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New Route to ABCD-Porphyrins via Bilanes

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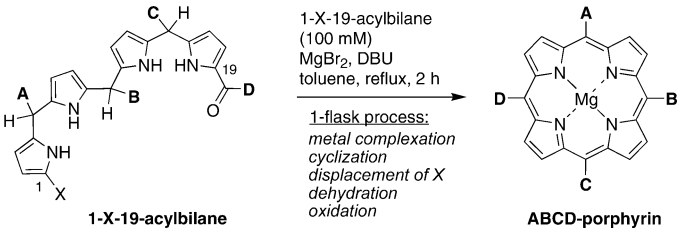

A new strategy for preparing porphyrins that bear up to four different meso-substituents (ABCD-porphyrins) relies on two key reactions. One key reaction entails a directed synthesis of a 1-protected 19-acylbilane by acid-catalyzed condensation at high concentration (0.5 M) of a 1-acyldipyrromethane and a 9-protected dipyrromethane-1-carbinol (derived from a 9-protected 1-acyldipyrromethane). Three protecting groups (X) were examined, including thiocyanato, ethylthio, and bromo, of which bromo proved most effective. The bilanes were obtained in 72−80% 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 basic, metal-templating conditions to give the corresponding metalloporphyrin. The reaction parameters investigated for cyclization of the bilane include solvent, metal salt, base, concentration, temperature, atmosphere, and time. The best conditions entailed the 1-bromo-19-acylbilane at 100 mM in toluene containing DBU (10 mol equiv) and $MgBr_2$ (3 mol equiv) at 115 °C exposed to air for 2 h, which afforded the magnesium porphyrin in 65% yield. The magnesium porphyrin is readily demetalated to give the free base porphyrin. A stepwise procedure (which entailed treatment of the 1-(ethylthio)-19-acylbilane to oxidation, metal complexation, desulfurization, carbonyl reduction, and acid-catalyzed condensation) was developed but was much less efficient than the one-flask process. The new route to ABCD-porphyrins retains the desirable features of the existing "2 + 2" (dipyrromethane + dipyrromethane-1,9-dicarbinol) method, such as absence of scrambling, yet has significant advantages. The advantages include the absence of acid in the porphyrin-forming step, the use of a metal template for cyclization, the ability to carry out the reaction at high concentration, the lack of a quinone oxidant, avoidance of use of dichloromethane, and the increased yield of macrocycle formation to give the target ABCD-metalloporphyrin.

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 1. The porphyrin-forming reaction entails acid-catalyzed condensation of a dipyrromethane-1,9-dicarbinol (**I**) + a dipyrromethane (**II**), which is believed to proceed via a bilanecarbinol (**III**) and a porphyrinogen (**IV**) with competing formation of polypyrromethanes (**V**). Treatment of the reaction mixture with an oxidant gives the porphyrin (**VI**).[1,2] 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)

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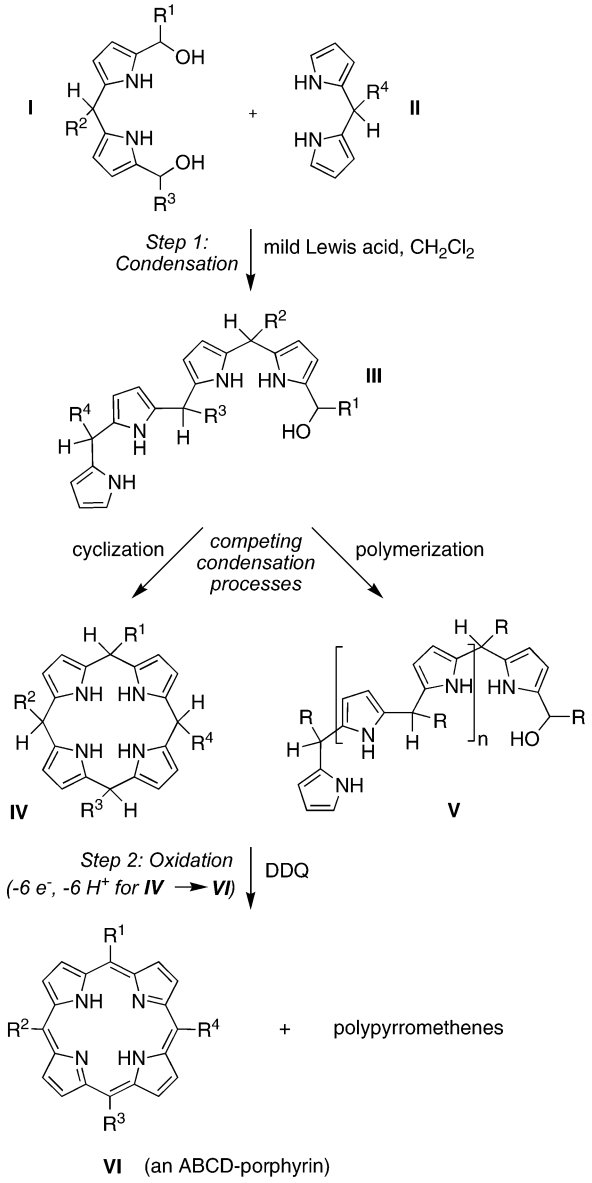
SCHEME 1. "2 + 2" Synthesis of an ABCD-Porphyrin (Free Base)



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.[3−8] However, the final porphyrin-forming step still presents a number of limitations despite extensive investigation.[2]

The drawbacks of the porphyrin-forming procedure include the following: (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 a dipyrromethane-1,9-dicarbinol (**I**) + a dipyrromethane (**II**).[2] 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** → **IV** versus **V**).[9,10] 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[11] also is increased.[2] 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.

Our approach has centered 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.[9]

The strategy initially envisaged is shown in Scheme 2. The key precursor to the ABCD-metalloporphyrin (**VI-M**) is a metal-complexed biladiene-*ac* bearing a 19-hydroxymethyl substituent (**VII**), which is obtained in several steps from a 1-protected 19-acylbilane (**VIII**). The latter is derived by selective condensation of an AB-substituted dipyrromethane (**IX**) and a CD-substituted dipyrromethane (**X**). The selective condensation stems from the presence of only a single reactive α-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.

The development of the synthesis of the bilane (**VIII**) shown in Scheme 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, nonacidic conditions. The common route to bilanes by hydrogenation of an unsaturated analogue (bilene or biladiene), which can be prepared in a number of ways,[12] was not suited for our needs. To gain rational entry to a bilane from dipyrromethane precursors requires the presence of only a single

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SCHEME 2. Stepwise Retrosynthesis for an ABCD-Metalloporphyrin

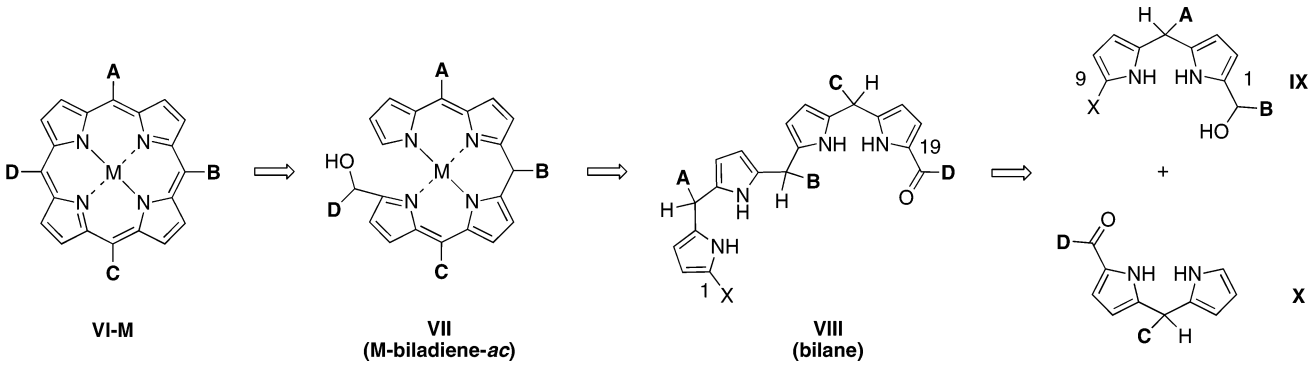
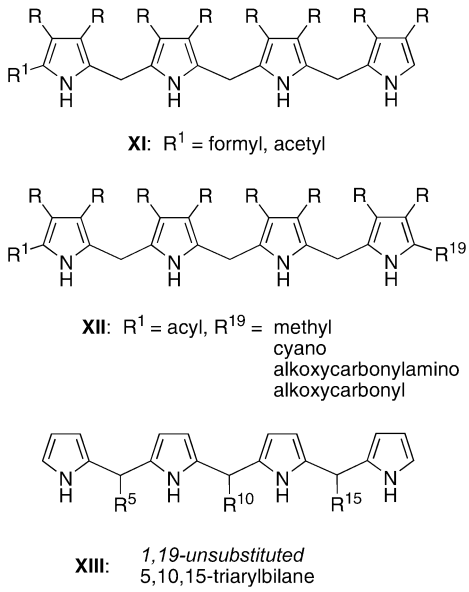


CHART 1. Known Bilanes Prepared from Dipyrromethanes



reactive α-pyrrolic site in each dipyrromethane, as is the case in Scheme 2.

Synthetic routes have been developed over the past few decades to provide access to bilanes bearing three distinct types of substitution patterns (Chart 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 (**XI**).[13−16] 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 (**XII**) have employed the reaction of a 1-acyldipyrromethane and a 9-protected 1-hydroxymethyldipyrromethane[17,18] (or 1-phenylselenylmethyl analogue)[19] wherein the 9-substituent includes alkoxycarbonyl,[19] alkoxycarbonylamino,[18] cyano,[17] or methyl.[17] (3) Meso-substituted, *β*-unsubstituted bilanes that contain three identical meso substituents have been isolated as byproducts of dipyrromethane syntheses,[20] prepared by acidolysis of a dipyrromethane in the presence of an aldehyde,[21] or obtained by one-flask aldehyde−pyrrole condensations.[22−24] Bilanes bearing BAB substituents at the meso positions (i.e., 5-B-10-A-15-B pattern) have been prepared by condensation of an A-aldehyde with a B-dipyrromethane in excess.[25,26] More generally, treatment of a BAB- or ABC-dipyrromethane-1,9-dicarbinol with excess pyrrole gives the BAB- or ABC-bilane (**XIII**).[24,27,28] Such bilanes are valuable precursors to BAB- or ABC-corroles,[24,28] 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,[21,25,27] the reaction typically proceeds with scrambling to give a mixture of porphyrins.

The relative dearth of methods for the direct synthesis of bilanes, suitable α-bilane protecting groups, and methods for converting bilanes to porphyrins may stem 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,[29] 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."[30] Regardless, none of the α-pyrrolic protecting groups that were employed previously appeared suited for the synthesis shown in Scheme 2. Accordingly, we investigated new α-pyrrolic protecting groups (X), including thiocyanato, alkylthio, and bromo groups.

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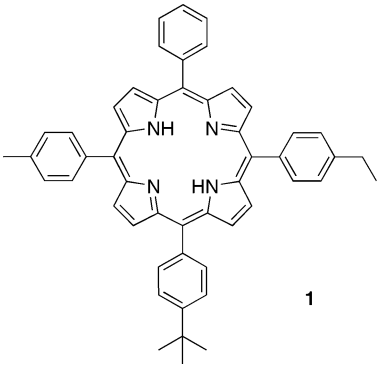
CHART 2. ABCD-Porphyrin Bearing Electron-Rich Substituents



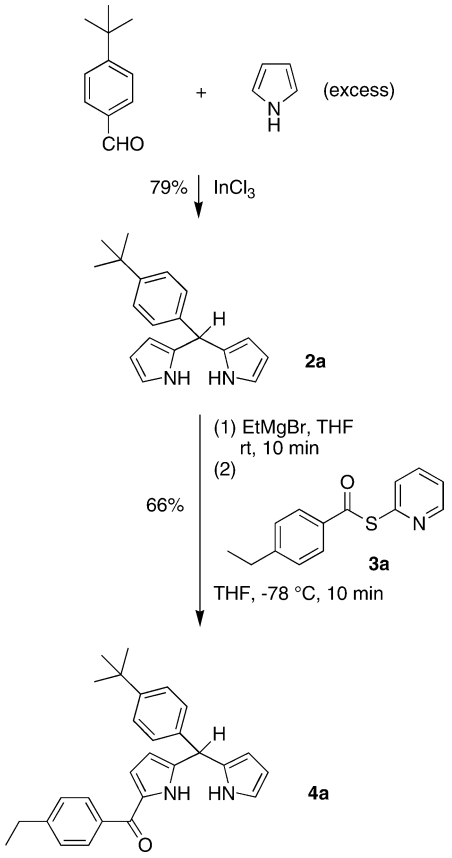
Upon preparing 19-acylbilanes (**VIII**) bearing a protecting group (X) at the 1-position (e.g., ethylthio), we began carrying out transformations to yield the porphyrin. The individual steps in the transformation included (i) oxidation to give the free base biladiene, (ii) metal complexation, (iii) displacement of X (e.g., desulfurization), and (iv) reduction of the acyl moiety to give the metal-templated biladiene-carbinol (**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 (**VIII**, X = −SEt) would undergo transformation in a one-flask process to give the metalloporphyrin (**VI-M**), thereby obviating the individual stepwise transformations. The one-flask transformation occurred under basic, metal-templating conditions.

In this article, we describe our studies of this new route to ABCD-porphyrins. The porphyrin (**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 2). Electron-rich, sterically unhindered substituents were chosen to accentuate any possible scrambling processes, whereas the distinct mass enables identification of such scrambling upon analysis by laser-desorption mass spectrometry (LD-MS).[11,31] 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.

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[4] and 1-acyldipyrromethanes[3,5] can easily be synthesized at high concentration with limited or no chromatography. Thus, the condensation of 4-*tert*-butylbenzaldehyde with excess pyrrole afforded known[3] dipyrromethane **2a** in 79% yield. Acylation of **2a** with Mukaiyama reagent **3a** (prepared herein by reaction[6] of 2-mercaptopyridine and 4-ethylbenzoyl chloride) gave the corresponding 1-acyldipyrromethane (**4a**) in 66% yield as shown in Scheme 3.

SCHEME 3. Synthesis of a 1-Acyldipyrromethane



A second 1-acyldipyrromethane (**4b**)[5] was treated with ammonium thiocyanate and iodine[32,33] to give the 1-acyl-9-thiocyanatodipyrromethane (**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 **4a** did not provide the expected bilane. Accordingly, the thiocyanato group was converted by treatment with EtMgBr (3 equiv)[33,34] to the corresponding ethylthio unit affording the 1-acyl-9-(ethylthio)dipyrromethane (**6-SEt**, Scheme 4) in 96% yield. In this reaction, 3 equiv of EtMgBr is necessary because the dipyrromethane possesses two relatively acidic pyrrolic protons.

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 synthe-

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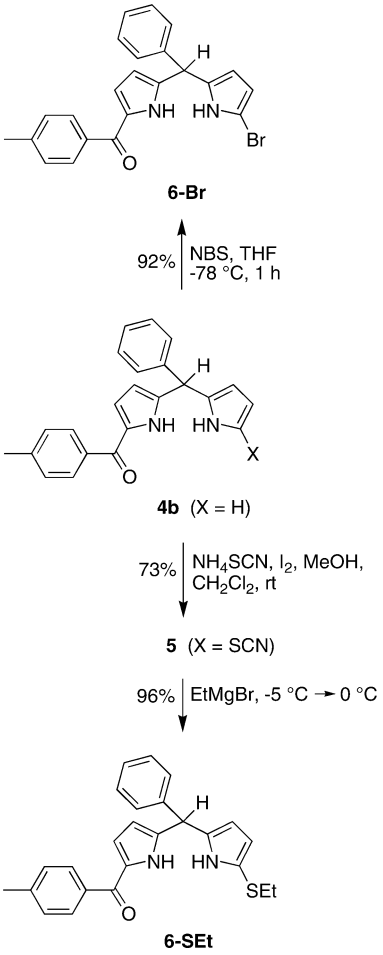
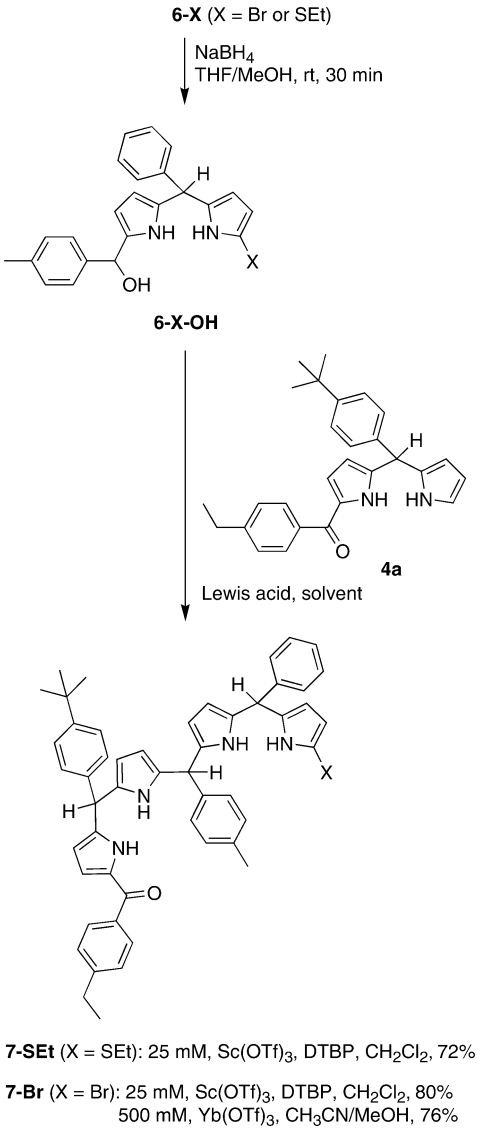
SCHEME 4. Synthesis of a 9-Protected 1-Acyldipyrromethane



ses.[35,36] The reduction of **6-SEt** or known[37] dipyrromethane **6-Br** to the corresponding carbinol **6-SEt-OH** or **6-Br-OH** was performed in THF/methanol (3:1), using 25 mol equiv of $NaBH_4$ (Scheme 5). The dipyrromethanecarbinol **6-SEt-OH** was noticeably more stable than **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.

ii. Acid Catalysis Conditions for Bilane Formation. The condensation of the crude **6-SEt-OH** with 1-acyldipyrromethane **4a** was carried out by using the conditions that emerged from extensive studies of the "2 + 2" (dipyrromethane + dipyrromethane-1,9-dicarbinol) condensation leading to porphyrins.[1,2,11,38,39] The conditions entail reaction in CH_2Cl_2 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 **6-SE-OH**, a trace amount of **4a**, and bilane **7-SEt**. Workup by

SCHEME 5. Synthesis of 1-Protected 19-Acylbilanes



quenching with excess TEA followed by column chromatography provided **7-SEt** in 72% yield (Scheme 5). Analogous reaction of **4a** and **6-Br-OH** afforded bilane **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 **6-Br-OH** and 1-acyldipyrromethane **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 LD-MS to assess scrambling.[11,31] The cleanliness was assessed qualitatively by 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 1.

In all cases where bilane **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

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

entry	acid (mM)	additive (mM)	solvent[b]	time (min)	cleanliness[c]	% yield[d] of **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
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

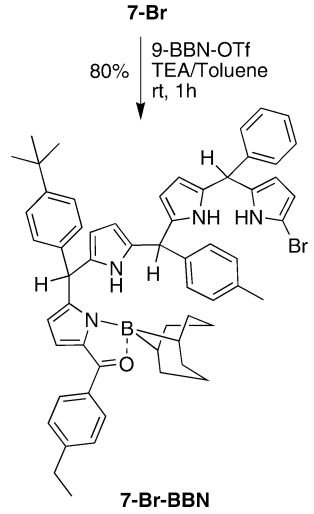
[a] Reactions were carried out with 0.125 mmol reactants unless noted otherwise. [b] Where mixed solvents are employed, the fraction of methanol is ~33%. [c] Crude reaction mixtures were assessed by TLC analysis [silica, hexanes/ethyl acetate (3:1)]. "E" (excellent) indicates the dominant presence of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

cleanliness. Following the conditions of entry 4, the reaction with $Yb(OTf)_3$ with 1.00 mmol of each reactant gave **7-Br** in 76% yield (0.619 g) as well as recovery of the unreacted **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,[17] montmorillonite clay in CH_2Cl_2,[18] $SnCl_4$,[40,41] and Cu(I), light, or heat.[19]

iii. 9-BBN Complex of a 19-Acylbilane. The bilane **7-Br** was converted to the corresponding 9-BBN complex, mirroring chemistry we have employed for the boron complexation of 1-acyldipyrromethanes.[5] The dialkylboron complexes of 1-acyldipyrromethanes are much more hydrophobic than the parent acyldipyrromethanes and crystallize easily, thereby facilitating isolation. Treatment of **7-Br** with TEA in toluene followed by addition of 9-BBN afforded **7-Br-BBN** in 80% yield (Scheme 6).

iv. Characterization of 19-Acylbilanes. Each bilane prepared herein (**7-SEt**, **7-Br**, **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 (^1H, ^{13}C, ^{15}N, and for **7-Br-BBN**, ^{11}B). The ^1H NMR resonances of the bilane **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 **7-SEt** and **7-Br** each gave a peak consistent with the protonated molecule ion

SCHEME 6. Dialkylboron Complexation of a 19-Acylbilane



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 **7-SEt** and **7-Br** are consistent with the presence of one molecule of water per bilane. The bilane **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).[42] We utilized this powerful method for characterization of the bilanes. The results are summarized in Table 2. The proton-coupled gHMBC analysis of each bilane (**7-Br**, **7-SEt**, **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 ^1H NMR spectra also show very close chemical shifts for the inner two pyrrolic NH protons. In the case of **7-Br-BBN**, the nitrogen atom (N^{24}) coordinated to

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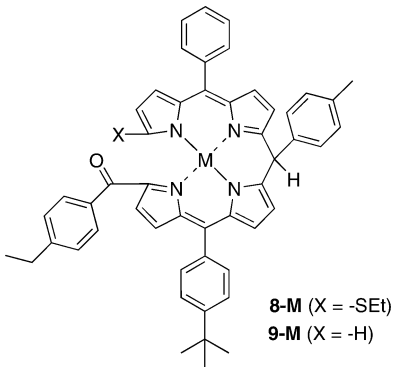
TABLE 2. ^{15}N NMR Spectroscopic Data for Bilanes[a]

		δ ^{15}N NMR resonances (ppm)		
compd	method	N^{21}	N^{22} and N^{23}	N^{24}
7-SEt	gHSQC	−215.1	−227.2	−223.5
	gHMBC	−215.1	−227.2	−223.5
7-Br	gHSQC	−220.7	−227.2	−223.5
	gHMBC	−220.7	−227.2	−223.5
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.[43] [b] The resonance from the boron-complexed pyrrolic nitrogen was not observed.

CHART 3. Biladiene-*ac*−Metal Complexes



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.[43] On the basis of the gHSQC spectra, the values of the NH one-bond coupling constant ($^1J_{N-H}$) ranged from −96 to −100 Hz for each bilane, which are consistent with those reported for shorter homologues (i.e., dipyrromethanes[42]).

v. Stability of 19-Acylbilanes. The bilanes, like most pyrromethanes, are susceptible to oxidation. 19-Acylbilanes **7-SEt**, **7-Br**, and **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 (**7-Br**, **7-SEt**, and **7-Br-BBN**) darkened both in solid form and upon dissolution in an NMR solvent (e.g., $CDCl_3$, THF-d_8) for 3−5 h on the benchtop under ambient light. The **7-Br-BBN** complex was noticeably less stable than the parent **7-Br** itself.

II. One-Flask Synthesis of Metalloporphyrins from Bilanes. The studies of the stepwise conversion of bilane **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 **8-M** (in the case only of M = Pd or Cu among seven metals examined) gave not the expected des-ethylthiobiladiene **9-M** (Chart 3) but rather the ABCD-porphyrin **1-M**. This finding prompted examination of the direct conversion of **7-SEt** → **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.[37] Thus, reaction of **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 **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.

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 **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 noncoordinating reaction milieu.[44] 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 nonnucleophilic 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 3 of crude porphyrin samples (determined spectroscopically[45]) encompass both the metalloporphyrin and the trace amount of free base porphyrin.

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

Application of the conditions of $MgBr_2$ and DBU to bilane **7-Br** (rather than **7-SEt**) in butyronitrile gave **1-Mg** in 47% yield (entry 3), whereas that in toluene gave **1-Mg** in 64% yield (entry 4). Thus, bilane **7-Br** is a much more effective precursor to the porphyrin than bilane **7-SEt**, and all subsequent studies were carried out with bilane **7-Br**. The essential ingredients in these conditions were assessed by omission experiments. The omission of $MgBr_2$ gave the free base porphyrin **1** in 10% yield (entry 5), whereas the omission of toluene gave **1-Mg** in 35% yield (entry 6). The reaction with $MgBr_2$ (3 equiv) and DBU (10 equiv) at 100 mM gave **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 zinc porphyrin **1-Zn** in yields ranging from 18% to 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 and 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 +

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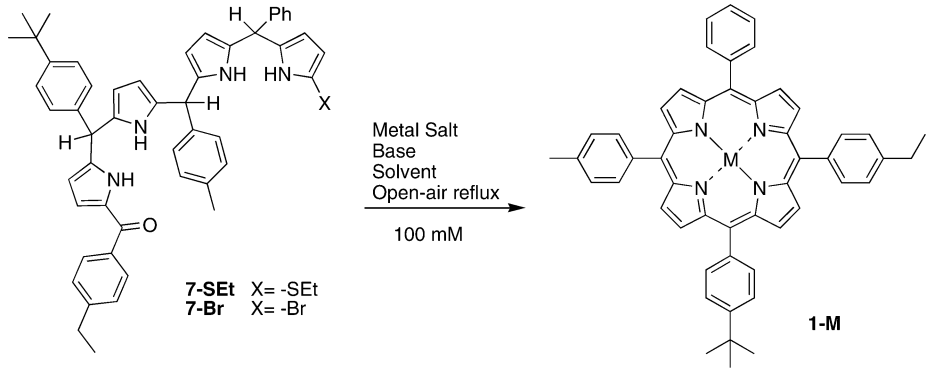
TABLE 3. One-Flask Bilane Cyclization[a]



entry	bilane	metal salt	DBU (equiv)	solvent	time (h)	product	yield (%)
1	**7-SEt**	$MgBr_2$	10	PrCN	2	**1-Mg**	15
2	**7-SEt**	$MgBr_2$	10	toluene	8	**1**	10[b]
3	**7-Br**	$MgBr_2$	10	PrCN	6	**1-Mg**	47[b]
4	**7-Br**	$MgBr_2$	10	toluene	2	**1-Mg**	64[b]
5	**7-Br**		10	toluene	24	**1**	10
6	**7-Br**	$MgBr_2$	10	*c*	3	**1-Mg**	35[b]
7[d]	**7-Br**	$MgBr_2$	10	toluene	1.5	**1-Mg**	69
8	**7-Br**	$Zn(OAc)_2$	10	toluene	1	**1-Zn**	50
9	**7-Br**	$ZnBr_2$	10	toluene	5	**1-Zn**	26[b]
10	**7-Br**	ZnI_2	10	toluene	4	**1-Zn**	31[b]
11	**7-Br**	$Zn(acac)_2$	10	toluene	3.5	**1-Zn**	37[b,e]
12	**7-Br**	$ZnEt_2$		toluene	3.5	**1-Zn**	18
13	**7-Br**	$NiCl_2$	10	toluene	2	**1-Ni**	29
14	**7-Br**	$InCl_3$	10	toluene	2	**1-InCl**	16

[a] The standard condition employs treatment of a solution of the bilane (0.062 mmol) in the specified solvent (100 mM) first 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 seconds, 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 **1** also was isolated (0.4% yield).

2" reaction. Accordingly, the effect of concentration was investigated for the reaction of **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 1A. (Note that concentrations stated in the text are calculated on the basis of the volume of toluene alone in the reaction, whereas the concentrations shown in Figure 1A refer to the volume of both toluene and DBU. For example, the reaction at "100 mM" refers only to the concentration of toluene but actually is ~87 mM upon taking into account the additional volume of DBU.)

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 **1-Mg** in 35% yield. The reaction at 1 or 10 mM concentration of **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 **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 **1-Mg**. The timecourse is displayed in Figure 1B. The reaction is very fast, with a half-time between 5 and 10 min. TLC analysis showed no detectable amount of **7-Br** by the 15-min timepoint; at the end of the reaction only **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 **7-Br** is shown in eq 1. The conversion of bilane **7-Br** to the corresponding porphyrin requires a $2e^-/2H^+$ oxidation. The reaction also produces 3 equiv 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 3 equiv of base.

$$\textbf{7-Br} + MgBr_2 \rightarrow \textbf{1-Mg} + H_2O + 3HBr + 2e^- + 2H^+ \quad (1)$$

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 **7-Br** was carried out under reflux with different atmospheric compositions. The reaction of **7-Br** in toluene containing $MgBr_2$ (3 equiv) and DBU (10 equiv) with a very slow oxygen flow (rather than air) afforded **1-Mg** in 31%

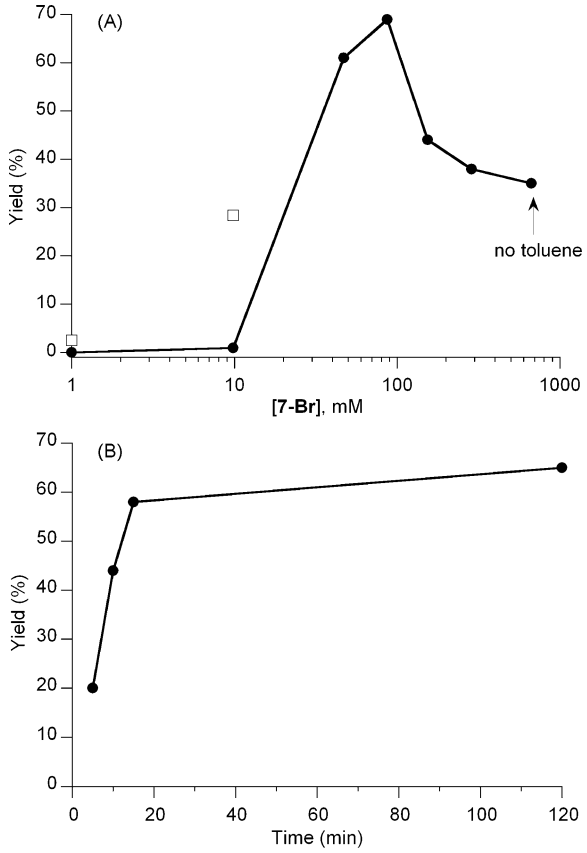


FIGURE 1. (A) The yield of porphyrin **1-Mg** as a logarithmic function of the concentration of **7-Br**. The data shown as solid circles (●) were obtained with **7-Br** (0.100 mmol), DBU (1.00 mmol, 10.0 equiv), and $MgBr_2$ (0.300 mmol, 3.00 equiv) in an appropriate amount of hot toluene exposed to air for 2 h. The two datapoints shown as open squares (□) were obtained in a similar manner but with 100 equiv of DBU and 30 equiv of $MgBr_2$. The *x*-axis shows the concentration of **7-Br** per the amount of toluene and DBU assuming additivity of volumes. The highest yield was obtained at 87 mM, which corresponds to a 100 mM concentration on the basis of only the amount of toluene. (B) The yield of porphyrin **1-Mg** as a function of time for **7-Br** at 100 mM (on the basis of the amount of toluene).

yield. Surprisingly, the reaction under a slow argon flow gave **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 **1-Mg** from **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[46] vs 24[47]) rather than ability to serve as oxidants. Further experimentation is required to elucidate the nature of the oxidant.

v. Preparative Synthesis. The best conditions identified from the above studies employed bilane **7-Br** (100 mM on the basis of toluene) in the presence of $MgBr_2$ (3 equiv) and DBU (10 equiv) at 115 °C open to the air for 2 h (entry 7 in Table 3). The reaction carried out in this manner at 10-fold larger scale than that in Table 3 (**7-Br**, 0.50 g, 0.62 mmol) gave the magnesium porphyrin **1-Mg** in 65% yield (0.295 g). A ~5-fold further increase in scale (2.44 g, 3 mmol of **7-Br**) afforded >1 g of crude **1-Mg** and a trace of the corresponding free base porphyrin **1**. The crude sample of **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 to 0.62 mmol scale) and was readily removed with flash column chromatography. The crude product was demetalated with TFA; workup and chromatography afforded the free base porphyrin **1** (1.123 g) in 53% yield.

Microwave-assisted synthesis often introduces shorter reaction times, hence we examined the synthesis of **1-Mg** under microwave irradiation. The condensation of **7-Br** was carried out at 115 °C under standard small-scale reaction conditions (0.1 mmol, toluene, 100 mM of **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 (**7-Br**) was observed after 15 min of irradiation time. In addition, no detectable scrambling was observed on the basis of LD-MS analysis. Subsequent purification via flash column chromatography afforded **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 **7-Br**, a small amount of unreacted 1-acyldipyrromethane (**4a**) typically remains. Any unreacted 1-acyldipyrromethane (**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.[48]

Outlook

The features of the one-flask bilane cyclization route are compared with the existing "2 + 2" route as shown in Table 4. The prior "2 + 2" route to ABCD-porphyrins requires seven steps,[1,2] 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).

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

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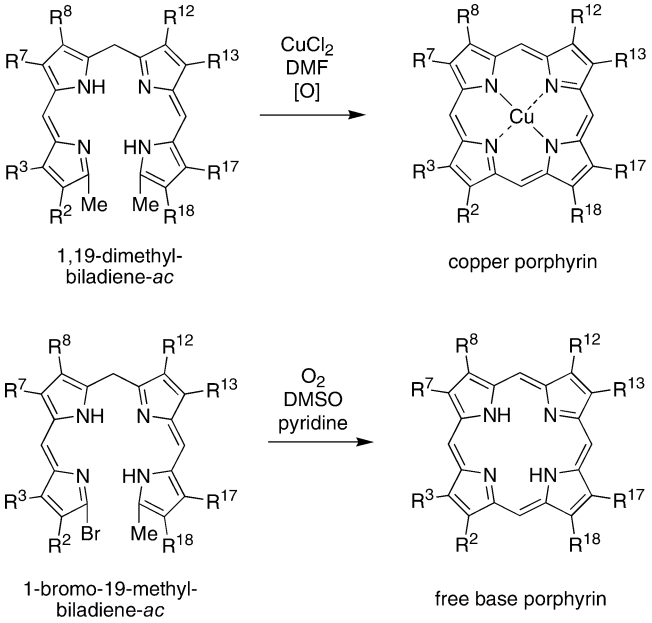
TABLE 4. Comparison of Routes to ABCD-Porphyrins

features	comparison: "2 + 2" route (DPM + DPM-diol)[a]	comparison: one-flask bilane cyclization
reactant concn, mM	2.5 (or 25)	100
effective pyrrole concn in cyclization, mM	10 (or 100)	400
theoretical porphyrin concn, mM	2.5 (or 25)	100
total no. of steps (from aldehydes)[b]	7	8
solvent for porphyrin formation	CH_2Cl_2	toluene
chromatography operations	1[c]	2[d]
oxidation	DDQ	in situ
conditions for porphyrin formation	Acidic	Basic
scrambling	ND[e] or low	ND[e]
yield of the porphyrin-forming step (%)	~20−30 (or 8−23)	65[e]
porphyrin metalation state	free base	magnesium chelate

[a] Dipyrromethane + dipyrromethane-1,9-dicarbinol. [b] Ignores steps to prepare the Mukaiyama reagents. [c] Purification of the crude product from the porphyrin-forming reaction. [d] Purification of bilane species (**7-SEt**, **7-Br**) and the metalloporphyrin. [e] Not detected.

SCHEME 7. Traditional Routes to Porphyrins



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 compound **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 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 α-methyl groups is lost upon copper-mediated oxidation, whereas the other α-methyl group provides the meso carbon atom. This reaction was pioneered by Johnson[49−51] and studied extensively by Smith.[52] Use of alkyl groups longer than alkyl can afford the corresponding monomeso-substituted porphyrin.[52] (2) Treatment of a 1-bromo-19-methylbiladiene-*ac* under basic, oxidative conditions gives the corresponding free base porphyrin.[50,51,53] 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.[52,54,55] The new ABCD-porphyrin synthesis has some conceptual similarity to the latter reaction, where the acyl carbon provides the meso site (and bears the D substituent) and the bromo substituent is the leaving group.

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,[56] are relatives of the bilin pigments,[57−59] exhibit a variety of conformational forms,[60] undergo three successive steps of $2e^-/2H^+$ oxidation,[12] and provide access to bilin derivatives that are potent antioxidants.[61] Moreover, bilanes **7-X** are homologues of dipyrromethanes **6-X**; the strategy used to prepare **7-X** can in principle be extended to provide rational access to longer pyrromethane chains bearing distinct meso substituents.

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Experimental Section

5-(4-*tert*-Butylphenyl)dipyrromethane (2a). Following a general procedure,[4] 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 × 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.[3] mp 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.[3]

***S*-2-Pyridyl 4-Ethylbenzothioate (3a).** Following a general procedure,[6] 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 water 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 (4a). Following a general procedure,[3] a solution of EtMgBr (37.5 mL, 38 mmol, 1.0 M in THF) was added slowly to a solution of **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 **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 diameter × 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 (5). Following a general procedure,[32] a solution of **4b** (3.40 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added in a dropwise manner to a solution of ammonium thiocyanate (1.14 g, 15.0 mmol) and iodine (1.27 g, 5.00 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, 5.00 mmol) in methanol (10 mL) was added dropwise into 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 (6-SEt). Following a general procedure,[34] a solution of EtMgBr (21 mL, 21 mmol, 1.0 M in THF) in THF (49 mL) at −5 °C was treated slowly with a solution of **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 (7-SEt). A solution of **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 dipyrromethanecarbinol as a yellow-orange paste. The resulting sample was dissolved in anhydrous CH_2Cl_2 (24 mL) and treated with **4a** (0.246 g, 0.600 mmol). The reaction mixture was stirred for 10 min to achieve complete dissolution of **4a**. Following the acid catalysis conditions used in porphyrin syntheses,[2] 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 (110 μL, 0.779 mmol, 32.5 mM) was added. The reaction mixture changed immediately from red to orange-yellow. The reaction mixture was diluted with CH_2Cl_2 (∼100 mL) and washed with water and brine. The organic layer was 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 (br s, 1H), 9.65−9.67 (br s, 1H), 9.92−10.22 (br s, 1H), 10.82−11.2 (br s, 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 mass spectrometric 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 (7-Br). The condensation conditions described below are identical with those of entry 4 in Table 1. A sample of **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 mixture 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 dipyrromethanecarbinol was concentrated to give an orange-yellow paste. For improved stability, the dipyrromethanecarbinol was handled as a paste containing residual diethyl ether rather than as a dry solid (see the Supporting Information). A sample of **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 [silica, hexanes/ethyl acetate (3:1)] and LD-MS. TLC analysis indicated the presence of **4a** and bilane **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 diameter × 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 **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 **7-Br** and **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 (br s, 1H), 9.64−9.72 (br s, 1H), 10.24−10.42 (br s, 1H), 10.86−11.04 (br s, 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, 109.6, 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 7-Br in Dilute Solution (25 mM). A sample of **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 [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 dipyrromethanecarbinol as a yellow-orange foam. The resulting sample was dissolved in anhydrous CH_2Cl_2 (48.0 mL) and treated with **4a** (0.492 g, 1.20 mmol). The reaction mixture was stirred for 10 min to achieve complete dissolution of **4a**. Following the acid catalysis conditions used in porphyrin syntheses,[2] 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 [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) and washed with water and brine. The organic phase was 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 (7-Br-9-BBN). By following the reported procedure for 1-acyldipyrromethanes,[5] a solution of **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 (2.00 mL, 1.00 mmol, 0.500 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 (br s, 1H), 0.72−0.78 (br s, 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 (br s, 2H), 10.36−10.46 (br s, 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, calcd

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) (1-Mg). A sample of **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 **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 **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 diameter × 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 δ 15.9, 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 (1). Following the procedure described for **1-Mg**, bilane **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 diameter × 30 cm, CH_2Cl_2 → CH_2Cl_2/ethyl acetate (5:3) → (1:1), ∼2.5 L of solvent]. The 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 **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 (br s, 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, 130.6−131.8 (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 1: Synthesis with $InCl_3$ (entry 2) of 7-Br. A sample of **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 **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 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 **6-Br-OH**, unreacted **4a**, bilane **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 diameter × 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 exhibited 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 3: (i) Standard Procedure Given for 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 **7-Br** (0.0500 g, 0.0620 mmol), dry toluene (0.620 mL), and DBU (0.0900 mL, 0.620 mmol, 10.0 mol equiv versus **7-Br**) at room temperature. The reaction mixture darkened while stirring over the course of 5 min. A sample of $Zn(OAc)_2$ (0.0350 g, 0.190 mmol, 3.00 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) 1-Mg. Application of the standard procedure with **7-Br** (0.050 g, 0.062 mmol) and $MgBr_2$ with chromatographic workup [alumina (40 g), 2.5 cm diameter × 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) 1-Ni. Application of the standard procedure with **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) 1-InCl. Application of the standard procedure with **7-Br** (0.082 g, 0.10 mmol) and $InCl_3$ with chromatographic workup [silica, $CH_2Cl_2 \rightarrow CH_2Cl_2$/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 (br s, 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.

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Supporting Information Available: Additional procedures; exploratory results; characterization data for selected new compounds; and NMR studies of bilanes. This material is available free of charge via the Internet at http://pubs.acs.org.

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