Synthesis of Meso-Substituted Chlorins via Tetrahydrobilene-*a* Intermediates

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Chlorin building blocks incorporating a geminal dimethyl group in the reduced ring and synthetic handles in specific patterns at the perimeter of the macrocycle are expected to have utility in biomimetic and materials chemistry. A prior route employed condensation of a dihydrodipyrrin (Western half) and a bromodipyrromethane-monocarbinol (Eastern half), followed by oxidative cyclization of the putative dihydrobilene-*a* to form the meso-substituted zinc chlorin in yields of ∼10%. The limited stability of the dihydrodipyrrin precluded study of the chlorin-forming process. We now have refined this methodology. A tetrahydrodipyrrin Western half (2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin) has been synthesized and found to be quite stable. The condensation of the Western half and an Eastern half (100 mM each) proceeded smoothly in CH_3CN containing 100 mM TFA at room temperature for 30 min. The resulting linear tetrapyrrole, a 2,3,4,5-tetrahydrobilene-*a*, also is quite stable, enabling study of the conversion to chlorin. Refined conditions for the oxidative cyclization were found to include the following: the tetrahydrobilene-*a* (10 mM), AgTf (3−5 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (15 molar equiv) in CH_3CN at reflux exposed to air for 4−6 h, affording the zinc chlorin. The chlorin-forming process could be implemented in either a two-flask process or a one-flask process. The two-flask process was applied to form six zinc chlorins bearing substituents such as pentafluorophenyl, 3,5-di-*tert*-butylphenyl, TMS-ethyl benzoate, iodophenyl, or ethynylphenyl (deprotection of the TMS-ethynyl group occurred during the oxidative cyclization process). The stepwise yields (isolated) for the condensation and oxidative cyclization processes forming the tetrahydrobilene and zinc chlorin were 32−72% and 27−62%, respectively, giving overall yields of zinc chlorin from the Eastern and Western halves of 12−45%. Taken together, the refinements introduced enable 100-mg quantities of chlorin building blocks to be prepared in a facile and rational manner.

Introduction

The synthesis of chlorins is an area of active interest owing to the photochemical properties of these green pigments.[1] We recently developed a synthetic route that provides access to chlorin building blocks bearing substituents at the meso- and/or β-positions.[2,3] In addition to selected patterns of functional group handles at the perimeter of the macrocycle, each chlorin bears a geminal dimethyl group to lock in the hydrogenation level yet lacks steric congestion or other unwanted functionality around the reduced ring. The synthesis involves the construction of an Eastern half and a Western half, which are joined to form the chlorin macrocycle in the final step (Scheme 1). This convergent coupling of the Eastern half and Western half is performed in a two-flask procedure involving acid-catalyzed condensation to give a dihydrobilene-*a*, followed by metal-mediated oxidative cyclization to give the chlorin. The Eastern half, a bromodipyrromethane-monocarbinol, is readily available by the acylation and bromination of a dipyrromethane at the 1- and 9-positions, respectively, followed by reduction. The Western half is a dihydrodipyrrin (**1**). The Western half has limited stability and generally must be prepared from the stable nitrohexanone-pyrrole precursor and used within a few days.

In our initial search for routes to a suitable Western half, we investigated the synthesis of a tetrahydrodipyrrin via an intermediate tetrahydrodipyrrin *N*-oxide (comprised of a pyrrole and a pyrroline *N*-oxide).[4] The formation of *N*-oxides by cyclization followed by deoxygenation affords a convenient entry to a number of nitrogen heterocycles.[5] Indeed, pyrroline *N*-oxides played a central role throughout Todd's studies related to the synthesis of vitamin B_{12}.[6] Battersby et al. synthesized a tetrahydrodipyrrin *N*-oxide, converted it to the corresponding tetrahydrodipyrrin, and upon reaction with a

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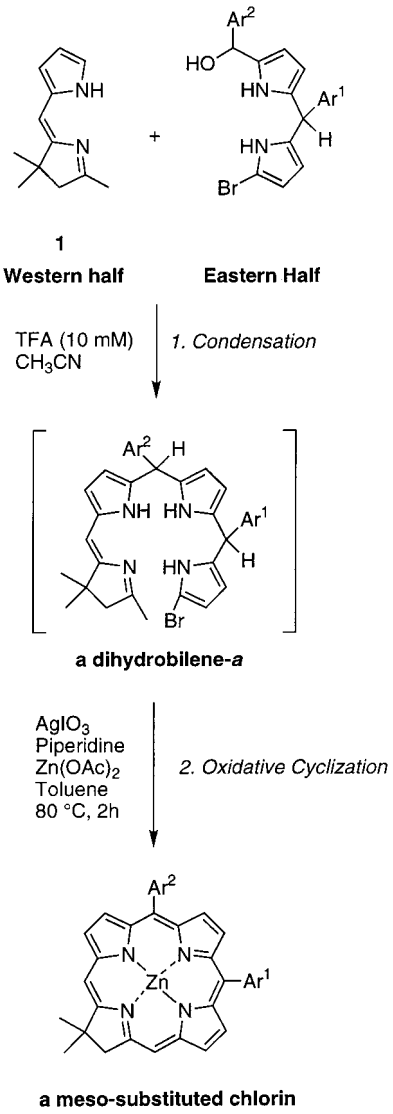
Scheme 1. Chlorin Synthesis via a Dihydrobilene-*a*



1-bromo-9-bromomethyldipyrrin in the presence of copper acetate obtained the copper chlorin in 6.9% yield (2.8 mg).[7] Though the pyrrole component in Battersby's Western half was substituted with one ester and two alkyl groups, the route employed also proved suitable for our synthesis of a tetrahydrodipyrrin *N*-oxide incorporating an unsubstituted pyrrole unit.[4] Thus, cyclization of nitrohexanone-pyrrole **2** afforded the corresponding tetrahydrodipyrrin *N*-oxide **3**, but attempted deoxygenation of the cyclic nitrone to form the tetrahydrodipyrrin Western half **4** afforded an unknown byproduct.[4] We resorted to the cyclization of the nitrohexanone-pyrrole **2** to give the dihydrodipyrrin **1** directly (without isolating the *N*-oxide) in yields of 20−30%.[2,3] The tetrahydrodipyrrin **4** remained quite attractive due to lack of π-conjugation between the pyrrole and pyrroline rings. We anticipated that compared with the dihydrodipyrrin Western half **1**, the tetrahydrodipyrrin **4** should (1) be more stable and (2) exhibit greater reactivity at the pyrrolic α-position to acid-catalyzed condensation, thereby facilitating formation of the corresponding tetrahydrobilene-*a* intermediate. We have since reinvestigated the synthesis of the tetrahydrodipyrrin Western half by deoxygenation of the corresponding *N*-oxide **3**.

In this paper, we describe a number of refinements that greatly facilitate access to meso-substituted chlorin building blocks. The synthesis of a new Western half (**4**) based on the tetrahydrodipyrrin nucleus is achieved by the deoxygenation of the corresponding *N*-oxide **3** under nonacidic conditions. The resulting tetrahydrobilene-*a* is stable, which enabled refinements to the conditions for both the condensation and the oxidation. We also have investigated a one-flask procedure for chlorin formation. Two new Eastern halves have been prepared for enhanced solubility of the resulting chlorin building blocks in organic solvents. The meso-substituted chlorin building blocks are of interest in the synthesis of multichlorin arrays.

Results and Discussion

Synthesis of a Tetrahydrodipyrrin Western Half. The synthesis of the unsubstituted tetrahydrodipyrrin Western half **4** is shown in Scheme 2. The desired nitrohexanone-pyrrole **2** was prepared from pyrrole-2-carboxaldehyde by reaction with nitromethane, affording 2-(2-*trans*-nitrovinyl)pyrrole, followed by reduction with sodium borohydride and fluoride-mediated Michael addition of mesityl oxide. Reductive cyclization of **2** in the presence of Zn in acetic acid at room temperature (but exothermic) as specified by Battersby[7] afforded the *N*-oxide **3** in <40% yield. A byproduct, observable by TLC analysis and estimated by ^{1}H NMR spectroscopy to be present in ∼3:2 ratio (byproduct/**3**), was isolated and assigned the annulated "pyrrolo-desmethyltropane" structure shown for **5**. Noteworthy features of the ^{1}H NMR spectrum of **5** include the following: (1) the presence of two resonances due to the pyrrole α-proton and β-proton, in contrast to the three resonances due to the α- and β-protons exhibited by the *N*-oxide **3**, and (2) disappearance of the singlets assigned to the amino and pyrrolic NH protons upon exchange with D_2O. The structure of **5** was confirmed by X-ray crystallography (Supporting Information). The formation of such a cyclic byproduct cannot occur with pyrrole precursors bearing a full complement of alkyl substituents at the α- and β-positions.[7] The same reaction performed in acetic acid diluted 1:1 with ethanol and held at 0 °C, with portionwise addition of the Zn, resulted in a >9:1 ratio of **3**:**5**. The residual byproduct **5** was readily removed by chromatography. Under these improved conditions, the desired *N*-oxide **3** was isolated in 86% yield.

The next step involved deoxygenation of *N*-oxide **3** to give the tetrahydrodipyrrin **4**. Numerous methods have been developed for the deoxygenation of heterocyclic

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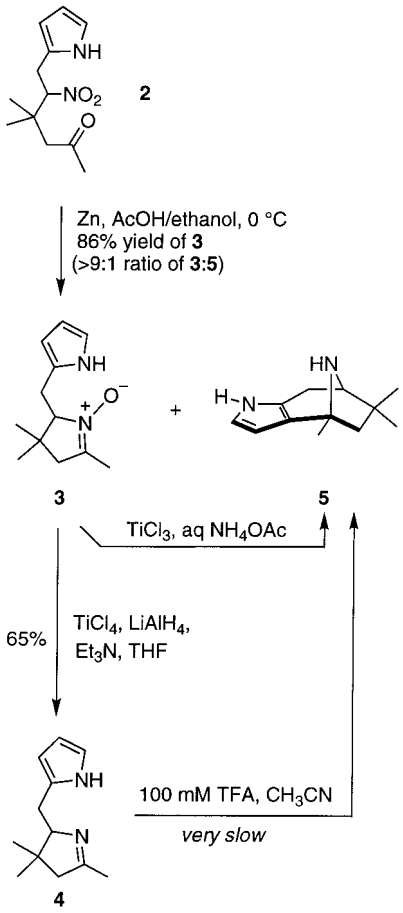
Scheme 2



N-oxides bearing various functional groups.[5] For the tetrahydrodipyrrin *N*-oxide, the ideal deoxygenation method must not be strongly acidic to avoid polymerizing the pyrrole unit and must not cause reduction of the imine. The deoxygenation of **3** was examined with a variety of reagents[8] at room temperature and at elevated temperatures, but the *N*-oxide was resistant to deoxygenation with each of these reagents as determined by TLC or ^{1}H NMR analysis. In addition, $NaBH_4$/THF[9] reduced the *N*-oxide and the double bond affording several products. Treatment with $TiCl_3$ in a buffered NH_4OAc solution[7] gave byproduct **5** (obtained previously but not identified)[4] rather than the desired pyrroline **4**. This failure is in contrast to the successful transformation (75% yield) achieved by Battersby and co-workers upon applying the same method to a tetrahydrodipyrrin *N*[10]-oxide, which differed from **3** only in bearing one ester and two alkyl substituents on the pyrrole unit.[7] Similar pyrrolo[3.2.1]azabicyclooctane products have been reported by rearrangement of tetrahydrodipyrrin derivatives (formed as intermediates in amine + ketoaldehyde condensations in studies of aging) and a plausible mechanism proposed involving electrophilic attack of the pyrroline imine at the pyrrole 3-position.[10]

Application of a procedure for the deoxygenation of *N*-oxides with Ti(0)/THF at room temperature[11] to **3** resulted in a variety of decomposition products as determined by ^{1}H NMR spectroscopy. Upon repeating the deoxygenation procedure with the addition of 2 molar equiv of triethylamine to the Ti(0)/THF slurry (to neutralize the HCl liberated from the preparation of Ti(0)) prior to addition to the solution of **3** in THF, the desired deoxygenated product **4** was obtained as a crystalline solid following column chromatography. The tetrahydrodipyrrin **4** is quite stable, exhibiting negligible decomposition over 1 month upon storage at 0 °C.

Investigation of the Synthesis of Chlorins. Our prior synthesis of chlorins involved (1) formation of the bromodipyrromethane-monocarbinol (Eastern half) by $NaBH_4$ reduction of the carbonyl group in the Eastern half precursor, (2) acid-catalyzed condensation of the Eastern half and the Western half to obtain the dihydrobilene-*a*, and (3) oxidative metal-mediated cyclization to give the chlorin.[2,3] All three steps were done in succession on the same day. However, condensation of **4** and **6a-OH** (100 mM TFA in CH_3CN at room temperature) followed by oxidation under the conditions employed with **1** (excess $AgIO_3$, $Zn(OAc)_2$ and piperidine in anhydrous toluene at 80 °C) gave chlorin **Zn-8a** in only 7% yield. Similarly, reaction of **4** and **6c-OH** afforded chlorin **Zn-8c** in 10% yield.

Studies of the Condensation. To understand whether the low yields of chlorin originated in the condensation process or the metal-mediated oxidative cyclization process, we sought to isolate the putative tetrahydrobilene-*a*, a linear tetrapyrrole derivative formed by condensation of the Western half and the Eastern half. The condensation of **4** and Eastern half **6a-OH** (100 mM each) was performed at room temperature in CH_3CN containing 100 mM TFA (eq 1). TLC analysis of the reaction mixture after 3 min showed the presence of a new component. Chromatographic workup after 30 min afforded the tetrahydrobilene-*a* **7a** in 72% yield. The ^{1}H NMR spectrum of the tetrahydrobilene-*a* showed resonances characteristic of the respective Western half **4** and Eastern half precursor **6a**. The three signals (7.75, 8.05, 9.29 ppm) assigned to the pyrrolic NH units each appeared as a broad multiplet. The appearance of multiple signals is not unexpected; the tetrahydrobilene-*a* contains three chiral centers, and the isolated product can comprise up to eight diastereomers. Bilanes and derivatives are known to be sensitive to oxidation as well as attack by electrophilic species (e.g., acids) and to undergo intermolecular exchange of the pyrrole rings.[12] However, the tetrahydrobilene-*a* sample showed no decomposition upon storage as a solid for several months or in a solution of $CDCl_3$ for more than 2 weeks under argon near 0 °C.

The surprising stability of the tetrahydrobilene-*a* and access to ~500 mg quantities of this compound enabled us to explore the reaction conditions of the separate condensation and oxidation steps. To modify the condi-

(8) Zn, NaOH/methanol (a); Zn, aqueous NH_4Cl/THF (b); $FeSO_4$, aqueous NH_4Cl/CH_3CN (c); Mg or Fe, $AcONH_4$/methanol (d); Ph_3P/toluene (e, f); S/toluene (g); NaN_3/toluene (h); Zn, NaI, Me_3SiCl/CH_3CN (i). (a) den Hertog, H. J.; Henkens, C. H.; Van Roon, J. H. *Rec. Trav. Chim. Pays-Bas* **1952**, *71*, 1145−1151. (b) Aoyagi, Y.; Abe, T.; Ohta, A. *Synthesis* **1997**, 891−894. (c) Talik, T.; Plazek, E. *Roczniki Chem.* **1961**, *35*, 463−473. (d) Hahn, W. E.; Lesiak, J. *Polish J. Chem.* **1985**, *59*, 627−629. (e) Lu, X.; Sun, J.; Tao, X. *Synthesis* **1982**, 185−186. (f) Read, R. W.; Spear, R. J.; Norris, W. P. *Aust. J. Chem.* **1983**, *36*, 1227−1237. (g) Relyea, D. I.; Tawney, P. O.; Williams, A. R. *J. Org. Chem.* **1962**, *27*, 477−481. (h) Di Nunno, L.; Florio, S. *La Chim. E L'Ind. (Milan)* **1975**, *57*, 243−244. (i) Morita, T.; Kuroda, K.; Okamoto, Y.; Sakurai, H. *Chem. Lett.* **1981**, 921−924.

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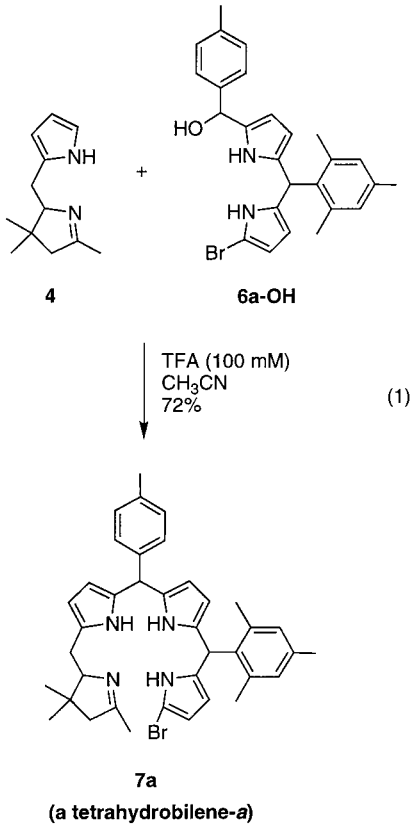

tions of the condensation, the concentration of TFA and the reaction time were examined. The condensation of Western half **4** and Eastern half **6a-OH** was performed for a given period of time; for quantitation, the resulting tetrahydrobilene-*a* **7a** was subjected to the oxidative cyclization to form the chlorin. The yield of chlorin **Zn-8a** was then determined by UV−vis spectroscopy. Refined conditions for the oxidative cyclization were employed (vide infra); these conditions employ AgTf, $Zn(OAc)_2$, and 2,2,6,6-tetramethylpiperidine in CH_3CN at reflux exposed to air for 4.5 h.

The effect of the concentration of TFA (10−316 mM) was examined at room temperature for condensations of 30 min in CH_3CN. The results are shown in Figure 1. The chlorin was formed in 36% yield upon use of 100 mM TFA. By contrast, the reaction of the dihydrodipyrrin **1** with 10 mM reactants and 10 mM TFA[2,13] gave chlorin in ∼10% yield.

Two possible side reactions during acid-catalyzed condensation were of considerable concern, including rearrangement of the Western half (**4** → **5**) and acidolysis yielding mixtures of chlorins and porphyrins: (1) A likely mechanism for formation of byproduct **5** involves electrophilic attack of the positively charged imine (or nitrone) on the 3-position of the pyrrole.[10] Treatment of **4** (100 mM) under the same acid catalysis conditions employed in chlorin formation (100 mM TFA in CH_3CN at room temperature) gave a ratio of 95:5 for compounds **4**/**5** after 30 min but ∼20:80 after 12 h. The same reaction with 1 M TFA gave a ratio of ∼15:85 after 30 min. These results show that the rearrangement of the Western half **4** to the byproduct **5** occurs under acid catalysis, but the reaction is too slow to be competitive with the condensation with an Eastern half giving the tetrahydrobilene-*a*. (2) A key concern upon exposure of dipyrromethanes to acidic media is the occurrence of acidolysis yielding

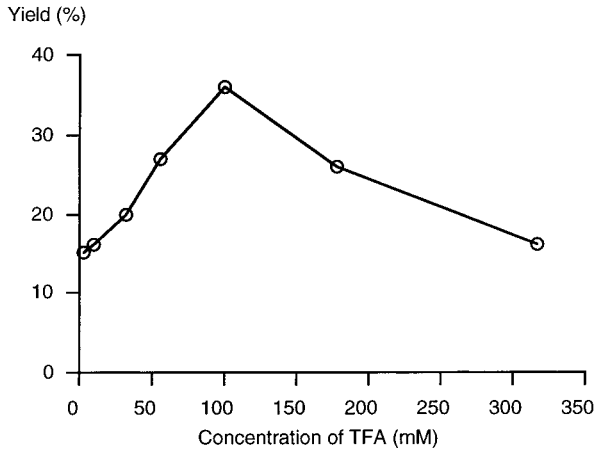

Figure 1. Effect of the concentration of TFA on the condensation of Eastern half (**6a-OH**) and Western half (**4**). The yield shown refers to the amount of chlorin formed upon treatment of the crude product to the oxidation conditions (analogous to a one-flask reaction) followed by UV−vis spectroscopy.

fragments that can recombine to form products with undesired substitution patterns (i.e., scrambling).[14] We have found that dipyrromethane-carbinols (and the resulting porphyrinogens) are stable to modest concentrations of TFA in CH_3CN but that scrambling occurs within 30 min upon exposure to 100 mM TFA.[15,16] LD-MS analysis of the crude reaction mixture showed no scrambling with condensations employing 100 mM TFA. The absence of scrambling in the condensation of the Eastern and Western halves at higher acid concentration than in dipyrromethane condensations can be explained by consideration of the basicity of the different reactants. The weakly basic nature of the pyrrolic unit in a dipyrromethane (protonated 2-methylpyrrole has $pK_a = -0.21$)[17] provides little capacity for buffering of the acid in reactions of the dipyrromethane. By comparison, the pyrroline motif in the Western half is basic (protonated 2,4,4-trimethyl-Δ^1-pyrroline has $pK_a = 7.6$).[18] With equal concentrations of TFA and the Western half (100 mM each), the latter likely buffers the former, affording an effective acidity within the range that safely avoids acidolysis of the dipyrromethane or tetrahydrobilene-*a* species.

The time course of the condensation for reaction with 100 mM TFA at room temperature is shown in Figure 2. These results show that the reaction is rapid and the yield changes only slightly over the course of 2 h, with a slight peak around 30 min. In summary, a condensation for 30 min at room temperature in CH_3CN containing 100 mM TFA results in the highest yield of chlorin.

Studies of the Metal-Mediated Oxidative Cyclization. The motivation for employing an oxidant, base, metal complex, and a silver salt for converting the

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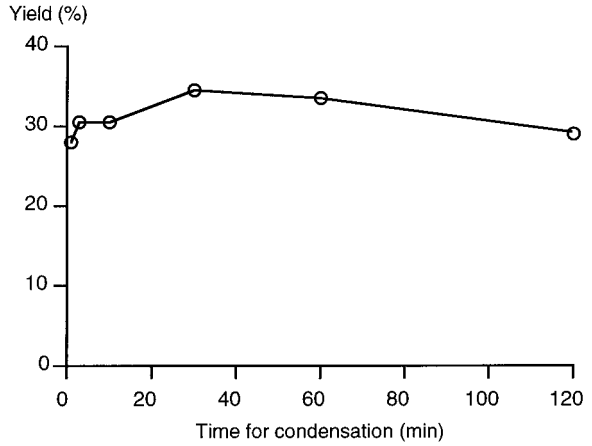


Figure 2. Effect of the duration of the condensation of Eastern half (**6a-OH**) and Western half (**4**) on the ultimate yield of chlorin. The yield (average of two experiments) shown refers to the amount of chlorin formed upon treatment of the crude product to the oxidation conditions (analogous to a one-flask reaction) followed by UV−vis spectroscopy.

tetrahydrobilene-*a* to the chlorin can be understood by examination of Scheme 3, which shows proposed steps in the transformation. While little is known either about the intermediates or the sequence of events in this process, consideration of the formal transformations in the overall process guided our thinking in the development of reaction conditions. The role of the oxidant is to remove six electrons and six protons. The role of the base is to neutralize the acetic acid (2 equiv) formed upon zinc insertion, to neutralize the HBr formed upon aromatization, and perhaps to facilitate imine−enamine tautomerization. The role of the metal complex is to template the electrocyclization. The role of the silver salt is to facilitate dehydrobromination.[19] The overall process is expected to be more complex than illustrated by Scheme 3. For example, complexation and tautomerization may be interspersed among stepwise oxidation processes.

The conversion of the tetrahydrobilene-*a* **7a** to the zinc chlorin **Zn-8a** was examined under a variety of conditions. The conditions employed previously used $AgIO_3$ (15 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and piperidine (15 molar equiv) in toluene at 80 °C for 2 h.[2,3] The same conditions with **7a** gave the desired zinc chlorin **Zn-8a**; the yield was low (7% overall yield), but a more severe problem was that iodinated chlorin byproducts were occasionally obtained. To avoid $AgIO_3$, we reexamined the use of high-potential quinones such as *p*-chloranil and DDQ, which are effective oxidants in the two-step one-flask synthesis of porphyrins.[20] We previously attempted to use *p*-chloranil but the chlorin product formed gave an incorrect molecule ion peak upon LD-MS analysis. The use of *p*-chloranil with the tetrahydrobilene-*a* gave two covalent chlorin−hydroquinone byproducts in greater yields than that of the desired chlorin (see the Supporting Information for isolation and characterization). Ultimately, we found that oxidation occurred without a deliberately added oxidant other than exposure of the hot reaction mixture to air. It is likely that the oxidant in the previous reaction conditions employing $AgIO_3$ also was O_2. With this finding in hand, an iterative optimization led to the following reaction conditions: AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (15 molar equiv) in a solvent exposed to air. The cleanliness of these reactions enabled the yield of chlorin to be determined by UV−vis spectroscopy. The following sections describe the optimization of the oxidative cyclization conditions.

Table 1. Effects of Solvent on Chlorin Formation (7a → Zn-8a)[a]

solvent	*T* (°C)	yield[b] (%)
CH_3CN	reflux	60
THF[c]	reflux	58
DMF	120 °C	57
1,2-dichloroethane	reflux	44
DMSO	120 °C	42
toluene	reflux	39
ethanol	reflux	35
pyridine	reflux	34[d]
$CHCl_3$	reflux	19
dioxane	reflux	17
methanol	reflux	<1[d]

[a] All reactions were performed under the standard conditions employing the following components: tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (15 molar equiv) under the specified conditions (solvent, temperature) exposed to air for 4.5 h. [b] Determined by absorption spectroscopy (ϵ_{609} = 43 600 M^{-1} cm^{-1}) in toluene. [c] Reagent-grade THF gave a slightly higher yield of chlorin (**Zn-8a**) compared to that with distilled THF. [d] The long wavelength λ_{max} was at 612 nm.

We first examined the conversion of **7a** to **Zn-8a** in 10 solvents of diverse polarity and composition (Table 1).

Scheme 3. Processes and Possible Intermediates in Chlorin Formation

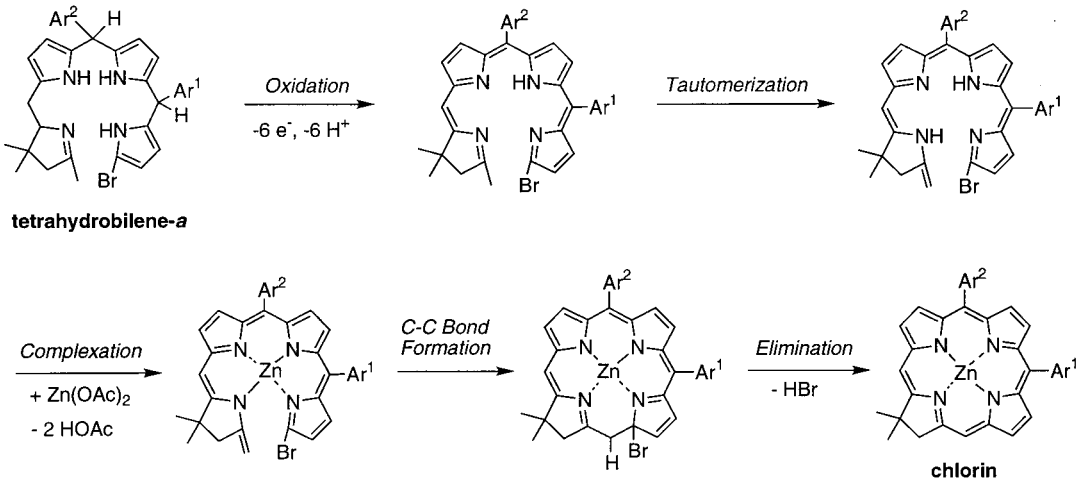


Table 2. Effects of Base on Chlorin Formation (7a → Zn-8a)[a]

base	yield[b] (%) THF	yield[b] (%) CH_3CN
2,2,6,6-tetramethylpiperidine	65	72
triethylamine	35	57
piperidine	41[c]	31[c]
2,5-di-*tert*-butylpyridine	<1	<1

[a] All reactions were performed under the standard conditions employing the following components: tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and specified base (15 molar equiv) at reflux in the specified solvent exposed to air for 4.5 h. [b] Determined by absorption spectroscopy (ϵ_{609} = 43 600 M^{-1} cm^{-1}) in toluene. [c] The long wavelength λ_{max} was at 612 nm.

Table 3. Effects of Amount of AgTf on Chlorin Formation (7a → Zn-8a)[a]

molar equiv of AgTf	yield[b] (%)
1	46
2	60
3	63
5	68
10	7
15	*c*

[a] All reactions were performed under the standard conditions employing the following components: tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (specified amount), $Zn(OAc)_2$ (15 molar equiv), 2,2,6,6-tetramethylpiperidine (15 molar equiv) at reflux in CH_3CN exposed to air for 4.5 h. [b] Determined by absorption spectroscopy (ϵ_{609} = 43,600 M^{-1} cm^{-1}) in toluene. [c] The broad bands in the absorption spectrum precluded accurate yield determination.

Table 4. Omission Experiments to Test Oxidative Cyclization Conditions (7A → Zn-8A)[a]

conditions	yield[b] (%) THF	yield[b] (%) CH_3CN
no omission (standard conditions)	58	60
omission of AgTf	15	35
omission of $Zn(OAc)_2$	-[c]	0
omission of 2,2,6,6-tetramethylpiperidine	-[c]	<1

[a] All reactions were performed under the following conditions (with omission of the specified component): tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (15 molar equiv) at reflux in the specified solvent exposed to air for 4.5 h. [b] Determined by absorption spectroscopy (ϵ_{609} = 43 600 M^{-1} cm^{-1}) in toluene. [c] Not examined.

The solvents CH_3CN, THF, and DMF proved superior (~60% yield), but we focused on CH_3CN and THF for further studies because of their ease of handling. Battersby also found CH_3CN to be the best solvent in his studies of chlorin formation.[7]

Four amine bases were examined (Table 2) in THF or CH_3CN. Of the four, 2,2,6,6-tetramethylpiperidine gave the best results in both CH_3CN and THF (72%, 65%). Piperidine, which was used in the previous method,[2,3] gave a lower yield than 2,2,6,6-tetramethylpiperidine.

We examined the amount of AgTf required for the reaction (Table 3). When a large excess of AgTf was used, little chlorin (**Zn-8a**) was formed. The best result was obtained using 2−5 molar equiv of AgTf.

To establish the absolute requirement for each of the reagents in the chlorin-forming reaction, omission experiments were performed (Table 4). In the absence of AgTf, chlorin was formed at only one-half to one-fourth of the normal level. No chlorin was observed in the absence of zinc acetate, and only a trace was obtained in the absence of 2,2,6,6-tetramethylpiperidine. The rigorous exclusion of oxygen proved difficult, and the omission of this putative reagent was not examined.

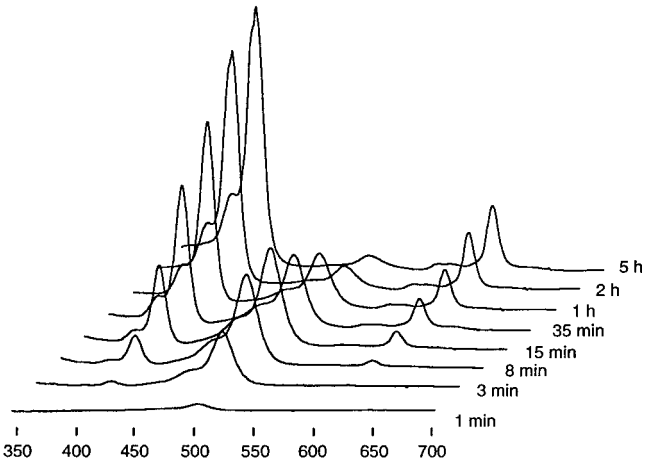


Figure 3. Spectral evolution of the conversion of **7a** to **Zn-8a** upon treatment under the oxidative cyclization conditions [tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), 2,2,6,6-tetramethylpiperidine (15 molar equiv) in CH_3CN at reflux in air]. The absorption due to the Soret band and the $Q_y(0,0)$ band steadily increases while the absorption at 505 nm rises and declines with time. (The clipping of the Soret band absorption in the spectra at 2 and 5 h is an instrumental artifact.)

The concentration dependence of the reaction was examined by performing the reaction of tetrahydrobilene-*a* **7a** at 1, 3, or 10 mM and scaling the concentrations of the reagents linearly. The yield of chlorin was essentially constant over this 10-fold change in concentration.

The time course of the reaction was monitored by absorption spectroscopy. The spectral evolution of the oxidative cyclization process is shown in Figure 3. Within 1 min, a sharp absorption band is evident at 505 nm, which resembles that of a bis(dipyrrinato)zinc(II) chromophore[4,21] though such an assignment is not certain (see the Supporting Information). A zinc−dipyrrin complex could form by chelation of a partially oxidized product of the initial tetrahydrobilene-*a* (not shown in Scheme 3). The peak at 505 nm increased for 15 min and then decreased. The absorption spectra also show the appearance after 8 min of the characteristic chlorin peaks at 413 and 609 nm, which continue growing in over 1 h. After 1 h, more than 40% of tetrahydrobilene-*a* **7a** had been converted into chlorin **Zn-8a**. The yield of chlorin as a function of time was readily assessed based on the intensity of the peak at 609 nm. The resulting yield versus time plot is shown in Figure 4. The formation of the chlorin **Zn-8a** is essentially complete within 5 h.

(19) Cromwell, N. H.; Ayer, R. P.; Foster, P. W. *J. Am. Chem. Soc.* **1960**, *82*, 130−132.
(20) Lindsey, J. S. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 1, pp 45−118.
(21) (a) Granick, S.; Gilder, H. In *Advances in Enzymology*; Nord, F. F., Ed.; Interscience: New York, 1947; Vol. 7, pp 358−363. (b) Johnson, A. W.; Kay, I. T.; Markham, E.; Price, R.; Shaw, K. B. *J. Chem. Soc.* **1959**, 3416−3424. (c) Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1970**, *9*, 1832−1839. (d) March, F. C.; Couch, D. A.; Emerson, K.; Fergusson, J. E.; Robinson, W. T. *J. Chem. Soc. A* **1971**, 440−448. (e) Murakami, Y.; Matsuda, Y.; Kobayashi, S. *J. Chem. Soc., Dalton Trans.* **1973**, 1734−1737. (f) Hill, C. L.; Williamson, M. M. *J. Chem. Soc., Chem. Commun.* **1985**, 1228−1229. (g) Brückner, C.; Karunaratne, V.; Rettig, S. J.; Dolphin, D. *Can. J. Chem.* **1996**, *74*, 2182−2193.

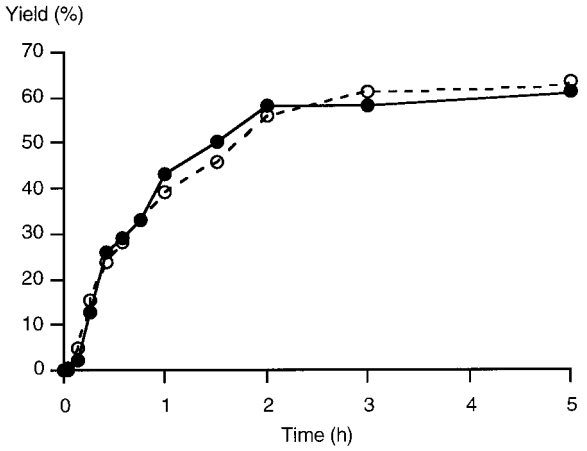


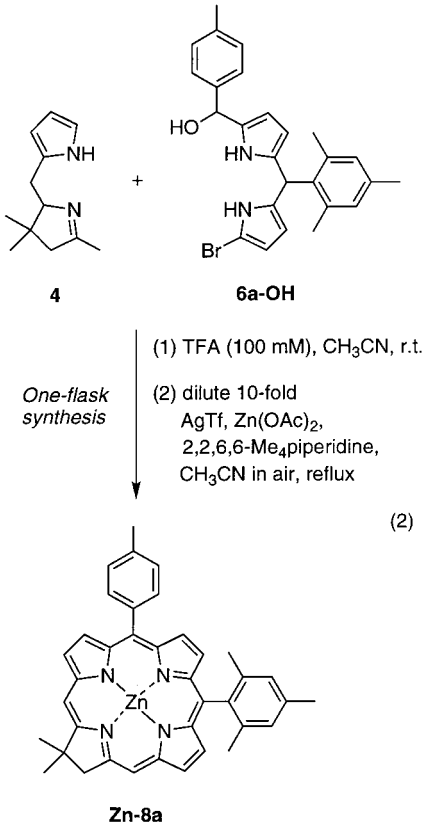
Figure 4. Yield of chlorin **Zn-8a** as a function of time upon treatment of **7a** to the oxidation conditions [tetrahydrobilene-*a* (**7a**) (10 mM), AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), 2,2,6,6-tetramethylpiperidine (15 molar equiv) in CH_3CN at reflux in air]. The yield was determined by absorption spectroscopy ($\epsilon_{609} = 43{,}600\ M^{-1}\ cm^{-1}$) in toluene. Legend: ●, THF; ○, CH_3CN.

In summary, the conditions for converting the tetrahydrobilene-*a* into the chlorin are as follows: tetrahydrobilene-*a* (10 mM), AgTf (3−5 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (15 molar equiv) in CH_3CN at reflux in air for 4−6 h. These conditions were applied to a larger-scale synthesis of chlorin **Zn-8a**. Thus, a 75.8-mg sample of tetrahydrobilene-*a* **7a** was converted to 45 mg of chlorin **Zn-8a** (62% yield).

One-Flask Procedure for Synthesis of Chlorins. The condensation yielding a tetrahydrobilene-*a* and subsequent oxidative cyclization yielding the chlorin has heretofore been implemented in a sequential two-flask procedure. The first step is an intermolecular reaction and should not require dilute conditions; the second step is an intramolecular cyclization and should proceed in greater yield under dilute conditions. Accordingly, we investigated a one-flask procedure employing 100 mM reactants in the condensation procedure and 10 mM reactants in the cyclization procedure. After condensation of Western Half **4** and Eastern half **6a-OH** using 100 mM of TFA in CH_3CN, the reaction mixture was diluted 10-fold by addition of CH_3CN. The components for the oxidation were added [AgTf (3 molar equiv), $Zn(OAc)_2$ (15 molar equiv), and 2,2,6,6-tetramethylpiperidine (30 molar equiv rather than 15 equiv, to neutralize the TFA)], and the mixture was refluxed with exposure to air. After 18 h, chromatographic workup afforded chlorin **Zn-8a** in 31% yield (eq 2). Although this one-flask approach is simple and readily implemented, the two-flask process affords a higher yield (45%) of chlorin.

Extension to the Synthesis of Meso-Substituted Chlorins. We investigated the synthesis of meso-substituted chlorins bearing two types of substituents: (1) strong electron-withdrawing groups and (2) synthetic handles at defined locations at the perimeter of the macrocycle. The former help to establish the scope of the methodology and the latter enable construction of chlorin-containing model systems in biomimetic or materials chemistry.

The synthesis of meso-substituted Eastern halves follows established methodology for the one-flask synthesis of meso-substituted dipyrromethanes,[22] monoacylation of a dipyrromethane,[16] and monobromination of a dipyrromethane.[2] Thus, a dipyrromethane (**9**) was treated with ethylmagnesium bromide followed by a pyridyl thioester (**10**, **11**, or **12**)[2,23] affording the corresponding monoacyldipyrromethane (**13b**−**e**) in 54−60% yield (Scheme 4). Bromination of the latter by treatment with NBS in THF at −78 °C afforded the desired precursor to the Eastern halves **6b**−**e** in 65−84% yield.[24]

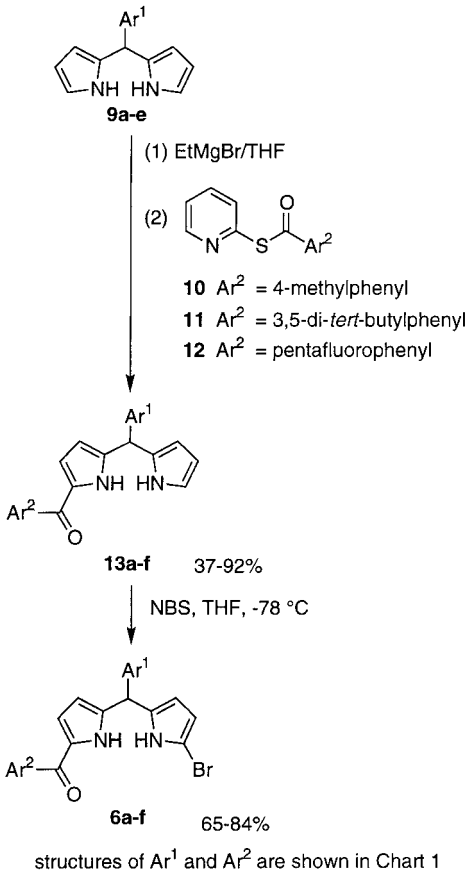


The synthesis of meso-substituted chlorin building blocks was carried out by the two-flask method as shown in Scheme 5. This route is to be compared with the previous route shown in Scheme 1. In each case, the new Western half **4** was employed. In these preparative syntheses, the oxidative cyclization process was monitored by absorption spectroscopy, showing the rise and fall of the intermediate (λ_{abs} ~505 nm) and the formation of the chlorin (λ_{abs} ~609 nm). In general, the oxidative cyclization was nearly complete at 4−8 h, but the reactions were often continued for up to 24 h.

The various meso-substituted chlorins prepared via this method are shown in Chart 1. The data shown are for reactions with 0.3−1.0 mmol of **4**, and then 0.10−0.23 mmol of tetrahydrobilene-*a*. The synthesis of chlorin **Zn-8a** provides a benchmark for yield comparisons. The reaction of **4** and **6a-OH** afforded tetrahydrobilene **7a** in 72% yield; oxidative conversion of the latter afforded **Zn-8a** in 62% yield. The scaled-up oxidative conversion beginning with 0.79 mmol of **7a** afforded 208 mg of

(22) Littler, B. J.; Miller, M. A.; Hung, C.-H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391−1396.
(23) Goto, T.; Onaka, M.; Mukaiyama, T. *Chem. Lett.* **1980**, 51−52.
(24) While all of the tetrahydrobilenes (**7a**−**f**) were stable for a period of ≥1 month, the Eastern half precursors (1-bromo-9-aroyldipyrromethanes) exhibited a range of stability. Compounds **6a**−**c** or **6d** showed decomposition after a few days or one week, respectively, while **6e** and **6f** were stable for >1 month.

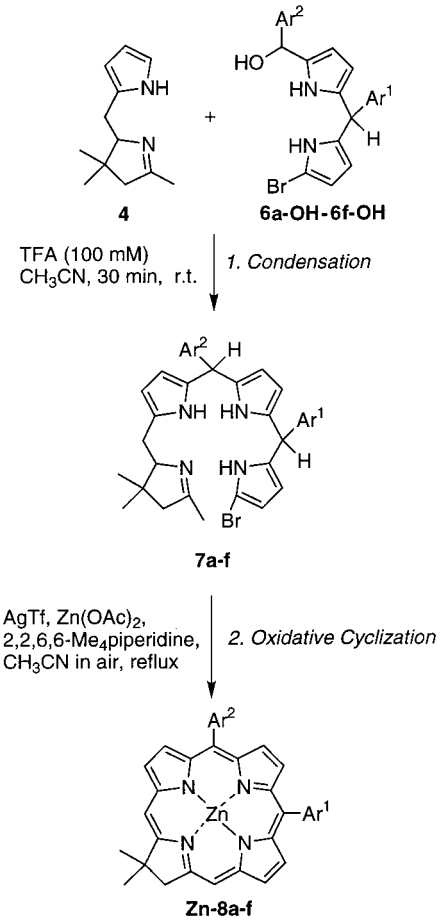
Scheme 4



chlorin **Zn-8a** (43% yield; 30% overall). The reaction of the bis(pentafluorophenyl)-substituted Eastern half with **4** gave the tetrahydrobilene **7b** in 32% yield and the chlorin **Zn-8b** in 38% yield. Several chlorin building blocks were prepared. The reaction of the Eastern half bearing a TMS-protected ester (**6c-OH**) with **4** gave the tetrahydrobilene **7c** and chlorin **Zn-8c** in reasonable yields (55%, 41%). An iodo-substituted chlorin (**Zn-8d**) was prepared by reaction of the corresponding Eastern half **6d**. We attempted to prepare a chlorin bearing a trimethylsilyl-protected ethyne by reaction of Eastern half **6e**. The tetrahydrobilene **7e** was formed smoothly. However, oxidative cyclization afforded the chlorin with the ethyne lacking the trimethylsilyl protecting group (**Zn-7e**). The synthesis of a similar trimethylsilyl-protected ethyne chlorin was attempted with oxidative cyclization of tetrahydrobilene **7f** in THF rather than CH_3CN, and again the deprotected ethynyl chlorin (**Zn-8f**) was obtained. In two cases, a comparison was made of the oxidative cyclization in CH_3CN or in THF; in each case (**7d**, **7e**), the yield of zinc chlorin was slightly higher in THF. Zinc chlorins **Zn-7d** and **Zn-7e** both incorporate the 3,5-di-*tert*-butyl group for increased solubility in organic solvents. In no case was scrambling yielding a mixture of chlorins detected.

It is noteworthy that in each synthesis the intermediate tetrahydrobilene-*a* was isolated in substantial quantities (73−460 mg), characterized, and found to be reasonably stable. The yields of chlorins were 2−4-fold greater than those obtained previously where comparisons could be made. For example, the prior synthetic method afforded chlorins **Zn-8a**, **Zn-8b**, or **Zn-8c** in yields of 10, 6, or 10%,[2] respectively, to be compared with

Scheme 5. Chlorin Synthesis via a Tetrahydrobilene-*a*

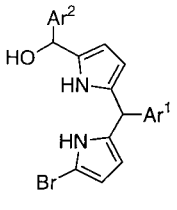


45, 12, or 23% in the current method. Note that the deprotected ethynyl chlorin **Zn-8f** was obtained herein in 30% yield, in contrast to the 9% yield of the protected ethynyl chlorin by the previous method.[2]

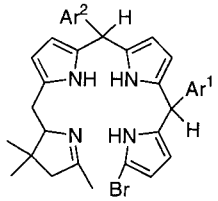
Outlook

We have refined a number of steps in the synthesis of meso-substituted chlorin building blocks. The limitations of the prior synthesis included the following: (1) chlorin was obtained in yields of ∼10% and quantities of ∼5−20 mg; (2) the Western half (a dihydrodipyrrin) had a short shelf life; (3) the putative dihydrobilene-*a* intermediate was not isolated or quantitated; (4) the use of $AgIO_3$ in the oxidation method in some cases resulted in iodinated chlorin byproducts. The refined method described herein affords a Western half (a tetrahydrodipyrrin) in good yield which is stable and can be prepared in multigram quantities. The Western half and the Eastern half undergo smooth condensation with mild acid catalysis, affording a stable tetrahydrobilene-*a* intermediate. No scrambling yielding a mixture of products, as can occur with dipyrromethanes under acid catalysis,[14−16] was detected under these conditions. Studies of the oxidative cyclization of the tetrahydrobilene-*a* intermediate revealed simple conditions [AgTf, $Zn(OAc)_2$, and 2,2,6,6-tetramethylpiperidine in CH_3CN at reflux exposed to air] that afford chlorin in a clean manner. Several zinc chlorins were synthesized in yields of 12−45% (based on the Eastern half and Western half precursors) and in quantities of 27−208 mg. The isolation of the intermedi-

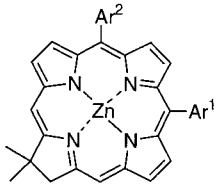
Chart 1



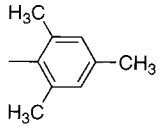
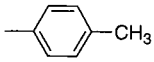
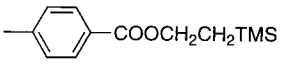
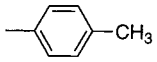
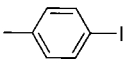
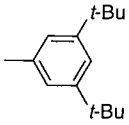
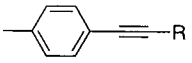
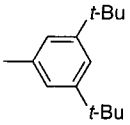
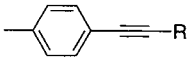
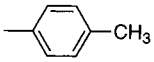
6a-f



7a-f



Zn-8a-f

	Ar^1	Ar^2	Stepwise Yields (%) Tetrahydrobilene **7**	Chlorin **Zn-8**	Total Yield (%)
a			72	62	45
b			32	38	12
c			55	41	23
d			40	40 (43)	16
e			59 R = TMS	27 (32) R = H	16
f			66 R = TMS	(45) R = H	30

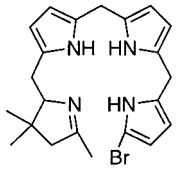
(yields in parentheses were obtained in THF rather than CH_3CN)

ate tetrahydrobilene-*a* in each case enabled determination of the yields of the separate condensation and oxidative cyclization processes.

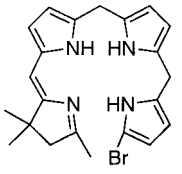
The conversion of the 2,3,4,5-tetrahydrobilene-*a* to the chlorin requires a $6e^-$, $6H^+$ oxidation. This change in oxidation level is identical to that in the conversion of a porphyrinogen to a porphyrin.[20] Other methods for forming chlorins by cyclization of a linear tetrapyrrole derived from an Eastern half and a Western half employ lesser changes in oxidation level. The intermediates (and oxidation required) in such syntheses include a 2,3-dihydrobilene-*a* ($4e^-$, $4H^+$),[2,3] a 2,3,4,5-tetrahydrobiladiene-*ac* ($4e^-$, $4H^+$),[7,25] a 2,3-dihydrobiladiene-*ab* ($2e^-$, $2H^+$),[26,27] and a 2,3-dihydrobilatriene (no change in oxidation level) (Chart 2; also see the Supporting Information for nomenclature).[27−31] The dihydrobilatriene was converted to the free base chlorin via a photochemical process in yields reaching 54% and in quantities reaching 10 mg.[27−31] All other routes require an oxidant, are performed thermally in the presence of a metal salt, and afford the metallochlorin rather than the free base chlorin. Battersby's pioneering studies to convert 2,3,4,5-tetrahydrobiladiene-*ac*[25] or 2,3-dihydrobiladiene-*ab*[25,26] species to the corresponding chlorin employed copper reagents; this approach afforded copper chlorins in yields of ≤7.4% and quantities of ≤3 mg.[7,25,26] However, the reaction with copper reagents in the presence of air sometimes affords the copper oxochlorin rather than the copper chlorin.[7] The use of zinc in place of copper provides distinct advantages because (1) the zinc chlorin is easily demetalated and (2) air can be employed as the oxidant without forming the oxochlorin. Relatively few tetrapyrrole intermediates in chlorin syntheses have been characterized.[7,26,29] The tetrahydrobilene-*a* intermediates

(25) Snow, R. J.; Fookes, C. J. R.; Battersby, A. R. *J. Chem. Soc., Chem. Commun.* **1981**, 524−526.
(26) Battersby, A. R.; Fookes, C. J. R.; Snow, R. J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2733−2741.
(27) Battersby, A. R.; Dutton, C. J.; Fookes, C. J. R.; Turner, S. P. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1235−1237.
(28) Dutton, C. J.; Fookes, C. J. R.; Battersby, A. R. *J. Chem. Soc., Chem. Commun.* **1983**, 1237−1238.
(29) Battersby, A. R.; Dutton, C. J.; Fookes, C. J. R.; Turner, S. P. D. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1557−1567.
(30) Battersby, A. R.; Dutton, C. J.; Fookes, C. J. R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1569−1576.
(31) Battersby, A. R.; Turner, S. P. D.; Block, M. H.; Sheng, Z.-C.; Zimmerman, S. C. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1577−1586.

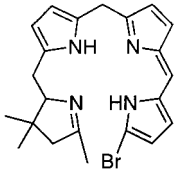
Chart 2. Tetrapyrrole Intermediates in Chlorin Syntheses (Most Substituents Omitted for Clarity)



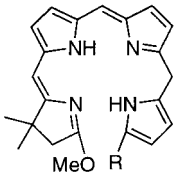
a 2,3,4,5-tetrahydrobilene-*a*



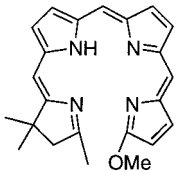
a 2,3-dihydrobilene-*a*



a 2,3,4,5-tetrahydrobiladiene-*ac*



a 2,3-dihydrobiladiene-*ab*



a 2,3-dihydrobilatriene

obtained herein from saturated starting materials (tetrahydrodipyrrin Western half, bromodipyrromethane-monocarbinol Eastern half) are stable and readily characterized. In summary, the approach we have developed enables study of the separate condensation and oxidative cyclization process, employs relatively mild conditions, and affords access to workable quantities of chlorin building blocks.

Experimental Section

General Methods. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were collected at room temperature in $CDCl_3$. The protons at the perimeter of the chlorins generally exhibited first-order spectra. Absorption spectra were obtained in toluene at room temperature. Chlorins were analyzed by laser desorption mass spectrometry (LD-MS) in the absence of a matrix.[32] Fast atom bombardment mass spectrometry (FAB-MS) data are reported for the molecule ion or protonated molecule ion. Pyrrole was distilled at atmospheric pressure from CaH_2. Melting points are uncorrected. *p*-Iodobenzaldehyde was obtained from Karl Industries, Inc. All other reagents and starting materials were obtained from Aldrich. Column chromatography was performed with flash silica (Baker). The reduction yielding the Eastern half was performed following a standard procedure for forming dipyrromethane-carbinols.[16]

Solvents. THF was distilled from sodium benzophenone ketyl as required. Toluene was distilled from CaH_2. CH_3CN (Fisher certified A.C.S.) for use in the condensation process was distilled from CaH_2 and stored over powdered molecular sieves. Nitromethane was stored over $CaCl_2$. Anhydrous methanol was prepared by drying over CaH_2 for 12 h followed by distillation. Other solvents were used as received.

Noncommercial Compounds. The compounds **2**,[2] **6a**,[2] **6b**,[2] **6f**,[2] **9a**−**d**,[22] **9e**,[33] **10**,[2] **12**,[2] **13a**,[2] **13b**,[2] and **13f**[2] were prepared as described in the literature.

2,3,4,5-Tetrahydro-1,3,3-trimethyldipyrrin *N*^{10}-Oxide (3). Following a general procedure,[7] to a vigorously stirred solution of **2** (1.26 g, 5.29 mmol) in 25 mL of acetic acid and 25 mL of ethanol at 0 °C, zinc dust (8.64 g, 132 mmol) was added slowly in small portions for 5 min. The reaction mixture was stirred at 0 °C for 15 min and then was filtered through Celite. The filtrate was concentrated under high vacuum. The resulting brown solid was purified by column chromatography [silica; packed and eluted with ethyl acetate/CH_2Cl_2 (1:1), then eluted with CH_2Cl_2/methanol (9:1)] affording a brown oil that solidified to brownish crystals on standing at room temperature (943 mg, 86%): mp 85−87 °C; ^{1}H NMR δ 1.12 (s, 3H), 1.17 (s, 3H), 2.04 (s, 3H), 2.28, 2.44 (AB, ^2J = 17.6 Hz, 2H), 2.95−3.10 (m, 2H), 3.82−3.96 (m, 1H), 5.85−5.97 (m, 1H), 6.02−6.11 (m, 1H), 6.64−6.72 (m, 1H), 10.50−10.72 (br, 1H); ^{13}C NMR δ 13.9, 23.4, 26.3, 28.5, 37.8, 47.7, 81.9, 107.0, 107.9, 118.1, 129.2, 147.3; FAB-MS obsd 206.1415, calcd 206.1419 ($C_{12}H_{18}N_2O$).

2,3,4,5-Tetrahydro-1,3,3-trimethyldipyrrin (4). Following a general procedure for the deoxygenation of *N*-oxides[11] with slight modification, $TiCl_4$ (2.87 mL, 26.2 mmol) was slowly added with stirring to dry THF (60 mL) under argon at 0 °C. To the resulting yellow solution was slowly added $LiAlH_4$ (665 mg, 17.5 mmol). The resulting black mixture was stirred at room temperature for 15 min, and then triethylamine (23.0 mL, 164 mmol) was added. The black mixture was then poured into a solution of **3** (725 mg, 3.65 mmol) in dry THF (45 mL). The mixture was stirred for 30 min at room temperature, and then water (45 mL) was added. The mixture was filtered. The filtrate was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure. The resulting yellow oil was purified by chromatography (silica, ethyl acetate) to give a pale yellow oil, which solidified to a pale yellow solid on cooling (448 mg, 65%): mp 53−54 °C; ^{1}H NMR δ 0.94 (s, 3H), 1.10 (s, 3H), 2.04 (s, 3H), 2.28, 2.44 (AB, ^2J = 16.9 Hz, 2H), 2.59 (ABX, ^3J = 11.7 Hz, ^2J = 14.7 Hz, 1H), 2.77 (ABX, ^3J = 3.3 Hz, ^2J = 14.7 Hz, 1H), 3.57−3.68 (m, 1H), 5.90−5.97 (m, 1H), 6.05−6.13 (m, 1H), 6.67−6.73 (m, 1H), 9.70−9.92 (br, 1H); ^{13}C NMR δ 20.3, 22.6, 27.0, 27.9, 41.8, 54.1, 80.1, 105.1, 107.1, 116.3, 131.4, 174.6; FAB-MS obsd 191.1551, calcd 191.1548 ($C_{12}H_{18}N_2$).

5,11-Diaza-1,9,9-trimethyltricyclo[6.2.1.0^{2,6}]undeca-2(6),3-diene (5). To a vigorously stirred solution of **2** (2.00 g, 8.39 mmol) in 40 mL of acetic acid at room temperature was added zinc dust (13.7 g, 210 mmol) all at once (***Caution:*** the reaction is exothermic). The reaction mixture was stirred at room temperature without temperature control for 1 h. The mixture was filtered through Celite. The filtrate was removed under vacuum, and CH_2Cl_2 (100 mL) was added. The solution was washed with 10% aqueous Na_2CO_3 (100 mL). The organic layer was separated and chromatographed, affording **3** (143 mg, 8.2%). The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and the resulting organic layer was dried (Na_2SO_4) and concentrated to give a dark pink solid that still contained about 10% of the *N*-oxide (720 mg). Recrystallization ($CHCl_3$) afforded dark pink crystals (254 mg, 16%): mp 145 °C; ^{1}H NMR δ 0.95 (s, 3H), 1.21 (s, 3H), 1.50 (s, 3H), 1.59, 1.74 (AB, ^2J = 11.7 Hz, 2H), 1.83−1.97 (br, 1H), 2.64 (ABX, ^3J < 1 Hz, ^2J = 16.1 Hz, 1H), 2.86 (ABX, ^3J = 5.1 Hz, ^2J = 16.1 Hz, 1H), 3.36 (ABX, ^3J < 1 Hz, ^2J = 5.1 Hz, 1H), 5.92−5.99 (m, 1H), 6.54−6.60 (m, 1H), 7.72−7.92 (br, 1H); ^{13}C NMR δ 24.5, 27.3, 28.5, 34.3, 42.0, 58.6, 60.6, 65.4, 103.4, 116.0, 123.6, 129.2; FAB-MS obsd 191.1553, calcd 191.1548 ($C_{12}H_{18}N_2$). The same

(32) (a) Fenyo, D.; Chait, B. T.; Johnson, T. E.; Lindsey, J. S. *J. Porphyrins Phthalocyanines* **1997**, *1*, 93−99. (b) Srinivasan, N.; Haney, C. A.; Lindsey, J. S.; Zhang, W.; Chait, B. T. *J. Porphyrins Phthalocyanines* **1999**, *3*, 283−291.

(33) Cho, W.-S.; Kim, H.-J.; Littler, B. J.; Miller, M. A.; Lee, C.-H.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 7890−7901.

product was obtained in 63% yield upon treatment of **3** in THF with $TiCl_3$ in aqueous ammonium acetate (pH = 6).[4]

Studies of the Western Half (4) + Eastern Half (6a-OH) Condensation. A sample of **6a** (64.6 mg, 140 μmol) was reduced with $NaBH_4$ (53.0 mg, 1.40 mmol) in 4 mL of anhydrous THF/methanol (4:1). The resulting **6a-OH** and **4** (26.6 mg, 140 μmol) were dissolved in 7 mL of anhydrous CH_2Cl_2, then 0.5 mL portions of the solution were placed in each of 14 vials (each vial contains 10 μmol of **6a-OH** and **4**). The solvent was evaporated and then 0.1 mL of CH_3CN containing the desired TFA concentration (10 to 316 mM) was added. After the desired reaction time (1 min to 2 h), the solution was diluted with 0.9 mL of CH_3CN [containing AgTf (7.7 mg, 30 μmol) and 2,2,6,6-tetramethylpiperidine (25.3 μL, 150 μmol)]. Then $Zn(OAc)_2$ (27.5 mg, 150 μmol) was added, and the mixture was refluxed for 4.5 h. The reaction yield was determined by UV−vis spectroscopy. In the yield determinations, CH_3CN was added to each reaction mixture to bring the volume to 4.0 mL (thereby negating any possible error due to solvent evaporation during the reflux period). A 25 μL aliquot was then removed and transferred to a cuvette containing 4 mL of toluene. Quantitation was then based on the absorption at 609 nm (ϵ_{609} = 43 600 M^{-1} cm^{-1}).

Studies of the Metal-Mediated Oxidative Cyclization. A solution of tetrahydrobilene **7a** (63.5 mg, 100 μmol) in 10 mL of anhydrous CH_2Cl_2 was divided into 0.5 mL portions in each of 20 vials (each vial contains 5 μmol of **7a**). For the study examining the effect of the reaction solvent, CH_2Cl_2 was then evaporated, and 0.5 mL of the solvent of interest was added. The corresponding reagents for the oxidation [2,2,6,6-tetramethylpiperidine (13 μL, 77 μmol) and $Zn(OAc)_2$ (14 mg, 76 μmol)] were added, and the mixture was refluxed for 4.5 h. The yield of chlorin was determined by UV−vis spectroscopy. In the yield determinations, CH_2Cl_2 was added to each reaction mixture to bring the volume to 4.0 mL (thereby negating any possible error due to solvent evaporation during the reflux period). A 50 μL aliquot was then removed and transferred to a 4 mL cuvette (containing toluene). Quantitation was then based on the absorption at 609 nm (ϵ_{609} = 43 600 M^{-1} cm^{-1}).

19-Bromo-2,3,4,5-tetrahydro-15-mesityl-1,3,3-trimethyl-10-(4-methylphenyl)bilene-*a* (7a). A sample of **6a** (461 mg, 1.00 mmol) was reduced with $NaBH_4$ (370 mg, 10.0 mmol) in 20 mL of anhydrous THF/methanol (4:1). The resulting **6a-OH** was dissolved in 10 mL of anhydrous CH_3CN, and then **4** (188 mg, 1.00 mmol) and TFA (77 μL, 1.0 mmol) were added. The reaction mixture was stirred at room temperature for 30 min under argon. Then 10% aqueous $NaHCO_3$ (50 mL) was added, and the mixture was extracted with distilled CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with water, dried (Na_2CO_3), and concentrated in vacuo without heating. The resulting brown solid was purified by chromatography [silica, hexanes/ethyl acetate (5:1), and then ethyl acetate] to give a brown solid (460 mg, 72%): mp 67−70 °C; ^{1}H NMR δ 0.90 (bs, 3H), 1.07 (bs, 3H), 1.91 (bs, 3H), 2.04 (bs, 6H), 2.25 (bs, 3H), 2.26−2.30 (m, 2H), 2.31 (bs, 3H), 2.48−2.60 (m, 1H), 2.66−2.72 (m, 1H), 3.52−3.63 (m, 1H), 5.28−5.32 (m, 1H), 5.67−5.81 (m, 6H), 6.00−6.04 (m, 1H), 6.77−6.83 (m, 2H), 7.06−7.11 (m, 4H), 7.67−7.79 (m, 1H), 7.99−8.13 (m, 1H), 9.23−9.32 (m, 1H); FAB-MS obsd 635.2749, calcd 635.2730 ($C_{38}H_{43}BrN_4$).

Zn(II)-17,18-dihydro-10-mesityl-18,18-dimethyl-5-(4-methylphenyl)porphyrin (Zn-8a). A solution of **7a** (75.8 mg, 0.120 mmol) in CH_3CN (12 mL) was treated with $Zn(OAc)_2$ (328 mg, 1.79 mmol), AgTf (91.9 mg, 0.360 mmol), and 2,2,6,6-tetramethylpiperidine (300 μL, 1.79 mmol). The reaction mixture was refluxed for 24 h exposed to air. The reaction mixture was concentrated under reduced pressure, and then the residue was chromatographed [silica, hexanes/CH_2Cl_2 (2:1)] to give a blue solid (45 mg, 62%). Analytical data were consistent with literature values.[2]

Two-Flask Procedure for Chlorin Formation, Exemplified for Zn(II)-17,18-Dihydro-10-mesityl-18,18-dimethyl-5-(4-methylphenyl)porphyrin (Zn-8a). The synthesis of the tetrahydrobilene-*a* (**7a**) was carried out as specified above. A sample of **6a** (531 mg, 1.15 mmol) was reduced with $NaBH_4$ (435 mg, 11.5 mmol) in 20 mL of anhydrous THF/methanol (4:1), affording **6a-OH**. The solvent was evaporated and the residue was dissolved in 11.5 mL of the anhydrous CH_3CN (100 mM **6a-OH**). Then Western half **4** (219 mg, 1.15 mmol, 100 mM) and TFA (89 μL, 1.15 mmol, 100 mM) were added. The reaction mixture was stirred at room temperature for 30 min under an atmosphere of argon. Then 10% aqueous $NaHCO_3$ (50 mL) was added and the mixture was extracted with distilled CH_2Cl_2 (100 mL). The combined organic layers were washed with water, dried (Na_2CO_3) and concentrated in vacuo without heating. The resulting brown solid was purified by chromatography [silica, hexanes/ethyl acetate (5:1), and then ethyl acetate] to give a brown solid (502 mg, 69%). The sample was shown to be pure by TLC [silica, hexanes/ethyl acetate (5:1); silica, ethyl acetate]. LD-MS proved ineffective for characterizing the tetrahydrobilene-*a*. This material could be characterized by mp, ^{1}H NMR spectroscopy, and FAB-MS. The metal-mediated oxidative cyclization to form the zinc chlorin (**Zn-8a**) was carried out as specified above. The tetrahydrobilene-*a* (**7a**), typically as a brown solid, was dissolved in CH_3CN [502 mg (0.79 mmol) in 79 mL; 10 mM] under an atmosphere of air. This solution was treated with $Zn(OAc)_2$ (2.16 g, 11.8 mmol), AgTf (609 mg, 2.37 mmol) and 2,2,6,6-tetramethylpiperidine (1.99 mL, 11.8 mmol). The reaction mixture was refluxed for 24 h. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed [silica, hexanes/CH_2Cl_2 (2:1)] to give a blue solid (208 mg, 43%; 30% overall yield). Analytical data were consistent with literature values.[2]

One-Flask Procedure for Chlorin Formation, Exemplified for Zn(II)-17,18-dihydro-10-mesityl-18,18-dimethyl-5-(4-methylphenyl)porphyrin (Zn-8a). A sample of **6a** (231 mg, 0.500 mmol) was reduced with $NaBH_4$ (185 mg, 5.00 mmol) in 20 mL of anhydrous THF/methanol (4:1). The resulting **6a-OH** was dissolved in 5 mL of anhydrous CH_3CN, and then **4** (94 mg, 0.50 mmol) and TFA (39 μL, 0.50 mmol) were added. The reaction mixture was stirred at room temperature for 30 min under argon, and then the reaction mixture was diluted with 45 mL of CH_3CN. AgTf (385 mg, 1.50 mmol), $Zn(OAc)_2$ (1.38 g, 7.50 mmol), and 2,2,6,6-tetramethylpiperidine (2.53 mL, 15.0 mmol, 30 molar equiv) were added. The resulting mixture was refluxed for 18 h exposed to air. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed [silica, hexanes/CH_2Cl_2 (2:1)], affording a blue solid (118 mg, 31%). Analytical data were consistent with literature values.[2]

(*S*)-2-Pyridyl 3,5-di-*tert*-butylbenzothioate (11). To a stirred solution of 2-mercaptopyridine (2.78 g, 25.0 mmol) in CH_2Cl_2 (50 mL) was added a solution of 3,5-di-*tert*-butylbenzoyl chloride (6.31 g, 25.0 mmol) in CH_2Cl_2 (125 mL) over 10 min. After 5 h, TLC showed complete consumption of the 2-mercaptopyridine, and then 2 N NaOH was added. The organic phase was isolated, washed with water, then dried (Na_2SO_4), and the solvent was removed to afford a white solid. The solid was recrystallized in hexane affording a white solid (5.05 g, 62%): mp 73−74 °C; ^{1}H NMR δ 1.36 (s, 18H), 7.31−7.36 (m, 1H), 7.67−7.70 (m, 1H), 7.75−7.80 (m, 2H), 7.85−7.88 (m, 2H), 8.66−8.69 (m, 1H); ^{13}C NMR δ 32.0, 35.7, 122.6, 124.2, 128.9, 131.4, 136.9, 137.7, 151.1, 152.3, 152.5, 190.8. Anal. Calcd for $C_{20}H_{25}NOS$: C, 73.35; H, 7.69; N, 4.28. Found: C, 73.40; H, 7.75; N, 4.23.

1-(4-Methylbenzoyl)-5-[4-[2-(trimethylsilyl)ethoxycarbonyl]phenyl]dipyrromethane (13c). Following a general procedure,[16] EtMgBr (13.1 mL, 13.1 mmol), 1.0 M in THF) was added to a solution of **9c** (2.00 g, 5.46 mmol) in dry THF (10 mL) at room temperature under argon. The mixture was stirred at room temperature for 10 min and then cooled to −78 °C. A solution of (*S*)-2-pyridyl 4-methylbenzothioate (**10**) (1.25 g, 5.45 mmol) in dry THF (10 mL) was added. The reaction mixture was maintained at −78 °C for 10 min, and then the cooling bath was removed. After 3 h, the reaction was quenched with 100 mL of saturated aqueous NH_4Cl. The reaction mixture was extracted with CH_2Cl_2, washed with water, and then dried (Na_2SO_4) and concentrated under reduced pressure to give a dark foam. Column chromatography

[silica packed with hexanes/ethyl acetate (10:1), eluted with hexanes/ethyl acetate (5:1)] afforded a golden amorphous solid (1.42 g, 54%): mp 67−70 °C; ^{1}H NMR δ 0.07 (s, 9H), 1.11 (t, J = 8.1 Hz, 2H), 2.42 (s, 3H), 4.39 (t, J = 8.1 Hz, 2H), 5.62 (s, 1H), 5.95−5.99 (m, 1H), 6.06−6.10 (m, 1H), 6.12−6.16 (m, 1H), 6.64−6.68 (m, 1H), 6.77−6.81 (m, 1H), 7.16−7.30 (m, 4H), 7.67 (d, J = 7.3 Hz, 2H), 7.89 (d, J = 7.3 Hz, 2H), 8.52−8.68 (br, 1H), 10.30−10.42 (br, 1H); ^{13}C NMR δ −0.8, 18.0, 22.2, 44.6, 63.9, 108.6, 109.0, 111.3, 118.7, 121.4, 128.9, 129.6, 129.7, 130.1, 130.4, 130.8, 131.6, 136.1, 141.4, 143.1, 146.5, 167.1, 185.3. Anal. Calcd for $C_{29}H_{32}N_2O_3Si$: C, 71.87; H, 6.65; N, 5.78. Found: C, 71.78; H, 6.61; N, 5.89.

1-(3,5-Di-*tert*-butylbenzoyl)-5-(4-iodophenyl)dipyrromethane (13d). Following the procedure for preparing **13c**, reaction of **9d** (1.80 g, 5.10 mmol) and **11** (1.70 g, 5.10 mmol) followed by column chromatography [silica hexanes/ethyl acetate (5:1)] afforded a golden amorphous solid (1.63 g, 56%): mp 119−120 °C; ^{1}H NMR δ 1.34 (s, 18H), 5.51 (s, 1H), 5.93−5.97 (m, 1H), 6.07−6.14 (m, 2H), 6.57−6.63 (m, 1H), 6.73−6.77 (m, 1H), 6.92 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 8.1 Hz, 2H), 7.60−7.67 (m, 3H), 8.57−8.70 (br, 1H), 10.38−10.52 (br, 1H); ^{13}C NMR δ 32.1, 35.6, 44.4, 93.3, 108.1, 108.5, 109.1, 111.3, 118.1, 118.8, 121.8, 124.1, 126.7, 130.9, 131.9, 138.3, 141.4, 141.8, 151.5, 186.6. Anal. Calcd for $C_{30}H_{33}IN_2O$: C, 63.83; H, 5.89; N, 4.96. Found: C, 63.59; H, 5.95; N, 4.83.

1-(3,5-Di-*tert*-butylbenzoyl)-5-[4-[2-(trimethylsilyl)ethynyl]phenyl]dipyrromethane (13e). Following the procedure for preparing **13c**, reaction of **9e** (2.00 g, 6.28 mmol) and **11** (2.06 g, 6.28 mmol) followed by column chromatography [silica hexanes/ethyl acetate (5:1)] afforded a golden amorphous solid (2.00 g, 60%): mp 108 °C dec; ^{1}H NMR δ 0.23 (s, 9H), 1.34 (s, 18H), 5.57 (s, 1H), 5.93−5.97 (m, 1H), 6.06−6.16 (m, 2H), 6.58−6.62 (m, 1H), 6.75−6.80 (m, 1H), 7.10 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.60−7.68 (m, 3H), 8.62−8.70 (br, 1H), 10.45−10.52 (br, 1H); ^{13}C NMR δ 0.7, 32.1, 35.6, 44.7, 94.9, 105.6, 108.4, 108.9, 111.4, 118.8, 122.1, 122.5, 124.2, 126.7, 128.9, 131.3, 131.8, 132.8, 138.4, 142.1, 142.4, 151.5, 186.8. Anal. Calcd for $C_{35}H_{42}N_2OSi$: C, 78.60; H, 7.92; N, 5.24. Found: C, 78.75; H, 7.96; N, 5.20.

1-Bromo-9-(4-methylbenzoyl)-5-[4-[2-(trimethylsilyl)-ethoxycarbonyl]phenyl]dipyrromethane (6c). Following a general procedure,[2,3] a solution of **13c** (470 mg, 0.970 mmol) in 25 mL of dry THF was cooled to −78 °C under argon. NBS (173 mg, 0.970 mmol) was added, and the reaction mixture was stirred for 1 h at −78 °C. Hexanes (50 mL) and water (50 mL) were added, and the mixture was allowed to warm to room temperature. The organic phase was extracted with CH_2Cl_2 and dried (Na_2SO_4). The solvent was removed under reduced pressure without heating. Column chromatography [silica; hexanes/ethyl acetate (4:1)] afforded a light brown powder (444 mg, 81%): mp 152 °C dec; ^{1}H NMR δ 0.07 (s, 9H), 1.11 (t, J = 8.1 Hz, 2H), 2.16 (s, 3H), 4.39 (t, J = 8.1 Hz, 2H), 5.57 (s, 1H), 5.89−5.93 (m, 1H), 6.02−6.06 (m, 1H), 6.09−6.13 (m, 1H), 6.76−6.80 (m, 1H), 7.17 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H), 9.10−9.26 (br, 1H), 10.82−10.94 (br, 1H); ^{13}C NMR δ −0.9, 17.9, 22.2, 44.6, 63.8, 98.8, 105.0, 110.4, 110.8, 111.2, 122.1, 128.7, 129.5, 129.8, 130.1, 130.3, 131.7, 132.4, 141.2, 143.2, 145.9, 167.0, 185.7. Anal. Calcd for $C_{29}H_{31}BrN_2O_3Si$: C, 61.81; H, 5.54; N, 4.97. Found: C, 61.96; H, 5.53; N, 4.93.

1-Bromo-9-(3,5-di-*tert*-butylbenzoyl)-5-(4-iodophenyl)-dipyrromethane (6d). Following the procedure for preparing **6c**, reaction of **13d** (800 mg, 1.42 mmol) with NBS (253 mg, 1.42 mmol) followed by column chromatography [silica hexanes/ethyl acetate (4:1)] afforded a light brown powder (770 mg, 84%): mp 88−91 °C; ^{1}H NMR δ 1.34 (s, 18H), 5.51 (s, 1H), 5.87−5.91 (m, 1H), 6.02−6.05 (m, 1H), 6.09−6.13 (m, 1H), 6.75−6.79 (m, 1H), 6.96 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.60−7.64 (m, 3H), 8.91−9.00 (br, 1H), 10.59−10.72 (br, 1H); ^{13}C NMR δ 32.1, 35.6, 44.5, 93.5, 98.8, 110.4, 111.1, 111.4, 122.2, 124.2, 126.9, 130.9, 132.0, 132.6, 138.2, 138.4, 140.7, 141.3, 151.6, 187.0. Anal. Calcd for $C_{30}H_{32}BrIN_2O$: C, 56.00; H, 5.01; N, 4.35. Found: C, 56.15; H, 5.19; N, 4.22.

1-Bromo-9-(3,5-di-*tert*-butylbenzoyl)-5-[4-[2-(trimethylsilyl)ethynyl]phenyl]dipyrromethane (6e). Following the procedure for preparing **6c**, reaction of **13e** (1.00 g, 1.87 mmol) with NBS (333 mg, 1.87 mmol) followed by column chromatography [silica hexanes/ethyl acetate (5:1)] afforded a golden amorphous solid (914 mg, 80%): mp 118 °C dec; ^{1}H NMR δ 0.23 (s, 9H), 1.33 (s, 18H), 5.56 (s, 1H), 5.86−5.91 (m, 1H), 6.01−6.04 (m, 1H), 6.08−6.12 (m, 1H), 6.74−6.79 (m, 1H), 7.15 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.58−7.67 (m, 3H), 8.94−9.06 (br, 1H), 10.62−10.76 (br, 1H); ^{13}C NMR δ 0.6, 32.1, 35.6, 44.8, 95.3, 98.7, 105.3, 110.3, 111.1, 111.4, 122.0, 122.8, 124.2, 126.7, 128.8, 131.9, 132.7, 132.9, 138.3, 141.2, 141.3, 151.5, 186.9. Anal. Calcd for $C_{35}H_{41}BrN_2OSi$: C, 68.50; H, 6.73; N, 4.56. Found: C, 68.48; H, 6.87; N, 4.47.

19-Bromo-2,3,4,5-tetrahydro-1,3,3-trimethyl-10,15-bis-(pentafluorophenyl)bilene-*a* (7b). Treatment of **6b** (176 mg, 0.300 mmol) with $NaBH_4$ (113 mg, 3.00 mmol) in 10 mL of anhydrous THF/methanol (4:1) afforded **6b-OH**. The reaction of **6b-OH** and **4** (57 mg, 0.30 mmol) in 3 mL of anhydrous CH_3CN containing TFA (23 μL, 0.30 mmol) for 30 min under argon followed by the standard workup afforded a brown solid (73 mg, 32%): mp 56−58 °C;^{1}H NMR δ 0.90 (bs, 3H), 1.11 (s, 3H), 1.92 (bs, 3H), 2.23−2.42 (m, 2H), 2.50−2.72 (m, 2H), 3.52−3.62 (m, 1H), 5.73−6.08 (m, 8H), 8.27−8.46 (m, 1H), 8.58−8.70 (m, 1H), 9.72−9.85 (m, 1H); FAB-MS obsd 759.1181, calcd 759.1215 ($C_{34}H_{25}BrF_{10}N_4$). Anal. Calcd for $C_{34}H_{25}BrF_{10}N_4$: C, 53.77; H, 3.32; N, 7.38. Found: C, 53.51; H, 3.41; N, 6.97.

Zn(II)-17,18-dihydro-18,18-dimethyl-5,10-bis(pentafluorophenyl)porphyrin (Zn-8b). Following the procedure for preparing **Zn-8a**, a solution of **7b** (77.7 mg, 0.102 mmol) in CH_3CN (10 mL) containing the oxidative cyclization reagents was refluxed for 24 h exposed to air. Standard workup and chromatography [silica, hexanes/CH_2Cl_2 (2:1)] gave a greenish blue solid (28.2 mg, 38%). Analytical data were consistent with literature values.[2]

19-Bromo-2,3,4,5-tetrahydro-1,3,3-trimethyl-10-(4-methylphenyl)-15-[4-[2-(trimethylsilyl)ethoxycarbonyl]-phenyl]bilene-*a* (7c). Treatment of **6c** (282 mg, 0.500 mmol) with $NaBH_4$ (189 mg, 5.00 mmol) in 30 mL of anhydrous THF/methanol (4:1) afforded **6c-OH**. The reaction of **6c-OH** and **4** (94 mg, 0.50 mmol) in 5 mL of anhydrous CH_3CN with TFA (39 μL, 0.50 mmol) for 30 min under argon followed by the standard workup afforded a brown solid (203 mg, 55%): mp 81−83 °C;^{1}H NMR δ 0.14 (bs, 9H), 0.96 (bs, 3H), 1.14 (bs, 3H), 1.15 (t, J = 8.1 Hz, 2H), 1.92−1.97 (m, 3H), 2.24−2.43 (m, 2H), 2.38 (bs, 3H), 2.53−2.67 (m, 1H), 2.71−2.80 (m, 1H), 3.57−3.68 (m, 1H), 4.47 (t, J = 8.1 Hz, 2H), 5.32−5.43 (m, 2H), 5.72−5.84 (m, 4H), 5.84−5.90 (m, 1H), 6.05−6.10 (m, 1H), 7.10−7.18 (m, 4H), 7.24−7.34 (m, 2H), 7.90−8.06 (m, 1H), 7.96−8.04 (m, 2H), 8.21−8.46 (m, 1H), 9.23−9.36 (m, 1H); FAB-MS obsd 737.2907, calcd 737.2886 ($C_{41}H_{49}BrN_4O_2Si$).

Zn(II)-17,18-dihydro-18,18-dimethyl-5-(4-methylphenyl)-10-[4-[2-(trimethylsilyl)ethoxycarbonyl]phenyl]-porphyrin (Zn-8c). Following the procedure for preparing **Zn-8a**, a solution of **7c** (110 mg, 0.150 mmol) in CH_3CN (15 mL) containing the oxidative cyclization reagents was refluxed for 14 h exposed to air. Standard workup and chromatography [silica, hexanes/CH_2Cl_2 (1:2)] gave a blue solid (43 mg, 41%): ^{1}H NMR δ 0.18 (s, 9H), 1.12 (t, J = 5.5 Hz, 2H), 2.03 (s, 6H), 2.66 (s, 3H), 4.52 (s, 2H), 4.65 (t, J = 5.5 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.94 (d, J = 8.1 Hz, 2H), 8.13 (d, J = 8.1 Hz, 2H), 8.31 (d, J = 4.4 Hz, 1H), 8.34 (d, J = 8.1 Hz, 2H), 8.42 (d, J = 4.4 Hz, 1H), 8.57−8.70 (m, 6H); LD-MS obsd 710.78; FAB-MS obsd 712.2232, calcd 712.2212 ($C_{41}H_{40}N_4O_2SiZn$); λ_{abs} 413, 609 nm.

19-Bromo-10-(3,5-di-*tert*-butylphenyl)-2,3,4,5-tetrahydro-15-(4-iodophenyl)-1,3,3-trimethylbilene-*a* (7d). Treatment of **6d** (322 mg, 0.500 mmol) with $NaBH_4$ (189 mg, 5.00 mmol) in 30 mL of anhydrous THF/methanol (4:1) afforded **6d-OH**. The reaction of **6d-OH** and **4** (94 mg, 0.50 mmol) in 5 mL of anhydrous CH_3CN containing TFA (39 μL, 0.50 mmol) for 30 min under argon followed by standard workup afforded a brown solid (163 mg, 40%): mp 70−73 °C;^{1}H NMR δ 0.91 (bs, 3H), 1.06 (bs, 3H), 1.25 (bs, 18H), 1.83−1.87 (m, 3H), 2.17−2.34 (m, 2H), 2.51−2.62 (m, 1H), 2.66−2.76 (m, 1H), 3.52−3.59 (m, 1H), 5.22−5.27 (m, 1H), 5.29−5.35 (m, 1H), 5.66−

5.88 (m, 5H), 5.97−6.03 (m, 1H), 6.87−6.93 (m, 2H), 7.00−7.07 (m, 3H), 7.54−7.62 (m, 2H), 7.79−7.94 (m, 1H), 8.08−8.28 (m, 1H), 9.08−9.22 (m, 1H); FAB-MS obsd 817.2317, calcd 817.2342 ($C_{42}H_{50}BrIN_4$). Anal. Calcd for $C_{42}H_{50}BrIN_4$: C, 61.69; H, 6.16; N, 6.85. Found: C, 61.57; H, 6.21; N, 6.70.

Zn(II)-5-(3,5-di-*tert*-butylphenyl)-17,18-dihydro-10-(4-iodophenyl)-18,18-dimethylporphyrin (Zn-8d). Following the procedure for preparing **Zn-8a**, a solution of **7d** (81.7 mg, 0.100 mmol) in CH_3CN (10 mL) containing the oxidative cyclization reagents was refluxed for 20 h exposed to air. Standard workup and chromatography [silica, hexanes/CH_2Cl_2 (1:2)] gave a blue solid (32 mg, 40%): ^{1}H NMR δ 1.49 (s, 18H), 2.03 (s, 6H), 4.51 (s, 2H), 7.72 (t, J = 1.5 Hz, 1H), 7.80 (d, J = 8.1 Hz, 2H), 7.91 (t, J = 1.5 Hz, 2H), 8.01 (d, J = 8.1 Hz, 2H), 8.35 (d, J = 4.5 Hz, 1H), 8.44 (d, J = 4.5 Hz, 1H), 8.58 (s, 1H), 8.61−8.63 (m, 2H), 8.65−8.69 (m, 2H), 8.72 (d, J = 4.5 Hz, 1H); LD-MS obsd 791.60; FAB-MS obsd 792.1667, calcd 792.1689 ($C_{42}H_{41}IN_4Zn$); λ_{abs} 412, 609 nm.

19-Bromo-10-(3,5-di-*tert*-butylphenyl)-2,3,4,5-tetrahydro-1,3,3-trimethyl-15-[4-[2-(trimethylsilyl)ethynyl]phenyl]bilene-*a* (7e). Treatment of **6e** (307 mg, 0.500 mmol) with $NaBH_4$ (189 mg, 5.00 mmol) in 30 mL of anhydrous THF/methanol (4:1) afforded **6e-OH**. The reaction of **6e-OH** and **4** (94 mg, 0.50 mmol) in 5 mL of anhydrous CH_3CN containing TFA (39 μL, 0.50 mmol) for 30 min under argon followed by the standard workup afforded a brown solid (233 mg, 59%): mp 61−63 °C;^{1}H NMR δ 0.24 (bs, 9H), 0.90 (bs, 3H), 1.06 (bs, 3H), 1.25 (bs, 18H), 1.83−1.90 (m, 3H), 2.21−2.47 (m, 2H), 2.49−2.62 (m, 1H), 2.66−2.75 (m, 1H), 3.51−3.60 (m, 1H), 5.25−5.35 (m, 2H), 5.65−5.88 (m, 5H), 5.96−6.02 (m, 1H), 6.97−7.04 (m, 3H), 7.04−7.14 (m, 2H), 7.32−7.42 (m, 2H), 7.81−7.96 (m, 1H), 8.07−8.21 (m, 1H), 9.08−9.20 (m, 1H); FAB-MS obsd 787.3802, calcd 787.3771 ($C_{47}H_{59}BrN_4Si$).

Zn(II)-5-(3,5-di-*tert*-butylphenyl)-10-(4-ethynyl]phenyl)-17,18-dihydro-18,18-dimethylporphyrin (Zn-8e). Following the procedure for preparing **Zn-8a**, a solution of **7e** (118 mg, 0.150 mmol) in CH_3CN (15 mL) containing the oxidative cyclization reagents was refluxed for 12 h exposed to air. Standard workup and chromatography [silica, hexanes/CH_2Cl_2 (2:1)] gave a blue solid (28 mg, 27%). Deprotection of the trimethylsilylethyne apparently occurred under these conditions: ^{1}H NMR δ 1.49 (s, 18H), 2.02 (s, 6H), 3.26 (s, 1H), 4.50 (s, 2H), 7.72 (t, J = 1.5 Hz, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.92 (t, J = 1.5 Hz, 2H), 8.03 (d, J = 8.1 Hz, 2H), 8.35 (d, J = 4.5 Hz, 1H), 8.45 (d, J = 4.5 Hz, 1H), 8.58 (s, 1H), 8.59−8.62 (m, 2H), 8.64 (s, 1H), 8.66 (d, J = 4.5 Hz, 1H), 8.72 (d, J = 4.5 Hz, 1H); LD-MS obsd 689.45; FAB-MS obsd 690.2748, calcd 690.2701 ($C_{44}H_{42}N_4Zn$); λ_{abs} 413, 609 nm.

19-Bromo-2,3,4,5-tetrahydro-1,3,3-trimethyl-10-(4-methylphenyl)-15-[4-[2-(trimethylsilyl)ethynyl]phenyl]-bilene-*a* (7f). Treatment of **6f** (309 mg, 0.600 mmol) with $NaBH_4$ (226 mg, 6.00 mmol) in 40 mL of anhydrous THF/methanol (4:1) afforded **6f-OH**. The reaction of **6f-OH** and **4** (113 mg, 0.600 mmol) in 6 mL of anhydrous CH_3CN containing TFA (46 μL, 0.60 mmol) for 30 min under argon followed by the standard workup afforded a brown solid (273 mg, 66%): mp 77−79 °C; ^{1}H NMR δ 0.27 (bs, 9H), 0.90 (bs, 3H), 1.08 (bs, 3H), 1.85 (bs, 3H), 2.27−2.31 (m, 2H), 2.32 (bs, 3H), 2.49−2.57 (m, 1H), 2.66−2.71 (m, 1H), 3.52−3.56 (m, 1H), 5.23−5.27 (m, 2H), 5.68−5.72 (m, 4H), 5.80−5.84 (m, 1H), 5.99−6.03 (m, 1H), 7.05−7.07 (m, 2H), 7.07−7.10 (m, 4H), 7.35−7.39 (m, 2H), 7.84−7.96 (m, 1H), 8.16−8.37 (m, 1H), 9.16−9.28(m,1H); FAB-MS obsd 689.2713, calcd 689.2675 ($C_{40}H_{45}BrN_4Si$). Anal. Calcd for $C_{40}H_{45}BrN_4Si$: C, 69.65; H, 6.58; N, 8.12. Found: C, 69.17; H, 6.69; N, 7.74.

Zn(II)-10-(4-ethynyl]phenyl)-17,18-dihydro-18,18-dimethyl-5-(4-methylphenyl)porphyrin (Zn-8f). Following the procedure for preparing **Zn-8a**, a solution of **7f** (158 mg, 0.229 mmol) in THF (23 mL) containing the oxidative cyclization reagents was refluxed for 24 h exposed to air. Standard workup and chromatography [silica, hexanes/CH_2Cl_2 (2:1)] gave a greenish blue solid (61 mg, 45%). Deprotection of the trimethylsilylethyne apparently occurred under these conditions: ^{1}H NMR δ 2.03 (s, 6H), 2.66 (s, 3H), 3.27 (s, 1H), 4.51 (s, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.1 Hz, 2H), 7.94 (d, J = 8.1 Hz, 2H), 8.03 (d, J = 8.1 Hz, 2H), 8.34 (d, J = 4.5 Hz, 1H), 8.41 (d, J = 4.5 Hz, 1H), 8.58 (s, 1H), 8.60−8.64 (m, 2H), 8.64−8.68 (m, 2H), 8.69 (d, J = 4.5 Hz, 1H); LD-MS obsd 591.68; FAB-MS obsd 592.1620, calcd 592.1605 ($C_{37}H_{28}N_4Zn$); λ_{abs} 413, 609 nm.

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Supporting Information Available: Isolation and characterization of chlorin byproducts obtained under nonoptimal conditions for the oxidative cyclization process; a discussion of possible oxidized intermediates during the oxidative cyclization process; a brief description of nomenclature of tetrapyrrole species; ^{1}H NMR spectra for **3**−**5**, **7a**,**c**,**e**,**f**; spectral data (^{1}H NMR, LD-MS) for all new chlorins; X-ray structural data for **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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