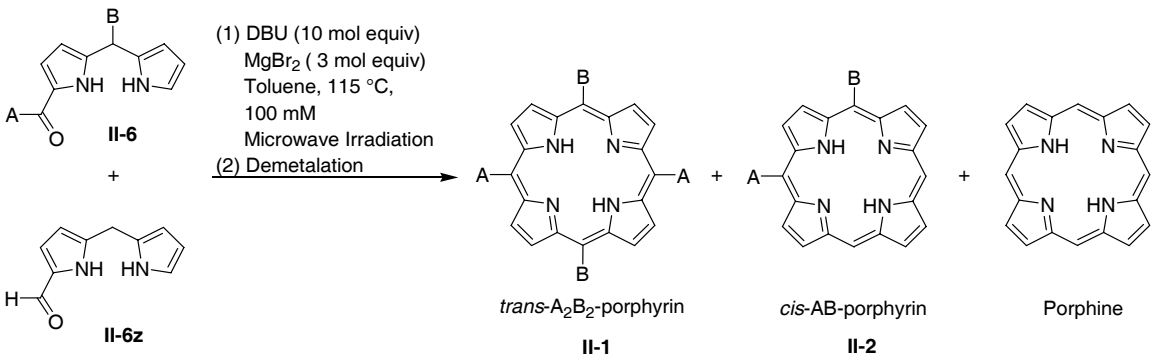


Table II.3. Statistical *cis*-AB-Porphyrin Synthesis from Two Non-Identical 1-Acyldipyrromethanes[a]

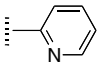
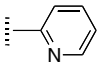
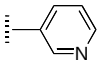
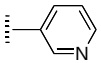
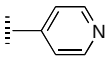
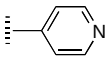
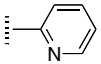
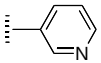
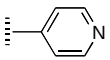
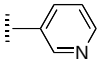
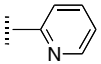
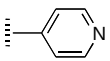
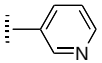
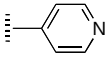
Entry	1-Acyldipyrromethane			Porphyrin **II-2**	Yield (%)	Porphyrin **II-1**	Yield (%)	Porphyrin	Yield (%)
	Cmpd	A (acyl)	B (meso)						
1	**II-6k**			**II-2a**	13	**II-1k**	12	Porphine	15
2	**II-6l**			**II-2b**	28	**II-1l**	3	Porphine	26
3[b]	**II-6m**			**II-2c**	27	**II-1m**	14	Porphine	16
4	**II-6n**			**II-2d**	9	**II-1n**	11	Porphine	7
5[c]	**II-6o**			**II-2e**	14	NI	-	NI	-
6	**II-6p**			**II-2f**	0	**II-1p**	11	Porphine	28

Table II.3 (continued)

7	**II-6v**			**II-2g**	32	**II-1v**	Trace	Porphine	6
8	**II-6w**			**II-2h**	21	**II-1w**	11	Porphine	trace

[a]All reactions were carried out under microwave irradiation with 0.2 mmol of 1-acyldipyrromethane unless noted otherwise. The porphyrin was purified by column chromatography followed by washing with hexanes. [b]0.1 mmol of 1-acyldipyrromethane was used. [c]NI: Not isolated.

When the 1-acyldipyrromethane contains only one substituent (A) and is condensed with 1-formyldipyrromethane, the expected porphyrins are the *trans*-A_2-porphyrin, porphine, and the hybrid A-porphyrin, which contains a single meso substituent. Access to such A-porphyrins was explored with 1-formyldipyrromethanes that contained one heterocycle at the 5-position (**II-6v**, **II-6w**). In this manner, two A-porphyrins were obtained (Table II.3, entries 7 and 8; 32 and 21% yields), each of which contains a single pyridyl substituent. It is noteworthy that relatively few porphyrins have been prepared that contain one or two pyridyl groups and no other substituents.[II18,II68-II70]

3. Route to *Cis*-ABC_2- or *Cis*-A_2B_2-Porphyrins. Amphipathic porphyrins are of interest for organization in monolayers and in lipid bilayers.[II71] We sought to exploit the present methodology to prepare *cis*-A_2B_2-porphyrins bearing two pyridyl groups and two pentyl groups. To our knowledge, only one example has been reported of a *cis*-A_2B_2-porphyrin bearing pyridyl/alkyl groups at the meso positions.[II44] Thus, a series of reactions was carried out where the 1-acyldipyrromethane bearing two pentyl substituents (**II-6r**) was condensed with a 1-acyldipyrromethane bearing two pyridyl substituents. The resulting reactions potentially afford *meso*-tetrapentylporphyrin, the *meso*-tetrapyridylporphyrin (A_4 or *trans*-A_2B_2), and the hybrid *cis*-A_2B_2- or *cis*-ABC_2-porphyrin. The results are summarized in Table II.4. In each case examined, the hybrid porphyrin was obtained in yields of 7 to 26%, the tetrapyridylporphyrin was obtained in yields of 5 to 23%, and no *meso*-tetrapentylporphyrin was isolated; the two porphyrins that were isolated were widely separated upon chromatography (see the Supporting Information). The failure to obtain the tetraalkylporphyrin was not unexpected given that the condensation alone of the dipentyl 1-acyldipyrromethane **II-6r** also fails altogether (Table II.2, entry 20). In this regard, the successful synthesis of the hybrid porphyrin is remarkable.

In summary, this study shows that the statistical condensation of 1-acyldipyrromethanes under microwave irradiation can provide entrée into a class of porphyrins having limited access with the current procedures (*cis*-ABC_2, *cis*-A_2B_2, *cis*-AB, and A). The *cis*-substituted porphyrins are obtained without accompaniment by the *trans* isomer, thereby facilitating purification.

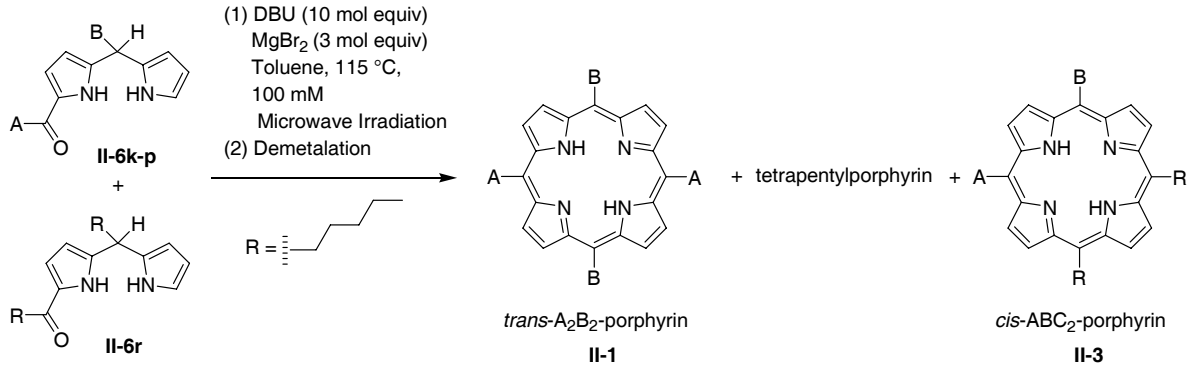
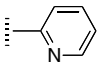
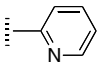
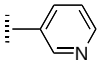
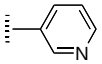
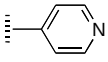
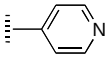
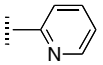
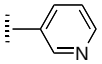
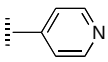
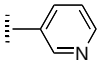
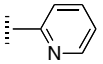
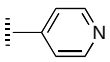
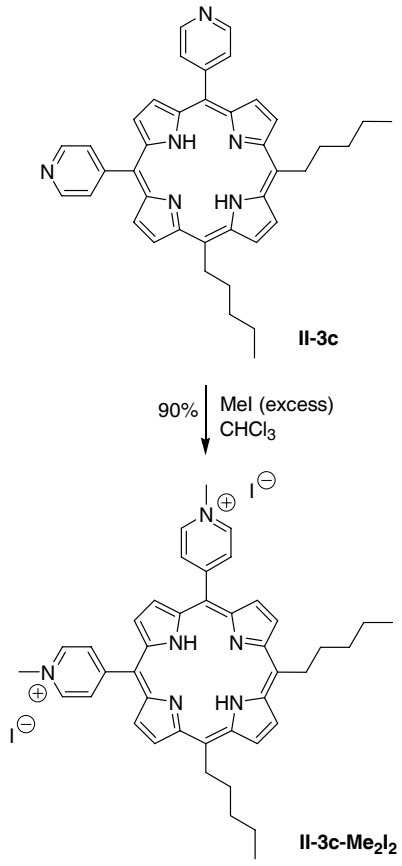


Table II.4. Statistical *Cis*-ABC_2-Porphyrin Synthesis from Two Non-Identical 1-Acyldipyrromethanes[a]

Entry	AB-1-Acyldipyrromethane			Porphyrin **II-3**	Yield (%)	Porphyrin **II-1**	Yield (%)
	Cmpd	A (acyl)	B (meso)				
1	**II-6k**			**II-3a**[b]	7	**II-1k**[c]	10
2	**II-6l**			**II-3b**[b]	17	**II-1l**[c]	23
3	**II-6m**			**II-3c**[b]	26	**II-1m**[c]	12
4	**II-6n**			**II-3d**	12	**II-1n**	14
5	**II-6o**			**II-3e**	16	**II-1o**	5
6	**II-6p**			**II-3f**	22	**II-1p**	15

[a]All reactions were carried out under microwave irradiation with 0.2 mmol of each 1-acyldipyrromethane unless noted otherwise. Each porphyrin was purified by column chromatography followed by washing with hexanes. [b]*Cis*-A_2B_2-porphyrin. [c]A_4-porphyrin.

4. Amphipathic Porphyrin. To accentuate the amphipathic character of the dipyridyl/dipentylporphyrins, one such porphyrin (**II-3c**) was treated with excess methyl iodide to form the quaternized product containing methyl pyridinium units (Scheme II.2). The bis-quaternized porphyrin (**II-3c-Me_2I_2**) was isolated in 90% yield simply by washing with hexanes. Porphyrin **II-3c-Me_2I_2** contains two pentyl groups in a *cis*-configuration and two methyl pyridinium groups in a *cis*-configuration, which provides an attractive amphipathic architecture for examination in bilayer lipid membranes. The synthetic route employed here is more versatile than a prior route to *cis*-A_2B_2-porphyrins that were designed for studies of bilayer lipid membranes.[II71]



Scheme II.2. Amphipathic Porphyrin.

II.C. Outlook

The non-acidic, magnesium-mediated conditions described here provide access to diverse meso-substituted porphyrins via the condensation of two 1-acyldipyrromethane molecules. The non-acidic nature of the conditions sidesteps acidolytic processes and enables the use of 1-acyldipyrromethanes that bear pyridyl or alkyl substituents. Pyridyl substituents have been some of the most sought after substituents yet also the most challenging owing to their facile acid-complexation behavior. The present method thus complements the methods shown in Scheme II.1 for gaining access to *trans*-A_2B_2- or *trans*-A_2-porphyrins via acid-catalyzed processes (routes I, IIa, IIb, and III). The conditions explored here for the reaction of a 1-acyldipyrromethane are more general than those in route IIc, which requires an expensive palladium reagent and affords the corresponding palladium porphyrin.

Much about mechanism remains unknown. The conversion of two 1-acyldipyrromethanes to the porphyrin entails, in unknown order, formation of two C-C bonds, elimination of two molecules of water, dehydrogenation (with an unknown oxidant), and metal complexation. The good yield at 100 or 200 mM reactions tends to suggest the formation of a magnesium complex with the two 1-acyldipyrromethanes early in the process, thereby favoring intramolecular over intermolecular reaction (i.e., cyclization over polymerization). The 1-acyldipyrromethanes containing an *o*-pyridyl group (but not *m*- or *p*-pyridyl) at the acyl site gave low yields of porphyrin, which may stem from competitive coordination of magnesium by the *o*-pyridyl and keto functional groups. Although early complexation with magnesium would seem reasonable, magnesium insertion into free base porphyrins is facile under these and analogous[II54] reaction conditions; thus, the isolation of the magnesium porphyrin alone is not sufficient proof of a templated reaction process (see Supporting Information). Concerning the course of reaction,

it should be noted that each 1-acyldipyrromethane that bears a 5-substituent presumably exists as a pair of enantiomers; the resulting intermediate(s) on the path to porphyrin may be diastereomeric with different reactivities. While studies to investigate these issues are beyond the scope of the present work, it deserves noting that attempts to apply these conditions to the reaction of a 1,9-diacyldipyrromethane and a dipyrromethane gave only a trace of the corresponding porphyrin. On the other hand, the condensation of 5-phenyldipyrromethane and *p*-tolualdehyde gave the *trans*-A_2B_2-porphyrin in 20% yield, but yields upon extension to other substrates were quite low (see Supporting Information). Thus, at present the basic, magnesium-mediated reaction conditions appear restricted to the condensation of 1-acyldipyrromethanes,[II8] the cyclization of 1-acylbilanes,[II53] and magnesium insertion into free base porphyrins.[II54]

The statistical condensations described herein have afforded entrée into porphyrins with substituent patterns that previously presented difficulties (including *cis*-A_2B_2 and *cis*-ABC_2, and the sparsely substituted analogues *cis*-A_2, *cis*-AB, A), do so in each case without concomitant formation of the *trans* isomer, and are compatible with pyridyl and alkyl substituents. Statistical condensations have long been used in porphyrin chemistry to access a desired porphyrin architecture, typically by chromatographic separation of the resulting mixture of porphyrins.[II67] The most prevalent statistical routes to porphyrins include (i) two aldehydes and pyrrole to give six porphyrins;[II67] (ii) two aldehydes and a dipyrromethane (or vice versa) to give three porphyrins;[II67] (iii) two dipyrromethane-1-carbinols to give three porphyrins;[II72] (iv) one aldehyde, 2-hydroxymethylpyrrole, and a dipyrromethane to give two porphyrins;[II73] and (v) one aldehyde, pyrrole, and tripyrrane to give two porphyrins.[II73] All of the methods that employ dipyrromethanes or tripyrranes (ii-v) also employ acid catalysis conditions, which may give poor results with pyridyl or alkyl groups.

Given the widespread acceptance of statistical routes in porphyrin synthesis, it is surprising that few efforts, other than the pioneering work of Drain,[II74-II76] Richert,[II77-II79] and Boyle[II80,II81] have been made toward the exploitation of such routes in the development of porphyrin libraries. The routes that have been examined rely on (1) the reaction of a collection of aldehydes with pyrrole,[II74,II77,II78,II82] (2) derivatization of a pure porphyrin,[II75,II76,II79,II83,II84] or (3) derivatization of a mixture of porphyrins.[II74,II78] Few combinatorial approaches have relied on routes that afford a more narrow set of porphyrins.[II80,II81] The condensation of 1-acyldipyrromethanes appears attractive in this latter regard for two reasons: (i) the ability to focus on selected architectures such as *cis*-A_2B_2-porphyrins, and (ii) the tolerance of the reaction conditions toward heterocyclic substituents. The ability to incorporate heterocyclic substituents in sparsely substituted architectures is of interest for a number of biomedical applications, where charged or amphipathic substituents are desired in a compact molecular design.

II.D. Experimental Section.

General. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were collected in $CDCl_3$ at room temperature unless noted otherwise. Melting points are uncorrected. THF was distilled from sodium/benzophenone under argon. LD-MS data were obtained in neat form in almost all cases, but with a matrix (POPOP) for porphyrins **II-Co-1a**, **II-Mg-1t**, **II-Mg-1s**, and **II-Mg-1r**. All other chemicals were reagent grade and were used as received. Anhydrous Anhydrous $MgBr_2$ and toluene were used as received. All reported yields of magnesium porphyrins ignore the presence of any apical ligand.

Synthesis of Mukaiyama Reagents (Method II.1).[II61] A solution of 2-mercaptopyridine (5.55 g, 50.0 mmol) in THF (50.0 mL) was treated slowly with an acid chloride (50.0 mmol). The resulting slurry was stirred for 30 min. The precipitate was collected by filtration and

washed with hexanes (70.0 mL) in a Buchner funnel. The filtered material was added into a biphasic solution of saturated aqueous $NaHCO_3$ (100 mL) and diethyl ether (100 mL). The mixture was stirred until the foaming subsided. The organic layer was removed, and the water layer was extracted with diethyl ether. The combined organic extract was dried (Na_2SO_4) and filtered. The filtrate was concentrated to give a solid, which was washed with hexanes (~20 mL) to afford the product.

***S*-2-Pyridyl hexanothioate (II-5c).** Following Method II.1, a solution of 2-mercaptopyridine (6.66 g, 60.0 mmol) in THF (60 mL) was treated with hexanoyl chloride (8.3 mL, 60 mmol) to afford a yellow liquid (12.2 g, 97%): ^{1}H NMR δ 0.89–0.91 (m, 3H), 1.31–1.34 (m, 4H), 1.70–1.74 (m, 2H), 2.69 (t, J = 7.6 Hz, 2H), 7.26–7.29 (m, 1H), 7.60– 7.62 (m, 1H), 7.71–7.76 (m, 1H), 8.61–8.62 (m, 1H); ^{13}C NMR δ 14.0, 22.5, 25.3, 31.2, 44.4, 123.7, 130.4, 137.4, 150.5, 151.7, 196.7; FAB-MS obsd 210.0958, calcd 210.0953 ($C_{11}H_{15}NOS$). Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 62.76; H, 7.19; N, 7.01.

Synthesis of 1-Acyldipyrromethanes (Method II.2).[II4] A solution of EtMgBr (38 mL, 38 mmol, 1.0 M in THF) was added slowly to a solution of the dipyrromethane (15.0 mmol) in THF (30.0 mL) under argon. The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of Mukaiyama reagent (15.0 mmol) in THF (30.0 mL) was added to the reaction mixture. The solution was stirred at –78 °C for 10 min, and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic layer was washed (water, brine), dried (Na_2SO_4) and filtered. The filtrate was concentrated. The resulting product was chromatographed [silica, CH_2Cl_2 (until all the unreacted dipyrromethane was eluted) → hexanes/ethyl acetate (3:1)] to afford the corresponding 1-acyldipyrromethane.

5-(4-Methylphenyl)-1-picolyldipyrromethane (**II-6e**). Following Method II.2, a solution of EtMgBr (38 mL, 38 mmol, 1.0 M in THF), 5-(4-methylphenyl)dipyrromethane (**II-4b**, 3.55 g, 15.0 mmol, in 30 mL of THF) and a solution of *S*-2-pyridyl picolinothioate (**II-5e**, 3.24 g, 15.0 mmol, in 30 mL of THF) afforded an oily product, which upon chromatography [silica, CH_2Cl_2/ethyl acetate (7:2), 4 cm dia x 30 cm] afforded a brown powder (3.91 g, 76%): mp 54 °C (dec.); ^{1}H NMR δ 2.35 (s, 3H), 5.53 (s, 1H), 6.01–6.02 (m, 1H), 6.10–6.12 (m, 1H), 6.19–6.21 (m, 1H), 6.73–6.74 (m, 1H), 7.13– 7.18 (m, 4H), 7.39–7.42 (m, 2H), 7.82–7.86 (m, 2H), 8.02–8.12 (m, 1H), 8.17–8.18 (brs, 1H), 8.44–8.58 (brs, 1H); ^{13}C NMR δ 21.3, 44.2, 107.77, 107.78, 108.7, 110.8, 118.0, 124.1, 126.3, 128.6, 129.7, 131.7 (brs), 137.2, 137.5, 138.2, 141.6, 148.2, 155.7, 171.5; FAB-MS obsd 341.1528, calcd 341.1526. Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 76.09; H, 5.77; N, 11.71. The elemental analysis data are consistent with the presence of one molecule of ethyl acetate per four molecules of product.

Synthesis of 1-Formyldipyrromethanes (Method II.3).[II64] A sample of dipyrromethane (15.0 mmol) in THF (30 mL) was treated with MesMgBr (30 mL, 30 mmol, 1 M in THF). After 10 min, the mixture was cooled to –78 °C. Phenyl formate (**II-5m**, 3.27 mL, 30.0 mmol) was added in one portion. The reaction mixture was stirred at –78 °C for 1 h. The cooling bath was removed, and stirring was continued for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (~150 mL). The organic extract was washed (water, brine) and concentrated. The resulting oil was dissolved in CH_3CN (150 mL) and treated with 2 M aqueous NaOH (90 mL). The resulting mixture was stirred vigorously at room temperature for 1 h. Water (~100 mL) was added, and the mixture was extracted with CH_2Cl_2. The organic phase was washed (saturated aqueous NH_4Cl, water, brine), dried

(Na_2SO_4), and concentrated. The resulting dark oil was chromatographed [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (10:1)] to afford the product.

1-Formyl-5-(3-pyridyl)dipyrromethane (**II-6v**)**.** Following Method II.3, reaction of 5-(3-pyridyl)dipyrromethane (**II-4k**, 1.12 g, 5.00 mmol in 20 mL of THF), MesMgBr (10.0 mL, 10 mmol, 1.0 M in THF) and phenyl formate (**II-5m**, 1.1 mL, 10. mmol) afforded an oily product. Column chromatography (silica, ethyl acetate) afforded a pure product (an orange solid, 0.304 g) and mixed fractions; the latter were rechromatographed (silica, ethyl acetate) to afford an additional 0.162 g of product. Total yield (0.466 g, 37%): mp 174–176 °C (dec.); ^{1}H NMR (300 MHz) (THF-d_8) δ 5.49 (s, 1H), 5.65–5.67 (m, 1H), 5.86–5.88 (m, 1H), 5.95–5.98 (m, 1H), 6.63–6.66 (m, 1H), 6.80–6.82 (m, 1H), 7.18–7.22 (m, 1H), 7.44–7.49 (m, 1H), 8.49–8.42 (m, 2H two signals overlapped), 9.40 (s, 1H), 9.84–9.98 (br, 1H), 11.20–11.29 (brs, 1H); ^{13}C NMR (THF-d_8) δ 42.8, 108.4, 111.1, 118.7, 121.2, 124.0, 131.9, 134.6, 136.4, 138.7, 142.9, 149.1, 151.1, 178.8 (signals derived from two carbon atoms are apparently overlapped); ESI-MS obsd 252.1134, calcd 252.1131 [$(M + H)^+$, M = $C_{15}H_{13}N_3O$]. Anal. Calcd for $C_{15}H_{13}N_3O$: C, 71.70; H, 5.21; N, 16.72. Found: C, 71.58.; H, 5.21; N, 16.44.

Condensation of a 1-Acyldipyrromethane via Conventional Heating at 135 °C (Method II.4A). A sample of 1-acyldipyrromethane (1.00 g) was placed in a 250 mL one-necked round bottom flask that was oven-dried and contained a magnetic stir bar. A teflon septum was attached, and toluene (~10 – ~25 mL) was added via syringe. The reaction mixture was stirred at room temperature for 1 min, where upon DBU (10 mol equiv versus **II-6a**) was added dropwise via syringe under vigorous stirring. The resulting mixture was stirred at room temperature for 5 min. The mixture darkened. The septum was removed, and $MgBr_2$ (3.0 mol equiv versus **II-6a**) was added in one portion under vigorous stirring. (Note that a dry flask is

essential, as is vigorous stirring, so that $MgBr_2$ does not clump as a solid on the bottom of the flask, which typically lowers the yield of porphyrin.) The septum was replaced, and the heterogeneous reaction mixture was stirred for 1 min at room temperature. The flask was fitted with a reflux condenser (4 cm dia × 30 cm) having the top end open to the atmosphere, and the flask was placed in an oil bath preheated to 135 °C. The reaction mixture was stirred under reflux. When porphyrin formation was complete (on the basis of TLC analysis and absorption spectroscopy, typically after overnight reaction), the crude reaction mixture was allowed to cool to room temperature and then concentrated. The resulting residue was dissolved in CH_2Cl_2 (2.0 mL) and filtered through a column [alumina, 500 g, 4 cm dia × 30 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:1 → 3:1), ~1.5 L]. The grade of alumina employed depended on the polarity of the porphyrin (see Supporting Information). The porphyrin-containing fraction was collected and concentrated to afford a purple solid.

5,15-Bis(4-*tert*-butylphenyl)-10,20-bis(4-ethylphenyl)porphinatomagnesium(II) (II-Mg-1a). Following Method II.4A, DBU (3.64 mL, 24.4 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (1.00 g, 2.44 mmol, 100 mM) in toluene (24.4 mL). $MgBr_2$ (1.35 g, 7.32 mmol, 3.00 mol equiv) was added. The reaction mixture was heated to reflux (oil bath temperature 135 °C) with exposure to air for the overnight duration of the reaction. TLC analysis (silica, CH_2Cl_2) showed the free base porphyrin, magnesium porphyrin and a trace amount of **II-6a** (although alumina chromatography was successful, TLC analysis on alumina did not give a successful separation whereas that on silica resulted in better separation). Chromatography [alumina, 500 g, 4 cm dia × 40 cm, CH_2Cl_2/ethyl acetate (4:1 → 3:1)] afforded a trace of free base porphyrin (**II-1a**), which eluted first and was easily isolated apart from the magnesium porphyrin (0.0040 g, 0.45%). The dominant porphyrin-containing fraction was

isolated to give a purple solid (0.511 g, 52%): ^{1}H NMR (THF-d_8) δ 1.54 (t, J = 7.6 Hz, 6H), 1.62 (s, 18H), 3.02 (q, J = 7.6 Hz, 4H), 7.56 (d, J = 7.8 Hz, 4H), 7.73 (d, J = 7.8 Hz, 4H), 8.10–8.15 (m, 8H), 8.77 (s, 8H); ^{13}C NMR (THF-d_8) δ 15.4, 28.9, 31.3, 34.7, 121.5, 123.1, 125.6, 131.3, 131.4, 134.9, 135.0, 141.7, 142.0, 142.8, 149.7, 149.8 (the signals of two carbons were not observed); LD-MS obsd 804.8; FAB-MS obsd 804.4073, calcd 804.4042 ($C_{56}H_{52}MgN_4$); λ_{abs} 405, 426, 564, 605 nm.

Condensation of a 1-Acyldipyrromethane via Conventional Heating at 115 °C (Method II.4B). The experimental protocol for *trans*-A_2B_2 magnesium porphyrin synthesis was carried out with the oil bath temperature set at 115 °C while keeping the rest of the procedure unchanged.

5,15-Bis(4-methylphenyl)-10,20-di-3-pyridylporphinatomagnesium(II) (II-Mg-1f). Following Method II.4B, **II-6f** (0.171 g, 0.500 mmol) in toluene (5 mL) was treated with DBU (1.49 mL, 10.0 mmol, 20 mol equiv) and $MgBr_2$ (0.276 g, 1.50 mmol, 3.0 mol equiv). The reaction was complete in 30 min. The crude reaction mixture was allowed to cool and then concentrated. The resulting residue was dissolved in CH_2Cl_2 and filtered through a column [alumina grade V,[II93] CH_2Cl_2/triethylamine (100:1)]. The porphyrin-containing fraction was collected and concentrated. The resulting solid was treated with methanol (5 mL), and the resulting suspension was centrifuged. Solvent was decanted, and the remaining purple solid was collected. This procedure (treat with methanol, centrifuge, and decant) was repeated twice to afford a purple solid (72 mg, 43%): LD-MS 666.6, ESI-MS obsd 667.2449, calcd 667.2455 [(M + H)$^+$, M = $C_{44}H_{32}N_4$]; λ_{abs} (hot THF) 408, 429, 571, 614 nm. Due to extensive aggregation upon attempted ^{1}H NMR spectroscopy, a sample of the magnesium porphyrin (42.5 mg, 0.0637 mmol) was demetalated in CH_2Cl_2 (10 mL) by addition of TFA (1.5 mL). The resulting crude

reaction mixture was neutralized by the addition of triethylamine (5.0 mL). Aqueous workup and washing with methanol afforded the free base porphyrin **II-1f** as a purple powder (32.5 mg, 80%): ^{1}H NMR (300 MHz) δ –2.75 (s, 2H), 2.72 (s, 6H), 7.58 (d, *J* = 7.4 Hz, 4H), 7.73–7.77 (m, 2H), 8.12 (d, *J* = 7.4 Hz, 4H), 8.52–8.56 (m, 2H), 8.82 (d, *J* = 4.8 Hz, 4H), 8.97 (d, *J* = 4.8 Hz, 4H), 9.06–9.08 (m, 2H), 9.50–9.51 (m, 2H); ^{13}C NMR (75 MHz) δ 21.7, 116.1, 121.2, 122.2, 127.7, 130.0–131.5 (brs), 131.8–132.8 (brs), 134.7, 137.8, 138.3, 139.0, 141.1, 149.3, 153.9; LD-MS 644.3, ESI-MS obsd 645.2765 calcd 645.2761 [$(M + H)^+$, M = $C_{44}H_{32}N_4$]; λ_{abs} 421, 517, 550, 592, 651 nm.

Condensation of a 1-Acyldipyrromethane via Microwave Irradiation (Method II.5, as used in Table II.2). A sample of 1-acyldipyrromethane (0.10 mmol) was placed in a 10 mL glass tubular reaction vessel containing a magnetic stir bar. Toluene (1.0 mL) and DBU (0.150 mL, 1.00 mmol) were added. The resulting mixture was stirred to obtain a homogenous solution, and then treated with $MgBr_2$ (0.055 g, 0.30 mmol). The vessel was sealed with a septum and subjected to microwave irradiation at 100 W. The protocol was as follows: (1) heat from room temperature to 115 °C (irradiate for 2 min), (2) hold at 115 °C (irradiate for 15 min; temperature typically overshot to 135 °C and then stabilized after 2 min), (3) allow to cool to room temperature (~1 min), (4) check the reaction mixture by TLC analysis and absorption spectroscopy, (5) repeat steps 1-3 until porphyrin formation is complete. The reaction mixture was transferred to a round bottom flask (using THF, which was HPLC-grade and lacked stabilizer) and concentrated. The resulting crude product was filtered through a column [alumina grade V,[II93] CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate → THF/MeOH (10:1)]. The porphyrin-containing fractions were concentrated. The resulting porphyrin was suspended in hexanes (5 mL). The suspension was sonicated for ~1 min, centrifuged, and decanted to obtain

the powder. The resulting porphyrin was suspended in methanol (5 mL) and treated likewise (sonication, centrifugation, decantation) to afford a purple powder.

5,15-Di-3-pyridyl-10,20-di-4-pyridylporphinatomagnesium(II) (II-Mg-1o). Following Method II.5, a sample of **II-6o** (0.0330 g, 0.100 mmol) gave porphyrin in 45 min. Chromatography [CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate → THF/MeOH (20:1)] followed by washing the porphyrin suspension with hexanes and methanol afforded a purple powder (14 mg, 21%): ^{1}H NMR (DMSO-d_6) δ 7.03–7.07 (m, 2H), 7.38–7.39 (br, 4H), 7.76–7.78 (m, 2H), 7.93 (d, J = 6.2 Hz, 4H), 7.98 (d, J = 6.2 Hz, 4H), 8.17–8.19 (m, 6H), 8.46–8.54 (brs, 2H); LD-MS obsd 640.6, ESI-MS obsd 641.2044, calcd 641.2047 [$(M + H)^+$, M = $C_{40}H_{24}MgN_8$]; λ_{abs} (toluene) 407, 428, 564, 604 nm.

Statistical Condensation of Two 1-Acyldipyrromethanes via Microwave Irradiation (Method II.6). Samples of a first 1-acyldipyrromethane (0.20 mmol) and a second 1-acyldipyrromethane (0.20 mmol) were placed in a 10 mL glass tubular reaction vessel containing a magnetic stir bar. Toluene (4.0 mL) and DBU (0.60 mL, 4.0 mmol) were added. The resulting mixture was stirred to obtain a homogenous solution, and then treated with $MgBr_2$ (0.221 g, 1.20 mmol). The vessel was sealed with a septum and subjected to microwave irradiation at 100 W. The protocol was as follows: (1) heat from room temperature to 115 °C (irradiate for 2 min), (2) hold at 115 °C (irradiate for 15 min; temperature typically overshot to 135 °C and then stabilized after 2 min), (3) allow to cool to room temperature (~1 min), (4) check the reaction mixture by TLC analysis and absorption spectroscopy, and (5) repeat steps 1-3 until porphyrin formation is complete. After porphyrin formation was complete, the crude reaction mixture was transferred to a round bottom flask (using THF, which was HPLC grade and lacked stabilizer) and concentrated. The resulting crude product was washed (water, brine), dried (Na_2SO_4) and

concentrated. The resulting crude reaction mixture was dissolved in CH_2Cl_2 (4 mL) and demetalated by the addition of TFA (0.032 mL). A sample of triethylamine was added (0.020 mL). The crude reaction mixture was washed (water, brine), dried (Na_2SO_4), and concentrated. The resulting product was chromatographed [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:3) → ethyl acetate → ethyl acetate/MeOH (10:1)]. Each porphyrin-containing fraction was concentrated. The resulting porphyrin was suspended in hexanes (5 mL). The suspension was sonicated for ~1 min, centrifuged, and decanted to obtain the powder. The resulting porphyrin was suspended in methanol (5 mL) and treated likewise (sonication, centrifugation, decantation) to afford a purple powder.

Note that when one of the 1-acyldipyrromethanes was 1-formyldipyrromethane (**II-6z**), the order of elution typically was porphine, the target 'hybrid' porphyrin, and the porphyrin derived from condensation of two molecules of the other 1-acyldipyrromethane. When one of the 1-acyldipyrromethanes was 1-hexanoyl-5-pentyldipyrromethane (**II-6r**), the order of elution typically was the target 'hybrid' porphyrin followed by the porphyrin derived from condensation of two molecules of the other 1-acyldipyrromethane; no tetrapentylporphyrin was obtained.

5,10-Di-3-pyridylporphyrin (II-2b). Following Method II.6, a mixture of **II-6l** (0.066 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by washing the porphyrin with hexanes (5 mL) and methanol (5 mL) afforded the title compound as a purple powder (0.026 g, 28%): ^{1}H NMR δ –3.47 (s, 2H), 7.73–7.78 (m, 2H), 8.50–8.52 (m, 2H), 8.90 (s, 2H), 8.96 (d, J = 6.6 Hz, 2H), 9.06–9.08 (m, 2H), 9.38 (d, J = 6.6 Hz, 2H), 9.41–9.43 (brs, 2H), 9.44–9.47 (brs, 2H), 10.24 (s, 2H); ^{13}C NMR δ 105.2, 115.9, 122.2, 131.1–132.9 (brs), 138.1, 141.2, 149.4, 153.9; LD-MS obsd 464.4; ESI-MS obsd 465.1819, calcd 465.1822 [$(M + H)^+$, M

= $C_{30}H_{20}N_6$]; λ_{abs} (toluene) 409, 502, 534, 577 nm. Two other porphyrins also were isolated, 5,10,15,20-tetra-3-pyridylporphyrin (**1l**, 4 mg, 3%) and porphine (0.0080 g, 13%). Data for **II-1l**: ^{1}H NMR (300 MHz) δ –2.84 (s, 2H), 7.68–7.72 (m, 4H), 8.05–8.11 (m, 4H), 8.19–8.21 (m, 4H), 8.84–8.8 (brs, 8H), 9.12–9.14 (brs, 4H); ^{13}C NMR δ 117.0, 122.3, 131.2–131.8 (brs), 137.8, 141.2, 149.6, 153.9, 160.8; ESI-MS obsd 619.2355, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 420, 515, 550, 592, 648 nm. The data (^{1}H NMR, ^{13}C NMR, FAB-MS) for porphine were consistent with those obtained from an authentic sample.[II8]

5-(4-Pyridyl)porphyrin (II-2h). Following Method II.6, a mixture of **II-6w** (0.050 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography [silica, THF → THF/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.016 g, 21%): ^{1}H NMR δ –3.69 (s, 2H), 8.17–8.19 (m, 2H), 9.02–9.06 (m, 4H), 9.43–9.44 (m, 2H), 9.42–9.48 (m, 4H), 10.28 (s, 1H), 10.34 (m, 2H); ^{13}C NMR δ 104.5, 105.2, 115.9, 129.9, 130.1, 130.7, 131.7, 132.2, 148.6, 150.2; ESI-MS obsd 388.1554, calcd 388.1556 [$(M + H)^+$, M = $C_{25}H_{17}N_5$]; λ_{abs} (toluene) 402, 495, 527, 569 nm. Two other porphyrins also were isolated, 5,15-di-4-pyridylporphyrin (**II-1w**, 0.010 g, 11%) and porphine (trace). No ESI-MS signal was observed for **II-1w** because of low solubility.

5,10-Dipentyl-15,20-di-4-pyridylporphyrin (II-3c). Following Method II.6, a mixture of **II-6m** (0.033 g, 0.10 mmol) and **II-6r** (0.031 g, 0.10 mmol) in toluene (2 mL) was treated with DBU (0.30 mL, 2.0 mmol) and $MgBr_2$ (0.11 g, 0.60 mmol). The reaction was monitored with TLC analysis [silica, THF/MeOH (10:1)] and absorption spectroscopy. Porphyrin formation was complete in ~2 h. TLC analysis of the crude reaction mixture [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → THF/MeOH (10:1)] revealed two green spots (R_f = 0.32 and 0.61).

The absorption spectrum of the crude reaction mixture revealed four bands (303, 405, 425, and 564 nm). The LD-MS analysis (with POPOP) of the crude reaction mixture indicated the presence of two porphyrins. The molecule ion peak, *m/z* = 626.9, was assigned to **II-Mg-3c**, whereas the peak at *m/z* = 640.6 was consistent with porphyrin **II-Mg-1m**. The crude product was dissolved in CH_2Cl_2 and demetalated by addition of TFA. The reaction mixture was neutralized with triethylamine. Aqueous workup and chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (10:1)] afforded the title compound as a purple powder (0.016 g, 26%): ^{1}H NMR δ –2.77 (s, 2H), 0.97 (t, *J* = 7.2 Hz, 6H), 1.54–1.57 (m, 4H), 1.75–1.83 (m, 4H), 2.50–2.58 (m, 4H), 4.98–5.01 (m, 4H), 8.10 (d, *J* = 5.8 Hz, 4H), 8.67–8.72 (brs, 2H), 8.79 (d, *J* = 4.4 Hz, 2H), 9.00 (d, *J* = 5.8 Hz, 4H), 9.48 (d, *J* = 4.4 Hz, 2H), 9.57–9.61 (brs, 2H); LD-MS obsd 604.7, ESI-MS obsd 605.3382, calcd 605.3387 [$(M + H)^+$, M = $C_{40}H_{40}N_6$]; λ_{abs} (toluene) 419, 517, 551, 595, 652 nm. 5,10,15,20-Tetra-4-pyridylporphyrin (**II-1m**) also was isolated (0.0076 g, 12%): ^{1}H NMR δ –2.93 (s, 2H), 8.15–8.17 (m, 8H), 8.85–8.88 (brs, 8H), 9.06–9.08 (m, 8H); ESI-MS obsd 619.2371, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_4$]; λ_{abs} (THF) 408, 429, 529, 569, 611 nm.

Quaternization Procedure to Yield 5,10-Dipentyl-15,20-bis[4-methylpyridin-4-ium-1-yl]porphyrin Diiodide (II-3c-Me_2I_2). A solution of **II-3c** (0.020 g, 0.033 mmol) in chloroform (3.3 mL) was treated with excess iodomethane (0.410 mL, 6.62 mmol). The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was concentrated, and the resulting product was washed with hexanes (5 mL x 2) to afford the title compound as a purple powder (0.0264 g, 90%): ^{1}H NMR (DMSO-d_6) δ –2.88 (s, 2H), 0.93 (t, *J* = 7.4, 6H), 1.46–1.54 (m, 4H), 1.73–1.78 (m, 4H), 2.53–2.55 (overlapped with DMSO signal), 4.70 (s, 6H), 4.98–5.11 (m, 4H), 8.94–8.96 (m, 8H), 9.43–9.45 (m, 4H), 9.14–8.16 (m, 4H); ^{13}C NMR

(DMSO-d_6) δ 14.7, 23.0, 32.6, 48.5, 113.0, 124.2, 132.9, 144.7, 157.9 (not all carbon signals were observed owing to limited solubility); ESI-MS obsd 317.1893, calcd 317.1886 [$(M - 2I)^{2+}$, $M = C_{42}H_{46}I_2N_6$]; λ_{abs} (water) 419, 525, 563, 646 nm.

Yield Calculations for Statistical Reactions (Tables II.3 and II.4). The yield of porphyrin formation via condensation of two non-identical 1-acyldipyrromethanes (e.g., 0.10 mmol each) was calculated as follows: (1) the theoretical yield of porphyrins in total was equal to the sum total number of moles of dipyrromethane species, (2) the actual yield in mmol of each porphyrin was determined experimentally, and (3) the ratio of the actual yield to the theoretical yield gives the reported % yield for each component. In this manner, the sum of all % yields can equal but not exceed 100%. Also, if each of the two 1-acyldipyrromethanes exclusively underwent homo-condensation to give the two porphyrins derived therefrom with no hetero-condensation to give hybrid porphyrin, the yield of each would be 50%, again giving a total of 100%.

The contents of this chapter have been published.[II94]

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II.F. Supporting Information.

I. Investigation of the Conditions for 1-Acyldipyrromethane Condensation.

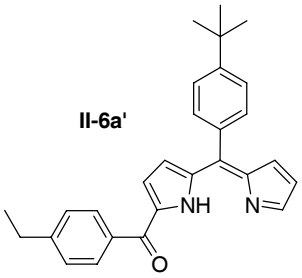
The chief metalloporphyrin examined for exploration of reaction conditions was **II-M-1a**. The porphyrin bears two *p*-*tert*-butylphenyl groups and two *p*-ethylphenyl groups in a *trans*-configuration (i.e., *trans*-A_2B_2-porphyrin). This set of substituents was chosen for the following reasons: (1) to facilitate detection of any scrambling processes while maintaining similar electronic effects, (2) to exhibit stability toward diverse reaction conditions, and (3) to facilitate analysis by ^{1}H NMR spectroscopy. Note that attempted preparation of porphyrin **II-M-1a** by route I (reaction of a dipyrromethane + an aldehyde) typically proceeds with at least a low level of scrambling.

The condensation of 1-acyldiprromethane **II-6a** was carried out under diverse conditions. The conditions examined included use of a metal salt and a base in a solvent exposed to air. The general protocol entails consecutive addition of a base and a metal salt to the solution of the 1-acyldipyrromethane in the corresponding solvent followed by heating (oil bath temperature 115 °C) exposed to air. The resulting mixture was heterogeneous, and the metalloporphyrin precipitated in the reaction mixture. Each reaction mixture was checked by absorption spectroscopy and TLC analysis. The reaction mixture was stirred (with a reflux condenser having the top end open to the air) until the intermediates at 390 and 529 nm disappeared. The results of the survey are listed in Table II.S-1.

(i) Metal Reagent. Metal reagents examined in place of $MgBr_2$ included $MnCl_2$, $FeCl_2$, $Co(OAc)_2{\cdot}4H_2O$, $NiCl_2$, $Cu(OAc)_2$, $Zn(OAc)_2$, $Pd(CH_3CN)_2Cl_2$, $CdCl_2$, and $InCl_3$. A trace amount of metalloporphyrin was observed with $MnCl_2$, $NiCl_2$, $Cu(OAc)_2$, or $CdCl_2$ after overnight stirring. $Co(OAc)_2{\cdot}4H_2O$ and $Pd(CH_3CN)_2Cl_2$ afforded the corresponding

metalloporphyrin in 6% yield and 37% yield, respectively. Among the metal salts examined, $MgBr_2$ afforded the best yield in 2 h (entries 1-10), which was 69%.

(ii) Solvent. Replacement of the solvent toluene with diisopropyl ether, *tert*-butyl methyl ether, or THF did not afford the expected porphyrin but instead gave dipyrrin **II-6a′** as the main product. Compound **II-6a′** was isolated (36% yield) from the reaction in diisopropyl ether. The absorption spectrum was typical of that with the reported data for 1-acyldipyrrins.[II5] Thus, the reaction was quite sensitive to the nature of the solvent. The condensation of 1-acyldipyrromethane **II-6a** did not afford any porphyrin in the ether solvents (entries 11-13).



(iii) Base. Replacement of DBU with the stronger bases EtMgBr and MesMgBr afforded a trace amount or no porphyrin, respectively, after 48 h (entries 14 and 15).

(iv) Temperature. At 70 °C, porphyrin formation was incomplete even upon stirring the reaction mixture for two days. At 115 °C, TLC analysis of the crude reaction mixture (alumina, CH_2Cl_2) after 6 h did not show any starting material, and **II-Mg-1a** was obtained in 69% yield (0.674 g). At 135 °C, the reaction mixture refluxed and was stirred overnight to give porphyrin **II-Mg-1a** in 52% yield (0.511 g). Partial solvent loss occurred under these refluxing conditions. It is possible that higher concentration resulting from solvent loss lowered the yield of porphyrin.

(v) Concentration. The condensation of **II-6a** (1.00 g, 2.44 mmol, 100 mM) was performed at three different concentrations (50 mM, 100 mM and 200 mM). The yield of porphyrin **II-Mg-1a** was 47%, 69% and 65% at 50 mM, 100 mM and 200 mM, respectively. A solventless reaction (no toluene) with **II-6a**, DBU, and $MgBr_2$ gave the porphyrin **II-Mg-1a** in 7% yield. In each case, a trace amount of the free base porphyrin **II-1** also was isolated.

In summary, the best conditions that emerged from this survey were as follows: the 1-acyldipyrromethane (100 mM) in toluene containing DBU (10 mol equiv) and $MgBr_2$ (3 mol equiv) at 115 °C exposed to air for 12 h. Application of these conditions to the condensation of **II-6a** gave the following results: (1) 0.12 mmol of **II-6a** (100 mM) gave 28 mg of **II-Mg-1a** (57%); (2) 0.49 mmol of **II-6a** (100 mM) gave 57 mg of **II-Mg-1a** (29%); and (3) 0.12 mmol of **II-6a** (200 mM) gave 21 mg of **II-Mg-1a** (43%).

(vi) Scale. The synthesis was carried out at increased scale in several cases. The results are as follows: **II-Mg-1a**, 52% yield, 0.511 g at 135 °C; **II-Mg-1a**, 69% yield, 0.674 g at 115 °C; **II-Mg-1b**, 46% yield, 0.454 g at 135 °C; **II-Mg-1c**, 31% yield, 0.209 g at 135 °C.

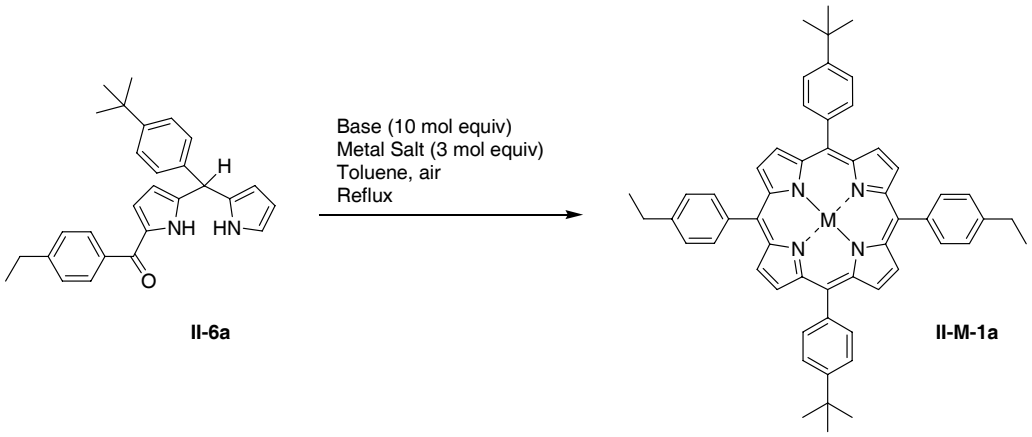


Table II.S-1. Survey of Conditions for *trans*-A_2B_2-Metalloporphyrin Synthesis from II.6a[a]

Entry	Metal salt	Base	Solvent	Time (h)	Product	Yield[b] (%)
1	$MnCl_2$	DBU	Toluene	48	**II-Mn-1a**	Trace
2	$FeCl_2$	DBU	Toluene	48	**II-Fe-1a**	0
3	$Co(OAc)_2$	DBU	Toluene	48	**II-Co-1a**	6[c]
4	$NiCl_2$	DBU	Toluene	48	**II-Ni-1a**	Trace
5	$Cu(OAc)_2$	DBU	Toluene	48	**II-Cu-1a**	Trace
6	$Zn(OAc)_2$	DBU	Toluene	48	**II-Zn-1a**	0
7[d]	$Pd(CH_3CN)_2Cl_2$	DBU	Toluene	48	**II-Pd-1a**	37
8	$CdCl_2$	DBU	Toluene	48	**II-In-1a**	Trace

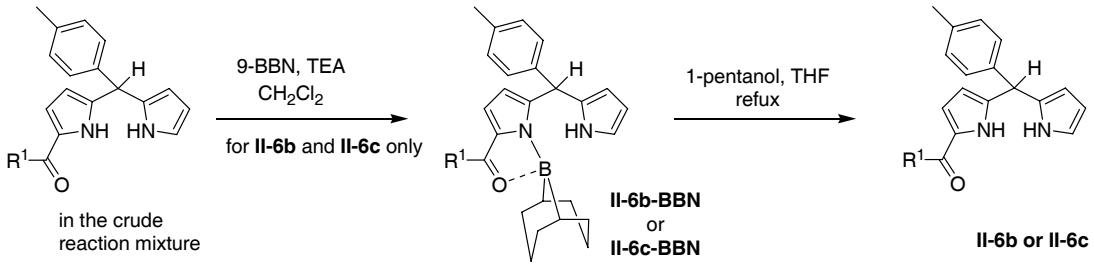
Table II.S-1 (continued)

9	$InCl_3$	DBU	Toluene	48	**II-In-1a**	0
10[e]	$MgBr_2$	DBU	Toluene	12	**II-Mg-1a**	57[f]
11[g]	$MgBr_2$	DBU	Diisopropyl ether	48	**II-Mg-1a**	0
12[g]	$MgBr_2$	DBU	*t*-butyl methyl ether	48	**II-Mg-1a**	0
13[g]	$MgBr_2$	DBU	THF	48	**II-Mg-1a**	0
14	---	EtMgBr	Toluene	48	**II-1a**	Trace
15	---	MesMgBr	Toluene	48	**II-1a**	0

[a]The standard conditions entail use of 1-acyldipyrromethane **II-6a** (0.060 mmol, 100 mM), a base (0.60 mmol, 10 mol equiv versus **II-6a**), a metal salt (0.180 mmol, 3 mol equiv versus **II-6a**) and a solvent (0.60 mL) at 115 °C exposed to air unless noted otherwise. The standard protocol entails consecutive addition of the base and the metal salt to the solution of **II-6a** in the reaction solvent followed by heating. [b]Isolated yield. [c]Yield determination on the basis of absorption spectrometry of the isolated porphyrin. [d]The same addition protocol was followed for $Pd(CH_3CN)_2Cl_2$. Addition of the $Pd(CH_3CN)_2Cl_2$ to a solution of DBU and **II-6a** in toluene afforded a black precipitate. [e]On the basis of TLC analysis (alumina, CH_2Cl_2), a trace amount of free base porphyrin also was observed. [f]One trial afforded **II-Mg-1a** in 43% at 200 mM. [g]Dipyrrin **II-6a′** was isolated as the main product in 36% yield.

II. Boron Complexation of 1-Acyldipyrromethanes.

The formation of dialkylboron complexes was attempted for **II-6b**, **II-6c**, and **II-6g**. The complexes were obtained only for **II-6b** and **II-6c** (Scheme II.S-1). In this process, the crude acylation mixture is treated with a dialkylboron triflate and triethylamine. The resulting hydrophobic dialkylboron complex of the 1-acyldipyrromethane can be isolated by precipitation/crystallization with limited or no chromatography. The 1-acyldipyrromethane-dialkylboron complexes **II-6b-BBN** and **II-6c-BBN** were decomplexed by treatment with 1-pentanol in refluxing THF, affording the 1-acyldipyrromethane **II-6b** and **II-6c**. The elemental analysis data for each of **II-6b-BBN** and **II-6c-BBN** are consistent with the presence of one molecule of water per two molecules of product, a phenomenon reported for other boron complexes.[II61]



Scheme II.S-1. Boron Complexation of 1-Acyldipyrromethanes

III. Alternative Routes to *trans*-A_2B_2-Porphyrins.

The success of the 1-acyldipyrromethane condensation to give *trans*-A_2B_2-porphyrins prompted examination of other routes to meso-substituted porphyrins under the same basic, magnesium-mediated conditions.

A. Condensation of a Dipyrromethane and an Aldehyde. As an alternative route to *trans*-A_2B_2-porphyrins, we explored the condensation of a dipyrromethane with an aldehyde in the presence of DBU (10 mol equiv versus dipyrromethane) and $MgBr_2$ (3-6 mol equiv versus dipyrromethane depending on the number of nitrogens possessing a non-bonding electron pair). The reaction was carried out overnight in toluene at 115 °C. The results from the exploratory study are shown in Table II.S-2. The condensation of aldehydes was examined initially with 5-phenyldipyrromethane (**II-4c**) or 5-(4-methylphenyl)dipyrromethane (**II-4b**) (entries 1-6). The scope of substituents examined includes electron-releasing groups, an electron-withdrawing group, bulky substituents, or –H. Among the aldehydes, the presence of an electron-withdrawing group or an alkyl chain afforded only a trace of the corresponding porphyrin (entries 2 and 3). Aldehydes having an electron-releasing group afforded better yields (entries 1 and 4), whereas poor yields were obtained with aldehydes bearing bulky substituents (entries 5 and 6). Paraformaldehyde and 1-formyldipyrromethane afforded only a trace of porphyrin (entry 7).

Except for one trial (entry 8), all other attempts to obtain porphyrins bearing meso-heteroaryl groups gave a trace of product (entries 9-15).

In summary, the condensation 5-phenyldipyrromethane (**II-4c**) and *p*-tolualdehyde gave the *trans*-A_2B_2-porphyrin **II-Mg-S10** in 20% yield (entry 1). A broad examination of this route with different substrates indicated somewhat limited scope; however, the success in a number of cases under the non-basic conditions may prove useful in selected applications.

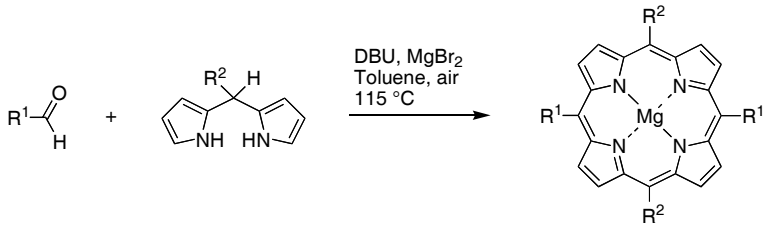


Table II.S-2. Synthesis of *trans*-A_2B_2-Porphyrins via a Dipyrromethane and an Aldehyde[a]

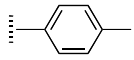
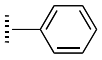
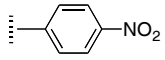
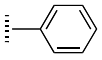
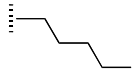
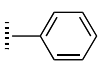
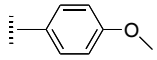
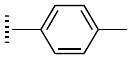
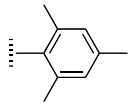
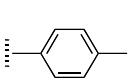
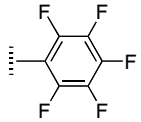
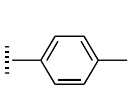
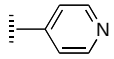
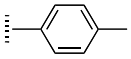
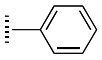
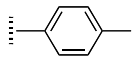
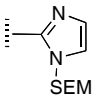
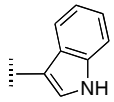
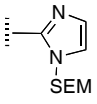
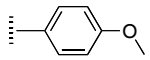
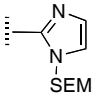
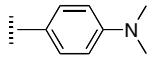
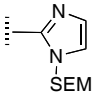
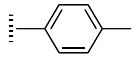
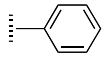
Entry	R^1	R^2	DBU (mol equiv)	$MgBr_2$ (mol equiv)	Porphyrin	Yield[b] (%)
1			10	3	**II-Mg-S10**	20
2			10	3	**II-Mg-S1**	trace
3			10	3	**II-Mg-S2**	trace
4			10	3	**II-Mg-1b**	33
5			10	3	**II-Mg-1i**	5
6			10	3	**II-Mg-1h**	trace
7			10	3	**II-Mg-porphine**	trace

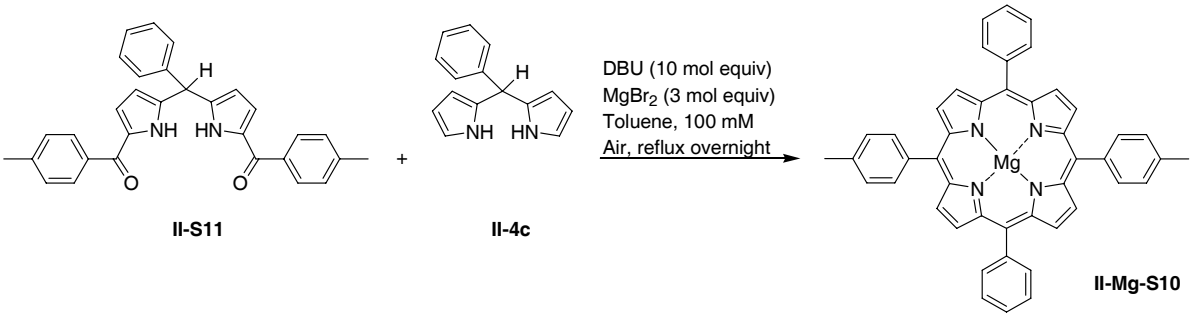
Table II.S-2. (continued)

8			10	3	**II-Mg-1g**	12
9			10	3	**II-Mg-S3**	trace
10			10	6	**II-Mg-S4**	2
11			10	6	**II-Mg-S5**	trace
12			10	6	**II-Mg-S6**	3
13			10	6	**II-Mg-S7**	5
14			10	3	**II-Mg-S8**	Trace
15		Pyrrole[c]	10	3	**II-Mg-S9**	Trace

[a]The standard conditions entail use of a dipyrromethane (0.20 mmol), an aldehyde (0.20 mmol), DBU (4.0 mmol), $MgBr_2$ (1.2–2.4 mmol depending on the number of nitrogens) and toluene (4.0 mL) at 115 °C exposed to air unless noted otherwise. [b]The porphyrin was purified by column chromatography. Owing to the small quantity of solid porphyrin, gravimetry was not performed. Instead, the solid sample was dissolved in a known volume of solvent, and the yield was determined by absorption spectrometry using the molar absorption coefficient of a metalloporphyrin at the Soret band of 500,000 $M^{-1}cm^{-1}$. This procedure is referred to as the "yield of isolated porphyrin determined by absorption spectrometry." [c]Pyrrole was used instead of a dipyrromethane.

B. Condensation of a Dipyrromethane and a 1,9-Diacyldipyrromethane. The basic, magnesium-mediated reaction conditions were applied to the condensation of a dipyrromethane and a 1,9-diacyldipyrromethane as an alternative means of obtaining *trans*-A_2B_2 porphyrins (Scheme II.S-2). Thus, the reaction of 1,9-bis(4-methylbenzoyl)-5-phenyldipyrromethane (**II-S11**)[II55] and 5-phenyldipyrromethane (**II-4c**)[II61] was performed under the standard conditions for

macrocycle formation [$MgBr_2$ (3 mol equiv) and DBU (10 mol equiv) in toluene at 115 °C exposed to air]. The method afforded the porphyrin **II-Mg-S10** in poor yield (3%) together with an unknown side product. No further study was performed on this route.



Scheme II.S-2. Condensation of a Dipyrromethane and 1,9-Diacyldipyrromethane.

IV. Chromatographic Separation of Porphyrins.

The isolation of the magnesium porphyrins often was carried out by chromatography on alumina. To assess the grade of alumina required, an initial TLC analysis was performed. The assessment was done on silica because alumina TLC gave poor separation.

Porphyrins that were fairly mobile on TLC analysis (silica, CH_2Cl_2) were then purified preparatively on alumina grade I. Those porphyrins that were bound very tightly on TLC analysis (silica, CH_2Cl_2) were chromatographed on alumina grade V. Grade V alumina was obtained by adding water to the alumina (15 g of water to 85 g of alumina).[II93] The magnesium porphyrins were isolated in a straightforward manner using this method.

The statistical reactions employed herein afford readily separable mixtures of at most three porphyrins. One example is shown in Figure S1, for the condensation of the 1-acyldipyrromethane bearing two 4-pyridyl groups (**II-6m**) and the 1-acyldipyrromethane bearing

two pentyl groups (**II-6r**). In this case, the meso-tetrapentylporphyrin is not observed; the A_4-porphyrin is *meso*-tetra-*p*-pyridylporphyrin, and the 'hybrid' porphyrin is a *cis*-A_2B_2-porphyrin that contains two pentyl groups and two *p*-pyridyl groups. The elution pattern shown in Figure II.S1 is typical for the statistical reactions described herein.

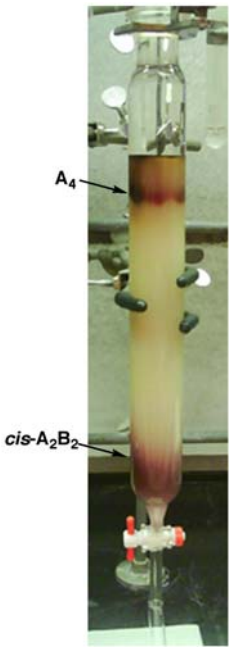


Figure II.S1. Chromatography column (silica, ~30 cm) showing elution of the mixture containing *meso*-tetra-*p*-pyridylporphyrin (denoted A_4) and the 5,10-dipentyl-15,20-di-p-pyridylporphyrin (denoted *cis*-A_2B_2).

V. Magnesiation of a Free Base Porphyrin.

We previously described a room-temperature method for magnesium insertion in free base porphyrins[II54] that entails a magnesium halide (e.g., MgI_2) and a non-nucleophilic nitrogenous base (e.g., triethylamine) in a non-coordinating solvent (e.g., CH_2Cl_2, toluene). Here, treatment of *trans*-A_2B_2-porphyrin **II-S10** with MgI_2 (10 mol equiv versus **II-S10**) and DBU (20 mol equiv versus **II-S10**) in CH_2Cl_2 at room temperature gave complete metalation in 4 h, whereupon **II-Mg-S10** was isolated in 91% yield. The same reaction was carried out using *trans*-A_2B_2-porphyrin **II-S10** with $MgBr_2$ (3 mol equiv) and DBU (10 mol equiv) in toluene at room temperature, which gave quantitative metalation upon examination after overnight reaction. The facile magnesium insertion into a free base porphyrin under these conditions indicates that formation of the magnesium porphyrin in the 1-acyldipyrromethane condensation in and of itself does not prove that the condensation proceeds via a templated process.

VI. Comparison of Routes to *trans*-A_2B_2-Porphyrins via 1-Acyldipyrromethanes.

1-Acyldipyrromethanes undergo condensation to afford the metal chelate of a *trans*-A_2B_2-porphyrin under basic conditions.[II5] The reaction entails condensation of two molecules of the 1-acyldipyrromethane in refluxing ethanol containing KOH (5-10 mol equiv) and

$Pd(CH_3CN)_2Cl_2$ (0.6 mmol equiv) exposed to air. The direct one-flask synthesis of magnesium *trans*-A_2B_2-porphyrins in the presence of $MgBr_2$ (3 mol equiv) and DBU (10 mol equiv) in hot toluene has a number of attractive features. A comparison of the two routes (palladium porphyrin synthesis and magnesium porphyrin synthesis) is provided in Table II.S-3.

Table II.S-3. Comparison of Routes to *trans*-A_2B_2-Porphyrins

Features	**Pd-porphyrin**[a]	**Mg-porphyrin**[b]
Porphyrin formation (mM)[c]	32	100
Chelate	Palladium(II)	Magnesium(II)
Solvent	Ethanol	Toluene
Base	KOH	DBU
Typical Yield (%)	25-53	45-69
Scale (mmol)	1	~3
Time (h)	2	overnight
Temperature (°C)	75	115 or 135[d]

[a]Route to palladium porphyrin. [b]Route to magnesium porphyrin. [c]Concentration of 1-acyldipyrromethane that was reported to give the highest yield of porphyrin, or most generally employed. [d]The oil bath temperature was set at 115 or 135 °C. The boiling point of toluene is 115 °C. The reaction mixture was generally found to be 115 °C upon direct measurement of the reaction contents for the two oil bath temperatures.

Similar to the one-flask synthesis of a *trans*-A_2B_2-palladium porphyrin[II5] and by contrast with the dipyrromethane-1-carbinol condensation, the synthesis described herein does not require (1) reduction of the 1-acyldipyrromethane, (2) acid-catalyzed condensation, (3) oxidation of the porphyrinogen intermediate with quinone derivatives, and (4) a separate step for metal insertion.

In both procedures, formation of porphyrin was achieved under basic conditions, which sidesteps acidolytic scrambling processes. Additionally, the route developed herein enables (1) use of an inexpensive metal reagent ($MgBr_2$) instead of an expensive palladium reagent [$Pd(CH_3CN)_2Cl_2$], (2) synthesis of free base porphyrins via demetalation of magnesium porphyrins, (3) synthesis at modestly high concentration (100 mM), (4) yields up to if not exceeding 65%, (5) synthesis of multimilligram quantities (e.g., 0.674 g), (6) synthesis of porphyrins possessing heterocycles at the meso-positions, (7) synthesis of porphyrins bearing bulky groups (e.g., pentafluorophenyl, mesityl) at the meso-positions, and (8) the use of basic groups (e.g., pyridyl), which are rather incompatible with acid-catalysis conditions.

VII. Experimental Section.

Microwave experiments were performed using a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC), which was equipped with an infrared sensor for temperature monitoring. The reaction vessels were 10 mL crimp-sealed thick-wall glass tubes equipped with a pressure sensor. The contents of each vessel were stirred with a magnetic stirrer. Silica gel (40 μm average particle size) was used for column chromatography. Alumina chromatography was carried out with alumina grade I unless noted otherwise (denoted "alumina"). In a number of

instances, alumina grade V[II93] was employed and is noted as such.

Noncommercial Compounds. Dipyrromethanes **II-4a**,[II53] **II-4b**,[II2] **II-4c**,[II55] **II-4d**,[II56] **II-4f**,[II55] **II-4g**,[II55] **II-4h**,[II57] **II-4i**,[II58] **II-4j**,[II16] **II-4k**,[II16] **II-4l**,[II16] and **II-4n**;[II59] Mukaiyama reagents **II-5a**,[II53] **II-5b**,[II61] **II-5h**,[II61] and **II-5i**;[II61] 1-acyldipyrromethanes **II-6a**,[II53] **II-6g**,[II12] **II-6j′**,[II65] and **II-6r**;[II65] 1-formyldipyrromethanes **II-6x**[II64] and **II-6z**;[II8] and 1,9-diacyldipyrromethane **II-S10**[II61] were synthesized as described in the literature. The known compounds **II-5c**,[II61] **II-5d**,[II62] **II-5g**,[II12] and **II-5k**[II63] were prepared according to a new procedure. Dipyrromethane **II-4e**, described previously without full characterization,[II48] was prepared here by the published procedure[II55] (with slight modification) in 32% yield, as described below.

New Porphyrins. The following porphyrins are new and the syntheses are described herein: metalloporphyrins **II-Mg-1a**, **II-Mg-1b**, **II-Mg-1c**, **II-Mg-1f**, **II-Mg-1g**, **II-Mg-1h**, **II-Mg-1j**, **II-Mg-1i**, **II-Mg-1o**, **II-Mg-1v**, **II-Mg-S5**, **II-Mg-S6**, **II-Mg-S7**, **II-Mn-1a**, **II-Fe-1a**, **II-Co-1a**, **II-Ni-1a**, **II-Cu-1a**, **II-Pd-1a**, and **II-In-1a**; and free base porphyrins **II-1a**, **II-1n**, **II-1o**, **II-1p**, **II-2b**, **II-2d**, **II-2e**, **II-2f**, **II-2g**, **II-3a**, **II-3b**, **II-3c**, **II-3c-MeI$_2$**, **II-3d**, **II- II-3e**, and **II-3f**.

Known Porphyrins. Metalloporphyrins **II-Mg-1e**,[II42] **II-Mg-1m**,[II85] **II-Mg-porphine**[II8] **II-Mg-S4**,[II59] and **II-Mg-S10**[II2] are known, as are free base porphyrins **II-1b**,[II86] **II-1e**,[II42] **II-1f**,[II17] **II-1g**,[II12] **II-1h**,[II87] **II-1j**,[II88] **II-1k**,[II89] **II-1l**,[II90] **II-1m**,[II91] **II-1r**,[II92] **II-1v**,[II23] **II-1w**,[II18] **II-1y**,[II58] **II-2c**,[II18] **II-2h**,[II18] and **II- S10**.[II4]

Yield Determination. In a small-scale reaction, the porphyrin was purified and isolated by column chromatography. Owing to the small quantity of solid porphyrin, gravimetry was not performed. Instead, the solid sample was dissolved in a known volume of solvent, and the yield was determined by absorption spectrometry, using the assumed molar absorption coefficient of a

metalloporphyrin at the Soret band of 500,000 $M^{-1}cm^{-1}$. This procedure is referred to as the "yield of isolated porphyrin determined by absorption spectrometry."

Dipyrromethanes

5-Ethyldipyrromethane (II-4d). Following a reported procedure[II55] with slight modification (degassing was omitted given the low boiling point of the aldehyde), a solution of propionaldehyde (3.61 mL, 50.0 mmol) in pyrrole (347 mL, 5.00 mol) at room temperature under argon was treated with $InCl_3$ (1.11 g, 5.00 mmol) for 1.5 h. Powdered NaOH (6.00 g, 150 mmol) was added. After stirring for 1 h, the mixture was suction filtered. Excess pyrrole was removed from the filtrate under high vacuum, leaving a brown oily product. Chromatography of the latter [silica, hexanes/CH_2Cl_2 (1:1) → (2:3)] afforded a yellow solid (4.31 g, 49%): mp 39–41 °C; ^{1}H NMR δ 0.91 (t, J = 7.4 Hz, 3H), 1.92–1.99 (m, 2H), 3.83 (m, J = 7.4 Hz, 1H), 6.07–6.11 (m, 2H), 6.14–6.16 (m, 2H), 6.57–6.58 (m, 2H), 7.46–7.62 (br, 2H); ^{13}C NMR δ 12.5, 27.8, 39.7, 105.8, 108.2, 117.3, 133.7; ESI-MS obsd 175.1231, calcd 175.1229 [$(M + H)^+$, M = $C_{11}H_{14}N_2$]. Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C 75.98; H, 8.26; N, 16.08.

5-Propyldipyrromethane (II-4e). Following a reported procedure[II55] with slight modification (degassing was omitted given the low boiling point of the aldehyde), a solution of butyraldehyde (4.48 mL, 50.0 mmol) in pyrrole (347 mL, 5.00 mol) at room temperature under argon was treated with $InCl_3$ (1.11 g, 5.00 mmol) for 1.5 h. Powdered NaOH (6.00 g, 150 mmol) was added. After stirring for 1 h, the mixture was suction filtered. Excess pyrrole was removed from the filtrate under high vacuum, leaving a white solid. Chromatography of the latter [silica, hexanes/CH_2Cl_2 (2:3) → (1:1) → CH_2Cl_2] afforded a colorless liquid (2.99 g, 32%): ^{1}H NMR (300 MHz) δ 0.88–0.93 (m, 3H), 1.25–1.35 (m, 2H), 1.89–2.03 (m, 2H), 3.97 (m, J = 7.5 Hz,

1H), 6.02–6.11 (m, 2H), 6.12–6.19 (m, 2H), 6.61–6.68 (m, 2H), 7.58–7.86 (br, 2H); ^{13}C NMR (75 MHz) δ 14.1, 20.9, 36.8, 37.5, 105.6, 108.2, 117.2, 133.8; ESI-MS obsd 189.1385, calcd 189.1386 [$(M + H)^+$, M = $C_{12}H_{16}N_2$]. Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88. Found: C 76.79; H, 8.53; N, 14.44.

5-(1-Methylsulfonylpyrrole-2-yl)dipyrromethane (II-4m). Following a reported procedure,[II55] a solution of 1-methylsulfonylpyrrole-2-carboxaldehyde[II60] (4.32 g, 25.0 mmol) in pyrrole (174 mL, 2.50 mol) was degassed by a stream of argon for 30 min. A sample of $InCl_3$ (0.555 g, 2.50 mmol) was added, and the resulting mixture was stirred at room temperature. After 1.5 h, GC analysis showed no starting material. Powdered NaOH (3 g) was added, and the reaction mixture was stirred for 45 min. The reaction mixture was filtered. The filter cake was washed with pyrrole. The filtrates were combined and concentrated. The resulting oil was entrained with hexanes, and volatile components were evaporated under vacuum. This entrainment and evaporation procedure was repeated four times. The resulting oil was filtered through a pad of silica (CH_2Cl_2) to afford a colorless oil, which slowly solidified to a white solid (6.46 g, 89%): mp 115–117 °C; ^{1}H NMR δ 2.43 (s, 3H), 5.92–5.94 (m, 1H), 5.96–5.98 (m, 2H), 6.06 (s, 1H), 6.14–6.16 (m, 1H), 6.16–6.20 (m, 2H), 6.70–6.72 (m, 2H), 7.12–7.13 (m, 1H), 8.02–8.12 (br, 2H); ^{13}C NMR δ 35.9, 41.8, 107.7, 108.9, 111.2, 113.6, 117.5, 122.8, 130.4, 136.6; ESI-MS obsd 290.0964 calcd 290.0957 [$(M + H)^+$, M = $C_{14}H_{15}N_3O_2S$]. Anal. Calcd for $C_{14}H_{15}N_3O_2S$: C, 58.11; H, 5.23; N, 14.52. Found: C, 58.10; H, 5.25; N, 14.37.

Mukaiyama Reagents (via Method II.1)

***S*-2-Pyridyl 2-(methoxycarbonyl)propionothioate (II-5d).** Following Method II.1 with slight modification, a solution of 2-mercaptopyridine (5.55 g, 50.0 mmol) in THF (50 mL) was treated with methyl 4-chloro-4-oxobutyrate (6.09 mL, 50.0 mmol) to give a crude oil. The oil

was treated with a biphasic solution of saturated aqueous $NaHCO_3$ and diethyl ether. The mixture was extracted. The organic layer was concentrated to afford a yellow oil (10.3 g, 92%): ^{1}H NMR δ 2.71 (t, *J* = 7.0 Hz, 2H), 3.06 (t, *J* = 7.0 Hz, 2H), 3.70 (s, 3H), 7.27–7.31 (m, 1H), 7.62–7.63 (m, 1H), 7.72–7.76 (m, 1H), 8.63 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR δ 29.0, 38.8, 52.2, 123.8, 130.4, 137.4, 150.7, 151.3, 172.4, 195.4; ESI-MS obsd 226.0531, calcd 226.0532 [$(M + H)^+$, M = $C_{10}H_{11}NO_3S$]. Anal. Calcd for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C 52.98; H, 5.08; N, 6.20.

***S*-2-Pyridyl picolinothioate (II-5e).** Following Method II.1, solution of 2-mercaptopyridine (2.78 g, 25.0 mmol) in THF (50 mL) was treated with picolinoyl chloride hydrochloride (4.45 g, 25.0 mmol) to afford a yellow solid (4.24 g, 81%): mp 89–91 °C; ^{1}H NMR δ 7.32–7.35 (m, 1H), 7.54–7.57 (m, 1H), 7.68–7.70 (m, 1H), 7.76–7.80 (m, 1H), 7.85–7.90 (m, 1H), 7.94–7.97 (m, 1H), 8.70–8.72 (m, 1H), 8.74–8.75 (m, 1H); ^{13}C NMR δ 121.0, 123.8, 128.5, 131.0, 137.3, 137.6, 149.4, 150.9, 151.3, 152.4, 191.8; FAB-MS obsd 217.0427, calcd 217.0436 [$(M + H)^+$, M = $C_{11}H_8N_2OS$]. Anal. Calcd for $C_{11}H_8N_2OS$: C, 61.09; H, 3.73; N, 12.95. Found: C 61.27; H, 3.70; N, 13.03.

***S*-2-Pyridyl nicotinothioate (II-5f).** Following Method II.1, a solution of 2-hydrochloride (8.90 g, 50.0 mmol) to afford a yellow oil. The resulting oil solidified upon entrainment with hexanes (7.95 g, 74%): mp 65–66 °C; ^{1}H NMR δ 7.35–7.40 (m, 1H), 7.44–7.48 (m, 1H), 7.72–7.76 (m, 1H), 7.80–7.85 (m, 1H), 8.25–8.29 (m, 1H), 8.69–8.71 (m, 1H), 8.83, 8.85 (m, 1H), 9.23–9.25 (m, 1H); ^{13}C NMR δ 123.9, 124.2, 131.1, 132.5, 135.1, 137.6, 148.9, 150.5, 151.0, 154.5, 188.3; FAB-MS obsd 217.0428, calcd 217.0436 [$(M + H)^+$, M = $C_{11}H_8N_2OS$]. Anal. Calcd for $C_{11}H_8N_2OS$: C, 61.09; H, 3.73; N, 12.95. Found: C, 61.08; H, 3.73; N, 12.92.

***S*-2-Pyridyl isonicotinothioate (II-5g).** Following Method II.1, a solution of 2-mercaptopyridine (5.55 g, 50.0 mmol) in THF (50.0 mL) was treated with isonicotinoyl chloride hydrochloride (8.46 g, 50.0 mmol) to afford a light yellow solid (11.2 g, 92%): mp 115 °C (lit.[II12] mp 115 °C); ^{1}H NMR δ 7.34–7.38 (m, 1H), 7.69–7.72 (m, 1H), 7.78–7.82 (m, 3H), 8.67–8.69 (m, 1H), 8.82–8.83 (m, 2H); ^{13}C NMR δ 120.6, 124.3, 130.9, 137.7, 142.9, 150.3, 151.0, 151.3, 189.1; FAB-MS obsd 217.0444, calcd 217.0436 ($C_{11}H_8N_2OS$). Anal. Calcd for $C_{11}H_8N_2OS$: C, 61.09; H, 3.73; N, 12.95. Found: C 59.05; H, 3.47; N, 12.39. The elemental analysis data are consistent with the presence of one molecule of water per two molecules of product.

***S*-2-Pyridyl pentanothioate (II-5j).** Following Method II.1, a solution of 2-mercaptopyridine (2.78 g, 25.0 mmol, in 25.0 mL of THF) and valeryl chloride (3.0 mL, 25 mmol) was stirred for 30 min. No precipitate was observed. The reaction mixture was stirred for 3 h. The general procedure afforded a yellow oil (4.66 g, 96%): ^{1}H NMR δ (300 MHz) 0.94 (t, *J* = 7.4 Hz, 3H), 1.35–1.47 (m, 2H), 1.67–1.77 (m, 2H), 2.71 (t, *J* = 7.4 Hz, 2H), 7.26–7.31 (m, 1H), 7.60–7.63 (m, 1H), 7.71–7.77 (m, 1H), 8.61–8.64 (m, 1H); ^{13}C NMR (75 MHz) δ 13.5, 21.8, 27.2, 43.7, 123.2, 129.8, 136.8, 150.1, 151.4, 196.1; ESI-MS obsd 196.0790, calcd 196.0790 [$(M + H)^+$, M = $C_{10}H_{13}NOS$]. Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.50; H, 6.71; N, 7.17. Found: C 61.26; H, 6.79; N, 7.20.

***S*-2-Pyridyl propionothioate** (**II-5k**). Following Method II.1 with slight modification, a solution of 2-mercaptopyridine (5.55 g, 50.0 mmol) in THF (50 mL) was treated with propionyl chloride (4.30 mL, 50.0 mmol) to give a crude oil. The oil was treated with a biphasic solution of saturated aqueous $NaHCO_3$ and diethyl ether. The mixture was extracted. The organic layer was concentrated to afford a yellow oil (8.01 g, 96%): ^{1}H NMR δ 1.24 (t, *J* = 5.8 Hz, 3H), 2.74 (q, *J* = 5.8 Hz, 2H), 7.26–7.30 (m, 1H), 7.60–7.62 (m, 1H), 7.72–7.76 (m, 1H), 8.61–8.63 (m,

1H); ^{13}C NMR δ 9.7, 37.9, 123.7, 130.4, 137.3, 150.6, 151.8, 197.5; FAB-MS obsd 168.0479, calcd 168.0477 [$(M + H)^+$, M = C_8H_9NOS]; Anal. Calcd for C_8H_9NOS: C, 57.46; H, 5.42; N, 8.38. Found: C 57.17; H, 5.44; N, 8.41.

Dialkylboron Complexation and Decomplexation of 1-Acyldipyrromethanes.

General Procedure for the Boron Complexation of 1-Acyldipyrromethanes.[II65] A solution of EtMgBr (30.0 mL, 30 mmol, 1.0 M in THF) was added slowly to a solution of the 1-acyldipyrromethane (15.0 mmol) in THF (30 mL) under argon. The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of Mukaiyama reagent (15.0 mmol) in THF (30 mL) was added. The solution was stirred at –78 °C for 10 min, and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and filtered. The filtrate was concentrated. The crude product (a brown oil) was dissolved in CH_2Cl_2 (30 mL) and treated with triethylamine (5.0 mL, 36 mmol) followed by 9-BBN-OTf (60.0 mL, 30 mmol, 0.5 M in hexane) with stirring at room temperature. A precipitate was formed that largely consisted of the salt of triethylamine and triflic acid. After 1 h, the crude product was filtered through a pad of silica [6 x 20 cm, CH_2Cl_2/hexanes (1:1)]. The product eluted as a fast-moving band, which upon concentration afforded the product.

General Procedure for Dialkylboron Decomplexation.[II65] A sample of 1-acyldipyrromethane–boron complex (2.04 mmol) in THF (3.2 mL) was treated with 1-pentanol (0.8 mL). The reaction mixture was heated at reflux. After 1 h, TLC (silica, CH_2Cl_2) examination showed complete consumption of the starting material. The mixture was concentrated, and the resulting oily residue was subjected to a high vacuum to remove trace

amount of pentanol. The resulting oily residue was treated with hexanes (25 mL). The oil solidified upon standing for 15 min, and the mixture was heated gently under reflux for 10 min whereupon the solid dissolved completely. The solution was cooled, affording a precipitate upon standing for a few hours. The hexanes was decanted and saved. The precipitate was collected and dissolved in a minimum amount of CH_2Cl_2 (0.5 mL); addition of hexanes afforded the title compound as a precipitate. The precipitate was collected and dried in vacuo to afford a yellow powder. The decanted hexanes solution from above was concentrated to half of the starting volume. The resulting precipitate was separated and dissolved in a minimum amount of CH_2Cl_2. Treatment with hexanes yielded additional title compound as a precipitate.

10-(9-Borabicyclo[3.3.1]non-9-yl)-1-(4-methoxybenzoyl)-5-(4-methylphenyl)-dipyrromethane (II-6b-BBN). Following the method for dialkylboron complexation, reaction of EtMgBr (30 mL, 30 mmol, 1.0 M in THF), **II-4b** (3.54 g, 15.0 mmol, in 30 mL of THF), **II-5b** (3.68 g, 15.0 mmol, in 30 mL of THF) and 9-BBN-OTf (60.0 mL, 30 mmol, 0.50 M in hexane) afforded a yellow–orange solid (3.49 g, 41%): mp 139–140 °C; ^{1}H NMR δ 0.65–0.69 (m, 2H), 1.71–2.32 (m, 12H), 2.32 (s, 3H), 3.92 (s, 3H), 5.81–5.85 (m, 1H), 5.97 (s, 1H), 6.13–6.16 (m, 1H), 6.31 (d, J = 4.0 Hz, 1H), 6.69–6.71 (m, 1H), 7.04–7.11 (m, 6H), 7.29 (d, J = 4.4 Hz, 1H), 7.81–7.85 (brs, 1H), 8.21 (d, J = 8.8 Hz, 2H); ^{13}C NMR δ 21.3, 24.0, 25.2, 26.1, 26.5, 30.7, 31.0, 34.7, 34.72, 44.5, 55.9, 108.0, 108.6, 114.7, 117.4, 117.8, 120.6, 123.6, 128.5, 129.4, 132.1, 132.9, 134.6, 136.7, 139.3, 151.7, 164.4, 173.9; FAB-MS obsd 490.2815, calcd 490.2792 ($C_{32}H_{35}BN_2O_2$). Anal. Calcd for $C_{32}H_{35}BN_2O_2$: C, 78.37; H, 7.19; N, 5.71. Found: C, 76.91; H, 7.50; N, 5.45. The elemental analysis data are consistent with the presence of one molecule of water per two molecules of product.

Decomplexation of II-6b-BBN affording II-6b. Following the method for dialkylboron decomplexation, a sample of **II-6b-BBN** (1.00 g, 2.04 mmol) was treated in pentanol at reflux to afford a yellow powder (0.631 g, 83%). Treatment with hexanes yielded additional precipitate (0.053 g). The combined yield was 0.684 g (91%): mp 61–62 °C; ^{1}H NMR δ 2.34 (s, 3H), 3.88 (s, 3H), 5.49 (s, 1H), 5.96–6.00 (m, 1H), 6.06–6.07 (m, 1H), 6.16–6.18 (m, 1H), 6.69–6.72 (m, 1H), 6.79–6.81 (m, 1H), 6.95 (d, *J* = 9.2 Hz, 2H), 7.10–7.15 (m, 4H), 7.87 (d, *J* = 9.2 Hz, 2H), 7.97–7.99 (brs, 1H), 9.33–9.34 (brs, 1H); ^{13}C NMR δ 21.3, 44.0, 55.7, 107.8, 108.5, 110.6, 113.8, 117.9, 120.5, 128.4, 129.6, 130.9, 131.2, 131.4, 131.6, 137.0, 138.2, 141.9, 162.9, 183.8; FAB-MS obsd 370.1697, calcd 370.1681 ($C_{24}H_{22}N_2O_2$). Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.64; H, 6.34; N, 7.77.

10-(9-Borabicyclo[3.3.1]non-9-yl)-1-hexanoyl-5-(4-methylphenyl)dipyrromethane (II-6c-BBN). Following the method for dialkylboron complexation, reaction of EtMgBr (30 mL, 30 mmol, 1.0 M in THF), **II-4b** (3.54 g, 15.0 mmol, in 30 mL of THF), **II-5c** (3.14 g, 15.0 mmol, in 30 mL of THF), and 9-BBN-OTf (60.0 mL, 30 mmol, 0.5 M in hexane) gave an oily product. Column chromatography afforded a brown paste (1.48 g, 23%): ^{1}H NMR δ 0.55–0.58 (m, 2H), 0.88–0.93 (m, 3H), 1.37–1.41 (m, 4H), 1.83–1.97 (m, 2H), 1.63–2.08 (m, 12H), 2.31 (s, 3H), 2.83 (t, *J* = 7.2 Hz, 2H), 5.81–5.85 (m, 1H), 5.90 (s, 1H), 6.12–6.14 (m, 1H), 6.31 (d, *J* = 4.4 Hz, 1H), 6.72–6.73 (m, 1H), 7.11–7.18 (m, 5H), 7.81–7.84 (brs, 1H); ^{13}C NMR δ 14.2, 21.3, 24.1, 25.1, 25.6, 25.7, 26.1, 26.4. 30.7, 31.0, 31.6, 32.0, 34.37, 34.4, 44.6, 108.1, 108.7, 117.2, 117.5, 120.0, 128.5, 129.5, 132.7, 136.8, 137.0, 139.3, 152.7, 185.2; FAB-MS obsd 454.3177, calcd 454.3155 ($C_{30}H_{39}BN_2O$). Anal. Calcd for $C_{30}H_{39}BN_2O$: C, 79.29; H, 8.65; N, 6.16. Found: C, 77.64; H, 8.62; N, 6.02. The elemental analysis data are consistent with the presence of one molecule of water per two molecules of product.

Decomplexation of II-6c-BBN affording II-6c. Following the method for dialkylboron decomplexation, a solution of **II-6c-BBN** (1.12 g, 2.45 mmol) in THF (4 mL) was treated with 1-pentanol (1.0 mL). The crude product was chromatographed [silica, CH_2Cl_2/ethyl acetate (5:1)] to afford a brown paste (0.785 g, 96%): ^{1}H NMR δ 0.87–0.91 (m, 3H), 1.33–1.35 (m, 4H), 2.32 (s, 3H), 2.59–2.68 (m, 4H), 5.46 (s, 1H), 5.94–5.96 (m, 1H), 6.01–6.03 (brs, 1H), 6.14–6.15 (m, 1H), 6.69–6.70 (m, 1H), 6.82–6.83 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 8.21–8.24 (brs, 1H), 9.46–9.48 (brs, 1H); ^{13}C NMR spectroscopy was precluded owing to decomposition during an overnight analysis; FAB-MS obsd 334.2061, calcd 334.2045 ($C_{22}H_{26}N_2O$). Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 78.99; H, 7.79; N, 8.17.

1-Acyldipyrromethanes (via Method II.2)

5-(4-Methylphenyl)-1-[2-(methoxycarbonyl)propionyl]dipyrromethane (II-6d). Following Method II.2, reaction of EtMgBr (38 mL, 38 mmol, 1.0 M in THF), **II-4b** (3.55 g, 15.0 mmol, in 30 mL of THF), and **II-5d** (3.38 g, 15.0 mmol, in 30 mL of THF) afforded an oil, which upon column chromatography [silica, hexanes/CH_2Cl_2 (4:1) → CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1) 4 cm dia x 30 cm] afforded a gray solid (1.03 g, 20%): mp 138–139 °C; ^{1}H NMR δ 2.32 (s, 3H), 2.65 (t, *J* = 7.0 Hz, 2H), 3.05 (m, 2H), 3.66 (s, 3H), 5.46 (s, 1H), 5.93–5.94 (m, 1H), 6.01–6.03 (m, 1H), 6.13–6.15 (m, 1H), 6.68–6.69 (m, 1H), 6.88–6.90 (m, 1H), 7.04–7.11 (m, 4H), 8.08–8.28 (brs, 1H), 9.46–9.68 (brs, 1H); ^{13}C NMR δ 21.3, 28.5, 32.3, 43.8, 52.1, 107.8, 108.6, 110.3, 117.89, 117.9, 128.4, 129.6, 130.9, 131.6, 137.0, 138.3, 141.9, 173.7, 188.4; FAB-MS obsd 350.1636, calcd 350.1630 ($C_{21}H_{22}N_2O_3$). Anal. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99. Found: C, 71.95; H, 6.40; N, 7.85.

5-(4-Methylphenyl)-1-nicotinoyldipyrromethane (II-6f). Following Method II.2, a

solution of EtMgBr (25 mL, 25 mmol, 1.0 M in THF), **II-4b** (2.36 g, 10.0 mmol, in 20 mL of THF) and **II-5f** (2.16 g, 10.0 mmol, in 20 mL of THF) gave an oily product. Column chromatography [silica, CH_2Cl_2/ethyl acetate (7:3), 4 cm dia x 30 cm] afforded an orange oil, which consisted of a mixture of products as determined by ^{1}H NMR spectroscopy. The oil was dissolved in acetonitrile (100 mL) and treated with 2 M NaOH. The mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated, washed (water, brine), and dried (Na_2SO_4). The organic phase was concentrated to afford an orange solid. The solid was dissolved in CH_2Cl_2 and washed with saturated aqueous NH_4Cl. The organic phase was collected with CH_2Cl_2. The organic phase was washed (water, brine), dried, and concentrated to afford an orange-yellow solid. The latter was chromatographed [silica, CH_2Cl_2/ethyl acetate, (7:3)] to afford a yellow solid (2.09 g 61%): mp 64–65 °C (dec.); ^{1}H NMR δ 2.34 (s, 3H), 5.52 (s, 1H), 5.99–6.00 (m, 1H), 6.11–6.13 (m, 1H), 6.17–6.18 (m, 1H), 6.71–6.72 (m, 1H), 6.81–6.83 (m, 1H), 7.09–7.13 (m, 4H), 7.40–7.43 (m, 1H), 8.07– 8.10 (m, 1H), 8.16–8.21 (brs, 1H), 8.75–8.77 (m, 1H), 9.03–9.04 (m, 1H), 9.72–9.81 (brs, 1H); ^{13}C NMR δ 21.3, 44.1, 108.0, 108.8, 111.3, 118.1, 121.5, 123.6, 128.5, 129.8, 130.5, 131.1, 134.3, 136.5, 137.4, 137.7, 143.2, 149.9, 152.5, 182.3; FAB-MS obsd 341.1545, calcd 341.1528. Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31. Found: C, 77.36; H, 5.59; N, 12.14.

5-(4-Methylphenyl)-1-(pentafluorobenzoyl)dipyrromethane (II-6h). Following Method II.2 with modification, a solution of MesMgBr (12.3 mL, 12.3 mmol, 1.0 M in THF) was added to a solution of **II-4b** (1.16 g, 4.92 mmol) in THF (5.00 mL) under argon. The resulting mixture was treated with a solution of **II-5h** (1.50 g, 4.92 mmol) in THF (5 mL) at –78 °C. Aqueous workup and column chromatography [silica, CH_2Cl_2/ethyl acetate (5:1), 4 cm dia x 30 cm] afforded a brown powder (1.69 g, 79%): mp 63–65 °C; ^{1}H NMR δ 2.36 (s, 3H), 5.51 (s,

1H), 6.01–6.02 (m, 1H), 6.11–6.13 (m, 1H), 6.17–6.20 (m, 1H), 6.64–6.65 (m, 1H), 6.72–6.73 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.94–7.98 (brs, 1H), 9.42–9.48 (brs, 1H); ^{13}C NMR δ 21.2, 44.1, 108.1, 108.8, 112.0, 118.2, 123.1, 128.5, 129.8, 130.6, 131.1, 136.3–136.6 (m), 137.2, 137.6, 138.9–139.2 (m), 141.0–141.3 (m), 142.8–142.9 (m), 143.5–143.8 (m), 145.3–145.5 (m), 145.6, 171.8; FAB-MS obsd 430.1123, calcd 430.1105 ($C_{23}H_{15}F_5N_2O$). Anal. Calcd for $C_{23}H_{15}F_5N_2O$: C, 64.19; H, 3.51; N, 6.51. Found: C, 63.71; H, 3.42; N, 6.33.

5-(4-Methylphenyl)-1-(2,4,6-trimethylbenzoyl)dipyrromethane (II-6i). Following Method II.2 with modification, **II-4b** (2.00 g, 8.46 mmol) in THF (8.50 mL) was treated with MesMgBr (17.0 mL, 17 mmol, 1.0 M in THF). The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of 2,4,6-trimethylbenzoyl chloride (**II-5l**, 1.55 g, 8.46 mmol) in THF (8.5 mL) was added. The solution was stirred at –78 °C for 10 min, then allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic extract was washed (water, brine), dried (Na_2SO_4) and concentrated. The resulting product was purified by column chromatography [silica, hexanes/CH_2Cl_2/ethyl acetate (7:2:1), 4 cm dia x 30 cm] to afford a yellow powder (0.874 g, 27%): mp 79–81 °C; ^{1}H NMR δ 2.14 (s, 3H), 2.16 (s, 3H), 2.30 (s, 3H), 2.34 (s, 3H), 5.48 (s, 1H), 5.95–5.97 (m, 1H), 6.01–6.02 (m, 1H), 6.15–6.17 (m, 1H), 6.34–6.44 (brs, 1H), 6.64–6.68 (m, 1H), 6.85 (s, 2H), 7.09–7.163 (m, 4H), 8.03–8.12 (brs, 1H), 9.21–9.38 (brs, 1H); ^{13}C NMR δ 19.6, 21.3, 21.4, 44.1, 107.8, 108.6, 110.9, 118.0, 121.1, 128.4, 128.5, 129.5, 129.8, 131.1, 132.4, 134.7, 134.8, 136.9, 137.2, 137.8, 138.5, 142.6, 189.1; FAB-MS obsd 382.2050, calcd 382.2045 ($C_{26}H_{26}N_2O$).

1- Picolinoyl-5-(2-pyridyl)dipyrromethane (II-6k). Following Method II.2 with slight modification, reaction of EtMgBr (12.5 mL, 12.5 mmol, 1.0 M in THF), **II-4j** (1.12 g, 5.00 mmol

in 10 mL of THF) and **II-5e** (1.08 g, 5.00 mmol, in 5 mL of THF) followed by chromatography [silica, CH_2Cl_2/ethyl acetate (4:1 → 3:1)] afforded the desired product, together with an unidentified byproduct (observed as a colorless spot on TLC, and by ^{1}H NMR spectroscopy). The resulting mixture was dissolved in CH_2Cl_2 (~50 mL) and washed with saturated aqueous $NaHCO_3$ (3 x 500 mL). The organic layer was dried (Na_2SO_4), and concentrated. The resulting product was chromatographed (silica, CH_2Cl_2/ethyl acetate (3:1)] to obtain a light yellow foam, which turned orange upon storage at room temperature (0.544 g, 33%): mp 108–110 °C; ^{1}H NMR (300 MHz, THF-d_8) δ 5.64 (s, 1H), 5.89–5.90 (m, 1H), 5.97–6.01 (m, 2H, two signals overlapped), 6.63–6.66 (m, 1H), 7.17–7.25 (m, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.41–7.45 (br, 1H), 7.44–7.48 (m, 1H), 7.67 (dt, J = 1.8 Hz, J = 8.2 Hz, 1H), 7.88 (dt, J = 1.8 Hz, J = 8.2 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.60–8.62 (m, 1H), 8.64–8.65 (m, 1H), 9.92–10.15 (br, 1H), 11.62–12.20 (br, 1H); ^{13}C NMR (75 MHz, THF-d_8) δ 47.1, 107.9, 108.3, 110.6, 118.6, 121.2 (br), 122.8, 123.7, 124.3, 126.9, 131.5, 132.0, 137.7, 138.0, 141.4, 149.2, 150.2, 156.9, 162.4 (the signal of the carbonyl carbon atom was not observed); ESI-MS obsd 329.1404 calcd 329.1396 [$(M + H)^+$, M = $C_{20}H_{16}N_4O$]. Note that although the title compound was quite soluble in $CDCl_3$, better peak separation was obtained for ^{1}H NMR spectroscopy in THF-d_8.

1-Isonicotinoyl-5-(4-pyridyl)dipyrromethane (**II-6m).** Following Method II.2 with slight modification, reaction of EtMgBr (9.50 mL, 9.5 mmol, 1.0 M in THF), **II-4l** (0.838 g, 3.75 mmol, in 15.0 mL of THF), and **II-5g** (0.813 g, 3.75 mmol, in 15.0 mL of THF) afforded a crude brown product. The crude product was stirred at room temperature for 4 h. The resulting oil was chromatographed [silica, ethyl acetate → CH_2Cl_2/MeOH (40:1)]. The fractions containing the product were collected and concentrated to afford a yellow solid (0.745 g, 60%): mp 180 °C (dec.); ^{1}H NMR (DMSO-d_6) δ 4.77 (s, 1H), 4.92–4.96 (m, 1H), 5.08–5.14 (m, 1H), 5.22–5.26

(m, 1H), 5.84–5.88 (m, 1H), 5.91–5.96 (m, 1H), 6.32 (d, *J* = 5.6 Hz, 2H), 6.81 (d, *J* = 5.6 Hz, 2H), 7.66 (d, *J* = 5.2 Hz, 2H), 7.90 (d, *J* = 5.2 Hz, 2H), 9.92–10.4 (br, 1H), 11.41–11.52 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 42.4, 107.0, 107.2, 110.3, 117.9, 121.2, 122.2, 123.3, 129.4, 129.9, 142.6, 145.2, 149.7, 150.2, 150.9, 181.8; ESI-MS obsd 329.1396, calcd 329.1396 ($C_{20}H_{16}N_4O$). Anal. Calcd for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.91; N, 17.06. Found: C, 72.91; H, 4.90; N, 16.61.

1-Picolinoyl-5-(3-pyridyl)dipyrromethane (II-6n). Following Method II.2, reaction of EtMgBr (12.5 mL, 12.5 mmol, 1.0 M in THF), **II-4k** (1.12 g, 5.00 mmol, in 10 mL of THF), and **II-5e** (1.08 g, 5.00 mmol, in 5 mL of THF) afforded a dark oil, which upon chromatography (silica, ethyl acetate) afforded a light-pink solid (0.768 g, 47%): mp 176–177 °C; ^{1}H NMR (DMSO-d_6) δ 5.67 (s, 1H), 5.72–5.73 (m, 1H), 5.94–5.96 (m, 1H), 6.03–6.05 (m, 1H), 6.69–6.70 (m, 1H), 7.33–7.36 (m, 1H), 7.40–7.41 (m, 1H), 7.56–7.60 (m, 2H, two signals overlapped), 7.98–8.00 (m, 2H, two signals overlapped); 8.44–8.45 (m, 2H, two signals overlapped), 8.69 (d, *J* = 4.8 Hz, 1H), 10.79–10.84 (br, 1H), 12.08–12.14 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 40.6, 106.7, 107.2, 109.8, 117.8, 121.9, 123.2, 123.5, 126.4, 129.7, 130.8, 135.5, 137.5, 138.1, 142.0, 147.7, 148.7, 149.3, 155.0, 179.3; ESI-MS obsd 329.1401 calcd 329.1396 [$(M + H)^+$, M = $C_{20}H_{16}N_4O$]. Anal. Calcd for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.91; N, 17.06. Found: C, 73.14; H, 4.82; N, 17.08.

1-Isonicotinoyl-5-(3-pyridyl)dipyrromethane (**II-6o**)**.** Following Method II.2 with slight modification, reaction of EtMgBr (25.0 mL, 25 mmol, 1.0 M in THF), **II-4k** (2.23 g, 10.0 mmol, in 20 mL of THF) and **II-5g** (2.16 g, 10.0 mmol, added as a solid) afforded an oil, which was chromatographed [silica, ethyl acetate → CH_2Cl_2/MeOH (10:1)]. The fractions containing the product [silica, CH_2Cl_2/MeOH (10:1)] were collected, concentrated, and chromatographed (silica, CH_2Cl_2/MeOH 20:1) to afford a yellow solid (0.956 g, 29%): mp 90–92 °C (dec.); ^{1}H

NMR δ 5.57 (s, 1H), 5.95–6.00 (m, 1H), 6.07–6.09 (m, 1H), 6.15–6.17 (m, 1H), 6.73–6.75 (m, 1H), 6.79–6.80 (m, 1H). 7.20–7.23 (m, 1H), 7.49–7.52 (m, 1H), 7.57–7.58 (m, 2H), 8.41–8.45 (m, 1H), 8.46–8.47 (m, 1H), 8.73–8.75 (m, 2H), 8.79–8.82 (brs, 1H), 10.29–10.32 (brs, 1H); ^{13}C NMR δ 42.0, 108.6, 108.9, 111.6, 118.8, 122.0, 122.5, 123.9, 129.7, 130.6, 136.2, 136.7, 142.3, 145.1, 148.8, 149.7, 150.5, 183.0; ESI-MS obsd 329.1396, calcd 329.1396 [$(M + H)^+$, M = $C_{20}H_{16}N_4O$].

1-Picolinoyl-5-(4-pyridyl)dipyrromethane (II-6p). Following Method II.2 with slight modification, reaction of EtMgBr (5.5 mL, 5.5 mmol, 1.0 M in THF), **II-4l** (0.490 g, 2.20 mmol, in 4.4 mL of THF), and **II-5e** (0.378 g, 2.20 mmol, in 2.2 mL of THF) gave an oil, which upon chromatography (silica, ethyl acetate) afforded a light-yellow-brown solid (0.385 g, 51%): mp 181–183 °C (dec.); ^{1}H NMR (THF-d_8) δ 5.57 (s, 1H), 5.76–5.78 (m, 1H), 5.94–5.96 (m, 1H), 6.00–6.02 (m, 1H), 6.67–6.69 (m, 1H), 7.14 (d, J = 6.0 Hz, 2H), 7.44–7.48 (m, 1H), 7.50–7.53 (br, 1H), 7.86–7.91 (m, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.46 (d, J = 6.0 Hz, 2H), 8.59–8.60 (m, 1H), 9.96–10.06 (br, 1H), 11.48–11.60 (br, 1H) (although compound **II-6p** is soluble in $CDCl_3$, THF-d_8 gave better peak separation); ^{13}C NMR (THF-d_8) δ 43.7, 108.6, 111.0, 118.8, 121.9 (br), 124.3, 124.5, 127.0, 131.3, 132.2, 138.0, 141.0, 148.3, 150.9, 152.0, 156.8 (the signal from the carbonyl carbon atom was not observed); ESI-MS obsd 329.1400 calcd 329.1396 [$(M + H)^+$, M = $C_{20}H_{16}N_4O$].

5-Propyl-1-pentanoyldipyrromethane (II-6s). Following Method II.2, reaction of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF), **II-4e** (1.41 g, 7.50 mmol, in 15.0 mL of THF), and **II-5j** (1.47 g, 7.50 mmol, in 15.0 mL of THF) afforded an oil, which upon chromatography [silica, CH_2Cl_2 → hexanes/ethyl acetate (3:1)] afforded a brown liquid (0.9479 g, 46%), which upon standing at –4 °C eventually solidified: mp 47–49 °C; ^{1}H NMR (300 MHz) δ 0.91 (t, J =

7.4 Hz, 6H), 1.23–1.35 (m, 4H), 1.70–1.75 (m, 2H), 1.96–2.03 (m, 2H), 2.74 (t, *J* = 7.5 Hz, 2H), 4.05–4.16 (m, 1H), 6.03–6.06 (m, 1H), 6.09–6.13 (m, 2H), 6.65–6.67 (m, 1H), 6.88–6.90 (m, 1H), 8.82–8.90 (brs, 1H), 10.06–10.24 (br, 1H); ^{13}C NMR (75 MHz) δ 14.1, 21.2, 22.9, 28.7, 36.0, 38.0, 38.1, 105.1, 108.1, 108.6, 117.4, 119.8, 131.2, 133.1, 145.2, 192.0; ESI-MS obsd 273.1962, calcd 273.1961 [$(M + H)^+$, M = $C_{17}H_{24}N_2O$]. Anal. Calcd for $C_{20}H_{16}N_4O$: C, 74.96; H, 8.88; N, 10.28. Found: C, 74.76; H, 9.03; N, 10.20.

5-Pentyl-1-propionyldipyrromethane (II-6t). Following Method II.2, reaction of EtMgBr (12.5 mL, 12.5 mmol, 1.0 M in THF), **II-4f** (1.08 g, 5.00 mmol, in 5.00 mL of THF), and **II-5k** (0.836 g, 5.00 mmol, in 5.00 mL of THF) afforded an oil, which upon chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:1)] afforded a light brown solid (0.907 g, 67%): mp 46–47 °C; ^{1}H NMR δ 0.85–0.88 (m, 3H), 1.20–1.28 (m, 9H), 1.99–2.08 (m, 2H), 2.81 (q, *J* = 5.5 Hz, 2H), 4.08 (t, *J* = 5.7 Hz, 2H), 6.03–6.05 (m, 1H), 6.10–6.13 (m, 1H), 6.65–6.67 (m, 1H), 6.91–6.93 (m, 1H), 9.05–9.12 (brs, 1H), 10.36–10.41 (brs, 1H); ^{13}C NMR δ 10.0, 14.3, 22.7, 27.6, 31.1, 31.8, 34.0, 38.3, 105.3, 108.3, 108.5, 117.4, 118.7, 130.8, 132.8, 144.0, 192.1; ESI-MS obsd 273.1962, calcd 273.1961 [$(M + H)^+$, M = $C_{17}H_{24}N_2O$].

5-Ethyl-1-propionyldipyrromethane (II-6u). Following Method II.2, reaction of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF), **II-4d** (1.31 g, 7.50 mmol, in 15.0 mL of THF), and **II-5k** (1.25 g, 7.50 mmol, in 15.0 mL of THF) afforded an oil, which upon chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (10:1)] afforded an off-white solid (1.39 g, 81%): mp 121–122°C; ^{1}H NMR δ 0.94 (t, *J* = 7.2 Hz, 3H), 1.23 (t, *J* = 7.8 Hz, 3H), 2.02–2.15 (m, 2H), 2.81 (q, *J* = 7.8 Hz, 2H), 3.99 (t, *J* = 8.0 Hz, 1H), 6.03–6.06 (m, 1H), 6.09–6.12 (m, 2H), 6.65–6.66 (m, 1H), 6.92–6.94 (m, 1H), 9.12–9.26 (br, 1H), 10.42–10.58 (br, 1H); ^{13}C NMR δ 10.0, 12.7, 27.1, 31.1, 40.1, 105.3, 108.2, 108.6, 117.4, 118.8, 130.8, 132.7, 143.9, 192.2; ESI-MS

obsd 231.1490, calcd 231.1491 [$(M + H)^+$, M = ($C_{14}H_{18}N_2O$)]. Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 72.83; H, 7.78; N, 12.04.

1-Formyldipyrromethanes (via Method II.3)

1-Formyl-5-(4-methylphenyl)dipyrromethane (II-6j). Following Method II.3, reaction of **II-4b** (3.54 g, 15.0 mmol), MesMgBr (30 mL, 30 mmol, 1 M in THF) and phenyl formate (**II-5m**, 3.27 mL, 30.0 mmol) followed by chromatography afforded a brown powder (1.616 g, 41%): mp 186–188 °C; ^{1}H NMR δ 2.34 (s, 3H), 5.47 (s, 1H), 5.95–5.96 (m, 1H), 6.09–6.11 (m, 1H), 6.16–6.17 (m, 1H), 6.70–6.72 (m, 1H), 6.89–6.91 (m, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.93–7.95 (brs, 1H), 9.09–9.12 (brs, 1H), 9.38 (s, 1H); ^{13}C NMR δ 21.3, 44.0, 108.0, 108.8, 111.0, 118.1, 122.1, 128.4, 129.8, 131.0, 132.2, 137.4, 138.2, 141.9, 178.9; FAB-MS obsd 264.1265, calcd 2364.1263 ($C_{17}H_{16}N_2O$). Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.16; H, 6.10; N, 10.58.

1-Formyl-5-(4-pyridyl)dipyrromethane (II-6w). Following Method II.3, reaction of **II-4l** (1.12 g, 5.00 mmol, in 20 mL of THF), MesMgBr (10 mL, 10 mmol, 1.0 M in THF) and **II-5m** (1.1 mL, 10 mmol) afforded a dark oil, which upon chromatography (silica, ethyl acetate) afforded a light pink solid (0.621 g, 49%): mp 181–183 °C; ^{1}H NMR (DMSO-d_6) δ 5.52 (s, 1H), 5.72–5.74 (m, 1H), 5.94–5.96 (m, 1H), 6.02–6.04 (m, 1H), 6.67–6.69 (m, 1H), 6.93–6.95 (m, 1H), 7.13 (d, *J* = 5.9 Hz, 2H), 8.48 (d, *J* = 5.9 Hz, 2H), 9.39 (s, 1H), 10.68–10.82 (br, 1H), 12.04–12.18 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 42.5, 106.9, 107.2, 109.9, 117.9, 123.3, 129.9, 132.3, 141.7, 149.6, 150.9, 178.8 (signals derived from two carbon atoms are overlapped); ESI-MS obsd 252.1132, calcd 252.1131 [$(M + H)^+$, M = $C_{15}H_{13}N_3O$].

5-Ethoxycarbonyl-1-formyldipyrromethane (II-6y). A Vilsmeier reagent was prepared by treatment of DMF (3.75 mL) with $POCl_3$ (0.56 mL, 6.0 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 10 min. A solution of **II-4i** (1.09 g, 5.00 mmol) in dry

DMF (15 mL) was treated with the freshly prepared Vilsmeier reagent (**II-5n**, 3.6 mL, 5.0 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 1.5 h, then the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature. The reaction mixture was poured into saturated aqueous sodium acetate (~50 mL) and dichloromethane (50 mL), and stirred for 1 h. The organic phase was separated, and the aqueous phase was washed with dichloromethane. The organic phase was washed (water, brine) and dried (Na_2SO_4). The mixture was concentrated, and DMF was removed under high vacuum. Chromatography of the resulting product [silica, CH_2Cl_2/ethyl acetate (5:1)] afforded an off-white solid (0.72 g, 58%): mp 129–131 °C; ^{1}H NMR (300 MHz) δ 1.30 (t, J = 7.0 Hz, 3H), 4.25 (q, J = 7.0 Hz, 2H), 5.14 (s, 1H), 6.09–6.11 (m, 1H), 6.15–6.18 (m, 1H), 6.19–6.21 (m, 1H), 6.78–6.79 (m, 1H), 6.88–6.90 (m, 1H), 8.70–8.80 (brs, 1H), 9.44 (s, 1H), 9.50–9.60 (s, 1H); ^{13}C NMR (75 MHz) δ 14.3, 44.3, 62.4, 108.2, 108.8, 110.7, 119.0, 122.6, 125.1, 132.9, 137.6, 170.6, 179.3; ESI-MS obsd 247.1078, calcd 247.1077 [$(M + H)^+$, M = $C_{13}H_{14}N_2O_3$]. Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.40; H, 5.84; N, 11.46.

1-Acyldipyrromethane Condensation (via Method II.4A). 5,15-Bis(4-methoxyphenyl)-10,20-bis(4-methylphenyl)porphinatomagnesium(II) (Mg-1b). Following Method II.4A, **II-6b** (1.00 g, 2.70 mmol, 100 mM) in toluene (27 mL) was treated with DBU (4.0 mL, 27 mmol) and $MgBr_2$ (1.50 g, 8.09 mmol). The crude product was concentrated and purified by column chromatography [alumina, 480 g, 4 cm dia × 40 cm, CH_2Cl_2/ethyl acetate (10:1 → 4:1)] to afford a purple powder (0.454 g, 46%): ^{1}H NMR (THF-d_8) δ 2.70 (s, 6H), 4.10 (s, 6H), 7.29 (d, J = 8.0 Hz, 4H), 7.55 (d, J = 8.0 Hz, 4H), 8.07–8.10 (m, 8H), 8.75–8.79 (m, 8H); ^{13}C NMR (THF-d_8) δ 22.6, 56.7, 113.5, 123.0, 123.1, 128.7, 133.0, 133.1, 136.6, 137.5, 138.2, 138.5, 143.6, 151.5, 151.8, 161.3; LD-MS obsd 724.9; FAB-MS obsd 724.2716, calcd

724.2689 ($C_{48}H_{36}MgN_4O_2$); λ_{abs} (toluene) 408, 429, 566, 604 nm.

5,15-Bis(4-methylphenyl)-10,20-dipentylporphinatomagnesium(II) (Mg-1c). Following Method II.4A, **II-6c** (0.688 g, 2.10 mmol, 100 mM) in toluene (21 mL) was treated with DBU (3.0 mL, 21 mmol) and $MgBr_2$ (1.14 g, 6.17 mmol). The crude product was concentrated and purified by column chromatography [alumina grade V, 450 g, 4 cm dia × 30 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (4:1 → 3:1), ~2.4 L] to afford a purple powder (0.209 g, 31%): ^{1}H NMR (THF-d_8) δ 0.99 (t, J = 7.4 Hz, 6H), 1.53–1.61 (m, 4H), 1.82–1.87 (m, 4H), 2.52–2.62 (m, 4H), 2.73 (s, 6H), 4.98–5.8 (m, 4H), 7.54 (d, J = 7.8 Hz, 4H), 8.08 (d, J = 7.8 Hz, 4H), 8.91 (d, J = 4.4 Hz, 4H), 9.46 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 14.5, 21.8, 23.1, 33.2, 36.2, 39.5, 120.6, 121.4, 127.2, 128.7, 132.4, 134.8, 136.7, 141.3, 149.4, 150.2; LD-MS obsd 652.8, FAB-MS obsd 652.3442, calcd 652.3416 ($C_{44}H_{44}MgN_4$); λ_{abs} (toluene) 408, 429, 569, 612 nm.

5,15-Bis(4-methylphenyl)-10,20-di-4-pyridylporphinatomagnesium(II) (II-Mg-1g). Following Method II.4A, **II-6g** (1.00 g, 2.93 mmol, 100 mM) in toluene (29 mL) was treated with DBU (4.4 mL, 29 mmol, 10 mol equiv) and $MgBr_2$ (3.24 g, 17.6 mmol, 6.0 mol equiv). The reaction mixture was concentrated and washed with MeOH to afford a purple powder (0.244 g, 25%): ^{1}H NMR (DMSO-d_6) δ 2.33–2.34 (m, 6H), 6.77 (d, J = 7.2, 4H), 7.22–7.24 (d, J = 7.2, 4H), 7.37–7.38 (m, 4H), 7.91–7.97 (m, 8H), 8.16–8.17 (m, 4H); LD-MS obsd 666.8; calcd 666.2382; no ESI-MS signal was observed because of low solubility ($C_{44}H_{30}MgN_6$); λ_{abs} (THF) 408, 429, 530, 569, 614 nm.

5,15-Bis(4-methylphenyl)-10,20-bis(pentafluorophenyl)porphinatomagnesium(II) (II-Mg-1h). Following Method II.4A, **II-6h** (0.100 g, 0.232 mmol, 100 mM) in toluene (2 mL) was treated with DBU (0.350 mL, 2.32 mmol) and $MgBr_2$ (0.128 g, 0.697 mmol). The crude product was concentrated and purified by column chromatography [alumina grade V, 450 g, 2

cm dia × 10 cm, CH_2Cl_2/ethyl acetate (1:1)] to afford a purple powder (2 mg, 2%): LD-MS obsd 844.16, calcd 844.1535 ($C_{46}H_{22}F_{10}MgN_4$); λ_{abs} 430, 562, 608 nm.

5,15-Bis(4-methylphenyl)porphinatomagnesium(II) (II-Mg-1j). Following Method II.4A, **II-6j** (1.00 g, 3.79 mmol, 100 mM) in toluene (38 mL) was treated with DBU (5.66 mL, 37.9 mmol) and $MgBr_2$ (2.09 g, 11.4 mmol). The crude product was concentrated and purified by column chromatography [alumina grade V, 450 g, 4 cm dia × 30 cm, CH_2Cl_2] to afford a purple powder (0.376 g, 39%): ^{1}H NMR δ 2.73 (s, 6H), 7.56–7.57 (m, 4H), 8.10–8.12 (m, 4H), 8.88–9.15 (m, 4H), 9.23–9.38 (m, 4H), 10.18 (s, 2H); LD-MS obsd 512.8; FAB-MS obsd 512.1848, calcd 512.1851 ($C_{34}H_{24}MgN_4$); λ_{abs} (toluene) 395, 416, 551, 589, 619, 644 nm. Note that the peaks at 619 and 644 nm were very weak, and are attributed to trace impurities. The peak at 644 nm is most likely a free base chlorin, given that this peak did not give any bathochromic shift upon use of pyridine as the solvent, and also appeared in the spectrum upon demetalation to give the free base porphyrin. The free base porphyrin **II-1j** so obtained exhibited absorption peaks in toluene at 503, 537, 577, 634, and 645 nm. Fluorescence excitation spectroscopy gave the expected result for the 644 nm peak to stem from the free base chlorin. The peak at 619 nm in the magnesium chelate disappeared upon demetalation; the origin of this peak is not known. Regardless, both peaks were quite weak. The yield of chlorin was 5% on the assumption of typical molar absorption coefficients for metalloporphyrins [Q(1,0) = 20,000 $M^{-1}cm^{-1}$] and free base chlorins [Q(0,0) = 35,000 $M^{-1}cm^{-1}$]. The peak at 619 nm was comparable in intensity to that of the peak at 644 nm.

Solventless Reaction (II-Mg-1a). A sample of **II-6a** (0.100 g, 0.244 mmol) was placed in an oven-dried flask (100 mL). A teflon septum was attached, and DBU (0.365 mL, 2.44 mmol, 10 mol equiv versus **II-6a**) was added via syringe. The reaction mixture was stirred for 5

min, whereupon the reaction mixture darkened. $MgBr_2$ (0.135 g, 0.732 mmol, 3.0 mol equiv versus **II-6a**) was added all at once. The heterogenous mixture was sonicated for few secs, and then stirred at room temperature for 1 min. The flask was fitted with a reflux condenser (4 cm dia × 30 cm) having the top end open to the atmosphere, and the flask was placed in an oil bath preheated to 115 °C. The reaction mixture was stirred for 6 h. TLC analysis (alumina, CH_2Cl_2) and absorption spectroscopy of a sample removed from the crude reaction mixture revealed formation of the magnesium porphyrin. The crude reaction mixture was dissolved in CH_2Cl_2 (~3 mL) and filtered through a column (alumina 300 g, 4 cm dia × 20 cm, CH_2Cl_2/ethyl acetate (5:1 → 3:1), ~2 L solvent was used). Free base porphyrin **II-1a** eluted near the solvent front, affording a purple powder (0.12% yield). The dominant porphyrin-contaning fraction eluted later (CH_2Cl_2/ethyl acetate) and was concentrated to give a purple powder (7% yield). The characterization data (^{1}H NMR, ^{13}C NMR, LD-MS and absorption spectrum) were consistent with those obtained from an authentic sample of **II-Mg-1a**. Data for free base porphyrin **II-1a**: LD-MS obsd 782.8, calcd 782.4348 ($C_{56}H_{54}N_4$); λ_{abs} 419, 516, 552.592, 650 nm. Both yields were determined by absorption spectrometry of the isolated porphyrin on the basis of an assumed molar absorption coefficient, ε = 430,000 $M^{-1}cm^{-1}$ for the free base porphyrin, and ε = 500,000 $M^{-1}cm^{-1}$ for the magnesium porphyrin.

5,15-Bis(4-*tert*-butylphenyl)-10,20-bis(4-ethylphenyl)porphinatocobalt(II) (II-Co-1a). Following Method II.4A with modification, DBU (0.0950 mL, 0.610 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (0.0250 g, 0.0610 mmol, 100 mM) in toluene (0.6 mL). $Co(OAc)_2 \cdot 4H_2O$ (0.0460 g, 0.183 mmol, 3.00 mol equiv) was added, and the mixture was heated at 115 °C. Porphyrin formation was complete in 24 h. Chromatography (silica, CH_2Cl_2) afforded an orange solid (6% yield determined by absorption spectrometry on

the basis of an assumed molar absorption coefficient, ε = 500,000 $M^{-1}cm^{-1}$): LD-MS obsd 839.7; FAB-MS obsd 839.3546, calcd 839.3524 ($C_{56}H_{52}CoN_4$); λ_{abs} (toluene) 412, 528, 577 nm.

5,15-Bis(4-*tert*-butylphenyl)-10,20-bis(4-ethylphenyl)porphinatopalladium(II) (II-Pd-1a). Following Method II.4A with modification, DBU (0.0950 mL, 0.610 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (0.0250 g, 0.0610 mmol, 100 mM) in toluene (0.6 mL). $Pd(CH_3CN)_2Cl_2$ (0.0470 g, 0.183 mmol, 3.00 mol equiv) was added, and the mixture was heated at 115 °C. Porphyrin formation was complete in 12 h. Chromatography [silica, hexanes/CH_2Cl_2 (1:4)] afforded an orange solid (10.0 mg, 37%): LD-MS obsd 886.7, calcd 886.32 ($C_{56}H_{52}N_4Pd$); λ_{abs} (toluene) 418, 524 nm; the low solubility precluded collection of a ^1H NMR spectrum.

5-(4-*tert*-Butylphenyl)-1-(4-ethylphenyl)dipyrrin (II-6a′). Following Method II.4A with modification, a sample of DBU (0.0950 mL, 0.610 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (0.0250 g, 0.0610 mmol, 100 mM) in diisopropyl ether (0.6 mL). The reaction mixture was stirred at room temperature for 5 min. The reaction mixture turned dark red. $MgBr_2$ (0.0340 g, 0.183 mmol, 3.00 mol equiv) was added. The reaction mixture was sonicated for a few secs, and then stirred at room temperature for 1 min. The reaction flask was fitted with a reflux condenser (4 cm dia × 30 cm) having the top end open to the atmosphere, and the flask was placed in an oil bath preheated to 135 °C. The crude reaction mixture was checked by absorption spectroscopy, whereby a 1-μL reaction aliquot was added to 3 mL of CH_2Cl_2. Two broad bands were observed (319 and 430 nm). TLC analysis (silica, CH_2Cl_2) revealed three tailing spots (yellow). After 5 h, the reaction mixture was checked with absorption spectroscopy, and a sharp band at 428 nm was observed. The reaction mixture was stirred overnight under reflux. The crude reaction mixture was concentrated. Chromatography

[silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)] afforded a purple powder **II-Mg-1a** (4% spectroscopic yield). The data (^{1}H NMR, ^{13}C NMR, absorption spectroscopy, and LD-MS) of the purified product were consistent with that reported above for **II-Mg-1a**. The title compound was isolated as a yellow-orange paste (9.0 mg, 36%): ^{1}H NMR δ 1.29 (t, *J* = 7.4 Hz, 3H), 1.39 (s, 9H), 2.74 (q, *J* = 7.4 Hz, 2H), 6.45 (d, *J* = 4.2 Hz, 1H), 6.58 (d, *J* = 4.8 Hz, 1H), 6.82 (d, *J* = 4.2 Hz, 1H), 6.89 (d, *J* = 4.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.42–7.49 (m, 4H), 7.90 (d, *J* = 8.4 Hz, 2H), 8.08 (s, 1H), the NH proton was not observed; ^{13}C NMR δ 15.5, 29.2, 29.9, 31.5, 35.0, 119.1, 122.5, 125.0, 125.2, 128.1, 129.7, 131.0, 133.9, 135.3, 136.0, 138.5, 139.4, 141.0, 149.3, 150.5, 152.8, 159.2, 185.6; LD-MS obsd 408.9, FAB-MS obsd 409.2289, calcd 409.2280 [(M + H)$^+$, M = $C_{28}H_{28}N_2O$]; λ_{abs} 433 nm.

1-Acyldipyrromethane Condensation (via Method II. 4B)

5,15-Bis(4-methylphenyl)-10,20-di-2-pyridylporphinatomagnesium(II) (II-Mg-1e). Following Method II.4B, **II-6e** (0.102 g, 0.300 mmol, 100 mM) in toluene (3.0 mL) was treated with DBU (1.57 mL, 10.5 mmol, 35.0 mol equiv) and $MgBr_2$ (0.497 g, 2.70 mmol, 9.0 mol equiv). The crude product was concentrated and chromatographed [alumina grade V, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)] to afford a purple powder (6 mg, 6%): no ESI-MS signal was observed because of low solubility; LD-MS obsd 666.5, calcd 666.2382 ($C_{44}H_{30}MgN_6$); λ_{abs} (toluene) 429, 555 nm.

5,15-Di-3-pyridyl-10,20-di-4-pyridylporphinatomagnesium(II) (II-Mg-1o). Following Method II.4B, **II-6o** (0.164 g, 0.500 mmol) in toluene (5 mL) was treated with DBU (2.23 mL, 10.0 mmol) and $MgBr_2$ (0.276 g, 1.50 mmol, 3.0 mol equiv). The reaction mixture was heated for 18 h. The reaction mixture was cooled and concentrated. The resulting residue was dissolved in CH_2Cl_2 and filtered through a column [alumina grade V, CH_2Cl_2 →

CH_2Cl_2/ethyl acetate (5:1)]. The porphyrin-containing fraction was collected and concentrated (~3%, spectroscopic yield). LD-MS obsd 640.6, calcd 640.1974 ($C_{40}H_{24}MgN_8$). No further purification or characterization was performed.

Condensation of 1-Acyldipyrromethanes Under Microwave Irradiation (via Method II.5). 5,15-Bis(4-methylphenyl)porphyrin (II-1j). Following Method II.5, samples of **II-6j** (0.0530 g, 0.200 mmol), DBU (0.300 mL, 1.99 mmol) and $MgBr_2$ (0.110 g, 0.598 mmol) were reacted. After 30 min the crude reaction mixture was chromatographed [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)]. The porphyrin-containing fractions were concentrated and checked with TLC analysis [silica, CH_2Cl_2]. A trace amount of impurity more polar than the porphyrin was observed. The product was dissolved in CH_2Cl_2 (1 mL) and demetalated by the addition of TFA (0.036 mL). The reaction mixture was stirred at room temperature for 30 min. A sample of triethylamine was added (0.020 mL). The crude reaction mixture was washed (water, brine), dried (Na_2SO_4), and concentrated. The resulting product was filtered through a column [silica, ethyl acetate/MeOH (40:1)] to afford a purple powder (0.019 g, 19%): ^{1}H NMR (pyridine-d_5) δ– 2.64 (s, 2H), 2.66 (s, 6H), 7.63–7.65 (m, 4H), 8.22–8.24 (m, 4H), 9.24–9.25 (m, 4H), 9.52–9.61 (brs, 4H), 10.59 (s, 2H); LD-MS obsd 490.2; ESI-MS obsd 491.2231, calcd 491.2230 [$(M + H)^+$, $M = C_{34}H_{26}N_4$]; λ_{abs} (toluene) 409, 503, 537, 576 nm.

5,10,15,20-Tetra-3-pyridylporphinatomagnesium(II) (II-Mg-1l). Following Method II.5, a sample of **II-6l** (0.0330 g, 0.100 mmol) gave porphyrin in 30 min. Chromatography [alumina, CH_2Cl_2 → CH_2Cl_2/MeOH (10:1) → THF/MeOH (10:1)] followed by washing the porphyrin suspension with hexanes and MeOH afforded a purple powder (39 mg, 61%): ^{1}H NMR (DMSO-d_6) δ 7.03–7.07 (m, 4H), 7.77–7.79 (m, 4H), 7.94–7.96 (br, 8H), 8.18–8.20 (m, 4H), 8.49–8.55 (brs, 4H); ^{13}C NMR (DMSO-d_6) δ 117.9, 122.1, 132.0, 138.7, 140.6, 148.6,

149.3, 153.0; LD-MS obsd 641.1; ESI-MS obsd 641.2043, calcd 641.2047 [$(M + H)^+$, M = $C_{40}H_{24}MgN_8$]; λ_{abs} (toluene) 407, 428, 565, 604 nm.

5,10,15,20-Tetra-4-pyridylporphinatomagnesium(II) (II-Mg-1m). Following Method II.5, a sample of **II-6m** (0.0330 g, 0.100 mmol) gave porphyrin in 45 min. Chromatography followed by washing the porphyrin suspension with hexanes and MeOH afforded a purple powder (15 mg, 47%): ^{1}H NMR (DMSO-d_6) δ 7.38 (d, J = 6.4 Hz, 8H), 7.94–8.02 (brs, 8H), 8.18 (d, J = 6.4 Hz, 8H); LD-MS obsd 640.7; ESI-MS obsd 641.2047, calcd 641.2047 [$(M + H)^+$, M = $C_{40}H_{24}MgN_8$]; λ_{abs} (toluene) 406, 427, 563, 602 nm.

5,15-Di-3-pyridylporphinatomagnesium(II) (II-Mg-1v). Following Method II.5, a sample of **II-6v** (0.050 g, 0.20 mmol) gave porphyrin in 30 min. Chromatography followed by washing the porphyrin suspension with hexanes and MeOH afforded a purple powder (3.8 mg, 4%): LD-MS obsd 486.2; ESI-MS obsd 487.1528, calcd 487.1516 [$(M + H)^+$, M = $C_{30}H_{18}MgN_6$]; λ_{abs} (toluene) 393, 413, 549, 588, 620 nm. A ^{1}H NMR spectrum could not be obtained because of low solubility. Note that the peak at 620 nm was very weak, and is attributed to an unknown trace impurity.

5,15-Bis(ethoxycarbonyl)porphyrin (II-1y). Following Method II.5, samples of **II-6y** (0.0490 g, 0.200 mmol), DBU (0.30 mL, 1.9 mmol) and $MgBr_2$ (0.110 g, 0.598 mmol) were reacted. After 45 min the crude reaction mixture was chromatographed [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate/MeOH (10:1:0.2)]. The porphyrin-containing fractions were concentrated and checked with TLC analysis [silica, CH_2Cl_2]. A trace amount of impurity was observed. The product was dissolved in CH_2Cl_2 (1.0 mL) and demetalated by addition of TFA (0.036 mL). The reaction mixture was stirred at room temperature for 30 min. A sample of triethylamine was added (0.020 mL). The crude reaction mixture was washed (water, brine), dried (Na_2SO_4) and

concentrated. The resulting product was filtered through a column [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)] to afford a purple powder (0.012 g, 13%): ^{1}H NMR δ –3.31 (s, 2H), 1.86 (t, *J* = 8.0 Hz, 6H), 5.12–5.14 (m, 4H), 9.45–9.46 (m, 4H), 9.68–9.69 (m, 4H), 10.32–10.36 (brs, 2H); LD-MS obsd 454.2; ESI-MS obsd 455.1712, calcd 455.1713 [$(M + H)^+$, M = $C_{26}H_{22}N_4O_4$]; λ_{abs} (toluene) 403, 501, 539, 577, 633 nm.

Statistical Condensation of 1-Acyldipyrromethanes Under Microwave Irradiation (via Method II.6).

5,10-Di-2-pyridylporphyrin (II-2a). Following Method II.6, a mixture of **II-6k** (0.066 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.012 g, 13%): ^{1}H NMR δ –3.41 (s, 2H), 7.69–7.74 (m, 2H), 8.06–8.12 (m, 2H), 8.22 (d, *J* = 7.8 Hz, 2H), 8.91–8.94 (brs, 2H), 9.03 (d, *J* = 4.6 Hz, 2H), 9.15–9.17 (m, 2H), 9.38 (d, *J* = 4.6 Hz, 2H), 9.43–9.46 (brs, 2H), 10.27 (s, 2H); ^{13}C NMR δ 105.1, 105.3, 115.8, 118.4, 122.2, 122.7, 130.7, 130.1–133.3 (brs), 135.1, 138.2, 141.2, 148.9, 149.3, 154.0, 160.7; ESI-MS obsd 465.1818, calcd 465.1822 [$(M + H)^+$, M = $C_{30}H_{20}N_6$]; λ_{abs} (toluene) 425, 514, 564, 602, 656 nm. Two other porphyrins were isolated, 5,10,15,20-tetra-2-pyridylporphyrin (**II-1k**, 0.0014 g, 12%) and porphine (0.0090 g, 15%). Data for **II-1k**: ^{1}H NMR δ –2.84 (s, 2H), 7.68–7.72 (m, 4H), 8.05–8.11 (m, 4H), 8.19–8.21 (m, 4H), 8.84–8.8 (brs, 8H), 9.12–9.14 (brs, 4H); ^{13}C NMR δ 119.1, 122.7, 130.7, 131.3–131.8 (brs), 135.0, 148.9, 160.8; ESI-MS obsd 619.2352, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$; λ_{abs} (toluene) 420, 513, 546, 590, 645 nm. The data (^{1}H NMR, ^{13}C NMR, FAB-MS, and absorption spectrum) for porphine were consistent with those obtained from an authentic sample.[II8]

5,10-Di-4-pyridylporphyrin (II-2c). Following Method II.6, a mixture of **II-6m** (0.033 g, 0.100 mmol) and **II-6z** (0.017 g, 0.098 mmol) in toluene (2 mL) was treated with DBU (0.30 mL, 2.0 mmol) and $MgBr_2$ (0.110 g, 0.600 mmol). The reaction was monitored with TLC analysis and absorption spectroscopy. Porphyrin formation was complete in ~ 90 min. The TLC analysis of the crude reaction mixture revealed three spots with R_f = 0.62, 0.67, and 0.79 [silica, THF/MeOH (10:1)]. The crude product was dissolved in CH_2Cl_2 (4 mL) and demetalated by addition of TFA. The reaction mixture was neutralized with triethylamine. Aqueous workup and chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (20:1)] afforded the title porphyrin in pure form without subsequent washing procedures (0.013 g, 27%): ^{1}H NMR (pyridine-d_5) δ –3.18 (s, 2H), 8.27–8.28 (m, 4H), 9.06–9.07 (brs, 4H), 9.24–9.25 (m, 4H), 9.59–9.60 (m, 2H), 9.68–9.72 (brs, 2H), 10.55 (s, 2H); LD-MS 464.1; ESI-MS obsd 465.1822 calcd 465.1822 [$(M + H)^+$, M = $C_{30}H_{20}N_6$]; λ_{abs} (toluene) 408, 501, 533, 576 nm. Two other porphyrins were isolated, 5,10,15,20-tetra-4-pyridylporphyrin (**II-1m**, 0.0085 g, 14%) and porphine (0.0050 g, 16%). Data for **II-1m** were consistent with those obtained for a sample via a different preparation. The data (^{1}H NMR, ^{13}C NMR, FAB-MS, and absorption spectrum) for porphine were consistent with those obtained from an authentic sample.[II8]

5-(2-Pyridyl)-10-(3-pyridyl)porphyrin (II-2d). Following Method II.6, a mixture of **II-6n** (0.066 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.0084 g, 9%): ^{1}H NMR (300 MHz) δ –3.44 (s, 2H), 7.71–7.76 (m, 2H), 8.08–8.13 (m, 1H), 8.23– 8.25 (m, 1H), 8.49–8.52 (m, 1H), 8.87–8.89 (m, 1H), 8.94–8.96 (m, 2H), 9.02–9.06 (m, 2H), 9.15–9.17 (m, 1H), 9.37–9.38 (m, 2H), 9.43 (s, 2H), 9.44–9.47 (brs, 1H), 10.25 (s, 2H); ^{13}C NMR δ 105.1,

105.3, 115.8, 118.4, 122.2, 122.7, 130.7, 131.74–131.78 (brs), 135.1, 138.2, 141.2, 148.9, 149.3, 154.0, 160.8; ESI-MS obsd 465.1821, calcd 465.1822 [$(M + H)^+$, M = $C_{30}H_{20}N_6$]; λ_{abs} (toluene) 408, 502, 532, 577, 632 nm. Two other porphyrins also were isolated, 5,15-di-2-pyridyl-10,20-di-3-pyridylporphyrin (**II-1n**, 0.013 g, 11%) and porphine (0.0043 g, 7%). Data for **II-1n**: ^{1}H NMR (300 MHz) δ –2.84 (s, 2H), 7.70–7.75 (m, 4H), 8.09–8.14 (m, 2H), 8.23–8.26 (m, 2H), 8.49–8.51 (m, 2H), 8.82–8.89 (m, 8H), 9.02–9.03 (m, 2H), 9.13–9.14 (m, 2H), 9.44–9.46 (m, 2H); ^{13}C NMR (75 MHz) δ 116.5, 119.5, 122.3, 122.8, 130.6, 130.7–132.0 (brs), 135.2, 138.0, 141.3, 148.9, 149.3, 153.9, 160.5; ESI-MS obsd 619.2355, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 420, 514, 548, 591, 647 nm. The data (^{1}H NMR, ^{13}C NMR, FAB-MS, and absorption spectrum) for porphine were consistent with those obtained from an authentic sample.[II8]

5-(3-Pyridyl)-10-(4-pyridyl)porphyrin (II-2e). Following Method II.6, a mixture of **II-6o** (0.066 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.013 g, 14%): ^{1}H NMR δ –3.47 (s, 2H), 7.74–7.78 (m, 1H), 8.12–8.22 (brs, 2H), 8.51–8.53 (m, 1H), 8.87–8.90 (brs, 2H), 8.96–8.97 (m, 2H), 9.04–9.07 (m, 3H), 9.38–9.40 (m, 2H), 9.45–9.48 (brs, 3H), 10.27 (s, 1H), 10.28 (s, 1H); ^{13}C NMR δ 105.3, 105.4, 116.0, 116.8, 122.3, 129.7, 130.0–134.0 (brs), 138.1, 141.2, 148.6, 149.4, 150.5, 153.9; LD-MS obsd 464.4; ESI-MS obsd 465.1821, calcd 465.1822 [$(M + H)^+$, M = $C_{30}H_{20}N_6$]; λ_{abs} (toluene) 408, 502, 533, 576 nm.

5,15-Di-2-pyridyl-10,20-di-4-pyridylporphyrin (II-1p). Following Method II.6, a mixture of **II-6p** (0.066 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). The reaction failed to

form the hybrid *cis*-AB-porphyrin **II-2f**. Chromatography [silica, THF → THF/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL) afforded the *trans*-A_2B_2-porphyrin title compound as a purple powder (0.014 g, 11%): ^{1}H NMR δ –2.89 (s, 2H), 7.72–7.75 (m, 2H), 8.11–8.15 (m, 6H), 8.25–8.27 (m, 2H), 8.82–8.90 (m, 8H), 9.02–9.04 (m, 4H), 9.13–9.14 (m, 2H); ^{13}C NMR δ 117.6, 119.6, 122.9, 129.7, 130.6, 130.7–132.0 (brs), 135.2, 148.6, 149.0, 150.3, 160.4; ESI-MS obsd 619.2350, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 419, 513, 545, 590, 647 nm. Porphine (0.017 g, 28%) also was isolated, which exhibited data (^{1}H NMR, ^{13}C NMR, FAB-MS, and absorption spectrum) consistent with those obtained from an authentic sample.[II8]

5-(3-Pyridyl)porphyrin (II-2g). Following Method II.6, a mixture of **II-6v** (0.050 g, 0.20 mmol) and **II-6z** (0.035 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography [silica, THF → THF/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.025 g, 32%): ^{1}H NMR δ –3.68 (s, 2H), 7.76–7.79 (m, 1H), 8.53–8.56 (m, 1H), 9.02 (d, *J* = 4.4 Hz, 2H), 9.07–9.08 (m, 1H), 9.44 (d, *J* = 4.4 Hz, 2H), 9.46–8.49 (m, 5H), 10.27 (s, 1H), 10.34 (m, 2H); ^{13}C NMR δ 104.3, 105.2, 115.1, 122.3, 130.9, 131.6, 132.1, 132.2, 137.9, 141.4, 146.0–148.0 (brs), 149.3, 154.1; ESI-MS obsd 388.1558, calcd 388.1556 [$(M + H)^+$, M = $C_{25}H_{17}N_5$]; λ_{abs} (toluene) 402, 496, 526, 570, 642 nm. Porphine (4 mg, 6%) also was isolated, which exhibited data (^{1}H NMR, ^{13}C NMR, FAB-MS, and absorption spectrum) consistent with those obtained from an authentic sample.[II8]

5,10-Dipentyl-15,20-di-2-pyridylporphyrin (II-3a). Following Method II.6, a mixture of **II-6k** (0.066 g, 0.20 mmol) and **II-6r** (0.063 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by

washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.008 g, 7%): ^{1}H NMR δ –2.69 (s, 2H), 0.96 (t, *J* = 7.4 Hz, 6H), 1.49–1.56 (m, 4H), 1.74–1.81 (m, 4H), 2.50–2.58 (m, 4H), 4.97–5.00 (m, 4H), 7.66–7.69 (m, 2H), 8.03–8.07 (m, 2H), 8.14 8.16 (m, 2H), 8.71–8.75 (brs, 2H), 8.82–8.84 (m, 2H), 9.11–9.13 (m, 2H), 9.46–9.48 (m, 2H), 9.53–9.56 (brs, 2H); ^{13}C NMR δ 14.4, 23.0, 32.9, 35.9, 38.8, 117.0, 121.3, 122.5, 128.9–130.4 (brs), 130.6, 134.9, 148.8, 161.1; ESI-MS obsd 605.3386, calcd 605.3387 [(M + H)$^+$, M = $C_{40}H_{40}N_6$]; λ_{abs} (toluene) 420, 517, 551, 594, 652 nm. 5,10,15,20-Tetra-2-pyridylporphyrin (**II-1k**) also was isolated (0.012 g, 10%), which exhibited data (^{1}H NMR, ^{13}C NMR, ESI-MS, and absorption spectrum) consistent with those obtained from an authentic sample.

5,10-Dipentyl-15,20-di-3-pyridylporphyrin (II-3b). Following Method II.6, a mixture of **II-6l** (0.066 g, 0.20 mmol) and **II-6r** (0.063 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography followed by washing the porphyrin suspension with hexanes (5 mL) afforded the title compound as a purple powder (0.020 g, 17%): ^{1}H NMR δ –2.74 (s, 2H), 0.98 (t, *J* = 7.2 Hz, 6H), 1.52–1.57 (m, 4H), 1.77–1.81 (m, 4H), 2.52–2.56 (m, 4H), 4.96–4.99 (m, 4H), 7.70–7.73 (m, 2H), 8.45–8.46 (m, 2H), 8.70–8.74 (brs, 2H), 8.78–8.79 (m, 2H), 9.02–9.03 (m, 2H), 9.39–9.41 (brs, 2H), 9.47–9.48 (m, 2H), 9.54–9.56 (brs, 2H); ^{13}C NMR δ 14.4, 23.0, 29.9, 32.9, 35.9, 38.9, 114.6, 121.4, 122.2, 129.1–130.4 (brs), 138.3, 141.1, 149.2, 153.8; ESI-MS obsd 605.3396, calcd 605.3387 [(M + H)$^+$, M = $C_{40}H_{40}N_6$]; λ_{abs} (toluene) 420, 518, 552, 595, 654 nm. 5,10,15,20-Tetra-3-pyridylporphyrin (**II-1l**) also was isolated (0.028 g, 23%), which exhibited data (^{1}H NMR, ^{13}C NMR, ESI-MS, and absorption spectrum) consistent with those obtained from an authentic sample.

5,10-Dipentyl-15-(2-pyridyl)-20-(3-pyridyl)porphyrin (II-3d). Following Method II.6, a mixture of **II-6n** (0.066 g, 0.20 mmol) and **II-6r** (0.063 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL) afforded the title compound as a purple powder (0.015 g, 12%): ^{1}H NMR δ –2.71 (s, 2H), 0.97 (m, 6H), 1.51–1.59 (m, 4H), 1.73–1.82 (m, 4H), 2.53–2.55 (m, 4H), 4.97–5.00 (m, 4H), 7.67–7.72 (m, 2H), 8.05–8.09 (m, 1H), 8.16–8.18 (m, 1H), 8.44–8.45 (m, 1H), 8.68–8.69 (m, 1H), 8.75–8.78 (m, 2H), 8.83–8.85 (m, 1H), 9.00–9.01 (m, 1H), 9.11–9.13 (m, 1H), 9.41–9.43 (m, 1H), 9.47–9.49 (m, 2H), 9.56–9.58 (m, 2H); ^{13}C NMR δ 14.4, 22.9, 32.9, 33.0, 35.9, 35.96, 38.8, 38.9, 114.4, 117.2, 121.2, 121.5, 122.1, 122.6, 129.09–132.3 (brs), 130.5, 135.0, 138.4, 141.1, 148.8, 149.1, 153.9, 161.0; ESI-MS obsd 605.3387, calcd 605.3387 [$(M + H)^+$, M = $C_{40}H_{40}N_6$]; λ_{abs} (toluene) 420, 517, 552, 595, 653 nm. 5,15-Di-2-pyridyl-10,20-di-3-pyridylporphyrin (**II-1n**) also was isolated (0.017 g, 14%): ^{1}H NMR δ –2.84 (s, 2H), 7.71–7.73 (m, 4H), 8.08–8.12 (m, 2H), 8.23–8.25 (m, 2H), 8.48–8.52 (m, 2H), 8.82–8.89 (m, 8H), 9.01–9.03 (m, 2H), 9.10–9.13 (m, 2H), 9.42– 9.46 (m, 2H); ^{13}C NMR δ 116.5, 119.5, 122.2, 122.8, 130.6, 130.7–131.8 (brs), 135.2, 138.1, 141.3, 148.9, 149.4, 153.9, 160.5; ESI-MS obsd 619.2352, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 420, 514, 548, 591, 647 nm.

5,10-Di-pentyl-15-(3-pyridyl)-20-(4-pyridyl)porphyrin (II-3e). Following Method II.6, a mixture of **II-6o** (0.066 g, 0.20 mmol) and **II-6r** (0.063 g, 0.20 mmol) in toluene (4 mL) was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL x 1) afforded the title compound as a purple powder

(0.019 g, 16%): ^{1}H NMR δ –2.73 (s, 2H), 0.99 (t, *J* = 7.2 Hz, 6H), 1.52–1.57 (m, 4H), 1.78–1.85 (m, 4H), 2.53–2.61 (m, 4H), 5.01–5.05 (m, 4H), 7.73–7.78 (m, 1H), 8.12–8.14 (m, 2H), 8.47–8.49 (m, 1H), 8.72–8.73 (m, 2H), 8.79–8.82 (m, 2H), 9.02–9.05 (m, 3H), 9.41–9.42 (m, 1H), 9.50–9.52 (m, 2H), 9.61 (s, 2H); ^{13}C NMR δ 14.4, 22.9, 32.9, 35.9, 38.9, 114.6, 115.5, 118.8, 119.3, 121.5, 121.6, 122.2, 123.4, 123.9, 129.6, 129.7–130.8 (brs), 136.7, 138.2, 141.0, 148.5, 149.2, 150.1, 150.7, 150.9, 153.6, 153.8; ESI-MS obsd 605.3384, calcd 605.3387 [(M + H)$^+$, M = $C_{40}H_{40}N_6$]; λ_{abs} (toluene) 420, 517, 552, 596, 653 nm. 5,15-Di-3-pyridyl-10,20-di-4-pyridylporphyrin (**II-1o**) also was isolated (0.0056 g, 5%): ^{1}H NMR δ–2.88 (s, 2H), 7.66–7.77 (m, 2H), 8.15–8.17 (brs, 4H), 8.52–8.53 (m, 2H), 8.83–8.87 (m, 8H), 9.05–9.06 (m, 6H), 9.41–9.44 (m, 2H); ^{13}C NMR δ 117.0, 117.9, 122.3, 129.6, 130.8–132.2 (brs), 137.7, 141.1, 148.6, 149.6, 150.1, 153.8; ESI-MS obsd 619.2352, calcd 619.2353 [(M + H)$^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 419, 514, 548, 590, 645 nm.

5,10-Dipentyl-15-(2-pyridyl)-20-(4-pyridyl)porphyrin (II-3f). Following Method II.6, a mixture of **II-6p** (0.066 g, 0.20 mmol) and **II-6r** (0.063 g, 0.20 mmol) in toluene was treated with DBU (0.60 mL, 4.0 mmol) and $MgBr_2$ (0.220 g, 1.20 mmol). Chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (10:1)] followed by washing the porphyrin with hexanes (5 mL x 1) afforded the title compound as a purple powder (0.026 g, 22%): ^{1}H NMR δ –2.73 (s, 2H), 0.97 (m, 6H), 1.51–1.59 (m, 4H), 1.77–1.79 (m, 4H), 2.53–2.54 (m, 4H), 4.96–5.00 (m, 4H), 7.69–7.71 (m, 1H), 8.07–8.11 (m, 3H), 8.16–8.18 (m, 1H), 8.68–8.69 (m, 1H), 8.74–8.75 (m, 1H), 8.78–8.79 (m, 1H), 8.45–8.47 (m, 1H), 8.99–9.00 (m, 2H), 9.11–9.13 (m, 1H), 9.47–9.48 (m, 2H), 9.56 (s, 2H); ^{13}C NMR δ 14.4, 22.9, 32.93, 32.97, 35.9, 38.8, 38.9, 115.3, 117.3, 121.4, 121.5, 122.6, 129.09–130.8 (brs), 135.0, 148.5, 148.9, 150.8, 160.9; ESI-MS obsd 605.3381, calcd 605.3387 [(M + H)$^+$, M = $C_{40}H_{40}N_8$]; λ_{abs} (toluene) 420,

517, 551, 594, 652 nm. 5,15-Di-2-pyridyl-10,20-di-4-pyridylporphyrin (**II-1p**) also was isolated (0.018 g, 15%): ^{1}H NMR δ –2.89 (s, 2H), 7.73–7.78 (m, 2H), 8.10–8.14 (m, 6H), 8.23–8.25 (m, 2H), 8.83–8.88 (m, 8H), 9.02–9.08 (brs, 4H), 9.13–9.16 (brs, 2H); ^{13}C NMR δ 117.6, 119.6, 122.9, 129.7, 130.6, 130.7–131.8 (brs), 135.2, 148.6, 149.0, 150.3; ESI-MS obsd 619.2350, calcd 619.2353 [$(M + H)^+$, M = $C_{40}H_{26}N_8$]; λ_{abs} (toluene) 419, 513, 546, 590, 647 nm.

Synthesis of a *trans*-A_2B_2-porphyrin from an Aldehyde and a Dipyrromethane (Method II.7)

5,15-Bis(4-methylphenyl)-10,20-diphenylporphinatomagnesium (II-Mg-S10): A sample of **II-4c** (52.0 mg, 0.233 mmol) was placed in a 10 mL one-necked round bottom flask that was oven-dried, contained a magnetic stir bar, and was fitted with a septum. Toluene (2.3 mL) was added via syringe. The reaction mixture was stirred at room temperature for 1 min, whereupon *p*-tolualdehyde (0.028 mL, 0.233 mmol, 1 mol equiv versus **II-4c**) was added dropwise via syringe under vigorous stirring. The resulting mixture was stirred at room temperature for 1 min. A sample of DBU (0.350 mL, 2.33 mmol, 10 mol equiv) was added via syringe. The mixture darkened. The septum was removed and $MgBr_2$ (0.258 g, 1.40 mmol, 3.0 mol equiv) was added in one portion under vigorous stirring. The septum was replaced, and the heterogeneous mixture was stirred for 1 min at room temperature. The flask was fitted with a reflux condenser (4 cm dia × 30 cm) having the top end open to the atmosphere, and the flask was placed in an oil bath preheated to 115 °C. The reaction mixture was stirred. When porphyrin formation was complete (on the basis of TLC analysis and absorption spectroscopy), the crude reaction mixture was concentrated. The resulting residue was dissolved in CH_2Cl_2 (2 mL) and filtered through a column. The porphyrin-containing fraction was concentrated to afford a purple powder (0.031 g, 20%): ^{1}H NMR (THF–d_8) 2.61 (s,6H), 7.55 (d, J = 7.6 Hz, 4H)

7.72–7.74 (m, 6H), 8.07 (d, J = 7.6 Hz, 4H), 8.20–8.22 (m, 4H), 8.75–8.80 (m, 8H); ^{13}C NMR δ 20.8, 121.4, 121.5, 126.1, 126.9, 127.0, 131.2, 131.3, 134.8, 134.83, 136.5, 141.6, 144.6, 149.6, 149.7; LD-MS obsd 664.5, FAB-MS obsd 664.2501, calcd 664.2477 ($C_{46}H_{32}MgN_4$); λ_{abs} 404, 425, 564, 604 nm.

5,15-Bis(4-methylphenyl)-10,20-bis(2,4,6-trimethylbenzoyl)porphyrin (II-1i). Following Method II.7 with slight modification, a mixture of **II-4c** (0.071 g, 0.30 mmol) and mesitaldehyde (0.045 mL, 0.30 mmol) in toluene (6 mL) was treated with DBU (0.90 mL, 6.0 mmol) and $MgBr_2$ (0.33 g, 1.8 mmol). The resulting crude product was washed (water, brine), dried (Na_2SO_4) and concentrated. The resulting crude reaction mixture was dissolved in CH_2Cl_2 (6 mL) and demetalated by addition of TFA (0.030 mL). A sample of triethylamine (0.020 mL) was added. The crude reaction mixture was washed (water, brine), dried (Na_2SO_4) and concentrated. Chromatography (silica, CH_2Cl_2) afforded the target compound as purple powder (0.011 g, 5%). The data (^{1}H NMR, LD-MS, and absorption spectrum) were consistent with those obtained from an authentic sample.[II12]

5,15-Bis(4-methylphenyl)-10,20-bis[1-(2-(trimethylsilyl)ethoxymethyl)imidazol-2-yl]porphinatomagnesium(II) (II-Mg-S4). Method II.7 was employed with a sample of *p*-tolualdehyde (0.028 mL, 0.23 mmol). The crude product was concentrated and purified by column chromatography (alumina grade V, CH_2Cl_2) to afford a purple powder (2%, spectroscopic yield): LD-MS obsd 905.3, calcd 904.39 ($C_{52}H_{56}MgN_8O_2Si_2$); λ_{abs} 412, 430, 590 nm.

5,15-Di-3-indolyl-10,20-bis[1-(2-(trimethylsilyl)ethoxymethyl)imidazol-2-yl]porphinatomagnesium(II) (II-Mg-S5). Method II.7 was employed with a sample of indole-3-carboxaldehyde (34 mg, 0.23 mmol). The crude product was concentrated and purified by

column chromatography [alumina grade V, CH_2Cl_2/ethyl acetate (1:1)] to afford a purple powder (2.0%, spectroscopic yield): LD-MS obsd 955.5, calcd 954.3820 ($C_{52}H_{56}MgN_8O_2Si_2$); λ_{abs} 428 (broad), 525, 542 nm.

5,15-Bis(4-methoxyphenyl)-10,20-bis[1-(2-(trimethylsilyl)ethoxymethyl)imidazol-2-yl]porphinatomagnesium(II) (II-Mg-S6). Method II.7 was employed with a sample of 4-methoxybenzaldehyde (0.028 mL, 0.23 mmol). The crude product was concentrated and purified by column chromatography [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate/MeOH (100:1)] to afford a purple powder (3.0%, spectroscopic yield): LD-MS obsd 937.6, calcd 936.3813 ($C_{52}H_{56}MgN_8O_4Si_2$); λ_{abs} (CH_2Cl_2/EtOH, 3:1) 425, 560 nm.

5,15-Bis(4-dimethylaminophenyl)-10,20-bis[1-(2 (trimethylsilyl)ethoxymethyl)imidazol-2-yl]porphinatomagnesium(II) (II-Mg-S7). Method II.7 was employed with a sample of 4-dimethylaminobenzaldehyde (0.035 g, 0.23 mmol). The crude product was concentrated and purified by column chromatography [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (1:1)] to afford a purple powder (5.0%, spectroscopic yield): LD-MS obsd 940.6, calcd 940.4752 ($C_{52}H_{56}MgN_8O_4Si_2$); λ_{abs} (CH_2Cl_2/ethyl acetate, 3:1) 429 (broad), 580 nm.

Other Reactions

Attempted Reaction of 1,9-(4-Methylbenzoyl)-5-phenyldipyrromethane (II-S11) and 5-phenyldipyrromethane (II-4c). A sample of DBU (75.0 μL, 0.500 mmol, 10.0 mol equiv versus **II-S11** and **II-4c**) was added dropwise to a solution containing **II-S11** (0.023 g, 0.050 mmol, 50 mM) and **II-4c** (0.011 g, 0.050 mmol, 50 mM) in toluene (1.0 mL). The reaction mixture was stirred at room temperature for 5 min. The reaction mixture became dark red. Solid $MgBr_2$ (0.0280 g, 0.150 mmol, 3.00 mol equiv) was added. The reaction mixture was sonicated for a few secs, and stirred at room temperature for 1 min. The heterogeneous reaction mixture was stirred at reflux (oil bath temperature 135 °C) exposed to air. The crude reaction mixture was checked with absorption spectroscopy, whereby a 1-μL reaction aliquot was added to 3 mL of CH_2Cl_2. Two broad bands were observed (322 and 428 nm). TLC analysis (silica, CH_2Cl_2) revealed an unknown byproduct and components corresponding to the 1,9-diacyldipyrromethane **II-S11**, dipyrromethane **II-4c** and metalloporphyrin **II-Mg-S10**. The reaction mixture was stirred at reflux exposed to air for 8 h. The crude reaction mixture was concentrated. Chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)] afforded an unknown byproduct (likely a 1,9-diacyldipyrrinato-magnesium complex of undetermined structure) and the magnesium porphyrin **II-Mg-S10** as a purple powder (3% spectroscopic yield).

Magnesiation to Give 5,15-Bis(4-methylphenyl)-10,20-diphenylporphinatomagnesium(II) (II-Mg-S10). A sample of **II-S10** (0.0210 g, 0.0330 mmol) in CH_2Cl_2 (2.20 mL) was treated with DBU (100 μL, 0.660 mmol, 20.0 mol equiv). The reaction mixture was stirred at room temperature for 2 min, and then MgI_2 was added (0.0920 g, 0.330 mmol, 10.0 mol equiv versus **II-S10**). The resulting heterogeneous reaction mixture was stirred at room temperature. On the basis of TLC analysis (alumina, CH_2Cl_2) and LD-MS, metalation of **II-S10** was complete in 4 h. The mixture was diluted with CH_2Cl_2 (20 mL) and

washed with 5% $NaHCO_3$ (2 x 25 mL). The organic layer was dried (Na_2SO_4) and filtered. The filtrate was concentrated. The resulting crude product was chromatographed (alumina, CH_2Cl_2) to afford a purple powder (20 mg, 91%): ^{1}H NMR (THF-d_8) δ 2.61(s, 6H), 7.55 (d, J = 7.6 Hz, 4H), 7.72–7.74 (m, 6H), 8.07 (d, J = 7.6 Hz, 4H), 8.20–8.22 (m, 4H), 8.75–8.80 (m, 8H); ^{13}C NMR (THF-d_8) δ 20.8, 121.4, 121.5, 126.1, 126.9, 127.0, 131.2, 131.3, 134.8, 134.83, 136.5, 141.6, 144.6, 149.6, 149.7; LD-MS obsd 664.5, FAB-MS obsd 664.2501, calcd 664.2477 ($C_{46}H_{32}MgN_4$); λ_{abs} 404, 425, 564, 604 nm.

Concentration Dependence Study

Synthesis of II-Mg-1a (50 mM). Following Method II.4B with modification, DBU (3.65 mL, 24.4 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (1.00 g, 2.44 mmol) in toluene (48.8 mL). The reaction mixture darkened, and $MgBr_2$ (1.35 g, 7.32 mmol, 3.00 mol equiv) was added. Porphyrin formation was complete in 6 h. Chromatography [alumina, CH_2Cl_2/ethyl acetate (5:1 → 3:1)] afforded a purple powder (0.461 g, 4.7%). The data from NMR spectroscopy (^{1}H NMR, ^{13}C NMR), LD-MS and absorption spectroscopy were consistent with that reported above for **II-Mg-1a**.

Synthesis of II-Mg-1a (100 mM). Following Method II.4B, DBU (3.65 mL, 24.4 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (1.00 g, 2.44 mmol) in toluene (24.4 mL). The reaction mixture darkened, and $MgBr_2$ (1.35 g, 7.32 mmol, 3.00 mol equiv) was added. Porphyrin formation was complete in 6 h. Chromatography [alumina, CH_2Cl_2/ethyl acetate (5:1 → 3:1)] afforded a purple powder (0.674 g, 69%). The data from NMR spectroscopy (^{1}H NMR, ^{13}C NMR), LD-MS and absorption spectroscopy were consistent with that reported above for **II-Mg-1a**.

Synthesis of II-Mg-1a (200 mM). Following Method II.4B with modification, DBU (3.65 mL, 24.4 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to a solution of **II-6a** (1.00 g, 2.44 mmol) in toluene (12 mL). The reaction mixture darkened, and $MgBr_2$ (1.35 g, 7.32 mmol, 3.00 mol equiv) was added. Porphyrin formation was complete in 6 h. Chromatography [alumina, CH_2Cl_2/ethyl acetate (5:1 → 3:1)] afforded a purple powder (0.634 g, 65%). The data from NMR spectroscopy (^{1}H NMR, ^{13}C NMR), LD-MS and absorption spectroscopy were consistent with that reported above for **II-Mg-1a**.

Synthesis of II-Mg-1a with $MgBr_2 \cdot O(C_2H_5)_2$. Following Method II.4B with modification, DBU (0.450 mL, 3.00 mmol, 10.0 mol equiv versus **II-6a**) was added dropwise to

a solution of **II-6a** (0.123 g, 0.300 mmol, 100 mM) in toluene (3 mL). $MgBr_2 \cdot O(C_2H_5)_2$ (0.232 g, 0.898 mmol, 3.0 mol equiv) was added, and the reaction was carried out at 115 °C. The reaction was complete in 4 h. The crude product was concentrated and purified by column chromatography [alumina, CH_2Cl_2/ethyl acetate (1:1)] to afford a purple powder (91 mg, 75%): The data from NMR spectroscopy (^{1}H NMR, ^{13}C NMR), LD-MS and absorption spectroscopy were consistent with that reported above for **II-Mg-1a**.

CHAPTER III.

NEW ROUTE TO ABCD-PORPHYRINS VIA BILANES

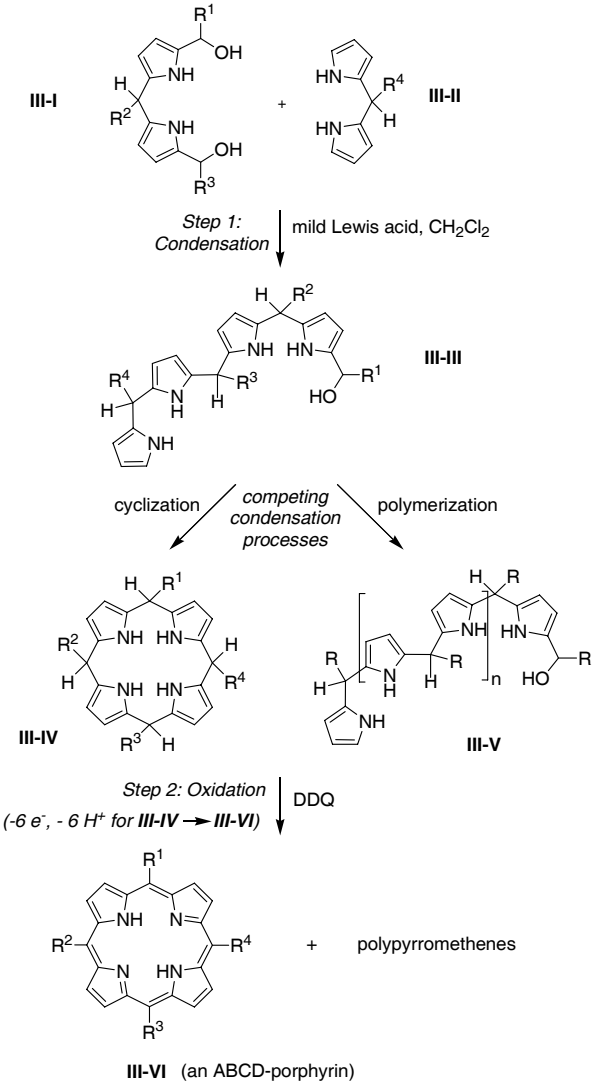
III.A. Introduction.

Porphyrins bearing four different meso substituents provide versatile building blocks for use in biomimetic and materials chemistry. The existing method for the synthesis of such ABCD-porphyrins is shown in Scheme III.1. The porphyrin-forming reaction entails acid-catalyzed condensation of a dipyrromethane-1,9-dicarbinol (**III-I**) + a dipyrromethane (**III-II**), which is believed to proceed via a bilane-carbinol (**III-III**) and a porphyrinogen (**III-IV**) with competing formation of polypyrromethanes (**III-V**). Treatment of the reaction mixture with an oxidant gives the porphyrin (**III-VI**).[III1,III2] This "2 + 2" method enables synthesis of ~1 g quantities of variously substituted ABCD-porphyrins with low or no detectable scrambling.

In developing access to ABCD-porphyrins, we have attempted to meet the following criteria: (1) no scrambling at any stage of the synthesis, (2) limited reliance on chromatography, (3) scalable syntheses affording at least 1 g of porphyrin, (4) straightforward implementation in a reasonable period (e.g., <1 week), (5) broad scope in terms of ABCD substituents, and (6) good yield. The procedures for forming the dipyrromethane and elaborating the dipyrromethane to give the dipyrromethane-1,9-dicarbinol are reasonably well developed and meet all six objectives. [III3-III8] However, the final porphyrin-forming step still presents a number of limitations despite extensive investigation. [III2]

The drawbacks of the porphyrin-forming procedure include: (1) low concentration (2.5 or 25 mM), (2) low yield (≤ 30%), and (3) requisite use of column chromatography to purify the porphyrin. Such drawbacks need to be overcome for widespread practical use. In this regard, a lengthy series of studies was carried out recently to identify improved conditions for the acid-catalyzed condensation of the dipyrromethane-1,9-dicarbinol (**III-I**) + a dipyrromethane (**III-II**).[III2] Although acid catalysis conditions were identified for carrying out the reaction at 25 mM, the highest yield is typically obtained at 2.5 mM reactants. Higher concentrations tend to give

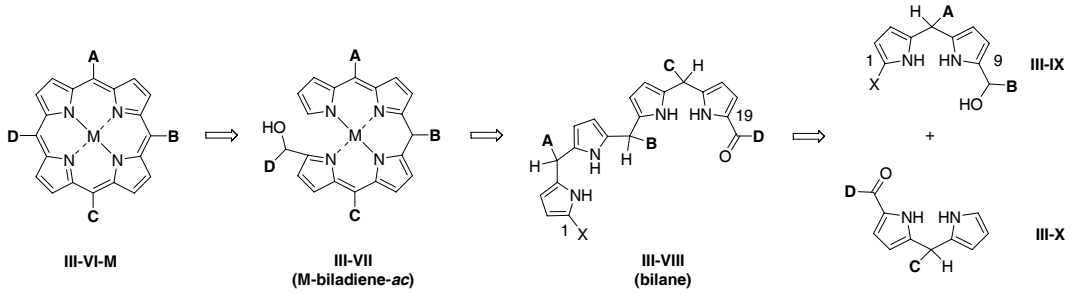
larger amounts of polymer owing to the well-known concentration dependence of the competition of cyclization versus polymerization (**III-III** → **III-IV** versus **III-V**).[III9,III10] Moreover, the use of higher concentrations typically requires an increased concentration of acid (to overcome the buffering effect of water of condensation), whereupon the risk of acid-induced scrambling[III11] also is increased.[III2] The difficulty in identifying further improvements to the conditions for the 2 + 2 condensation has prompted us to investigate fundamentally new approaches for constructing the porphyrin macrocycle.



Scheme III.1. "2 + 2" Synthesis of a ABCD-Porphyrin (Free Base).

Our approach has centred on developing a strategy for constructing the porphyrinic macrocycle wherein a linear tetrapyrrole species is cyclized under metal-templating conditions. Metal-templating is expected to juxtapose the reactant groups at the termini of the linear tetrapyrrole and thereby favor intramolecular cyclization over competing polymerization. The use of a metal template requires the tetrapyrrole species to contain a motif that participates in metal coordination (e.g., pyrromethene or acylpyrrole); such a tetrapyrrole cannot be a porphyrinogen, given the absence of metal-templating of pyrrolic units in fully saturated pyrromethane species.[III9]

The strategy initially envisaged is shown in Scheme III.2. The key precursor to the ABCD-metalloporphyrin (**III-VI-M**) is a metal-complexed biladiene-*ac* bearing a 19-hydroxymethyl substituent (**III-VII**), which is obtained in several steps from a 1-protected 19-acylbilane (**III-VIII**). The latter is derived by selective condensation of an AB-substituted dipyrromethane (**III-IX**) and a CD-substituted dipyrromethane (**III-X**). The selective condensation stems from the presence of only a single reactive a-position in each dipyrromethane: the latter bears one α-acyl moiety and has one α-site open for condensation, whereas the former bears one α-protecting group (X) and has one α-carbinol group for bilane formation. Note that the terminal α-positions in a dipyrromethane are numbered 1 and 9; those in a bilane are 1 and 19.



Scheme III.2. Stepwise Retrosynthesis of an ABCD-Metalloporphyrin.

The development of the synthesis of the bilane (**III-VIII**) shown in Scheme III.2 presented several challenges. A key objective was to identify a suitable protecting group X that could be introduced at the pyrrole α-position and could be removed at a later stage under mild, non-acidic conditions. The common route to bilanes by hydrogenation of an unsaturated analogue (bilene or biladiene), which can be prepared in a number of ways,[III12] was not suited for our needs. To gain rational entry to a bilane from dipyrromethane precursors requires the presence of only a single reactive α-pyrrolic site in each dipyrromethane, as is the case in Scheme III.2.

Synthetic routes have been developed over the past few decades to provide access to bilanes bearing three distinct types of substitution patterns (Chart III.1). (1) Early routes to β-substituted bilanes that met the needs of biosynthetic studies employed the condensation of a 1-formyldipyrromethane and a 1-hydroxymethyldipyrromethane to give a 19-formylbilane (**III-XI**).[III13-III16] This approach lacks an α-protecting group on the latter dipyrromethane and is not general. (2) More directed routes to β-substituted 1-protected 19-acylbilanes (**III-XII**) have employed the reaction of a 1-acyldipyrromethane and a 9-protected 1-hydroxymethyldipyrromethane[III17,III18] (or 1-phenylselenylmethyl analogue)[III19] wherein the 9-substituent includes alkoxycarbonyl,[III19] alkoxycarbonylamino,[III18] cyano,[III17] or methyl.[III17] (3) Meso-substituted, β-unsubstituted bilanes that contain three identical meso substituents have been isolated as byproducts of dipyrromethane syntheses,[III20] prepared by acidolysis of a dipyrromethane in the presence of an aldehyde,[III21] or obtained by one-flask aldehyde-pyrrole condensations.[III22-III24] Bilanes bearing BAB substituents at the meso positions (i.e., $B^{III5}A^{III10}B^{III15}$ pattern) have been prepared by condensation of an A-aldehyde with a B-dipyrromethane in excess.[III25,III26] More generally, treatment of an BAB- or ABC-dipyrromethane-1,9-dicarbinol with excess pyrrole gives the BAB- or ABC-bilane

(**XIII**).[III24,III27,III28] Such bilanes are valuable precursors to BAB- or ABC-corroles,[III24,III28] but the lack of provisions for substituents at the 1 and 19-positions precludes use in the ABCD-porphyrin synthesis envisaged here. Although such bilanes can be condensed with an aldehyde under acid-catalysis,[III21,III25,III27] the reaction typically proceeds with scrambling to give a mixture of porphyrins.

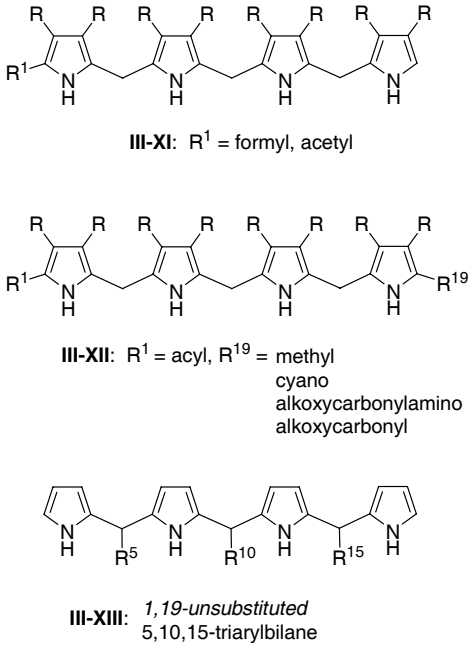


Chart III.1. Known Bilanes Prepared from Dipyrromethanes.

The relative dearth of methods for the direct synthesis of bilanes, suitable α-bilane protecting groups, and methods for converting bilanes to porphyrins, stems in part from the perception of bilanes as unstable compounds. Indeed, Jackson emphasized 40 years ago that "it became clear from our own, and from other,[III29] work that the bilanes were very unstable, particularly towards oxidation, and towards acid catalysed redistribution reactions which caused 'jumbling' of the pyrrole rings and led to mixtures of porphyrins on attempted cyclisation."[III30]

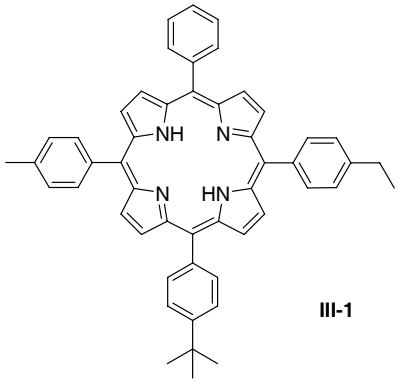
Regardless, none of the α-pyrrolic protecting groups that was employed previously appeared suited for the synthesis shown in Scheme III.2. Accordingly, we investigated new α-pyrrolic protecting groups (X), including thiocyanato, alkylthio, and bromo groups.

Upon preparing 19-acylbilanes (**III-VIII**) bearing a protecting group (X) at the 1-position (e.g., ethylthio), we began carrying out transformations to yield the porphyrin. The individual steps in the transformation included (i) oxidation to give the free base biladiene, (ii) metal complexation, (iii) desulfurization, and (iv) reduction of the acyl moiety to give the metal-templated biladiene-carbinol (**III-VII**), which upon (v) acid-catalyzed condensation and (vi) oxidation would give the free base or metalloporphyrin. During the course of this work, we found serendipitously that the 1-(ethylthio)-19-acylbilane (**III-VIII**, X = -SEt) would undergo transformation in a one-flask process to give the metalloporphyrin (**III-VI-M**), thereby obviating the individual stepwise transformations. The one-flask transformation occurred under basic, metal-templating conditions.

In this chapter, we describe our studies of this new route to ABCD-porphyrins. The porphyrin (**III-1**) chosen for demonstration of the methodology contains four different meso substituents (phenyl, *p*-tolyl, 4-ethylphenyl, and 4-*tert*-butylphenyl), each of which is electron-rich, sterically unhindered, and of distinct mass (Chart III.2). Electron-rich, sterically unhindered substituents were chosen to accentuate any possible scrambling processes, whereas the distinct mass enables identification of such scrambling upon LD-MS analysis.[III11,III31] We first describe the synthesis of 9-protected 1-acyldipyrromethanes and their elaboration to the corresponding 1-protected 19-acylbilanes. The bilanes have been characterized extensively by 1D and 2D NMR spectroscopy. The stepwise conversion of the bilane to the porphyrin, which has provided insight into the properties and reactivity of novel tetrapyrrolic species, is described

in the Supporting Information. The final section describes the one-flask conversion of the 1-protected 19-acylbilane to the porphyrin.

Taken together, the new route described herein should enable synthesis of porphyrins in good yield and at reasonable concentrations, thereby facilitating practical use and large-scale syntheses.



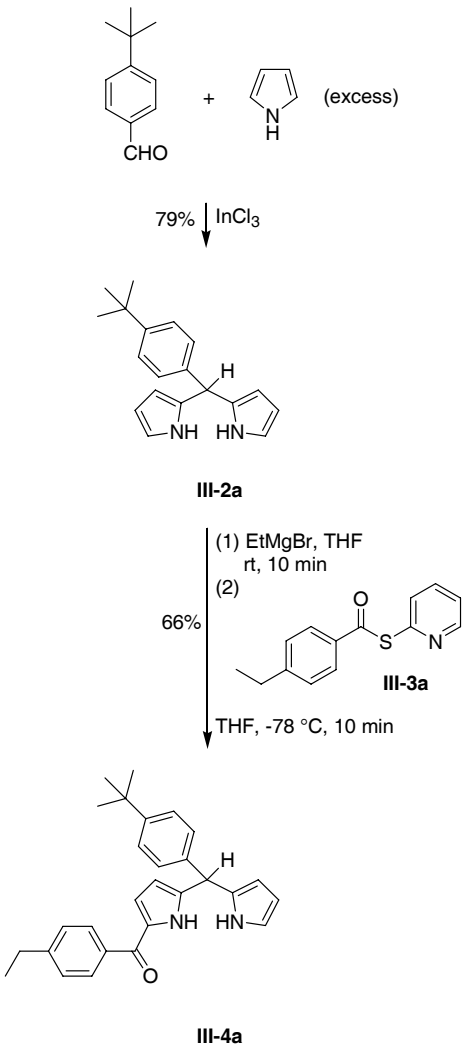
III-1

Chart III.2. ABCD-Porphyrin Bearing Electron-Rich Substituents.

III.B. Results and Discussion.

I. Directed Synthesis of Bilanes.

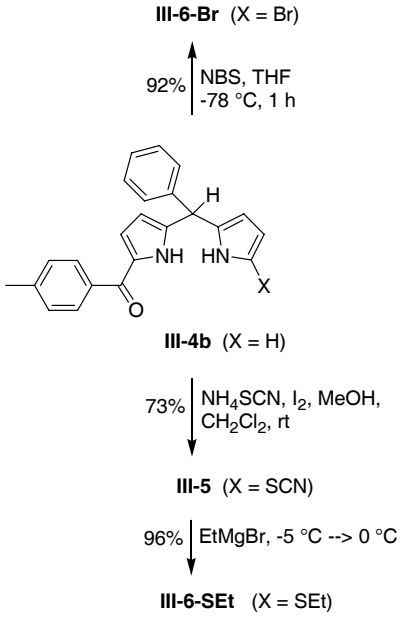
(i) Preparation of Dipyrromethane Precursors. The initial approach focused on use of a 1-acyldipyrromethane and a 9-protected 1-acyldipyrromethane as precursors to the target bilane. Multigram quantities of dipyrromethanes[III4] and 1-acyldipyrromethanes[III3,III5] can easily be synthesized at high concentration with limited or no chromatography. Thus, the condensation of 4-*tert*-butylbenzaldehyde with excess pyrrole afforded known[III3] dipyrromethane **III-2a** in 79% yield. Acylation of **III-2a** with Mukaiyama reagent **III-3a** (prepared herein by reaction[III6] of 2-mercaptopyridine and 4-ethylbenzoylchloride) gave the corresponding 1-acyldipyrromethane (**III-4a**) in 66% yield as shown in Scheme III.3.



Scheme III.3. Synthesis of a 1-Acyldipyrromethane.

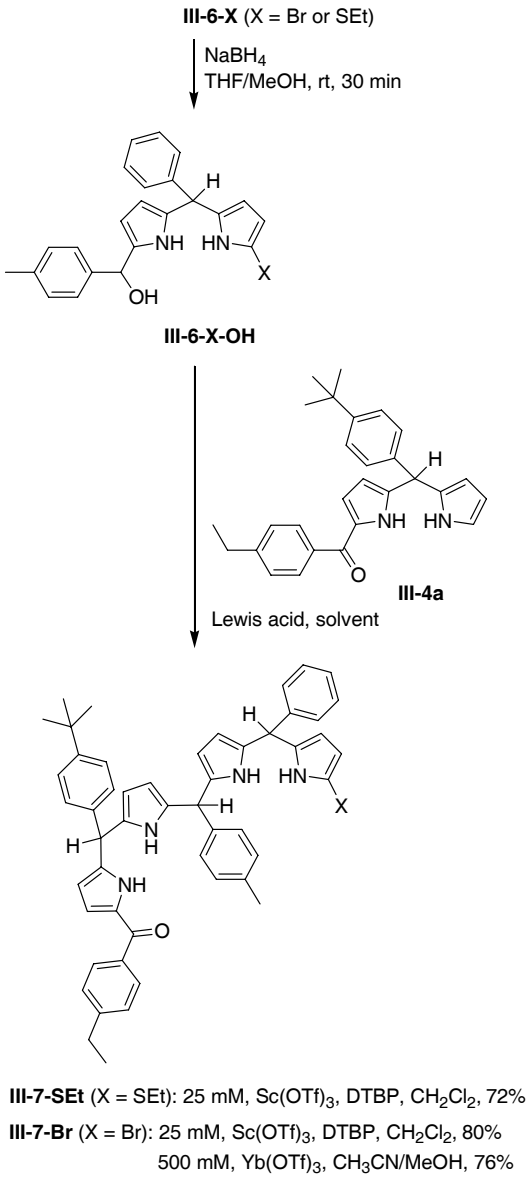
A second 1-acyldipyrromethane (**III-4b**)[III5] was treated with ammonium thiocyanate and iodine[III32,III33] to give the 1-acyl-9-thiocyanatodipyrromethane (**III-5**) in 73% yield. Attempts to use this species in the synthesis of a bilane encountered difficulties owing, apparently, to loss of the cyano group upon reduction of the acyl unit. Condensation of the resulting putative 9-thiodipyrromethane-1-carbinol with 1-acyldipyrromethane **III-4a** did not provide the expected bilane. Accordingly, the thiocyanato group was converted by treatment with EtMgBr (3 mol

equiv)[III33,III34] to the corresponding ethylthio unit affording the 1-acyl-9-(ethylthio)dipyrromethane (**III-6-SEt**, Scheme III.4) in 96% yield. In this reaction, three equiv of EtMgBr is necessary because the dipyrromethane possesses two relatively acidic pyrrolic protons.



Scheme III.4. Synthesis of a 9-Protected 1-Acyldipyrromethane.

We also prepared a precursor that bears a 1-bromo substituent, given the better leaving group character of –Br versus –SEt, as well as our extensive experience with the preparation of the precursor 1-acyl-9-bromodipyrromethanes in chlorin syntheses.[III35,III36] The reduction of **III-6-SEt** or known[III37] dipyrromethane **III-6-Br** to the corresponding carbinol **III-6-SEt-OH** or **III-6-Br-OH** was performed in THF/methanol (3:1) using 25 mol equiv of $NaBH_4$ (Scheme III.5). The dipyrromethane-carbinol **III-6-SEt-OH** was noticeably more stable than that of **III-6-Br-OH** in the sense that a sample of the former could be taken to dryness whereas the latter could not without some decomposition.



Scheme III.5. Synthesis of 1-Protected 19-Acylbilanes**.**

(ii) Acid Catalysis Conditions for Bilane Formation. The condensation of the crude **III-6-SEt-OH** with 1-acyldipyrromethane **III-4a** was carried out using the conditions that emerged from extensive studies of the "2 + 2" (dipyrromethane + dipyrromethane-1,9-dicarbinol) condensation leading to porphyrins.[III1,III2,III11,III38,III39] The conditions entail reaction in CH_2Cl_2 (anhydrous) at 25 mM in the presence of $Sc(OTf)_3$ (3.25 mM) and 2,6-di-*tert*-butylpyridine (DTBP, 32.5 mM) under argon. After 20 min of condensation, TLC analysis

revealed complete consumption of **III-6-SEt-OH**, a trace amount of **III-4a**, and bilane **III-7-SEt**. Workup by quenching with excess TEA followed by column chromatography provided **III-7-SEt** in 72% yield (Scheme III.5). Analogous reaction of **III-4a** and **III-6-Br-OH** afforded bilane **III-7-Br** in 80% yield.

A survey of conditions was carried out to identify high-concentration reaction conditions that afford the bilane in high yield, without scrambling, and enable a straightforward purification. The concentration was set at 0.5 M, and the study was applied to the condensation of **III-6-Br-OH** and 1-acyldipyrromethane **III-4a**. Four solvents (CH_2Cl_2, toluene, THF/MeOH, CH_3CN/MeOH) and seven Lewis acids [$MgBr_2$, $Mg(OTf)_2$, $Sc(OTf)_3$, $Zn(OTf)_2$, $InCl_3$, $Sn(OTf)_2$, $Yb(OTf)_3$] were examined with or without the presence of the Brønsted acid scavenger DTBP. The condensations were monitored by TLC analysis to assess cleanliness and by laser-desorption mass spectrometry (LD-MS) to assess scrambling.[III11,III31] The cleanliness was assessed qualitatively using an EGFP scale (excellent, good, fair, poor) on the basis of the relative amount of the desired bilane and the number of other components present. The bilane was isolated by chromatography to determine the yield. The results of the study are shown in Table III.1.

Table III.1. Survey of Diverse Acids in the Condensation of III-4a + III-6-Br-OH (0.5 M each)[a]

Entry	Acid (mM)	Additive (mM)	Solvent[b]	Time (min)	Cleanliness[c]	% Yield[d] of **III-7-Br**
1	$InCl_3$ (1.0–2.5)	----	THF/MeOH or CH_3CN/MeOH	180	P	Trace
2	$InCl_3$ (3.3)	----	CH_3CN/MeOH	45	G	66
3	$Sc(OTf)_3$(3.3)	----	CH_3CN/MeOH	45	G	51

Table III.1 (continued)

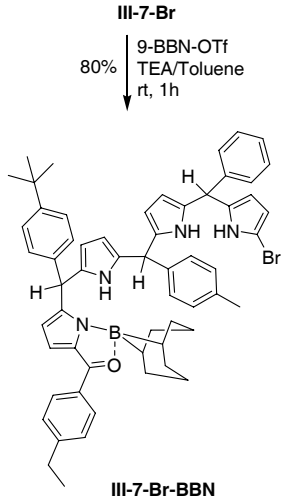
4	$Yb(OTf)_3$ (3.3)	----	CH_3CN/MeOH	45	E	60
5	$Zn(OTf)_2$ (3.3)	---	CH_3CN/MeOH	45	G	53
6	$Sn(OTf)_2$ (3.3)	----	CH_3CN/MeOH	45	F	49
7	$Mg(OTf)_2$ (3.3)	----	CH_3CN/MeOH	360	P	Trace
8	$MgBr_2$ (3.3)	----	CH_3CN/MeOH	overnight	P	Trace
9[e]	$Sc(OTf)_3$ (32)	DTBP (320)	THF/MeOH	120	G	50
10[e]	$Sc(OTf)_3$ (32)	DTBP (320)	CH_3CN/MeOH	20	G	84
11[f]	$Sc(OTf)_3$ (3.25)	DTBP (32.5)	CH_2Cl_2	30	F	35
12	$Sc(OTf)_3$ (3.25)	DTBP (32.5)	Toluene	120	P	Trace

[a]Reactions were carried out with 0.125 mmol reactants unless noted otherwise. [b]Where mixed solvents are employed, the fraction of methanol is ~33%. [c]Crude reaction mixtures were assessed by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. "E" (excellent) indicates the dominant presence of **III-7-Br**, a small amount of unreacted **III-4a**, no **III-6-Br-OH**, and no other components. "G" (good) indicates the dominant presence of **III-7-Br**, a small amount of unreacted **III-4a**, little or no **III-6-Br-OH**, and a few other components. "F" (fair) indicates the presence of some **III-7-Br**, significant quantities of unreacted **III-4a** and **III-6-Br-OH**, and significant quantities of other components. "P" (poor) indicates little or no **III-7-Br**, a large amount of unreacted **III-4a**, no **III-6-Br-OH**, and/or a large amount of other components. [d]Isolated yields. [e]0.250 mmol reactants. [f]0.500 mmol reactants.

In all cases where bilane **III-7-Br** was detected, no scrambling was observed. Of the various reaction conditions, the use of $Yb(OTf)_3$ (entry 4) provided an attractive balance of yield

and cleanliness. The reaction with $Yb(OTf)_3$ with 1.00 mmol of each reactant gave **III-7-Br** in 76% yield (0.619 g) as well as recovery of the unreacted **III-4a** (0.073 g). The conditions in entry 10 [$Sc(OTf)_3$ and DTBP] also appeared quite attractive from a yield standpoint; however, removal of DTBP from the crude bilane required column chromatography. Given that the reaction with $Yb(OTf)_3$ employed 1/10 as much acid, did not require an additive, and afforded a simpler purification procedure, we focused all subsequent work on the use of $Yb(OTf)_3$ in methanolic acetonitrile for bilane formation. In summary, the study on bilane synthesis allowed the condensation to be performed (1) at high concentration (0.5 M), (2) without any detectable scrambling, (3) in high yield (76%), (4) with a low acid concentration (3.3 mM), (5) without chlorinated solvents (CH_2Cl_2 vs methanolic acetonitrile), and (6) in a few hour period. The condensation conditions are comparable to if not milder than those used previously for directed syntheses of β-substituted bilanes, which include triethylammonium acetate in CH_2Cl_2,[III17] montmorillonite clay in CH_2Cl_2,[III18] $SnCl_4$,[III40,III41] and Cu(I), light, or heat.[III19]

(iii) III-9-BBN Complex of a 19-Acylbilane. The bilane **III-7-Br** was converted to the corresponding 9-BBN complex, mirroring chemistry we have employed for the boron complexation of 1-acyldipyrromethanes.[III5] The dialkylboron complexes of 1-acyldipyrromethanes are much more hydrophobic than the parent acyldipyrromethanes and crystallize easily, thereby facilitating isolation. Treatment of **III-7-Br** with TEA in toluene followed by addition of 9-BBN afforded **III-7-Br-BBN** in 80% yield (Scheme III.6).



Scheme III.6. Dialkylboron Complexation of a 19-Acylbilane.

(iv) Characterization of 19-Acylbilanes. Each bilane prepared herein (**III-7-SEt**, **III-7-Br**, **III-7-Br-BBN**) contains three stereogenic centers; thus, the isolated bilane is expected to consist of a mixture of 8 stereoisomers. The bilanes were characterized by LD–MS, FAB-MS, elemental analysis, and NMR spectroscopy (^{1}H, ^{13}C, ^{15}N, and for **III-7-Br-BBN**, ^{11}B). The ^{1}H NMR resonances of the bilane **III-7-Br** were examined by NOESY and H–H gCOSY, enabling assignment of all protons in the molecule. The high-resolution exact mass spectrum of **III-7-SEt** and **III-7-Br** each gave a peak consistent with the protonated molecule ion derived from the $2e^{-}$ /$2H^{+}$-oxidized analogue. Bilanes are known to be prone to oxidation, which may have occurred during the mass spectrometric process. The elemental analysis data for **III-7-SEt** and **III-7-Br** are consistent with the presence of one molecule of water per bilane. The bilane **III-7-Br-BBN** gave expected elemental analysis and mass spectral data. Thompson and co-workers recently described the use of ^{15}N NMR spectroscopy, including proton-coupled gHMBC and gHSQC analysis for the characterization of diverse pyrrolic compounds including dipyrromethanes, dipyrrins, and bis(dipyrrins).[III42] We utilized this powerful method for characterization of the

bilanes. The results are summarized in Table III.2. The proton-coupled gHMBC analysis of each bilane (**III-7-Br**, **III-7-SEt**, **III-7-Br-BBN**) showed three distinct peaks for the four nitrogen atoms. This pattern stems from the two terminal pyrroles (N^{21}, N^{24}), which bear distinct α-substituents (acyl vs bromo or ethylthio) and give distinct resonances, and the two inner pyrroles (N^{22}, N^{23}), which are similarly substituted and give an overlapped resonance. The ^{1}H NMR spectra also show very close chemical shifts for the inner two pyrrolic protons. In the case of **III-7-Br-BBN**, the nitrogen atom (N^{24}) coordinated to the 9-BBN moiety gave a large downfield chemical shift upon gHMBC analysis (and no peak upon gHSQC analysis), which is consistent with that of the dialkylboron complex of a 1-acyldipyrromethane.[III43] On the basis of the gHSQC spectra, the values of the NH one bond coupling constant ($^{1}J_{N-H}$) ranged from –96 to –100 Hz for each bilane, which are consistent with those reported for shorter homologues (i.e., dipyrromethanes[III42]).

Table III.2. ^{15}N NMR Spectroscopic Data for Bilanes[a]

Compound	Method	δ ^{15}N NMR Resonances (ppm)		
		N^{21}	N^{22} and N^{23}	N^{24}
III-7-SEt	gHSQC	–215.1	–227.2	–223.5
	gHMBC	–215.1	–227.2	–223.5
III-7-Br	gHSQC	–220.7	–227.2	–223.5
	gHMBC	–220.7	–227.2	–223.5
III-7-Br-BBN	gHSQC	–220.9	–227.4	___[b]
	gHMBC	–220.9	–227.4	–151.5

[a] ^{15}N NMR spectroscopic data were collected with 0.2 M samples in THF-d_8 at room temperature. Chemical shifts were standardized with respect to 1.0 M $MeNO_2$ (δ = 0.0 ppm) as an internal standard.[III43] [b] The resonance from the boron-complexed pyrrolic nitrogen was not observed.

(v) Stability of 19-Acylbilanes. The bilanes, like most pyrromethanes, are susceptible to oxidation. 19-Acylbilanes **III-7-SEt**, **III-7-Br**, and **III-7-Br-BBN** were found to be stable in the solid (foam-like) form upon storage at –15 °C for at least several weeks. The bilanes darkened both in solid form and upon dissolution (**III-7-Br**, **III-7-SEt**, and **III-7-Br-BBN**) in an NMR solvent (e.g., $CDCl_3$, THF-d_8) for 3–5 hours on the benchtop under ambient light. The **III-7-Br-BBN** complex was noticeably less stable than the parent **III-7-Br** itself**.**

II. One-Flask Synthesis of Metalloporphyrins from Bilanes. The studies of the stepwise conversion of bilane **III-7-SEt** to the corresponding metalloporphyrin are described in the Supporting Information. A key finding was that attempted desulfurization of the biladiene-*ac*–metal complex **III-8-M** (in the case only of M = Pd or Cu among seven metals examined) gave not the expected des-ethylthiobiladiene **III-9-M** (Chart III.3) but rather the ABCD-porphyrin **III-1-M**. This finding prompted examination of the direct conversion of **III-7-SEt** → **III-1-M** without explicit preparation and isolation of the intermediate biladiene-*ac*–metal complex. The conditions employed initially were those for the self-condensation of a 1-acyldipyrromethane to give the *trans*-A_2B_2-palladium(II)porphyrin.[III37] Thus, reaction of **III-7-SEt** (100 mM) in the presence of a palladium salt (1.1 equiv) and KOH (5 equiv) in refluxing ethanol exposed to air afforded palladium porphyrin **III-1-Pd** (13–38% yield). The one-flask transformation is remarkable, given that porphyrin formation requires (in unknown order) formation of a carbon-carbon bond, displacement of the alkylthio unit, deoxygenation, oxidation, and metalation.

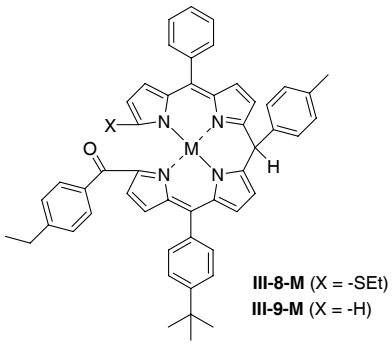


Chart III.3. Biladiene-*ac*–Metal Complexes.

An immediate objective was to gain access to a broader set of metalloporphyrins, particularly metal chelates that could be readily demetalated [e.g., Zn(II) or Mg(II)] so that the resulting free base porphyrin could be metalated as desired. Attempts to extend the KOH/ethanol conditions to metals other than palladium for the cyclization of **III-7-SEt** were generally unsuccessful. A key conceptual approach, derived from our studies of magnesium metalation of porphyrins, was to employ a magnesium reagent in a relatively non-coordinating reaction milieu.[III44] This led to the studies described below. The reader is referred to the Supporting Information for a comprehensive listing of conditions explored.

(i) Survey of Reaction Conditions. The reaction of a bilane was carried out with a metal salt and the strong, relatively non-nucleophilic base DBU in a solvent at small scale. Each reaction was analyzed by absorption spectroscopy to assess the yield of porphyrin and by TLC. In each case where a metalloporphyrin formed, TLC showed the presence of a trace quantity (~0.01 times that of the metalloporphyrin) of the free base porphyrin. Thus, the reported yields in Table III.3 of crude porphyrin samples (determined spectroscopically[III45]) encompass both the metalloporphyrin and the trace amount of free base porphyrin.

The reaction of **III-7-SEt** with $MgBr_2$ and DBU in butyronitrile gave **III-1-Mg** in 15% yield (entry 1, Table III.3). The use of toluene rather than butyronitrile gave **III-1-Mg** in 10%

yield (entry 2). Weaker bases such as 1,1,3,3-tetramethylguanidine or 2,2,6,6-tetramethylpiperidine in place of DBU gave **III-1-Mg** in 5 or 2% yield. No free base porphyrin was obtained in the absence of $MgBr_2$, even upon using much stronger bases such as ethylmagnesium bromide or lithium bis(trimethylsilyl)amide, or the weaker base diisopropylethylamine (see Supporting Information).

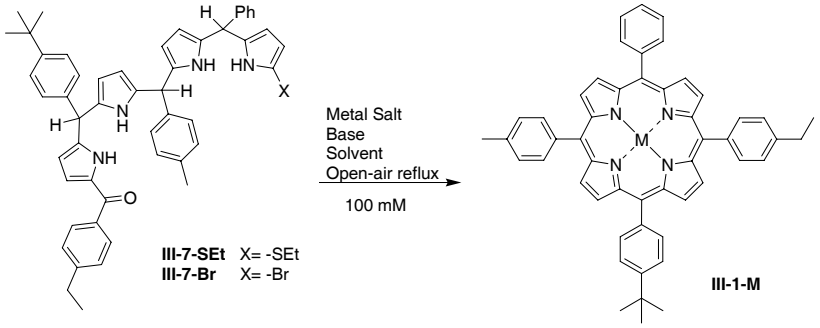


Table III.3. One-Flask Bilane Cyclization[a]

Entry	Bilane	Metal Salt	DBU (equiv)	Solvent	Time (h)	Product	Yield (%)
1	**III-7-SEt**	$MgBr_2$	10	PrCN	2	**III-1-Mg**	15
2	**III-7-SEt**	$MgBr_2$	10	Toluene	8	**III-1**	10[b]
3	**III-7-Br**	$MgBr_2$	10	PrCN	6	**III-1-Mg**	47[b]
4	**III-7-Br**	$MgBr_2$	10	Toluene	2	**III-1-Mg**	64[b]
5	**III-7-Br**	---	10	Toluene	24	**III-1**	10
6	**III-7-Br**	$MgBr_2$	10	---[c]	3	**III-1-Mg**	35[b]
7[d]	**III-7-Br**	$MgBr_2$	10	Toluene	1.5	**III-1-Mg**	69
8	**III-7-Br**	$Zn(OAc)_2$	10	Toluene	1	**III-1-Zn**	50
9	**III-7-Br**	$ZnBr_2$	10	Toluene	5	**III-1-Zn**	26[b]
10	**III-7-Br**	ZnI_2	10	Toluene	4	**III-1-Zn**	31[b]
11	**III-7-Br**	$Zn(acac)_2$	10	Toluene	3.5	**III-1-Zn**	37[b,e]
12	**III-7-Br**	$ZnEt_2$	---	Toluene	3.5	**III-1-Zn**	18

Table III.3. (continued)

13	**III-7-Br**	$NiCl_2$	10	Toluene	2	**III-1-Ni**	29
14	**III-7-Br**	$InCl_3$	10	Toluene	2	**III-1-InCl**	16

[a]The standard condition employs treatment of a solution of the bilane (0.062 mmol) in the specified solvent first (100 mM) with DBU (10 mol equiv versus bilane) and after 5 min with the corresponding metal reagent (3 mol equiv versus bilane). The resulting heterogeneous reaction mixture was sonicated for a few secs, and then stirred at room temperature for 1 min. The reaction mixture was stirred and heated under open-air reflux. [b]Yield of isolated pure porphyrin was determined by absorption spectroscopy. [c]Reaction concentration was estimated to be 0.67 M. [d]Larger scale reaction (0.62 mmol bilane). [e]Free base porphyrin **III-1** also was isolated (0.4% yield).

Application of the conditions of $MgBr_2$ and DBU to bilane **III-7-Br** (rather than **III-7-SEt**) in butyronitrile gave **III-1-Mg** in 47% yield (entry 3), whereas that in toluene gave **III-1-Mg** in 64% yield (entry 4). Thus, bilane **III-7-Br** is a much more effective precursor to the porphyrin than bilane **III-7-SEt**, and all subsequent studies were carried out with bilane **III-7-Br**. The essential ingredients in these conditions were assessed by omission experiments. The omission of $MgBr_2$ gave the free base porphyrin **III-1** in 10% yield (entry 5), whereas the omission of toluene gave **III-1-Mg** in 35% yield (entry 6). The reaction using $MgBr_2$ (3 equiv) and DBU (10 equiv) at 100 mM gave **III-1-Mg** in high yield (69%, entry 7), which prompted examination of other metal reagents under the same conditions. A series of zinc reagents gave **III-1-Zn** in yields ranging from 18 – 50% (entries 8–12). The reaction with $NiCl_2$ or $InCl_3$ gave the corresponding metalloporphyrin in 29% or 16% isolated yield, respectively (entries 13–14).

(ii) Reaction Concentration. A key consideration in developing this approach was that metal-templating would provide effective reaction at higher concentration than that of the 2 + 2 reaction. Accordingly, the effect of concentration was investigated for the reaction of **III-7-Br**. For the concentration-dependence study, the mol ratio of $MgBr_2$ (3 equiv) and DBU (10 equiv) was kept constant, and only the relative amount of toluene was altered. The reactions were performed for 2 h and the isolated yield of porphyrin was determined. The results are

displayed in Figure III-1A. Note that concentrations stated herein are calculated on the basis of the volume of toluene in the reaction, whereas the concentrations shown in Figure III-1A refer to the volume of toluene and DBU.

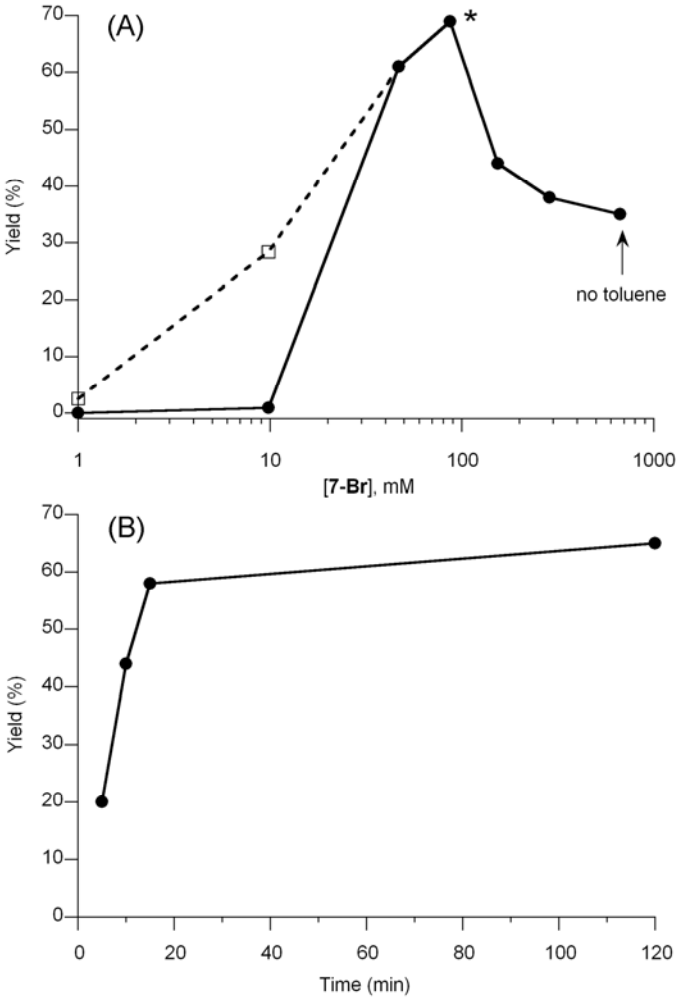


Figure III.1. (A) The yield of porphyrin **III-1-Mg** as a logarithmic function of the concentration of **III-7-Br**. The data shown in solid circles (●) were obtained with **III-7-Br** (0.100 mmol), DBU (1.00 mmol, 10.0 equiv), and $MgBr_2$ (0.300 mmol, 3.00 equiv) in an appropriate amount of hot toluene exposed to air for 2 h. The two datapoints shown in open squares (□) were obtained in similar manner but with 100 equiv of DBU and 30 equiv of $MgBr_2$. The x-axis shows the concentration of **III-7-Br** per the amount of toluene and DBU assuming additivity of volumes. The * denoted on the graph indicates a 100 mM concentration of **III-7-Br** on the basis of the amount of toluene. (B) The yield of porphyrin **III-1-Mg** as a function of time for **III-7-Br** at 100 mM on the basis of the amount of toluene.

The highest yield (69%) was observed at 100 mM (on the basis of toluene). At the

highest concentration investigated, the reaction was carried out in the absence of toluene, which gave **III-1-Mg** in 35% yield. The reaction at 1 mM or 10 mM concentration of **III-7-Br** gave no detectable porphyrin or 0.9% spectroscopic yield, respectively, despite allowing these low-concentration reactions to proceed overnight. When the same dilute reactions were performed with a 10-fold increase in DBU (100 equiv) and $MgBr_2$ (30 equiv), the falloff in yield with increasing dilution was somewhat mitigated. In each case, LD-MS analysis of the crude reaction mixture did not show the presence of any scrambled porphyrin product.

(iii) Reaction Time. The rate of porphyrin formation was examined with bilane **III-7-Br**. Because the reaction under the standard conditions (in toluene containing $MgBr_2$ and DBU) is heterogeneous, individual reactions were sacrificed at a specific time and each crude reaction mixture was then dissolved in CH_2Cl_2 to obtain accurate yield determinations of **III-1-Mg**. The timecourse is displayed in Figure III.1B. The reaction is very fast, with a half-time between 5–10 min. TLC analysis showed no detectable amount of **III-7-Br** by the 15-min timepoint; at the end of the reaction only **III-1-Mg** and a polar component were observed. Absorption spectroscopy showed the time-dependent appearance and disappearance of an absorption band with a very broad peak at 462 nm (consistent with a magnesium-coordinated biladiene-*ac* species).

(iv) Balanced Equation. The balanced equation for porphyrin synthesis directly from bilane **III-7-Br** is shown in Equation III.1. The conversion of bilane **III-7-Br** to the corresponding porphyrin requires a $2e^-/2H^+$ oxidation. The reaction also produces three equivalents of acid, one (HBr) from the bilane upon cyclization and two (HX) from the metal reagent MX_2 upon metalation. Thus, to maintain a basic medium over the course of the reaction requires at least three equivalents of base.

III-7-Br + $MgBr_2$ → **III-1-Mg** + H_2O + 3HBr + $2e^-$ + $2H^+$ (Equation III.1)

The requirement for a $2e^-/2H^+$ oxidant naturally suggested the role of molecular oxygen given that the reactions were performed in the presence of air. To test the essential role of oxygen, the condensation of **III-7-Br** was carried out under reflux with different atmospheric compositions. The reaction of **III-7-Br** in toluene containing $MgBr_2$ (3 equiv) and DBU (10 equiv) with a very slow oxygen flow (rather than air) afforded **III-1-Mg** in 31% yield. Surprisingly, the reaction under a slow argon flow gave **III-1-Mg** in 51% yield. Thus, the absence of oxygen does not impede the reaction while the presence of increased oxygen gave a lower yield.

The reaction carried out in the presence of 2,2,6,6-tetramethylpiperidine rather than DBU resulted in 6% spectroscopic yield of **III-1-Mg** from **III-7-Br** (standard aerobic conditions). It is tempting to suggest that the imine unit in DBU may provide the oxidizing equivalent; however, the lower yield with 2,2,6,6-tetramethylpiperidine versus DBU may also stem from the great difference in strength of the two bases (the conjugate acids have pK_a 11.2^{III46} vs 24^{III47}) rather than ability to serve as oxidants. Further experimentation is required to elucidate the nature of the oxidant.

(v) Preparative Synthesis. The reaction of **III-7-Br** (0.50 g, 0.62 mmol) in the presence of $MgBr_2$ and DBU gave the magnesium porphyrin **III-1-Mg** in 65% yield (0.295 g). A ~5-fold larger-scale reaction (2.44 g, 3 mmol of **III-7-Br**) afforded >1 g of crude **III-1-Mg** and a trace of the corresponding free base porphyrin **III-1**. The crude sample of **III-1-Mg** could not be purified via flash column chromatography owing to the presence of a closely chromatographing impurity. The same impurity was observed in the small-scale reactions (0.062 mmol to 0.62 mmol scale) and was readily removed with flash column chromatography. The

crude product was demetalated with TFA; work-up and chromatography afforded the free base porphyrin **III-1** (1.123 g) in 53% yield.

Microwave-assisted synthesis often introduces shorter reaction times, hence we examined the synthesis of **III-1-Mg** under microwave irradiation. The condensation of **III-7-Br** was carried out at 115 °C under standard small-scale reaction conditions (0.1 mmol, toluene, 100 mM of **III-7-Br**, 3 equiv of $MgBr_2$ and 10 equiv of DBU). The reaction was completed in 15 min. The crude reaction mixture was checked by TLC analysis, LD-MS and absorption spectrum. No starting material (**III-7-Br**) was observed after 15 min irradiation time. In addition, no detectable scrambling was observed on the basis of LD-MS analysis. Subsequent purification via flash column chromatography afforded **III-1-Mg** in 51% yield.

The success of the bilane cyclization process depends in part on the purity of the starting bilane. In the synthesis of bilane **III-7-Br**, a small amount of unreacted 1-acyldipyrromethane (**III-4a**) typically remains. Any unreacted 1-acyldipyrromethane (**III-4a**) can undergo self-condensation to give the corresponding *trans*-A_2B_2-porphyrin. Purification of the bilane ensures that only one porphyrin is formed in the cyclization process. The self-condensation of the 1-acyldipyrromethane, while a potential side reaction in the ABCD-porphyrin synthesis, alone constitutes a viable means for constructing a *trans*-A_2B_2-porphyrin and will be described elsewhere. A limited version of this route, the self-condensation of 1-formyldipyrromethane to give the fully unsubstituted magnesium(II)porphine, has recently been described.[III48]

III.C. Outlook.

The features of the one-flask bilane cyclization route are compared with the existing 2 + 2 route as shown in Table III.4. The prior "2 + 2" route to ABCD-porphyrins requires seven steps,[III1,III2] including (1, 2) synthesis of the two dipyrromethanes, (3–5) 1,9-diacylation of one

dipyrromethane and conversion to the dipyrromethane-1,9-dicarbinol, (6) dipyrromethane + dipyrromethane-dicarbinol condensation/oxidation to give the ABCD-porphyrin, and optionally (7) metalation. The entire synthesis requires only one chromatography operation (for purification of the porphyrin).

Table III.4. Comparison of Routes to ABCD-Porphyrins

Features	Comparison	
Method	"2 + 2" route (DPM + DPM-diol)	One-flask bilane cyclization
[reactant]	2.5 (or 25) mM	100 mM
Effective [pyrrole] in cyclization	10 (or 100) mM	400 mM
Theoretical porphyrin concentration	2.5 (or 25) mM	100 mM
Total steps (from aldehydes)[a]	7	8
Solvent for porphyrin formation	CH_2Cl_2	Toluene
Chromatography operations	1[b]	2[c]
Oxidation	DDQ	In situ
Conditions for porphyrin formation	Acidic	Basic
Scrambling	ND[d] or low	ND[d]
Yield of the porphyrin-forming step (%)	~20–30 (or 8–23)	65[e]
Porphyrin metalation state	Free base	Magnesium chelate

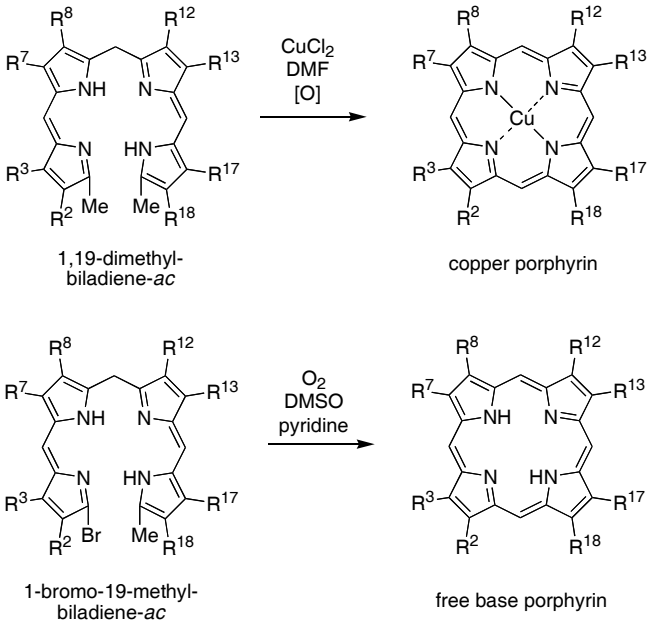
[a]Ignores steps to prepare the Mukaiyama reagents. [b]Purification of the crude product from the porphyrin-forming reaction. [c]Purification of bilane species (**III-7-SEt**, **III-7-Br**) and the metalloporphyrin. [d]Not detected.

The new synthesis described herein requires eight steps, including (1, 2) synthesis of the two dipyrromethanes, (3, 4) 1-acylation of each dipyrromethane, (5) protection of one of the 1-acyldipyrromethanes at the 9-position, (6) reduction of the latter to give the 9-protected dipyrromethane-1-carbinol, (7) condensation of the 9-protected dipyrromethane-1-carbinol with

the other 1-acyldipyrromethane to give the corresponding bilane, and (8) ring closure to give the ABCD-metalloporphyrin.

The new route includes one additional step versus the prior synthesis, yet is more convergent and provides several operational improvements: (i) cyclization at higher concentration [100 mM bilane concentration = 400 mM total pyrrole concentration, versus 10 (or 100) mM total pyrrole concentration], (ii) avoidance of chlorinated solvents in all reaction steps (except purification of **II-4a** and the metalloporphyrins), (iii) formation of the ABCD-metalloporphyrin under basic conditions, which sidesteps acidolytic scrambling, (iv) no addition of a chemical reagent for oxidation of the intermediate(s), (v) better yield for ring closure (up to ~65% versus 20–30%), and (vi) no separate metalation step. The good yield at reasonably high concentration is consistent with expectation for, but not proof of, a metal-templated process.

The synthesis also can be compared with two more traditional methods for preparing porphyrins from unsaturated bilane species (Scheme III.7). (1) Treatment of a 1,19 dimethylbiladiene-*ac* or 1,19-dimethylbilene-*b* (not shown) with copper acetate in DMF affords the corresponding copper(II) porphyrin. In this reaction, one of the a-methyl groups is lost upon copper-mediated oxidation whereas the other α-methyl group provides the meso carbon atom. This reaction was pioneered by Jackson[III49-III51] and studied extensively by Smith.[III52] Use of alkyl groups longer than alkyl can afford the corresponding mono-meso-substituted porphyrin.[III52] (2) Treatment of a 1-bromo-19-methylbiladiene-*ac* under basic, oxidative conditions gives the corresponding free base porphyrin.[III50,III51,III53] The methyl group provides the meso carbon atom whereas the bromo substituent is the leaving group. The two routes have proved very versatile for the synthesis of β-substituted porphyrins.[III52,III54,III55] The ABCD-porphyrin synthesis has some conceptual similarity to the latter reaction, where the acyl carbon provides the meso site (and the D substituent) and the bromo substituent is the leaving group.



Scheme III.7. Traditional Routes to Porphyrins.

In summary, the new route described herein should be attractive for large-scale syntheses of diverse porphyrins bearing up to four different meso substituents. Although the chief focus of this work was to gain access to porphyrins, meso-substituted bilanes can now be synthesized and handled in a straightforward manner. Such access may provide entrée into a variety of studies, given that bilanes constitute open-chain analogues of calixpyrroles,[III56] are relatives of the bilin pigments,[III57-III59] exhibit a variety of conformational forms,[III60] undergo three successive steps of $2e^-/2H^+$ oxidation,[III12] and provide access to bilin derivatives that are potent antioxidants.[III61] Moreover, bilanes **III-7-X** are homologues of dipyrromethanes **III-6-X**; the strategy used to prepare **III-7-X** can in principle be extended to provide rational access to longer pyrromethane chains bearing distinct meso substituents.

III.D. Experimental Section

1. General. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were collected in $CDCl_3$ at room temperature unless noted otherwise. Melting points are uncorrected.

Silica gel (40 μm average particle size) was used for column chromatography. THF and toluene were distilled from sodium/benzophenone under argon. Methanol (anhydrous) and CH_2Cl_2 (anhydrous) were used as received. All other chemicals were reagent grade and were used as received. The dipyrromethanes, 1-acyldipyrromethanes, and bilanes are easily detected in TLC upon exposure to Br_2 vapor. LD-MS data for bilanes III-7-SEt and III-7-Br were obtained with the matrix POPOP. Grade V alumina was prepared by adding 15 mL of distilled H_2O to 85 g of alumina with vigorous mechanical stirring.

5-(4-*tert*-Butylphenyl)dipyrromethane (III-2a). Following a general procedure,[III4] a solution of 4-*tert*-butylbenzaldehyde (16.2 g, 100 mmol) in pyrrole (0.694 L, 10.0 mol) at room temperature under argon was treated with $InCl_3$ (2.21 g, 10.0 mmol) for 1.5 h. Powdered NaOH (12.0 g, 300 mmol) was added. After stirring for 1 h, the mixture was suction filtered. Excess pyrrole was removed from the filtrate under high vacuum. The resulting residue was treated with hexanes (3 x 100 mL) to facilitate removal of traces of pyrrole. The resulting solid was recrystallized [EtOH/H_2O (6:1)] to afford a grayish white solid (21.6 g, 79%): mp 155–157 °C (lit.[III3] 160 °C); ^{1}H NMR δ 1.31 (s, 9H), 5.45 (s, 1H), 5.94–5.96 (m, 2H), 6.15–6.17 (m, 2H), 6.68–6.70 (m, 2H), 7.13–7.16 (m, 2H), 7.32–7.35 (m, 2H), 7.89–7.95 (br, 2H); ^{13}C NMR δ 31.5, 34.6, 43.6, 107.2, 108.5, 117.2, 125.7, 128.2, 132.9, 139.1, 149.9; FAB-MS obsd 278.1788, calcd 278.1783 ($C_{19}H_{22}N_2$). Anal. Calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.82; H, 7.96; N, 10.05. The mp, ^{1}H NMR spectrum, and elemental analysis data are consistent with those obtained from a sample prepared via an earlier route.[III3]

***S*-2-Pyridyl 4-ethylbenzothioate (III-3a).** Following a general procedure,[III6] a solution of 2-mercaptopyridine (11.1 g, 100 mmol) in THF (100 mL) was treated with 4-ethylbenzoyl chloride (16.9 g, 100 mmol). The resulting slurry was stirred for 30 min. The precipitate was collected by filtration and washed with hexanes (150 mL) in a Buchner funnel. The filtered

material was added into a biphasic solution of saturated aqueous $NaHCO_3$ (100 mL) and diethyl ether (100 mL). The mixture was stirred until the foaming subsided. The organic layer was removed, and the aqueous layer was extracted with diethyl ether. The combined organic extract was dried (Na_2SO_4), and filtered. The filtrate was concentrated. The resulting solid was washed with hexanes (~20 mL) to afford a pale yellow solid (20.9 g, 86%): mp 48–50 °C; ^{1}H NMR δ 1.27 (t, *J* = 7.6 Hz, 3H), 2.73 (q, *J* = 7.6 Hz, 2H), 7.31–7.35 (m, 3H), 7.72–7.74 (m, 1H), 7.77–7.81 (m, 1H), 7.94–7.96 (m, 2H), 8.67–8.69 (m, 1H); ^{13}C NMR δ 15.3, 29.1, 123.7, 127.9, 128.5, 131.0, 134.3, 137.3, 150.5, 151.2, 151.6, 189.0; FAB-MS obsd 244.0812, calcd 244.0796 [(M + H)$^+$, M = $C_{14}H_{13}NOS$]. Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.10; H, 5.39; N, 5.76. Found: C, 68.96; H, 5.38; N, 5.70.

5-(4-*tert*-Butylphenyl)-1-(4-ethylbenzoyl)dipyrromethane (III-4a). Following a general procedure,[III3] a solution of EtMgBr (37.5 mL, 38 mmol, 1.0 M in THF) was added slowly to a solution of **III-2a** (4.17 g, 15.0 mmol) in THF (30 mL) under argon. The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of **III-3a** (3.45 g, 15.0 mmol) in THF (30 mL) was added. The solution was stirred at –78 °C for 10 min, and then allowed to warm to room temperature. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and filtered. The filtrate was concentrated to a minimum amount, whereupon silica gel was added. The mixture was concentrated to dryness. The resulting powder was loaded on top of a column (5 cm dia x 20 cm), followed by elution with hexanes/CH_2Cl_2/ethyl acetate (7:2:1) to afford a light yellow powder (4.06 g, 66%): mp 71–73 °C; ^{1}H NMR δ 1.27 (t, *J* = 7.6 Hz, 3H), 1.31 (s, 9H), 2.73 (q, *J* = 7.6 Hz, 2H), 5.50 (s, 1H), 5.99–6.01 (m, 1H), 6.08–6.09 (m, 1H), 6.16–6.18 (m, 1H), 6.70–6.72 (m, 1H), 6.81–6.82 (m, 1H),

7.15 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.93–7.99 (br, 1H), 9.24–9.30 (br, 1H); ^{13}C NMR δ 15.4, 29.1, 31.5, 34.6, 43.9, 107.8, 108.6, 110.6, 117.8, 120.5, 125.9, 127.9, 128.1, 129.3, 130.9, 131.3, 136.1, 137.8, 141.6, 148.6, 150.3, 184.5; FAB-MS obsd 410.2367, calcd 410.2358 ($C_{28}H_{30}N_2O$). Anal. Calcd for $C_{28}H_{30}N_2O$: C, 81.91; H, 7.37; N, 6.82. Found: C, 82.16; H, 7.49; N, 6.74.

1-(4-Methylbenzoyl)-5-phenyl-9-thiocyanatodipyrromethane (III-5). Following a general procedure,[III32] a solution of **III-4b** (3.40 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added slowly in a dropwise manner to a solution of ammonium thiocyanate (1.14 g, 15.0 mmol) and iodine (1.27 g, 5.0 mmol) in methanol (10.0 mL) with stirring at room temperature. After 1 h, TLC analysis showed some starting material. Hence, a second portion of a solution of ammonium thiocyanate (1.14 g, 15.0 mmol) and iodine (1.27 g, 5.0 mmol) in methanol (10 mL) was added dropwise in the reaction mixture, and the reaction mixture was stirred for 2 h. The reaction mixture was concentrated (~10 mL) and filtered (Buchner funnel). The filtered material was washed with methanol and dried in vacuo to afford a grayish white solid (2.91 g, 73%): mp 183–185 °C; ^{1}H NMR δ 2.42 (s, 3H), 5.59 (s, 1H), 6.01–6.03 (m, 1H), 6.11–6.12 (m, 1H), 6.51–6.53 (m, 1H), 6.81–6.83 (m, 1H), 7.15–7.17 (m, 2H), 7.24–7.30 (m, 5H), 7.61–7.63 (m, 2H), 9.34–9.40 (br, 1H), 10.64–10.70 (br, 1H); ^{13}C NMR δ 21.8, 44.4, 103.1, 110.7, 111.1, 111.2, 120.7, 121.5, 127.8, 128.4, 129.0, 129.3, 129.4, 131.3, 135.5, 138.5, 139.7, 140.7, 142.9, 185.2; FAB-MS obsd 398.1312, calcd 398.1327 ($C_{24}H_{19}N_3OS$); Anal. Calcd for $C_{24}H_{19}N_3OS$: C, 72.52; H, 4.82; N, 10.57. Found: C, 72.28 ; H, 4.99; N, 10.51.

1-Ethylsulfanyl-9-(4-methylbenzoyl)-5-phenyldipyrromethane (III-6-SEt). Following a general procedure,[III34] a solution of EtMgBr (21 mL, 21 mmol, 1.0 M in THF) in THF (49 mL) cooled at –5 °C was treated slowly with a solution of **III-5** (2.78 g, 7.00 mmol) in

THF (35 mL). After stirring at 0 °C for 30 min, TLC showed complete consumption of starting material. The mixture was poured into an ice-cold solution of 20% aqueous NH_4Cl (~100 mL), to which Et_2O (~100 mL) was added. The organic layer was washed with water, dried and concentrated. Hexanes was added. The resulting suspension was filtered on a Buchner funnel to afford a pink solid (2.69 g, 96%): mp 179–181 °C; ^{1}H NMR δ 1.18 (t, *J* = 7.2 Hz, 3H), 2.42 (s, 3H), 2.60 (q, *J* = 7.2 Hz, 2H), 5.49 (s, 1H), 5.94–5.96 (m, 1H), 6.05–6.06 (m, 1H), 6.30–6.31 (m, 1H), 6.80–6.81 (m, 1H), 7.21–7.36 (m, 7H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.98–8.02 (br, 1H), 9.39–9.43 (br, 1H); ^{13}C NMR δ 15.3, 21.7, 32.1, 44.5, 109.7, 110.7, 117.2, 119.4, 120.3, 127.7, 128.5. 129.12, 129.18, 129.3, 131.0, 133.8, 135.8, 140.4, 140.7, 142.5, 184.5; FAB-MS obsd 400.1609, calcd 400.1609 ($C_{25}H_{24}N_2OS$); Anal. Calcd for $C_{25}H_{24}N_2OS$: C, 74.97; H, 6.04; N, 6.99. Found: C, 74.83; H, 6.14; N, 6.77.

19-(4-Ethylbenzoyl)-1-ethylsulfanyl-10-(4-methylphenyl)-5-phenyl-15-(4-*tert*-butylphenyl)bilane (III-7-SEt). A solution of **III-6-SEt** (0.240 g, 0.600 mmol) in dry THF/methanol (48 mL, 3:1) under argon at room temperature was treated with $NaBH_4$ (0.567 g, 15.0 mmol, 25.0 mol equiv) in small portions with rapid stirring. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. The reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl and CH_2Cl_2 (250 mL). The organic phase was separated, washed (water and brine), dried (K_2CO_3), and concentrated under reduced pressure to yield the carbinol as a yellow-orange paste. The resulting sample was dissolved in anhydrous CH_2Cl_2 (24 mL) and treated with **III-4a** (0.246 g, 0.600 mmol). The reaction mixture was stirred for 10 min to achieve complete dissolution of **III-4a**. Following the acid catalysis conditions used in porphyrin syntheses,[III2] 2,6-di-*tert*-butylpyridine (175 μL, 0.779 mmol, 32.5 mM) and $Sc(OTf)_3$ (0.0384 g, 0.0779 mmol, 3.25 mM)

were added. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. The reaction mixture was stirred at room temperature for 1 h. A sample of TEA was added (110 μL, 0.779 mmol, 32.5 mM). The reaction mixture changed immediately from red to orange-yellow. The reaction mixture was diluted with CH_2Cl_2 (~100 mL), washed with water and brine, dried (Na_2SO_4) and concentrated to afford an orange paste. Further drying under high vacuum for 10 min afforded an orange foam. Column chromatography [silica, hexanes/ethyl acetate (3:1)] afforded a brown foam (0.343 g, 72%), presumably as a mixture of 8 stereoisomers: mp 87–90 °C; ^{1}H NMR (THF-d_8) δ 1.30 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.6 Hz, 3H), 1.29 (s, 9H), 2.28 (s, 3H), 2.53 (q, J = 7.2 Hz, 2H), 2.72 (q, J = 7.6 Hz, 2H), 5.22–5.24 (m, 1H), 5.29–5.31 (m, 1H), 5.41-5.44 (m, 1H), 5.48–5.51 (m, 2H), 5.53–5.50 (m, 1H), 5.57–5.60 (m, 1H), 5.62–5.63 (m, 1H), 5.82–5.92 (m, 1H), 6.08–6.14 (m, 1H), 6.68–6.74 (m, 1H), 7.02–7.06 (m, 4H), 7.11–7.14 (m, 5H), 7.19–7.23 (m, 2H), 7.27–7.32 (m, 4H), 7.77 (d, J = 7.6 Hz, 2H), 9.52–9.58 (brs, 1H), 9.65–9.67 (brs, 1H), 9.92–10.22 (brs, 1H), 10.82–11.2 (brs, 1H); ^{13}C NMR (THF-d_8) δ 15.6, 16.0, 21.3, 29.8, 31.9, 32.4, 35.2, 44.8, 45.1, 45.4, 107.6, 107.8, 109.6, 110.6, 117.1, 118.9, 119.6, 125.9, 127.1, 128.4, 128.8, 129.2, 129.4, 129.5, 130.0, 131.9, 132.65, 132.68, 132.7, 133.36, 133.4, 134.4, 134.5, 134.72, 134.75, 134.8, 136.2, 137.62, 137.68, 138.0, 140.8, 141.9, 142.0, 143.2, 143.3, 144.48, 144.5, 148.7, 150.0, 170.7, 183.8; ^{15}N NMR (THF-d_8) δ –215.1, –223.5, –227.2 (two nitrogen atoms) (gHSQC and gHMBC). The high resolution exact mass spectrum gave m/z = 793.3978, which is assigned to the protonated molecule ion of the $2e^-/2H^+$-oxidized derivative of the title compound, *i.e.*, the protonated bilene [calcd 793.3940 for $(M' + H)^+$, $M' = C_{53}H_{52}N_4OS$, where the title compound has $C_{53}H_{54}N_4OS$], owing to oxidation during the ionization process. LD-MS (POPOP) obsd 794.0, calcd 794.4018 ($C_{53}H_{54}N_4OS$). Anal. Calcd for $C_{53}H_{54}N_4OS$: C, 80.06; H, 6.85; N, 7.05. Anal. Calcd for

$C_{53}H_{54}N_4OS \cdot H_2O$: C, 78.29; H, 6.94; N, 6.89. Found: C, 78.39; H, 6.87; N, 6.84.

1-Bromo-19-(4-ethylbenzoyl)-10-(4-methylphenyl)-5-phenyl-15-(4-*tert*-butylphenyl)bilane (III-7-Br). The condensation conditions described below are identical with those of entry 4 in Table III.1. A sample of **III-6-Br** (0.420 g, 1.00 mmol) in dry THF/methanol (80.0 mL, 3:1) under argon at room temperature was treated with $NaBH_4$ (0.946 g, 25.0 mmol, 25.0 mol equiv). The reaction was complete in 30 min. The reaction was poured into a mixture of saturated aqueous NH_4Cl (50 mL) and diethyl ether (250 mL). The organic phase was extracted with diethyl ether (~300 mL), washed with water and brine, dried (K_2CO_3), and concentrated under reduced pressure at ambient temperature. The resulting orange-yellow paste was transferred to an oven-dried round-bottomed flask (25 mL) with diethyl ether. The diethyl ether solution of the carbinol was concentrated to give an orange-yellow paste. The carbinol was handled as a paste containing residual diethyl ether rather than a dry solid for improved stability (see Supporting Information). A sample of **III-4a** (0.411 g, 1.00 mmol) was added. A septum was fitted to the flask, and anhydrous acetonitrile (1.34 mL) was added under a slow argon flow. The resulting orange-red reaction mixture was stirred for 1 min, whereupon $Yb(OTf)_3$ (0.660 mL of a 10.0 mM stock solution in anhydrous MeOH) was slowly added. The reaction mixture immediately turned dark brown. The reaction mixture was stirred for 20 min. An aliquot was removed from the reaction mixture and checked by TLC analysis [silica, hexanes/ethyl acetate (3:1)] and LD-MS. TLC analysis indicated the presence of **III-4a** and bilane **III-7-Br**. No detectable scrambling was observed by LD-MS analysis. The reaction mixture was neutralized by the addition of TEA [10 μL, 0.0660 mmol, 10 mol equiv vs $Yb(OTf)_3$]. The reaction mixture immediately turned light brown. The resulting mixture was diluted with diethyl ether (~30 mL), washed with water and brine, dried (K_2CO_3), and concentrated to afford a light brown foam. The

crude product was chromatographed [silica (0.530 g), 4 cm dia × 15 cm, hexanes/ethyl acetate (3:1), ~1.5 L solvent]. The bilane-containing fractions were concentrated to afford the title compound as a light-brown foam (0.619 g, 76%), presumably as a mixture of 8 stereoisomers. Unreacted **III-4a** was eluted from the column as a second component, which upon concentration gave an orange foam (73 mg). A small mixed fraction was obtained as an orange-yellow paste that contained **III-7-Br** and **III-4a** (15 mg). Data for the title compound: mp 95–97 °C; ^{1}H NMR (THF-d_8) δ 1.29 (m, 12H), 2.27 (s, 3H), 2.69 (q, J = 7.5 Hz, 2H), 5.21–5.23 (m, 1H), 5.25–5.27 (m, 1H), 5.41–5.45 (m, 1H), 5.49–5.55 (m, 5H), 5.86–5.89 (m, 2H), 6.76–6.81 (m, 1H), 7.06–7.10 (m, 4H), 7.14–7.18 (m, 5H), 7.19–7.25 (m, 2H), 7.27–7.30 (m, 4H), 7.76 (d, J = 8.4 Hz, 2H), 9.52–9.62 (brs, 1H), 9.64–9.72 (brs, 1H), 10.24–10.42 (brs, 1H), 10.86–11.04 (brs, 1H); ^{13}C NMR (THF-d_8) δ 15.1, 20.3, 28.8, 30.9, 34.2, 43.8, 44.1, 44.5, 96.3, 106.6, 106.8, 106.9, 108.8, 109.2, 109.64, 118.5, 125.0, 126.2, 127.5, 127.9, 128.3, 128.4, 128.56, 128.60, 129.0, 130.9, 131.8, 131.83, 132.2, 132.23, 133.5, 133.6, 133.7, 133.8, 133.85, 133.9, 135.3, 135.5, 137.1, 139.9, 141.0, 142.3, 143.3, 147.8, 149.1, 182.8; ^{15}N NMR (THF-d_8) δ –220.7, –223.5, –227.2 (two nitrogen atoms), (gHSQC, gHMBC). The high resolution exact mass spectrum gave m/z = 811.3035, which is assigned to the protonated molecule ion of the $2e^{-}/2H^{+}$-oxidized derivative of the title compound, *i.e.*, a protonated bilene [calcd 811.3011 for $(M' + H)^{+}$, M′ = $C_{51}H_{47}BrN_4O$, where the title compound has $C_{51}H_{49}BrN_4O$]. LD-MS (POPOP) obsd 810.0, 811.1, 812.0, 813.0, 814.1, calcd 812.309 ($C_{51}H_{49}BrN_4O$). Anal. Calcd for $C_{51}H_{49}BrN_4O$: C, 75.26; H, 6.07; N, 6.88. Anal. Calcd for $C_{51}H_{49}BrN_4O\cdot H_2O$: C, 73.63; H, 6.18; N, 6.73. Found: C, 73.19; H, 5.90; N, 6.69.

Alternative Synthesis of III-7-Br in Dilute Solution (25 mM). A sample of **III-6-Br** (0.500 g, 1.20 mmol) in dry THF/methanol (100 mL, 3:1) under argon at room temperature was

treated with $NaBH_4$ (1.14 g, 30.0 mmol, 25.0 mol equiv) in small portions with rapid stirring. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. The reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl and CH_2Cl_2 (350 mL). The organic phase was separated, washed with water and brine, dried (K_2CO_3), and concentrated under reduced pressure to yield the carbinol as a yellow-orange foam. The resulting sample was dissolved in anhydrous CH_2Cl_2 (48.0 mL) and treated with **III-4a** (0.492 g, 1.20 mmol). The reaction mixture was stirred for 10 min to achieve complete dissolution of **III-4a**. Following the acid catalysis conditions used in porphyrin syntheses,[III2] 2,6-di-*tert*-butylpyridine (345 μL, 1.56 mmol, 32.5 mM) and $Sc(OTf)_3$ (0.0770 g, 0.156 mmol, 3.25 mM) were added. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (3:1)].

The reaction mixture was stirred at room temperature for 1 h. A sample of TEA (220 μL, 0.0780 mmol, 32.5 mM) was added. The reaction mixture immediately changed from red to orange-yellow. The reaction mixture was diluted with CH_2Cl_2 (~100 mL), washed with water and brine, dried (Na_2SO_4) and concentrated to give a brown-yellow paste. Column chromatography [silica, hexanes/ethyl acetate (3:1)] afforded a brown foam (0.79 g, 80%). The data (^{1}H NMR, ^{13}C NMR, LD-MS, FAB-MS, and mp) were consistent with those obtained from samples prepared via earlier routes.

24-[9-Borabicyclo[3.3.1]non-9-yl]-1-bromo-19-(4-ethylbenzoyl)-10-(4-methylphenyl)-5-phenyl-15-(4-*tert*-butylphenyl)bilane (III-7-Br-9-BBN). By following the reported procedure for 1-acyldipyrromethanes,[III5] a solution of **III-7-Br** (0.410 g, 0.500 mmol) in toluene (1 mL) was treated with TEA (170 μL, 1.20 mmol) followed by 9-BBN-OTf (2.0 mL, 1.0 mmol, 0.50 M in hexanes). The reaction was complete in ~30 min. The mixture was

passed through an alumina column eluting with CH_2Cl_2. The product eluted as a fast-moving yellow band, which upon concentration afforded a yellow solid (0.380 g, 80%), presumably as a mixture of 8 stereoisomers: mp 103–105 °C; ^{1}H NMR (THF-d_8) δ 0.56–0.62 (brs, 1H), 0.72–0.78 (brs, 1H), 1.26 (s, 12H), 1.61–1.96 (m, 12H), 2.26 (s, 3H), 2.69–2.82 (m, 2H), 5.22–5.26 (m, 2H), 5.44–5.58 (m, 6H), 5.85–5.89 (m, 2H), 6.35–6.38 (m, 1H), 7.01–7.03 (m, 6H), 7.13–7.15 (m, 3H), 7.18–7.21 (m, 2H), 7.25–7.27 (m, 2H), 7.43–7.45 (m, 2H), 8.19–8.21 (m, 2H), 9.58–9.63 (brs, 2H), 10.36–10.46 (brs, 1H); ^{13}C NMR (THF-d_8) δ 15.5, 21.3, 24.0, 25.2, 26.1, 26.4, 29.4, 30.3, 31.3, 31.4, 31.6, 34.6, 34.7, 34.8, 43.9, 44.4, 44.5, 97.1, 107.4, 107.5, 107.8, 108.2, 109.3, 110.7, 118.3, 120.8, 125.6, 127.3, 128.1, 128.4, 128.5, 128.6, 128.8, 128.9, 129.4, 129.44, 130.0, 131.4, 131.5, 131.8, 131.9, 132.4, 133.1, 133.2, 134.2, 134.8, 136.67, 136.70, 139.2, 139.4, 141.6, 149.9, 151.2, 152.5, 174.3; ^{11}B NMR (THF-d_8) δ 22.5; ^{15}N NMR (THF-d_8) δ –220.9, –227.4 (two nitrogen atoms) (gHSQC); –151.5, –220.9, –227.4 (two nitrogen atoms) (gHMBC); LD-MS (POPOP) obsd 934.1, 935.1, 936.1, calcd 932.42; FAB-MS obsd 932.4196, cald 932.4200 ($C_{59}H_{62}BBrN_4O$). Anal. Calcd for $C_{59}H_{62}$ $BBrN_4O$: C, 75.88; H, 6.69; N, 6.00. Found: C, 76.33; H, 7.17; N, 5.78.

5-(4-Ethylphenyl)-15-(4-methylphenyl)-10-phenyl-20-(4-*tert*-butylphenyl)porphinatomagnesium(II) (III-1-Mg). A sample of **III-7-Br** (0.500 g, 0.620 mmol) was placed in a dry, one-necked, 25 mL round-bottomed flask containing a magnetic stir bar and fitted with a vented Teflon septum. Dry toluene (to ensure a free-flowing suspension at the outset of the reaction) was added (6.2 mL) followed by DBU (0.940 mL, 6.20 mmol, 10.0 mol equiv versus **III-7-Br**). The reaction mixture was stirred for 5 min at room temperature, during which time the mixture darkened. A sample of $MgBr_2$ (0.340 g, 1.86 mmol, 3 mol equiv versus bilane **III-7-Br**) was added in one portion. The mixture was stirred for 1 min at room

temperature. The flask was fitted with a reflux condenser and placed in an oil bath preheated to 115 °C. The reaction mixture (heterogeneous) was stirred under open-air reflux. On the basis of TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy of crude reaction samples, porphyrin formation was complete in 2 h. The crude reaction mixture was concentrated and then chromatographed [alumina (480 g), 4 cm dia × 30 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), ~1.5 L of solvent]. The porphyrin-containing fraction was concentrated to give a purple solid (0.295 g, 65%): ^{1}H NMR δ 1.56 (t, *J* = 7.6 Hz, 3H), 1.62 (s, 9H), 2.71 (s, 3H), 3.00 (q, *J* = 7.6 Hz, 2H), 7.52–7.57 (m, 4H), 7.72–7.74 (m, 5H), 8.10–8.14 (m, 6H), 8.21–8.23 (m, 2H), 8.85–8.87 (m, 2H), 8.89–8.92 (m, 6H); ^{13}C NMR δ15.9, 21.7, 29.1, 31.9, 35.1, 121.5, 121.7, 121.8, 122.0, 123.4, 126.0, 126.5, 127.2, 131.8, 131.9, 132.0, 132.03, 132.1, 134.7, 134.86, 134.9, 134.94, 136.8, 140.9, 141.0, 141.2, 143.1, 144.1, 149.9, 150.0, 150.19, 150.22, 150.25; LD-MS obsd 735.3; FAB-MS obsd 734.3257, calcd 734.3260 ($C_{51}H_{42}MgN_4$); λ_{abs} (toluene) 407, 428, 565, 605 nm.

5-(4-Ethylphenyl)-15-(4-methylphenyl)-10-phenyl-20-(4-*tert*-butylphenyl)porphyrin (III-1). Following the procedure described for **III-1-Mg**, bilane **III-7-Br** (2.44 g, 3.00 mmol) in toluene (30 mL) was reacted with DBU (4.50 mL, 30.0 mmol) and $MgBr_2$ (1.66 g, 9.00 mmol) at 115 °C for 2 h. The reaction mixture was concentrated and chromatographed [alumina (550 g), 4 cm dia × 30 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), ~2.5 L of solvent]. This resulting purple product contained a trace amount of impurity as determined by ^{1}H NMR spectroscopy. The crude product was washed with methanol several times, but no improvement was observed. The crude product was dissolved in CH_2Cl_2 (60 mL), and TFA (2.3 mL) was added. The resulting reaction mixture was stirred for 1 h at room temperature. TLC analysis (silica, CH_2Cl_2) showed the free-base porphyrin close to the solvent front. LD-MS analysis

revealed a single peak at *m/z* = 712.89 (molecular mass of free base porphyrin **III-1**). The reaction mixture was neutralized with TEA (5 mL) and concentrated by half. The resulting reaction mixture was washed with water and brine, dried (Na_2SO_4) and concentrated. The crude product was filtered through a column [silica, 4 cm × 10 cm, CH_2Cl_2]. The porphyrin-containing fraction was concentrated to afford a purple solid (1.123 g, 53%): ^{1}H NMR δ – 2.77 (brs, 2H), 1.53 (t, *J* = 7.2 Hz, 3H), 1.61 (s, 9H), 2.70 (s, 3H), 3.00 (q, *J* = 7.2 Hz, 2H), 7.54–7.59 (m, 4H), 7.74–7.76 (m, 5H), 8.09–8.15 (m, 6H), 8.21–8.22 (m, 2H), 8.81–8.87 (m, 8H); ^{13}C NMR δ 15.9, 21.8, 29.1, 31.9, 35.1, 120.0, 120.3, 120.5, 120.6, 123.8, 126.4, 126.9, 127.6, 127.9, 130.6̃131.8 (br), 134.7, 134.8, 134.9, 137.5, 139.4, 139.5, 139.7, 142.5, 143.8, 150.7; LD-MS obsd 712.8, FAB-MS obsd 712.3560, calcd 712.3566 ($C_{51}H_{44}N_4$); λ_{abs} (toluene) 420, 515, 550, 592, 650 nm.

Protocol for Table III.1: Synthesis Using $InCl_3$ (entry 2) of III-7-Br. A sample of **III-6-Br** (0.053 g, 0.125 mmol) in dry THF/methanol (10.0 mL, 3:1) was treated with $NaBH_4$ (0.120 g, 3.13 mmol, 25.0 mol equiv) at once under argon at room temperature. The reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl in diethyl ether (~20 mL). The organic phase was extracted with diethyl ether, washed with water and brine, dried (K_2CO_3), and concentrated. The resulting orange-yellow paste was transferred to an oven-dried round-bottomed flask (5 mL) with diethyl ether. A sample of **III-4a** (0.051 g, 0.125 mmol) was added. A septum was fitted on the flask, and a sample of anhydrous acetonitrile (0.165 mL) was added under a very slow argon flow. The resulting orange-red reaction mixture was stirred for 1 min, whereupon $InCl_3$ (0.0850 mL of a 10.0 mM stock solution in anhydrous MeOH) was slowly added. The reaction mixture immediately turned dark brown. An aliquot was removed from the reaction mixture at various times and checked by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. Up to four components were observed (unreacted **III-6-Br-**

OH, unreacted **III-4a**, bilane **III-7-Br**, and an unknown red spot; R_f = 0.3, 0.4, 0.6, and ~0.65 respectively). The components on the TLC plate were further identified by exposure to bromine, affording dark pink, orange, dark brown, and light brown spots, respectively. The reaction mixture was stirred for ~45 min. LD-MS (POPOP) analysis of the crude reaction mixture gave a peak (*m/z* = 813.0) consistent with the title compound; the spectrum did not reveal any detectable scrambling. The reaction was neutralized with TEA [5 μL, 50 mol equiv vs $InCl_3$]. The resulting mixture was diluted with diethyl ether (~10 mL) and washed with water and brine. The organic layer was dried (K_2CO_3) and concentrated to afford a light brown foam. The crude product was chromatographed [silica (0.350 g), 3 cm dia × 10 cm, hexanes/ethyl acetate (3:1), ~650 mL]. The elution was performed quickly given concerns about limited stability of the bilane. (In some cases, a green band eluted prior to the bilane band. The green substance gave λ_{abs} = 360, 465 nm; LD-MS (POPOP) gave *m/z* = 809.5 which is consistent with the free base biladiene-*ac*; a ^{1}H NMR spectrum could not be obtained because of the low stability.) The bilane-containing fractions were concentrated to afford a light-brown foam (0.065 g, 66%). The data (^{1}H NMR, ^{13}C NMR, LD-MS (POPOP), FAB-MS, and mp) were consistent with those obtained from samples obtained via the preparative route. The same experimental protocol was applied to other Lewis acids [$MgBr_2$, $Mg(OTf)_2$, $Sc(OTf)_3$, $Zn(OTf)_2$, $Sn(OTf)_2$, $Yb(OTf)_3$]. Note that a methanol stock solution was employed in each case with the exception of the reactions in CH_2Cl_2 and toluene.

Protocol for Table III.3:

(i) Standard Procedure Given for III-1-Zn. An oven-dried microscale reaction vial containing a dry stir bar and fitted with a vented Teflon septum was treated successively with a sample of **III-7-Br** (0.050 g, 0.062 mmol), dry toluene (0.620 mL), and DBU (0.090 mL,

0.62 mmol, 10 mol equiv versus **III-7-Br**) at room temperature. The reaction mixture darkened while stirring over the course of 5 min. A sample of $Zn(OAc)_2$ (0.035 g, 0.19 mmol, 3.0 mol equiv) was added in one portion. The reaction mixture was stirred for 1 min at room temperature. The flask was placed in a benchtop sonication bath for a few seconds. Then the flask was fitted with a reflux condenser and placed in an oil bath preheated to 115 °C. The reaction mixture was stirred under open-air reflux. The crude reaction mixture was checked by absorption spectroscopy and TLC (silica, CH_2Cl_2). The formation of metalloporphyrin was complete in 1 h. The crude reaction mixture was concentrated to dryness. The resulting residue was chromatographed (silica, CH_2Cl_2). Porphyrin-containing fractions were concentrated to afford a purple solid (24 mg, 50%): ^{1}H NMR δ 1.54 (t, *J* = 7.6 Hz, 3H), 1.62 (s, 9H), 2.70 (s, 3H), 3.00 (q, *J* = 7.6 Hz, 2H), 7.53–7.57 (m, 4H), 7.73–7.75 (m, 5H), 8.08–8.14 (m, 6H), 8.19–8.22 (m, 2H), 8.91–8.92 (m, 2H), 8.95–8.97 (m, 6H); ^{13}C NMR δ 15.9, 21.8, 29.1, 30.4, 32.2, 35.1, 121.1, 121.4, 121.5, 121.6, 123.7, 126.3, 126.7, 126.8, 127.5, 127.6, 127.7, 131.9, 132.0, 132.1, 132.17, 132.2, 132.3, 132.9, 134.5, 134.6, 134.65, 134.7, 134.8, 137.3, 140.0, 140.1, 140.12, 140.3, 143.1, 143.2, 143.6, 150.3, 150.4, 150.5, 150.56,150.6; LD-MS obsd 774.7, FAB-MS obsd 774.2729, calcd 774.2701 ($C_{51}H_{42}N_4Zn$); λ_{abs} (toluene) 424, 550, 590 nm.

(ii) III-1-Mg. Application of the standard procedure with **III-7-Br** (0.050 g, 0.062 mmol) and $MgBr_2$ with chromatographic workup [alumina (40 g), 2.5 cm dia × 10 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), ~250 mL of solvent] afforded a purple solid (0.032 g, 69%). The characterization data (^{1}H NMR, ^{13}C NMR, LD-MS and absorption spectrum) were consistent with those obtained from samples obtained via the preparative synthesis.

(iii) III-1-Ni. Application of the standard procedure with **III-7-Br** (0.082 g, 0.10 mmol) and $NiCl_2$ with chromatographic workup [silica, hexanes/CH_2Cl_2, (4:1)] gave an orange solid (22

mg, 29%): ^{1}H NMR δ 1.49 (t, *J* = 7.6 Hz, 3H), 1.57 (s, 9H), 2.65 (s, 3H), 2.96 (q, *J* = 7.6 Hz, 2H), 7.48–7.53 (m, 4H), 7.69–7.72 (m, 5H), 7.90–7.97 (m, 6H), 8.02–8.04 (m, 2H), 8.74–8.77 (m, 2H), 8.79–8.82 (m, 6H); ^{13}C NMR δ 15.9, 21.7, 29.1, 31.9, 35.1, 118.9, 119.2, 119.3, 119.32, 124.1, 126.6, 127.1, 127.8, 127.9, 132.2, 132.3, 132.40, 132.43, 132.5, 133.8, 133.90, 133.96, 134.0, 137.6, 138.1, 138.2, 138.4, 141.2, 142.7, 142.96, 142.98, 143.9, 150.8; LD-MS obsd 769.2, FAB-MS obsd 768.2769, calcd 768.2763 ($C_{51}H_{42}NiN_4$); λ_{abs} (toluene) 417, 528 nm.

(iv) III-1-InCl. Application of the standard procedure with **III-7-Br** (0.082 g, 0.10 mmol) and $InCl_3$ with chromatographic workup [silica, CH_2Cl_2 → CH_2Cl_2/MeOH (200:1)] gave a purple solid (13 mg, 15%; counterion assumed to be chloride): ^{1}H NMR δ 1.57 (t, *J* = 7.8 Hz, 3H), 1.65 (s, 9H), 2.74 (s, 3H), 3.05 (q, *J* = 7.8 Hz, 2H), 7.56–7.67 (m, 4H), 7.76–7.82 (m, 5H), 8.04–8.06 (m, 3H), 8.13–8.15 (m, 1H), 8.27–8.31 (m, 3H), 8.40 (brs, 1H), 9.06–9.07 (m, 2H), 9.08–9.11(m, 6H); ^{13}C NMR δ 15.9, 21.8, 29.1, 31.9, 35.2, 121.7, 122.0, 122.1, 122.3, 123.9, 124.0, 126.5, 126.6, 126.9, 127.1, 127.7, 127.9, 128.2, 137.9, 139.0, 139.10, 139.3, 142.1, 144.2, 149.5, 149.6, 149.7, 149.8, 149.83, 151.1; LD-MS obsd 905.3, 861.3, 826.1; FAB-MS obsd 825.2412, calcd 825.2448 (M′ = M – Cl; M′ = $C_{51}H_{42}InN_4$); λ_{abs} (toluene) 408, 429, 562, 603 nm.

The contents of this chapter have been published.[III62]

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III.F. Supporting Information for New Route to ABCD-Porphyrins via Bilanes.

I. Additional Experimental Procedures

The microwave-assisted reactions were performed inside the cavity of a CEM Discover focused microwave synthesis system equipped with an infrared sensor for temperature monitoring. The reaction vessels were 10 mL crimp-sealed thick-wall glass tubes equipped with a pressure sensor. The contents of each vessel were stirred with a magnetic stirrer.

All solvents used for the metal-templated bilane cyclization were anhydrous. The use of dry conditions at the outset of the reaction (despite the liberation of water during the reaction process) is important to ensure a free-flowing suspension of the metal salt, particularly for $MgBr_2$.

Each bilane contains three stereogenic centers and hence is expected to exist as a mixture of eight stereoisomers. The multiplicity of the resonances for substituents (e.g., 4-methyl group of the 4-methylphenyl moiety) far removed from the stereogenic centers appear as they would for a pure compound. Such resonances are listed on the basis of their appearance in the spectra.

1. Noncommercial Compounds. 1-Acyldipyrromethanes **III-4b**[III5] and **III-6-Br**[III37] were prepared as described in the literature.

2. Yield Determinations. The yield of porphyrin was determined in three ways depending on the reaction scale and experimental objective. (1) In reactions of all scales, the crude reaction mixtures often were examined by absorption spectroscopy. The resulting yield is specified as a "spectroscopic yield" determined with use of a molar absorption coefficient of a metalloporphyrin at the Soret band of 500,000 $M^{-1}cm^{-1}$. This procedure permitted an assessment of yield without employing a purification procedure. This procedure has been described in detail.[III45] (2) In other small-scale reactions, the porphyrin was purified and isolated by

chromatography. Owing to the small quantity of solid porphyrin, gravimetry was not performed. Instead, the solid sample was dissolved in a known volume of solvent, and the yield was determined by absorption spectroscopy, again using the molar absorption coefficient of a metalloporphyrin at the Soret band of 500,000 $M^{-1}cm^{-1}$. When free base porphyrins were isolated, a molar absorption coefficient of the Soret band of 430,000 $M^{-1}cm^{-1}$ was employed. This procedure is referred to as the "isolated yield determined by absorption spectroscopy." (3) Larger scale reactions afforded sufficient porphyrin for yield determination by gravimetry, which was the method employed unless specified otherwise. In some cases this method is emphasized by stating "isolated yield."

3. Microwave-Assisted Synthesis of III-1-Mg. A sample of **III-7-Br** (0.082 g, 0.10 mmol) was placed in a 10 mL glass tube containing a magnetic stir bar. Toluene (1 mL) and DBU (0.150 mL, 1.00 mmol) were added. The resulting mixture was stirred for 5 min and treated with $MgBr_2$ (0.055 g, 0.30 mmol). The vessel was sealed with a septum and subjected to microwave irradiation at 300 W. The protocol was as follows: (1) room temperature to 115 °C (irradiation ~30 s), (2) hold at 115 °C (irradiation for 10 min; temperature overshot to 135 °C and then stabilized after 1-2 min), (3) allow to cool to ~60 °C (~2 min), (4) heat to 115 °C (irradiation ~20-30 sec), (5) hold at 115 °C (irradiation for 3 min), and (6) allow to cool to room temperature. The reaction mixture was concentrated and filtered through an alumina column [4 cm dia x 15 cm, ~300 g alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3)]. The porphyrin-containing fraction was concentrated to afford a purple solid (38 mg, 51%). The characterization data (^{1}H NMR, LD-MS, FAB-MS, and λ_{abs}) were consistent with those for the product obtained via the preparative route.

4. Stability of 1-Bromodipyrromethane-9-carbinol for Preparation of III-7-Br. The

synthesis of 1-bromodipyrromethane-9-carbinol (**III-6-Br-OH)** at any reasonable scale (e.g., > 1 mmol) requires a low boiling point solvent to facilitate the work-up procedure. We observed partial decomposition of **III-6-Br-OH** during the evaporation of ethyl acetate at room temperature. Upon concentrating the crude reaction mixture, the intermediate **III-6-Br-OH** decomposed completely yielding a red-brown material. We chose the low boiling point solvent diethyl ether to shorten the time for work-up procedure. Therefore, the carbinol was maintained in an orange-yellow oil-paste form containing a residual amount of diethyl ether, and was carried on to the bilane-forming step in this form.

The only disadvantage of using diethyl ether is that it is difficult to remove completely from bilanes. Accordingly, we routinely carried the sample of **III-7-Br** containing a trace amount of diethyl ether on to the porphyrin synthesis. Subsequent ^{1}H NMR spectroscopic examination of the isolated magnesium porphyrin typically revealed the presence of diethyl ether, even after vacuum-oven drying the sample at 80 °C for 24 h. The coordination of solvents to magnesium is well known, including to magnesium porphyrins. In this regard, it is likely that the diethyl ether was retained by coordination to the apical site of the centrally coordinated magnesium ion. The upfield chemical shifts of protons from diethyl ether in the ^{1}H NMR spectrum of the magnesium porphyrin sample also confirm the coordination. Note that all the characterization data for magnesium porphyrin **III-1-Mg** are consistent with the product prepared via the preparative route.

5. Examination of Effects of Atmosphere on Porphyrin Formation. (i) Porphyrin Formation Under Oxygen. A sample of **III-7-Br** (0.0200 g, 0.0246 mmol) was placed in an oven-dried round bottomed flask (5 mL). The flask was sealed with a teflon septum, and dry toluene was added at room temperature (0.250 mL). The mixture was stirred at room

temperature for 1 min, whereupon DBU (0.0380 mL, 0.246 mmol, 10.0 mol equiv versus **III-7-Br**) was added. The reaction mixture was stirred for 5 min. The reaction mixture darkened. $MgBr_2$ (0.0140 g, 0.0738 mmol, 3.00 mol equiv versus bilane **III-7-Br**) was added. The heterogeneous reaction mixture was sonicated for a few secs, and then stirred at room temperature for 1 min. The reaction mixture at reflux (oil bath temperature 135 °C) was stirred under a very slow flow of oxygen at reflux for 3 h. TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy of crude reaction samples revealed the formation of (i) the magnesium porphyrin and (ii) an intermediate that is more polar than the porphyrin and which exhibits a broad band at 468 nm. No further change was observed even after 8 h under reflux with a slow oxygen flow. The crude reaction mixture was concentrated and filtered through a column (alumina 280 g, 4 cm dia × 15 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), 600 mL). A trace amount of free base porphyrin **III-1** eluted near the solvent front (CH_2Cl_2) and was obtained in 0.8% spectroscopic yield. The dominant porphyrin-containing fraction eluted later (CH_2Cl_2/ethyl acetate) and was concentrated to give a purple solid (7 mg, 40% isolated yield, 31% spectroscopic yield). The characterization data (^{1}H NMR, ^{13}C NMR, LD-MS and absorption spectrum) were consistent with those obtained from samples of **III-1-Mg** and **III-1** obtained from the preparative routes.

(ii) Porphyrin Formation Under Argon. A sample of **III-7-Br** (0.082 g, 0.1 mmol) was placed in an oven-dried vial (1 mL). The vial was sealed with a teflon septum and purged with argon for 5 min. Toluene was added at room temperature (1 mL) under a constant flow of argon. The mixture was stirred at room temperature for 1 min, and DBU (0.150 mL, 1 mmol) was added. The reaction mixture was stirred for 5 min, whereupon $MgBr_2$ (0.055 g, 0.3 mmol) was added. The heterogeneous reaction mixture was stirred at room temperature for 1 min under

a slow flow of argon. The reaction vial was placed in an oil bath (preheated to 115 °C) and was equipped with a reflux condenser, still maintaining a slow flow of argon. The reaction mixture was stirred for 2 h. An aliquot was removed from the reaction mixture. TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy of the sample revealed the formation of the magnesium porphyrin. The crude reaction mixture was concentrated and filtered through a column (alumina 280 g, 4 cm dia × 15 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), ~ 800 mL) to afford a purple solid (35 mg, 51%). A trace amount of free base porphyrin **III-1** eluted near the solvent front (CH_2Cl_2) and was obtained in 0.3% spectroscopic yield. The characterization data (^{1}H NMR, ^{13}C NMR, LDMS and absorption spectrum) were consistent with those obtained from samples of **III-1-Mg** and **III-1** obtained from the preparative routes.

6. Protocols for Figure III.1A. (i) 10 mM Reaction. A solution of **III-7-Br** (0.0820 g, 0.100 mmol) in dry toluene (10.0 mL) in an oven-dried round-bottomed flask (100 mL, equipped with a stir bar and fitted with a Teflon septum) was treated with DBU (0.15 mL, 1.0 mmol, 10.0 mol equiv vs **III-7-Br**). The reaction mixture was stirred vigorously for 5 min. The reaction mixture darkened. A sample of $MgBr_2$ (0.055 g, 0.30 mmol, 3.0 mol equiv vs bilane **III-7-Br**) was added. The reaction mixture was stirred at room temperature for 1 min. The flask was fitted with a reflux condenser and placed in an oil bath preheated to 115 °C. The reaction mixture was stirred under open-air reflux. On the basis of TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy of crude reaction samples, porphyrin formation was complete in 2 h. The crude reaction mixture was concentrated and dried under high vacuum for 10 min. The spectroscopic yield was determined to be 0.9%. The same experimental protocol was applied for the other concentrations, keeping the mol ratio of DBU (10.0 mol equiv vs **III-7-Br**) and $MgBr_2$ (3.0 mol equiv vs **III-7-Br**) constant, while altering the relative amount of toluene.

(ii) Highest Concentration (Toluene-Free) Reaction. A sample of **III-7-Br** (0.0500 g, 0.0615 mmol) was placed in an oven-dried round-bottomed flask (5 mL, equipped with a stir bar and fitted with a Teflon septum). DBU (0.0900 mL, 0.615 mmol, 10.0 mol equiv versus **III-7-Br**) was added. The reaction mixture was stirred vigorously for 5 min. The reaction mixture darkened. A sample of $MgBr_2$ (0.0340 g, 0.186 mmol, 3.00 mol equiv versus bilane **III-7-Br**) was added. The heterogeneous reaction mixture was sonicated for a few secs, and then stirred at room temperature for 1 min. The flask was fitted with a reflux condenser and placed in an oil bath preheated to 135 °C. The reaction mixture was stirred under open-air reflux. TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy of crude reaction samples revealed formation of the magnesium porphyrin and two, more polar products (a green spot and a red spot). On the basis of TLC analysis, no change was observed even upon stirring the reaction mixture for 4 h. The crude reaction mixture was concentrated and chromatographed [alumina (280 g), 4 cm dia × 15 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1)]. A trace amount of free base porphyrin **III-1** eluted near the solvent front (CH_2Cl_2) and was obtained in 1% spectroscopic yield. The dominant porphyrin-containing fraction eluted later (CH_2Cl_2/ethyl acetate) and was concentrated to give a purple solid (16.0 mg, 35). The characterization data (^{1}H NMR, ^{13}C NMR, LD-MS and absorption spectrum) were consistent with those obtained from samples of **III-1-Mg** and **III-1** obtained from the preparative routes.

(iii) Variations in Concentrations of DBU and $MgBr_2$. A sample of **III-7-Br** (0.082 g, 0.1 mmol) was placed in an oven-dried round-bottomed flask (100 mL, equipped with a stir bar and fitted with a Teflon septum) and treated with dry toluene (8.5 mL). A sample of DBU (1.5 mL, 10.0 mmol, 100 mol equiv vs **III-7-Br**) was added. The reaction mixture changed to dark brown-red in ~1 min. A sample of $MgBr_2$ (0.55 g, 3.0 mmol, 30 mol equiv vs **III-7-Br**) was

added at once. The reaction mixture was stirred vigorously for 1 min. The flask was fitted with a reflux condenser and placed in an oil bath preheated to 115 °C. The reaction mixture was stirred under open-air reflux for 2 h. An aliquot was removed from the reaction mixture and checked by TLC analysis (silica, CH_2Cl_2) and absorption spectroscopy. A trace amount of starting material (**III-7-Br**) was observed upon TLC analysis. The absorption spectrum revealed three peaks (405, 428, 468 nm). The reaction mixture was stirred for 1 h, whereupon TLC analysis indicated no starting material was present. No change was observed in the absorption spectrum of the crude reaction mixture. The crude reaction mixture was concentrated, and the spectroscopic yield was determined to be 29%.

7. Protocol for Figure 1B: 5 min Timepoint. A solution of **III-7-Br** (0.0820 g, 0.100 mmol) in dry toluene (1.0 mL) in an oven-dried round-bottomed flask (5 mL, equipped with a stir bar and fitted with a Teflon septum) was treated with DBU (0.15 mL, 1.0 mmol, 10 mol equiv vs **III-7-Br**). The reaction mixture was stirred at room temperature for 5 min. The reaction mixture darkened. A sample of $MgBr_2$ (0.055 g, 0.30 mmol, 3.0 mol equiv vs bilane **III-7-Br**) was added. The reaction mixture was stirred at room temperature for 5 min. The flask was fitted with a reflux condenser and placed in an oil bath preheated to 115 °C. The reaction mixture was stirred under open-air reflux. The flask was removed from the oil bath after 5 min and allowed to cool to room temperature. TLC analysis (silica, CH_2Cl_2) indicated the presence of unreacted starting material. The crude reaction mixture was concentrated and dried under high vacuum for 10 min. The spectroscopic yield was determined to be 20%. The same experimental protocol was applied for the other timepoints.

II. Studies of the One-Flask Cyclization of Bilanes

1. Survey of Metal Reagents for One-Flask Bilane Cyclization III-7-SEt. The reaction conditions for the one-flask cyclization of bilane III-7-SEt were surveyed.

Table III.S1. Survey of Metal Reagents for One-Flask Cyclization of Bilane III-7-SEt[a]

Entry	Metal Salt (equiv)	Base (equiv)	Solvent	Time (h)	Yield (%)	Porphyrin **III-1-M**
1	$Pd(CH_3CN)_2Cl_2$[b] (1.1)	KOH (5)	EtOH	1	38[c]	**III-1-Pd**
2	$Pd(OAc)_2$[b](1.1)	KOH (5)	EtOH	1	13	**III-1-Pd**
3	$Pd(CF_3COO)_2$[b] (1.1)	KOH (5)	EtOH	1	28	**III-1-Pd**
4	$PdBr_2$[b] (1.1)	KOH (5)	EtOH	1	22	**III-1-Pd**
5	$Pd(acac)_2$[b] (1.1)	KOH (5)	EtOH	1	32	**III-1-Pd**
6	$Zn(OAc)_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
7	$FeCl_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
8	$Fe(OAc)_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
9	$SnCl_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
10	$Sn(OAc)_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
11	$Co(OAc)_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
12	$CdCl_2$ (2)	KOH (5)	EtOH	48	----	**III-1-M**
13	$NiCl_2$ (2)	KOH (5)	EtOH	48	12[c]	**III-1-Ni**
14	$Ni(OAc)_2$ (2)	KOH (5)	EtOH	48	8	**III-1-Ni**
15	$InCl_3$ (2)	KOH (5)	EtOH	48	trace	**III-1-In**
16	$MgBr_2$ (15)	DBU (60)	Acetonitrile	72	trace	**III-1-M**
17	MgI_2 (15)	DBU (60)	Acetonitrile	72	trace	**III-1-M**
18	$InCl_3$ (15)	DBU (60)	Acetonitrile	72	trace	**III-1-M**
19	$InBr_3$ (15)	DBU (60)	Acetonitrile	72	trace	**III-1-M**
20	$MgBr_2$ (15)	DBU (60)	Butyronitrile	12	15	**III-1-Mg**
21	MgI_2 (15)	DBU (60)	Butyronitrile	12	10	**III-1-Mg**
22	$Mg(OTf)_2$ (15)	DBU (30)	Isovaleronitrile	3	8	**III-1-Mg**
23	$Zn(OTf)_2$ (15)	DBU (30)	Isovaleronitrile	8	---	**III-1-Zn**
24	$InCl_3$ (15)	DBU (30)	Valeronitrile	12	trace	**III-1-In**
25	$MgBr_2$ (15)	TMG[d] (60)	Toluene	12	5	**III-1-Mg**
26	$MgBr_2$ (15)	TMPi[e] (60)	Toluene	24	2	**III-1-Mg**
27	$MgBr_2$ (3)	DBU(10)	Toluene	8	10[c]	**III-1-Mg**
28	---	EtMgBr (5)	Toluene	48	---	**III-1**
29	---	LiHMDS[f] (5)	Toluene	48	---	**III-1**
30	---	DIEA[g] (5)	Toluene	48	---	**III-1**

[a]The reactions were carried out with 0.013 mmol of **III-7-SEt** at 100 mM concentration. The standard condition employs (1) treatment of bilane **III-7-SEt** with the specified solvent, (2) addition of a base, (3) stirring the reaction mixture for 5 min at room temperature, (4) addition of the corresponding metal salt, (5) sonication of the resulting heterogeneous reaction mixture for a few secs, (6) heating the reaction mixture under open-air reflux, and isolation of the porphyrin product with yield determined by absorption spectroscopy. [b]The reaction was carried out at 25

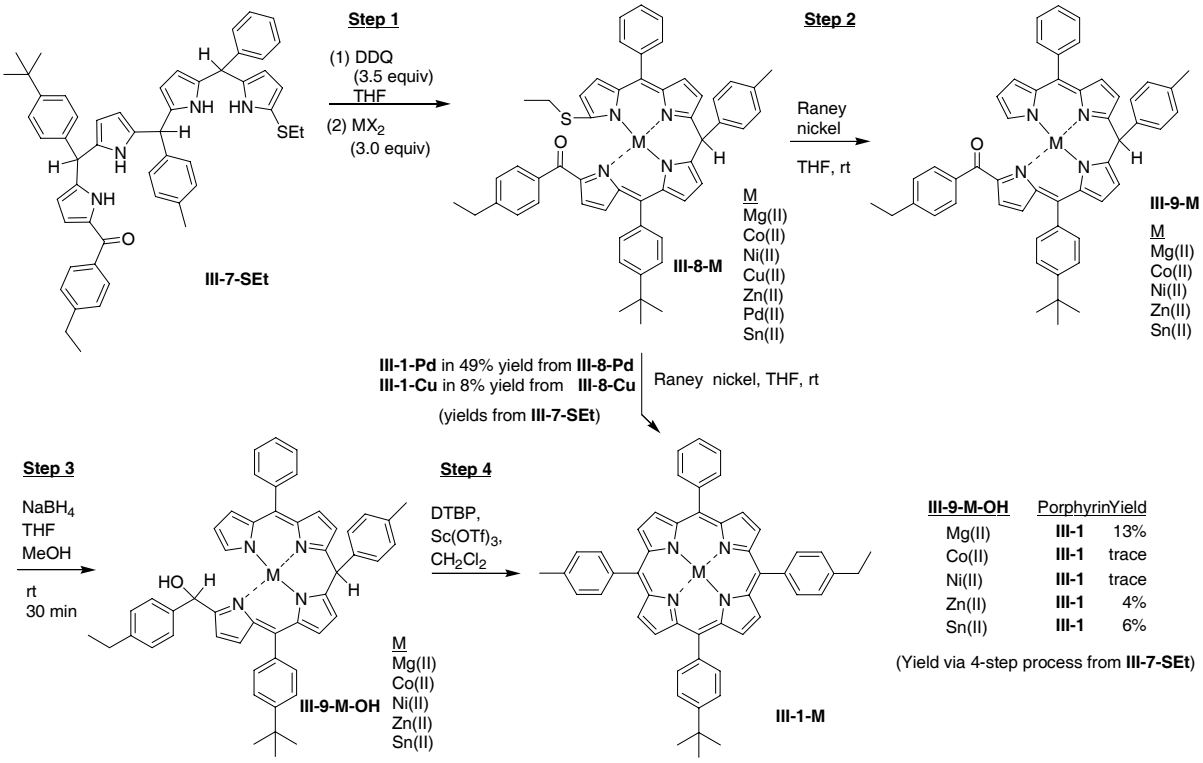
mM concentration. For palladium reagents the standard conditions were changed. Bilane **III-7-SEt** and the palladium reagent were placed in the reaction vial, and ethanol was added. The reaction mixture was heated under open-air reflux. By contrast, the addition of the palladium reagent to the solution of bilane **III-7-SEt** in ethanol afforded black material. [c]Spectroscopic yield. [d]1,1,3,3-Tetramethylguanidine. [e]2,2,6,6-Tetramethylpiperidine. [f]Lithium hexamethyldisilazane. [g]*N*,*N*-diisopropylethylamine.

2. Protocols for Table III.S1. (i) Synthesis of III-1-Pd, Exemplified for $Pd(CH_3CN)_2Cl_2$ with Bilane III-7-SEt (25 mM, entry 1). Samples of bilane **III-7-SEt** (0.010 g, 0.013 mmol), KOH (0.0040 g, 0.065 mmol) and $Pd(CH_3CN)_2Cl_2$ (0.0040 g, 0.013 mmol) were placed in a 2 mL microscale reaction vial sealed with a rubber septum. Ethanol (0.520 mL) was added and a needle was placed through the septum. The heterogeneous reaction mixture was stirred and heated at 75 °C for 2 h. The progress of the reaction was monitored by TLC analysis (silica, CH_2Cl_2). The reaction was complete in ~2 h. The residue was concentrated. The resulting crude product was dissolved in CH_2Cl_2 and passed through a pad of alumina (CH_2Cl_2). The resulting porphyrin-containing fraction was concentrated. Methanol was added, and the resulting suspension was placed in a sonication bath for a few minutes followed by centrifugation. Methanol was decanted to afford a red-orange solid (isolated yield determined by absorption spectroscopy: 38%): ^{1}H NMR 1.53 δ (t, *J* = 7.5 Hz, 3H), 1.60 (s, 9H), 2.70 (s, 3H), 3.00 (q, *J* = 7.5 Hz, 2H), 7.53–7.57 (m, 4H), 7.71–7.76 (m, 5H), 8.04–8.10 (m, 6H), 8.16–8.18 (m, 2H), 8.78–8.80 (m, 2H), 8.82–8.85 (m, 6H); ^{13}C NMR δ 15.9, 21.7, 29.1, 31.2, 31.9, 35.1, 121.7, 122.0, 122.2, 123.8, 126.4, 127.0, 127.6, 127.9, 131.0, 131.1, 131.2, 131.3, 134.2, 134.3, 134.4, 134.5, 137.6, 139.0, 139.1, 139.3, 141.7, 141.9, 142.1, 143.9, 150.8; LD-MS obsd 816.8, FAB-MS obsd 817.2554 calcd 817.2522 [$(M + H)^+$, M = $C_{51}H_{42}N_4Pd$]; λ_{abs} (toluene) 418, 525 nm.

(ii). Synthesis of III-1-Ni, Exemplified for $NiCl_2$ with Bilane III-7-SEt (100 mM, entry 13). Samples of bilane **III-7-SEt** (0.010 g, 0.013 mmol), KOH (0.0040 g, 0.065 mmol)

and $NiCl_2$ (0.0030 g, 0.026 mmol) were placed in 2 mL microscale reaction vial sealed with a rubber septum. Ethanol (0.5 mL) was added, and a needle was placed through the septum. The reaction vial was sonicated, and the heterogeneous reaction mixture was heated overnight at 70 °C. The progress of the reaction was monitored by TLC analysis (silica, CH_2Cl_2). After the reaction was complete (~12 h) the solvent was evaporated. The residue was dissolved in CH_2Cl_2 and passed through a column (silica, CH_2Cl_2). The resulting porphyrin-containing fractions were concentrated to give an orange solid. Methanol was added, and the resulting suspension was placed in a sonication bath for a few minutes followed by centrifugation. Methanol was decanted to afford an orange solid (isolated spectroscopic yield 12%): ^{1}H NMR δ 1.50 (t, J = 7.6 Hz, 3H), 1.58 (s, 9H), 2.66 (s, 3H), 2.94 (q, J = 7.4 Hz, 2H), 7.47–7.52 (m, 4H), 7.67–7.71 (m, 5H), 7.90–7.96 (m, 6H), 8.02–8.03 (m, 2H), 8.73–8.80 (m, 8H); ^{13}C NMR δ 15.9, 21.7, 29.1, 31.9, 35.1, 118.9, 119.2, 119.3, 119.32, 124.1, 126.6, 127.1, 127.8, 127.9, 132.2, 132.3, 132.40, 132.43, 132.5, 133.8, 133.90, 133.96, 134.0, 137.6, 138.1, 138.2, 138.4, 141.2, 142.7, 142.96, 142.98, 143.87, 150.8; LD-MS obsd 768.6, FAB-MS obsd 768.2761, calcd 768.2763 ($C_{51}H_{42}NiN_4$); λ_{abs} (toluene) 415, 528 nm.

III. Stepwise Synthesis of ABCD-Porphyrins



Scheme III.S1. Stepwise Synthesis of ABCD-Porphyrins.

We examined porphyrin formation from bilane **III-7-SEt** in the presence of a metal reagent. The porphyrin-forming process was performed in a stepwise manner including (i) oxidation/metalation, (ii) desulfurization, (iii) reduction, and (iv) ring closure (Scheme III.S1). Putative intermediates (e.g., **III-8-M**, **III-9-M**, **III-9-M-OH)** were not purified. In all trials the final condensation was performed at 100 mM. In this study seven metal salts [MX_2 = MgI_2, $Co(OAc)_2$, $NiCl_2$, $Cu(OAc)_2$, $Zn(OAc)_2$, $Pd(OAc)_2$, $Sn(OAc)_2$] were examined and carried through the process.

Step One: Oxidation and Metalation of Bilane III-7-SEt. Treatment of bilane **III-7-SEt** (50 mM) with DDQ (3.5 equiv versus **III-7-SEt**) at room temperature in THF (Scheme III.S1) caused the reaction mixture to change immediately from light yellow to dark green. The absorption spectrum of the crude reaction mixture showed three bands (348, 443 and a broad band at 592 nm). LD-MS (POPOP) of the crude reaction mixture gave a peak at m/z 789.5 consistent with the corresponding free base biladiene-ac. The crude biladiene-*ac* was treated in situ with excess metal salt MX_2 (3 equiv versus III-7-SEt). The reaction mixture darkened slowly, affording a broad peak at ~490 nm (Figure III.S1). Each crude sample was analyzed by LD-MS (POPOP) whereupon the expected molecule ion peak was observed. The reaction mixture was neutralized by addition of TEA (10 mol equiv versus metal salt), and aqueous workup was performed.

The biladiene-*ac* metal salts **III-8-M** [M = Mg(II), Co(II), Ni(II), Cu(II), Zn(II), Pd(II), and Sn(II)] were isolated and found to be stable in the solid state at –15 °C for several weeks. In general, the product was not purified, but the crude reaction mixture was used in the next step without purification. For each metal investigated, the absorption spectrum and LD-MS spectrum was obtained. The zinc(II)-biladiene-*ac* complex was characterized in detail, and the data are listed below. It is assumed that the biladiene-*ac* species exists as a pair of enantiomers owing to the stereogenic center at the 10-position. If the biladiene assumes a helical conformation[III60] owing to steric hindrance of the substituents at the 1- and 19-positions, diastereomers may be obtained.

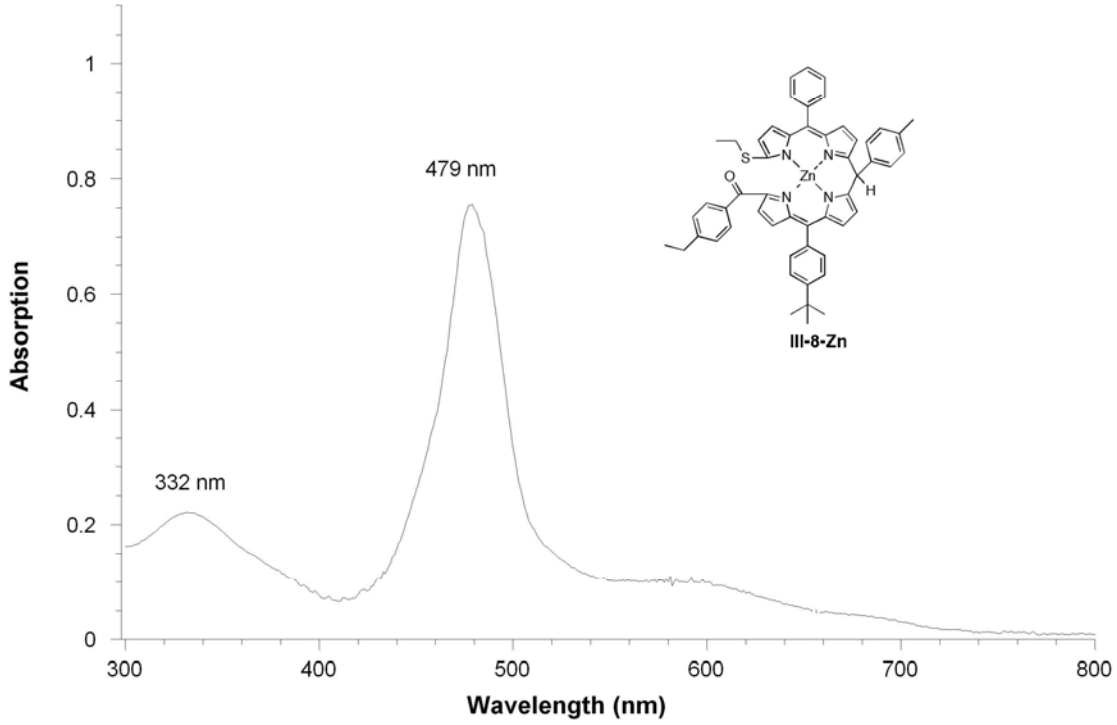


Figure III.S1. Absorption Spectrum of Zn(II)biladiene-ac Metal Complex **(III-8-Zn)** in CH_2Cl_2/ethanol (3:1) at Room Temperature.

The ^{1}H NMR spectrum of **III-8-Zn** exhibits the following features:

(1) loss of four pyrrolic NH resonances found in the bilane precursor **III-7-SEt** [^{1}H NMR in THF-d_8 δ 9.52–9.58 (brs, 1H), 9.65–9.67 (brs, 1H), 9.92–10.22 (brs, 1H), 10.82–11.21 (brs, 1H)].

(2) loss of resonances attributed to 2 of the 3 meso protons [e.g., 5.22–5.24 (m, 1H), 5.29–5.31 (m, 1H) in THF-d_8].

(3) ^{13}C NMR spectroscopy (in $CDCl_3$) revealed chemical shifts at 115.6 and 115.9 ppm, which are tentatively assigned as meso carbons C5 and C15 given the resemblance to the chemical shift of the resonance for *meso* carbon atoms in dipyrrinic compounds.[IIIS1]

(4) a ^{13}C chemical shift at 34.9 ppm, tentatively assigned to the third *meso* carbon (C10), is

consistent with that for the *meso* carbon in dipyrromethanes.[III4]

The absorption band at 490 nm (Figure III.S1) was consistent with that of *meso* unsubstituted biladiene-*ac* metal complexes,[IIIS2] and can be contrasted with the literature spectra of *meso* unsubstituted bilene-*b* metal complexes (~235, 392 and 500 nm),[III49] the protonated bilene-*b* (broad band at ~505 nm),[IIIS3] the bilatriene-*abc* salt (~420 and 750 nm), and a free base bilatriene-*abc* (~400 and 680 nm).[III53] To our knowledge, there are no reports of bilatriene-metal complexes (although metal complexes have been reported for the structurally quite different biliverdin[IIIS4]). Finally, it should be noted that DDQ oxidation of bilanes lacking 1,19-substituents often affords corroles rather than biladienes.[IIIS4]

Step Two: Desulfurization of III-8-M. Desulfurization of the biladiene-ac metal complex **III-8-M** [M = Mg(II), Co(II), Ni(II), Zn(II), and Sn(II)] was carried out according to a reported procedure for 1,9-bis(alkylthio)dipyrromethanes[III33] (**Scheme III.S1**). A solution of **III-8-M** in THF (5.0 mL, 12.5 mM) was treated with Raney nickel for 1 h. The absorption spectrum showed the intact biladiene-metal complex in each case. LD-MS analysis of the crude mixture gave a peak attributed to the desulfurized biladiene product (**III-9-M**) accompanied by demetalation for Mg(II), Co(II), Ni(II), Zn(II), and Sn(II). In each case only partial desulfurization occurred; regardless, the crude product was used in the next step without purification. For Cu(II) or Pd(II), attempted desulfurization with Raney nickel gave, surprisingly, not the biladiene III-9-M, but the metalloporphyrin **III-1-Cu** or **III-1-Pd** in 8% and 49% yield, respectively.

Step Three: Keto-Reduction of III-9-M. Reduction of the crude biladiene-ac metal complex **III-9-M** [M = Mg(II), Co(II), Ni(II), Zn(II), and Sn(II)] was performed according to the modified procedure reported for 1,9-diacyldipyrromethanes.[III2] Thus, treatment with $NaBH_4$ (25

mol equiv) in THF/MeOH (3:1) afforded the carbinol **III-9-M-OH** (Scheme III.S1). The absorption spectrum showed the intact biladiene-metal complex in each case. LD-MS analysis of the crude reaction mixture proved more erratic: a peak corresponding to the starting material was not observed; however, peaks corresponding to the carbinol were often accompanied by a peak corresponding to the fragment lacking the OH unit or the 4-ethylbenzyl moiety altogether.

Step Four: Cyclization of III-9-M-OH to Give the Porphyrin. The crude putative biladiene-carbinol **III-9-M-OH** [M = Mg(II), Co(II), Ni(II), Zn(II), and Sn(II)] in anhydrous CH_2Cl_2 was treated with $Sc(OTf)_3$ (3.25 mM) in the presence of 2,6-di-tert-butylpyridine (DTBP, 32.5 mM). The acid-catalyzed condensation was performed with the sample of **III-9-M-OH** set equal to 100 mM, assuming quantitative yields in each of steps 1–3. After 20 min, the absorption spectrum showed a strong band at 419 nm, corresponding to the Soret band of the free base meso-tetraarylporphyrin. The LD-MS spectrum of the purified sample was consistent with free base porphyrin **III-1** (**Scheme III.S1**). The isolated yield of porphyrin from each sample of biladiene **III-9-M-OH** ranged from trace quantities to 13% (from **III-7-SEt**). The origin of the variation in yields is attributed in large part to the desulfurization using Raney nickel. The highest yield (13%) was obtained with MgI_2.

In the studies of the stepwise synthesis, magnesium(II) appeared to give efficient formation of the metal-complexed biladiene-*ac*, and also gave the highest yield of porphyrin among all metal reagents other than those containing palladium.

1. Procedures and Results for the Stepwise Synthesis with $Zn(OAc)_2$.

Step 1: Oxidation and Metalation of III-7-SEt to Give III-8-Zn. A solution of bilane **III-7-SEt** (0.0900 g, 0.113 mmol) in THF (2.20 mL, 52.0 mM) was treated with DDQ (0.0560 g, 0.247 mmol, 2.20 mol equiv) under vigorous stirring. The reaction mixture changed from yellow

to dark green. $Zn(OAc)_2$ (0.0620 g, 0.340 mmol, 3.00 mol equiv) was added. The reaction mixture darkened. TLC analysis [silica, hexanes/CH_2Cl_2 (5:3)] showed the reaction was completed in ~30 min, whereupon water was added (~20 mL). The resulting mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated to give a dark green-purple solid. Methanol (~10 mL) was added, and the resulting suspension was placed in a sonication bath for a few minutes followed by centrifugation. The methanol layer was decanted leaving behind a dark green-purple solid (0.029 g, 30%): mp 92–95 °C; ^{1}H NMR δ 1.19 (t, *J* = 7.5 Hz, 3H), 1.36 (s, 9H), 1.40 (t, *J* = 7.5 Hz, 3H), 2.24 (s, 3H), 2.63 (q, *J* = 7.5 Hz, 2H), 3.04 (q, *J* = 7.5 Hz, 2H), 5.24–5.28 (br, 1H), 5.74–5.75 (m, 1H), 6.11–6.13 (m, 1H), 6.22–6.24 (m, 1H), 6.33 (m, 2H), 6.46–6.48 (m, 1H), 6.75 (m, 3H), 6.82–6.83 (m, 1H), 6.91–6.93 (m, 1H), 6.97–7.00 (m, 2H), 7.26–7.34 (m, 10H), 7.49–7.51 (m, 2H); ^{13}C NMR δ 15.1, 16.4, 21.9, 28.4, 29.1, 29.9, 31.6, 34.9, 80.0, 115.6, 115.9, 123.8, 123.9, 124.0, 124.4, 125.4, 126.6, 127.0, 127.1, 127.7, 127.9, 129.1, 130.5, 130.6, 130.8, 130.9, 131.1, 131.4, 132.7, 135.7, 135.9, 136.3, 136.4, 138.1, 139.1, 141.1, 142.3, 143.2, 144.0, 145.0, 145.1, 147.0, 148.0, 151.5, 155.5, 165.1, 178.6, 190.7; LD-MS (POPOP) obsd 851.9, calcd 852.284; λ_{abs} 332, 479 nm ($C_{53}H_{48}N_4OSZn$).

Step 2: Desulfurization of III-8-Zn to Give Biladiene-Metal Complex III-9-Zn. A sample of **III-8-Zn** (0.005 g, 0.006 mmol) was placed in a microscale reaction vial. Following the reported procedure for desulfurizing 1,9-bis(alkylthio)dipyrromethanes,[III33] a solid portion of wet Raney nickel (1 g) was removed from a Raney-nickel–water slurry by a spatula and washed with THF (~10 mL) three times. The washed Raney nickel was transferred to the reaction vial with 0.5 mL THF. The reaction mixture changed from green-purple to dark red. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (8:3)] and LD-MS. The reaction was complete in 1 h. The residue was filtered through a sintered glass funnel and

the filtered material was washed with THF (~20 mL). The filtrate was concentrated to afford a dark red paste (0.015 g): LD-MS (POPOP) obsd 791.8 calcd 792.2807 ($C_{51}H_{44}N_4OZn$).

Step 3: Keto-Reduction of III-9-Zn to Give Zn-Biladiene-carbinol III-9-Zn-OH. A crude sample (0.015 g) of **III-9-Zn** from the previous step was placed in a microscale reaction vial, sealed with a rubber septum and flooded with argon for 5 min. The sample was dissolved in dry THF/methanol (1.5 mL, 4:1) at room temperature The septum was removed to add $NaBH_4$ (0.0110 g, 0.300 mmol, 50.0 mol equiv) in one batch. The reaction was checked with LD-MS. The starting material was consumed in ~40 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl and CH_2Cl_2 (50 mL). The organic phase was separated, washed with water and brine, dried (K_2CO_3), and concentrated under reduced pressure to yield a dark red paste (0.025 g), which was dried under high vacuum for 10 min: LD-MS (POPOP) obsd 794.5, calcd 794.2963 ($C_{51}H_{46}N_4OZn$).

Step 4: Cyclization of III-9-Zn-OH to Give Free base ABCD-porphyrin III-1. The crude sample of **III-9-Zn-OH** (0.025 g) was dissolved in anhydrous CH_2Cl_2 (0.50 mL, 12 mM) at room temperature in a microscale reaction vial, which was fitted with a vented septum and flooded with argon. A sample of 2,6-di-*tert*-butylpyridine (4.00 μL, 0.0160 mmol, 32.5 mM) was added into the reaction vial. $Sc(OTf)_3$ (0.001 g, 0.002 mmol, 4 mM) was added. The reaction mixture darkened immediately. The progress of the reaction was monitored by absorption spectroscopy of oxidized reaction aliquots (1 μL aliquot is placed into 3 mL of CH_2Cl_2, to which 1 drop of 10 mM DDQ in toluene is added prior to absorption spectroscopy in CH_2Cl_2). The intermediate (biladiene-*ac*–zinc(II) complex, 476 nm) disappeared after ~40 min, whereupon DDQ (0.003 g, 0.01 mmol) was added. The reaction mixture was stirred for an additional 20 min. A sample of TEA (3.0 μL, 0.020 mmol) was added. The crude reaction

mixture was diluted with CH_2Cl_2 (20 mL) and poured into water. The organic phase was separated and the water layer was extracted with CH_2Cl_2. The combined organic extract was washed with water and brine, dried (Na_2SO_4) and concentrated. Filtration through a pad of alumina (CH_2Cl_2) afforded porphyrin (2%, spectroscopic yield). The characterization data (LD-MS and absorption spectrum) were consistent with **III-1** those obtained from samples prepared via the preparative route.

2. Procedures and Results for the Stepwise Synthesis with MgI_2.

Step 1: Oxidation and Metalation of III-7-SEt to Give III-8-Mg. A solution of bilane **III-7-SEt** (0.050 g, 0.063 mmol) in THF (1.25 mL, 50.0 mM) was treated with DDQ (0.050 g, 0.22 mmol, 3.5 mol equiv) under vigorous stirring. The reaction mixture changed from yellow to dark green immediately. After 10 min, MgI_2 (0.053 g, 0.19 mmol, 3.0 mol equiv) was added. The reaction mixture darkened. TLC analysis [silica, hexanes/ethyl acetate (3:1)] revealed consumption of starting material after ~30 min, whereupon TEA (265 μL, 1.89 mmol) was added. Water (~20 mL) was added and the resulting mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated. The crude product was dried under high vacuum for 10 min affording a dark green paste (0.068 g): LD-MS (POPOP) obsd 811.6; calcd 812.3399 ($C_{53}H_{48}MgN_4OS$); λ_{abs} 440 nm (broad).

Step 2: Desulfurization of III-8-Mg to Give III-9-Mg. Following a reported procedure,[33] a solid portion of wet Raney nickel (4 g) was removed from a Raney-nickel–water slurry by a spatula and washed with THF (~10 mL) five times. The washed Raney nickel was transfered to the reaction flask by pipette (THF 2.5 mL) under vigorous stirring. The reaction mixture changed from dark green to dark red. On the basis of TLC analysis (silica, CH_2Cl_2) and LD-MS (POPOP), the reaction was complete in 1 h. The mixture was filtered through a sintered glass funnel. The filtered material was washed with THF (~100 mL), concentrated and dried

under high vacuum affording a dark red paste: LD-MS (POPOP) obsd 753.4, calcd 752.3366 ($C_{51}H_{44}MgN_4O$).

Step 3: Keto-Reduction of III-9-Mg to give III-9-Mg-OH. The entire quantity of **III-9-Mg** was dissolved in dry THF/methanol (5 mL, 3:1) under argon at room temperature and treated with $NaBH_4$ (0.0600 g, 1.58 mmol, 25.0 mol equiv) in one batch. The progress of the reaction was checked with LD-MS. The starting material was consumed in ~40 min. The reaction mixture poured into a mixture of saturated aqueous NH_4Cl and CH_2Cl_2 (50 mL). The organic phase was separated, washed with water and brine, dried (K_2CO_3) and concentrated under reduced pressure. The resulting product was dried under high vacuum for 10 min affording a dark red paste (0.035 g): LD-MS (POPOP) obsd 753.7, calcd 754.3522 ($C_{51}H_{46}MgN_4O$).

Step 4: Cyclization of III-9-Mg-OH to Give Free base ABCD-porphyrin III-1. A solution of **III-9-Mg-OH** in anhydrous CH_2Cl_2 (2.50 mL, 12.5 mM) under argon was treated with a sample of 2,6-di-*tert*-butylpyridine (18.0 μL, 0.0810 mmol, 32.5 mM). The reaction mixture was stirred for 5 min and then $Sc(OTf)_3$ (0.004 g, 0.008 mmol, 3.25 mM) was added. The reaction mixture darkened immediately. The reaction was monitored with absorption spectroscopy. Three bands (319, 446, 501 nm) were observed. A sample of TEA (22.0 μL, 0.0810 mmol) was added. The reaction was checked by absorption spectroscopy and a strong band was observed at 419 nm. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and poured into water. The organic phase was separated washed with water, and brine, dried (Na_2SO_4) and concentrated affording a dark brown-black paste. The crude reaction mixture was filtered through a column (silica, CH_2Cl_2). The resulting porphyrin-containing fraction was concentrated. Methanol was added, and the resulting suspension was placed in sonication bath for few minutes followed by centrifugation. Methanol was decanted to afford a purple solid (13

mg, 27%) with characterization data (^{1}H NMR, ^{13}C NMR, LD-MS, λ_{abs}) consistent with that for the product obtained via the preparative route described in the paper.

3. Procedures and Results for the Attempted Stepwise Synthesis with $Pd(OAc)_2$.

Step 1: Oxidation and Metalation of III-7-SEt to Give III-8-Pd. A solution of bilane **III-7-SEt** (0.050 g, 0.063 mmol) in THF (1.25 mL, 50.0 mM) was treated with DDQ (0.0500 g, 0.221 mmol, 3.50 mol equiv) under vigorous stirring. The reaction mixture changed from yellow to dark green immediately. $Pd(OAc)_2$ (0.0430 g, 0.189 mmol, 3.00 mol equiv) was added. The reaction mixture darkened. The reaction mixture was checked by TLC analysis [silica, CH_2Cl_2/ethyl acetate (1:1)]. The reaction was completed in 20 min, whereupon TEA (265 μL, 1.89 mmol) was added. The reaction mixture was treated with water (~20 mL) and the resulting mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried (Na_2SO_4), and concentrated affording a brown paste: LD-MS (POPOP) obsd 894.0; calcd 894.2584 ($C_{53}H_{48}N_4OPdS$); λ_{abs} 347, 445 nm (broad).

Steps 2-4: Attempted Desulfurization Resulting in Formation of Porphyrin III-1-Pd. The entire quantity of **III-8-Pd** was dissolved in THF (2.5 mL, 25 mM) and treated with a solid portion of wet Raney nickel (4 g), removed from a Raney-nickel-water slurry by a spatula and washed with THF (~10 mL) five times. Washed Raney nickel was transfered to the reaction flask by pipette (THF 2.5 mL) under vigorous stirring. The reaction mixture changed from dark brown to dark red. The progress of the reaction was monitored by TLC analysis [silica, CH_2Cl_2]. Starting material was consumed ~30 min affording palladium porphyrin. The mixture was filtered through a sintered glass funnel to remove the Raney nickel. The filtered material was washed with THF (~100 mL). The filtrate was concentrated affording a dark red orange paste. The crude reaction mixture was filtered through a column (silica, CH_2Cl_2). The resulting porphyrin-containing fraction was concentrated. Methanol was added, and the resulting

suspension was placed in sonication bath for few minutes followed by centrifugation. Methanol was decanted affording a purple solid (25 mg, 49%). The characterization data (^{1}H NMR, ^{13}CNMR, LD-MS and absorption spectrum) were consistent with those obtained from samples of **III-1-Pd** obtained from the earlier route.

4. Procedures and Results for the Attempted Stepwise Synthesis with $Cu(OAc)_2$.

Step 1: Oxidation and Metalation of III-7-SEt to Give III-8-Cu. A solution of bilane **III-7-SEt** (0.050 g, 0.063 mmol) in THF (1.25 mL, 50.0 mM) was treated with DDQ (0.0500 g, 0.221 mmol, 3.50 mol equiv) under vigorous stirring. The reaction mixture changed from yellow to dark green immediately. $Cu(OAc)_2$ (0.0340 g, 0.188 mmol, 3.00 mol equiv) was added. The reaction mixture darkened. The reaction mixture was checked by TLC analysis [silica, CH_2Cl_2/ethyl acetate (1:1)]. The reaction was completed in 15 min, whereupon TEA (265 μL, 1.89 mmol) was added. The reaction mixture was treated with water (~20 mL) and the resulting mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried (Na_2SO_4) and concentrated affording a brown paste: LD-MS (POPOP) obsd 850.8; calcd 851.3 ($C_{53}H_{48}CuN_4OS$); λ_{abs} 348, 443 nm (broad).

Steps 2-4: Attempted Desulfurization Resulting in Formation of Porphyrin III-1-Cu. The entire quantity of **III-8-Cu** was dissolved in THF (2.5 mL, 25 mM) and treated with a solid portion of wet Raney nickel (4 g), removed from a Raney-nickel-water slurry by a spatula and washed with THF (~10 mL) five times. Washed Raney nickel was transfered to the reaction flask by pipette (THF 2.5 mL) under vigorous stirring. The reaction mixture changed from dark brown to dark red. The progress of the reaction was monitored by TLC analysis [silica, CH_2Cl_2]. Starting material was consumed ~15 min affording copper porphyrin. The mixture was filtered through a sintered glass funnel to remove the Raney nickel. The filtered material was washed with THF (~100 mL). The filtrate was concentrated affording a paste. The crude reaction

mixture was filtered through a column (silica, CH_2Cl_2). The resulting porphyrin-containing fraction was concentrate affording a purple solid (4 mg, 9%): LD-MS obsd 773.2, calcd 773.2705 ($C_{51}H_{42}CuN_4$); λ_{abs} 416, 539, 616 nm.

IV. Characterization of Bilanes

1. Nomenclature. The bilanes have been numbered according to the numbering system originally introduced by Fischer and Haberland.[58] On the bilane structure shown below, first the carbon atoms have been numbered starting with the carbon atom bearing protecting group X consecutively (omitting the C^{20}), and then the nitrogen atoms. For the numbering system of hydrogen atoms, basically the same number with the carbon that it is attached to shared between carbon and hydrogen atoms.

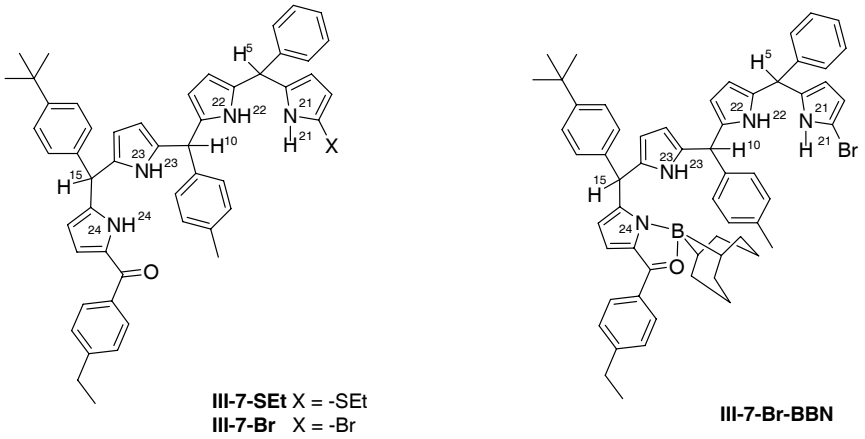


Chart III.S1. Numbering System of Bilanes**.**

2. ^{15}N NMR Studies of Bilanes. ^{15}N NMR spectroscopy (41 MHz) was performed at room temperature using a 400 MHz spectrometer as described previously for analogous compounds.[III42,III43] The procedures are described in detail here for completeness. All data for ^{15}N NMR chemical shifts are reported relative to that of nitromethane (δ 0.0 ppm) as an indirect

reference using pyrrole as a direct reference. Although nitromethane is typically used as a direct reference in ^{15}N NMR spectroscopy, nitromethane can not be used as a reference for gHSQC spectroscopy due to the lack of N-H bond. In addition, in some cases, artifacts in the region of –5 to 5 ppm (which arise from the NMR spectrometer filters) often accompany CH_3NO_2, which make this solvent less desirable reference. Thus, pyrrole in an NMR microtube insert was used as a reference for the gHSQC and gHMBC spectroscopy measurements. An NMR tube containing 8.0 M pyrrole in THF-d_8 (70 μL) was placed in an NMR tube containing 1.0 M CH_3NO_2 in THF-d_8 (500 μL). The pseudo-concentration of each component in the entire NMR tube was ~0.9 M (CH_3NO_2) and ~1 M (pyrrole). The gHMBC (N-H) spectrum showed the resonance of the pyrrole nitrogen at –230.4 ppm relative to nitromethane (δ 0.0 ppm). The pyrrole-containing NMR microtube was placed in an NMR tube containing the bilane sample (0.2 M) in THF-d_8 (500 μL), whereupon gHSQC and gHMBC spectroscopy was carried out. Each gHSQC experiment was carried out with 32 scans, requiring ~3 h. Each gHMBC experiments was performed with 128 scans, requiring ~16 h. Each gHSQC and gHMBC spectrum was referenced from the resonance of pyrrole (–230.4 ppm). The assignments of the resonance of nitrogen atoms on the bilane structures are displayed in Table III.2.

3. NOESY and HH-gCOSY NMR Studies of Bilane III-7-Br. On the basis of the NOESY spectrum of **III-7-Br**, the structure has the following features: (1) the pyrrolic proton that resonates most downfield appears as a broad singlet at δ 10.84–11.20 ppm and couples only with H^{15} (previously assigned by ^{15}N NMR spectroscopy); (2) the pyrrolic proton that resonates as a broad singlet at δ 10.28–10.42 ppm couples only with H^5 (previously assigned by ^{15}N NMR spectroscopy), (3) the pyrrolic proton that resonates as a broad singlet at δ ~9.62–9.72 ppm couples with H^{10} and H^{15} (previously assigned by ^{15}N NMR spectroscopy), (4) a pyrrolic proton

that resonates as a broad singlet at δ~9.48–9.62 ppm couples with H^{10} and H^{5}. These observations indicate that the pyrrolic protons that couple with H^{10} are located in the inner portion of the structure. A complete assignment of the meso and β-pyrrole protons of bilane **III-7-Br** is shown in the ^{1}H NMR spectra (Figures III.S2–III.S4).

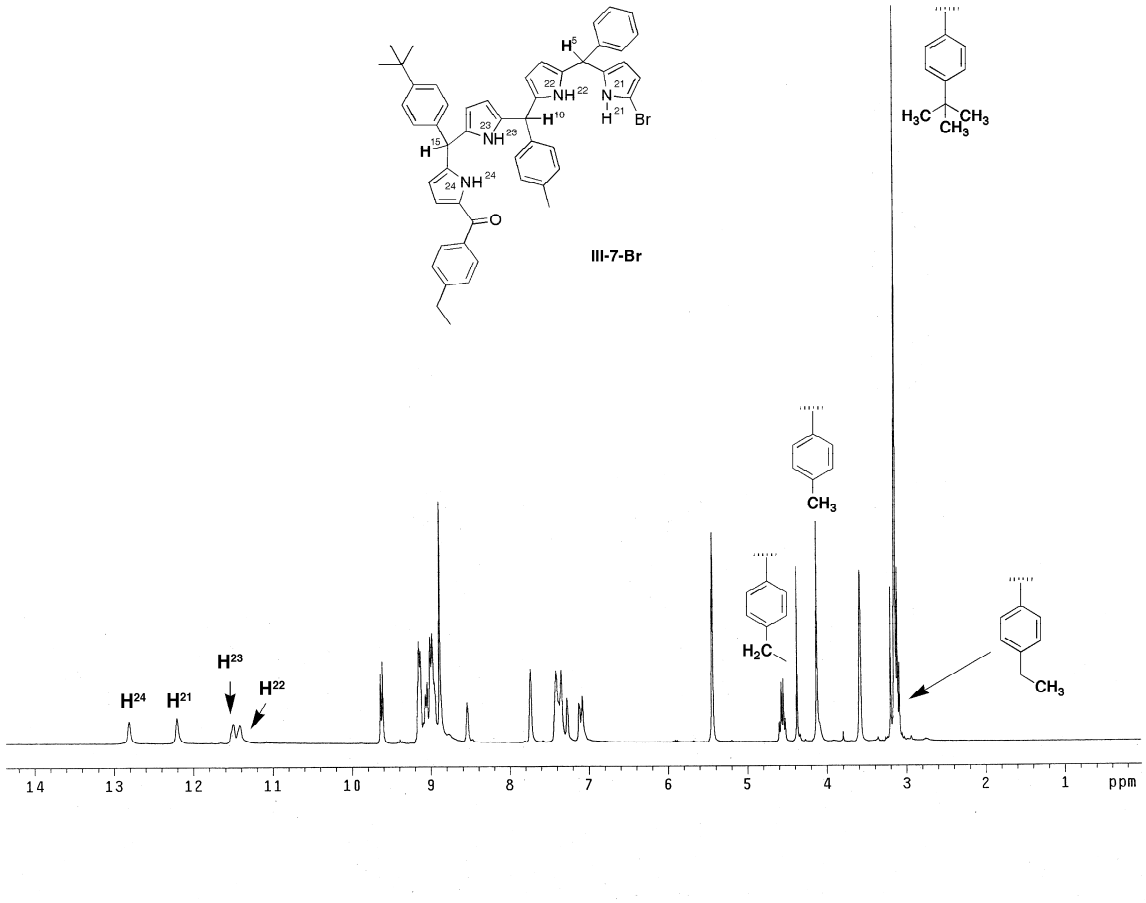


Figure III.S2. ^{1}H NMR Spectrum of Bilane **III-7-Br** with Display of Selected Assigned Resonances.

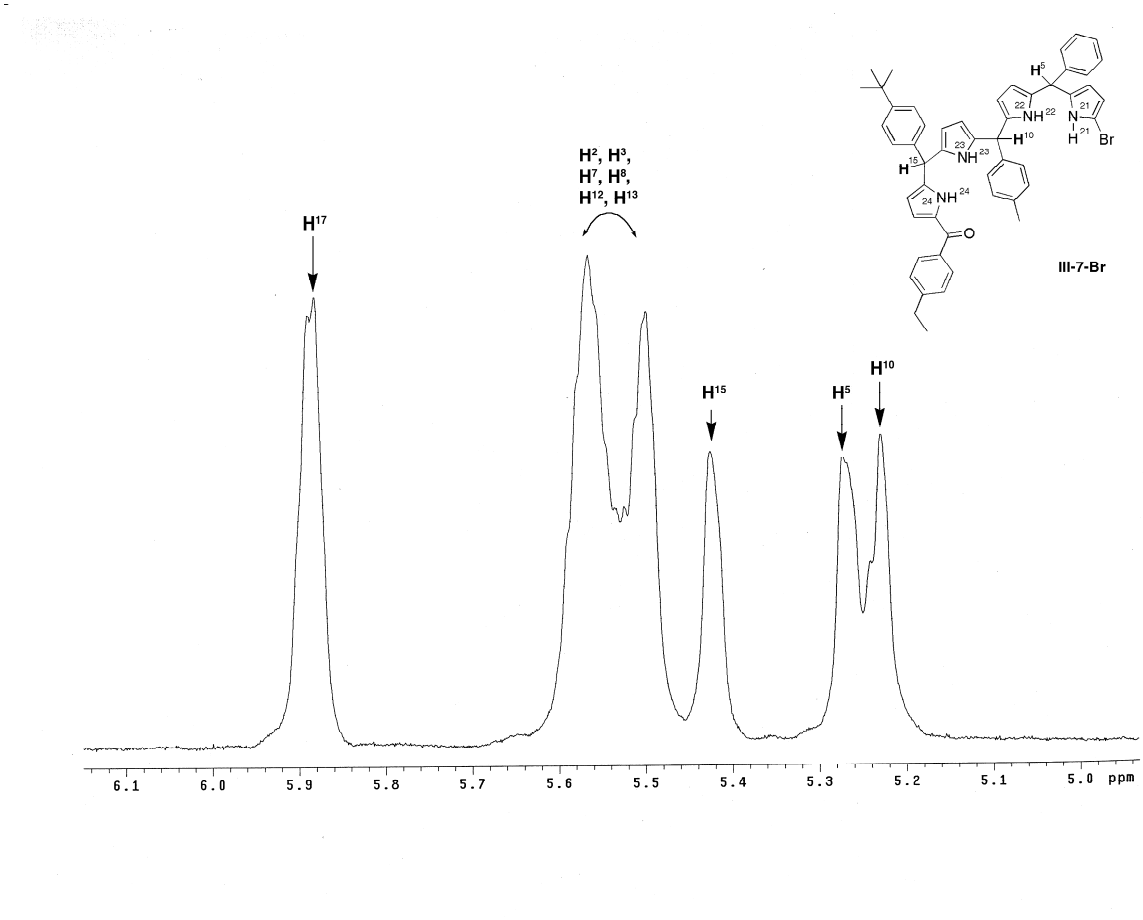


Figure III.S3. ^{1}H NMR Spectrum of Bilane **III-7-Br** with Assigned meso Protons.

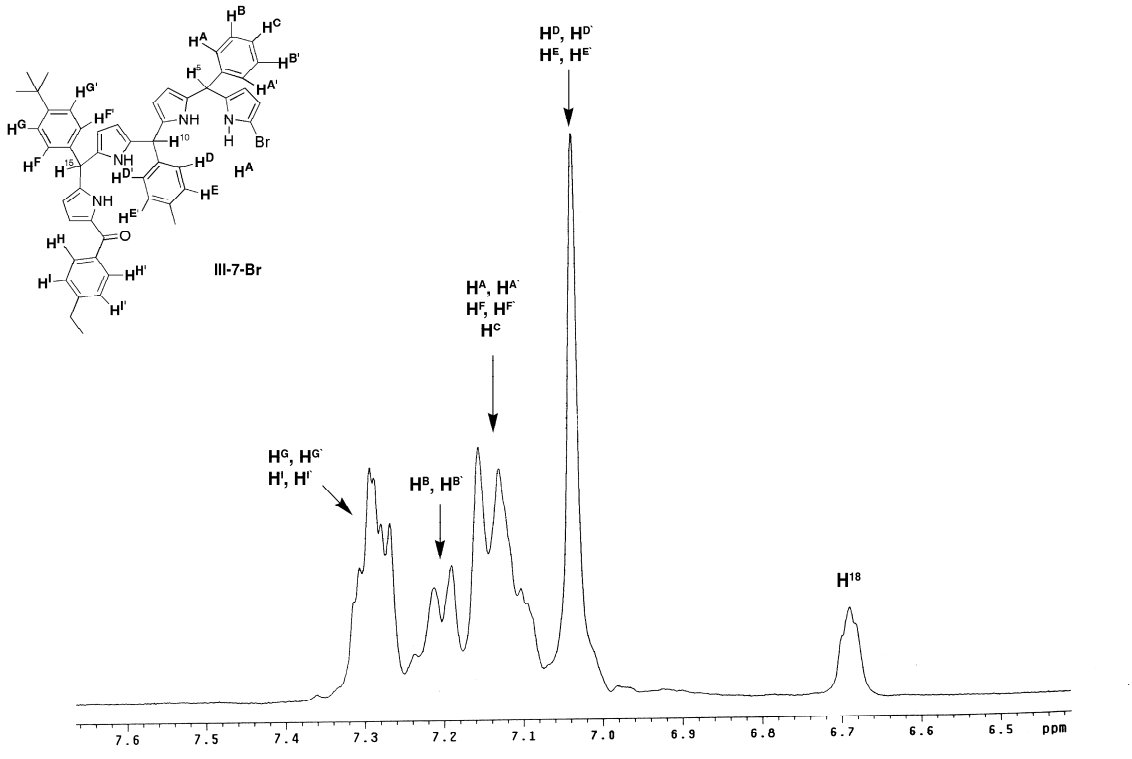


Figure III.S4. ^{1}H NMR Spectrum of Bilane **III-7-Br** with Assigned Aromatic Protons.

III.V. References.

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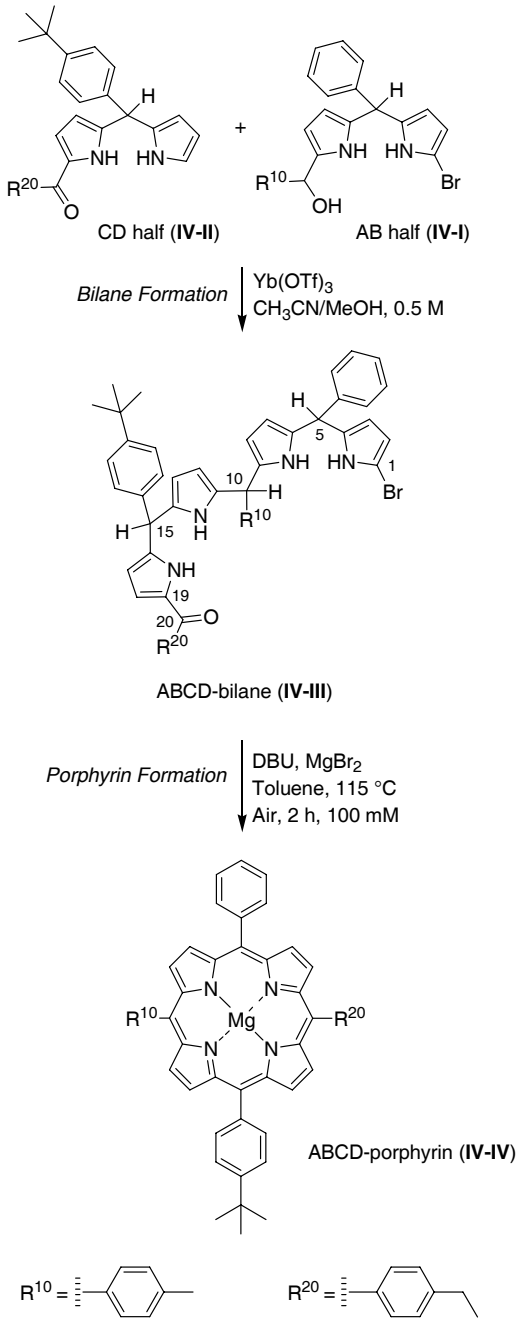
CHAPTER IV

INVESTIGATION OF THE SCOPE OF A NEW ROUTE TO ABCD-BILANES AND ABCD-PORPHYRINS

IV. Introducation

Porphyrins bearing multiple substituents in distinct patterns are valuable constituents in biomimetic and materials chemistry. One route to porphyrins bearing four different meso substituents (i.e., ABCD-porphyrins) relies on the condensation of an ABC-dipyrromethane-1,9-dicarbinol and a D-dipyrromethane followed by oxidation of the resulting porphyrinogen.[IV1-IV3] The reaction is compatible with a variety of substituents, and proceeds without detectable scrambling in many cases. (Scrambling refers to the cleavage of pyrromethane moieties and recombination of fragments thereof to form undesired macrocycles containing distinct patterns or combinations of substituents.[IV4-IV8]) The chief limitations of this "2 + 2" method reside in the macrocycle-forming step: the reaction is carried out in dilute solution (2.5-25 mM reactants), the yield is low (20-30%), dichloromethane is typically used as the solvent, and an added chemical oxidant (DDQ) is employed for porphyrinogen → porphyrin conversion. In addition, certain types of substituents afford poor results (e.g., alkyl,[IV2] heterocyclic,[IV2] no substituent[IV9,IV10]). An alternative route relies on treatment of an intact porphyrin with nucleophiles (e.g., organolithiums) followed by oxidation to form the porphyrin bearing distinct patterns of substituents.[IV11]

We recently developed a new strategy for the synthesis of ABCD-porphyrins that relies on two key reactions: (1) acid-catalyzed condensation of an AB-substituted 1-bromo-dipyrromethane-9-carbinol (**IV-I**) and a CD-substituted 1-acyldipyrromethane (**IV-II**) to give the corresponding 19-acyl-1-bromobilane (**IV-III**), and (2) cyclization of the bilane (**IV-III**) in the presence of a non-nucleophilic base (DBU), a non-coordinating solvent (toluene), and a metal reagent ($MgBr_2$) at 115 °C exposed to air. In the one case examined, cyclization to give the ABCD-porphyrin **IV-IV** proceeded in 65% yield (Scheme 1).[IV12]

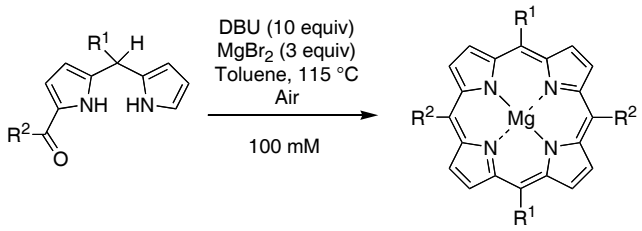


Scheme IV.1. Porphyrins via Bilanes.

The "porphyrins via bilanes" strategy has several attractive features: (i) no detectable scrambling at any stage of the synthesis, (ii) good yield (up to 60%) at high concentration (100

mM) for the macrocycle-forming step, (iii) synthesis of the porphyrin in a relatively short period of time (e.g., < 1 week), (iv) no added chemical oxidant for porphyrin formation, (v) magnesium porphyrins as the products, which easily undergo demetalation, and (vi) facile chromatographic purification. Our chief focus in developing this approach has been to broaden access to porphyrins, yet the accompanying entrée to meso-substituted bilanes may be of comparable value.

The reaction conditions for the intramolecular cyclization of a 19-acyl-1-bromobilane also have been applied to the condensation of two 1-acyldipyrromethane molecules to give the corresponding *trans*-A_2B_2-porphyrin without formation of an isolable bilane (Scheme IV.2). Upon examination of a wide variety of 1-acyldipyrromethanes,[IV13] the reaction conditions were found to be particularly well suited to the synthesis of porphyrins that bear less than four meso substituents (e.g., *trans*-A_2-porphyrins). The limiting example of such sparsely substituted porphyrins entails the condensation of two 1-formyldipyrromethane molecules to give porphine (all meso-substituents = H).[IV14] The reaction conditions also were well suited to the presence of pyridyl groups, which enabled the synthesis of a variety of novel porphyrins bearing pyridyl groups via rational (e.g., *trans*-A_2B_2-, *trans*-A_2-porphyrin) or statistical (e.g., *cis*-A_2-, *cis*-AB-, A-porphyrin) approaches. Greater structural diversity was not achievable owing to the use of 1-acyldipyrromethanes (i.e., ABCD-porphyrins were not accessible), however, and the reaction conditions were poorly compatible with alkyl substituents (e.g., *trans*-A_2B_2-porphyrins bearing four alkyl groups could not be prepared).



Scheme IV.2. *trans*-A_2B_2-Porphyrin Synthesis.

The prior study of the new methodology for the intramolecular cyclization of a 19-acyl-1-bromobilane did not examine the scope of application.[IV12] In the study described herein, we investigated the scope of substituents that can be introduced to ABCD-bilanes and the corresponding ABCD-porphyrins. The groups of interest include alkyl chains, aryl units with electron-withdrawing or electron-releasing groups, bulky substituents, heterocycles, and no substituent (-H). Elucidating the type of substituents that could be tolerated at the 10- and 20-positions (R^{10}, R^{20}) was of most immediate interest, because such sites engage in reaction to form the bilane and porphyrin, respectively. The R^{10} substituent derives from the 1-bromodipyrromethane-9-carbinol (**IV-I)**; this substituent must tolerate acylation of the dipyrromethane, reduction to the α-carbinol, and acid-catalyzed condensation to give the bilane. The R^{20} substituent is not involved in bilane formation but resides at the β-position where carbon-carbon bond formation must occur in the cyclization to give the porphyrin (**IV-IV**) under magnesium-mediated, oxidative conditions. The substituents at positions 5 and 15 (R^5, R^{15}) are also of interest; however, studies of numerous porphyrin-forming reactions indicate that there is greater latitude for diverse substituents at the center of dipyrromethane moieties than at the reacting α-positions.[IV2]

The paper is divided into three parts. In part I, we describe the synthesis of 1-bromo-9-acyldipyrromethanes and 1-acyldipyrromethanes, and their elaboration to the corresponding bilanes under acid-catalyzed condensation. Part II describes the one-flask conversion of the 1-

bromo-19-acylbilanes to the corresponding ABCD-porphyrins. In part III, the findings from the prior sections are applied in the synthesis of two types of porphyrins: (i) porphyrins bearing three pyridyl groups, and (ii) tetraalkylporphyrins. The study reveals the types of meso-substituted bilanes and porphyrins that can be synthesized via this new methodology.

IV.II. Results and Discussion

I. Synthesis of Bilanes. The groups chosen to explore the scope of the methodology include alkyl (pentyl), electron-withdrawing (pentafluorophenyl), electron-releasing (4-methoxyphenyl), heterocyclic (4-pyridyl), bulky (mesityl), alkyl ester (3-methoxy-3-oxopropyl), and no substituent (-H). In this study, two sets of bilanes were prepared. In the first set, all bilanes vary only at the 10-position, whereas in the second set, all bilanes vary only at the 20-position. Such variation is achieved by condensation of a series of 1-bromodipyrromethane-9-carbinols with a 1-acyldipyrromethane. The invariant substituents are identical with that of the benchmark bilane **IV-1a** (vide infra), namely phenyl and 4-*tert*-butylphenyl, whereas 4-methylphenyl (10-position) or 4-ethylphenyl (20-position) is swapped out in bilane set 1 or 2, respectively. The two sets of bilanes (**IV-1**, **IV-2**) and the corresponding porphyrins (**IV-MgP-1**, **IV-MgP-2**) are shown in Chart IV.1.

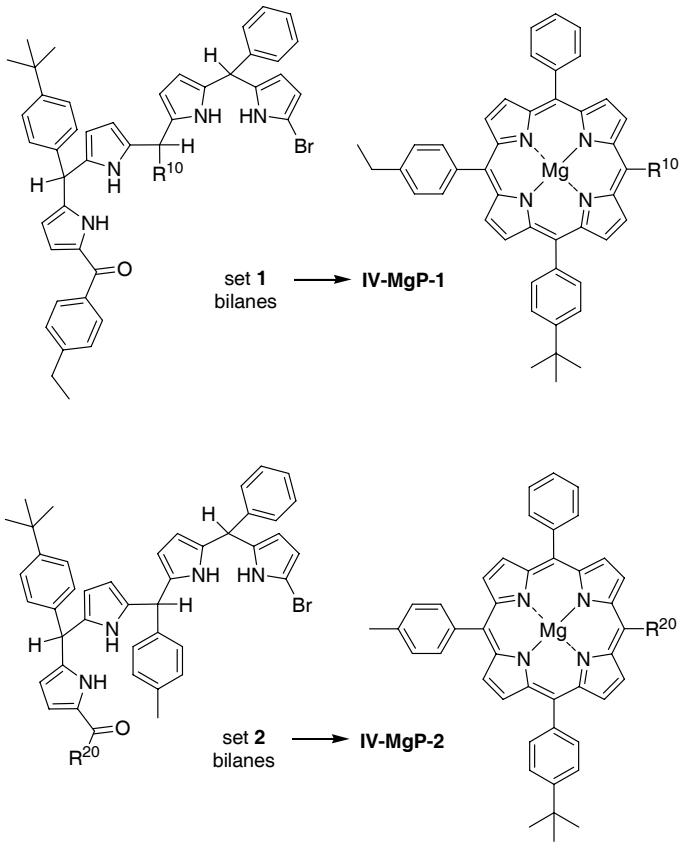


Chart. IV.I. The two sets of bilanes (**IV-1**, **IV-2**) and the corresponding porphyrins (**IV-MgP-1**, **IV-MgP-2**)

A. Preparation of Dipyrromethane Species. Established routes were followed to obtain the dipyrromethane species required herein, a sizable number of which are known compounds. Multigram quantities of 5-phenyldipyrromethane **IV-3a**[IV15] and 5-(4-*tert*-butylphenyl)dipyrromethane **IV-3b**[IV12] were synthesized by condensation of the corresponding aldehyde with excess pyrrole.[IV15] Dipyrromethane **IV-3a** was acylated[IV16] with known Mukaiyama reagents (**IV-4a**,[IV17] **IV-4b**,[IV13] **IV-4c**,[IV17] **IV-4d**,[IV17] **IV-4e**,[IV13] **IV-4f**[IV13]) to give the corresponding 1-acyldipyrromethanes **IV-5a-f** in 71-93% yield (Table IV.1, entries 1-6), of which **IV-5a**,[IV16] **IV-5b-d**,[IV18] and **IV-5e**[IVI7] are known compounds (**IV-5b-e** were prepared previously by a different route). The acylation[IV17] of **IV-3a** with 2,4,6-trimethylbenzoyl chloride (**IV-4g**) afforded the corresponding 1-acyldipyrromethane **IV-5g**[IV18] in 21% yield (entry 7).

Formylation[IV14] of **IV-3a** with the Vilsmeier reagent (**IV-4h**) afforded **IV-5h**[IV19] in 43% yield (entry 8). The 1-acyldipyrromethanes **IV-5a-h** were subjected to regioselective α-bromination [IV20,IV21] with NBS to give 1-bromo-9-acyldipyrromethanes **IV-5a-h-Br** in 54-92% yield (Table IV.1, entries 1-8), of which **IV-5a-Br**[IV18] is a known compound. The resulting 1-bromo-9-acyldipyrromethanes constitute precursors for the AB-half of each bilane.

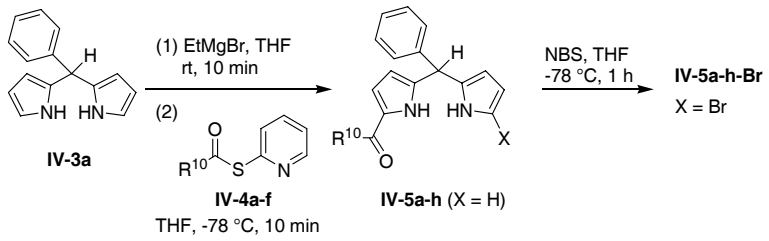
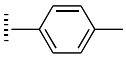
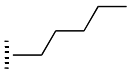
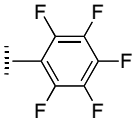
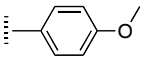
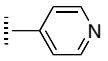
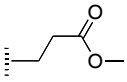
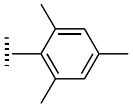


Table IV.1. Synthesis of 1-Bromo-9-Acyldipyrromethanes

Entry	**IV-4**	R^{10}	**IV-5**	Yield (%)	**IV-5-Br**	Yield (%)
1	**IV-4a**		**IV-5a**	83[a]	**IV-5a-Br**	92[b]
2	**IV-4b**		**IV-5b**	72	**IV-5b-Br**	63
3	**IV-4c**		**IV-5c**	93	**IV-5c-Br**	69
4	**IV-4d**		**IV-5d**	83	**IV-5d-Br**	84
5	**IV-4e**		**IV-5e**	71	**IV-5e-Br**	88
6	**IV-4f**		**IV-5f**	72	**IV-5f-Br**	Mixture[c]
7	**IV-4g**[d]		**IV-5g**	21	**IV-5g-Br**	58
8	**IV-4h**[e]		**IV-5h**	43	**IV-5h-Br**	54

[a]Ref IV16. [b]Ref IV18. [c]Inseparable mixture of 1-bromo and 2-bromo-9-acyldipyrromethanes. [d]Acylation was performed with 2,4,6-trimethylbenzoyl chloride.[IV17] [e]Via Vilsmeier formylation.[IV14]

The precursors for the CD-half of each bilane were derived by acylation of dipyrromethane **IV-3b** in the same manner as for dipyrromethane **IV-3a**. The acylations entailed use of Mukaiyama reagents **IV-4i**[IV12] (Table IV.2, entry 1) and **IV-4b-f** (entries 2-6), 2,4,6-trimethylbenzoyl chloride (entry 7), and the Vilsmeier reagent (entry 8). In so doing, new 1-acyldipyrromethanes **IV-6a-h** were obtained in 27-66% yield.

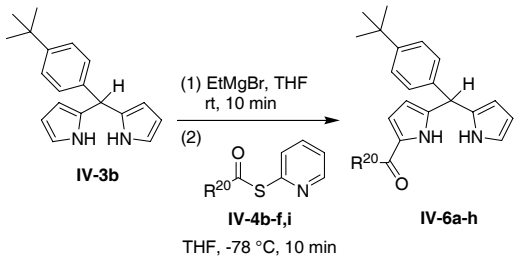
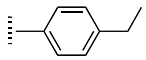
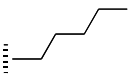
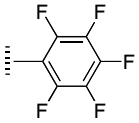
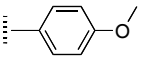
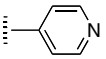
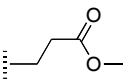
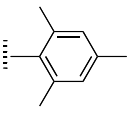


Table IV.2. Synthesis of 1-Acyldipyrromethanes

Entry	**IV-4**	R^{20}	**IV-6**	Yield (%)
1	**IV-4i**		**IV-6a**[a]	66
2	**IV-4b**		**IV-6b**	52
3	**IV-4c**		**IV-6c**	41
4	**IV-4d**		**IV-6d**	56
5	**IV-4e**		**IV-6e**	52
6	**IV-4f**		**IV-6f**	65
7	**IV-4g**[a]		**IV-6g**	33
8	**IV-4h**[b]		**IV-6h**	27

[a]Acylation was performed with 2,4,6-trimethylbenzoyl chloride. [b]Via Vilsmeier formylation.

B. Bilane Formation. We followed the protocol[IV12] employed previously for the synthesis of the target bilanes: (i) each 1-bromo-9-acyldipyrromethane (**IV-5a-h-Br**) was reduced to the corresponding carbinol (**IV-5a-h-Br-OH**) in THF/methanol (3:1) using $NaBH_4$. Each crude carbinol (**IV-5a-h-Br-OH**, 0.5 M) was condensed with a 1-acyldipyrromethane (**IV-6a-h**, 0.5 M) in CH_3CN/MeOH (3:1) containing $Yb(OTf)_3$ (3.3 mM) at room temperature. In most cases, after 2 h of condensation, TLC analysis of the crude reaction mixture revealed complete consumption of the carbinol, a trace of unreacted 1-acyldipyrromethane (**IV-6a-h**), and the corresponding bilane (**IV-1a-h**). Workup entailed quenching with excess triethylamine followed by column chromatography. For the preparation of bilane set 1 (R^{10} variation), 1-acyldipyrromethane **IV-6a** was condensed with each of the 1-bromodipyrromethane-9-carbinols **IV-5a-h-Br-OH** to give bilanes **IV-1a-h**. For set 2 (R^{20} variation), each of the 1-acyldipyrromethanes **IV-6b-h** was condensed with 1-bromodipyrromethane-9-carbinol **IV-5a-Br-OH** to give bilanes **IV-2b-h.**

The results are displayed in Table IV.3. Application of the standard method only worked well in the first set of bilanes (entries 1-8) in three cases (**IV-1a**, **IV-1b**, **IV-1d**) but afforded good yields for all members of the second set of bilanes (**IV-2b-h**; entries 9-15). In the first set of bilanes, the R^{10} substituent is varied, and reaction must occur at this (carbinol) site for bilane formation. By contrast, in the second set of bilanes, the R^{IV20} substituent is varied, which does not participate in bilane formation. Modified conditions for bilane formation were investigated where reaction failed as described in the following.

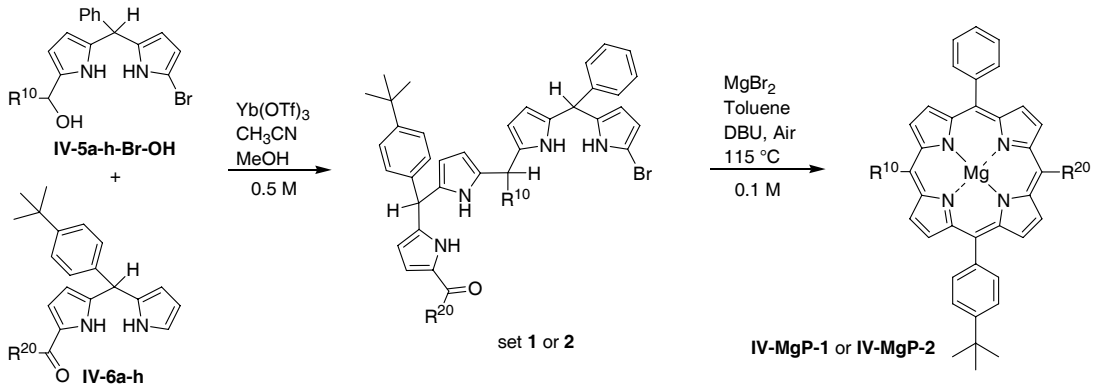


Table IV.3. Synthesis of Bilanes (1, 2) and ABCD-porphyrins (IV-MgP-1, IV-MgP-2)

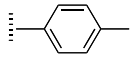
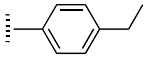
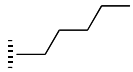
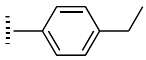
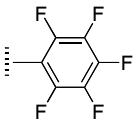
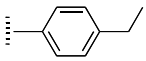
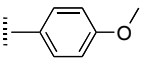
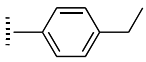
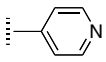
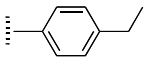
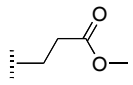
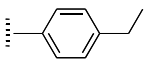
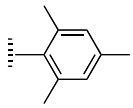
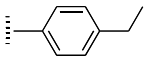
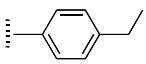
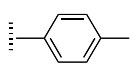
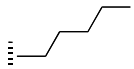
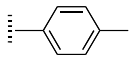
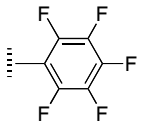
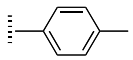
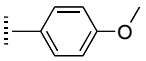
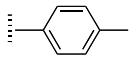
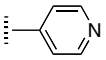
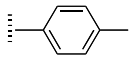
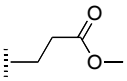
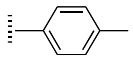
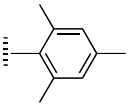
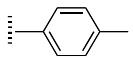
Entry	Reactants		R^{10}	R^{20}	**Bilane**[a]	Yield (%)	**Porphyrin**[b]	Yield (%)
1[c]	**IV-5a-Br-OH**	**IV-6a**			**IV-1a**	76	**IV-MgP-1a**	69
2	**IV-5b-Br-OH**	**IV-6a**			**IV-1b**	85	**IV-MgP-1b**	46
3	**IV-5c-Br-OH**	**IV-6a**			**IV-1c**	87[d]	**IV-MgP-1c**	29[e]
4	**IV-5d-Br-OH**	**IV-6a**			**IV-1d**	76	**IV-MgP-1d**	45
5	**IV-5e-Br-OH**	**IV-6a**			**IV-1e**	36[f]	**IV-MgP-1e**	57
6	**IV-5f-Br-OH**	**IV-6a**			**IV-1f**	0	**IV-MgP-1f**	NA
7	**IV-5g-Br-OH**	**IV-6a**			**IV-1g**	0[g]	**IV-MgP-1g**	NA
8	**IV-5h-Br-OH**	**IV-6a**			**IV-1h**	0[h]	**IV-MgP-1h**	NA
9	**IV-5a-Br-OH**	**IV-6b**			**IV-2b**	57	**IV-MgP-2b**	37

Table IV.3. (continued)

10	**IV-5a-Br-OH**	**IV-6c**			**IV-2c**	35	**IV-MgP-2c**	42[e]
11	**IV-5a-Br-OH**	**IV-6d**			**IV-2d**	64	**IV-MgP-2d**	60
12	**IV-5a-Br-OH**	**IV-6e**			**IV-2e**	61	**IV-MgP-2e**	54
13	**IV-5a-Br-OH**	**IV-6f**			**IV-2f**	68	**IV-MgP-2f**	17
							IV-P-2f-OH	4
14	**IV-5a-Br-OH**	**IV-6g**			**IV-2g**	64	**IV-MgP-2g**	<2
15	**IV-5a-Br-OH**	**IV-6h**			**IV-2h**	56[i]	**IV-MgP-2h**	0[j]
							IV-ZnP-2h	25[k]

[a]The bilanes were prepared with 1 mmol or 0.5 mmol of each reactant in CH_3CN/MeOH (3:1) containing $Yb(OTf)_3$ (3.3 mM) in 2-5 h at room temperature (Method IV.3). [b]Each porphyrin was prepared by reaction of a bilane in toluene containing $MgBr_2$ and DBU exposed to air under conventional heating (Method IV.4). [c]Ref IV12. [d]Performed in CH_3CN without methanol. [e]A more polar porphyrin, a putative covalent adduct with DBU, was isolated in ~6% yield. [f]Perfomed with 230 mM $Yb(OTf)_3$. [g]The reduction of **IV-5g-Br** was not successful. [h]**IV-5h-Br-OH** decomposed during bilane formation (Method IV.1). [i]Performed with 23 mM $Yb(OTf)_3$ at 55 °C. [j]An inseparable mixture of porphyrin and chlorin was obtained. [k]Performed using $Zn(OAc)_2$ in place of $MgBr_2$.

(i) R^{10} = pentafluorophenyl (IV-1c). Only a trace of **IV-1c** was observed after 8 h under the standard conditions. Upon increasing the concentration of $Yb(OTf)_3$ to 23 mM (while maintaining the 3:1 ratio of CH_3CN/MeOH), the resulting heterogeneous reaction mixture after 30 min contained the bilane **IV-1c**, a trace amount of unreacted **IV-6a**, and a polar unidentified component (TLC analysis). Alternatively, the concentration of $Yb(OTf)_3$ was maintained at 3.3 mM while carrying out the reaction in CH_3CN in the absence of MeOH. After 5 h, TLC analysis

revealed complete consumption of **IV-5-c-Br-OH**, a trace amount of **IV-6a**, and bilane **IV-1c**. Subsequent workup afforded bilane **IV-1c** in 87% yield (Table IV.3, entry 3).

(ii) R^{10} = 4-pyridyl (IV-1e). No bilane was observed after 5 h under the standard conditions, or upon increasing the concentration of $Yb(OTf)_3$ to 23 mM. Upon increasing the concentration of acid to 230 mM, reaction proceeded in 3 h to give bilane **IV-1e** together with two more polar, unidentified products. MALDI-MS analysis revealed the molecule ion peak expected for bilane **IV-1e** together with multiple fragments, none of which was consistent with any scrambling processes. The standard workup and purification with column chromatography afforded the target bilane **IV-1e** in 36% yield (Table IV.3, entry 5).

Because heterocyclic substituents have presented notorious difficulties in porphyrin synthesis,[IV2,IV22-24] we also examined several other mild Lewis acid catalysts [$Zn(OTf)_2$, $InCl_3$, $Er(OTf)_3$, $Bi(OTf)_3$] over a range of concentrations (3.30, 23.0, and 230 mM) in CH_3CN for the synthesis of **IV-1e**. $Zn(OTf)_2$ gave no product even after overnight stirring at room temperature. $InCl_3$, $Er(OTf)_3$, and $Bi(OTf)_3$ at 230 mM each afforded the target bilane upon 6–8 h of reaction. The cleanest reaction was observed with $InCl_3$ (no starting materials remained). The success of these reaction conditions augurs well for the synthesis of elaborate bilanes bearing heterocyclic substituents.

(iii) R^{10} = 3-methoxy-3-oxopropyl (IV-1f). The reduction of the ketone in **IV-5f-Br** to give **IV-5f-Br-OH** proceeded smoothly; however, the standard condensation protocol afforded three new components but no bilane was detected by MALDI-MS or by ^{1}H NMR spectroscopy (entry 6).

(iv) R^{10} = mesityl (IV-1g). All attempts to reduce the mesitoyl group of **IV-5g-Br** failed to give the corresponding carbinol **IV-5g-Br-OH** (entry 7). The conditions examined include

use of excess $NaBH_4$ (100 mol equiv versus **IV-5g-Br**, 8.25 mM) in anhydrous THF/MeOH (2:1),[IV25] twice this amount of $NaBH_4$, or $LiBH_4$.

(v) R^{10} = H (IV-1h). The reaction of **IV-5h-Br-OH** and **IV-6a** under standard conditions afforded three components (a streaking component, unreacted **IV-6a**, and a polar material). Standard workup gave mostly decomposition products rather than the desired bilane (entry 8).

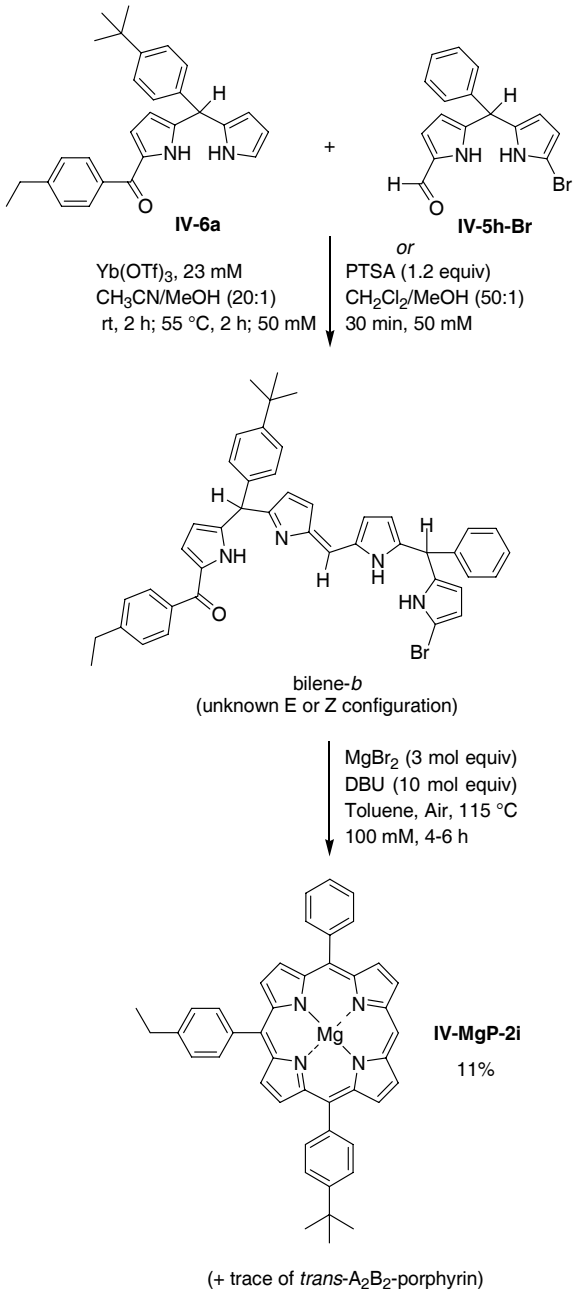
In summary, modified acid-catalysis conditions proved useful for dipyrromethane-carbinols bearing pentafluorophenyl or *p*-pyridyl groups at the carbinol site. However, bilanes bearing a 10-mesityl group or no substituent (R^{10} = H) cannot be prepared via this approach. The bilanes were characterized by NMR spectroscopy (^1H, ^{13}C) and mass spectrometry (MALDI-MS, ESI-MS).

II. Synthesis of Metalloporphyrins from Bilanes. The synthesis of ABCD-porphyrins was carried out using bilanes that possess a variety of substituents at the 10-position (set 1, **IV-1a-e**) and 20-position (set 2, **IV-2b-h**). The standard protocol[IV12] entails bilane (100 mM) in toluene (115 °C) containing DBU (10.0 mol equiv versus the bilane) and $MgBr_2$ (3.0 mol equiv versus the bilane) with exposure to air. The results are displayed in Table IV.3. Of 11 new trials (**IV-MgP-1a**[IV12] was made previously), nine ABCD-porphyrins were obtained in yields of 17-60% yield in 2-4 h.

The standard reaction with bilane **IV-2h** to obtain ABC-porphyrin **IV-MgP-2h** (which contains one unsubstituted meso position) afforded an inseparable mixture of porphyrin and chlorin as evidenced by absorption spectroscopy (λ_{abs} = 624 nm, consistent with expectation for a magnesium-triarylchlorin[IV26,IV27]) and laser-desorption mass spectrometry (LD-MS) in the absence of a matrix[IV28] (Table IV.3, entry 15). A traditional method for handling such mixtures entails DDQ-mediated oxidation to convert chlorin to porphyrin;[IV29-IV31] however, treatment of

the mixture gave an unknown byproduct in low yield rather than the desired porphyrin. Meso-unsubstituted porphyrins are known to be susceptible to reactions at the unsubstituted meso site, particularly upon oxidation to give meso,meso-linked dimers.[IV32] Given that magnesium porphyrins are more susceptible to one-electron oxidation than zinc porphyrins,[IV33] and zinc reagents have been employed in place of $MgBr_2$ in the bilane → porphyrin conversion,[IV12] we carried out the macrocycle-forming reaction in the presence of $Zn(OAc)_2$. The use of $Zn(OAc)_2$ with bilane **IV-2h** afforded a lesser amount of chlorin (λ_{abs} = 620 nm), and upon oxidation with DDQ, the target zinc ABC-porphyrin **IV-ZnP-2h** was obtained in 25% yield.

An alternative approach to prepare ABC-porphyrins was investigated by the reaction of 1-formyl-9-bromodipyrromethane **IV-5h-Br** (without reduction) and 1-acyldipyrromethane **IV-6a** to give the bilene-*b* intermediate. This approach was pursued because (i) chlorin contaminants are believed to derive upon tautomeric rearrangement of polypyrromethane precursors (e.g., porphyrinogens),[IV34] (ii) we felt that pre-formation of the unsaturated unit at the position lacking an aryl substituent (i.e., the 10-position) would thereby avoid tautomeric rearrangement at this apparently problematic site, and (iii) the requisite 1-bromo-9-formyldipyrromethanes have been used succesfully in analogous condensation reactions in chlorin chemistry.[IV21,IV35] The reaction with the standard acid-catalysis conditions with $Yb(OTf)_3$ was sluggish and required mild heating (55 °C) for 2 h to give the bilene (λ_{max} = 490 nm), whereas the same reaction could be carried out in 30 min with *p*-toluenesulfonic acid at room temperature. Subsequent treatment of the bilene to the porphyrin-forming conditions indeed gave **IV-MgP-2i** in 11% yield (Scheme IV.3). On the other hand, prolonged heating of the reaction mixture in air gave the corresponding meso,meso-linked porphyrin dimer.

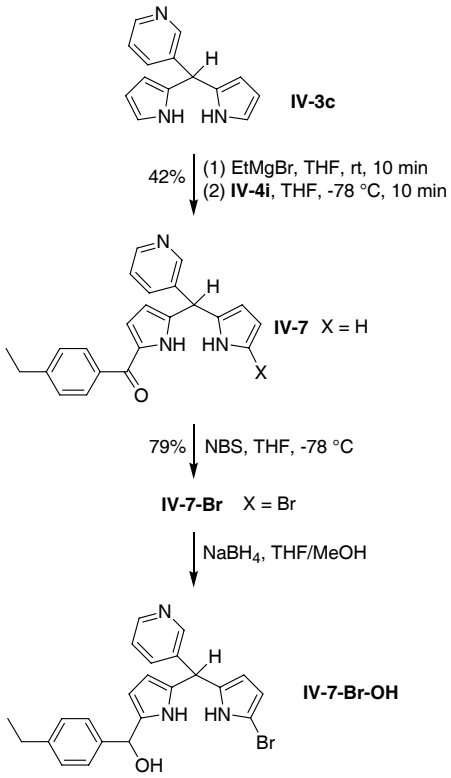


Scheme IV.3. Synthesis of ABC-porphyrin from Bilene-*b* Intermediate.

III. Applications. The scope was explored further by preparation of bilanes and porphyrins bearing three pyridyl groups or four alkyl groups. In this study, the substituent variation was focused at the R^5, R^{15}, and R^{20} sites while maintaining the R^{10} substituent of a type that is known to afford successful reaction in bilane formation.

A. Porphyrins Bearing Three Pyridyl Substituents.

(i) Bilane Synthesis. We investigated the synthesis of target molecules bearing three heterocyclic substituents (*o*-, *m*-, *p*-pyridyl). In each target bilane, the R^5 substituent was *m*-pyridyl, the R^{10} substituent was 4-ethylphenyl, and the 15 and 20 positions were varied (*o*-, *m*-, *p*-pyridyl). The synthesis of each bilane employed 1-bromodipyrromethane-9-carbinol **IV-7-Br**, which was prepared as shown in Scheme IV.4. The dipyrromethane bearing a *m*-pyridyl group (**IV-3c**)[IV22] was treated with Mukaiyama reagent **IV-4i** to give the corresponding 1-acyldipyrromethane **IV-7** in 42% yield. α-Bromination[IV20,IV21] of the latter afforded 1-acyl-9-bromodipyrromethane **IV-7-Br** in 79% yield. Reduction with $NaBH_4$ gave **IV-7-Br-OH**, which constitutes the precursor for the AB-half of each bilane.



Scheme IV.4. Synthesis of **IV-7-Br**.

The bilane synthesis entailed condensation of the carbinol **IV-7-Br-OH** with a 1-

acyldipyrromethane (0.5 M each) in neat acetonitrile (without MeOH) containing $Yb(OTf)_3$ (230 mM). The rationale for the use of neat acetonitrile stemmed from our findings that bilanes that contain a heterocyclic group (**IV-1e**, *p*-pyridyl) or a bulky electron-withdrawing substituent (**IV-1c**, pentafluorophenyl) at the 10-position are formed faster and in higher yield upon reaction in neat acetonitrile. [Note that the acid catalyst is not entirely dissolved; the reaction mixture is heterogeneous. We use the concentration term (e.g., 230 mM) for consistency and purposes of comparison.] Each of the four 1-acyldipyrromethanes (**IV-8a-d**) employed bears two pyridyl groups and is a known compound[IV13] (Table IV.4).

In each bilane-forming reaction, chromatographic purification proved difficult given the tendency of the tripyridyl-substituted bilanes to streak. In each case, TLC analysis of the purified fraction revealed one component; however, ^{1}H NMR spectroscopy showed the presence of the target bilane and an unidentified impurity. Although the 1-acyldipyrromethane generally was not detected, its presence was ostensibly revealed upon subsequent porphyrin formation. Our prior studies have shown that prolonged chromatographic purification of a bilane results in formation of a green byproduct, presumably owing to oxidation.[IV12] Accordingly, in each case the crude bilane was carried on to the porphyrin-forming reaction without further purification.

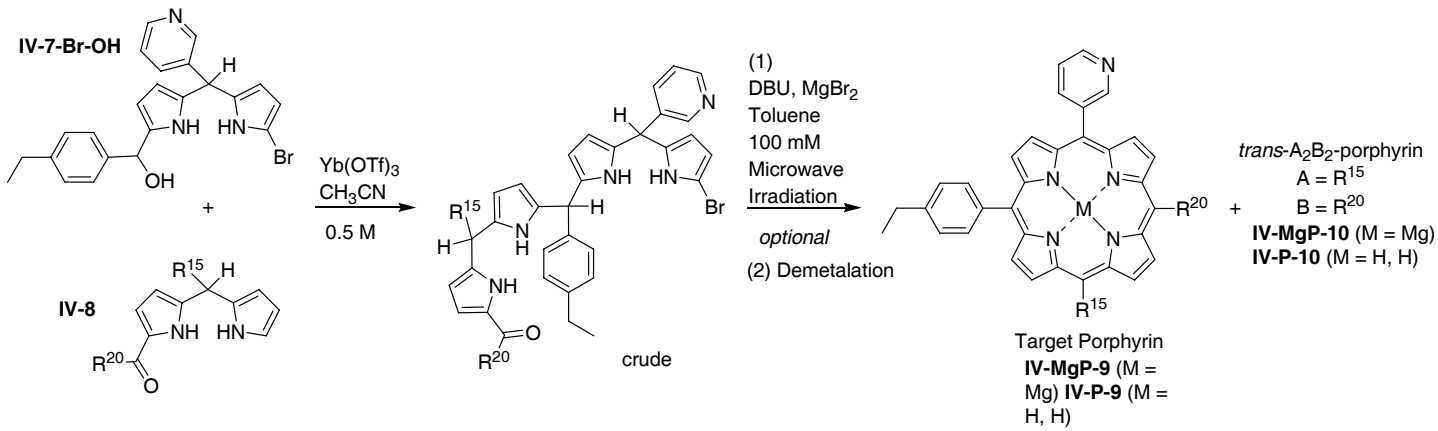
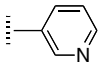
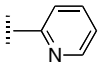
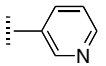
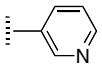
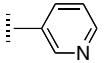
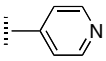
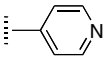
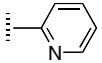


Table IV.4. Porphyrins Bearing Three Pyridyl Substituents[a]

R^{15}	R^{20}	Cmpd **IV-8**	Target Porphyrin	Type	M	Yield (%)	*trans*-A_2B_2-Porphyrin	Yield (%)
		**IV-8a**	**IV-MgP-9a**	*trans*-A_2BC	Mg	12	**IV-MgP-10a**	trace
		**IV-8b**	**IV-MgP-9b**	A_3B	Mg	8	**IV-MgP-10b**	trace
		**IV-8c**	**IV-P-9c**	A_2BC	H, H[b]	17	**IV-P-10c**	7
		**IV-8d**	**IV-P-9d**	ABCD	H, H[b]	25	**IV-P-10d**	15

[a]The formation of the bilane and the porphyrin was prepared following Method IV.5 (see text). Microwave irradiation was used in each porphyrin-forming reaction. [b]Demetalation was performed

(ii) Porphyrin Synthesis. Microwave irradiation can provide a superior method versus conventional heating for the synthesis of porphyrins bearing heterocyclic substituents.[IV13] Accordingly, in each case the crude bilane was subjected to the porphyrin-forming conditions [DBU (10 mol equiv) and $MgBr_2$ (3 mol equiv) in toluene] via microwave irradiation. In each case, the TLC and LD-MS analyses of the crude reaction mixture revealed the presence of two porphyrin products, the target porphyrin and a *trans*-A_2B_2-porphyrin. The *trans*-A_2B_2-porphyrin is believed to derive from the condensation of unreacted 1-acyldipyrromethane (**IV-8**) that was present as a contaminant in the crude bilane.

The results are shown in Table IV.4. Porphyrin **IV-MgP-9a** contains an *o*-pyridyl group flanked by two *m*-pyridyl groups (*trans*-AB_2C-porphyrin) and was isolated in 12% yield. Porphyrin **IV-MgP-9b** contains three *m*-pyridyl groups (A_3B-porphyrin) and was obtained in 8% yield upon alumina column chromatography. In each case, a trace of the *trans*-A_2B_2-porphyrin (**IV-MgP-10a**, **IV-MgP-10b**) also was isolated.

The chromatographic purification of the magnesium porphyrin was not successful in the case of putative **IV-MgP-9c** and **IV-MgP-9d**, each of which bears one *p*-pyridyl group and two other pyridyl groups. Hence, demetalation was performed and the target porphyrin was isolated as the free base. Thus, free base porphyrin **IV-P-9c** contains a sequence of *m*-, *p*-, and *m*-pyridyl groups (*trans*-AB_2C-porphyrin) and was isolated in 17% yield accompanied by the free base *trans*-A_2B_2-porphyrin **IV-P-10c** in 7% yield. Similarly, free base porphyrin **IV-P-9d**, which contains a sequence of *m*-, *o*-, and *p*-pyridyl groups (ABCD-porphyrin), was isolated in 25% yield accompanied by the free base *trans*-A_2B_2-porphyrin **IV-P-10d** in 15% yield.

B. Tetraalkylporphyrins. The synthesis of porphyrins bearing four meso-alkyl groups also was examined. A variety of meso-alkyl/aryl-porphyrins have been prepared;[IV7,IV36-38] however, the most elaborate meso-tetraalkylporphyrins prepared to date apparently are limited to

A_4-[IV39-42] and A_3B-[IV43] substituent patterns. The dipyrromethanes used are shown in Chart IV.2. All of the dipyrromethanes are known compounds; those bearing the meso substituent H (**IV-3d**),[IV15] ethyl (**IV-3e**),[IV13] propyl (**IV-3f**)[IV13] and pentyl (**IV-3h**)[IV15] were previously prepared by condensation with pyrrole in the presence of $InCl_3$. 5-Butyldipyrromethane (**IV-3g**), previously described without complete characterization,[IV44,IV45] was prepared herein by reaction with pyrrole containing $InCl_3$. A new Mukaiyama reagent, *S*-2-pyridyl butanothioate (**IV-4k**), was prepared by reaction of 2-mercaptopyridine and butyryl chloride.

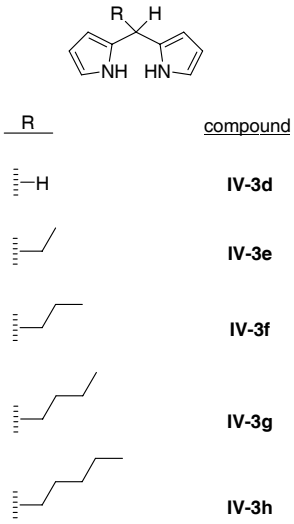


Chart IV.2. Alkyl Substituted Dipyrromethanes**.**

A series of 1-acyldipyrromethanes was prepared as shown in Table IV.5. The reaction of dipyrromethane **IV-3d-h** with the Mukaiyama reagents **IV-4b**, **IV-4j**,[IV13] **IV-4k**, and **IV-4l**[IV13] following the standard acylation procedure[IV16] afforded the target 1-acyldipyrromethanes in 42-79% yields. 1-Acyldipyrromethanes **IV-11b**,[IV13] **IV-11e**,[IV13] and **IV-11h**[IV46] are known compounds, whereas **IV-11a**, **IV-11c**, **IV-11d**, **IV-11f**, and **IV-11g** are new. 1-Acyldipyrromethanes **IV-11b-d** and **IV-11h** were subjected to regioselective α-bromination[IV20,IV21] with NBS to afford the corresponding 1-bromo-9-acyldipyrromethanes (Table IV.5). Compound **IV-11c-Br** was very unstable and underwent discoloration upon

warming a stored sample above –4 °C. Surprisingly, the analogous compound **11d-Br** was sufficiently stable to obtain full characterization data (^{1}H NMR and ^{13}C NMR spectra in THF-d_8; ESI-MS and elemental analysis).

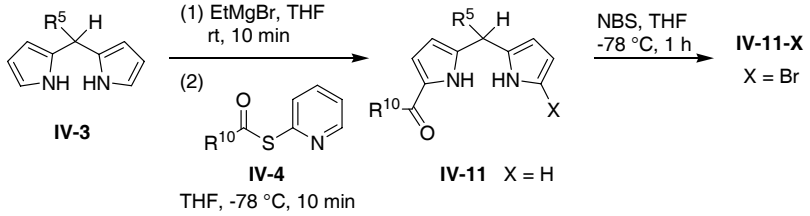


Table IV.5. Synthesis of Alkyl-Substituted 1-Acyldipyrromethanes

Entry	**IV-3**	**IV-4**	R^5	R^{10}	**IV-11**	Yield (%)
1	**IV-3d**	**IV-4j**	—H		**IV-11a**	42
2	**IV-3e**	**IV-4j**			**IV-11b**	81[a]
					IV-11b-Br	88
3	**IV-3e**	**IV-4k**			**IV-11c**	64
					IV-11c-Br	89
4	**IV-3e**	**IV-4l**			**IV-11d**	62
					IV-11d-Br	94
5	**IV-3f**	**IV-4l**			**IV-11e**	46[a]
6	**IV-3f**	**IV-4b**			**IV-11f**	52
7	**IV-3g**	**IV-4b**			**IV-11g**	79
8	**IV-3h**	**IV-4b**			**IV-11h**	65[b]
					IV-11h-Br	85

[a]Ref IV13. [b]Ref IV46.

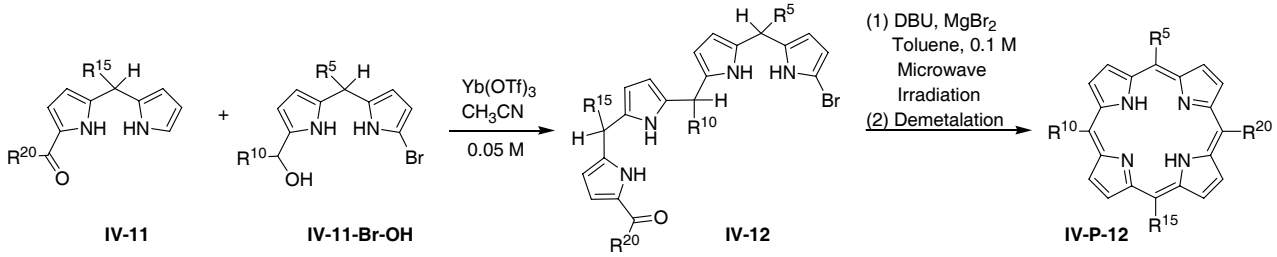


Table IV.6. Bilanes and Porphyrins Bearing Alkyl Substituents[a]

Entry	IV-11-Br-OH	IV-11	R^5	R^{10}	R^{15}	R^{20}	Bilane	Yield (%)	Porphyrin	Type	Yield (%)
1	**IV-11h-Br-OH**	**IV-11b**					**IV-12a**	37	**IV-MgP-12a**	*cis*-A_2B_2	16[b]
2	**IV-11b-Br-OH**	**IV-11a**			H		**IV-12b**	86	**IV-P-12b**	A_3	--[b]
3	**IV-11h-Br-OH**	**IV-11a**			H		**IV-12c**	62	**IV-P-12c**	*cis*-A_2B	16[c]
4	**IV-11d-Br-OH**	**IV-11e**					**IV-12d**	78	**IV-P-12d**	*trans*-A_2BC	23
5	**IV-11d-Br-OH**	**IV-11f**					**IV-12e**	63	**IV-P-12e**	ABCD	18
6	**IV-11c-Br-OH**	**IV-11g**					**IV-12f**	81	**IV-P-12f**	ABCD	24

[a]The bilane was prepared in CH_3CN containing $Yb(OTf)_3$ (3.3 mM) for 30 min at room temperature (Method IV.6). Each porphyrin was prepared by reaction of a bilane in toluene containing $MgBr_2$ and DBU exposed to air under microwave irradiation unless noted otherwise. [b]By use of conventional heating (Method IV.4; no demetalation, giving the magnesium chelate). [c]No porphyrin was obtained upon conventional heating.

The bilane synthesis was performed under conditions slightly modified from the standard protocol given that all of the dialkyl 1-bromo-9-acyldipyrromethane-carbinols were found to be unstable in the solid form. Reduction of a dialkyl 1-bromo-9-acyldipyrromethane (**IV-11b-Br**, **IV-11c-Br**, **IV-11d-Br**, **IV-11h-Br**) was carried out in the standard way with excess $NaBH_4$ to give the corresponding carbinol. The modifications to the procedure were as follows: (i) the dipyrromethane-carbinol was concentrated in a mixture of ethyl ether/acetonitrile (1:5) until most of the ether was removed, (ii) the resulting carbinol was used directly in the bilane-forming reaction, and (iii) acid-catalyzed condensation was carried out at 0.05 M (rather than 0.5 M) in acetonitrile containing $Yb(OTf)_3$. In this manner, the subsequent standard workup with chromatography afforded the target tetraalkylbilanes in 62-86% yields (Table IV.6).

Treatment of tetraalkyl-substituted bilane **IV-12a** to the reaction conditions including conventional heating for 8 h gave the target *cis*-A_2B_2-porphyrin **IV-MgP-12a** in 16% yield. However, attempts to perform the reaction of bilane **IV-12b** or **IV-12c** under conventional heating gave no porphyrin. The promising results obtained for the synthesis of porphyrins bearing heterocyclic substituents under microwave irradiation[IV13] encouraged the analogous synthesis of tetraalkylporphyrins. Thus, a given bilane (**IV-12c-f**) was treated with DBU (10 mol equiv) and $MgBr_2$ (3 mol equiv) in toluene (Table IV.6). The reaction mixture was subjected to microwave irradiation for 30 min. In each case, examination of the crude reaction mixture by absorption spectroscopy showed the characteristic porphyrin Soret band and two broad peaks (303 nm, 525 nm; unassigned origin). TLC analysis showed consumption of the bilane, formation of the porphyrin, and a polar tailing component. Microwave irradiation was continued until TLC analysis and absorption spectroscopy did not

show any intermediate, which typically required ~36 h. The crude reaction mixture was subjected to demetalation followed by column chromatography. In each case, the porphyrin was obtained in yield ranging from 16 to 24%. The resulting porphyrins include two ABCD-porphyrins (**IV-P-12e**, **IV-P-12f**), each of which contains an ethyl, propyl, butyl and pentyl group (and hence are isomers), and one *trans*-A_2BC-porphyrin (**IV-P-12d**).

IV.III. Outlook

The data obtained herein provide extensive information concerning the scope of the route to ABCD-bilanes and ABCD-porphyrins. The key findings are as follows:

(1) The pentyl unit gave better yields at the 10- versus 20-position in both bilane and porphyrin formation (Table IV.3, entries 2, 9).

(2) The pentafluorophenyl unit at the 10- versus 20-position of the bilane gave somewhat better yields upon bilane formation (Table IV.3, entries 3, 10), but the reverse was observed in porphyrin formation.

(3) The 4-methoxyphenyl group at the 20- versus 10-position of the bilane resulted in a higher yield in the porphyrin-forming reaction (Table IV.3, entries 4, 11).

(4) No significant difference in porphyrin yield was observed by having the 4-pyridyl group at the 10 or 20-position of the bilane (Table IV.3, entries 5, 12).

(5) An alkyl ester unit can be introduced to the porphyrin macrocycle via the 20- but not the 10-position of the bilane (Table IV.3, entries 6, 13).

(6) A mesityl group cannot be introduced at the 10-position of the bilane, and a 20-mesityl substituted bilane does not give significant amounts of the porphyrin (Table IV.3, entries 7, 14).

(7) A 10-unsubstituted porphyrin can be prepared via a bilene-*b* but not a bilane because a dipyrromethane containing a primary carbinol does not give the bilane (Table IV.3, entry 8; Scheme IV.3).

(8) A 20-unsubstituted porphyrin can be prepared as the zinc but not the magnesium chelate (Table IV.3, entry 15).

(9) The synthesis of sparsely substituted alkylporphyrins via conventional heating was rather unsuccessful but could be achieved via microwave irradiation (Table IV.6, entries 2 and 3).

(10) Bilanes and porphyrins bearing up to three different pyridyl groups in distinct arrangements can be prepared (Table IV.4). A change in the ratio of reagents was not necessary for successful reaction despite the presence of three alternative coordination sites (in addition to the acyl moiety) for the acid catalyst or $MgBr_2$ in the reacting species.

(11) Bilanes and porphyrins bearing up to four different alkyl groups can be prepared (Table IV.6).

(12) The 1-bromo-19-acylbilanes bearing bearing aryl or heteroaryl substituents were stable to routine handling on the open benchtop and upon prolonged storage at –4 °C. By contrast, the analogous bilanes bearing alkyl substituents were rather unstable and were used shortly after preparation (see Supporting Information).

Alkyl and pyridyl groups were of particular interest in this study because both types of groups have afforded poor results with the standard dipyrromethane + dipyrromethane-dicarbinol route to ABCD-porphyrins.[IV2] The alkyl-substituted dipyrromethanes give rise to multiple porphyrin products (owing to acidolytic scrambling) whereas the pyridyl groups tend to complex with the acid catalysts and thereby impede reaction. The new method for condensation of a 1-acyldipyrromethane (Scheme IV.2) to give *trans*-A_2B_2-porphyrins is

broadly compatible with pyridyl substituents but only marginally so with alkyl groups; regardless, the route does not provide access to ABCD patterns for porphyrins, and offers no access to bilanes at all.[IV13] The conditions employed herein rely on (i) a mild Lewis acid in a polar medium [e.g., $Yb(OTf)_3$ in acetonitrile] for bilane formation, and (ii) non-acidic conditions for macrocycle formation. The conditions support reaction in the presence of alkyl and pyridyl substituents without detectable scrambling. Thus, the new capabilities with pyridyl and alkyl groups fill a longstanding lacuna in porphyrin chemistry.

The scope demonstrated herein is quite promising for a number of applications. The applications for the porphyrins are manifold, yet the bilanes may prove equally versatile. Almost all prior studies of bilanes have focused on naturally occurring analogues, which bear β-pyrrole substituents and lack meso substituents.[IV47-IV56] The bilanes (and their various oxidized analogues: bilenes, biladienes, and bilatrienes) may prove very attractive in studies of coordination chemistry, supramolecular chemistry, redox chemistry, materials chemistry, and photochemistry (as phytochrome or phycobilin analogues). Regardless of application, significant features of the route will require further development. One limitation is the necessity for elevated temperature to achieve macrocycle formation: the reaction proceeds well at ~115 °C but poorly at lower temperatures. Much about the mechanism of macrocycle formation remains unknown, particularly the nature of the reactive end groups (acylpyrrole, bromopyrrole) upon carbon-carbon bond formation, the nature of any metal-coordination complexes (i.e., templating), the course of oxidation prior to or following macrocycle formation, and the relative reactivity of the different (up to eight) stereoisomeric forms of the bilane. Understanding such aspects of the reaction may lead to milder conditions for macrocycle formation and thereby further broaden the scope of application.

The contents of this chapter are in press.[IV57]

IV.IV. Experimental Section

General. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were collected in $CDCl_3$ at room temperature unless noted otherwise. Melting points are uncorrected. Silica gel (40 μm average particle size) was used for column chromatography. Alumina (grade I) was used as received for column chromatography. THF was distilled from sodium/benzophenone under argon. Methanol (anhydrous) and CH_2Cl_2 (anhydrous) were used as received. Anhydrous toluene was obtained from commercial sources or by distillation from sodium/benzophenone under argon. All other chemicals were reagent grade and were used as received. The dipyrromethanes, 1-acyldipyrromethanes, and bilanes are easily detected in TLC analysis upon exposure to Br_2 vapor.

5-Butyldipyrromethane (IV-3g). Following a reported procedure,[IV15] a solution of valeraldehyde (5.31 mL, 50.0 mmol) in pyrrole (347 mL, 5.00 mol) at room temperature under argon was treated with $InCl_3$ (1.11 g, 5.00 mmol) for 1.5 h. Powdered NaOH (6.00 g, 150 mmol) was added. After stirring for 1 h, the mixture was suction filtered. Excess pyrrole was removed from the filtrate under high vacuum, leaving a brown oil. Chromatography of the latter [silica, hexanes/CH_2Cl_2 (1:1) → (2:3)] afforded a yellow liquid (4.26 g, 42%): ^{1}H NMR δ 0.87 (t, J = 7.2 Hz, 3H), 1.25–1.33 (m, 4H), 1.91 (app q, J = 7.2 Hz, 2H), 3.90 (t, J = 7.6 Hz, 1H), 6.06–6.09 (m, 2H), 6.11–6.16 (m, 2H), 6.54–6.56 (m, 2H), 7.54–7.58 (br, 2H); ^{13}C NMR δ 14.3, 22.9, 30.0, 34.5, 37.8, 105.5, 108.2, 117.3, 133.7. ESI-MS obsd 202.14735, calcd 202.14700 ($C_{13}H_{18}N_2$). Anal. Calcd for $C_{13}H_{18}N_2$: C, 77.18; H,

8.97; N, 13.85. Found: C, 77.29; H, 8.99; N, 13.60.

***S*-2-Pyridyl butanothioate (IV-4k).** Following a reported procedure,[IV17] a solution of 2-mercaptopyridine (5.55 g, 50.0 mmol) in THF (50.0 mL) was treated slowly with butyryl chloride (5.33 g, 50.0 mmol). The resulting reaction mixture was stirred for 30 min. The reaction mixture was added to a biphasic solution of saturated aqueous $NaHCO_3$ (100 mL) and diethyl ether (100 mL). The mixture was stirred until the foaming subsided. The organic layer was extracted with diethyl ether. The organic extract was washed (water, brine), dried (Na_2SO_4) and concentrated to afford a yellow oil (8.066 g, 89%): ^{1}H NMR δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.73–1.78 (m, 2H), 2.68 (t, *J* = 7.4 Hz, 2H), 7.26–7.29 (m, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.71–7.75 (m, 1H), 8.60–8.61 (m, 1H); ^{13}C NMR δ 13.7, 19.2, 46.2, 123.6, 130.3, 137.3, 150.6, 151.8, 196.6; ESI-MS obsd 181.05612, calcd 181.05613 ($C_9H_{11}NOS$). Anal. Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.69; H, 6.10; N, 7.63.

General Protocol for the Synthesis of 1-Acyldipyrromethanes (Method IV.1). Following the standard procedure,[IV16] a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added slowly to a solution of a dipyrromethane (**IV-3a–i**, 7.50 mmol) in THF (15.0 mL) under argon. The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of a Mukaiyama reagent (**IV-4a-d**, **IV-4f**, **IV-4i-4l**, 7.50 mmol) in THF (15.0 mL) was added to the reaction mixture (**IV-4e**[IV134] was added as a solid). The solution was stirred at –78 °C for 10 min, and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic layer was washed (water, brine), dried (Na_2SO_4), and filtered. The filtrate was concentrated. Column chromatography

[silica, CH_2Cl_2 (until all the unreacted dipyrromethane was eluted) → hexanes/ethyl acetate (3:1)] afforded the corresponding 1-acyldipyrromethane.

1-(4-Ethylbenzoyl)-5-(3-pyridyl)dipyrromethane (IV-7). Following Method IV.1, a solution of EtMgBr (10.0 mL, 10. mmol, 1.0 M in THF) was added to a solution of **IV-3c** (0.893 g, 4.00 mmol) in THF (8.0 mL). A solution of **IV-4i** (0.973 g, 4.00 mmol) in THF (8.0 mL) was added to the reaction mixture. The resulting crude product was chromatographed [silica, CH_2Cl_2/ethyl acetate (3:2) → CH_2Cl_2/ethyl acetate (1:1) → ethyl acetate] to afford a light-brown foam (0.594 g, 42%): mp 68–70 °C; ^{1}H NMR d 1.27 (t, *J* = 7.6 Hz, 3H), 2.72 (q, *J* = 7.6 Hz, 2H), 5.57 (s, 1H), 5.93–5.96 (m, 1H), 6.07–6.09 (m, 1H), 6.12–6.14 (m, 1H), 6.69–6.70 (m, 1H), 6.79–6.81 (m, 1H), 7.12–7.16 (m, 1H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.47–7.49 (m, 1H), 7.72 (d, *J* = 7.8 Hz, 2H), 8.39–8.42 (m, 2H), 9.22–9.41 (br, 1H), 10.55–10.62 (br, 1H); ^{13}C NMR d 15.5, 29.1, 42.0, 108.4, 108.5, 110.9, 118.7, 121.3, 123.6, 128.1, 129.5, 130.3, 131.3, 135.8, 136.1, 137.1, 140.9, 148.5, 149.1, 149.8, 185.1; ESI-MS obsd 356.1756, calcd 356.1757 [$(M + H)^+$, M = $C_{23}H_{21}N_3O$]. Anal. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82. Found: C, 77.88; H, 5.97; N, 11.48.

General Protocol for the Bromination of 1-Acyldipyrromethanes (Method IV.2). Following a general procedure,[IV20,IV21] a solution of 1-acyldipyrromethane (**IV-5a-h**, **IV-11b-d**, **IV-11h**; 1.00-5.40 mmol, 0.1 M) in dry THF (10.0–54.0 mL) was cooled to –78 °C under argon. A solid sample of NBS (1.00-5.40 mmol) was added to give a concentration of 0.1 M, and the reaction mixture was stirred at –78 °C for 1 h. Hexanes (20.0 mL) and water (20.0 mL) were added, and the reaction mixture was allowed to warm to room temperature. Ethyl acetate was added. The organic phase was washed (water, brine), dried (K_2CO_3), and concentrated under reduced pressure without heating. The crude product was purified by

column chromatography [silica, hexanes/ethyl acetate (3:1)] to afford the corresponding 1-acyl-9-bromodipyrromethane.

1-Bromo-9-hexanoyl-5-phenyldipyrromethane (IV-5b-Br). Following Method IV.2, a solution of **IV-5b** (1.728 g, 5.40 mmol) in THF (54.0 mL) was treated with NBS (0.961 g, 5.4 mmol) to afford a brown paste (1.36 g, 63%): ^{1}H NMR δ 0.87–0.90 (m, 3H), 1.31–1.33 (m, 4H), 1.61–1.65 (m, 2H), 2.52–2.69 (m, 2H), 5.45 (s, 1H), 5.89–5.91 (m, 1H), 6.04–6.07 (m, 2H), 6.82–6.84 (m, 1H), 7.12–7.14 (m, 2H), 7.25–7.30 (m, 3H), 8.52–8.66 (br, 1H), 9.72–9.92 (br, 1H); ^{13}C NMR δ 14.2, 22.7, 25.5, 31.9, 37.9, 44.3, 98.0, 109.9, 110.56, 110.6, 117.7, 127.6, 128.4, 128.9, 131.9, 132.7, 140.2, 140.4, 191.8; FAB-MS obsd 399.1073, calcd 399.1072 [$(M + H)^+$, M = $C_{21}H_{23}BrN_2O$]. Anal. Calcd for $C_{21}H_{23}BrN_2O$: C, 63.16; H, 5.81; N. 7.02. Found: C, 62.94; H, 5.88; N, 6.85.

1-Bromo-9-(pentafluorobenzoyl)-5-phenyldipyrromethane (IV-5c-Br). Following Method IV.2, a solution of **IV-5c** (0.833, 2.00 mmol) in THF (20.0 mL) was treated with NBS (0.354 g, 2.00 mmol) at –78 °C to afford a brown foam (0.686 g, 69%): mp 85–87 °C; ^{1}H NMR δ 5.49 (s, 1H), 5.86–5.96 (m, 1H), 6.09–6.11 (m, 2H), 6.62–6.72 (m, 1H), 7.16–7.22 (m, 2H), 7.31–7.37 (m, 3H), 8.02–8.22 (br, 1H), 9.68–9.84 (br, 1H); ^{13}C NMR (THF-d_8) δ 45.3, 98.3, 110.3, 110.4, 110.5, 112.0, 112.2, 122.5, 127.8, 128.0, 129.6, 132.6, 134.4, 137.4, 139.9, 141.7, 142.1, 143.7, 144.3, 145.8, 146.2, 171.7; ESI-MS obsd 495.01176, calcd 495.01259 [$(M + H)^+$, M = $C_{22}H_{12}BrF_5N_2O$]. Anal. Calcd for $C_{22}H_{12}BrF_5N_2O$: C, 53.36; H, 2.44; N, 5.66. Found: C, 53.28; H, 2.16; N, 6.02.

General Protocol for the Synthesis of Bilanes (Method IV.3). Following the published procedure,[IV12] a solution of a 1-bromo-9-acyldipyrromethane (**IV-5a-h-Br**) in dry

THF/methanol (3:1, 0.0125 M) under argon at room temperature was treated with $NaBH_4$ (25.0 mol equiv versus **IV-5a-h-Br**) in small portions with rapid stirring. The progress of the reaction was monitored by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. The reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl (25 mL) and ethyl ether (25 mL). The organic phase was separated, washed (water, brine), dried (K_2CO_3), and concentrated under reduced pressure at ambient temperature to yield the corresponding dipyrromethane-carbinol (**IV-5a-h-Br-OH**) as a yellow-orange paste. The resulting product was transferred to an oven-dried round-bottom flask with diethyl ether (10.0 mL). The diethyl ether solution of the dipyrromethane-carbinol was concentrated to give an orange paste. For improved stability, the dipyrromethane-carbinol was handled as a paste containing residual diethyl ether rather than as a dry solid. A sample of a 1-acyldipyrromethane **IV-6a-h** (1.00 mmol, 0.5 M) was added. A septum was fitted to the flask, and anhydrous acetonitrile was added under a slow argon flow. The resulting reaction mixture was stirred for 1 min, whereupon $Yb(OTf)_3$ (as a 10 mM stock solution in methanol, or as a solid, to give a final acid concentration of 3.3 – 230 mM) was slowly added. The reaction mixture darkened. The reaction mixture was stirred until all of the dipyrromethane-carbinol was consumed [0.5-5 h; TLC analysis: silica, hexanes/ethyl acetate (3:1)]. An aliquot was removed from the reaction mixture and checked by MALDI-MS (POPOP). No detectable scrambling was observed. The reaction mixture was neutralized by the addition of triethylamine [10 mol equiv versus $Yb(OTf)_3$]. The reaction mixture turned light brown. The resulting mixture was diluted with diethyl ether (~50 mL), washed (water, brine), dried (K_2CO_3), and concentrated to afford a light-brown foam. The

crude product was chromatographed to afford the bilane as a light-brown foam, presumably as a mixture of stereoisomers.

1-Bromo-15-(4-*tert*-butylphenyl)-19-(isonicotinoyl)-10-(4-methylphenyl)-5-phenylbilane (IV-2e). Following Method IV.3, a solution of **IV-5a-Br** (0.105 g, 0.250 mmol) in dry THF/methanol (20.0 mL, 3:1) was treated with $NaBH_4$ (0.236 g, 6.25 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.340 mL) was treated with **IV-6e** (0.096 g, 0.250 mmol) and $Yb(OTf)_3$ (0.160 mL of a 10.0 mM stock solution in anhydrous MeOH). The resulting reaction mixture was stirred at room temperature for 4 h. The standard workup and column chromatography [silica, hexanes/ethyl acetate (1:4)] afforded a brown foam (0.119 g, 61%), presumably as a mixture of 8 stereoisomers: mp 92–95 °C; ^{1}H NMR (THF-d_8) δ 1.29 (s, 9H), 2.27 (s, 3H), 5.22–5.25 (m, 1H), 5.27–5.29 (m, 1H), 5.41–5.45 (m, 1H), 5.49–5.56 (m, 5H), 5.85–5.89 (m, 1H), 5.91–5.95 (m, 1H), 6.71–6.74 (m, 1H), 7.01–7.06 (m, 4H), 7.09–7.14 (m, 5H), 7.19–7.21 (m, 2H), 7.29–7.31 (m, 2H), 7.61–7.62 (m, 2H), 8.68 (m, 2H), 9.54–9.61 (br, 1H), 9.66–9.69 (br, 1H), 10.31–10.42 (br, 1H), 11.18–11.26 (br, 1H); ^{13}C NMR (THF-d_8) δ 21.3, 31.9, 35.2, 44.8, 45.0, 45.4, 97.2, 107.7, 107.9, 109.8, 110.2, 111.3, 109.8, 110.1, 111.3, 120.9, 123.2, 125.9, 127.2, 128.9, 129.4, 129.5, 129.53, 131.2, 132.3, 132.4, 132.44, 133.1, 133.2, 134.3, 134.4, 134.5, 134.9, 134.93, 135.0, 136.3, 136.4, 140.5, 141.9, 144.1, 144.2, 145.1, 146.7, 150.2, 151.1, 182.5; MALDI-MS (POPOP) obsd 782.1, 783.1, 784.1, 785.1, 786.1, 787.1, 788.1, 789.1, calcd 785.27292 ($C_{48}H_{44}BrN_5O$); ESI-MS obsd 786.2777, calcd 786.2801 [$(M + H)^+$, M = $C_{48}H_{44}BrN_5O$].

General Protocol for the Synthesis of Porphyrins (Method IV.4). Following the reported procedure,[IV12] an oven-dried one-necked round bottom flask (10 mL) containing a dry stir bar and fitted with a vented Teflon septum was treated successively with a sample of

a bilane (**IV-1b-e**, 0.300 mmol) and dry toluene (3.00 mL). DBU (0.450 mL, 3.00 mmol, 10.0 mol equiv versus the bilane) was added dropwise at room temperature. The reaction mixture darkened while stirring over the course of 5 min. A sample of $MgBr_2$ (0.166 g, 0.900 mmol, 3.00 mol equiv versus the bilane) was added in one portion under vigorous stirring. (Note that a dry flask is essential, as is vigorous stirring, so that $MgBr_2$ does not clump as a solid on the bottom of the flask, which typically lowers the yield of porphyrin.) The reaction mixture was stirred for 1 min at room temperature. The flask was fitted with a reflux condenser (4 cm dia × 30 cm) having the top end open to the atmosphere, and the flask was placed in an oil bath preheated to 115 °C. The reaction mixture (heterogeneous) was stirred at 115 °C. The crude reaction mixture was checked by absorption spectroscopy and TLC analysis (silica CH_2Cl_2). In most cases the formation of porphyrin was complete in 2-3 h. The crude reaction mixture was checked by LD-MS analysis for possible scrambling. The crude reaction mixture was concentrated and then chromatographed [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (4:1) → (2:1)]. The porphyrin-containing fraction was concentrated to afford a purple solid.

20-(4-*tert*-Butylphenyl)-15-(4-methylphenyl)-10-phenyl-5-(4 pyridyl)porphinatomagnesium(II) (IV-MgP-2e). Application of Method IV.4 with **IV-2e** (0.059 g, 0.0750 mmol), DBU (0.113 mL, 0.750 mmol), and $MgBr_2$ (0.042 g, 0.250 mmol) in toluene (0.750 mL) with chromatographic workup [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate → (3:1) → (2:1) → ethyl acetate/MeOH (30:1)] afforded a solid. The resulting product was washed with hexanes (5 mL x 3) to afford a purple solid (0.029 g, 54%): ^{1}H NMR δ 1.64 (s, 9H), 2.69 (s, 3H), 7.59 (m, 2H), 7.74–7.76 (m, 3H), 7.83–7.86 (m, 2H), 8.08–8.20 (m, 8H),

8.75–8.80 (m, 2H), 8.83–8.85 (m, 8H); LD-MS obsd 708.2; ESI-MS obsd 707.2893, calcd 707.2901 ($C_{48}H_{37}MgN_5$); λ_{abs} (toluene) 407, 427, 564, 604 nm.

General Protocol for the Synthesis of Porphyrins Bearing Three Pyridyl Substituents (Method IV.5). The procedure described from Method IV.4 in the following ways: (1) Bilane formation was carried out in neat acetonitrile (no methanol). (2) The bilane was not readily purified and hence was used in crude form, whereupon a small amount of unreacted 1-acyldipyrromethane gave the corresponding *trans*-A_2B_2-porphyrin. (3) Porphyrin formation was carried out under microwave irradiation. (4) The magnesium porphyrin was demetalated and the free base porphyrin was isolated.

(i) Bilane formation. A sample of **IV-7-Br** (0.217 g, 0.500 mmol) in dry THF/methanol (40.0 mL, 3:1) was treated all-at-once with $NaBH_4$ (0.473 g, 12.5 mmol, 25.0 mol equiv) under argon at room temperature. On the basis of TLC analysis of the crude reaction mixture (silica, ethyl acetate) the reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl (~10 mL) and diethyl ether (~10 mL). The organic phase was separated, washed (water, brine), dried (K_2CO_3), and concentrated until some diethyl ether (~5 mL) remained. The resulting orange-yellow solution (**IV-7-Br-OH**) was transferred to an oven-dried round-bottomed flask (25 mL). A sample of 1-acyldipyrromethane (0.164 g, 0.500 mmol) was added followed by anhydrous acetonitrile (1 mL) under a slow flow of argon. The resulting solution was concentrated under low pressure with a rotary evaporator (ambient temperature) to largely remove the ethyl ether and give a volume of ~1 mL (predominantly acetonitrile). The resulting orange-red solution was stirred for 1 min, whereupon $Yb(OTf)_3$ (0.142 g, 0.230 mmol) was added. The reaction mixture immediately turned dark red-orange. An aliquot was removed from the

reaction mixture at various times and checked by TLC analysis (silica, ethyl acetate). Up to four components were observed [trace of unreacted 1-acyldipyrromethane, target bilane, unknown streaking red component; and the carbinol (R_f = 0.19, 0.39, 0.58, and 0.81, respectively), which upon exposure to bromine were orange, dark brown, dark pink, and dark red, respectively]. The reaction mixture was stirred until all of the carbinol was consumed. MALDI-MS (POPOP) analysis of the crude reaction mixture gave a peak (*m/z* = 745.9) consistent with the target bilane. The reaction was neutralized by the addition of triethylamine (0.020 mL). The resulting mixture was diluted with ethyl acetate (~30 mL) and washed with water and brine. The organic layer was dried (K_2CO_3) and concentrated to afford a dark red-brown paste.

(ii) Porphyrin formation under microwave conditions. The crude bilane was transferred to a 10-mL glass tubular reaction vessel containing a magnetic stir bar and toluene (5 mL). The headspace contained air. A sample of DBU (0.750 mL, 5.00 mmol) was added via syringe. The vessel was sealed with a septum. The resulting mixture was stirred for 5 min at room temperature. The reaction mixture darkened. The septum was removed and $MgBr_2$ (0.276 g, 1.50 mmol) was added all at once. The vessel was sealed with a septum and the resulting heterogeneous reaction mixture was stirred at room temperature for 1 min. The vessel was subjected to microwave irradiation at 100 W. The protocol was as follows: (1) heat from room temperature to 115 °C (irradiate for 2 min), (2) hold at 115 °C (irradiate for 15 min; the temperature typically overshot to 135 °C and then stabilized after 2 min), (3) allow to cool to room temperature (~1 min), (4) check the reaction mixture by TLC analysis and absorption spectroscopy, (5) repeat steps 1-3 until porphyrin formation is complete (typically 3-4 h overall). After porphyrin formation was complete, the crude

reaction mixture was dissolved in THF (HPLC-grade and stabilizer-free). The solution was concentrated and chromatographed [alumina, THF (HPLC-grade and stabilizer-free) → THF/MeOH (10:1)]. The porphyrin-containing fraction was concentrated. The resulting porphyrin was suspended in MeOH (5 mL). The suspension was sonicated for ~1 min, centrifuged, and decanted to obtain the magnesium porphyrin. In some cases purification of the crude reaction mixture by alumina column chromatography [alumina, CH_2Cl_2 → THF → THF/MeOH (10:1)] was not successful due to extensive streaking of the magnesium porphyrin. In such cases, the porphyrin-containing fractions were combined, subjected to demetalation, and the product was purified as the free base porphyrin.

(iii) Demetalation. The crude magnesium porphyrin was dissolved in CH_2Cl_2 (5 mL) and demetalated by the addition of TFA (0.030 mL). The reaction mixture was stirred for 1 h, whereupon a sample of triethylamine was added (0.020 mL). The crude reaction mixture was washed (water, brine), dried (Na_2SO_4), and concentrated. The resulting product was chromatographed [silica, CH_2Cl_2 → CH_2Cl_2/THF (1:10) → THF]. The porphyrin-containing fractions were concentrated and combined to afford the free base porphyrin.

10-(4-Ethylphenyl)-5,15-di-3-pyridyl-20-(2-pyridyl)porphinatomagnesium(II) (IV-MgP-9a). Following Method IV.5, **IV-7-Br** (0.217 g, 0.500 mmol) and **IV-8a** (0.164 g, 0.500 mmol) gave a red-brown paste. The crude bilane was treated with DBU (0.750 mL, 5.00 mmol) and $MgBr_2$ (0.276 g, 1.50 mmol) in toluene (5 mL) under microwave conditions followed by standard workup to afford a purple solid (39 mg, 12%): ^{1}H NMR (DMSO-d_6) δ 1.44 (t, J = 7.6 Hz, 3H), 2.93 (q, J = 7.6 Hz, 2H), 7.59 (d, J = 7.0 Hz, 2H), 7.76–7.84 (m, 3H), 8.05–8.06 (m, 2H), 8.18–8.19 (m, 1H), 8.24–8.26 (m, 1H), 8.56 (d, J = 7.0 Hz, 2H), 8.68–8.72 (m, 6H), 8.78 (d, J = 4.6 Hz, 2H), 8.96 (d, J = 4.6 Hz, 2H), 9.01 (d, J = 4.6 Hz,

1H), 9.28–9.36 (m, 2H); LD-MS obsd 667.4; ESI-MS obsd 667.2339, calcd 667.2335 [(M + H)$^+$, M = $C_{43}H_{29}MgN_7$]; λ_{abs} (THF) 409, 430, 571, 612 nm.

General Protocol for the Synthesis of Bilanes and Porphyrins Bearing Alkyl Substituents (Method IV.6). The procedure differs from Method IV.4 in the following ways: (1) The 1-acyldipyrromethane (typically a paste) was handled as a solution in acetonitrile. (2) Bilane formation was carried out in neat acetonitrile (no methanol) and at 50 mM instead of 500 mM. (3) Porphyrin formation was carried out under microwave irradiation. (4) The magnesium porphyrin was demetalated and the free base porphyrin was isolated.

(i) Bilane formation: A sample of 9-bromo-1-acyldipyrromethane **IV-11-Br** (0.250 mmol) in dry THF/methanol (20.0 mL, 3:1) was treated with $NaBH_4$ (0.236 g, 6.25 mmol, 25.0 mol equiv versus **IV-11-Br**) to give the carbinol. On the basis of TLC analysis of the crude reaction mixture [silica, hexanes/ethyl acetate (3:1)] the reaction was complete in ~30 min. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl in diethyl ether (~40 mL). The organic phase was extracted with diethyl ether, washed (water, brine), dried (K_2CO_3) and transferred to a round-bottom flask. A solution of 1-acyldipyrromethane **IV-11** in acetonitrile (5 mL) was transferred to the resulting carbinol solution via syringe. (Note that alkyl-substituted 1-acyldipyrromethanes typically exist as a paste at room temperature; therefore, the 1-acyldipyrromethane was weighed in a vial and transferred as a solution). The resulting solution was concentrated under low pressure with a rotary evaporator (ambient temperature) to largely remove the ethyl ether and give a volume of ~5 mL (predominantly acetonitrile). The resulting orange-red solution (containing a residual amount of ethyl ether) was treated with $Yb(OTf)_3$ (10.0 mg, 0.0165 mmol, ~3.3 mM) under a

slow flow of argon. An aliquot was removed from the reaction mixture after 30 min and checked by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. A trace amount of unreacted **IV-11** and bilane **IV-12** were observed. Exposure of the TLC plate to bromine further identified the components by the characteristic orange spot and dark brown spot, respectively. The reaction was neutralized with triethylamine [0.025 mL, 0.165 mmol, 10 mol equiv versus $Yb(OTf)_3$]. The resulting mixture was diluted with ethyl acetate (~30 mL) and washed with water and brine. The organic layer was dried (K_2CO_3) and concentrated to afford a dark brown paste. The resulting crude product was chromatographed [silica, hexanes/ethyl acetate (3:1)] to afford a brown paste.

(ii) Porphyrin formation under microwave conditions. A sample of bilane **IV-12** (0.10 mmol) was transferred to a 10 mL glass reaction vessel containing a magnetic stir bar and toluene (1 mL). The headspace contained air. A sample of DBU (0.15 mL, 1.0 mmol) was added via syringe. The vessel was sealed with a septum. The resulting mixture was stirred for 5 min at room temperature. The reaction mixture darkened. The septum was removed, and $MgBr_2$ (0.055 g, 0.30 mmol) was added. The vessel was sealed with a septum, and the resulting heterogeneous reaction mixture was stirred at room temperature for 1 min. The vessel was subjected to microwave irradiation at 100 W. The protocol was as follows: (1) heat from room temperature to 115 °C (irradiate for 2 min), (2) hold at 115 °C (irradiate for 30 min; temperature typically overshot to 135 °C and then stabilized after 2 min), (3) allow to cool to room temperature (~1 min), (4) check the reaction mixture by TLC analysis [silica, CH_2Cl_2, a streaking red-brown unidentified product and a magnesium porphyrin typically were observed] and absorption spectroscopy (3 bands were observed at 303, 425, and 525 nm), (5) repeat steps 1-4 until the intermediate was largely consumed. Most

reactions were quite sluggish, in which case the reaction flask was treated with microwave irradiation for a longer period of time (~6 h) prior to analysis. The total overall microwave irradiation time typically was ~24 h. The crude reaction mixture was transferred to a round bottom flask with THF (HPLC-grade and lacking stabilizer) and concentrated. The crude product was washed (water, brine), dried (Na_2SO_4) and concentrated.

(iii) Demetalation. The procedure was identical to that in Method IV.5.

1-Bromo-15-butyl-5-ethyl-19-hexanoyl-10-propylbilane (IV-12f). Following Method IV.6, a solution of **IV-11c-Br** (0.242 g, 0.750 mmol) in dry THF/methanol (60.0 mL, 3:1) was treated with $NaBH_4$ (0.708 g, 18.75 mmol). The standard workup procedure was followed. A solution of **IV-11g** (0.225 g, 0.750 mmol) in acetonitrile (15 mL) was added to the carbinol solution in ethyl ether (~45 mL). The ether was removed, and $Yb(OTf)_3$ (31.0 mg, 0.0495 mmol, 3.30 mM) was added. The reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography afforded a brown paste (0.370 g, 81%), presumably as a mixture of 8 stereoisomers: ^{1}H NMR (THF-d_8) δ 0.81–0.92 (m, 12H), 1.28–1.34 (m, 8H), 1.59–1.66 (m, 4H), 1.83–1.93 (m, 6H), 2.64 (t, J = 7.2 Hz, 2H), 3.67 (t, J = 7.6 Hz, 1H), 3.79 (t, J = 7.6 Hz, 1H), 3.89 (t, J = 7.8 Hz, 1H), 5.67–5.69 (m, 3H), 5.73–5.74 (m, 2H), 5.85–5.87 (m, 2H), 6.72–6.75 (m, 1H), 9.01–9.08 (br, 1H), 9.16–9.24 (m, 1H), 10.04–10.16 (br, 1H), 10.42–10.54 (br, 1H); ^{13}C NMR (THF-d_8) δ 22.6, 24.2, 24.3, 31.5, 33.3, 33.4, 38.9, 40.8, 42.5, 45.7, 45.72, 47.9, 48.2, 48.3, 48.6, 49.0, 50.8, 105.9, 115.1, 115.3, 117.2, 117.6, 119.8, 126.5, 141.9, 142.4, 142.5, 143.1, 143.8, 143.9, 144.1, 144.2, 146.9, 153.6; ESI-MS obsd 606.29350, calcd 606.29333 ($C_{34}H_{47}BrN_4O$).

5-Butyl-15-ethyl-10-pentyl-20-propylporphyrin (IV-P-12f). Application of Method IV.6 with **IV-12f** (0.122 g, 0.200 mmol), DBU (0.300 mL, 2.00 mmol), and $MgBr_2$

(0.111 g, 0.600 mmol) in toluene (2.0 mL) afforded a crude product. Demetalation of the crude product was followed by chromatographic workup [silica, hexanes/CH_2Cl_2 (1:1)] to afford a purple solid (0.025 g, 24%): ^{1}H NMR δ –2.68 (s, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 1.13 (t, *J* = 7.4 Hz, 3H), 1.32 (t, *J* = 7.4 Hz, 3H), 1.51–1.57 (m, 2H), 1.76–1.84 (m, 4H), 2.11 (t, *J* = 7.4 Hz, 3H), 2.48–2.56 (m, 6H), 4.87–4.99 (m, 8H), 9.45–9.46 (m, 8H); ^{13}C NMR δ 14.4, 14.6, 15.2, 22.9, 23.0, 23.9, 29.0, 31.8, 32.9, 35.5, 35.7, 37.6, 38.6, 41.0, 118.3, 118.6, 118.7, 119.9, 127.2–129.3 (br); MALDI-FT-ICR-MS obsd 507.35271, calcd 507.34877 [$(M + H)^+$, M = $C_{34}H_{42}N_4$]; λ_{abs} (toluene) 419, 521, 554, 602, 662 nm.

Porphyrin Formation via a Bilene: 20-(4-*tert*-Butylphenyl)-5-(4-ethylphenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-2i). Bilene formation was accomplished with catalysis either by (i) $Yb(OTf)_3$ or (ii) *p*-toluenesulfonic acid followed by (iii) porphyrin formation. (i) $Yb(OTf)_3$ catalysis: A solution of **IV-5h-Br** (0.105 g, 0.250 mmol) in acetonitrile (2.35 mL) was treated with $Yb(OTf)_3$ (1.15 mL, 0.0115 mmol, from a 10.0 mM stock solution). The reaction mixture was stirred for 5 min and **IV-6a** (0.106 g, 0.250 mmol) was added. The resulting heterogeneous mixture was stirred at room temperature for 30 min. No product was observed. A sample of $Yb(OTf)_3$ (0.0420 g, 0.069 mmol, total acid concentration 23.0 mM) was added. The resulting heterogeneous mixture was stirred at room temperature for 2 h. On the basis of TLC analysis [silica, hexanes/ethyl acetate (3:1)] only a trace amount of product was observed. The reaction mixture was placed in an oil bath preheated to 55 °C. The reaction mixture became homogeneous in 10 min, and was maintained at 55 °C for 2 h. The TLC analysis revealed the presence of a streaking component and a trace amount of unreacted **IV-6a**. The reaction mixture was concentrated. The resulting crude product was washed (water, brine), dried (Na_2SO_4) and concentrated to

give the crude bilene-*b*. (ii) *p*-Toluenesulfonic acid catalysis: A solution of **IV-5h-Br** (0.052 g, 0.125 mmol) in CH_2Cl_2 (0.600 mL) was treated with *p*-toluenesulfonic acid (PTSA) solution [0.030 g, 0.150 mmol in CH_2Cl_2/MeOH (0.625 mL, 24:1)]. The reaction mixture was stirred for 5 min and **IV-6a** (0.053 g, 0.125 mmol) was added. The resulting heterogeneous mixture was stirred at room temperature for 30 min. TLC analysis (silica, CH_2Cl_2) revealed the presence of a streaking component. A sample of triethylamine (0.020 mL) was added. The resulting crude product was washed (water, brine), dried (Na_2SO_4) and concentrated to give the crude bilene-*b*. (iii) The crude bilene-*b* (here reported from $Yb(OTf)_3$ catalysis) was dissolved in toluene (2.5 mL) and treated with DBU (0.375 mL, 2.50 mmol) and $MgBr_2$ (0.138 g, 0.750 mmol) at 115 °C with exposure to air for ~4-6 h. Column chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (4:1) → (2:1)] afforded 5,15-bis(4-*tert*-butylphenyl)-10,20-bis(4-ethylphenyl)porphinatomagnesium(II) (<2% yield on the basis of absorption spectroscopy with an assumed molar absorption coefficient at the Soret band of 500,000 $M^{-1}cm^{-1}$) followed by the title compound. Fractions containing the latter were concentrated to give a purple solid (0.016 g, 11%): ^{1}H NMR δ 1.54 (t, *J* = 7.6 Hz, 3H), 1.63 (s, 9H), 2.99 (q, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.74–7.76 (m, 5H), 8.10–8.16 (m, 4H), 8.22–8.23 (m, 2H), 8.89–8.95 (m, 4H), 8.98–9.04 (m, 2H), 9.29 (s, 2H), 10.12 (s, 1H); ^{13}C NMR δ 15.9, 29.0, 32.0, 35.1, 106.3, 121.0, 121.5, 122.3, 123.5, 125.9, 126.5, 127.2, 131.6, 131.7, 132.1, 132.2, 132.5, 132.8, 134.8, 134.82, 134.9, 135.0, 140.8, 141.3, 143.1, 143.9, 149.8, 149.9, 150.0, 150.2; LD-MS obsd 644.5, ESI-MS obsd 644.2784, calcd 644.2792 ($C_{44}H_{36}MgN_4$); λ_{abs} (toluene) 422, 558, 597 nm. When the porphyrin-forming reaction was carried out for 15 h, the product was the singly fused porphyrin dimer, which was isolated following column chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl

acetate (4:1) → (2:1)] as a purple solid (0.013 g, 8%). Data for the singly fused porphyrin dimer (**IV-MgP-2i-dimer**): ^{1}H NMR δ 1.52–1.59 (m, 24H), 3.05 (q, *J* = 9.6 Hz, 4H), 7.59–7.63 (m, 16H), 7.94–8.21 (m, 4H), 8.12–8.15 (m, 4H), 8.21–8.23 (m, 6H), 8.52–8.59 (m, 4H), 8.88–8.97 (m, 8H); ^{13}C NMR δ 15.9, 29.1, 31.9, 35.0, 121.2, 122.2, 122.5, 122.7, 123.3, 126.0, 126.4, 127.1, 131.5, 131.6, 131.8, 131.9, 132.1, 132.2, 134.2, 134.6, 134.9, 135.0, 140.8, 141.3, 143.2, 144.0, 149.6, 149.8, 149.9, 150.1, 150.2, 150.4, 150.7, 155.2, 155.3; LD-MS obsd 1286.9, FAB-MS obsd 1286.5554, calcd 1286.5424 ($C_{88}H_{70}Mg_2N_8$); λ_{abs} (toluene) 427 (br), 465 (br), 577 (br), 620 nm.

IV.V. References

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IV.VI. Supporting Information for Investigation of the Scope of a New Route to ABCD-Bilanes and ABCD-Porphyrins.

I. Bilanes

(i) Stability of Bilanes. The 1-bromo-19-acylbilanes bearing aryl and heteroaryl substituents were stable to routine handling. No decomposition was observed upon silica column chromatography (~1 h) or vacuum drying (~ 4 h) at ambient temperature. Upon drying, the bilanes existed as amorphous, foam-like solids (light or dark brown). The dried sample upon storage at –4 °C and protected from light gave no noticeable decomposition for up to 2 months. By contrast, the analogous bilanes bearing alkyl rather than aryl substituents were rather unstable. Vacuum drying (~2 h) at ambient temperature afforded a paste (rather than a solid foam), which became dark or red and exhibited impurities upon ^{1}H NMR spectroscopy. The alkylbilanes were used within 2-3 days of storage at –4 °C.

(ii) ^{1}H NMR Spectroscopy of Bilanes. For the bilanes prepared herein, each meso position (5, 10, 15) that bears one non-hydrogen substituent is a stereogenic center. Given that the bilanes have non-equivalent substituents at the 1- and 19-positions, all bilanes synthesized herein that have three meso-substituents are expected to exist as a mixture of 8 stereoisomers. Consequently, it is expected, and was observed, that the resonances of selected protons upon ^{1}H NMR spectroscopy appear broad. Indeed, all such bilanes exhibited the following typical features: (1) each of the three meso protons gave a broad resonance (for a meso-aryl substituent) or a broad triplet (for a meso-alkyl substituent), and (2) each of the four NH protons (from the four pyrrolic nitrogens) was clearly observed as a broad signal upon analysis in THF-d_8.

Although the bilanes that contain three stereogenic centers are expected to exist as amixture of eight stereoisomers, the multiplicity of the resonances for substituents (e.g., the 4-methyl group of the 4-methylphenyl moiety) far removed from the stereogenic centers appear (at 400 MHz) as they would for a pure compound. Such resonances are listed on the basis of their appearance in the spectra.

(iii) Mass Spectrometry of Bilanes. MALDI-MS data for bilanes were obtained using the matrix POPOP.

(iv) Oxidation of Bilanes. The identity of the oxidant in the bilane → porphyrin conversion is not known. We previously noted that the reaction in the absence of oxygen did not diminish the yield of porphyrin, whereas the use of an oxygen atmosphere in place of air gave a diminished yield.[IV12] These data were obtained for the synthesis of **IV-MgP-1a**. In the event that oxygen does serve as the oxidant for other bilanes, the volume of air required for stoichiometric oxidation deserves consideration. The reactions carried out under conventional heating are performed with a reflux condenser that is open at the top, allowing access to the aerobic environment. On the other hand, the reactions carried out under microwave irradiation are performed in sealed reaction vessels. Here the issue of oxygen as a possible limiting reagent was raised. The bilane → porphyrin conversion requires a $2e^-/2H^+$ oxidation, which if supplied by oxygen, would require ½ mol of oxygen per mol of bilane. The reaction vessels are sealed at room temperature. Hence, given PV = nRT (where P = 1 atm, R = 0.082 l-atm $mol^{-1}K^{-1}$, T = 298 K), the oxidation of 1 mmol of bilane would require 12.2 mL of oxygen gas. In air, oxygen is present at approximately 21% v/v. Hence the volume of air required, assuming all of the oxygen in air is available to serve as an oxidant, is 58 mL. The reactions performed here typically were carried out in 10-mL reaction

vessels at two scales: 0.1 mmol or 0.5 mmol. Consider the volumes for each. For the reaction at 0.1mmol, the reaction volume was ~1 mL, in which case the headspace was ~9 mL (filled with air). The stoichiometric requirement for oxygen would be met by an air volume of 5.8 mL, which is readily satisfied. For the reaction at 0.5 mmol, the reaction volume was ~5 mL, in which case the headspace was ~5 mL (filled with air). The stoichiometric requirement for oxygen would be met by an air volume of 29 mL, which is not satisfied under this experimental arrangement. However, in each case the reaction vessels were opened at least four times during the course of the reaction to perform analytical measurements, in which case the headspace volume was exchanged.

II. Experimental Section

The microwave-assisted reactions were performed inside the cavity of a CEM Discover focused microwave synthesis system equipped with an infrared sensor for temperature monitoring. The reaction vessels were 10 mL crimp-sealed thick-wall glass tubes equipped with a pressure sensor. The contents of each vessel were stirred with a magnetic stirrer.

All solvents used for the metal-templated bilane cyclization were anhydrous. The use of dry conditions at the outset of the reaction (despite the liberation of water during the reaction process) is important to ensure a free-flowing suspension of the metal salt, particularly for $MgBr_2$.

Mass spectrometry was carried out via MALDI-TOF-MS using the matrix POPOP (referred to as MALDI-MS), via MALDI-FT-ICR-MS (designated as such), or in the absence of a matrix[IV28] (referred to as LD-MS).

Noncommercial Compounds. The following compounds were prepared as described in the literature.

Dipyrromethanes: **IV-3a**,[IV15] **IV-3b**,[IV12] **IV-3c**,[IV22] **IV-3d**,[IV15] **IV-3e**,[IV13] **IV-3f**,[IV13] **IV-3h**.[IV15]

Mukaiyama reagents: **IV-4a**,[IV17] **IV-4b**,[IV13] **IV-4c**,[IV17] **IV-4d**,[IV17] **IV-4e**,[IV13] **IV-4f**,[IV13] **IV-IV-4i**,[IV12] **IV-4j**,[IV13] **IV-4l**.[IV13]

1-Acyldipyrromethanes: **IV-5a**,[IV16] **IV-5b-d**,[IV18] **IV-5e**,[IV7] **IV-5g**,[IV18] **IV-5h**,[IV19] **IV-8a-d**,[IV13] **IV-11b**,[IV13] **IV-11e**.[IV13]

1-Acyl-9-bromodipyrromethanes: **IV-5a-Br**.[IV18]

Yield Determinations. Unless noted otherwise, the yield of porphyrin was determined by gravimetry of isolated samples without consideration of the presence of any apical ligands on the magnesium porphyrin or solvents of crystallization.

Chromatograpic Separation of ABCD-Porphyrins Bearing Three Heterocyclic Substituents. In some cases where the bilane was not completely purified, the target porphyrin was accompanied by a second porphyrin, which was ostensibly derived from unreacted 1-acyldipyrromethane. In all such cases encountered herein, the chromatographic separation of the two porphyrins was straightforward. One example is shown in Figure IV.S1, for the intramolecular cyclization of a crude bilane bearing three non-identical heterocyclic substituents. The ABCD-porphyrin (**IV-P-9d**) contains *o*-, *m*-, *p*- pyridyl and 4-ethylphenyl groups. The contaminating *trans*-A_2B_2-porphyrin (**IV-P-10d**) contains two *o*-pyridyl and two *p*-pyridyl groups. The elution pattern shown in

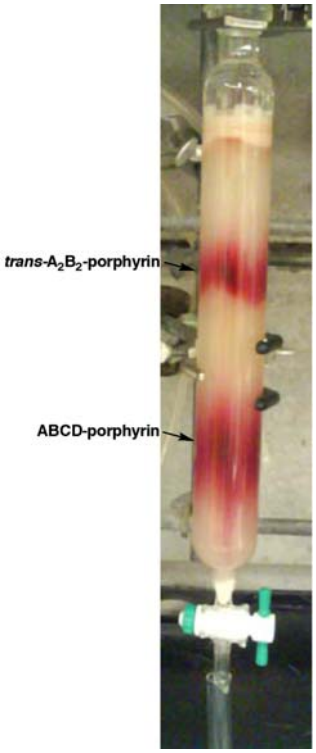

Figure IV.S1 is typical for the purification of the porphyrins shown in Table IV.4.

Figure IV.S1. Chromatographic separation (silica, 30 cm x 4 cm dia) of a mixture composed of two porphyrins.

1-Acyldipyrromethanes (Method IV.1): Compounds **IV-5b-e** were previously prepared and isolated via the dialkylboron complexes; here the compounds were prepared directly.

1-Hexanoyl-5-phenyldipyrromethane (IV-5b). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3a** (1.67 g, 7.50 mmol) in THF (15.0 mL). A solution **IV-4b** (1.57 g, 7.50 mmol, in 15.0 mL of THF) was added to the reaction mixture. The resulting crude product was chromatographed to afford a brown paste (1.73 g, 72%). The data (^{1}H NMR, ^{13}C NMR, FAB-MS, and elemental analysis) were consistent with those obtained from an authentic sample.[IV18]

1-(Pentafluorobenzoyl)-5-phenyldipyrromethane (IV-5c). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3a** (1.67 g, 7.50 mmol) in THF (15.0 mL). A solution of **IV-4c** (2.29 g, 7.50 mmol) in THF (15.0 mL) was added to the reaction mixture. The resulting crude product was chromatographed to afford a golden-brown amorphous powder (2.90 g, 93%). The data (mp, ^{1}H NMR, ^{13}C NMR, FAB-MS, and elemental analysis) were consistent with those obtained from an authentic sample.[IV18]

1-(4-Methoxybenzoyl)-5-phenyldipyrromethane (IV-5d). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3a** (1.67 g, 7.50 mmol) in THF (15.0 mL). A solution of **IV-4d** (1.84 g, 7.50 mmol) in THF

(15.0 mL) was added to the reaction mixture. The resulting crude product was chromatographed to afford a brown amorphous powder (2.21 g, 83%). The data (mp, ^{1}H NMR, ^{13}C NMR, FAB-MS, and elemental analysis) were consistent with those obtained from an authentic sample.[IV18]

1-Isonicotinoyl-5-phenyldipyrromethane (IV-5e). Following Method IV.1 with slight modification, a solution of EtMgBr (25.0 mL, 1.0 M in THF, 25 mmol) was added to a solution of **IV-3a** (2.22 g, 10.0 mmol) in THF (20.0 mL). A solid sample of **IV-4e** (2.16 g, 10.0 mmol) was added in one batch to the reaction mixture at –78 °C. The resulting mixture was stirred at –78 °C for 20 min, and allowed to warm to room temperature with stirring for 3 h. The standard workup and chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1)] afforded a yellow solid (2.32 g, 71%). The data (mp, ^{1}H NMR, ^{13}C NMR, FAB-MS, and elemental analysis) were consistent with those obtained from an authentic sample.[IV7]

1-(4-Methoxy-4-oxobutanoyl)-5-phenyldipyrromethane (IV-5f). Following Method IV.1 with slight modification, a solution of EtMgBr (25.0 mL, 25 mmol, 1.0 M in THF) was added to a solution of **IV-3a** (2.22 g, 20.0 mmol) in THF (10 mL). A solution of **IV-4f** (2.25 g, 10.0 mmol) in THF (20 mL) was added to the reaction mixture at –78 °C. The resulting crude product was purified by washing with ethyl ether (15 mL x 3) to afford a pale yellow powder (2.44 g, 73%): mp 139 °C; ^{1}H NMR δ 2.67 (t, J = 7.0 Hz, 2H), 3.07 (t, J = 7.0 Hz, 2H), 3.67 (s, 3H), 5.48 (s, 1H), 5.92–5.96 (m, 1H), 6.01–6.04 (m, 1H), 6.12–6.18 (m, 1H), 6.68–6.72 (m, 1H), 6.88–6.92 (m, 1H), 7.17–7.18 (m, 2H), 7.28–7.32 (m, 3H), 7.98–8.16 (br, 1H), 9.28–9.32 (br, 1H); ^{13}C NMR δ 28.4, 32.3, 44.3, 52.1, 107.9, 108.1, 108.8, 108.9, 110.3, 110.4, 117.4, 117.5, 118.0, 127.6, 128.5, 129.1, 131.1, 140.9, 173.7,

188.1; FAB-MS obsd 336.14866, calcd 336.14739 ($C_{20}H_{20}N_2O_3$). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.89; H, 6.40; N, 7.85.

5-Phenyl-1-(2,4,6-trimethylbenzoyl)dipyrromethane (IV-5g). Following the reported procedure,[IV193] a sample of **IV-3a** (1.10 g, 5.00 mmol) in THF (6 mL) was treated with MesMgBr (10.0 mL, 10 mmol, 1.0 M in ether). The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of 2,4,6-trimethylbenzoyl chloride (**IV-4g**, 0.913 g, 5.00 mmol) in THF (8.50 mL) was added to the reaction mixture. The solution was stirred at –78 °C for 10 min, and allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic extract was washed (water, brine), dried (Na_2SO_4) and concentrated. The resulting product was purified by column chromatography [silica, CH_2Cl_2 (until all unreacted **IV-3a** was eluted) → hexanes/ethyl acetate (3:1)] to afford a brown powder (0.390 g, 21%). The data (mp, ^{1}H NMR, ^{13}C NMR, FAB-MS, and elemental analysis) were consistent with those obtained from an authentic sample.[IV18]

5-(4-*tert*-Butylphenyl)-1-hexanoyldipyrromethane (IV-6b). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3b** (2.09 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4b** (1.57 g, 7.50 mmol) in THF (15.0 mL) was added to the reaction mixture. The resulting crude product was chromatographed [silica, hexanes/CH_2Cl_2 (1:2) → CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:1)] to afford a brown paste (1.73 g, 72%): ^{1}H NMR δ 0.87 (t, J = 6.8 Hz, 3H), 1.27 (s, 9H), 1.29–1.30 (m, 2H), 1.57–1.61 (m, 2H), 2.41–2.45 (m, 2H), 2.55–2.61 (m, 2H), 5.48 (s, 1H), 5.99–6.04 (m, 1H), 6.05–6.08 (m, 1H), 6.10–6.16 (m, 1H), 6.66–6.72 (m, 1H), 6.78–6.80 (m; 1H),

7.01 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 8.86–8.96 (br, 1H), 10.26–10.36 (br, 1H); ^{13}C NMR δ 14.1, 22.6, 25.4, 31.5, 31.8, 34.5, 37.6, 43.6, 107.7, 108.2, 110.4, 117.9, 118.1, 125.5, 127.9, 131.5, 131.7, 138.2, 141.8, 149.9, 191.7; ESI-MS obsd 376.25131, calcd 376.25146 ($C_{25}H_{32}N_2O$). Anal. Calcd for $C_{25}H_{32}N_2O$: C, 79.75; H, 8.57; N, 7.44. Found: C, 79.97; H, 8.59; N, 7.42.

5-(4-*tert*-Butylphenyl)-1-(pentafluorobenzoyl)dipyrromethane (IV-6c). Following Method IV.I, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3b** (2.09 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4c** (2.29 g, 7.50 mmol) in THF (15.0 mL) was added to the reaction mixture. The resulting crude product was chromatographed [silica, hexanes/CH_2Cl_2 (3:1) → (2:1)]. An unidentified side product (green) eluted with the target compound. A second column [silica, hexanes/ethyl acetate (3:1)] afforded a light-brown foam (1.45 g, 41%): mp 73 °C; ^{1}H NMR δ 1.30 (s, 9H), 5.47 (s, 1H), 5.98–6.20 (m, 1H), 6.10–6.12 (m, 1H), 6.16–6.18 (m, 1H), 6.58–6.66 (m, 1H), 6.68–6.74 (m, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.88–8.04 (br; 1H), 9.34–9.42 (br, 1H); ^{13}C NMR δ 31.5, 34.7, 44.0, 108.0, 108.9, 111.9, 118.1, 122.7, 126.2, 128.2, 130.5, 131.0, 136.3–136.6 (m), 137.0, 138.8–139.1 (m), 141.0–141.2 (m), 142.7–142.9 (m), 143.6–143.7 (m), 145.2–145.4 (m), 150.8, 171.8; ESI-MS obsd 473.16445, calcd 473.16468 [$(M + H)^+$, M = $C_{26}H_{21}F_5N_2O$]. Anal. Calcd for $C_{26}H_{21}F_5N_2O$: C, 66.10; H, 4.48; N, 5.93. Found: C, 65.90; H, 4.59; N, 5.85.

5-(4-*tert*-Butylphenyl)-1-(4-methoxybenzoyl)dipyrromethane (IV-6d). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3b** (2.09 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4d** (1.84 g, 7.50 mmol) in THF (15 mL) was added to the reaction mixture. The resulting crude product

was chromatographed [silica, CH_2Cl_2 → hexanes/ethyl acetate (3:1) → (2:1)] to afford a brown foam (1.73 g, 56%): mp 69–71 °C; ^{1}H NMR δ 1.28 (s, 9H), 3.86 (s, 3H), 5.49 (s, 1H), 5.96–6.02 (m, 1H), 6.06–6.10 (m, 1H), 6.14–6.18 (m, 1H), 6.62–6.68 (m, 1H), 6.72–6.78 (m, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H), 8.12–8.22 (br, 1H), 9.54–9.62 (br, 1H); ^{13}C NMR δ 31.5, 34.5, 43.8, 55.5, 107.7, 108.2, 110.7, 113.7, 117.9, 120.9, 125.6, 128.0, 130.9, 131.1, 131.4, 131.6, 138.1, 142.2, 149.9, 162.7, 183.9; ESI-MS obsd 413.2222, calcd 413.2223 [$(M + H)^+$, M = $C_{27}H_{28}N_2O_2$]. Anal. Calcd for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79. Found: C, 78.62; H, 6.75; N, 6.54.

5-(4-*tert*-Butylphenyl)-9-isonicotinoyldipyrromethane (IV-6e). Following Method IV.1 with slight modification, a solution of EtMgBr (12.5 mL, 12.5 mmol, 1.0 M in THF) was added to a solution of **IV-3b** (1.39 g, 5.00 mmol) in THF (10 mL). A sample of **IV-4e** (1.08 g, 5.00 mmol) was added as a solid to the reaction mixture. The reaction mixture was stirred at –78 °C for 10 min and allowed to warm to room temperature. The resulting reaction mixture was stirred at room temperature for 1 h. The standard workup and chromatography [silica, CH_2Cl_2/ethyl acetate (7:3)] afforded a yellow solid. The resulting product was washed with hexanes (5 mL x 3). The mixture was filtered to give a yellow solid (0.982 g, 52%): mp 81–82 °C; ^{1}H NMR δ 1.28 (s, 9H), 5.40 (s, 1H), 5.98–6.02 (m, 1H), 6.13–6.16 (m, 2H), 6.66–6.72 (m, 1H), 6.78–6.82 (s, 1H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 6.0 Hz, 2H), 8.26–8.38 (br, 1H), 8.72 (d, *J* = 6.0 Hz, 2H), 10.02–10.12 (br, 1H); ^{13}C NMR δ 31.5, 34.7, 43.9, 108.0, 108.7, 111.4, 113.7, 118.0, 122.0, 122.6, 126.0, 128.1, 130.1, 131.0, 134.2, 137.4, 143.9, 145.4, 150.4, 150.6, 182.6; ESI-MS obsd

384.2068, calcd 384.2070 [$(M + H)^+$, M = $C_{25}H_{25}N_3O$]. Anal. Calcd for $C_{25}H_{25}N_3O$: C, 78.30; H, 6.57; N, 10.96. Found: C, 78.25; H, 6.57; N, 10.42.

5-(4-*tert*-Butylphenyl)-9-[4-methoxy-4-oxobutanoyl]dipyrromethane (IV-6f). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3b** (2.09 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4f** (1.69 g, 7.50 mmol) in THF (15 mL) was added to the reaction mixture. Chromatography [silica, CH_2Cl_2 → hexanes/ethyl acetate (3:1)] afforded a brown foam (1.91 g, 65%): mp 49–51 °C; ^{1}H NMR δ 1.32 (s, 9H), 2.63 (t, *J* = 6.8 Hz, 2H), 2.99–3.03 (m, 2H), 3.63 (s, 3H), 5.50 (s, 1H), 5.94–6.02 (m, 1H), 6.04–6.08 (m, 1H), 6.12–6.16 (m, 1H), 6.64–6.72 (m, 1H), 6.88–6.92 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 8.62–8.72 (br, 1H), 10.28–10.36 (br, 1H); ^{13}C NMR δ 28.3, 31.4, 32.0, 34.4, 43.4, 51.8, 107.5, 108.2, 110.2, 117.7, 118.1, 125.5, 127.9, 130.6, 131.4, 138.2, 142.1, 149.8, 173.5, 188.3; ESI-MS obsd 415.19894, calcd 415.19921 [$(M + Na)^+$, M = $C_{24}H_{28}N_2O_3$]. Anal. Calcd for $C_{24}H_{28}N_2O_3$: C, 73.44; H, 7.19; N, 7.14. Found: C, 73.22; H, 6.95; N, 7.93.

5-(4-*tert*-Butylphenyl)-9-(2,4,6-trimethylbenzoyl)dipyrromethane (IV-6g). Following the reported procedure,[IV17] a sample of **IV-3b** (2.09 g, 7.50 mmol) in THF (7.50 mL) was treated with MesMgBr (15.0 mL, 1.0 M in THF, 15.0 mmol). The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of 2,4,6-trimethylbenzoyl chloride (**IV-4g**, 1.37 g, 7.50 mmol) in THF (7.5 mL) was added to the reaction mixture. The solution was stirred at –78 °C for 10 min, and allowed to warm to room temperature. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic extract was washed (water, brine), dried (Na_2SO_4) and concentrated. Chromatography [silica,

hexanes/CH_2Cl_2/ethyl acetate (7:2:1)] afforded a brown powder. The TLC analysis of the product revealed the presence of an additional component. A second column [silica, hexanes/ethyl acetate (3:1)] afforded a light-brown powder (1.06 g, 33%): mp 81 °C; ^{1}H NMR (m, 1H), 6.22–6.28 (br, 1H), 6.36–6.42 (br, 1H), 6.66–6.72 (m, 1H), 6.88 (s, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 8.12–8.16 (br; 1H), 9.24–9.28 (br, 1H); ^{13}C NMR δ 19.5, 19.6, 21.3, 31.5, 34.7, 43.9, 107.7, 108.5, 110.9, 111.3, 117.9, 121.2, 125.9, 128.1, 128.4, 131.2, 132.3, 134.7, 136.8, 137.8, 138.4, 142.6, 150.3, 189.0; ESI-MS obsd 425.2588, calcd 425.2587 [$(M + H)^+$, M = $C_{29}H_{32}N_2O$]; ESI-MS obsd 424.25166, calcd 424.25146 ($C_{29}H_{32}N_2O$).

5-(4-*tert*-Butylphenyl)-9-formyldipyrromethane (IV-6h). Following the reported procedure,[IV14] a sample of DMF (6 mL) was treated with $POCl_3$ (0.900 mL, 9.84 mmol) at 0 °C under argon with stirring (Vilsmeier reagent). A solution of **IV-3b** (2.22 g, 8.0 mmol) in DMF (24.0 mL) at 0 °C under argon was treated with the freshly prepared Vilsmeier reagent (5 mL, 8.2 mmol) and the resulting solution was stirred for 1.5 h at 0 °C. The reaction mixture was poured into a mixture of 2 M NaOH (30.0 mL) and CH_2Cl_2 (20.0 mL) at 0 °C. The resulting reaction mixture was stirred for 20 min at 0 °C. The reaction mixture turned orange-brown. The organic phase was washed [saturated aqueous NH_4Cl (20.0 mL), water, and brine], dried (Na_2SO_4), and concentrated to afford a red oil. The remaining DMF was removed under high vacuum (1 h, 50 °C) to give a dark red solid. Column chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (50:1)] gave a brown solid (0.620 g, 27%): mp 119–121 °C; ^{1}H NMR (300 MHz) δ 1.29 (s, 9H), 5.46 (s, 1H), 5.92–5.98 (m, 1H), 6.06–6.12 (m, 1H), 6.14–6.18 (m, 1H), 6.66–6.74 (m, 1H), 6.84–6.92 (m, 1H), 7.09 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.88–8.02 (br, 1H), 9.06–9.22 (br, 1H), 9.35 (s, 1H);

^{13}C NMR δ 31.5, 34.7, 43.9, 108.0, 108.9, 111.0, 118.0, 122.3, 126.2, 128.2, 130.8, 132.4, 137.3, 142.7, 150.7, 178.8; ESI-MS obsd 307.1806, calcd 307.1804 [$(M + H)^+$, M = $C_{20}H_{22}N_2O$]. Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.53; H, 7.28; N, 9.17.

1-Propionyldipyrromethane (IV-11a). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3d** (1.09 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4j** (1.25 g, 7.50 mmol, in THF 15.0 mL) was added to the reaction mixture. Chromatography [silica, hexanes/CH_2Cl_2 (5:1) → CH_2Cl_2 → CH_2Cl_2/ethyl acetate (10:1) → (4:1)] afforded a white solid (0.637 g, 42%): mp 119 °C; ^{1}H NMR δ 1.27 (t, *J* = 7.2 Hz, 3H), 2.82 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 2H), 6.03–6.05 (m, 1H), 6.09–6.14 (m, 2H), 6.67–6.70 (m, 1H), 6.91–6.93 (m, 1H), 9.42–9.48 (br, 1H), 10.68–10.96 (br, 1H); ^{13}C NMR δ 10.0, 26.8, 31.0, 106.5, 108.5, 109.7, 117.7, 119.0, 128.3, 131.0, 139.9, 192.4; ESI-MS obsd 203.1177, calcd 203.1178 [$(M + H)^+$, M = $C_{12}H_{14}N_2O$]. Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85 Found: C, 71.24; H, 6.99; N, 13.76.

1-Butanoyl-5-ethyldipyrromethane (IV-11c). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3e** (1.31 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4k** (1.36 g, 7.50 mmol, in 15 mL of THF) was added to the reaction mixture. The resulting crude product was chromatographed [silica, hexanes/ethyl acetate (6:1)] to afford a light orange oil. Vacuum drying afforded an off-white solid (1.176 g, 64%): mp 55 °C; ^{1}H NMR δ 0.89–0.98 (m, 6H), 1.69–1.78 (m, 2H), 2.02–2.10 (m, 2H), 2.72 (t, *J* = 7.4 Hz, 2H), 3.96 (t, *J* = 8.0 Hz, 1H), 6.02–6.04 (m, 1H), 6.08–6.10 (m, 2H), 6.63–6.65 (m, 1H), 6.89–6.91 (m, 1H), 9.12–9.21 (br, 1H), 10.42–10.51 (br, 1H); ^{13}C NMR δ 12.7, 14.2, 19.8, 26.9, 40.0, 40.1, 105.0, 108.0, 108.6, 117.3, 119.6,

131.1, 132.8, 144.9, 191.8; ESI-MS obsd 244.15689, calcd 244.15756 ($C_{15}H_{20}N_2O$). Anal. Calcd for $C_{15}H_{20}N_2O$: C, 73.74; H, 8.25; N, 11.47. Found: C, 73.84; H, 8.22; N, 11.37.

5-Ethyl-1-pentanoyldipyrromethane (IV-11d). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3e** (1.31 g, 7.50 mmol) in THF (15 mL). A solution of **IV-4l** (1.47 g, 7.50 mmol, in 15 mL of THF) was added to the reaction mixture. The resulting crude product was chromatographed [silica, hexanes/ethyl acetate (4:1)] to afford a light pink solid (1.192 g, 62%): mp 59–60 °C; ^{1}H NMR δ 0.97–1.03 (m, 6H), 1.43–1.50 (m, 2H), 1.76–1.84 (m, 2H), 2.12–2.26 (m, 2H), 2.86 (t, *J* = 7.6 Hz, 2H), 4.09 (t, *J* = 7.6 Hz, 1H), 6.10–6.11 (m, 1H), 6.16–6.18 (m, 2H), 6.71–6.72 (m, 1H), 7.02–7.03 (m, 1H), 9.74–9.82 (br, 1H), 11.18–11.24 (br, 1H); ^{13}C NMR δ 12.7, 14.0, 22.8, 26.9, 28.6, 37.8, 40.1, 104.9, 107.9, 108.5, 117.2, 119.7, 131.1, 132.8, 145.0, 191.9; ESI-MS obsd 258.17419 calcd 258.17321 ($C_{16}H_{22}N_2O$). Anal. Calcd for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.33; H, 8.61; N, 10.94.

1-Hexanoyl-5-propyldipyrromethane (IV-11f). Following Method IV.1, a solution of EtMgBr (4.0 mL, 4.0 mmol, 1.0 M in THF) was added to a solution of **IV-3f** (0.290 g, 1.50 mmol) in THF (3 mL). A solution **IV-4b** (0.320 g, 1.50 mmol, in 3 mL of THF) was added to the reaction mixture. The resulting crude product was chromatographed [silica, hexanes → hexanes/ethyl acetate (6:1)] to afford a brown paste (0.231 g, 52%): ^{1}H NMR δ 0.83–0.89 (m, 6H), 1.25–1.32 (m, 6H), 1.64–1.70 (m, 2H), 1.94–2.01 (m, 2H), 2.69 (t, *J* = 7.6 Hz, 2H), 4.04 (t, *J* = 7.6 Hz, 1H), 6.01–6.03 (m, 1H), 6.07–6.10 (m, 2H), 6.62–6.64 (m, 1H), 6.85–6.86 (m, 1H), 8.72–8.78 (br, 1H), 9.92–10.02 (br, 1H); ^{13}C NMR δ 14.1, 21.1, 22.6, 26.2, 28.5, 31.8, 35.9, 38.0, 38.1, 105.0, 108.1, 108.5, 117.3, 119.5, 131.1, 132.9, 144.9,

191.9; ESI-MS obsd 286.20439, calcd 286.20451 ($C_{18}H_{26}N_2O$). Anal. Calcd for $C_{18}H_{26}N_2O$: C, 75.48; H, 9.15; N, 9.78 Found: C, 75.26; H, 9.12; N, 9.72.

5-Butyl-1-hexanoyldipyrromethane (IV-11g). Following Method IV.1, a solution of EtMgBr (19.0 mL, 19 mmol, 1.0 M in THF) was added to a solution of **IV-3g** (1.52 g, 7.50 mmol) in THF (15 mL). A solution **IV-4b** (1.57 g, 7.50 mmol, in 15 mL of THF) was added to the reaction mixture. The resulting crude product was chromatographed [silica, CH_2Cl_2 → hexanes/ethyl acetate (3:1)] to afford a brown oil (1.783 g, 79%): ^{1}H NMR δ 0.86–0.91 (m, 6H), 1.31–1.37 (m, 8H), 1.76 (m, 2H), 2.08–2.11 (m, 2H), 2.79 (t, J = 7.8 Hz, 2H), 4.12 (t, J = 8.0 Hz, 1H), 6.04–6.05 (m, 1H), 6.10–6.13 (m, 2H), 6.65–6.66 (m, 1H), 6.95–6.97 (m, 1H), 9.62–9.76 (br, 1H), 11.02–11.16 (br, 1H); ^{13}C NMR δ 14.2, 14.23, 22.76, 22.8, 26.4, 30.3, 32.0, 33.6, 38.2, 38.4, 105.0, 108.1, 108.6, 117.4, 119.8, 131.2, 133.1, 145.3, 192.1; ESI-MS obsd 300.22062, calcd 300.22016 ($C_{19}H_{28}N_2O$). Anal. Calcd for $C_{19}H_{28}N_2O$: C, 75.96; H, 9.39; N, 9.32. Found: C, 76.04; H, 9.48; N, 9.37.

1-Bromo-9-acyldipyrromethanes (Method IV.2):

1-Bromo-9-(4-methoxybenzoyl)-5-phenyldipyrromethane (IV-5d-Br). Following Method IV.2, a solution of **IV-5d** (1.93 g, 5.40 mmol) in THF (54 mL) was treated with NBS (0.961 g, 5.40 mmol) at –78 °C to afford a brown foam (1.98 g, 84%): mp 68–70 °C; ^{1}H NMR (THF-d_8) δ 3.82 (s, 3H), 5.52 (s, 1H), 5.65–5.66 (m, 1H), 5.89–5.91 (m, 1H), 5.94–5.95 (m, 1H), 6.72–6.74 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 7.19–7.28 (m, 5H), 7.86 (d, J = 8.8 Hz, 2H), 10.48–10.58 (br; 1H), 11.12–11.22 (br, 1H); ^{13}C NMR (THF-d_8) δ 45.1, 55.8, 97.9, 110.2, 110.3, 110.4, 110.6, 110.8, 114.25, 114.3, 119.1, 119.2, 127.6, 129.17, 129.2, 131.0, 131.2, 131.8, 134.2, 140.8, 141.9, 162.8, 182.3 (partial decomposition was observed

during spectral acquisition); ESI-MS obsd 435.07018, calcd 435.07027 [(M + H)$^+$, M = $C_{23}H_{19}BrN_2O_2$].

1-Bromo-9-isonicotinoyl-5-phenyldipyrromethane (**IV-5e-Br**)**.** Following Method IV.2, a solution of **IV-5e** (0.65 g, 2.0 mmol) in THF (20 mL) was treated with NBS (0.354 g, 2.0 mmol) at –78 °C. The resulting crude product was purified by column chromatography [silica, hexanes/ethyl acetate (1:1) → ethyl acetate] to afford a light yellow foam (0.717 g, 88%): mp 75 °C; ^{1}H NMR δ 5.53 (s, 1H), 5.91–5.92 (m, 1H), 6.07–6.08 (m, 1H), 6.13–6.15 (m, 1H), 6.78–6.80 (m, 1H), 7.16 –7.18 (m, 2H), 7.26–7.32 (m, 3H), 7.53 (d, *J* = 5.2 Hz, 2H), 8.71 (d, *J* = 5.2 Hz, 2H), 8.76–8.84 (br, 1H), 10.18–10.26 (br, 1H); ^{13}C NMR (THF-d_8) δ 45.2, 98.2, 110.3, 110.5, 111.45, 111.5, 121.1, 123.2, 127.8, 129.3, 129.5, 131.5, 134.7, 142.5, 143.9, 146.6, 151.1, 182.7; ESI-MS obsd 406.0548, calcd 406.0549 [(M + H)$^+$, M = $C_{21}H_{16}BrN_3O$].

1-Bromo-5-phenyl-9-(2,4,6-trimethylbenzoyl)dipyrromethane (IV-5g-Br). Following Method IV.2, a solution of **IV-5g** (0.368 g, 1.0 mmol) in THF (10 mL) was treated with NBS (0.178 g, 1.0 mmol). The resulting crude product was purified by column chromatography [silica, hexanes/ethyl acetate (3:1)] to afford a brown foam (0.263 g, 59%): mp 89 °C (dec.); ^{1}H NMR (THF-d_8) δ 2.27 (s, 3H), 2.56 (s, 6H), 5.46 (s, 1H), 5.56–5.62 (m, 1H), 5.74–5.80 (m, 1H), 5.92–5.96 (m, 1H), 6.16–6.22 (br, 1H), 6.83 (m, 2H), 7.18 –7.21 (m, 3H), 7.25–7.29 (m, 2H), 10.50–10.58 (br, 1H), 11.10–11.18 (br, 1H); ^{13}C NMR (THF-d_8) δ 19.7, 21.3, 45.2, 98.0, 110.1, 110.2, 110.3, 110.4, 110.9, 111.1, 119.4, 127.7, 128.8, 128.9, 129.2, 129.5, 134.0, 135.1, 135.2, 138.5, 139.0, 142.5, 142.8, 188.3; ESI-MS obsd 447.10566, calcd 447.10665 [(M + H)$^+$, M = $C_{25}H_{23}BrN_2O$].

1-Bromo-9-(4-ethylbenzoyl)-5-(3-pyridyl)dipyrromethane (IV-7-Br). Following Method IV.2, a solution of **IV-7** (0.531 g, 1.49 mmol) in THF (15 mL) was treated with NBS (0.264 g, 1.49 mmol) at –78 °C. The resulting crude product was purified by column chromatography [silica, ethyl acetate → ethyl acetate/THF (1:1) → THF] to afford an orange solid (0.434 g, 69%): ^{1}H NMR (THF-d_8) δ 1.25 (t, J = 7.4 Hz, 3H), 2.69 (q, J = 7.4 Hz, 2H), 5.55 (s, 1H), 5.62–5.64 (m, 1H), 5.90–5.93 (m, 1H), 5.95–5.97 (m, 1H), 6.72–6.75 (m, 1H), 7.23–7.25 (m, 1H), 7.28 (d, J = 7.4 Hz, 2H), 7.53 (d, J = 7.4 Hz, 1H), 7.77 (d, J = 7.4 Hz, 2H), 8.41–8.43 (m, 1H), 8.44–8.47 (m, 1H), 10.61–10.65 (br, 1H), 11.25–11.29 (br, 1H); ^{13}C NMR (THF-d_8) δ 15.0, 28.8, 41.8, 97.6, 109.4, 109.6, 109.8, 118.5, 123.2, 127.6, 129.1, 131.5, 133.3, 135.8, 136.8, 137.4, 140.0, 148.0, 149.0, 183.1; ESI-MS obsd 433.0790, calcd 433.0790 ($C_{23}H_{20}BrN_3O$).

1-Bromo-5-ethyl-9-propionyldipyrromethane (IV-11b-Br). Following Method IV.2, treatment of a solution of **11b** (0.460 g, 2.00 mmol) in THF (20.0 mL) with NBS (0.354 g, 2.0 mmol) afforded a dark brown paste (0.546 g, 88%): ^{1}H NMR δ 0.93 (t, J = 7.4 Hz, 3H), 1.27 (t, J = 7.4 Hz, 3H), 2.01–2.13 (m, 2H), 2.81 (q, J = 7.4 Hz, 2H), 3.92 (t, J = 8.0 Hz, 1H), 5.96–5.98 (m, 1H), 6.01–6.02 (m, 1H), 6.10–6.12 (m, 1H), 6.95–6.97 (m, 1H), 9.48–9.62 (br, 1H), 10.52–10.68 (br, 1H); a ^{13}C NMR spectrum could not obtained because of instability of the compound; ESI-MS obsd 309.0598, calcd 309.0597 [$(M + H)^+$, M = $(C_{14}H_{17}BrN_2O)$].

1-Bromo-9-butanoyl-5-ethyldipyrromethane (IV-11c-Br). Following Method IV.2, treatment of a solution of **IV-11c** (0.977 g, 4.0 mmol) in THF (40 mL) with NBS (0.708 g, 4.00 mmol) afforded a white solid (1.22 g, 94%). The title compound changed from off-white to dark brown within 2 min upon removal from storage at –4 °C, hence only

limited characterization were obtained: ^{1}H NMR (THF-d_8) δ 0.87–0.96 (m, 6H), 1.65–1.69 (m, 3H), 1.93–2.04 (m, 2H), 2.65–2.67 (m, 2H), 3.87 (m, 1H), 5.85–5.86 (m, 1H), 5.89–5.94 (m, 1H), 5.97–5.99 (m, 1H), 6.84–6.87 (m, 1H), 10.31–10.34 (br, 1H), 10.88–11.12 (br, 1H); ESI-MS obsd 322.06727, calcd 322.06808 ($C_{15}H_{19}BrN_2O$).

1-Bromo-5-ethyl-1-pentanoyldipyrromethane (IV-11d-Br). Following Method IV.2, treatedment of **IV-11d** (1.03 g, 4.00 mmol) in THF (40.0 mL) with NBS (0.708 g, 4.00 mmol) gave a pink solid (1.271 g, 94%): mp 70 °C (dec.); ^{1}H NMR (THF-d_8) δ 0.87–0.93 (m, 6H), 1.31–1.40 (m, 2H), 1.59–1.66 (m, 2H), 1.93–2.01 (m, 2H), 2.65 (t, J = 7.4 Hz, 2H), 3.84 (t, J = 7.6 Hz, 1H), 5.83–5.84 (m, 1H), 5.89–5.92 (m, 2H), 6.76–6.78 (m, 1H), 10.22–10.32 (br, 1H), 10.58–10.62 (br, 1H); ^{13}C NMR (THF-d_8) δ 14.2, 21.2, 22.8, 26.4, 32.0, 36.0, 38.2, 105.1, 108.1, 108.7, 117.4, 119.8, 131.2, 133.1, 145.2, 192.1. (Note that partial decomposition was observed after 1 h upon attempted ^{13}C NMR measurement at room temperature.) ESI-MS obsd 336.08371 calcd 336.08373 ($C_{16}H_{21}BrN_2O$). Anal. Calcd for $C_{16}H_{21}BrN_2O$: C, 56.98; H, 6.28; N, 8.31. Found: C, 56.93; H, 6.31; N, 8.35.

1-Bromo-9-hexanoyl-5-pentyldipyrromethane (IV-11h-Br). Following Method IV.2, a solution of **IV-11h** (0.629 g, 2.00 mmol) in THF (20.0 mL) was treated with NBS (0.354 g, 2.0 mmol) at –78 °C. The resulting crude product was purified by column chromatography [silica, hexanes/ethyl acetate (3:1)] to afford a red-brown liquid (0.668 g, 85%): ^{1}H NMR δ 0.84–0.87 (m, 6H), 1.26–1.28 (m, 6H), 1.32–1.38 (m, 4H), 1.72–1.78 (m, 2H), 1.96–2.06 (m, 2H), 2.81 (t, J = 7.8 Hz, 2H), 3.97 (t, J = 7.8 Hz, 1H), 5.95–5.96 (m, 1H), 6.00–6.02 (m, 1H), 6.08–6.11 (m, 1H), 6.93–6.94 (m, 1H), 9.39–9.43 (br, 1H), 10.45–10.51 (br, 1H); a ^{13}C NMR spectrum could not be recorded because of instability of the compound;

ESI-MS obsd 393.1535, calcd 393.1536 ($C_{20}H_{29}BrN_2O$).

Aryl-Substituted Bilanes (Method IV.3):

1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-ethylbenzoyl)-10-(hexanoyl)-5-phenylbilane (IV-1b). Following Method IV.3, a solution of **IV-5b-Br** (0.399 g, 1.00 mmol) in dry THF/methanol (80 mL, 3:1) was treated with $NaBH_4$ (0.951 g, 25.0 mmol). The resulting carbinol **IV-5b-Br-OH** in dry acetonitrile (1.34 mL) was treated with **IV-6a** (0.41 g, 1.0 mmol) and $Yb(OTf)_3$ (0.660 mL of a 10.0 mM stock solution in anhydrous MeOH). The resulting product was chromatographed to afford a light-brown foam (0.673 g, 85%), presumably as a mixture of 8 stereoisomers: mp 72–74 °C; ^{1}H NMR (THF-d_8) δ 0.84–0.91 (m, 4H), 1.23–1.29 (m, 15H), 1.84–1.88 (br, 2H), 2.70 (q, J = 7.6 Hz, 2H), 3.79 (t, J = 7.4 Hz, 2H), 5.22–5.28 (m, 1H), 5.41–5.43 (m, 1H), 5.45–5.48 (m, 1H), 5.52–5.54 (m, 2H), 5.68–5.72 (m, 2H), 5.84–5.88 (m, 2H), 6.66–6.71 (m, 1H), 7.08–7.15 (m, 5H), 7.19–7.22 (m, 3H), 7.27–7.30 (m, 4H), 7.77 (d, J = 7.6 Hz, 2H), 9.31–9.39 (br, 1H), 9.45–9.52 (br, 1H), 10.29–10.38 (br, 1H), 10.89–11.1 (br, 1H); ^{13}C NMR (THF-d_8) δ 15.9, 23.7, 28.6, 29.8, 31.9, 33.0, 35.2, 36.3, 36.6, 39.4, 44.8, 45.4, 97.2, 105.4, 107.9, 108.1, 109.7, 110.1, 110.6, 119.5, 125.9, 127.2, 128.4, 128.9, 129.2, 129.5, 130.0, 131.8, 131.9, 132.34, 135.12, 135.17, 135.2, 135.3, 135.4, 135.5, 135.6, 136.5, 136.6, 138.0, 140.8, 143.3, 143.4, 144.3, 148.7, 150.0, 183.8. The high-resolution exact mass spectrum gave m/z = 791.3345, which is assigned to the protonated molecule ion of the $2e^-/2H^+$-oxidized derivative of the title compound, i.e., a protonated bilene [calcd 791.3324 for $(M' + H)^+$, M' = $C_{49}H_{51}BrN_4O$, where the title compound has $C_{49}H_{53}BrN_4O$]. MALDI-MS (POPOP) obsd 789.9, 791.0, 792.0, 792.9, calcd 792.3403 ($C_{49}H_{53}BrN_4O$). Anal. Calcd for $C_{51}H_{49}BrN_4O$: C, 74.13; H, 6.73; N, 7.06.

Found: C, 72.94; H, 6.78; N, 6.69. (The elemental analysis data are consistent with the presence of one molecule of water per one molecule of product.)

\1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-ethylbenzoyl)-10-(pentafluorophenyl)-5-phenylbilane (IV-1c). Following Method IV.3 with slight modification, a solution of **IV-5c-Br** (0.099 g, 0.20 mmol) in dry THF/methanol (16 mL, 3:1) was treated with $NaBH_4$ (0.19 g, 5.0 mmol). The resulting carbinol **IV-5c-Br-OH** in dry acetonitrile (1.34 mL) was treated with **6a** (0.0820 g, 0.200 mmol) and $Yb(OTf)_3$ (0.660 mL of a 10.0 mM stock solution in anhydrous acetonitrile). The resulting reaction mixture was stirred at room temperature for 5 h. The standard workup and column chromatography afforded a light-brown foam (0.154 g, 87%), presumably as a mixture of 8 stereoisomers: mp 79–81 °C; ^{1}H NMR (THF-d_8) δ 1.24–1.29 (m, 12H), 2.70 (q, J = 7.8 Hz, 2H), 5.26–5.29 (m, 1H), 5.41–5.43 (m, 1H), 5.51–5.54 (m, 1H), 5.58–5.62 (m, 2H), 5.71–5.79 (m, 3H), 5.88–5.89 (m, 2H), 6.68–6.69 (m, 1H), 7.09–7.16 (m, 5H), 7.20–7.24 (m, 2H), 7.27–7.31 (m, 4H), 7.77 (d, J = 8.0 Hz, 2H), 9.65–9.72. (br, 1H), 9.74–9.82 (br, 1H), 10.34–10.46 (br, 1H), 10.92–11.1 (br, 1H); ^{13}C NMR (THF-d_8) δ 16.0, 29.8, 31.9, 34.6, 44.8, 45.3, 45.4, 97.4, 107.7, 108.4, 109.8, 110.1, 110.3, 110.4, 110.6, 119.5, 125.9, 126.0, 127.3, 128.4, 128.5, 129.1, 129.3, 129.5, 130.0, 131.9, 133.49–133.52 (m), 133.8–133.9 (m), 136.1–136.2 (m), 137.37–137.39 (m), 138.0, 139.9–139.2 (m), 140.5–140.6 (m), 142.9, 143.0, 143.9, 144.3, 145.1–145.2 (m), 147.5–147.6 (m), 148.8, 150.2, 183.9; MALDI-MS (POPOP) obsd 885.1, 886.1, 887.1, 888.1, calcd 888.25 ($C_{50}H_{42}BrF_5N_4O$); ESI-MS obsd 911.23434, calcd 911.23544 [$(M + Na)^+$, M = $C_{50}H_{42}BrF_5N_4O$].

1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-ethylbenzoyl)-10-(4-methoxybenzoyl)-5-phenylbilane (IV-1d). Following Method IV.3, a solution of **IV-5d-Br** (0.435 g, 1.00

mmol) in dry THF/methanol (80.0 mL, 3:1) was treated with $NaBH_4$ (0.951 g, 25.0 mmol). The resulting carbinol **IV-5d-Br-OH** in dry acetonitrile (1.34 mL) was treated with **IV-6a** (0.411 g, 1.00 mmol) and $Yb(OTf)_3$ (0.660 mL of a 10.0 mM stock solution in anhydrous MeOH). The standard workup and column chromatography afforded a brown foam (0.627 g, 76%), presumably as a mixture of 8 stereoisomers: mp 89–91 °C; ^{1}H NMR (THF-d_8) δ 1.27 (t, J = 7.4 Hz, 3H), 1.27–1.29 (m, 12H), 2.69 (q, J = 7.4 Hz, 2H), 5.21–5.22 (m, 1H), 5.26–5.28 (m, 1H), 5.41–5.44 (m, 1H), 5.48–5.55 (m, 5H), 5.86–5.88 (m, 2H), 6.66–6.71 (m, 1H), 6.77 (d, J = 8.4 Hz, 2H), 7.04–7.06 (m, 2H), 7.09–7.14 (m, 5H), 7.19–7.20 (m, 2H), 7.26–7.33 (m, 4H), 7.76 (d, J = 8.4 Hz, 2H), 9.52–9.58 (br, 1H), 9.62–9.68 (br, 1H), 10.32–10.38 (br, 1H), 10.88–11.96 (br, 1H) (partial decomposition was observed).

1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-ethylbenzoyl)-10-(4-pyridyl)-5-phenylbilane (IV-1e). Following Method IV.3 with slight modification, a solution of **IV-5e-Br** (0.406 g, 1.00 mmol) in dry THF/methanol (80.0 mL, 3:1) was treated with $NaBH_4$ (0.951 g, 25.0 mmol). The resulting carbinol **IV-5e-Br-OH** in dry acetonitrile (1.34 mL) was treated with **IV-6a** (0.411 g, 1.00 mmol) and $Yb(OTf)_3$ (0.660 mL of a 10.0 mM stock solution in anhydrous acetonitrile). The resulting reaction mixture was stirred at room temperature for 5 h. On the basis of TLC analysis (silica, ethyl acetate) of the crude reaction mixture, no product was observed. A sample of $Yb(OTf)_3$ was added (24.0 mg, 0.0390 mmol, total acid concentration = 23.0 mM). The reaction mixture was stirred at room temperature for 1 h. The TLC analysis of the crude reaction mixture did not reveal any product. A sample of $Yb(OTf)_3$ was added (0.257 g, 0.414 mmol, total acid concentration = 230 mM). The reaction mixture was stirred at room temperature for 3 h. The TLC analysis (silica, ethyl acetate) of the crude reaction mixture revealed the presence of the product and

two more polar (unidentified) products. The standard workup and column chromatography [silica, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (2:1) → ethyl acetate] afforded a green foam (0.288 g, 36%), presumably as a mixture of 8 stereoisomers: mp 98–101 °C; ^{1}H NMR (THF-d_8) δ 1.24–1.29 (m, 12H), 2.70 (q, J = 7.8 Hz, 2H), 5.24–5.31 (m, 2H), 5.41–5.43 (m, 1H), 5.49–5.62 (m, 6H), 5.86–5.91 (m, 2H), 6.67–6.71 (m, 1H), 7.04–7.15 (m, 5H), 7.18–7.25 (m, 3H), 7.25–7.32 (m, 4H), 7.77 (d, J = 7.2 Hz, 2H), 8.39 (d, J = 7.2 Hz, 2H), 9.67–9.73 (br, 1H), 9.75–9.83 (br, 1H), 10.35–10.42 (br, 1H), 10.93–11.3 (br, 1H); ^{13}C NMR (THF-d_8) δ 16.2, 28.8, 31.0, 34.3, 43.8, 44.4, 44.5, 96.4, 107.1, 108.8, 108.9, 109.1, 109.4, 109.5, 109.7, 118.5, 118.6, 123.6, 123.8, 124.9, 125.1, 127.4, 127.6, 128.1, 128.5, 128.7, 129.1, 131.0, 131.7, 131.8, 131.9, 132.0, 132.1, 132.39, 132.4, 132.5, 132.8, 132.9, 135.3, 137.0, 139.7, 142.1, 143.07, 147.8, 149.2, 149.5, 149.7, 152.4, 182.9; MALDI-MS (POPOP) obsd 796.3.1, 797.3, 798.3, 799.3, 800.3, 801.3, 802.3, 803.3, calcd 799.2886 ($C_{49}H_{46}BrN_5O$); ESI-MS obsd 800.29506, calcd 800.29585 [$(M + H)^+$, M = $C_{49}H_{46}BrN_5O$].

1-Bromo-15-(4-*tert*-butylphenyl)-19-(hexanoyl)-10-(4-methylphenyl)-5-phenylbilane (IV-2b). Following Method IV.3, a solution of **IV-5a-Br** (0.210 g, 0.500 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.67 mL) was treated first with **IV-6b** (0.205 g, 0.50 mmol) and then $Yb(OTf)_3$ (0.330 mL of a 10.0 mM stock solution in anhydrous MeOH). The resulting product was chromatographed [silica, hexanes/ethyl acetate (3:1)] to afford a light-brown foam (0.220 g, 57%), presumably as a mixture of 8 stereoisomers: mp 65–68 °C; ^{1}H NMR (THF-d_8) δ 0.89 (t, J = 7.2 Hz, 3H), 1.28 (s, 9H), 1.31–1.36 (br, 4H), 1.62–1.68 (br, 2H), 2.27 (s, 3H), 2.64 (t, J = 7.6 Hz, 2H), 5.20–5.22 (m, 1H), 5.25–5.28 (m, 1H), 5.31–5.36 (m, 1H), 5.47–5.59 (m, 5H), 5.77–5.81 (m, 1H), 5.85–

5.89 (m, 1H), 6.66–6.71 (m, 1H), 7.08–7.15 (m, 6H), 7.12–7.18 (m, 3H), 7.19–7.23 (m, 2H), 7.25–7.28 (m, 2H), 9.52–9.62 (m, 2H), 10.31–10.39 (br, 1H), 10.65–10.72 (br, 1H); ^{13}C NMR (THF-d_8) δ 14.5, 21.3, 23.6, 31.9, 32.8, 35.2, 38.3, 44.7, 45.0, 45.4, 97.2, 107.6, 107.8, 107.9, 109.8, 110.1, 116.4, 125.8, 127.2, 128.9, 129.2, 129.4, 129.5, 129.54, 132.8, 132.83, 133.1, 133.2, 134.2, 134.4, 134.5, 134.65, 134.7, 134.8, 136.3, 136.4, 140.9, 141.9, 142.0, 142.2, 142.3, 142.5, 144.18, 144.2, 150.0, 189.6 (one aliphatic carbon was not observed); MALDI-MS (POPOP) obsd 775.8, 776.9, 777.9, 778.8, 779.9, 780.9, calcd 778.3246 ($C_{48}H_{51}BrN_4O$); ESI-MS obsd 801.3138, calcd 801.3134 [$(M + Na)^+$, M = $C_{48}H_{51}BrN_4O$].

1-Bromo-15-(4-*tert*-butylphenyl)-10-(4-methylphenyl)-19-(pentafluorobenzoyl)-5-phenylbilane (IV-2c). Following Method IV.3 with slight modification, a solution of **IV-5a-Br** (0.21 g, 0.50 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.67 mL) was treated with **IV-6c** (0.236 g, 0.500 mmol) and $Yb(OTf)_3$ (0.330 mL of a 10.0 mM stock solution in anhydrous MeOH). The resulting reaction mixture was stirred at room temperature for 1 h. The TLC analysis [silica, hexanes/ethyl acetate (3:1)] of the crude reaction mixture revealed the presence of the bilane and unreacted starting materials (**IV-5a-Br-OH** and **IV-6c**). A sample of $Yb(OTf)_3$ (0.012 g, 0.019 mmol, total acid concentration = 23 mM) was added. The reaction mixture was stirred for 1 h. The TLC analysis of the crude reaction revealed the presence of the product and a trace amount of unreacted **IV-6c**. The standard workup and column chromatography afforded a dark brown foam (0.152 g, 35%), presumably as a mixture of 8 stereoisomers: mp 79–81 °C; ^{1}H NMR (THF-d_8) δ 1.29 (s, 9H), 2.27 (s, 3H), 5.21–5.22 (m, 1H), 5.23–5.26 (m, 1H), 5.38–5.42 (m, 1H), 5.48–5.55 (m, 5H), 5.86–5.89 (m, 2H), 6.57–6.61 (br, 1H), 7.02–7.03 (m, 4H), 7.09–7.14 (m, 5H), 7.19–7.21 (m,

2H), 7.29–7.32 (m, 2H), 9.51–9.59 (br, 1H), 9.67–9.72 (br, 1H), 10.31–10.37 (br, 1H), 11.46–11.51 (br, 1H); ^{13}C NMR (THF-d_8) δ 21.2, 31.9, 35.2, 44.9, 45.0, 45.4, 97.2, 107.6, 107.62, 107.7, 107.74, 108.0, 109.8, 110.1, 112.0, 122.5, 126.0, 127.2, 128.9, 129.2, 129.4, 129.5, 129.53, 132.1, 132.2, 132.4, 133.1, 133.14, 133.2, 134.3, 134.4, 134.47, 134.98, 135.0, 135.1, 135.13, 136.3, 136.33, 136.4, 140.1, 141.9, 144.16, 144.2, 147.1, 147.2, 150.3, 171.4; ESI-MS obsd 897.21900, calcd 897.21979 [$(M + Na)^+$, M = $C_{49}H_{40}BrF_5N_4O$].

1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-methoxybenzoyl)-10-(4-methylphenyl)-5-phenylbilane (IV-2d). Following Method IV.3, a solution of **IV-5a-Br** (0.210 g, 0.50 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.670 mL) was treated with **IV-6d** (0.205 g, 0.50 mmol) and $Yb(OTf)_3$ (0.33 mL of a 10.0 mM stock solution in anhydrous MeOH). The standard workup and column chromatography afforded a light-brown foam (0.322 g, 79%), presumably as a mixture of 8 stereoisomers: mp 75–77 °C; ^{1}H NMR (THF d_8) δ 1.29 (s, 9H), 2.27 (s, 3H), 3.83 (s, 3H), 5.22–5.24 (m, 1H), 5.25–5.28 (m, 1H), 5.41–5.43 (m, 1H), 5.49–5.56 (m, 5H), 5.85–5.92 (m, 2H), 6.65–6.72 (m, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.02–7.06 (m, 4H), 7.10–7.15 (m, 5H), 7.19–7.21 (m, 2H), 7.28–7.30 (m, 2H), 7.85 (d, *J*= 8.4 Hz, 2H), 9.55–9.58 (m, 1H), 9.62–9.66 (br, 1H), 10.29–10.38 (br, 1H), 10.85–10.92 (br, 1H); ^{13}C NMR (THF-d_8) δ 20.3, 31.0, 34.3, 43.8, 44.1, 44.5, 54.9, 96.3, 106.7, 106.8, 107.0, 108.9, 109.2, 109.6, 113.3, 118.0, 124.9, 126.2, 127.9, 128.3, 128.5, 128.56, 128.6, 130.8, 131.0, 131.8, 131.9, 132.1, 132.2, 133.5, 133.6, 133.78, 133.8, 133.9, 135.3, 135.5, 139.9, 141.1, 141.8, 141.9, 142.0, 143.27, 143.3, 149.1, 162.7, 182.0; MALDI-MS (POPOP) obsd 812.2, 813.2, 814.2, 815.2, 816.2, 817.2, 818.2, calcd 814.2882 ($C_{50}H_{47}BrN_4O_2$); ESI-

MS gave *m/z* = 813.2798, which is assigned to the protonated molecule ion of the $2e^-/2H^+$-oxidized derivative of the title compound, i.e., a protonated bilene [calcd 813.2796 for $(M' + H)^+$, $M' = C_{50}H_{46}BrN_4O_2$, where the title compound has $C_{50}H_{47}BrN_4O_2$].

1-Bromo-15-(4-*tert*-butylphenyl)-19-(4-methoxy-4-oxobutanoyl)-10-(4-methylphenyl)-5-phenylbilane (IV-2f). Following Method IV.3, a solution of **IV-5a-Br** (0.210 g, 0.500 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.67 mL) was treated with **IV-6f** (0.196 g, 0.500 mmol) and $Yb(OTf)_3$ (0.33 mL of a 10.0 mM stock solution in anhydrous MeOH). The standard workup and column chromatography afforded a light-brown foam (0.259 g, 68%), presumably as a mixture of 8 stereoisomers: mp 79–83 °C; ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 9H), 2.30 (s, 3H), 2.59 (t, *J* = 6.8 Hz, 2H), 3.01 (t, *J* = 6.8 Hz, 2H), 3.62 (s, 3H), 5.22–5.25 (m, 1H), 5.26–5.28 (m, 1H), 5.31–5.35 (m, 1H), 5.67–5.72 (m, 3H), 5.73–6.75 (m, 2H), 5.42– 5.49 (m, 1H), 5.92–6.04 (m, 1H), 6.83–6.89 (m, 1H), 6.99–7.08 (m, 6H), 7.13–7.15 (m, 2H), 7.22–7.29 (m, 5H), 7.80–7.92 (m, 2H), 8.22–8.32 (br, 1H), 9.18–9.23 (br, 1H); ^{13}C NMR (THF-d_8) δ 21.2, 28.8, 31.9, 33.0, 35.2, 44.7, 44.0, 45.4, 51.6, 97.2, 107.6, 107.7, 107.8, 109.8, 110.1, 110.3, 116.7, 125.8, 127.2, 128.9, 129.2, 129.4, 129.47, 129.5, 132.2, 132.7, 132.8, 133.0, 133.1, 133.2, 134.37, 134.4, 134.5, 134.6, 134.7, 134.8, 136.3, 136.4, 140.8, 142.0, 142.6, 142.7, 144.16, 144.2, 150.1, 173.6, 187.6; MALDI-MS (POPOP) obsd 790.9, 791.9, 792.8, 793.8, 794.8, 795.8, 796.8, calcd 794.2832 ($C_{47}H_{47}BrN_4O_3$); ESI-MS obsd 817.2723, calcd 817.2723 [$(M + Na)^+$, $M = C_{47}H_{47}BrN_4O_3$].

1-Bromo-15-(4-*tert*-butylphenyl)-10-(4-methylphenyl)-5-phenyl-19-(2,4,6-trimethylbenzoyl)bilane (IV-2g). Following Method IV.3, a solution of **IV-5a-Br** (0.21 g,

0.50 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.67 mL) was treated with **IV-6g** (0.196 g, 0.50 mmol) and $Yb(OTf)_3$ (0.33 mL of a 10.0 mM stock solution in anhydrous MeOH). The reaction mixture was stirred for 4 h at room temperature. The standard workup and column chromatography afforded a reddish brown foam (0.262 g, 64%), presumably as a mixture of 8 stereoisomers: mp 98–102 °C; ^{1}H NMR (THF-d_8) δ 1.29 (s, 9H), 2.08–2.14 (m, 6H), 2.22–2.26 (m, 6H), 5.18–5.22 (m, 1H), 5.25–5.29 (m, 1H), 5.37–5.41 (m, 1H), 5.49–5.55 (m, 5H), 5.71–5.77 (m, 1H), 5.85– 5.91 (m, 1H), 6.13–6.21 (br, 1H), 6.81–6.85 (m, 2H), 7.01–7.08 (m, 4H), 7.07–7.10 (m, 2H), 7.12–7.15 (m, 3H), 7.19–7.23 (m, 2H), 7.28–7.30 (m, 2H), 9.52–9.60 (br, 1H), 9.65–9.72 (m, 1H), 10.25–10.38 (br, 1H), 10.85–11.05 (br, 1H); ^{13}C NMR (THF-d_8) δ 19.7, 21.2, 21.4, 31.9, 35.2, 44.8, 45.0, 45.4, 97.2, 107.6, 107.7, 107.8, 107.9, 109.8, 110.1, 110.8, 119.5, 125.9, 127.2, 128.8, 128.9, 129.2, 129.4, 129.5, 132.7, 132.8, 133.1, 133.2, 133.7, 134.38, 134.4, 134.5, 134.7, 134.75, 134.8, 134.9, 135.1, 136.3, 136.4, 136.5, 138.3, 139.1, 140.7, 142.0, 143.7, 144.16, 144.2, 150.1, 188.1; MALDI-MS (POPOP) obsd 824.3, 825.4, 826.4, 827.4, 828.4, 829.4, 830.4, calcd 826.3246 ($C_{52}H_{51}BrN_4O$); ESI-MS obsd 849.3138, calcd 849.3138 [$(M + Na)^+$, M = $C_{52}H_{51}BrN_4O$].

1-Bromo-15-(4-*tert*-butylphenyl)-19-formyl-10-(4-methylphenyl)-5-phenylbilane (IV-2h). Following Method IV.3, a solution of **IV-5a-Br** (0.210 g, 0.500 mmol) in dry THF/methanol (40.0 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The resulting carbinol **IV-5a-Br-OH** in dry acetonitrile (0.670 mL) was treated with **IV-6h** (0.196 g, 0.500 mmol) and $Yb(OTf)_3$ (0.330 mL of a 10.0 mM stock solution in anhydrous MeOH). The

reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography afforded a brown foam (0.198 g, 56%), presumably as a mixture of 8 stereoisomers: mp 92–94 °C; ^{1}H NMR (THF-d_8) δ 1.29 (s, 9H), 2.23 (s, 3H), 5.21–5.23 (m, 1H), 5.25–5.30 (m, 1H), 5.35–5.39 (m, 1H), 5.49–5.57 (m, 5H), 5.83–5.91 (m, 2H), 6.75–6.79 (m, 1H), 7.02–7.06 (m, 4H), 7.07–7.11 (m, 2H), 7.13–7.17 (m, 3H), 7.19–7.25 (m, 2H), 7.27–7.32 (m, 2H), 9.36 (s, 1H), 9.51–9.59 (br, 1H), 9.63–9.69 (m, 1H), 10.32–10.40 (br, 1H), 11.02–11.12 (br, 1H); ^{13}C NMR (THF-d_8) δ 21.3, 31.9, 35.2, 44.8, 45.0, 45.4, 97.2, 107.6, 107.7, 107.8, 107.9, 109.8, 110.1, 111.0, 121.1, 125.9, 127.2, 128.9, 129.2, 129.4, 129.47, 129.5, 132.4, 132.44, 132.5, 133.1, 133.2, 134.2, 134.3, 134.4, 134.5, 134.8, 134.85, 134.9, 136.3, 136.4, 140.5, 142.0, 144.2, 144.4, 150.1, 178.5; ESI-MS obsd 731.2355, calcd 731.2357 [$(M + Na)^+$, M = $C_{43}H_{41}BrN_4O$].

Aryl-Substituted Porphyrins (Method IV.4): 20-(4-*tert*-Butylphenyl)-5-(4-ethylphenyl)-15-pentyl-10-phenylporphinatomagnesium(II) (IV-MgP-1b). Application of Method IV.4 with **IV-1b** (0.24 g, 0.30 mmol), DBU, and $MgBr_2$ in toluene (3 mL) with chromatographic workup afforded a purple solid (0.098 g, 46%): ^{1}H NMR δ 0.96 (t, J = 7.2 Hz, 3H), 1.52–1.61 (m, 3H), 1.64 (s, 9H), 1.81–1.88 (m, 2H), 2.56–2.68 (br, 2H), 2.95– 3.01 (m, 4H), 5.04–5.14 (m, 2H), 7.52– 7.54 (m, 2H), 7.31–7.75 (m, 5H), 8.08–8.14 (m, 4H), 8.20–8.21 (m, 2H), 8.79–8.85 (m, 4H), 8.92–8.97 (m, 2H), 9.45–9.52 (m, 2H); ^{13}C NMR δ 14.5, 15.9, 23.1, 29.0, 32.0, 33.2, 35.1, 36.2, 39.5, 120.9, 121.0, 121.3, 122.2, 123.3, 125.9, 126.4, 127.1, 128.7, 128.8, 131.8, 131.9, 132.0, 132.1, 132.4, 134.7, 134.9, 134.94, 141.1, 141.3, 142.9, 144.2, 149.5, 149.7, 149.8, 149.8, 149.85, 149.87, 149.94, 150.0, 150.36, 150.4, LD-MS obsd 714.6, calcd 714.357; FAB-MS obsd 714.3596, calcd 714.3573 ($C_{49}H_{46}MgN_4$);

λ_{abs} (toluene) 406, 428, 566, 607 nm.

20-(4-*tert*-Butylphenyl)-5-(4-ethylphenyl)-15-(pentafluorophenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-1c). Application of Method IV.4 with **IV-1c** (0.267 g, 0.300 mmol), DBU, and $MgBr_2$ in toluene (3 mL) with chromatographic workup afforded two porphyrins, the title porphyrin (0.071 g, 29%) and a more polar porphyrin (0.017 g, LD-MS obsd 961.2; 6% presumed yield). Data for **IV-MgP-1c**: ^{1}H NMR δ 1.57 (t, *J* = 7.4 Hz, 3H), 1.66 (s, 9H), 3.05 (q, *J* = 7.4 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.76–7.79 (m, 5H), 8.15–8.18 (m, 4H), 8.25–8.26 (m, 2H), 8.79–8.83 (m, 2H), 8.88–8.89 (m, 1H), 8.92–8.96 (m, 3H), 8.97–8.99 (m, 1H), 9.02–9.04 (m, 1H); ^{13}C NMR δ 15.9, 29.1, 31.9, 35.1, 100.8, 118.7, 122.3, 122.8, 123.6, 124.1, 126.0, 126.2, 126.6, 127.5, 129.4, 129.5, 129.6, 129.7, 131.9, 132.1, 132.3, 132.4, 132.5, 132.6, 132.7, 132.8, 133.5, 133.6, 133.8, 133.9, 134.7, 134.9, 135.1, 138.81–133.89 (m), 140.5, 141.0, 143.4, 143.7, 145.64–145.68 (m), 147.9–148.1 (m), 149.4, 150.1, 150.3, 150.4, 150.7, 151.0; LD-MS obsd 810.8; FAB-MS obsd 801.26191, calcd 801.26268 ($C_{50}H_{35}F_5MgN_4$); λ_{abs} (toluene) 406, 427, 523, 604 nm.

20-(4-*tert*-Butylphenyl)-5-(4-ethylphenyl)-15-(4-methoxyphenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-1d). Application of Method IV.4 with **IV-1d** (0.249 g, 0.300 mmol), DBU, and $MgBr_2$ in toluene (3 mL) with chromatographic workup afforded a purple solid (0.113 g, 45%): ^{1}H NMR (THF-d_8) δ 1.53 (t, *J* = 7.6 Hz, 3H), 1.63 (s, 9H), 3.01 (q, *J* = 7.6 Hz, 2H), 4.06 (s, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.58 (q, *J* = 8.0 Hz, 2H), 7.71–7.73 (m, 3H), 7.79 (d, *J* = 8.0 Hz, 2H), 8.09–8.11 (m, 6H), 8.19–8.21 (m, 2H), 8.73–8.79 (m, 8H); ^{13}C NMR (THF-d_8) δ 17.3, 30.8, 33.2, 36.6, 56.8, 113.5, 123.1, 123.2, 123.3, 123.4, 125.0, 127.5, 128.0, 128.8, 132.9–133.2 (m), 136.7, 136.8, 137.6, 138.6, 143.5, 143.8,

144.7, 146.5, 151.4, 151.45, 151.5, 151.6, 151.7, 151.9, 161.3; LD-MS obsd 750.7; FAB-MS obsd 750.3237, calcd 750.3209 ($C_{51}H_{42}MgN_4O$); λ_{abs} (toluene) 406, 428, 566, 607 nm.

20-(4-*tert*-Butylphenyl)-5-(4-ethylphenyl)-10-phenyl-15-(4-pyridyl)porphinatomagnesium(II) (IV-MgP-1e). Application of Method IV.4 with **IV-1e** (0.120 g, 0.150 mmol), DBU (0.225 mL, 1.50 mmol) and $MgBr_2$ (0.166 g, 0.450 mmol) in toluene (0.75 mL) with chromatographic workup [alumina, CH_2Cl_2/ethyl acetate → (3:1) → ethyl acetate → ethyl acetate/MeOH (80:1)] afforded a purple solid. The resulting product was washed with hexanes (5 mL x 3) to afford a purple solid (0.062 g, 57%): ^{1}H NMR (THF-d_8) δ 1.55 (t, J = 7.8 Hz, 3H), 1.64 (s, 9H), 3.05 (q, J = 7.8 Hz, 2H), 7.59 (d, J = 7.8 Hz, 2H), 7.73–7.75 (m, 3H), 7.82 (d, J = 7.8 Hz, 2H), 8.12–8.17 (m, 6H), 8.21–8.22 (m, 2H), 8.75–8.77 (m, 3H), 8.79–8.81 (m, 4H), 8.84–8.85 (m, 3H); ^{13}C NMR (THF-d_8) δ 16.4, 29.8, 32.3, 35.7, 118.8, 122.6, 123.0, 123.4, 124.1, 126.6, 127.1, 128.0, 130.76, 130.8, 130.9, 131.4, 131.5, 132.2, 132.5, 132.6, 132.8, 133.0, 135.8, 135.9, 142.4, 142.7, 144.0, 145.4, 148.5, 148.7, 149.5, 150.6, 150.7, 150.8, 151.0, 153.1; LD-MS obsd 721.9; calcd 721.3056 ($C_{49}H_{39}MgN_5$); insufficient solubility for FAB-MS; λ_{abs} (toluene) 407, 427, 525, 564, 605 nm.

20-(4-*tert*-Butylphenyl)-5-(4-methylphenyl)-15-pentyl-10-phenylporphinatomagnesium(II) (IV-MgP-2b). Application of Method IV.4 with **IV-2b** (0.059 g, 0.075 mmol), DBU (0.113 mL, 0.75 mmol) and $MgBr_2$ (0.0420 g, 0.225 mmol) in toluene (0.75 mL) with chromatographic workup [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (3:1) → (1:1)] afforded a purple solid (0.0196 g, 37%): ^{1}H NMR δ 0.99 (t, J = 7.2 Hz, 3H), 1.54–1.61 (s, 2H), 1.63 (s, 9H), 1.82–1.91 (m, 2H), 2.52–2.53 (m, 2H), 2.69 (s, 3H), 5.05–5.09 (m, 2H), 7.50 (d, J = 7.6 Hz, 2H), 7.24–7.74 (m, 5H), 8.09 (d, J = 7.2 Hz, 2H), 8.11 (d, J

= 7.6 Hz, 2H), 8.12–8.20 (m, 2H), 8.78–8.84 (m, 4H), 8.91–8.96 (m, 2H), 9.45– 9.54 (br, 2H); ^{13}C NMR δ 14.4, 21.7, 23.1, 32.0, 33.2, 35.1, 36.2, 39.5, 120.9, 121.0, 121.4, 122.2, 123.4, 126.4, 127.2, 128.8, 128.9, 131.8, 131.9, 132.1, 132.2, 132.5, 134.7, 134.8, 134.9, 136.7, 141.0, 141.1, 144.2, 149.5, 149.7, 149.8, 149.93, 149.97, 150.0, 150.4; LD-MS obsd 700.9; ESI-MS obsd 700.3410, calcd 700.3409 ($C_{48}H_{44}MgN_4$); λ_{abs} (toluene) 407, 428, 566, 607 nm.

20-(4-*tert*-Butylphenyl)-5-(4-methylphenyl)-15-(pentafluorophenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-2c). Application of Method IV.4 with **IV-2c** (0.067 g, 0.075 mmol), DBU (0.113 mL, 0.750 mmol), and $MgBr_2$ (0.166 g, 0.450 mmol) in toluene (0.750 mL) with chromatographic workup [alumina, CH_2Cl_2/ethyl acetate → (4:1) →CH_2Cl_2/ethyl acetate (1:1)] afforded the title porphyrin (0.025 g, 42%) and a more polar porphyrin (0.004 g, LD-MS obsd 947.0; 7% presumed yield). Data for **IV-MgP-2c**: ^{1}H NMR δ 1.66 (s, 9H), 2.70 (s, 3H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.72–7.77 (m, 5H), 8.08–8.13 (m, 4H), 8.20–8.21 (m, 2H), 8.73–8.77 (m, 2H), 8.83–8.89 (m, 4H), 8.92–8.98 (m, 2H); ^{13}C NMR δ 21.7, 31.9, 35.1, 122.3, 122.8, 123.5, 124.0, 126.5, 127.3, 127.4, 129.5, 129.6, 132.0, 132.3, 132.5, 132.6, 133.5, 133.8, 134.7, 134.8, 134.9, 137.1, 140.5, 140.7, 143.6, 145.2–145.6 (m), 148.4–148.9 (m), 149.3, 149.4, 150.1, 150.2, 150.22, 150.3, 150.7, 150.9; LD-MS obsd 797.0; ESI-MS obsd 796.24750, calcd 796.24703 ($C_{49}H_{33}F_5MgN_4$); λ_{abs} (toluene) 405, 426, 562, 604 nm.

20-(4-*tert*-Butylphenyl)-5-(4-methylphenyl)-15-(4-methoxyphenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-2d). Application of Method IV.4 with **IV-2d** (0.123 g, 0.150 mmol), DBU (0.225 mL, 1.50 mmol), and $MgBr_2$ (0.083 g, 0.45 mmol) in

toluene (1.5 mL) with chromatographic workup [alumina, CH_2Cl_2/ethyl acetate → (4:1) → (2:1)] afforded a purple solid (0.067 g, 60%): ^{1}H NMR δ 1.63 (s, 9H), 3.01(s, 3H), 4.06 (s, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.71–7.73 (m, 3H), 7.79 (m, 2H), 8.09–8.16 (m, 4H), 8.22–8.23 (m, 2H), 8.19–8.21 (m, 2H), 8.73–8.79 (m, 8H); ^{13}C NMR δ 21.7, 32.0, 35.1, 55.8, 112.0, 121.3, 121.5, 121.7, 122.0, 123.4, 126.4, 127.2, 128.8, 131.8, 131.9, 131.91, 131.96, 132.0, 132.1, 134.7, 134.88, 134.9, 135.8, 136.6, 136.7, 141.0, 141.1, 144.1, 149.9, 150.0, 150.3, 150.4, 158.9; LD-MS obsd 736.8; ESI-MS obsd 736.3047, calcd 736.3044 ($C_{50}H_{40}MgN_4O$); λ_{abs} (toluene) 407, 428, 565, 606 nm.

20-(4-*tert*-Butylphenyl)-15-[3-methoxy-3-oxopropyl]-5-(4-methylphenyl)-10-phenylporphinatomagnesium(II) (IV-MgP-2f). Application of Method IV.4 with **IV-2f** (0.115 g, 0.150 mmol), DBU (0.225 mL, 1.50 mmol), and $MgBr_2$ (0.083 g, 0.450 mmol) in toluene (1.5 mL) with chromatographic workup [alumina, CH_2Cl_2 → CH_2Cl_2/ethyl acetate → (3:1) → (2:1) → (1:1)] afforded the title porphyrin as a purple solid (0.020 g, 17%). A second more polar porphyrin eluted with ethyl acetate/MeOH (40:1) to give a purple solid (0.005 g, 5%). The latter was demetalated with TFA (0.007 mL) in CH_2Cl_2 (3.00 mL) followed by chromatography [silica, ethyl acetate/MeOH (30:1) → (15:1) → (5:1) → (3:1)] to give free base porphyrin 20-(4-*tert*-butylphenyl)-15-(2-carboxyethyl)-5-(4-methylphenyl)-10-phenylporphyrin **IV-P-2f-OH (**0.0042 g, 83%). Data for **IV-MgP-2f**: ^{1}H NMR δ 1.58–1.59 (s, 3H), 1.65 (s, 9H), 2.71 (s, 3H), 3.67–3.72 (m, 4H), 7.49–7.51 (m, 2H), 7.72–7.74 (m, 5H), 8.06–8.13 (m, 4H), 8.21–8.23 (m, 2H), 8.84–8.93 (m, 8H); LD-MS obsd 716.8; ESI-MS obsd 716.29964, calcd 716.29962 ($C_{47}H_{40}MgN_4O_2$); λ_{abs} (toluene) 407, 428, 567, 607 nm. Data for **IV-P-2f-OH**: ^{1}H NMR δ 0.86–1.12 (br, 2H), 1.28 (m, 9H), 2.63 (s, 3H), 3.62–3.68

(m, 4H), 6.67–7.02 (br, 2H), 7.42–7.45 (m, 3H), 7.62–7.65 (br, 2H), 7.85–7.89 (br, 4H), 8.24–8.28 (br, 2H), 8.45–8.58 (br, 5H), 9.24–9.26 (br, 3H) (the carboxylic acid proton was not observed); LD-MS obsd 680.6; ESI-MS obsd 680.31073, calcd 680.31458 ($C_{46}H_{40}N_4O_2$); λ_{abs} (toluene) 420, 517, 551, 595, 652 nm.

20-(4-*tert*-Butylphenyl)-5-(4-methylphenyl)-10-phenylporphinatozinc(II) (IV-ZnP-2h). Application of Method IV.4 with **IV-2h** (0.071 g, 0.10 mmol), DBU (0.150 mL, 1.00 mmol), and $Zn(OAc)_2$ (0.055 g, 0.30 mmol) in toluene (1 mL) afforded two products, which, on the basis of the absorption spectrum and LD-MS analysis, were assigned to the title porphyrin and the corresponding chlorin. The crude reaction mixture exhibited an enhanced absorption band at λ_{abs} = 620 nm. The reaction mixture was washed (water, brine), dried (Na_2SO_4) and concentrated. A solution of the crude product in toluene (63 mL) was treated with DDQ (0.027 g, 0.12 mmol, 1.2 equiv versus **IV-2h**) at 55 °C and stirred for 1 h, whereupon no chlorin was observed. The crude reaction mixture was washed (water, brine), dried (Na_2SO_4) and concentrated. Column chromatography [silica, CH_2Cl_2 → hexanes (3:1) → (2:1)] afforded a purple solid (0.016 g, 25%): ^{1}H NMR δ 1.63 (s, 9H), 2.71 (s, 3H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.75–7.78 (m, 5H), 8.09 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 8.21–8.23 (m, 2H), 8.95–8.97 (m, 1H), 8.98–8.99 (m, 2H), 9.02–9.03 (m, 2H), 9.08 (app d, *J* = 4.4 Hz, 1H), 9.30 (app d, *J* = 4.4 Hz, 2H), 10.12 (s, 1H); ^{13}C NMR δ 21.7, 32.0, 35.1, 105.8, 120.6, 121.0, 121.7, 121.8, 123.8, 126.8, 127.5, 127.7, 131.7, 131.8, 131.9, 132.2, 132.3, 132.7, 132.9, 134.6, 134.63, 134.8, 137.3, 139.8, 140.2, 143.0, 149.9, 150.0, 150.1, 150.13, 150.2, 150.3, 150.45, 150.5; LD-MS obsd 671.3; ESI-MS obsd 670.2069, calcd 670.2071 ($C_{43}H_{34}N_4Zn$); λ_{abs} (toluene) 418, 508, 544, 582 nm.

Pyridyl-Substituted Porphyrins (Method IV.5):

5-(4-Ethylphenyl)-10,15,20-tri-3-pyridylporphinatomagnesium(II) (IV-MgP-9b). Following Method IV.5, **IV-7-Br** (0.217 g, 0.500 mmol) and **IV-8b** (0.164 g, 0.500 mmol) gave a red-brown paste. The crude bilane was chromatographed (silica, THF). Although TLC analysis (silica, THF) revealed only one component (R_f = 0.51), the ^{1}H NMR spectrum showed the expected bilane together with an unidentified species. The crude bilane was treated with DBU (0.750 mL, 5.00 mmol) and $MgBr_2$ (0.276 g, 1.52 mmol) in toluene (5 mL) under microwave conditions followed by standard workup to afford a purple solid (27 mg, 8%): ^{1}H NMR (DMSO-d_6) δ 1.49 (t, J = 7.4 Hz, 3H), 2.98 (q, J = 7.4 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.86–7.89 (m, 3H), 8.06–8.16 (m, 2H), 8.58–8.66 (m, 3H), 8.74 (d, J = 4.4 Hz, 2H), 8.75–8.78 (m, 4H), 8.83 (d, J = 4.4 Hz, 2H), 9.00– 9.01 (m, 3H), 9.34–9.41 (m, 3H); ^{13}C NMR (DMSO-d_6) δ 15.6, 28.1, 117.3, 117.6, 122.1, 122.4, 125.9, 131.5, 131.8, 131.9, 132.5, 134.4, 138.8, 140.2, 140.6, 142.8, 148.6, 149.2, 149.3, 149.6, 152.9; LD-MS obsd 667.549; ESI-MS obsd 667.2330, calcd 667.2335 [$(M + H)^+$, M = $C_{43}H_{29}MgN_7$]; λ_{abs} (THF) 409, 430, 572, 613 nm.

5-(4-Ethylphenyl)-10,20-di-3-pyridyl-15-(4-pyridyl)porphyrin (IV-P-9c). Following Method IV.5, **IV-7-Br** (0.0550 g, 0.125 mmol) in dry THF/methanol (10 mL, 3:1) was treated with $NaBH_4$ (0.118 g, 3.13 mmol) to afford the corresponding carbinol. A sample of **IV-8c** (0.0410 g, 0.125 mmol) was added to a solution of the carbinol in anhydrous acetonitrile (0.25 mL). The crude reaction mixture was stirred at room temperature for 1 min, and $Yb(OTf)_3$ (0.036 g, 0.058 mmol) was added. The resulting mixture was stirred at room temperature for 4 h. The reaction mixture was neutralized with triethylamine

(0.02 mL), washed (water, brine), dried (K_2CO_3) and concentrated to afford a red paste. The crude bilane was treated with DBU (0.187 mL, 1.25 mmol) and $MgBr_2$ (0.069 g, 0.375 mmol) in toluene (1.25 mL) under microwave conditions followed by standard workup to afford the magnesium porphyrin. The demetalation procedure and column chromatography afforded the title porphyrin (14 mg, 17%) and the *trans*-A_2B_2-porphyrin 5,15-di-3-pyridyl-10,20-di-4-pyridylporphyrin (**IV-P-10c**, 5 mg, 7%). Data for the title porphyrin: ^{1}H NMR δ –2.84 (s, 2H), 1.52 (t, *J* = 7.7 Hz, 3H), 2.93 (q, *J* = 7.7 Hz, 2H),7.58 (d, *J* = 7.8 Hz, 2H), 7.73–7.76 (m, 2H), 8.10 (d, *J* = 6.8 Hz, 2H), 8.15 (d, *J* = 4.8 Hz, 2H), 8.50 (d, *J* = 7.8 Hz, 2H), 8.78 (d, *J* = 4.8 Hz, 2H), 8.82–8.84 (m, 4H), 8.94 (d, *J* = 4.8 Hz, 2H), 9.02–9.04 (m, 4H), 9.44–9.46 (m, 2H); ^{13}C NMR δ 15.9, 29.1, 116.6, 117.0, 122.2, 122.3, 126.6, 129.6, 131.1–131.5 (br), 134.9, 138.2, 139.1, 141.1, 144.3, 148.5, 149.5, 150.3, 153.8; LD-MS obsd 645.4; ESI-MS obsd 645.2636, calcd 645.2641 ($C_{43}H_{31}N_7$); λ_{abs} (THF) 417, 513, 547, 591, 647 nm. Data for **IV-P-10c**: ^{1}H NMR δ –2.91 (s, 2H), 7.74–7.77 (m, 2H), 8.15 (d, *J* = 4.4 Hz, 4H), 8.49–8.51 (m, 2H), 8.84–8.85 (m, 8H), 9.03–9.06 (m, 6H), 9.43–9.47 (m, 2H); ^{13}C NMR δ 117.0, 117.9, 122.3, 129.6, 131.2–131.8 (br), 137.7, 141.1, 148.7, 149.6, 150.1, 153.8; LD-MS obsd 618.3; ESI-MS obsd 618.22803, calcd 618.22804 ($C_{40}H_{26}N_8$); λ_{abs} (THF) 416, 512, 546, 589, 645 nm.

10-(4-Ethylphenyl)-5-(3-pyridyl)-15-(4-pyridyl)-20-(2-pyridyl)porphyrin (IV-P-9d). Following Method IV.5, **IV-7-Br** (0.0550 g, 0.125 mmol) in dry THF/methanol (10 mL, 3:1) was treated with $NaBH_4$ (0.118 g, 3.13 mmol, 25.0 mol equiv) to afford the corresponding carbinol. A sample of **IV-8d** (0.0410 g, 0.125 mmol) was added to a solution of the carbinol in anhydrous acetonitrile (0.25 mL). The crude reaction mixture was stirred

at room temperature for 1 min, and $Yb(OTf)_3$ (0.036 g, 0.058 mmol) was added. The resulting mixture was stirred at room temperature for 3 h. The reaction mixture was neutralized with triethylamine (0.020 mL), washed (water, brine), dried (K_2CO_3) and concentrated to afford a red paste. The crude bilane was treated with DBU (0.187 mL, 1.25 mmol) and $MgBr_2$ (0.0690 g, 0.375 mmol) in toluene (1.25 mL) under microwave conditions followed by standard workup to afford the magnesium porphyrin. The demetalation procedure and column chromatography afforded the title porphyrin (20 mg, 25%) and the *trans*-A_2B_2-porphyrin 5,15-di-4-pyridyl-10,20-di-2-pyridylporphyrin (**IV-P-10d**, 11 mg, 14%). Data for the title porphyrin: ^{1}H NMR δ –2.84 (s, 2H), 1.52 (t, *J* = 7.7 Hz, 3H), 2.99 (q, *J* = 7.7 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.73–7.76 (m, 2H), 8.11 (d, *J* = 7.6 Hz, 2H), 8.13–8.16 (m, 3H), 8.23–8.26 (m, 1H), 8.49–8.52 (m, 1H), 8.77–8.83 (m, 4H), 8.87 (d, *J* = 4.4 Hz, 2H), 8.94 (d, *J* = 4.4 Hz, 2H), 9.02–9.04 (m, 3H), 9.12–9.14 (m, 1H), 9.44–9.45 (m, 1H); ^{13}C NMR δ 15.9, 29.1, 116.5, 117.2, 118.8, 122.1, 122.2, 122.8, 126.6, 129.7, 130.6, 131.4–131.6 (br), 134.8, 135.2, 138.2, 139.1, 141.2, 144.2, 148.5, 148.9, 149.3, 150.5, 153.8, 160.6; LD-MS obsd 645.5; ESI-MS obsd 645.2638, calcd 645.2641 ($C_{43}H_{31}N_7$); λ_{abs} (THF) 417, 513, 546, 589, 645 nm. Data for **IV-P-10d**: ^{1}H NMR δ –2.89 (s, 2H), 7.72–7.75 (m, 2H), 8.10–8.16 (m, 6H), 8.24 (d, *J* = 8.0 Hz, 2H), 8.82–8.89 (m, 8H), 9.02–9.04 (m, 4H), 9.14 (d, *J* = 4.4 Hz, 2H); ^{13}C NMR δ 117.6, 119.6, 122.9, 129.7, 130.6, 131.2–131.8 (br), 135.2, 148.6, 149.0, 150.3, 160.4; LD-MS obsd 618.6; ESI-MS obsd 618.2281, calcd 618.2280 ($C_{40}H_{26}N_8$); λ_{abs} (THF) 415, 511, 544, 588, 644 nm.

Alkyl-Substituted Bilanes and Porphyrins (Method IV.6):

1-Bromo-15-ethyl-5,10-dipentyl-19-propionylbilane (IV-12a). Following Method

IV.6 with slight modification, a solution of **IV-11h-Br** (0.197 g, 0.500 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The standard workup procedure was followed. Acetonitrile (10 mL) was added to the crude product in ethyl ether (~30 mL). The resulting carbinol was concentrated until the ethyl ether was removed. The solution of **IV-11h-Br-OH** (in dry acetonitrile, ~10 mL containing residual ethyl ether) was treated first with **IV-11b** (0.115 g, 0.500 mmol) and then $Yb(OTf)_3$ (21 mg, 0.033 mmol, 3.3 mM) under argon. The reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography [silica, hexanes/ethyl acetate (2:1)] afforded a yellow paste (0.113 g, 37%), presumably as a mixture of 8 stereoisomers. The compound partially decomposed during attempted ^{1}H NMR spectroscopy in THF-d_8. ESI-MS obsd 629.2820, calcd 629.2825 [$(M + Na)^+$, M = $C_{34}H_{47}BrN_4O$].

5,10-Diethyl-15,20-dipentylporphinatomagnesium(II) (IV-MgP-12a). Application of Method IV.4 with **IV-12a** (0.061 g, 0.15 mmol), DBU (0.225 mL, 1.50 mmol) and $MgBr_2$ (0.083 g, 0.45 mmol) in toluene (1.5 mL) with chromatographic workup afforded a purple solid (0.013 g, 16%): ^{1}H NMR (THF-d_8) δ 1.15–1.59 (m, 6H), 1.82–1.86 (m, 5H), 2.14–2.16 (m, 7H), 2.51–2.59 (m, 6H), 4.97–5.04 (m, 8H), 8.48–9.52 (br, 8H); ^{13}C NMR δ 14.5, 23.1, 23.5, 29.3, 33.2, 36.2, 39.4, 120.1, 121.3, 128.8, 128.9, 129.0, 129.04, 149.1, 149.4; LD-MS 527.4; ESI-MS obsd 528.3085, calcd 528.3097 ($C_{34}H_{40}MgN_4$); λ_{abs} (toluene) 408, 428, 575, 615 nm.

1-Bromo-5,10-diethyl-19-propionylbilane (IV-12b). Following Method IV.6 with slight modification, a solution of **IV-11b-Br** (0.155 g, 0.500 mmol) in dry THF/methanol(40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The standard workup procedure was

followed. Acetonitrile (10 mL) was added to the crude product in ethyl ether (~30 mL). The resulting carbinol was concentrated until the ethyl ether was removed. The solution of **IV-11b-Br-OH** (in dry acetonitrile, ~10 mL containing residual ethyl ether) was treated first with **IV-11a** (0.101 g, 0.500 mmol) and then $Yb(OTf)_3$ (21 mg, 0.033 mmol, 3.3 mM) under argon. The reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography afforded a brown paste (0.213 g, 86%), presumably as a mixture of 4 stereoisomers: ^{1}H NMR (300 MHz) (THF-d_8) δ 0.81 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 1.51–1.57 (m, 3H), 3.38–3.43 (m, 2H), 2.39 (q, J = 7.5 Hz, 2H), 3.75 (q, J = 7.5 Hz, 2H), 5.36–5.45 (m, 5H), 5.46–5.49 (m, 2H), 5.54–5.56 (m, 2H), 5.59–5.61 (m, 1H), 5.49–5.57 (m, 1H), 6.75–6.79 (m, 1H), 8.71–8.79 (br, 1H), 9.02–9.11 (m, 1H), 9.74–9.81 (br, 1H), 10.48–11.51 (br, 1H); the compound decomposed during attempted ^{13}C NMR spectroscopy in THF-d_8; MALDI-MS (POPOP) obsd 492.3, 493.3, 494.3, 495.3 calcd 494.16812 ($C_{26}H_{31}BrN_4O$); ESI-MS obsd 517.1574, calcd 517.1573 [$(M + Na)^+$, M = $C_{26}H_{31}BrN_4O$].

1-Bromo-5,10-dipentyl-19-propionylbilane (IV-12c). Following Method IV.6 with slight modification, a solution of **IV-11h-Br** (0.197 g, 0.500 mmol) in dry THF/methanol (40 mL, 3:1) was treated with $NaBH_4$ (0.473 g, 12.5 mmol). The standard workup procedure was followed. Acetonitrile (10 mL) was added to the crude product in ethyl ether (~30 mL). The resulting carbinol was concentrated until the ethyl ether was removed. The solution of **IV-11h-Br-OH** (in dry acetonitrile, ~10 mL containing residual ethyl ether) was treated first with **IV-11a** (0.101 g, 0.500 mmol) and then $Yb(OTf)_3$ (21 mg, 0.033 mmol, 3.3 mM) under argon. The reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography [silica, hexanes/ethyl acetate (2:1)] afforded a yellow

paste (0.178 g, 62%), presumably as a mixture of 4 stereoisomers: ^{1}H NMR (THF-d_8) δ 0.84–0.854 (m, 6H), 1.10 (t, J = 7.4 Hz, 3H), 1.19 (t, J = 7.2 Hz, 4H), 1.21–1.29 (br, 6H), 1.79–1.88 (br, 2H), 2.67 (q, J = 7.2 Hz, 2H), 3.74–3.79 (m, 2H), 3.83–3.86 (m, 2H), 5.65–5.68 (m, 5H), 5.73–5.75 (m, 2H), 5.80–5.83 (m, 2H), 5.85–5.88 (m, 2H), 6.72–6.75 (m, 1H), 9.05–9.04 (br, 1H), 9.31–9.37 (m, 1H), 10.11–10.14 (br, 1H), 10.65–10.72 (br, 1H); the compound decomposed during attempted ^{13}C NMR spectroscopy in THF-d_8; ESI-MS obsd 601.2508 calcd 601.2512 [$(M + Na)^+$, M = $C_{32}H_{43}BrN_4O$].

5-Ethyl-10,15-dipentylporphyrin (IV-P-12c). Application of Method IV.6 with **IV-12c** (0.030 g, 0.052 mmol), DBU (0.078 mL, 0.52 mmol), and $MgBr_2$ (0.0290 g, 0.156 mmol) in toluene (0.5 mL) afforded a crude product. Demetalation of the crude product was followed by chromatographic workup [silica, hexanes/CH_2Cl_2 (1:2)] to afford a purple solid (0.0043 g, 16%): ^{1}H NMR δ –2.89 (s, 2H), 0.93–0.99 (m, 6H), 1.56–1.59 (m, 4H, overlapped with water signal), 1.73–1.84 (m, 4H), 2.11 (t, J = 7.4 Hz, 3H), 2.47–2.59 (m, 4H), 4.92–5.06 (m, 6H), 9.25–9.27 (m, 2H), 9.47–9.53 (m, 4H), 9.56–9.58 (m, 2H), 9.91 (s, 1H); MALDI-FT-ICR-MS obsd 479.30515, calcd 479.31747 [$(M + H)^+$, M = $C_{32}H_{38}N_4$]; λ_{abs} (toluene) 413, 513, 544, 591, 649 nm.

1-Bromo-10-butyl-5-ethyl-19-pentanoyl-15-propylbilane (IV-12d). Following Method IV.6, a solution of **IV-11d-Br** (0.084 g, 0.25 mmol) in dry THF/methanol (20 mL, 3:1) was treated with $NaBH_4$ (0.236 g, 6.25 mmol). The standard workup procedure was followed. A solution of **IV-11e** (0.068 g, 0.25 mmol) in acetonitrile (5 mL) was added to the carbinol solution in ethyl ether (~15 mL). Ether was removed, and $Yb(OTf)_3$ (10.0 mg, 0.0165 mmol, 3.30 mM) was added. The reaction mixture was stirred for 30 min at

room temperature. The standard work up and column chromatography afforded a brown paste (0.115 g, 78%), presumably as a mixture of 8 stereoisomers: ^{1}H NMR (THF-d_8) δ 0.82–0.93 (m, 12H), 1.26–1.40 (m, 8H), 1.59–1.66 (m, 2H), 1.83–1.93 (m, 6H), 2.65 (t, J = 7.6 Hz, 2H), 3.67 (t, J = 7.6 Hz, 1H; partially overlapped with the signal from THF), 3.77 (t, J = 7.6 Hz, 1H), 3.90–3.94 (m, 1H), 5.68–5.70 (m, 3H), 5.73–5.74 (m, 2H), 5.86–5.87 (m, 2H), 6.74–6.76 (m, 1H), 9.01–9.03 (br, 1H), 9.18–9.22 (m, 1H), 10.08–10.12 (br, 1H), 10.48–10.54 (br, 1H); ^{13}C NMR (THF-d_8) δ 12.9, 14.5, 14.6, 22.0, 23.6, 23.8, 28.5, 29.2, 31.1, 36.0, 36.1, 37.9, 38.4, 39.0, 39.2, 41.2, 96.3, 105.5, 105.6, 105.7, 107.6, 108.0, 110.1, 117.0, 132.3, 132.6, 132.7, 133.4, 134.3, 134.5, 137.2, 144.0, 189.5; ESI-MS obsd 592.27744, calcd 592.27767 ($C_{33}H_{45}BrN_4O$).

5,15-Dibutyl-10-ethyl-20-propylporphyrin (IV-P-12d). Application of Method IV.6 with **IV-12d** (0.0590 g, 0.100 mmol), DBU (0.150 mL, 1.00 mmol), and $MgBr_2$ (0.0550 g, 0.300 mmol) in toluene (1 mL) afforded a crude product. Demetalation of the crude product was followed by chromatographic workup [silica, hexanes/CH_2Cl_2 (1:1)] to afford a purple solid (0.011 g, 23%): ^{1}H NMR δ –2.68 (s, 2H), 1.11 (t, J = 7.6 Hz, 6H), 1.31 (t, J = 7.2 Hz, 3H), 1.77–1.82 (m, 4H), 2.10 (t, J = 7.6 Hz, 3H), 2.46–2.53 (m, 6H), 4.88–4.99 (m, 8H), 9.44–9.45 (m, 8H); ^{13}C NMR δ 14.1, 14.2, 15.0, 22.6, 22.7, 23.7, 28.8, 31.6, 35.2, 37.4, 40.8, 118.1, 118.4, 119.7, 128.0–128.1 (br); ESI-MS obsd 492.32554, calcd 492.32530 ($C_{33}H_{40}N_4$); λ_{abs} (toluene) 419, 521, 554, 602, 662 nm.

1-Bromo-10-butyl-5-ethyl-19-hexanoyl-15-propylbilane (IV-12e). Following Method IV.6, a solution of **IV-11d-Br** (0.253 g, 0.750 mmol) in dry THF/methanol (60 mL, 3:1) was treated with $NaBH_4$ (0.708 g, 18.8 mmol). The standard workup procedure was

followed. A solution of **IV-11f** (0.215 g, 0.750 mmol) in acetonitrile (15 mL) was added to the carbinol solution in ethyl ether (~45 mL). The ether was removed, and $Yb(OTf)_3$ (31.0 mg, 0.0495 mmol, 3.30 mM) was added. The reaction mixture was stirred for 30 min at room temperature. The standard workup and column chromatography afforded a brown paste (0.285 g, 63%), presumably as a mixture of 8 stereoisomers: ^{1}H NMR (300 MHz, THF-d_8) δ 0.81–0.91 (m, 12H), 1.26–1.33 (m, 8H), 1.59–1.66 (m, 2H), 1.77–1.90 (m, 6H), 2.51–2.52 (m, 2H), 2.63 (t, J = 7.6 Hz, 2H), 3.67 (t, J = 7.2 Hz, 1H), 3.77 (t, J = 7.2 Hz, 1H), 3.92 (t, J = 7.2 Hz, 1H), 5.67–5.68 (m, 3H), 5.72–5.74 (m, 2H), 5.86–5.87 (m, 2H), 6.73–6.74 (m, 1H), 9.01–9.04 (br, 1H), 9.16–9.22 (m, 1H), 10.04–10.12 (br, 1H), 10.42–10.51 (br, 1H); ^{13}C NMR (THF-d_8) δ 12.9, 14.5, 14.6, 21.9, 23.6, 23.7, 26.1, 29.1, 29.2, 31.1, 32.8, 36.1, 38.2, 38.3, 39.0, 39.2, 41.1, 96.3, 105.5, 105.6, 105.7, 107.6, 108.0, 110.1, 117.0, 132.3, 132.6, 132.7, 133.4, 134.3, 134.5, 137.2, 144.0, 189.5; ESI-MS obsd 606.29292, calcd 606.29333 ($C_{34}H_{47}BrN_4O$).

5-Butyl-10-ethyl-15-pentyl-20-propylporphyrin (IV-P-12e). Application of Method IV.6 with **IV-12e** (0.122 g, 0.200 mmol), DBU (0.300 mL, 2.00 mmol), and $MgBr_2$ (0.111 g, 0.600 mmol) in toluene (2 mL) afforded a crude product. Demetalation of the crude product was followed by chromatographic workup [silica, hexanes/CH_2Cl_2 (1:1)] to afford a purple solid (0.018 g, 18%): ^{1}H NMR δ –2.68 (s, 2H), 0.97 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.4 Hz, 3H), 1.32 (t, J = 7.2 Hz, 3H), 1.51–1.58 (m, 2H), 1.73–1.83 (m, 4H), 2.11 (t, J = 7.6 Hz, 3H), 2.44–2.56 (m, 6H), 4.87–4.99 (m, 8H), 9.44–9.45 (m, 8H); ^{13}C NMR δ 14.1, 14.5, 15.2, 22.9, 23.0, 23.9, 29.0, 31.8, 32.9, 35.5, 35.7, 37.6, 38.6, 41.0, 118.3, 118.57, 118.6, 119.9, 120.6–130.2 (br), 129.0, 131.1; ESI-MS obsd 506.34140, calcd 506.34095 ($C_{34}H_{42}N_4$); λ_{abs} (toluene) 419, 521, 554, 602, 662 nm.