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Investigation of Streamlined Syntheses of Porphyrins Bearing Distinct Meso Substituents

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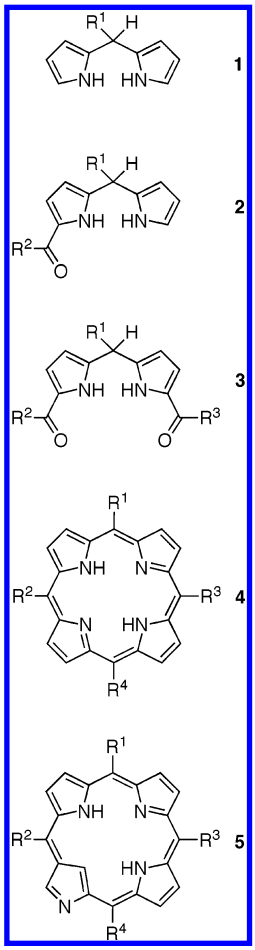
Abstract:

The use of porphyrins in fundamental studies and diverse applications requires facile access to ample quantities of material in pure form. The existing conditions for the condensation of a dipyrromethane plus a dipyrromethane−dicarbinol employ 2.5 mM reactants and afford ∼30% yields with no detectable scrambling. Large-scale syntheses require condensation and oxidation conditions that function at higher concentrations. Thirty-one acids (plus additives) have been examined for reactions at 25 mM reactants using the synthesis of a *trans*-A_2B_2-porphyrin as a model. The porphyrin was formed in ∼20% yield upon condensation in CH_2Cl_2 at room temperature using (1) $Sc(OTf)_3$ (3.2 mM) + 2,6-di-*tert*-butylpyridine (32 mM), or (2) $Zn(OTf)_2$ (10 mM). Nine porphyrins were prepared in this manner in yields of 15−22% with no detectable scrambling, whereas three other porphyrins afforded low levels of scrambling and/or lower yields (8−14%). Conditions for the oxidation also have been investigated. The reaction of 5-mesityldipyrromethane and the dicarbinol derived from 1-(4-methoxybenzoyl)-9-(4-methylbenzoyl)-5-phenyldipyrromethane (18 mmol each in 720 mL of CH_2Cl_2; 25 mM) with catalysis by $Sc(OTf)_3$/2,6-di-*tert*-butylpyridine and aerobic oxidation [(t-$Bu_4FePc)_2O$ and DDQ, 2.5 mol % each with a stream of O_2] afforded 2.88 g (22.8% yield) of the corresponding ABCD-porphyrin. The present synthesis (25 mM), at 4.5-times larger scale than the largest prior analogous synthesis (2.5 mM reactants with stoichiometric use of DDQ), afforded 4.0 times as much porphyrin on a molar basis while employing about one-half the amount of solvent and $<^1/_{25}$ the amount of DDQ. A three-step one-flask process also was developed that employs (i) condensation at 25 mM reactants, (ii) aerobic oxidation, and (iii) metal insertion to afford the metalloporphyrin [Mg(II), Ni(II), Cu(II), Zn(II), Pd(II)] in a streamlined manner. Taken together, the various improvements facilitate gram-scale syntheses of diverse porphyrins.

Introduction

Porphyrins bearing meso substituents are crucial building blocks in biomimetic and materials chemistry. The quantity of such porphyrins that can be readily obtained is closely tied to the availability of the corresponding precursors, including dipyrromethanes (**1**), 1-acyldipyrromethanes (**2**), and 1,9-diacyldipyrromethanes (**3**) (Chart 1). Symmetrical 1,9-diacyldipyrromethanes serve as precursors to A_3B-, *trans*-A_2B_2-, and *trans*-AB_2C-porphyrins, whereas unsymmetrical

Chart 1



1,9-diacyldipyrromethanes are precursors for *cis*-A_2B_2-, *cis*-A_2BC-, and ABCD-porphyrins (**4**). Simple procedures are now available for the preparation of dipyrromethanes,[1] 1-acyldipyrromethanes,[2] and 1,9-diacyldipyrromethanes[3,4] at high concentration and in ≥10−20-g quantities with limited or no chromatography. On the other hand, the porphyrin-forming reaction is carried out in dilute solution, employing 2.5 mM each of a dipyrromethane and a dipyrromethane−dicarbinol.[5] Consequently, a 100-mL reaction that proceeds

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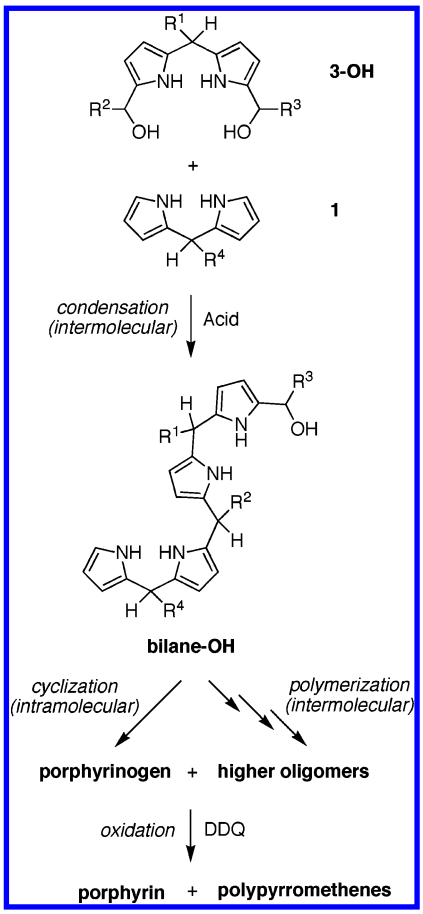
10.1021/op050193g CCC: $33.50

Scheme 1



in 30% yield would afford only 60 mg of a porphyrin having a molecular weight of 800 Da.

There are two considerations that have led to the use of dilute-solution conditions in the porphyrin-forming reaction, both of which have a bearing on the acid-catalyzed condensation rather than the oxidation step of the overall process:

The first consideration lies in the competition between cyclization and polymerization that is inherent in the "2 + 2" condensation of a dipyrromethane plus a dipyrromethane−dicarbinol. The first step yielding the bilane is an intermolecular process, which increases in rate with increasing concentration. The second step entails intramolecular cyclization of the bilane to give the porphyrinogen, which is in competition with intermolecular condensation to give higher oligomers (Scheme 1). Given that one intermolecular reaction precedes intramolecular cyclization, and the latter is in competition with continued intermolecular polymerization, it is expected that the highest yield of the porphyrinogen would be observed at modest concentrations.[6,7] This expectation has been observed in the pyrrole + aldehyde condensation, where analogous cyclization/polymerization issues also are extant. Studies of the room-temperature pyrrole + aldehyde condensation[8,9] as a function of concentration revealed that (1) the highest yield of porphyrin is achieved upon condensation at ∼10 mM reactants,[6] (2) increasing the concentration (>10 mM) of reactants while keeping the concentration of acid fixed (at the value found optimal for 10 mM reactants) results in a decline in yield,[6] and (3) the decline in yield with increasing concentration of reactants can be mitigated partially by a commensurate increase in acid concentration.[10,11]

The second consideration lies in the challenge of identifying acid-catalysis conditions that afford condensation without altering the integrity of the pattern of meso substituents in the reacting components. The substituent patterns of a dipyrromethane or a dipyrromethane−carbinol are vulnerable upon exposure to acid.[12] Indeed, acidolysis of dipyrromethane, dipyrromethane−dicarbinol, or polypyrrane species followed by undesired recombination of the fragmentation products (to form undesired polypyrrane or porphyrinogen species) leads to a mixture of porphyrin products.[13] Such "scrambling" processes must be expressly avoided in any rational synthesis of porphyrins. Given the difficulty of separating mixtures of porphyrins, preventing scrambling is generally a more important objective in porphyrin chemistry than achieving a high yield of reaction.

After lengthy study, two sets of conditions were identified that afford no detectable scrambling in the condensation of a dipyrromethane + a dipyrromethane−dicarbinol (or the self-condensation of a dipyrromethane-1-carbinol): (1) condensation in CH_3CN containing TFA at room temperature[5,14] and (2) condensation in CH_2Cl_2 containing a mild Lewis acid [($Yb(OTf)_3$, $Dy(OTf)_3$, $Sc(OTf)_3$, or $InCl_3$] at room temperature.[15] The latter conditions afford modest yield (15−40%) and convenient workup. However, both conditions were identified for condensation with 2.5 mM reactants, a concentration chosen to give identical concentrations of pyrrolic species as in the 10 mM pyrrole + aldehyde condensation. Although the reactions generally proceed with no detectable scrambling, such a modest reaction concentration crimps applications where sizable quantities of porphyrins are required.

In this contribution we describe the investigation of conditions for the synthesis of meso-substituted porphyrins at concentrations higher than those employed previously. The use of high concentrations of reactants (dipyrromethane and dipyrromethane−dicarbinol) lessens solvent consumption and the time required for reaction workup. A lengthy study has been performed of the acid-catalyzed condensation of a dipyrromethane + dipyrromethane−dicarbinol to achieve the highest possible yield without detectable scrambling. The

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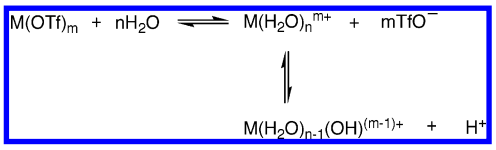
distribution of products [porphyrin and *N*-confused porphyrin (**5**, Chart 1)] also has been characterized. In addition to studies of the acid-catalyzed condensation, conditions for the oxidation as well as in situ metalation to afford the metalloporphyrin have been investigated. Taken together, the procedures described herein enable more rapid and facile preparation of meso-substituted porphyrins bearing distinct patterns of substituents.

Results and Discussion

I. Acid-catalysis Conditions at Higher Concentration. I.A. Background. Our approach was guided by studies of the pyrrole + aldehyde condensation, where the yield declined by less than 2-fold upon a 10-fold increase (from 10 to 100 mM) in reactant concentration and use of commensurably higher concentrations of acid.[10,11] Accordingly, we chose 25 mM as the target concentration for the dipyrromethane + dipyrromethane−dicarbinol reaction, which corresponds to a 100 mM pyrrole + aldehyde condensation. In seeking to identify acid catalysis conditions suitable for the 25 mM condensation, avoiding scrambling (which is not an issue in the pyrrole + aldehyde condensation) was of paramount concern.

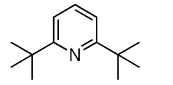
The mechanism of acidolytic scrambling is believed to proceed by protonation of a dipyrromethane species, liberating the pyrrole and an azafulvene species, which upon undesired recombination can yield scrambled porphyrin products.[13,16] In principle, such protonation cannot occur upon strict Lewis acid catalysis. In practice however, the use of a Lewis acid is often accompanied by Brønsted acid catalysis owing to the presence of water in the reaction mixture.[17] The formation of a Brønsted acid catalyst is shown in Scheme 2.[18] The concentration of H_2O in reagent-grade CH_2Cl_2 typically is ∼8−10 mM.[19] While the residual water in CH_2Cl_2 can be removed in a variety of ways, the presence of water in the reaction mixture is not easily avoided in a condensation; for example, for 25 mM reactants the concentration of water formed upon complete condensation is 50 mM.

Scheme 2



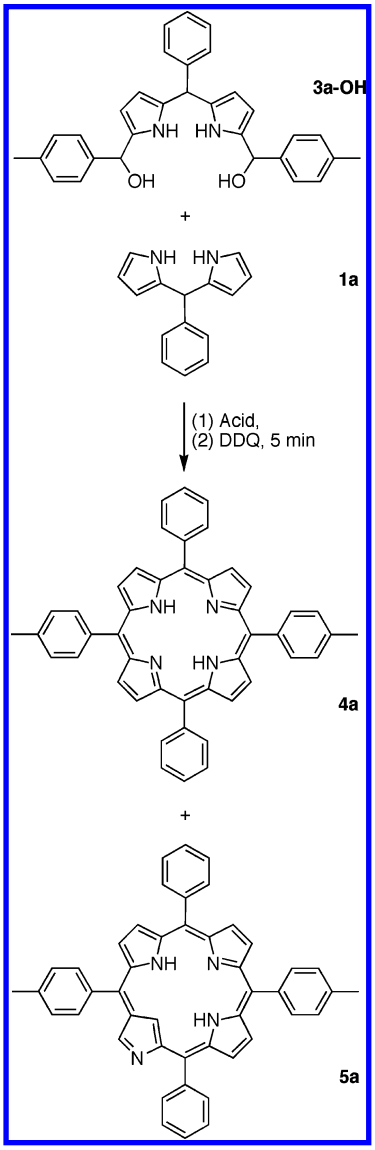
Two approaches to suppress acidolysis in a Lewis-acid-catalyzed dipyrromethane condensation entail the inclusion of a Brønsted-acid scavenger such as 2,6-di-*tert*-butylpyridine[20] (DTBP, Chart 2), or the inclusion of a desiccant such as molecular sieves. The former has been employed to good effect in porphyrin chemistry.[21] In principle, molecular sieves also should be quite effective, but complications can arise, given that molecular sieves are typically composed of aluminosilicates, which can function as acid buffers (i.e., ion-exchange resins). Both approaches were investigated herein.

Chart 2



2,6-di-*tert*-butylpyridine
(DTBP)

Scheme 3



I.B. Survey. A survey of acid catalysts was carried out using the model reaction of 5-phenyldipyrromethane (**1a**) and the dicarbinol derived from 5-phenyl-1,9-di-*p*-toluoyldipyrromethane (**3a-OH**) at 25 mM each in CH_2Cl_2 at room temperature (Scheme 3). The reactions were monitored over time (1, 5, 15, 60, and 90 min) by removing an aliquot, oxidizing the aliquot with DDQ, and collecting the absorption spectrum of the oxidized sample to determine the spectro-

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Table 1. **Survey of diverse acids in the condensation of 1a + 3a-OH (25 mM each in CH_2Cl_2)**

entry	acid (mM)[a]	additive (mM)	time (min)	% yield (scrambling level)[b]	entry	acid (mM)[a]	additive (mM)	time (min)	% yield (scrambling level)[b]
1	BF_3•OEt_2 (10)	−	1	26 (3)	25	AgOTf (10)	−	90	7
2	BF_3•OEt_2 (10)	NaCl (625)	1	26 (3)	26	$InCl_3$ (10)	−	5	12 (1)
3	$MgBr_2$ (10)	−	90	6	27	$InBr_3$ (3.2)	−	15	17 (2)
4	$Mg(OTf)_2$ (10)	−	90	7	28	$In(OTf)_3$ (10)	−	15	22 (2)
5	TMSOTf (10)	−	1	26 (2)	29	$SnCl_4$ (25)	Et_3N (100)	90	9
6	TMSOTf (10)	DTBP (25)	5	7	30	$SnCl_2$ (10)	−	90	3
7	TMSOTf (50)	DTBP (125)	5	13	31	$Sn(OTf)_2$ (3.2)	−	15	20
8	$CaCl_2$ (10)	−	60	1	32	$Sn(OTf)_2$ (10)	−	1	25 (1)
9	$Sc(OTf)_3$ (3.2)	−	15	20 (0)	33	$Sn(OTf)_2$ (10)	MS 4Å[d]	1	20 (0)
10	$Sc(OTf)_3$ (10)	−	5	22 (0)	34	$Sn(OTf)_2$ (25)	DTBP (250)	1	13 (0)
11	$FeBr_3$ (10)	−	15	17 (2)	35	$La(OTf)_3$ (10)	−	90	3
12	$Fe(ClO_4)_3$ (10)	−	15	20 (2)	36	$Sm(OTf)_3$ (10)	−	15	16 (0)
13	$CuCl_2$ (25)	−	15	22 (2)	37	$Eu(OTf)_3$ (10)	−	60	16 (0)
14	CuOTf (10)	−	15	13	38	$Dy(OTf)_3$ (10)	−	15	16 (2)
15	$Cu(OTf)_2$ (10)	−	60	19 (0)	39	$Yb(OTf)_3$ (3.2)	−	60	18 (2)
16	−	NH_4Cl (250)	90	6	40	$Yb(OTf)_3$ (10)	−	60	22
17	−	Bu_4NCl (10)	90	ND[c]	41	$Yb(OTf)_3$ (32)	−	15	22 (0)
18	$ZnCl_2$ (10)	Bu_4NCl (10)	90	2	42	$Hf(OTf)_4$ (3.2)	−	60	24
19	$Zn(OTf)_2$ (10)	−	60	22 (0)	43	$Hf(OTf)_4$ (10)	−	1	25 (2)
20	$Zn(OTf)_2$ (10)	Bu_4NCl (10)	60	10	44	$BiCl_3$ (10)	−	90	11
21	$Zn(OTf)_2$ (10)	Ph_4NCl (10)	60	9	45	$Bi(OTf)_3$ (1.0)	−	5	24 (1)
22	$Ga(OTf)_3$ (10)	−	60	20 (3)	46	$Bi(OTf)_3$ (3.2)	−	5	29 (1)
23	$Y(OTf)_3$ (3.2)	−	15	20 (0)	47	$Bi(OTf)_3$ (3.2)	DTBP (32)	15	20 (0)
24	$Pd(OCOCF_3)_2$ (10)	−	90	4	48	$Bi(OTf)_3$ (10)		15	28 (2)
					49	ionic liquid[e]	−	90	7.4 (3)

[a] In this and subsequent tables, the quantity of acid is denoted by molarity even though the acid may not be completely dissolved [b] The yield and scrambling level[14] are reported for the data point collected at the time indicated. [c] Not detected. [d] The quantity of molecular sieves was 8-fold (w/w) relative to **3a-OH**. [e] The ionic liquid 3-butyl-1-(4-sulfobutyl)imidazolium triflate[28] was used in equal volume with CH_2Cl_2 as described for a pyrrole + aldehyde condensation.[25]

scopic yield of the reaction. The reactions also were monitored for scrambling by examination of reaction aliquots by laser-desorption mass spectrometry (LD-MS) using a scale from level 0 (no detectable scrambling) to level 4 (complete scrambling).[14] The combination of phenyl and *p*-tolyl substituents allows resolution of scrambled porphyrins upon LD-MS while minimizing steric and electronic differences. The yield of *N*-confused porphyrin was determined by HPLC.[22]

Thirty-one Lewis acids were screened with and without additives. The Lewis acids were chosen from three general categories, including (1) acids previously used in porphyrin synthesis,[15,23−25] (2) acids used in organic reactions such as condensations of carbonyl-containing compounds, and (3) acids that are water-stable such as rare-earth triflates and lanthanide triflates.[26] The additives include 2,6-di-*tert*-butylpyridine (DTBP), molecular sieves 4 Å or 3 Å, and a variety of salts. Salts have been found to serve as cocatalysts with BF_3•$O(Et)_2$ in pyrrole + aldehyde condensations.[19,27] Several salts, including an ionic liquid,[28] also were investigated as catalysts in the absence of Lewis acids.

The data are summarized in Table 1. The yield data reported are for the highest yield observed during the course of reaction. In some cases, the yields plateaued and remained constant over time, while in other cases the yields peaked and then declined. The constant yield over time typically was accompanied by little or no scrambling (level 0 or 1); on the other hand, any decline in yield over time typically was accompanied by a higher level of scrambling. The data from the acid screening enabled categorization of the acids:

(1) Acids with good yield (≥20%) but scrambling: BF_3•$O(Et)_2$, TMSOTf, $Fe(ClO_4)_3$, $CuCl_2$, $Ga(OTf)_3$, $In(OTf)_3$, $Hf(OTf)_4$, and $Bi(OTf)_3$.

(2) Acids with poor yield (<20%): $MgBr_2$, $Mg(OTf)_2$, $CaCl_2$, $FeBr_3$, CuOTf, $ZnCl_2$, $Pd(OCOCF_3)_2$, AgOTf, $InCl_3$, $InBr_3$, $SnCl_2$, $SnCl_4$, $La(OTf)_3$, $Dy(OTf)_3$, $BiCl_3$, and an ionic liquid (3-butyl-1-(4-sulfobutyl)imidazolium triflate).

(3) Acids with reasonable yield (∼15−20%) and no scrambling: $Sc(OTf)_3$, $Cu(OTf)_2$, $Zn(OTf)_2$, $Y(OTf)_3$, $Sn(OTf)_2$, $Sm(OTf)_3$, $Eu(OTf)_3$, and $Yb(OTf)_3$.

Three acids from the latter set [$Sc(OTf)_3$, $Zn(OTf)_2$, and $Sn(OTf)_2$] were selected for further study. A more in-depth study of the effects of various reaction parameters was carried out using $Sc(OTf)_3$, owing in part to its high solubility in CH_2Cl_2 versus that of $Zn(OTf)_2$ and $Sn(OTf)_2$. Unless stated otherwise, each reaction of **1a** + **3a-OH** (25 mM each) was carried out in CH_2Cl_2 containing 10 mM $Sc(OTf)_3$ at room temperature.

I.B.1. Amount of $Sc(OTf)_3$. The yield observed at 1 min increased with an increase in the amount of $Sc(OTf)_3$ from

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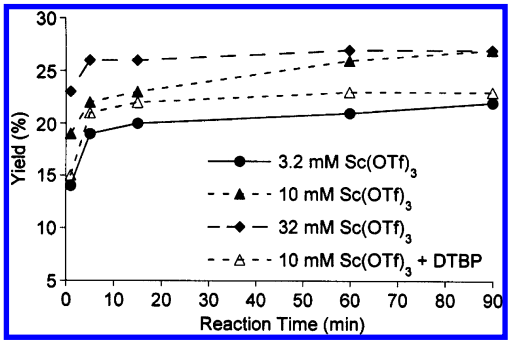

Figure 1. **Yield of porphyrin 4a as a function of time upon condensation of 1a + 3a-OH (25 mM each) under various acid catalysis conditions. One reaction with 10 mM $Sc(OTf)_3$ contained 100 mM DTBP (2,6-di-*tert*-butylpyridine). The reactions were performed in CH_2Cl_2 at room temperature. The yield of porphyrin was determined spectroscopically.**

3.2 to 32 mM (Figure 1). [The acid may not be entirely dissolved; however, the molarity term is used herein for ease of comparison with the concentration of reactants.]

I.B.2. Effect of a Proton Scavenger. The inclusion of DTBP had little effect on the rate or yield of reaction (Figure 1), and, again, scrambling was not detected. By contrast, the more dilute reaction at 2.5 mM reactants with a mild Lewis acid and DTBP gave a much slower rate than that without DTBP. The slower rate in the latter case was attributed to Lewis acid catalysis alone versus concurrent catalysis by the added Lewis acid and a Brønsted acid formed in situ.[21]

I.B.3. Temperature. The reaction at −78 °C give 17% yield after 5 min.

I.B.4. Other Additives. The inclusion of molecular sieves slowed the reaction and gave a lower yield. Other additives examined such as salts or the use of lower temperature gave either lower yields, or higher yields accompanied by scrambling (see Supporting Information).

I.B.5. Solvents. The acid $Sc(OTf)_3$ has been reported to function effectively in aqueous solutions.[18] The reaction was attempted in water containing a surfactant, as reported by Bonar-Law for pyrrole + aldehyde condensations,[29] but the yield was only 2%. Other solvents spanning a range of static dielectric constants (∼2−37 for toluene to acetonitrile) gave yields of <15% (see the Supporting Information).

In summary, the best conditions for porphyrin formation with $Sc(OTf)_3$ employ the acid at 3.25 or 10 mM and DTBP at 32.5 or 100 mM. The timecourse data for $Sc(OTf)_3$, $Sn(OTf)_2$, and $Zn(OTf)_2$ (including use of DTBP or molecular sieves) are listed in Table 2. $Sc(OTf)_3$ gave no detectable scrambling with DTBP even after 1 h of condensation, while with molecular sieves after 1 h there was level 1 scrambling (entries 1 and 2). On the other hand, $Sn(OTf)_2$ with molecular sieves gave no detectable scrambling even after 1 h, while $Sn(OTf)_2$ with DTBP gave level 1 scrambling after 1 h (entries 3 and 4). With $Zn(OTf)_2$, no additive was required for moderate yield with no detectable scrambling (entry 5).

I.C. Distribution of Porphyrins and *N*-confused Porphyrins. Condensations leading to porphyrins are known to give other pyrrolic macrocycles, including the corresponding *N*-confused porphyrin (i.e., **5**, Chart 1) and sapphyrin. In our prior studies of pyrrole + aldehyde condensations, the *N*-confused porphyrin was found to be a ubiquitous byproduct present in quantities one-fifth to one-tenth that of the porphyrin.[9,22,24]

Table 2. **Time course data for selected acids in the condensation of 1a + 3a-OH (25 mM each in CH_2Cl_2)[a]**

			% yield (scrambling level) at given times				
entry	acid[b]	additive	1 min	5 min	15 min	1 h	1.5 h
1	$Sc(OTf)_3$	DTBP[c]	15	22	22	23 (0)	23
2	$Sc(OTf)_3$	MS 4Å[d]	15	15 (0)	14	15 (1)	13
3	$Sn(OTf)_2$[e]	MS 4Å[d]	20 (0)	21	19	18 (0)	18
4	$Sn(OTf)_2$	DTBP[c]	9	11 (0)	10	11 (1)	11
5	$Zn(OTf)_2$	−	11	20 (0)	18	−	22 (0)

[a] Each reaction was performed at 25 mM reactants in CH_2Cl_2 at room temperature. [b] 10 mM each. [c] 100 mM. [d] The quantity of molecular sieves was 8-fold (w/w) relative to **3a-OH**. [e] Scrambling was detected when the reaction was carried out at 5-times larger scale.

We examined the amount of *N*-confused porphyrin formed under the new reaction conditions (25 mM reactants), where the yield of porphyrin was ∼20%. A small amount of *N*-confused porphyrin (<0.5%) was detected with each of the best acid-catalysis conditions (Table 3, entries 1−4). Note that the formation of the *N*-confused porphyrin does not stem from a scrambling process (i.e., the dipyrromethane and dipyrromethane−dicarbinol remain intact) but instead results from reaction at the β-position of the dipyrromethane. In addition, the amount of *N*-confused porphyrin formed in the prior, low-concentration (2.5 mM) conditions also was examined. The five conditions include the following: $Yb(OTf)_3$, $Dy(OTf)_3$, $Sc(OTf)_3$, or $InCl_3$ (in CH_2Cl_2);[15] or TFA in acetonitrile.[5] The yield of *N*-confused porphyrin had previously been examined upon catalysis with TFA (and found to be <1% after 1 h)[12] but not with the mild Lewis acids. In each of the five acid-catalysis conditions, the yield of porphyrin was ∼30%, whereas the yield of *N*-confused porphyrin was ≤1.4% (entries 5−9). Thus, the condensation performed at higher concentration (25 vs 2.5 mM) affords no increase in the yield of *N*-confused porphyrin. Regardless, *N*-confused porphyrins are more polar than the corresponding porphyrin and are readily removed by crystallization or passage of the crude reaction mixture over a pad of chromatographic media.

I.D. Semipreparative Synthesis. To confirm key analytical-scale experiments, semipreparative reactions were performed, and the yield of isolated porphyrin was determined. In each case, the reaction of **3a-OH** + **1a** was carried out with 0.25 mmol of each reactant (25 mM) in CH_2Cl_2 at room temperature. The reactions were monitored spectroscopically to determine when the condensation leveled off, and then DDQ was added, and the porphyrin product was purified.

I.D.1. The reaction in the presence of $Sc(OTf)_3$ (10 mM) and DTBP (100 mM) afforded porphyrin in a spectroscopic yield of 23% by 15 min. Upon filtration through a single alumina pad with CH_2Cl_2 elution, porphyrin **4a** was obtained in 21% yield with no detectable scrambling. Essentially identical results were obtained upon reaction at the 1 mmol scale using 3.25 mM $Sc(OTf)_3$ and 32.5 mM DTBP.

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Table 3. **Product distribution under various reaction conditions**[a]

entry	acid (mM)	additive	concentration, mM	time, min	% yield of **4a**	% yield of **5a**	scrambling (level)
1	$Sc(OTf)_3$ (3.2)	DTBP[b]	25	15	21	0.2	0
2	$Sc(OTf)_3$ (10)	DTBP[c]	25	15	22	0.3	0
3	$Sn(OTf)_2$ (10)	MS 4Å[d]	25	15	22	0.5	0
4	$Zn(OTf)_2$ (10)	-	25	15	18	0.3	0
5	$Yb(OTf)_3$ (3.2)	-	2.5	15	33	0.9	0
6	$Dy(OTf)_3$ (1.0)	-	2.5	60	31	0.8	0
7	$Sc(OTf)_3$ (0.32)	-	2.5	15	33	1.4	0
8	$InCl_3$ (0.32)	-	2.5	15	26	0.9	0
9	TFA (30)[e]	-	2.5	15	31	0.5	0

[a] All reactions were performed in CH_2Cl_2 unless noted otherwise. [b] 32 mM. [c] 100 mM. [d] The quantity employed was 8-fold (w/w) relative to **3a-OH**. [e] Performed in CH_3CN.

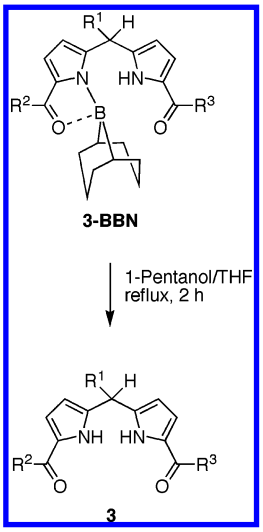
I.D.2. The reaction in the presence of $Sn(OTf)_2$ (10 mM) and molecular sieves (8-fold w/w with respect to **3a-OH**) and similar workup gave porphyrin **4a** in 19% yield with level 1 scrambling.

I.D.3. The reaction in the presence of $Zn(OTf)_2$ (10 mM) gave a spectroscopic yield of 22% after 15 min. Similar workup gave porphyrin **4a** in 21% yield with no detectable scrambling.

Thus, both $Sc(OTf)_3$ and $Zn(OTf)_2$ gave porphyrin **4a** in ~20% yield with no detectable scrambling. The isolation of the porphyrin was straightforward. No *N*-confused porphyrin was detected in the isolated porphyrin product upon HPLC analysis.

II. Scope of Application of Catalysis Conditions. The conditions using $Sc(OTf)_3$ (3.25 mM) and DTBP (32.5 mM) were applied to a wider array of dipyrromethane−dicarbinols and dipyrromethanes. In addition to the previously examined phenyl and *p*-tolyl groups, substituents included the more challenging cases of alkyl groups, electron-releasing groups, and substrates lacking substituents. Dipyrromethanes bearing distinct substituents including phenyl (**1a**),[1] 4-methoxyphenyl (**1b**),[1] pentafluorophenyl (**1c**),[1] 4-iodophenyl (**1d**),[30] no substituent (dipyrromethane itself, **1f**),[1] and mesityl (**1g**)[1] were prepared as described in the literature by reaction of an aldehyde with excess pyrrole under a refined procedure. The procedure entails solventless condensation in the presence of a mild Lewis acid (e.g., $InCl_3$) with workup that relies on crystallization (avoiding any aqueous−organic extraction or chromatography).[1] 5-(4-Methylphenyl)dipyrromethane (**1e**), prepared by earlier small-scale procedures with more cumbersome workup methods,[31,32] was prepared herein by the refined route at the 0.15 mol scale, affording 27 g of **1e** (76%) upon crystallization. Many of the requisite 1,9-diacyldipyrromethanes (**3**) have been prepared previously (**3a**,[4] **3c**,[5] and **3e**[33]), while others were previously obtained as the 9-BBN complexes (**3-BBN**). The latter (**3b-BBN**,[4] **3d-BBN**,[4] and **3f-BBN**−**3h-BBN**[4]) were decomplexed in a straightforward manner (Scheme 4). The structures of the various 1,9-diacyldipyrromethanes are conveyed in Table 4.

Scheme 4



The results of the condensations are shown in Table 4. The use of various dipyrromethane species enabled examination of 12 different substituents. Generally, the yields were in the 15−22% range with no detectable scrambling. Three exceptions occurred where lower yields were observed with dipyrromethane−dicarbinols bearing the following substituents: two anisyl groups (**3g**), a pentafluorophenyl group at the carbinol carbon (**3h**), or no meso substituent (**3f**). Reactions with the latter compounds provided the only instances where a trace of scrambling was observed, and the resulting porphyrin products were not fully characterized.

III. Oxidation Conditions. III.A. Bulk Oxidations with Quinones. One set of experiments was performed to examine whether a less-than-stoichiometric amount of DDQ could be employed without loss in yield. Given that DDQ is a $2e^-/2H^+$ acceptor, and the conversion of porphyrinogen → porphyrin requires removal of $6e^-/6H^+$, stoichiometry requires the use of 3 mol of DDQ per mol of porphyrinogen.[7] One porphyrinogen should be formed from each dipyrromethane + dipyrromethane−dicarbinol condensation. However, the porphyrinogen yield is typically ≤30%, with the preponderance of material consisting of acyclic products.[5,12] The extent to which reaction products other than the porphyrinogen would consume DDQ was not evident.

The condensation of **3a-OH** (0.175 mmol, 25 mM) and **1a** (0.175 mmol, 25 mM) was carried out with $Sc(OTf)_3$ (3.2

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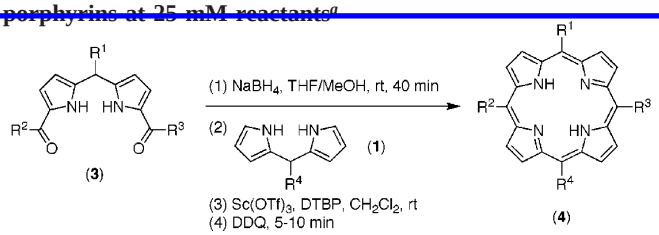
***Table 4.* Synthesis of a set of porphyrins at 25 mM reactants[a]**



R^1	R^2	R^3	Component **3**	R^4	Component **1**	Porphyrin	Yield (%)
Ph	Ph	Ph	**3a**	Ph	**1a**	**4a**	19
Ph	Ph	Ph	**3a**	4-OMePh	**1b**	**4b**	21
Ph	Ph	Ph	**3a**	2,3,5,6-tetrafluorophenyl	**1c**	**4c**	15
Ph	Ph	4-OMePh	**3b**	4-IPh	**1d**	**4d**	17
4-IPh	4-*t*-BuPh	4-*t*-BuPh	**3c**	Ph	**1e**	**4e**	19
n-pentyl	*n*-pentyl	Ph	**3d**	Ph	**1e**	**4f**	19
4-TMSethynylPh	3,5-di-*t*-BuPh	3,5-di-*t*-BuPh	**3e**	Ph	**1e**	**4g**	22
Ph	Ph	4-OMePh	**3b**	H	**1f**	**4h**	21
H	Ph	Ph	**3f**	Ph	**1a**	**4i**	14[b]
4-OMePh	4-OMePh	4-BrPh	**3g**	Ph	**1a**	**4j**	9
Ph	Ph	2,3,5,6-tetrafluorophenyl	**3h**	Ph	**1e**	**4k**	8[b]
Ph	Ph	4-OMePh	**3b**	2,3-dimethylphenyl	**1g**	**4l**	22.8[c]

[a] All reactions were carried out at room temperature in CH_2Cl_2 containing $Sc(OTf)_3$ (3.25 mM) and DTBP (32.5 mM) followed by oxidation with DDQ. The reaction scale ranged from 0.20 to 1.0 mmol of reactants. [b] Level 1 or level 0 scrambling. [c] The reaction was carried out with 18 mmol reactants, and aerobic oxidation was employed.

mM) and DTBP (32 mM) in CH_2Cl_2 (7 mL) at room temperature for 15 min. The reaction mixture was divided into seven portions. Each one-seventh portion of the crude reaction mixture was treated with a given quantity of DDQ. The yield of porphyrin increased linearly with the increasing amount of DDQ in the substoichiometric range until the stoichiometric quantity was reached. An increase above the stoichiometric quantity of DDQ caused no increase in yield (Figure 2). Accordingly, a stoichiometric amount of DDQ is required to quench the reactions and give full conversion of the porphyrinogen to the porphyrin.

The oxidation of porphyrinogen to porphyrin is most often performed with either *p*-chloranil or DDQ.[7] If the oxidant is added in the presence of the acid, the porphyrinogen is susceptible to acidolytic processes leading to scrambling until oxidation is accomplished. On the other hand, the presence of acid renders the quinone a more potent oxidant.[34] Thus, it was of interest to characterize the rate of oxidation with DDQ and *p*-chloranil, both in the presence of acid and in neutralized reaction mixtures (achieved by treatment with TEA, a stronger base than DTBP).

The condensation of **3a-OH** (0.10 mmol, 25 mM) and **1a** (0.10 mmol, 25 mM) was carried out with $Sc(OTf)_3$ (3.2 mM) and DTBP (32 mM) in CH_2Cl_2 (4 mL) at room temperature for 15 min. The reaction mixture was divided

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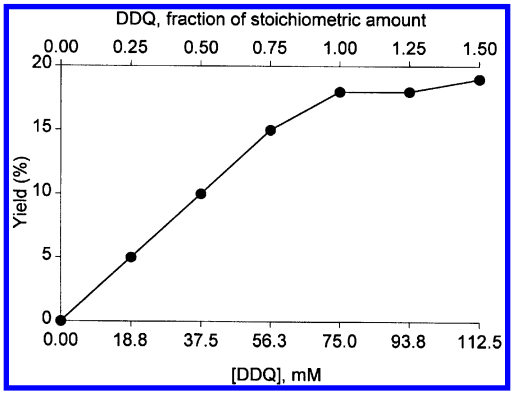

Figure 2. **Yield of porphyrin 4a as a function of the amount of DDQ used for oxidation. The corresponding porphyrinogen was obtained upon condensation of 1a + 3a-OH with $Sc(OTf)_3$ in the presence of DTBP. The reactions were performed in CH_2Cl_2 at room temperature, and the yield of porphyrin was determined spectroscopically. The concentrations are as follows: [1a] = [3a-OH] = 25 mM; [$Sc(OTf)_3$] = 3.2 mM; [DTBP] = 32 mM. The stoichiometric quantity of DDQ corresponds to a concentration of 75 mM.**

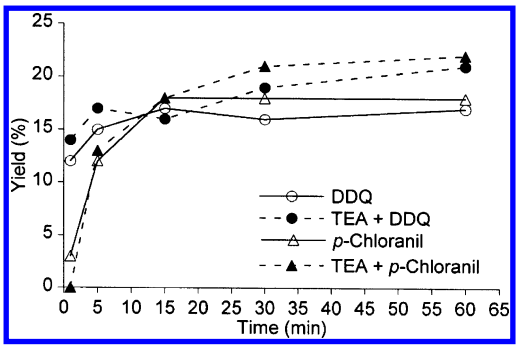

Figure 3. **Yield of porphyrin 4a as a function of time upon oxidation with DDQ or *p*-chloranil (with or without triethylamine). The corresponding porphyrinogen was obtained upon condensation of 1a + 3a-OH with $Sc(OTf)_3$ in the presence of DTBP in CH_2Cl_2 at room temperature. The condensation mixture was split into four portions. Each portion was treated to the oxidation conditions. Samples were removed periodically for spectroscopic determination of the yield of porphyrin. The concentrations are as follows: [1a] = [3a-OH] = 25 mM; [$Sc(OTf)_3$] = 3.2 mM; [DTBP] = 32 mM.**

into four portions. Two portions (each containing 0.025 mmol of each reactant) were treated with stoichiometric quantities of DDQ or *p*-chloranil (0.075 mmol). The other two portions were neutralized with 10 mol equiv of TEA (with respect to acid) followed by addition of DDQ or *p*-chloranil (0.075 mmol). Absorption spectroscopy for each reaction mixture was recorded over time. The results are shown in Figure 3. The addition of DDQ at room temperature gives a nearly instantaneous conversion of porphyrinogen to porphyrin. *p*-Chloranil is a milder oxidant,[10,35] requires a slightly longer exposure time for complete reaction, and affords a yield slightly higher than that of DDQ. Neutralization of the acid catalyst (by addition of TEA) prior to the addition of oxidant (DDQ or *p*-chloranil) caused no effect on the porphyrin yield, as observed previously in pyrrole + aldehyde condensations.[6] Accordingly, DDQ was employed to provide rapid quenching during exploratory studies of reaction conditions, and all reported data were obtained with DDQ unless noted otherwise.

III.B. Aerobic Oxidations. Aerobic oxidation processes are potentially superior to the use of stoichiometric oxidants from the standpoint of cost, environmental impact, and ease of workup. In a porphyrin synthesis, the diminished amount of quinone and hydroquinone byproducts in an aerobic oxidation process should facilitate workup of the reaction mixture. An efficient aerobic oxidation process for oxidation of secondary alcohols was developed by Bäckvall.[36−39] We adapted this process for use in porphyrin-forming reactions.[10] The process entails the use of catalytic quantities of DDQ and an iron phthalocyanine species; a steady stream of oxygen serves as the stoichiometric oxidant. Upon probing the iron phthalocyanine species, we found that (1) the μ-oxo dimer, not the parent iron(II) phthalocyanine, is the active species[40] and (2) little difference is observed with soluble versus insoluble μ-oxo dimers of iron phthalocyanine species.[40] The resulting aerobic oxidation process shown in Scheme 5 was implemented for the pyrrole + aldehyde reaction. In this application, an anaerobic condensation was performed at room temperature with pyrrole + benzaldehyde (0.1 M each) and 0.01 M $BF_3{\cdot}O(Et)_2$ in CH_2Cl_2 for 30 min; oxidation was then initiated by adding catalytic quantities of the μ-oxo dimer of the iron phthalocyanine and DDQ (typically 1−5 mol % each) as solid samples and by bubbling the mixture with air or O_2 for 90 min at room temperature.[10,40]

The only disadvantage to the established aerobic oxidation process was the slow rate of oxidation. Herein, we explored a broad set of alternative oxidation processes. A model system was developed that consisted of the $2e^-/2H^+$ oxidation of a dipyrromethane (e.g., **1a**) in the presence of zinc acetate, which affords the bis(dipyrrinato)zinc(II) complex. This model system was attractive for several reasons: (1) the dipyrromethane and dipyrrin represent three-eighths of a porphyrinogen and a porphyrin, respectively; (2) the dipyrromethane is a stable compound that can be prepared in bulk for oxidation studies; and (3) the absorption spectrum of the bis(dipyrrinato)zinc(II) complex is very sharp and distinct (ϵ_{483} = 115,000 M^{-1} cm^{-1}), unlike the very broad spectrum of the free base dipyrrin.[41] The systems studied included the following: CuCl·phenanthroline + diethyl azodicarboxylate;[42] $Pd(OAc)_2$/pyridine;[43] *N*-hydroxyphthalimide, benzoic

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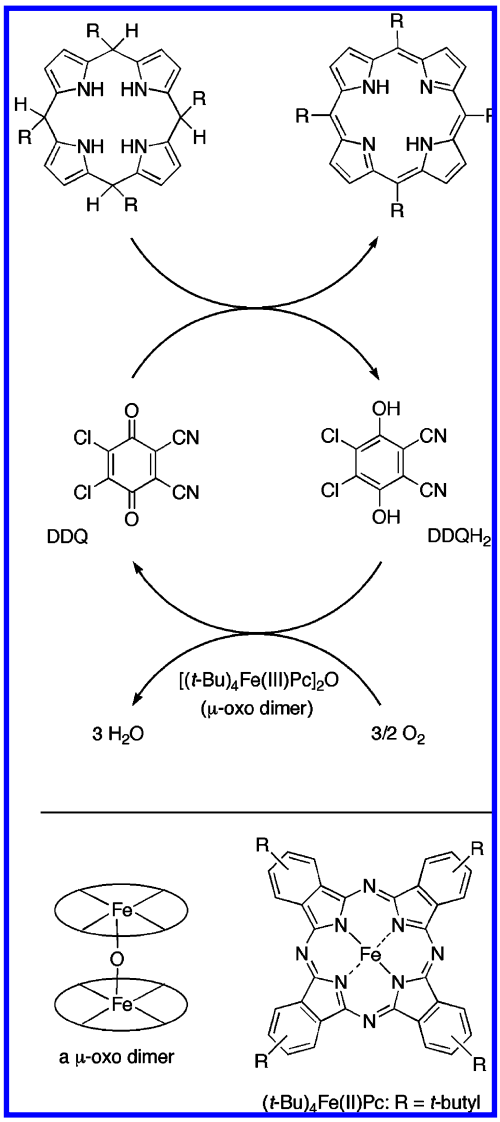
Scheme 5



acid and $Co(OAc)_2$;[44] 2,2,6,6-tetramethyl-piperidyl-1-oxy, $NaNO_2$ and 1,3-dibromo-5,5-dimethylhydantoin;[45] bis(salicylideniminato-3-propyl)methylaminocobalt(II) and DDQ;[46] and $Ru(PPh_3)_3Cl_2$, DDQ and K_2CO_3.[39,47,48] No improvement over the established aerobic oxidation system was achieved. We also explored the use of an inexpensive bulk chemical reagent [$Mn(OAc)_3$,[49] $FeCl_3$,[50] or PbO_2[51]] for recycling catalytic amounts of DDQ or *p*-chloranil. Although good results were obtained with PbO_2, this approach was decidedly unattractive from an environmental standpoint. These oxidation studies are described in the Supporting Information.

Accordingly, the established aerobic oxidation process was employed in conjunction with the reactions described herein. The condensation of **3a-OH** (0.50 mmol, 25 mM) and **1a** (0.50 mmol, 25 mM) was carried out with $Sc(OTf)_3$ (3.2 mM) and DTBP (32 mM) in CH_2Cl_2 (20 mL) at room temperature for 15 min. Oxidation was initiated by adding [(*t*-Bu)$_4$Fe(III)Pc]$_2$O (the μ-oxo dimer of (*t*-Bu)$_4$Fe(II)Pc) and DDQ (5 mol % each) as solid samples, followed by gently bubbling the mixture with O_2 for 90 min at room temperature. The reaction mixture was chromatographed, affording porphyrin **4a** (0.055 g, 17% yield). The yield in this preparation is comparable to that obtained with a stoichiometric amount of DDQ.

IV. Direct Synthesis of Metalloporphyrins. In many instances the synthetic target is a metalloporphyrin rather than a free base porphyrin. We explored treating the crude reaction mixture (following oxidation) with a metalation reagent, because (1) one purification process could be eliminated, and (2) the purification of metalloporphyrins often is more simple than that of free base porphyrins.

Metalation generally entails treatment of a free base porphyrin with a metal salt.[52] Although the specific conditions (solvent, temperature, presence of a base, duration) depend on the desired metal, a large number of metalloporphyrins can be prepared by reaction of the free base porphyrin with a metal acetate in a warm solvent. Other metals can be quite finicky. For example, magnesium insertion does not work well with magnesium acetate but can be achieved with a heterogeneous mixture of a reactive magnesium halide (e.g., $MgBr_2$ or MgI_2) and a nonnucleophilic amine in a noncoordinating solvent.[53]

Each condensation of **1a** + **3a-OH** was performed at 25 mM using $Sc(OTf)_3$ and DTBP in CH_2Cl_2 at room temperature for 15 min. The mixture was oxidized aerobically upon addition of catalytic amounts of [(*t*-Bu)$_4$FePc]$_2$O and DDQ followed by a steady stream of oxygen for 90 min. Then the reaction mixture was treated with the respective metalation reagent. Metalation with zinc or copper was achieved with methanolic $Zn(OAc)_2 \cdot 2H_2O$ or $Cu(OAc)_2 \cdot H_2O$, respectively, upon stirring overnight at room temperature. For metalation with palladium, the reaction mixture was concentrated, and then $Pd(O_2CCF_3)_2$[54] in 1,2-dichloroethane and methanol were added, and the mixture was heated at 45 °C for 1 h. For metalation with nickel, the reaction mixture was concentrated, then toluene and $Ni(acac)_2$ in toluene were added, and the mixture was refluxed overnight. For metalation with magnesium, MgI_2 and DIEA were employed in CH_2Cl_2 at room temperature.[53] The course of each reaction was monitored by TLC and fluorescence spectroscopy. In each case, after completion of the metalation only one porphyrinic

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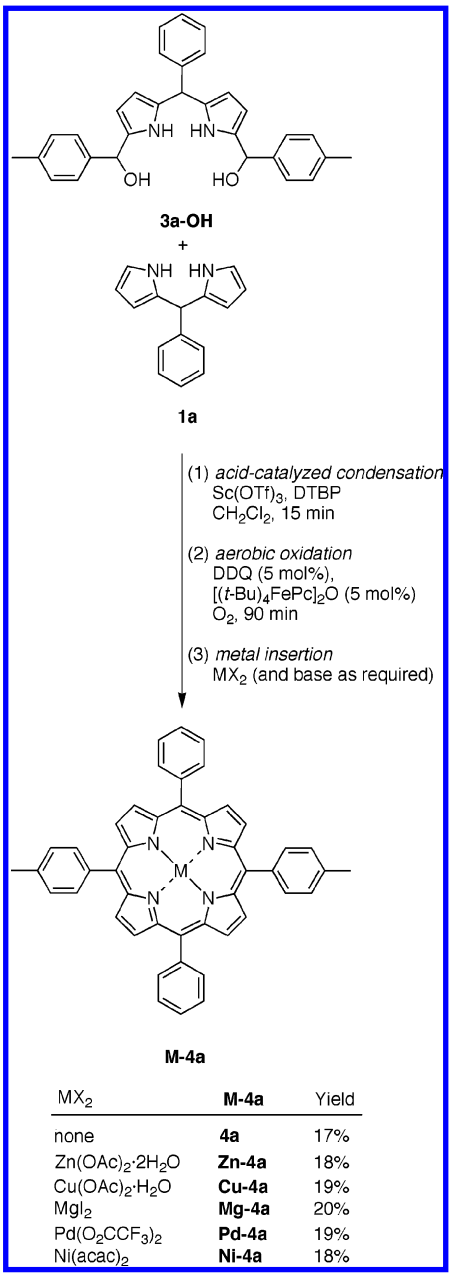
Scheme 6



MX_2	M-4a	Yield
none	**4a**	17%
$Zn(OAc)_2{\cdot}2H_2O$	**Zn-4a**	18%
$Cu(OAc)_2{\cdot}H_2O$	**Cu-4a**	19%
MgI_2	**Mg-4a**	20%
$Pd(O_2CCF_3)_2$	**Pd-4a**	19%
$Ni(acac)_2$	**Ni-4a**	18%

product was observed upon TLC analysis. The metalloporphyrin was easily isolated by chromatography in 18−20% overall yield (Scheme 6). This three-step one-flask synthesis provided the metalloporphyrin without isolation of the intermediate free base porphyrin.

V. Application. The synthesis of an ABCD-porphyrin was performed using the three-step procedure. Thus, the reaction of **3b-OH** and **1g** was carried out with 18.0 mmol of each reactant (25 mM, 720 mL of CH_2Cl_2) with catalysis by $Sc(OTf)_3$ (2.34 mmol) and DTBP (23.4 mmol). Aerobic oxidation was subsequently performed for 90 min using [(*t*-Bu)$_4$FePc]$_2$O and DDQ (2.5 mol % each) and a stream of O_2. Workup including passage over a short pad of silica afforded 2.88 g (4.11 mmol, 22.8% yield) of the corresponding porphyrin **4l** (molecular mass 701 Da). The porphyrin contained no detectable scrambled products or *N*-confused porphyrin. To our knowledge, the largest previous synthesis of an ABCD-porphyrin was carried out at the 4.00 mmol scale in 1600 mL of CH_3CN (2.5 mM) and proceeded in 25% yield with the use of a stoichiometric quantity of DDQ, affording 1.12 g (1.02 mmol, 1094 Da).[5] Thus, in comparison with this particular previous synthesis, the present synthesis at 4.5-times larger scale afforded 4.0-times as much porphyrin on a molar basis while requiring 0.45-times the amount of solvent and 0.0375-times the amount of DDQ.

Conclusions

The procedures described herein enable porphyrin synthesis by reaction of a dipyrromethane + dipyrromethane−dicarbinol at 25 mM in ∼20% yield with little or no scrambling. The acid catalysis conditions entail a mild Lewis acid catalyst at somewhat higher concentration than that for the 2.5 mM condensations examined previously. The acid catalysis conditions were identified by examination of a challenging substrate (i.e. one that is particularly sensitive to acidolysis). For less challenging substrates, other acid conditions may prove effective, including those described herein that were not examined for scale-up purposes. A very broad survey of aerobic oxidation catalysts did not identify a system superior to that employed previously, namely the use of a μ-oxo dimer of an iron phthalocyanine (either soluble or insoluble) and DDQ in catalytic quantities, accompanied by a stream of air or O_2. A three-step one-flask procedure encompassing (1) acid-catalyzed condensation of a dipyrromethane + dipyrromethane−dicarbinol, (2) aerobic oxidation of the resulting porphyrinogen, and (3) in situ metalation of the resulting free base porphyrin provides a streamlined approach for the rational synthesis of metalloporphyrins bearing a distinct pattern of substituents. The procedures outlined herein should provide the foundation for extensions to larger-scale syntheses of porphyrins, as required for fundamental studies and diverse applications.

Experimental Section

General. The following procedures were employed unless noted otherwise. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained in $CDCl_3$. Absorption spectra were collected in CH_2Cl_2/ethanol (3:1) for spectroscopic yield determinations or in THF for characterization of purified samples. The solvents were used as received from commercial sources, including THF (HPLC grade), CH_2Cl_2 (anhydrous or reagent-grade), and methanol (anhydrous). The oxygen employed for aerobic oxidation experiments was 99.5% (Medical grade, National Welders, Inc.). Porphyrin-forming reactions were carried out in anhydrous CH_2Cl_2.

The progress of the porphyrin-forming reactions was monitored spectroscopically,[6] and the extent of scrambling in the crude reaction mixture was determined by laser desorption ionization mass spectrometry (LD-MS) without a matrix as described previously.[14,55] A sonication bath (Fisher FS 14) was used to sonicate samples during purifica-

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tion. Melting points are uncorrected. Silica gel (40 μm average particle size) and alumina (80−200 mesh) were used for column chromatography.

Noncommercial Compounds. Dipyrromethanes **1a,b,c,f,g**[1] and **1d**[30] were prepared as described in the literature and analyzed for purity by gas chromatography.[1] Compounds **3a**, **3b-BBN**, **3d-BBN**, and **3f-BBN**−**3h-BBN**;[4] **3c**,[5] **3e**,[33] $Bi(OTf)_3$,[56] 3-butyl-1-(4-sulfobutyl)imidazolium triflate,[28] and $[(t\text{-}Bu)_4FePc]_2O$[40] were prepared as described in the literature.

Quantitation of *N*-Confused Porphyrin. The quantitation was carried out using HPLC analysis as described previously.[22] Shortly after DDQ oxidation, the samples were basified by addition of TEA (10-fold molar excess relative to acid). Addition of TEA was crucial for accurate detection of the *N*-confused porphyrin, otherwise the *N*-confused porphyrin was removed during the pre-HPLC sample cleanup. Strongly adsorbing black materials were removed prior to HPLC sample analysis by passing a carefully measured volume of the crude reaction mixture (1.5 mL for 2.5 mM reactions or 0.25 mL for reactions at 25 mM concentration) through a Pasteur pipet column packed with 1.4 g of activity II basic alumina (obtained by adding 3 mL of H_2O to 100 g of alumina with intermittent shaking). The sample was eluted with three 1-mL portions of CH_2Cl_2. Solvent was driven off the column by application of mild pressure using a handheld pipet bulb. The eluant was transferred immediately to an autosampler vial and capped.

HPLC analysis was performed using a silica gel analytical column (Econosphere, CN, 4.6 mm × 250 mm) with an isocratic solvent mixture of 92.5% hexanes (containing 0.1% TEA) and 7.5% acetone. The solvent flow rate was controlled as follows: 0−5 min, 1.0 mL/min; 5−7 min, linear increase to 2.5 mL/min; 7−10.5 min, 2.5 mL/min; 10.5−11.5 min, linear decrease to 1 mL/min; and 11.5−13 min, 1 mL/min. The solvent front occurred at 3.5 min, porphyrin **4a** eluted at 4.2 min, and *N*-confused porphyrin **5a** eluted at 6.6 min. Detection was performed at 417 nm for **4a**, and 438 nm for **5a**. The detection limits for **4a** and **5a** were 1 and 3 pmol, respectively. For 2.5 mM reactions, the detection limits correspond to the following yields: **4a** = 0.1%, **5a** = 0.3%. For 25 mM reactions, these detection limits correspond to the following yields: **4a** = 0.04%, **5a** = 0.1%.

Two peaks (t_R = 6.6, 6.7 min; HPLC analysis) were initially observed in the region expected for the *N*-confused porphyrin, both of which exhibited an absorption spectrum consistent with an *N*-confused porphyrin. The dipyrromethane employed in the condensation step had been purified by recrystallization, and contained 2−5% of *N*-confused dipyrromethane. When the dipyrromethane free from *N*-confused dipyrromethane (obtained by chromatography) was used, only one peak in the region corresponding to the *N*-confused porphyrin was observed (6.7 min). [Note that the data shown in Table 3 were obtained from dipyrromethane samples free from *N*-confused dipyrromethane.] Although no *N*-confused porphyrins were isolated and fully characterized, it is reasonable to assign the two peaks to *N*-confused porphyrin isomers. The peak at 6.7 min is attributed to 10,20-diphenyl-5,15-di-*p*-tolyl-2-aza-21-carbaporphyrin (**5a**), which must originate by reaction of dipyrromethane **1a** at the pyrrolic 3-position with the dipyrromethane−dicarbinol **3a-OH**. The peak at 6.6 min is attributed to 10,20-diphenyl-5,15-di-*p*-tolyl-3-aza-21-carbaporphyrin (**5a-isomer**), which must originate by reaction at the pyrrolic 5′-position of the *N*-confused dipyrromethane with the dipyrromethane−dicarbinol **3a-OH**. See the Supporting Information for illustrative schemes concerning these reactions. Although the relative amount of the putative **5a-isomer** was surprising, *N*-confused dipyrromethanes and related species are known to undergo porphyrin-forming reactions.[57]

Acid-Screening Experiments. Immediately prior to the condensation reactions, a sample of **3a** (0.092 g, 0.20 mmol) was reduced to the corresponding dicarbinol with $NaBH_4$ (0.38 g, 10 mmol, 50 mol equiv) in 16 mL of THF/methanol (3:1).[5] After drying under vacuum for 15−30 min, the flask containing the dipyrromethane−dicarbinol (0.20 mmol assuming quantitative reduction) was treated with anhydrous CH_2Cl_2 (8 mL) and dipyrromethane **1a** (0.044 g, 0.20 mmol). The mixture was stirred for 5 min to ensure mixing. This mixture was equally divided into four tightly capped 20-mL vials (via Hamilton syringe) that were stirred with a microstir bar. The condensation was performed with the dipyrromethane−dicarbinol and the dipyrromethane (25 mM each) in CH_2Cl_2. The acid was weighed and transferred immediately into the reaction vials. The reaction was monitored by absorption spectroscopy, whereby a 10-μL reaction aliquot was injected into a solution of DDQ (1 mL, 0.01 M in toluene) (at 1, 5, 15, 60, and 90 min timepoints). This solution was diluted with 2.5 mL of CH_2Cl_2. A 25-μL aliquot of the resulting oxidized solution was dissolved in CH_2Cl_2/ethanol (3 mL, 3:1), and the absorption spectrum was recorded. Prior to LD-MS analysis, the aliquot of the crude, oxidized reaction mixture (3.5 mL) was passed through a pipet column packed with alumina, and the eluant was concentrated.

5-(4-Methylphenyl)dipyrromethane (1e). Following a standard procedure,[1] a solution of *p*-tolualdehyde (18.0 g, 150 mmol) in pyrrole (1.04 L, 15.0 mol) at room temperature under argon was treated with $InCl_3$ (3.32 g, 15.0 mmol) for 1.5 h. Powdered NaOH (18.0 g, 0.450 mol) was added. After stirring for 1 h, the mixture was suction filtered, and excess pyrrole was removed under high vacuum. The residue was treated with hexanes (3 × 100 mL) to facilitate removal of traces of pyrrole. The resulting solid was recrystallized [MeOH/H_2O (4:1)], affording a brown solid (27.0 g, 76%): mp 113−114 °C; ^{1}H NMR δ 2.36 (s, 3H), 5.45 (s, 1H), 5.92−5.94 (m, 2H), 6.15−6.17 (m, 2H), 6.68−6.70 (m, 2H), 7.10−7.12 (m, 4H), 7.91−7.95 (br, 2H); ^{13}C NMR δ 21.3, 43.8, 107.3, 108.6, 117.3, 128.5, 129.5, 132.9, 136.8, 139.2; FAB-MS obsd 236.1313, calcd 236.1313 ($C_{16}H_{16}N_2$). The

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data are consistent with those obtained from samples prepared via earlier routes.[31,32]

Decomplexation of a 1,9-Diacyldipyrromethane−BBN Complex: 1-(4-Methoxybenzoyl)-9-(4-methylbenzoyl)-5-phenyldipyrromethane (3b). Following a general procedure,[4] a solution of **3b-BBN** (5.94 g, 10.0 mmol) in THF (16.0 mL) was treated with 1-pentanol (4.0 mL). The reaction mixture was heated at reflux. After 2 h, TLC [silica, hexanes/ethyl acetate (4:1)] examination showed complete consumption of boron complex **3b-BBN**. The mixture was concentrated to dryness. The resulting oily residue was treated with 50 mL of hexanes to afford a solid residue. The resulting mixture was filtered through a Büchner funnel. The precipitate was collected and dried in vacuo to afford a light-pink powder (3.98 g, 84%). The filtrate was concentrated by 4-fold. The resulting precipitate was filtered, dissolved in a minimal volume of CH_2Cl_2, and precipitated upon addition of hexanes, affording an additional 0.284 g of the title compound. The combined yield (4.26 g) is 90%: mp 106−108 °C; ^{1}H NMR δ 2.39 (s, 3H), 3.84 (s, 3H), 5.66 (s, 1H), 5.92−5.93 (m, 2H), 6.50−6.53 (m, 2H), 6.88 (d, J = 8.0 Hz, 2H), 7.18−7.20 (d, J = 8.0 Hz, 2H), 7.33−7.34 (m, 1H), 7.38−7.42 (m, 2H), 7.54 (d, J = 8.0 Hz, 2H) 7.68 (d, J = 8.0 Hz, 2H), 7.77−7.79 (m, 2H), 11.47−11.51 (br, 2H); ^{13}C NMR δ 21.8, 45.3, 55.6, 111.30, 111.32, 113.4, 120.2 120.7, 127.5, 128.9, 129.0, 130.0, 131.1, 131.2, 131.3, 132.0, 135.8, 140.7, 141.1, 142.3, 162.6, 183.5, 184.5; FAB-MS obsd 475.2040, calcd 475.2022 [$(M + H)^+$, M = $C_{31}H_{26}N_2O_3$].

1-(Hexanoyl)-9-(4-methylbenzoyl)-5-pentyldipyrromethane (3d). Following a general procedure,[4] a solution of **3d-BBN** (1.10 g, 2.00 mmol) in THF (3.2 mL) was treated with 1-pentanol (0.8 mL). The reaction mixture was heated at reflux. After 2 h, TLC [silica, hexanes/ethyl acetate (4:1)] examination showed complete consumption of boron complex **3d-BBN**. The reaction mixture was concentrated (∼1 mL) and filtered through a pad of alumina [CH_2Cl_2/ethyl acetate (4:1 → 1:1)], affording a yellow oil. Methanol was added, affording a pink precipitate on standing for 10 min. The solvent was decanted. The residue was dried under vacuum to afford a pink amorphous powder (0.671 g, 75%): mp 130 °C; ^{1}H NMR δ 0.82−0.90 (m, 6H), 1.26−1.35 (m, 10H), 1.67−1.73 (m, 2H), 2.03−2.07 (m, 2H), 2.39 (s, 3H), 2.75 (t, J = 7.6 Hz, 2H), 4.03−4.17 (t, J = 7.6 Hz, 1H), 6.10−6.14 (m, 2H), 6.73−6.74 (m, 1H), 6.83−6.84 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 10.42−10.50 (br, 2H); ^{13}C NMR δ 14.1, 14.2, 21.7, 22.7, 25.5, 27.6, 31.7, 31.9, 33.7, 38.0, 38.4, 108.5, 108.8, 118.1, 120.9, 129.0, 129.4, 131.0, 131.7, 141.7, 142.1, 142.2, 184.6, 191.7; FAB-MS obsd 433.2860, calcd 433.2855 [$(M + H)^+$, M = $C_{28}H_{36}N_2O_2$]. Anal. Calcd for $C_{28}H_{36}N_2O_2$: C, 77.74; H, 8.39; N, 6.48. Found C, 77.66; H, 8.46; N, 6.52.

1,9-Bis(4-methylbenzoyl)dipyrromethane (3f). Following a general procedure,[4] a solution of **3f-BBN** (1.50 g, 3.00 mmol) in THF (4.8 mL) was treated with 1-pentanol (1.2 mL). The reaction mixture was heated at reflux. After 2 h, TLC [silica, hexanes/ethyl acetate (4:1)] examination showed complete consumption of boron complex **3f-BBN**. The mixture was concentrated to dryness. The resulting oily residue was treated with 30 mL of hexanes to afford a solid residue. The resulting mixture was filtered through a Büchner funnel. The precipitate was collected and dried in vacuo to afford a pale-yellow powder (0.940 g, 82%): mp 260 °C (dec); ^{1}H NMR δ 2.41 (s, 6H), 4.14 (s, 2H), 6.14−6.16 (m, 2H), 6.72−6.74 (m, 2H), 7.25 (d, J = 8.0 Hz, 4H), 7.76 (d, J = 8.0 Hz, 4H), 10.22−10.28 (br, 2H); FAB-MS obsd 383.1752, calcd 383.1760 [$(M + H)^+$, M = $C_{25}H_{22}N_2O_2$]. Due to poor solubility in $CDCl_3$, a ^{13}C NMR spectrum was not recorded.

1-(4-Bromobenzoyl)-9-(4-methoxybenzoyl)-5-(4-methoxyphenyl)dipyrromethane (3 g). Following a general procedure,[4] a solution of **3g-BBN** (1.03 g, 1.50 mmol) in THF (2.4 mL) was treated with 1-pentanol (0.6 mL). The reaction mixture was heated at reflux. After 2 h, TLC [silica, hexanes/ethyl acetate (4:1)] examination showed complete consumption of boron complex **3g-BBN**. The mixture was concentrated to dryness. The resulting oily residue was treated with 15 mL of hexanes to afford a solid residue. The resulting mixture was filtered through a Büchner funnel. The precipitate was collected and dried in vacuo to afford a light-pink powder (0.743 g, 87%): mp 113−115 °C; ^{1}H NMR δ 3.83 (s, 3H), 3.84 (s, 3H), 5.60 (s, 1H), 5.91−5.92 (m, 1H), 5.94−5.95 (m, 1H), 6.48−6.49 (m, 2H), 6.88 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 11.57−11.65 (br, 2H); ^{13}C NMR δ 44.5, 55.5, 55.6, 111.2, 111.5, 113.4, 114.3, 120.2, 121.2, 126.6, 130.1, 130.8, 131.0, 131.2, 131.42, 131.48, 132.02, 132.7, 137.2, 140.9, 142.5, 159.0, 162.7, 183.2, 183.5; FAB-MS obsd 569.1071, calcd 569.1076 [$(M + H)^+$, M = $C_{31}H_{25}BrN_2O_4$]. Anal. Calcd for $C_{31}H_{25}BrN_2O_4$: C, 65.38; H, 4.43; N, 4.92. Found C, 65.79; H, 4.77; N, 4.82.

1-(4-Methylbenzoyl)-9-(pentafluorobenzoyl)-5-phenyldipyrromethane (3h). Following a general procedure,[4] a solution of **3h-BBN** (1.96 g, 3.00 mmol) in THF (4.8 mL) was treated with 1-pentanol (1.2 mL). The reaction mixture was heated at reflux. After 2 h, TLC [silica, hexanes/ethyl acetate (4:1)] examination showed complete consumption of boron complex **3h-BBN**. The mixture was concentrated to dryness. The resulting oily residue was treated with 30 mL of hexanes to afford a solid residue. The resulting mixture was filtered through a Büchner funnel. The precipitate was collected and dried in vacuo to afford a light-pink powder (1.31 g, 82%): mp 165 °C; ^{1}H NMR δ 2.42 (s, 3H), 5.65 (s, 1H), 6.08−6.10 (m, 1H), 6.11−6.13 (m, 1H), 6.63−6.65 (br, 1H), 6.79−6.81 (m, 1H), 7.23−7.27 (m, 4H), 7.31−7.37 (m, 3H), 7.74 (m, 2H), 9.79−9.83 (br, 1H), 9.99−10.03 (br, 1H); ^{13}C NMR δ 21.8, 44.5, 111.13, 112.2, 120.6, 122.5, 128.1, 128.6, 129.2, 129.3, 129.4, 131.44, 131.48, 135.6, 139.1, 139.3, 142.8, 143.5, 172.1, 184.9; FAB-MS obsd 535.1420, calcd 535.1445 [$(M + H)^+$, M = $C_{30}H_{19}F_5N_2O_2$]. Anal. Calcd for $C_{30}H_{19}F_5N_2O_2$: C, 67.42; H, 3.58; N, 5.24. Found C, 67.62; H, 3.89; N, 5.15.

Synthesis of 5,15-Bis(4-methylphenyl)-10,20-diphenylporphyrin at 25 mM Reactants Using Zn(OTf)$_2$. A sample of **3a** (0.11 g, 0.25 mmol) was dissolved in dry THF/methanol (20 mL, 3:1) at room temperature in a round-

bottom flask, fitted with a vented rubber septum, and flooded with argon. The septum was removed as needed to add $NaBH_4$ (0.47 g, 12.5 mmol, 50 mol equiv) in small portions with rapid stirring. The progress of the reduction was monitored by TLC analysis [alumina, CH_2Cl_2/methanol (97:3)] of reaction aliquots. After the reaction was complete (about 40 min), the reaction mixture was poured into a stirred mixture of saturated aqueous NH_4Cl and CH_2Cl_2. The organic phase was separated, washed with water, dried (K_2CO_3), and concentrated under reduced pressure to yield the dicarbinol (0.25 mmol, assuming quantitative reduction) as a foamlike solid. The flask containing the dipyrromethane−dicarbinol was treated with anhydrous CH_2Cl_2 (10 mL) and **1a** (0.055 g, 0.25 mmol). The mixture was stirred for 5 min to achieve dissolution, whereupon $Zn(OTf)_2$ (0.036 g, 0.10 mmol, 10 mM) was added. The reaction was monitored by absorption spectroscopy, whereby a 10 μL reaction aliquot was injected into a solution of DDQ (1.0 mL, 0.01 M in toluene); this solution then was diluted with 2.5 mL of CH_2Cl_2. Then 25 μL of the resulting oxidized mixture was dissolved in CH_2Cl_2/EtOH (3 mL, 3:1), and the absorption spectrum was recorded. After 15 min (following the addition of $Zn(OTf)_2$), DDQ (0.17 g, 0.75 mmol) was added to the bulk reaction mixture, and the mixture was stirred at room temperature for 15 min. TEA (0.14 mL, 1.0 mmol) was added. The reaction mixture was filtered (to remove quinone species) through a pad of alumina (6 cm dia × 7.5 cm) and eluted with CH_2Cl_2 until the eluant was no longer purple. The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was placed in a sonication bath for a few minutes, followed by centrifugation. The methanol was decanted, affording a crystalline purple solid (0.032 g, 21%): ^{1}H NMR δ −2.77 (s, 2H), 2.70 (s, 6H), 7.56 (d, J = 8.0 Hz, 4H), 7.68−7.80 (m, 6H), 8.10 (d, J = 8.0 Hz, 4H), 8.20−8.23 (m, 4H), 8.83 (d, J = 4.4 Hz, 4H), 8.87 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 21.7, 120.1, 120.4, 126.9, 127.8, 127.9, 130.4−132.0 (br), 134.74, 134.77, 137.5, 139.4, 142.5; LD-MS obsd 642.7; FAB-MS obsd 643.2881, calcd 643.2862 [$(M + H)^+$, $M = C_{46}H_{34}N_4$]; λ_{abs} 417, 513, 548, 592, 647 nm.

Exemplary Procedure Using 25 mM Reactants With $Sc(OTf)_3$ and DTBP, Given for 5,15-Bis(4-methylphenyl)-10,20-diphenylporphyrin (4a). A sample of **3a** (0.458 g, 1.00 mmol) was dissolved in THF/methanol (80 mL, 3:1) at room temperature in a round-bottom flask, fitted with a vented rubber septum, and flooded with argon. The septum was removed as needed to add $NaBH_4$ (1.89 g, 50.0 mmol, 50.0 mol equiv) in small portions with rapid stirring. The progress of the reduction was monitored by TLC analysis [alumina, CH_2Cl_2/methanol (97:3)] of reaction aliquots. After the reaction was complete (about 40 min), the reaction mixture was poured into a stirred mixture of saturated aqueous NH_4Cl and CH_2Cl_2. The organic phase was separated, dried (K_2CO_3), and concentrated under reduced pressure to yield the dicarbinol as a foamlike solid. The flask containing the dipyrromethane−dicarbinol (1.00 mmol, assuming quantitative reduction) was treated with anhydrous CH_2Cl_2 (40 mL) and **1a** (0.222 g, 1.00 mmol). The mixture was stirred for 5 min to achieve dissolution, whereupon 2,6-di-*tert*-butylpyridine (0.293 mL, 1.30 mmol, 32.5 mM) and $Sc(OTf)_3$ (0.0640 g, 0.130 mmol, 3.25 mM) were added. The reaction was monitored by absorption spectroscopy, whereby a 10 μL reaction aliquot was injected into a solution of DDQ (1.0 mL, 0.01 M in toluene); this solution then was diluted with 2.5 mL of CH_2Cl_2. Then 25 μL of the resulting oxidized mixture was dissolved in CH_2Cl_2/EtOH (3 mL, 3:1), and the absorption spectrum was recorded. After 15 min (following the addition of $Sc(OTf)_3$), DDQ (0.681 g, 3.00 mmol) was added to the bulk reaction mixture, and the mixture was stirred at room temperature for 5 min. The reaction mixture was filtered (to remove quinone species) through a pad of alumina (6 cm dia × 7.5 cm) and eluted with CH_2Cl_2 containing 0.1% TEA until the eluant was no longer purple. The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting slurry was sonicated for a few minutes and then filtered through a Büchner funnel. The filtered material was dried in vacuo, affording a crystalline purple solid (0.125 g, 19%): ^{1}H NMR δ −2.76 (s, 2H), 2.71 (s, 6H), 7.56 (d, J = 8.0 Hz, 4H), 7.68−7.81 (m, 6H), 8.10 (d, J = 8.0 Hz, 4H), 8.21−8.23 (m, 4H), 8.83 (d, J = 4.4 Hz, 4H), 8.87 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 21.7, 120.1, 120.4, 126.8, 127.6, 127.8, 130.2−132.1 (br), 134.73, 134.77, 137.6, 139.4, 142.5; LD-MS obsd 643.7; FAB-MS obsd 643.2900, calcd 643.2862 [$(M + H)^+$, $M = C_{46}H_{34}N_4$]; λ_{abs} 417, 514, 548, 593, 647 nm.

5-(4-Methoxyphenyl)-10,20-bis(4-methylphenyl)-15-phenylporphyrin (4b). The condensation of dicarbinol **3a-OH** [derived from reduction of **3a** (0.458 g, 1.00 mmol) with $NaBH_4$ (1.89 g, 50.0 mmol, 50.0 mol equiv) in THF/methanol (80 mL, 3:1)] and dipyrromethane **1b** (0.252 g, 1.00 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.293 mL, 1.30 mmol) and $Sc(OTf)_3$ (0.0640 g, 0.130 mmol) in CH_2Cl_2 (40 mL) at room temperature for 10 min followed by the addition of DDQ (0.681 g, 3.0 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol and dried in vacuo, affording a crystalline purple solid (0.142 g, 21%): ^{1}H NMR δ −2.76 (s, 2H), 2.70 (s, 6H), 4.09 (s, 3H), 7.29 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 4H), 7.67−7.79 (m, 3H), 8.10 (d, J = 8.0 Hz, 4H), 8.12 (d, J = 8.0 Hz, 2H), 8.20−8.22 (m, 2H), 8.82 (d, J = 4.8 Hz, 2H), 8.86 (s, 6H); ^{13}C NMR δ 21.7, 55.7, 94.5, 112.4, 120.0, 120.4, 126.9, 127.6, 127.8, 130.0−132.3 (br), 134.7, 134.80, 134.87, 135.8, 137.5, 139.5, 142.5, 159.6; LD-MS obsd 673.9; FAB-MS obsd 672.2889, calcd 672.2889 ($C_{47}H_{36}N_4O$); λ_{abs} 418, 515, 550, 593, 649 nm.

5,15-Bis(4-methylphenyl)-10-(pentafluorophenyl)-20-phenylporphyrin (4c). The condensation of dicarbinol **3a-OH** [derived from reduction of **3a** (0.229 g, 0.500 mmol) with $NaBH_4$ (0.947, 25.0 mmol, 50.0 mol equiv) in THF/

methanol (40 mL, 3:1)] and dipyrromethane **1c** (0.156 g, 0.500 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.147 mL, 0.650 mmol) and $Sc(OTf)_3$ (0.0320 g, 0.0650 mmol) in CH_2Cl_2 (20 mL) at room temperature for 10 min followed by the addition of DDQ (0.340 g, 1.50 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol and dried in vacuo, affording a crystalline purple solid (0.0440 g, 11%). The filtrate was concentrated. The concentrated product was passed though a silica column, which was eluted with CH_2Cl_2 until the eluant was no longer purple. The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder to afford an additional 0.0110 g of porphyrin. The precipitates were combined to afford a purple solid (0.0550 g, 15%): ^{1}H NMR δ −2.76 (s, 2H), 2.71 (s, 6H), 7.56 (d, J = 8.0 Hz, 4H), 7.72−7.81 (m, 3H), 8.09 (d, J = 8.0 Hz, 4H), 8.19−8.21 (m, 2H), 8.75 (d, J = 4.4 Hz, 2H), 8.84 (d, J = 4.4 Hz, 2H), 8.86 (d, J = 4.4 Hz, 2H), 8.96 (d, J = 4.4 Hz, 2H); ^{13}C NMR δ 21.7, 100.1, 121.2, 122.2, 126.9, 127.7, 128.0, 129.1, 130.5, 130.8−132.9 (br), 132.8−133.8 (br), 134.7, 137.8, 138.9, 142.2, 145.2−145.8 (m), 147.8−148.2 (m); LD-MS obsd 734.0; FAB-MS obsd 733.2365, calcd 733.2391 [$(M + H)^+$, $M = C_{46}H_{29}F_5N_4$]; λ_{abs} 416, 512, 546, 589, 646 nm.

5-(4-Iodophenyl)-10-(4-methoxyphenyl)-20-(4-methylphenyl)-15-phenylporphyrin (4d). The condensation of dicarbinol **3b-OH** [derived from reduction of **3b** (0.474 g, 1.00 mmol) with $NaBH_4$ (1.89 g, 50.0 mmol, 50.0 mol equiv) in THF/methanol (80 mL, 3:1)] and dipyrromethane **1d** (0.348 g, 1.00 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.293 mL, 1.30 mmol) and $Sc(OTf)_3$ (0.0640 g, 0.130 mmol) in CH_2Cl_2 (40 mL) at room temperature for 10 min followed by the addition of DDQ (0.681 g, 3.00 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol followed by hexanes and dried in vacuo, affording a crystalline purple solid (0.135 g, 17%): ^{1}H NMR δ −2.79 (s, 2H), 2.71 (s, 3H), 4.10 (s, 3H), 7.29 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.72−7.77 (m, 3H), 7.95 (d, J = 8.0 Hz, 2H), 8.10 (d, J = 8.0 Hz, 4H), 8.12(d, J = 8.0 Hz, 2H), 8.20−8.22 (m, 2H), 8.80−8.84 (m, 4H), 8.86−8.89 (m, 4H); ^{13}C NMR δ 21.7, 55.8, 94.2, 112.4, 118.5, 120.3, 120.5, 120.6, 126.8, 127.6, 127.9, 130.0−131.9 (br), 134.6, 134.72, 134.76, 135.8, 136.0, 136.3, 137.6, 139.2, 142.0, 142.3, 159.6; LD-MS obsd 785.8; FAB-MS obsd 785.1745, calcd 785.1777 [$(M + H)^+$, $M = C_{46}H_{33}IN_4O$]; λ_{abs} 418, 514, 550, 593, 648 nm.

5,15-Bis(4-*tert*-butylphenyl)-10-(4-iodophenyl)-20-(4-methylphenyl)porphyrin (4e). The condensation of dicarbinol **3c-OH** [derived from reduction of **3c** (0.334 g, 0.500 mmol) with $NaBH_4$ (0.947 g, 25.0 mmol, 50.0 mol equiv) in THF/methanol (40 mL, 3:1)] and dipyrromethane **1e** (0.118 g, 0.500 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.147 mL, 0.650 mmol) and $Sc(OTf)_3$ (0.0320 g, 0.0650 mmol) in CH_2Cl_2 (20 mL) at room temperature for 10 min followed by the addition of DDQ (0.340 g, 1.50 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated and dried in vacuo, affording a crystalline purple solid (0.0821 g, 19%): ^{1}H NMR δ −2.79 (s, 2H), 1.61 (s, 18H), 2.71 (s, 3H), 7.55 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.0 Hz, 4H), 7.95 (d, J = 8.0 Hz, 2H), 8.08−8.14 (m, 8H), 8.80 (d, J = 4.4 Hz, 2H), 8.86−8.90 (m, 6H); LD-MS obsd 868.0; FAB-MS obsd 867.2853, calcd 867.2924 [$(M + H)^+$, $M = C_{53}H_{47}IN_4$]; λ_{abs} 418, 515, 550, 592, 648 nm. Due to poor solubility in various solvents (including $CDCl_3$), a ^{13}C NMR spectrum was not recorded.

5,10-Bis(4-methylphenyl)-15,20-dipentylporphyrin (4f). The condensation of dicarbinol **3d-OH** [derived from reduction of **3d** (0.216 g, 0.500 mmol) with $NaBH_4$ (0.947 g, 25.0 mmol, 50.0 mol equiv) in THF/methanol (40 mL, 3:1)] and dipyrromethane **1e** (0.118 g, 0.500 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.147 mL, 0.650 mmol) and $Sc(OTf)_3$ (0.0320 g, 0.0650 mmol) in CH_2Cl_2 (20 mL) at room temperature for 10 min followed by the addition of DDQ (0.340 g, 1.50 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated. The product was recrystallized (CH_2Cl_2/methanol) and dried in vacuo, affording a crystalline purple solid (0.0603 g, 19%): ^{1}H NMR δ −2.70 (s, 2H), 0.96−1.00 (m, 6H), 1.54−1.58 (m, 4H), 1.78−1.82 (m, 4H), 2.53−2.57 (m, 4H), 2.70 (s, 6H), 4.98−5.02 (m, 4H), 7.53 (d, J = 8.0 Hz, 4H), 8.05 (d, J = 8.0 Hz, 4H), 8.74 (s, 2H), 8.87 (d, J = 4.4 Hz, 2H), 9.43 (d, J = 4.4 Hz, 2H), 9.56 (s, 2H); ^{13}C NMR δ 14.3, 21.7, 22.9, 32.9, 35.7, 38.7, 119.0, 120.0, 127.6, 127.9−129.6 (br), 130.1−131.0 (br), 134.6, 137.3, 139.6; LD-MS obsd 631.4; FAB-MS obsd 631.3781, calcd 631.3801 [$(M + H)^+$, $M = C_{44}H_{46}N_4$]; λ_{abs} 417, 516, 550, 597, 655 nm.

5,15-Bis(3,5-di-*tert*-butylphenyl)-10-(4-methylphenyl)-20-[4-[2-(trimethylsilyl)ethynyl]phenyl]porphyrin (4g). The condensation of dicarbinol **3e-OH** [derived from reduction of **3e** (0.150 g, 0.200 mmol) with $NaBH_4$ (0.379 g, 10.0 mmol, 50.0 mol equiv) in THF/methanol (16 mL, 3:1)] and dipyrromethane **1e** (0.0470 g, 0.200 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.0590 mL, 0.260 mmol) and $Sc(OTf)_3$ (0.0130 g, 0.0260 mmol) in CH_2Cl_2 (8 mL) at room temperature for 10 min followed by the addition of DDQ (0.136 g, 0.600 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min

and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol and dried in vacuo, affording a crystalline purple solid (0.0420 g, 22%): ^{1}H NMR δ −2.74 (s, 2H), 0.37 (s, 9H), 1.52 (s, 36H), 2.69 (s, 3H), 7.54 (d, J = 8.0 Hz, 2H), 7.79 (s, 2H), 7.86 (d, J = 8.0 Hz, 2H), 8.07 (s, 4H), 8.10 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 2H), 8.79 (d, J = 4.4 Hz, 2H), 8.86−8.89 (m, 6H); ^{13}C NMR δ 0.3, 21.7, 31.9, 35.2, 95.6, 105.3, 118.9, 120.5, 121.2, 121.8, 122.6, 127.5, 130.1, 130.5, 130.7−132.1 (br), 134.58, 134.62, 137.5, 139.5, 141.3, 143.0, 148.9; LD-MS obsd 950.2; FAB-MS obsd 949.5577, calcd 949.5605 [(M + H)$^+$, M = $C_{66}H_{72}N_4Si$]; λ_{abs} 419, 515, 550, 592, 650 nm.

5-(4-Methoxyphenyl)-15-(4-methylphenyl)-10-phenylporphyrin (4h). The condensation of dicarbinol **3b-OH** [derived from reduction of **3b** (0.474 g, 1.00 mmol) with $NaBH_4$ (1.89 g, 50.0 mmol, 50.0 mol equiv) in THF/methanol (80 mL, 3:1)] and dipyrromethane **1f** (0.146 g, 1.00 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.293 mL, 1.30 mmol) and $Sc(OTf)_3$ (0.0640 g, 0.130 mmol) in CH_2Cl_2 (40 mL) at room temperature for 10 min followed by the addition of DDQ (0.681 g, 3.00 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol and dried in vacuo, affording a crystalline purple solid (0.123 g, 21%): ^{1}H NMR δ −2.98 (s, 2H), 2.72 (s, 3H), 4.10 (s, 3H), 7.32 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.71−7.80 (m, 3H), 8.13 (d, J = 8.0 Hz, 2H), 8.15 (d, J = 8.0 Hz, 2H), 8.21 (d, J = 8.0 Hz, 2H), 8.86 (d, J = 4.4 Hz, 2H), 8.93 (d, J = 4.4 Hz, 2H), 9.04 (d, J = 4.4 Hz, 2H), 9.33 (d, J = 4.4 Hz, 2H), 10.19 (s, 1H); ^{13}C NMR δ 21.8, 55.7, 104.9, 112.5, 119.6, 119.8, 120.6, 126.7, 127.7, 127.8, 130.9, 131.3, 131.5, 134.3, 134.7, 134.8, 135.9, 137.5, 139.0, 142.8, 144.0−146.0 (br), 159.6; LD-MS obsd 583.1; FAB-MS obsd 583.2503, calcd 583.2498 [(M + H)$^+$, M = $C_{40}H_{30}N_4O$]; λ_{abs} 412, 508, 543, 585, 642 nm.

5-(4-Bromophenyl)-10,15-bis(4-methoxyphenyl)-20-phenylporphyrin (4j). The condensation of dicarbinol **3g-OH** [derived from reduction of **3g** (0.285 g, 0.500 mmol with $NaBH_4$ (0.947, 25.0 mmol, 50.0 mol equiv) in THF/methanol (40 mL, 3:1)] and dipyrromethane **1a** (0.111 g, 0.500 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.147 mL, 0.650 mmol) and $Sc(OTf)_3$ (0.0320 g, 0.0650 mmol) in CH_2Cl_2 (20 mL) at room temperature for 10 min followed by the addition of DDQ (0.340 g, 1.50 mmol). After 5 min, the reaction mixture was filtered through a pad of alumina (CH_2Cl_2 containing 0.1% TEA). The resulting porphyrin-containing solution was concentrated to give a purple solid. Methanol was added. The resulting suspension was sonicated for 5 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed with methanol and dried in vacuo, affording a crystalline purple solid (0.034 g, 9%): ^{1}H NMR δ −2.78 (s, 2H), 4.10 (s, 6H), 7.28−7.30 (m, 4H), 7.74−7.79 (m, 3H), 7.89 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.0 Hz, 2H), 8.11−8.13 (m, 4H), 8.20−8.22 (m, 2H), 8.79−8.85 (m, 4H), 8.80 (s, 4H); ^{13}C NMR δ 55.7, 112.4, 118.3, 120.2, 120.3, 120.5, 122.5, 126.9, 127.9, 130.1, 130.3−132.4 (br), 134.6, 134.7, 135.8, 136.0, 141.4, 142.3, 159.6; LD-MS obsd 753.3; FAB-MS obsd 753.1877, calcd 753.1865 [(M + H)$^+$, M = $C_{46}H_{33}BrN_4O_2$]; λ_{abs} 419, 515, 550, 593, 648 nm.

Exemplary Procedure for Aerobic Oxidation: Synthesis of 5,15-Bis(4-methylphenyl)-10,20-diphenylporphyrin (4a). The condensation of dicarbinol **3a-OH** [derived from reduction of **3a** (0.229 g, 0.500 mmol) with $NaBH_4$ (0.947 g, 25.0 mmol, 50.0 mol equiv) in THF/methanol (40 mL, 3:1)] and dipyrromethane **1a** (0.111 g, 0.500 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.147 mL, 0.650 mmol) and $Sc(OTf)_3$ (0.0320 g, 0.0650 mmol) in CH_2Cl_2 (20 mL) at room temperature. After 15 min (following the addition of $Sc(OTf)_3$), samples of DDQ (0.0056 g, 5 mol %) and [(*t*-Bu)$_4$FePc]$_2$O (0.0400 g, 5 mol %) were added, and the reaction mixture was gently bubbled with oxygen for 90 min. The gas purge caused a slight but continual decrease in the reaction volume. The loss of solvent was offset by occasional addition of 1−2 mL of CH_2Cl_2 via syringe as required prior to acquisition of samples (total volume 20 mL over 105 min). The reaction mixture was filtered through a pad of alumina (6 cm dia × 7.5 cm) with CH_2Cl_2 as eluent. The resulting porphyrin-containing solution was concentrated to give a purple solid. Hexanes was added. The resulting suspension was sonicated for 5 min and then filtered through a Büchner funnel. The filtered material was washed with hexanes and dried in vacuo, affording a crystalline purple solid (0.055 g, 17%). The characterization data (^{1}H NMR, ^{13}C NMR, LD-MS, and UV−vis spectra) were consistent with the above-reported values.

Exemplary Gram-Scale Synthesis: 5-Mesityl-10-(4-methoxyphenyl)-20-(4-methylphenyl)-10-phenylporphyrin (4l). A sample of **3b** (8.54 g, 18.0 mmol) was placed in a 1-L round-bottom flask equipped with a pressure-equalizing addition funnel. Reagent grade THF (72 mL) and $NaBH_4$ (6.82 g, 180 mmol, 10.0 mol equiv) were added under an inert atmosphere followed by slow addition of reagent grade MeOH (30 mL; a water cooling bath was used to maintain the temperature). When no more starting material was detected by TLC analysis (∼1 h) [alumina, CH_2Cl_2/methanol (97:3)], the reaction mixture was diluted with CH_2Cl_2 (350 mL). Saturated aqueous NH_4Cl (500 mL) was poured slowly into the reaction mixture. The biphasic mixture was stirred for 15 min. The organic layer was separated, washed with water (500 mL), dried (K_2CO_3), and filtered. The filtrate was concentrated, affording a yellow foam. The condensation of dicarbinol **3b-OH** and dipyrromethane **1g** (4.76 g, 18.0 mmol) was carried out in a 1-L one-neck flask in the presence of 2,6-di-*tert*-butylpyridine (5.28 mL, 23.4 mmol) and $Sc(OTf)_3$ (1.15 g, 2.34 mmol) in reagent grade CH_2Cl_2 (720 mL) at room temperature. Then [15 min after the addition of $Sc(OTf)_3$] samples of DDQ (0.102 g, 2.5 mol %) and [(*t*-Bu)$_4$FePc]$_2$O (0.721 g, 2.5 mol %) (see Note 1 below) were added, a Claisen adapter equipped with a rubber septum and

a condenser was fitted over one neck of the round-bottom flask, and the reaction mixture was gently bubbled with oxygen (see Note 2 below) for 90 min. The reaction mixture was washed with water (1 L). The organic layer was separated, dried (Na_2SO_4), and concentrated to a volume of ~20 mL. The resulting mixture was filtered through a pad of silica (175 g; 8.0 cm dia × 8.0 cm) with CH_2Cl_2 as eluent. The resulting porphyrin-containing solution was concentrated to give a purple solid. Hexanes was added to the solid. The resulting suspension was sonicated for 1 min and then filtered through a filter paper secured in a fritted glass filter holder. The filtered material was washed (first with hexanes and second with methanol) and then dried in vacuo at room temperature, affording a crystalline purple solid (2.88 g, 22.8%): (see Note 3 below) ^{1}H NMR δ −2.68 (s, 2H), 1.85 (s, 6H), 2.64 (s, 3H), 2.71 (s, 3H), 4.10 (s, 3H), 7.28−7.30 (m, 4H), 7.56 (d, J = 8.0 Hz, 2H), 7.73−7.79 (m, 3H), 8.11 (d, J = 8.0 Hz, 2H), 8.14 (d, J = 8.0 Hz, 2H), 8.20−8.22 (m, 2H), 8.68−8.70 (m, 2H), 8.80−8.87 (m, 6H); ^{13}C NMR δ 21.6, 21.7, 21.8, 55.7, 112.4, 118.4, 119.6, 119.9, 120.1, 126.8, 127.6, 127.8, 127.9, 129.5−132.4 (br), 134.7, 135.7, 137.5, 137.9, 138.6, 139.3, 139.6, 142.6, 159.5; LD-MS obsd 700.5; FAB-MS obsd 700.3188, calcd 700.3202 ($C_{49}H_{40}N_4O$); λ_{abs} 418, 514, 549, 591, 649 nm.

Note 1: The 2.5 mol % level is referenced against the number of moles of the dipyrromethane. The theoretical amount of DDQ is 300 mol % (assuming a 100% yield of porphyrinogen and three moles of DDQ per mole of porphyrinogen). Accordingly, the quantity of DDQ employed herein is 0.83% of the amount required for a stoichiometric synthesis.

Note 2: The aerobic oxidation was carried out using oxygen of 99.999% purity (Research grade, National Welders, Inc.).

Note 3: No *N*-confused porphyrin (or any other porphyrin byproduct) was detected in the isolated porphyrin sample upon HPLC analysis.

Exemplary Three-Step One-Flask Synthesis of Metalloporphyrins. The condensation of dicarbinol **3a-OH** [derived from reduction of **3a** (0.275 g, 0.600 mmol) with $NaBH_4$ (1.13 g, 30.0 mmol, 50.0 mol equiv) in THF/methanol (48 mL, 3:1)] and dipyrromethane **1a** (0.133 g, 0.600 mmol) was carried out in the presence of 2,6-di-*tert*-butylpyridine (0.176 mL, 0.780 mmol) and $Sc(OTf)_3$ (0.0380 g, 0.0780 mmol) in CH_2Cl_2 (24 mL) at room temperature. After 15 min (following the addition of $Sc(OTf)_3$), samples of DDQ (0.0068 g, 5 mol %) and $[(t\text{-Bu})_4FePc]_2O$ (0.0480 g, 5 mol %) were added, and the reaction mixture was gently bubbled with oxygen for 90 min. The gas purge caused a slight but continual decrease in the reaction volume. The solvent loss was offset by occasional addition of 1−2 mL of CH_2Cl_2 via syringe as required prior to acquisition of samples (total volume 24 mL after 105 min). The reaction mixture was divided into portions and employed for metalation as described below. The condensation/oxidation was performed twice to generate all of the fractional portions listed below.

Magnesium Insertion: Mg(II)-5,15-bis(4-methylphenyl)-10,20-diphenylporphyrin (Mg-4a). A one-third portion of the crude reaction mixture from the aerobic oxidation (corresponding to 0.200 mmol of each reactant) was treated with CH_2Cl_2 (12 mL, giving a reaction volume of 20 mL) followed by MgI_2 (0.556 g, 2.00 mmol) and DIEA (0.697 mL, 4.00 mmol). The reaction mixture was stirred at room temperature for 30 min. The reaction mixture was poured over a chromatography column [alumina, 3 cm dia × 15 cm, CH_2Cl_2 → CH_2Cl_2/acetone (1:1)], affording purple fractions (accompanied by some black residue) that were combined, concentrated, and dried in vacuo. Hexanes was added. The resulting purple suspension was filtered. The filtrate was concentrated and dried in vacuo to afford a purple solid (0.0274 g, 20%): ^{1}H NMR δ 2.70 (s, 6H), 7.53 (d, J = 8.0 Hz, 4H), 7.69−7.76 (m, 6H), 8.10 (d, J = 8.0 Hz, 4H), 8.20−8.22 (m, 4H), 8.83 (d, J = 4.4 Hz, 4H), 8.87 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 21.7, 121.6, 121.8, 126.4, 127.2, 131.9, 132.0, 134.7, 134.8, 136.8, 141.0, 143.9, 149.9, 150.1; LD-MS obsd 664.5; FAB-MS obsd 664.2486, calcd 664.2477 ($C_{46}H_{32}N_4Mg$); λ_{abs} 429, 571, 613 nm; λ_{em} (λ_{ex} = 570 nm) 619, 650 nm.

Nickel Insertion: Ni(II)-5,15-bis(4-methylphenyl)-10,20-diphenylporphyrin (Ni-4a). A one-third portion of the crude reaction mixture from the aerobic oxidation (corresponding to 0.200 mmol of each reactant) was concentrated (to ~1 mL), whereupon toluene (10 mL) was added. The reaction mixture was treated with $Ni(acac)_2$ (0.514 g, 2.00 mmol). The mixture was refluxed overnight. The reaction mixture was poured over a chromatography column [silica, 3 cm dia × 15 cm, CH_2Cl_2/hexanes (3:1)]. The purple fraction was collected and washed with methanol and hexanes to afford a purple solid (0.0247 g, 18%): ^{1}H NMR δ 2.64 (s, 6H), 7.47 (d, J = 8.0 Hz, 4H), 7.67−7.70 (m, 6H), 7.89 (d, J = 8.0 Hz, 4H), 8.00−8.02 (m, 4H), 8.73 (d, J = 4.8 Hz, 4H), 8.77 (d, J = 4.8 Hz, 4H); ^{13}C NMR δ 21.6, 127.0, 127.8, 127.9, 132.2, 132.4, 133.8, 133.9, 137.6, 138.1, 141.1, 142.7, 142.9; LD-MS obsd 698.3; FAB-MS obsd 698.1968, calcd 698.1980 ($C_{46}H_{32}N_4Ni$); λ_{abs} 414, 527 nm.

Copper Insertion: Cu(II)-5,15-bis(4-methylphenyl)-10,20-diphenylporphyrin (Cu-4a). A one-third portion of the crude reaction mixture from the aerobic oxidation (corresponding to 0.200 mmol of each reactant) was treated with CH_2Cl_2 (7 mL, giving a reaction volume of 15 mL) followed by methanolic $Cu(OAc)_2 \cdot H_2O$ (0.199 g, 1.00 mmol, 5 mL). The reaction mixture was stirred overnight at room temperature. The reaction mixture was poured over a chromatography column [silica, 3 cm dia × 15 cm, CH_2Cl_2/hexanes (3:1)]. The purple fraction was collected and concentrated. The product was washed with methanol to afford a dark-purple solid (0.027 g, 19%): ^{1}H NMR δ 2.54 (s, 6H), 7.64−7.29 (m, 18H); LD-MS obsd 704.1; FAB-MS obsd 703.1951, calcd 703.1923 ($C_{46}H_{32}N_4Cu$); λ_{abs} 415, 540 nm.

Zinc Insertion: Zn(II)-5,15-bis(4-methylphenyl)-10,20-diphenylporphyrin (Zn-4a). A one-third portion of the crude reaction mixture from the aerobic oxidation (corre-

sponding to 0.200 mmol of each reactant) was treated with CH_2Cl_2 (7 mL, giving a reaction volume of 15 mL) followed by methanolic $Zn(OAc)_2 \cdot 2H_2O$ (0.219 g, 1.00 mmol, 5 mL). The reaction mixture was stirred overnight at room temperature. The reaction mixture was poured over a chromatography column [silica, 3 cm dia × 15 cm, CH_2Cl_2/hexanes (3:1)]. The purple fraction was collected and washed with methanol to afford a purple solid (0.0254 g, 18%): ^{1}H NMR δ 2.71 (s, 6H), 7.56 (d, J = 8.0 Hz, 4H), 7.77−7.74 (m, 6H), 8.10 (d, J = 8.0 Hz, 4H), 8.21−8.23 (m, 4H), 8.94 (d, J = 4.4 Hz, 4H), 8.98 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 21.7, 121.2, 121.4, 126.7, 127.5, 127.6, 132.0, 132.2, 134.5, 134.6, 137.3, 140.0, 143.0, 150.3, 150.5; LD-MS obsd 705.1; FAB-MS obsd 704.1928, calcd 704.1918 ($C_{46}H_{32}N_4Zn$); λ_{abs} 423, 556, 595 nm; λ_{em} (λ_{ex} = 550 nm) 605, 655 nm.

Palladium Insertion: Pd(II)-5,15-bis(4-methylphenyl)-10,20-diphenylporphyrin (Pd-4a). A one-third portion of the crude reaction mixture from the aerobic oxidation (corresponding to 0.200 mmol of each reactant) was concentrated (to ∼1 mL), whereupon a solution of 1,2-dichloroethane/methanol (4:1, 4 mL) was added. The reaction mixture was treated with $Pd(O_2CCF_3)_2$ (0.133 g, 0.400 mmol). The resulting heterogeneous mixture was stirred and heated at 45 °C for 1 h. The reaction mixture was poured over a chromatography column [silica, 3 cm dia × 15 cm, CH_2Cl_2/hexanes (3:1)]. The orange fraction was collected and washed with methanol to afford an orange-purple solid (0.0284 g, 19%): ^{1}H NMR δ 2.69 (s, 6H), 7.536 (d, J = 8.0 Hz, 4H), 7.76−7.71 (m, 6H), 8.04 (d, J = 8.0 Hz, 4H), 8.15−8.17 (m, 4H), 8.79 (d, J = 4.4 Hz, 4H), 8.83 (d, J = 4.4 Hz, 4H); ^{13}C NMR δ 21.7, 122.0, 123.0, 126.9, 127.6, 127.9, 131.0, 131.2, 134.2, 134.3, 137.6, 139.0, 141.7, 141.9, 142.0; LD-MS obsd 747.2; FAB-MS obsd 746.1729, calcd 746.1662 ($C_{46}H_{32}N_4Pd$); λ_{abs} 416, 523 nm.

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Supporting Information Available

Additional data concerning acid catalysis, interpretation of data concerning *N*-confused porphyrins, and description of aerobic oxidation studies and results. This material is available free of charge via the Internet at http://pubs.acs.org.

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