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De Novo Synthesis of Stable Tetrahydroporphyrinic Macrocycles: Bacteriochlorins and a Tetradehydrocorrin

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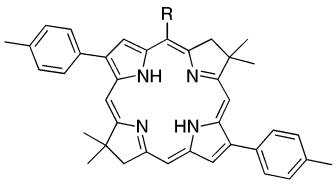
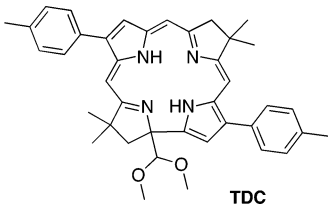


H-BC, R = H
MeO-BC, R = MeO



TDC

Bacteriochlorins (tetrahydroporphyrins) are attractive for diverse photochemical applications owing to their strong absorption in the near-infrared spectral region, as exemplified by the bacterial photosynthetic pigment bacteriochlorophyll *a*, yet often are labile toward dehydrogenation to give the chlorin. Tetradehydrocorrins (ring-contracted tetrahydroporphyrins) are attractive for studies of catalysis analogous to that of vitamin B_{12}. An eight-step synthesis toward such tetrahydroporphyrinic macrocycles begins with *p*-tolualdehyde and proceeds to a dihydrodipyrrin-acetal (**1**) bearing a geminal dimethyl group and a *p*-tolyl substituent. Self-condensation of **1** in CH_3CN containing $BF_3{\cdot}OEt_2$ at room temperature afforded a readily separable mixture of two free base bacteriochlorins and a free base B,D-tetradehydrocorrin. Each bacteriochlorin contains two geminal dimethyl groups to lock-in the bacteriochlorin hydrogenation level, *p*-tolyl substituents at opposing (2,12) β-positions, and the absence (**H**−**BC**) or presence (**MeO**−**BC**) of a methoxy group at the 5- (meso) position. The B,D-tetradehydrocorrin (**TDC**) lies equidistant between the hydrogenation levels of corrin and corrole, is enantiomeric, and contains two geminal dimethyl groups, 2,12-di-*p*-tolyl substituents, and an acetal group at the pyrroline−pyrrole junction. Examination of the effect of the concentrations of **1** (2.5−50 mM) and $BF_3{\cdot}OEt_2$ (10−500 mM) revealed a different response surface for each of **H**−**BC**, **MeO**−**BC**, and **TDC**, enabling relatively selective preparation of a given macrocycle. The highest isolated yield of each was 49, 30, and 66%, respectively. The macrocycles are stable to routine handling in light and air. The bacteriochlorins display characteristic spectral features; for example, **H**−**BC** exhibits near-IR absorption (λ_{Q_y} = 737 nm, ϵ_{Q_y} = 130 000 M^{-1} cm^{-1}) and emission (λ_{em} = 744 nm, Φ_f = 0.14). In summary, this simple entry to stable bacteriochlorins and tetradehydrocorrins should facilitate a wide variety of applications.

Introduction

The progressive $2e^-/2H^+$ reduction of the porphyrinic macrocycle along the series porphyrin, chlorin (a dihydroporphyrin), and bacteriochlorin (a tetrahydroporphyrin) causes profound changes in chemical and physical properties (Chart 1). The reduction alters the symmetry, yet each macrocycle maintains an 18-π-electron-conjugated system as required for aromaticity. One striking change upon reduction is the large increase in absorption in the red or near-IR region of the spectrum.[1] The changes in physical properties have been famously exploited by biological systems; the chlorin macrocycle provides the basis for chlorophylls *a* and *b* in plant photosynthesis, while the bacteriochlorin macrocycle provides the basis for bacteriochlorophyll *a* in bacterial photosynthesis. The strong absorption in the near-IR makes bacteriochlorins well suited for a wide variety of applications in the life sciences, medicine, and materials chemistry.

Surprisingly few methods exist for the preparation of bacteriochlorins despite the importance of this class of compounds.[2] To our knowledge, no total syntheses of photosynthetic bacteriochlorophylls have been reported.

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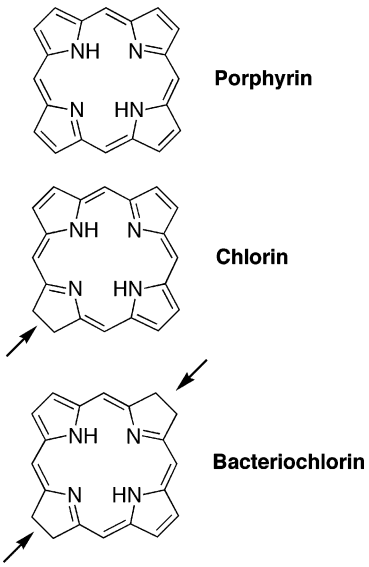
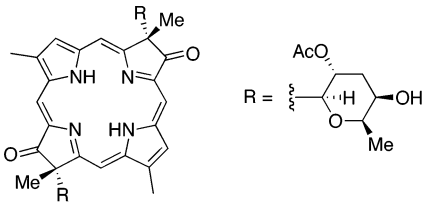
CHART 1



A chief obstacle to handling bacteriochlorophyll *a* is its pronounced tendency to undergo dehydrogenation to give the corresponding chlorin.[3] Bacteriochlorophyll *b*[4,5] and bacteriochlorophyll *g*[6] are even more labile given their susceptibility to tautomerization, also affording the corresponding chlorin. For example, both bacteriochlorophylls *b* and *g* undergo conversion to the chlorin with half-lives of a few minutes upon exposure to light in vitro.[5,6] Both oxidation and tautomerization processes are illustrated in Scheme 1.

A simple method developed several decades ago for preparing synthetic bacteriochlorins entails reduction with diimide of a porphyrin or chlorin.[7] This direct reduction method is accompanied by several problems, including (1) the difficulty of separating chlorin and bacteriochlorin species, (2) the adventitious dehydrogenation of the bacteriochlorin yielding the chlorin and porphyrin, and (3) the possible formation of bacteriochlorin isomers depending on the nature of meso or β-pyrrole substituents. More resilient bacteriochlorins have been prepared by derivatization of porphyrins or chlorins, including vicinal dihydroxylation (with optional subsequent pinacol rearrangement), photooxygenation of divinylporphyrins, Diels–Alder reactions, 1,3-dipolar cycloadditions, and successive addition of carbon nucleophiles.[2] Each method has merit yet also suffers from the potential formation of regioisomers owing to reaction at distinct pyrrole rings or at the same or opposite faces of the macrocycle. Elaborate bacteriochlorins have been obtained by modification of naturally occurring chlorophylls[8–10] or bacteriochlorophylls,[9,11] but the inherent lability of the naturally available starting materials and the presence of a nearly full complement of peripheral substituents restrict synthetic flexibility.

The bacteriochlorin chromophore is not inherently unstable. Tolyporphin A, a nonphotosynthetic bacteriochlorin pigment from the Pacific microalga *Tolypothrix nodosa*,[12] is a stable compound. The total synthesis of the *O*,*O*-diacetate of tolyporphin A was reported by Kishi, entailing >20 steps and affording <5 mg of product.[13] A key structural difference between tolyporphins and photosynthetic bacteriochlorophylls is the presence of two geminal dialkyl units in each reduced, pyrroline ring; such groups lock-in the reduction level of the bacteriochlorin.



Tolyporphin A

A similar geminal dialkyl motif is present in diverse naturally occurring hydroporphyrins, including vitamin B_{12}, isobacteriochlorins (Factor II, Factor III, siroheme), and nonphotosynthetic chlorins (bonellin, Factor I).[14] Indeed, vitamin B_{12} contains a geminal dialkyl group in each reduced ring (Chart 2). Syntheses of most of these stable hydroporphyrins have been achieved. However, the rich pattern of substituents in natural hydroporphyrins has resulted in elegant yet elaborate syntheses that afford minute quantities of products. Consequently, fully unsaturated synthetic analogues of the naturally occurring hydroporphyrins are typically employed as surrogates given the greater ease of preparation of the unsaturated analogues. Thus, porphyrins are employed as models of bacteriochlorins in a wide variety of photochemical studies, and corroles or octadehydrocorrins are

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SCHEME 1

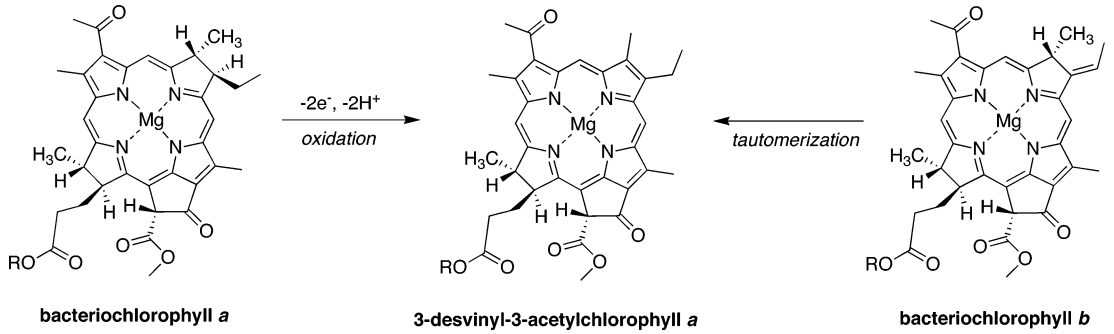
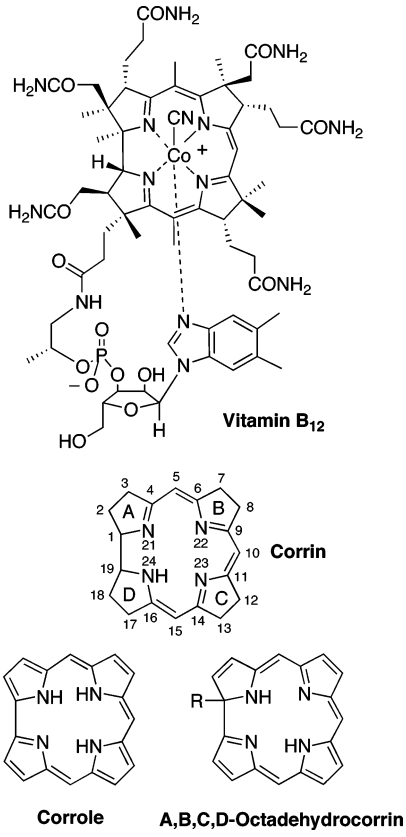


CHART 2

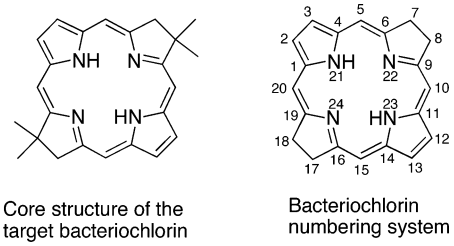


used as model corrins in organometallic chemistry and studies of catalysis. A corrole is an aromatic tautomer of an octadehydrocorrin, as illustrated for R = H in Chart 2.

The use of hydroporphyrins in applications and fundamental studies requires simple synthetic methods that afford access to ample quantities of stable compounds. Specific attributes of the desired methodology include the ability (1) to construct a macrocycle that is locked at the desired hydroporphyrin reduction level through the use of geminal dialkyl groups and (2) to place a limited number of substituents at designated sites around the perimeter of the macrocycle. The structure of a target bacteriochlorin core (lacking peripheral substituents other than the geminal dimethyl groups) is shown in Chart 3.

In this paper, we describe a de novo synthesis of bacteriochlorins where structural features in acyclic precursors establish the bacteriochlorin reduction level.

CHART 3



While our goal was solely to prepare bacteriochlorins, a tetradehydrocorrin has emerged as a fortuitous byproduct. The route employs the self-condensation of a dihydrodipyrrin-acetal. We describe the synthesis of the dihydrodipyrrin-acetal, a study of conditions for the self-condensation, and the characterization of the resulting tetrahydroporphyrinic macrocycles.

Results and Discussion

1. Exploration. The route that we developed draws on our prior work concerning the rational synthesis of chlorins.[15,16] The chlorins, which contain one geminal dialkyl unit, were prepared by reaction of a dihydrodipyrrin (**A**) (or a tetrahydrodipyrrin) and a 1-bromodipyrromethane-9-carbinol (**B**). In the hydrodipyrrins (e.g., **A**), both pyrrole and pyrroline entities served as nucleophiles, while component **B** reacted as a bis-electrophile. For the synthesis of bacteriochlorins, the condensation of two hydrodipyrrins requires complementary reactivity of pyrrole and pyrroline sites. We prepared a number of hydrodipyrrins each containing one pyrrole and one pyrroline unit with complementary reactivity, and eventually found that a dihydrodipyrrin (**C**) bearing a dimethyl acetal moiety attached to the α-pyrroline position underwent self-condensation to give bacteriochlorins (Scheme 2). This result validated the approach of employing a dihydrodipyrrin bearing pyrrole/pyrroline moieties with complementary nucleophilic/electrophilic reactivity, respectively, although the yield was very low (∼1%). The synthesis of **C** and other new hydrodipyrrins developed in the course of the exploratory work will be described elsewhere.

Dihydrodipyrrin analogues that bear a *β*-substituent in the pyrrole ring (**D**) are known to be more stable than the unsubstituted species (**A**).[16] Accordingly, we focused

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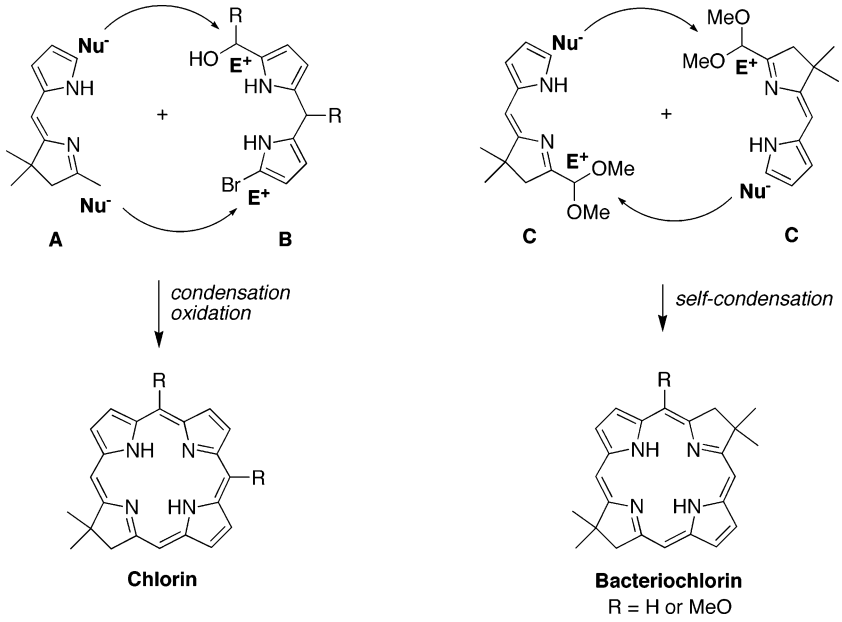
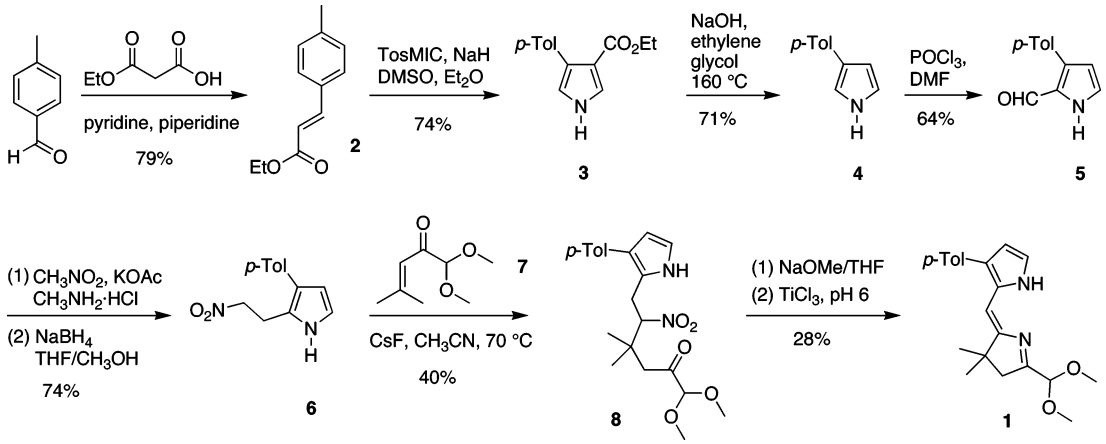
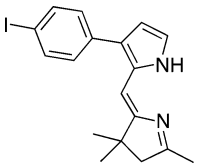


SCHEME 3



on the development of a route to dihydrodipyrrin-acetal **1**, a β-pyrrole-substituted analogue of **C**. The *p*-tolyl group was chosen as an inert substituent that is readily characterized by ^{1}H NMR spectroscopy.



D

2. Synthesis of Bacteriochlorin Precursors. The synthesis of dihydrodipyrrin-acetal **1** was initiated in a fashion similar to that of dihydrodipyrrin **D** (Scheme 3).[16] Components **2**−**4** of the synthesis have been prepared via different routes or have been reported with incomplete characterization data. A full description is reported here.

Application of the previously unused Knoevenagel condensation[17] of *p*-tolualdehyde with malonic acid monoethyl ester[18] in pyridine containing a catalytic amount of piperidine gave the known α,β-unsaturated ester **2**[19] in 79% yield. Reaction of **2** with (*p*-tolylsulfonyl)methyl isocyanide (TosMIC) afforded β-substituted pyrrole **3** (a known compound with incomplete data[20]) in 74% yield. Removal of the ethoxycarbonyl group of pyrrole **3** by treatment with NaOH in ethylene glycol at 160 °C gave the known β-substituted pyrrole **4**[21−23] in 71% yield. Vilsmeier−Haack formylation of **4** yielded a mixture of regioisomers owing to substitution at the 2- or 5-position.

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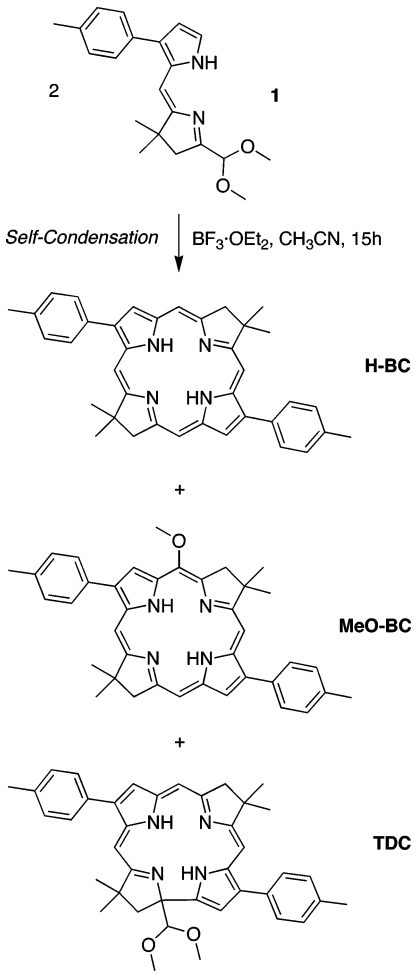
After column chromatography, the two regioisomers were determined to be present in ~13:1 ratio by ^{1}H NMR integration of the methyl unit of the *p*-tolyl group. Selective precipitation readily afforded the major regioisomer **5** in 64% yield. The same formylation method was used to prepare 2-formyl-3-(4-iodophenyl)pyrrole, which was characterized by ^{1}H NMR spectroscopy and X-ray crystallography.[16] The chemical shift of the two peaks (δ 6.42−6.44 and 7.10−7.13 ppm) from the pyrrolic protons of the major isomer **5** were quite similar to those for 2-formyl-3-(4-iodophenyl)pyrrole (δ 6.42 and 7.14 ppm)[16] or 2-formyl-3-phenylpyrrole (δ 6.50 and 7.30 ppm).[24] The minor isomer, 2-formyl-4-(4-methylphenyl)pyrrole (δ 7.20−7.22 and 7.36−7.38 ppm), also showed similar chemical shifts for the respective pyrrolic protons of the previously characterized 2-formyl-4-(4-iodophenyl)pyrrole (δ 7.21 and 7.39 ppm).[16]

Treatment of **5** to the standard conditions[16] for condensation of a pyrrole-2-carboxaldehyde with nitromethane afforded the crude 2-(2-nitrovinyl)pyrrole as a brown solid. Reduction of the latter with $NaBH_4$ gave the β-substituted nitroethylpyrrole **6**. The α-keto acetal (**7**) required for the next step, previously prepared at the 2 mmol scale by reaction of mesityl oxide with a catalytic amount of diphenyl diselenide and excess ammonium peroxydisulfate,[25] was carried out at the 160 mmol scale, affording **7** (~7 g) in 29% yield. The Michael reaction of **6** with excess **7** (10 equiv) in the presence of CsF at 65 °C gave **8** in 40% yield, accompanied by recovery of **7** (~50%) upon bulb-to-bulb distillation and column chromatography. Treatment of **8** with NaOMe followed by a buffered $TiCl_3$ solution afforded the dihydrodiyrrin-acetal **1** as a yellow solid in 28% yield.

3. Investigation of Reaction Conditions for Bacteriochlorin Formation. A series of microscale studies (~1−2 mg of **1** per reaction) was performed to investigate the effects of reaction parameters that are known to influence the course of condensations leading to porphyrinic macrocycles, including concentration of **1**, acid composition, acid concentration, solvent, and time.[26] The standard conditions employed initially included acetal **1** (5 mM) in CH_3CN containing acid (50 mM) at room temperature, which closely resemble those employed in the self-condensation of the unsubstituted dihydrodipyrrin-acetal **A**. Samples were removed periodically over the course of ~24 h, neutralized with TEA, and examined by absorption spectroscopy. Yields were calculated on the basis of the assumption (vide infra) that each bacteriochlorin has $\epsilon_{Q_y} = 120\ 000\ M^{-1}\ cm^{-1}$. The intense absorption of the bacteriochlorin enabled quantitative analysis of crude reaction mixtures.

A. Acids. A screening study was performed to identify the effects of a variety of acids on the self-condensation of **1**. Brønsted acids (4) and Lewis acids (11) (previously employed in porphyrin chemistry)[27] were examined in CH_3CN exposed to air. The acids can be categorized on the basis of bacteriochlorin yields: $BF_3{\cdot}OEt_2$ (31%); $InCl_3$, $Sc(OTf)_3$, or $SnCl_4$ (18−16%); *p*-TsOH·H_2O (4.9%); $Yb(OTf)_3$, SnF_4, $TiCl_4$, BBr_3, or HCl (1.5−0.4%); and AcOH, TFA, $MgBr_2$, $ZnCl_2$, or $Zn(OAc)_2$ (~0%). The acids $InCl_3$ and $Yb(OTf)_3$ afforded a free base bacteriochlorin, a metalated bacteriochlorin, and a non-bacteriochlorin macrocycle. This work will be described elsewhere.

SCHEME 4



B. Solvents. The effect of solvent on the self-condensation of **1** was examined with $BF_3{\cdot}OEt_2$ catalysis under the standard conditions. The bacteriochlorin yields were ~30% (CH_3CN), <2% ($CHCl_3$ or $ClCH_2CH_2Cl$), and not detectable (CH_2Cl_2, toluene, DMF, DMSO, THF, 1,4-dioxane, methanol, ethanol).

The standard reaction was scaled-up using $BF_3{\cdot}OEt_2$ in CH_3CN at room-temperature exposed to air for 6 h (Scheme 4). Chromatographic workup on silica followed by ^{1}H NMR spectroscopy and laser-desorption mass spectrometry (LD-MS) analysis led to two surprises. The first surprise was that two bacteriochlorins were isolated: one relatively nonpolar bacteriochlorin (**H**−**BC**) has no meso substituent, while one more polar bacteriochlorin (**MeO**−**BC**) has a methoxy group at the 5-position. The two bacteriochlorins were isolated in 11 and 30% yield, respectively. The second surprise emerged

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upon carrying out the reaction at lower concentrations of $BF_3{\cdot}OEt_2$, whereupon another porphyrinic macrocycle was identified. The macrocycle proved to be a B,D-tetradehydrocorrin (**TDC**), a ring-contracted tetrahydroporphyrinic species containing two opposing pyrroline rings. The tetradehydrocorrin is a $4e^-/4H^+$ oxidized analogue of a corrin and hence lies equidistant between the reduction levels of a corrin and a corrole or octadehydrocorrin.[28] Each macrocycle was characterized by absorption spectroscopy, ^1H NMR spectroscopy, LD-MS, and high-resolution FAB-MS (vide infra). In summary, the dramatic increase in yield (versus the <1% yield with the unsubstituted dihydrodipyrrin-acetal **A**) validated our hunch that β-substitution would afford a more stable dihydrodipyrrin and more efficient reaction.

C. Effect of Reactant and Acid Concentrations. To broadly characterize the effect of reactant concentration and acid concentration on the yield of each of the macrocycles, a grid-search experiment was performed at the microscale level (0.5−2 mL reactions). The search space was defined by the concentrations of dihydrodipyrrin-acetal **1** (2.5−50 mM) and $BF_3{\cdot}OEt_2$ (10−500 mM). Points at the corners, faces, core, and center of the search space were examined. Each reaction was monitored over time (23 h), and the total yield of bacteriochlorins (but not **TDC**) was determined spectroscopically from the crude mixture. Each reaction mixture was then separated chromatographically to determine the isolated yield (by spectrophotometry of purified fractions) of bacteriochlorins (**H**−**BC**, **MeO**−**BC**) and the tetradehydrocorrin **TDC**.

The time course for bacteriochlorin formation is shown in Figure 1 for the reactions carried out at the lowest, midpoint, and highest concentrations of both **1** and $BF_3{\cdot}OEt_2$. The data from the crude reaction samples estimate the summed yield of **H**−**BC** + **MeO**−**BC**. The bacteriochlorins form smoothly, and the yields generally remain constant over time. Little variation in rate was observed upon increasing the concentration of $BF_3{\cdot}OEt_2$ from 10 to 500 mM.

The isolated yields at each point in the search space are shown in Figure 2. The segmented histogram shows the yield of each of the three macrocycles and the summed yields. Note that the ratio of **H**−**BC**:**MeO**−**BC**:**TDC** changes with alteration in the concentration of acid and reactant. The yield of **TDC** is highest at the lowest acid concentration examined, and no **TDC** is observed at the highest acid concentrations. On the other hand, the yield of **H**−**BC** generally increased with increasing acid concentration. The yield of **MeO**−**BC** was highest at modest concentrations of acid and reactant. From a practical standpoint, this limited study has identified

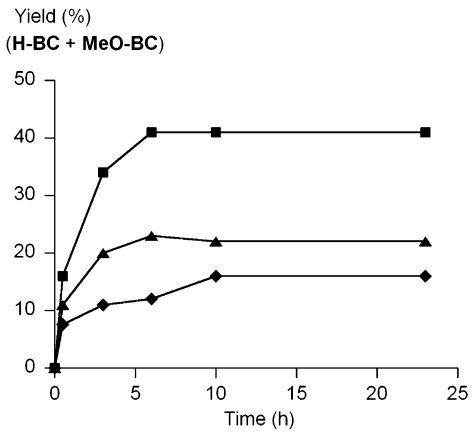

FIGURE 1. Yield of bacteriochlorins (sum of **H**−**BC** + **MeO**−**BC**) as a function of time. The data points were taken for concentrations of **1** and $BF_3{\cdot}OEt_2$ located along the diagonal of the grid described in Figure 2 (◆, 2.5 mM **1**, 10 mM $BF_3{\cdot}OEt_2$; ■, 11 mM **1**, 71 mM $BF_3{\cdot}OEt_2$; ▲, 50 mM **1**, 500 mM $BF_3{\cdot}OEt_2$). The yield values were determined by absorption spectroscopy of crude reaction samples (assuming ϵ_{Q_y} = 120 000 M^{-1} cm^{-1} for both bacteriochlorins).

conditions that afford a relatively good, albeit not exclusive, yield of each of the macrocycles.

Three semipreparative reactions were performed. In each reaction, the concentrations of **1** and $BF_3{\cdot}OEt_2$ were chosen on the basis of the response-surface data to favor one of the three macrocycles (**H**−**BC**, **MeO**−**BC**, **TDC**). The results are listed in Table 1. The reaction designed to favor **H**−**BC** gave **H**−**BC** in 49% yield (20 mg; entry 1). The reaction designed to favor **MeO**−**BC** gave **MeO**−**BC** in 30% yield (24 mg; entry 2). The reaction to favor **TDC** gave **TDC** in 66% yield (30 mg; entry 3). In each case, the desired macrocycle was readily isolated, as was a lesser amount of one (but not both) of the other macrocycles. The product ratios generally mirrored the trends observed in the microscale work (Figure 2), although the isolated yields were somewhat higher. These results augur well for relatively selective preparation of workable quantities of each tetrahydroporphyrinic macrocycle.

4. Mechanistic Considerations. At present, we know very little about the mechanistic course leading from the dihydrodipyrrin-acetal to the bacteriochlorin or tetradehydrocorrin species. The balanced reaction for formation of each product is shown in Scheme 5. The conversion of two molecules of **1** to give **MeO**−**BC** proceeds with elimination of three molecules of methanol. Note that the acetal unit of **1** serves as an electrophile for the bacteriochlorin-forming reaction. Examples are known where an acetal functions as an electrophile, leaving one alkyl ether unit intact.[29] The formation of **TDC** entails elimination of two molecules of methanol. Thus, the self-condensation of **1** to give **MeO**−**BC** and **TDC** does not require any change in oxidation state. By contrast, the formation of **H**−**BC** must proceed with elimination of four molecules of methanol and addition of $2e^-$ and $2H^+$. Neither the source of the reductant nor the nature of the

(28) Nomenclature of dehydrogenated corrinoids is not yet fully systematized. Many workers would refer to **TDC** as a didehydrocorrin because two double bonds have been introduced relative to the corrin; by the same token, a corrole would be a tetradehydrocorrin tautomer. In IUPAC recommendations, **TDC** is a tetradehydrocorrin ($4e^-/4H^+$ removed from the corrin), and corrole is an octadehydrocorrin tautomer ($8e^-/8H^+$ removed from corrin).[28a] A clear review concerning octadehydrocorrins is provided by Genokhova et al.[28b] **TDC** is at the same reduction level as a tetrahydrocorrole, but given the interrupted path of conjugation and lack of aromatic character, **TDC** is named as a dehydrogenated corrin rather than as a hydrogenated corrole. (a) *Pure Appl. Chem.* **1976**, *48*, 495−502. (b) Genokhova, N. S.; Melent'eva, T. A.; Berezovskii, V. M. *Russ. Chem. Rev.* **1980**, *49*, 1056−1067.

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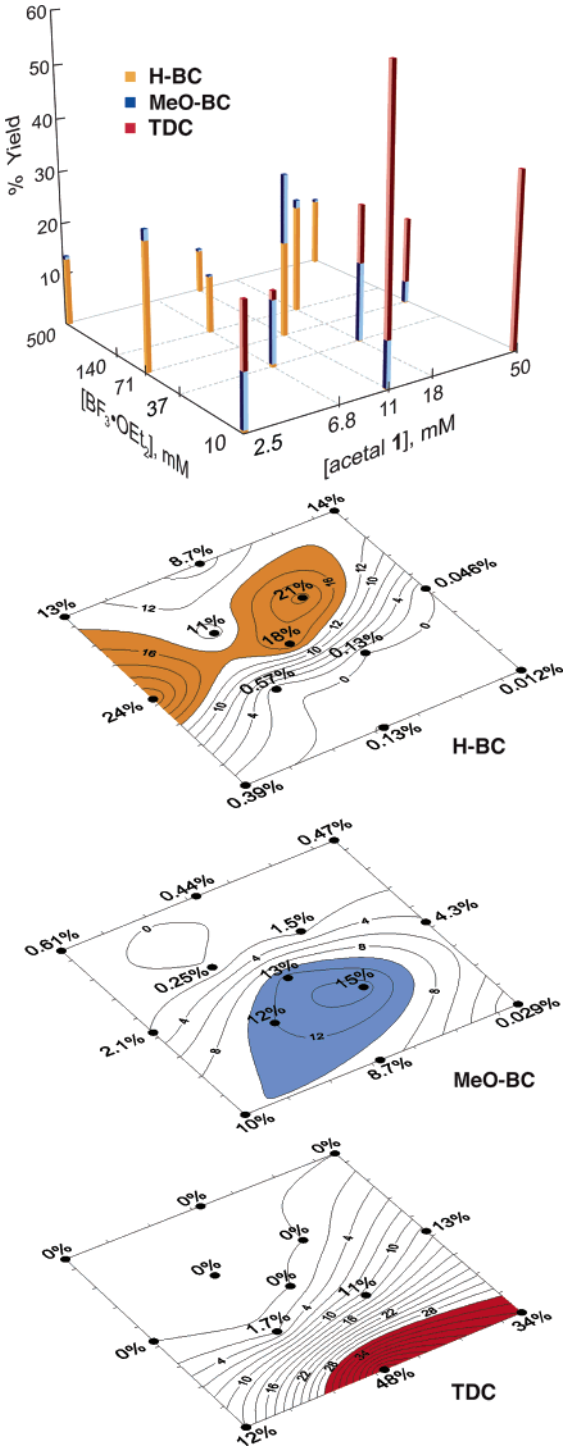
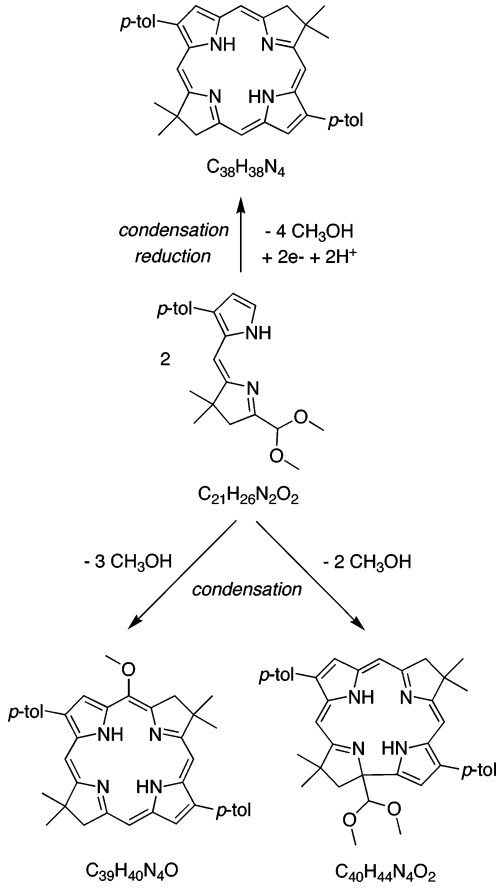


FIGURE 2. Yields of **H**−**BC**, **MeO**−**BC**, and **TDC** as a function of the concentrations of **1** and $BF_3{\cdot}OEt_2$. The reactions were performed at the microscale level. Each reaction was worked up after 23 h. The yields are based on spectrophotometry of purified fractions using the known molar absorption coefficients of each species. The segmented histogram (top) shows the yield of each species and the summed yield of macrocycles. The contour diagrams below illustrate the yield of each species **H**−**BC**, **MeO**−**BC**, and **TDC** in the same search space. The actual numerical data are listed; the interpolated contours are provided to guide the eye. In each contour, coloration is provided to illustrate the 60% cutset data (i.e., those regions that afford a yield that is at least 60% of the highest value recorded anywhere in the search space).

SCHEME 5



intermediate that undergoes reduction is known. It is worthwhile to contrast this overall transformation with that of porphyrin formation from an aldehyde and pyrrole, which proceeds via condensation to give a hexahydroporphyrin (porphyrinogen) intermediate; the latter is converted via a $6e^-/6H^+$ oxidation to give the porphyrin.[26]

From the standpoint of oxidation-state and structural considerations, the B,D-tetradehydrocorrin is to a bacteriochlorin what an octadehydrocorrin is to a porphyrin. Syntheses of octadehydrocorrins were developed several decades ago,[28b] and more recent activity has been devoted to methodology for preparing substituted corroles,[30,31] the aromatic counterpart of octadehydrocorrins.[28] Recent directed routes to corroles entail cyclization of a 1,19-unsubstituted bilane,[32,33] *a*,*c*-biladiene,[34] or 22,24-dihydro-*a*,*b*,*c*-bilatriene.[34] The conversion of each such acyclic species to give the A−D ring junction of the corrole requires oxidation (the mechanisms of which remain under active investigation). A typical oxidant is DDQ or

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TABLE 1. Isolated Yields of Macrocycles from Semipreparative Reactions[a]

entry	[**1**], mM	[BF_3·OEt_2], mM	**H**−**BC** yield	**MeO**−**BC** yield	**TDC** yield
1[b]	18	140	49% (21%)[c]	1.9% (1.5%)[c]	
2[d]	5.0	50	11%	30%	
3[b]	11	10		6.3% (8.7%)[c]	66% (48%)[c]

[a] Yields were determined gravimetrically. [b] Reaction was performed using 0.15 mmol of **1**. [c] Yield obtained in the microscale grid-search experiment (Figure 2). [d] Reaction was performed using 0.27 mmol of **1**.

p-chloranil. By contrast, the self-condensation of **1** provides a very facile, nonoxidative entry into B,D-tetradehydrocorrins. It is interesting that both **1** and corroles[31−33] are formed in the presence of quite low acid concentrations.

5. Characterization. A. The B,D-Tetradehydrocorrin. The absorption spectrum of **TDC** shows λ_{max} at 341 nm, a shoulder at 438 nm, and a broad, weaker band in the region 500−1000 nm (Figure 3). The absorption spectral features are similar to a Ni(II) 1-methyloctadehydrocorrin.[35,36] The ^{1}H NMR spectrum showed relatively complex features due to the lack of symmetry (C_1) of **TDC** (see Supporting Information for assignments). Two noteworthy features are that (1) the NH protons exhibit two broad peaks in the region of δ 11.34−11.40 ppm and δ 11.89−11.96 ppm, to be contrasted with the resonance at δ ca. −1 to −3 ppm of aromatic porphyrinic compounds, and (2) all peripheral alkenyl protons (5-, 8-, 10-, 15-, and 18-positions) fall in the range δ 5.4−6.6 ppm, to be contrasted with δ ca. 8−9.5 ppm for aromatic porphyrinic compounds. LD-MS and FAB-MS analysis of **TDC** gave a molecule ion peak (*m/z* = 612.7 and 612.3447, respectively) consistent with the proposed structure (Scheme 4). Further proof of structure for **TDC** came from a single-crystal X-ray analysis, which will be published elsewhere.

The progressive reduction along the series from corrole to **TDC** to corrin alters the path of conjugation in the macrocycle. The reduction state of the pyrrolic rings that form the A−D ring junction as well as the hybridization of the joined carbon atoms (C_1−C_{19}) also change along the series of corrole (pyrrole−pyrrole; sp^2−sp^2), **TDC** (pyrroline−pyrrole, sp^3−sp^2), and corrin (pyrroline−pyrrolidine, sp^3−sp^3). On account of the interrupted path of conjugation and the presence of only 16-π-electrons due to reduction in rings A and C, **TDC** is not aromatic. **TDC** is a B,D-tetradehydrocorrin where the 1-acetal substituent defines the A ring, and the B and D rings are dehydrogenated relative to corrin (Chart 2).[28] While a number of dehydrocorrins have been prepared (e.g., D-didehydrocorrin,[37] C,D-tetradehydrocorrin,[38,39] B,C-tetradehydrocorrin,[40] B,C,D-hexadehydrocorrin,[41] and A,B,C,D-octadehydrocorrin;[28b] each defined using IUPAC nomenclature[28]) by direct synthesis or by reduction of an existing macrocycle,[42] to our knowledge there are no prior reports concerning the synthesis of B,D-tetradehydrocorrins.

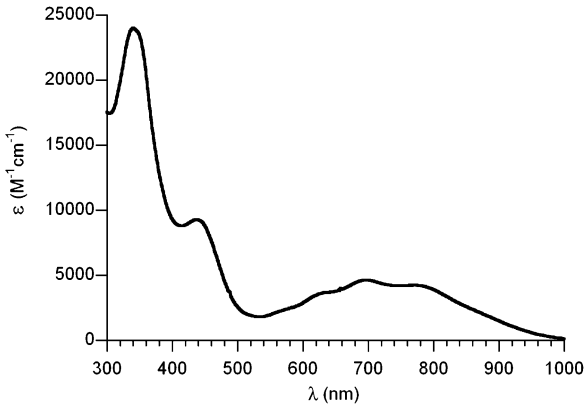

FIGURE 3. Absorption spectrum of **TDC** in toluene at room temperature.

B. Bacteriochlorins. Absorption Spectra. The absorption spectra of **H**−**BC** and **MeO**−**BC** in toluene are shown in Figure 4. Bacteriochlorin **H**−**BC** exhibits strong bands (B_y, B_x) at 351 and 374 nm, a weak $Q_x(0,0)$ band at 499 nm, and a strong $Q_y(0,0)$ band at 737 nm. Bacteriochlorin **MeO**−**BC** exhibits a broadened B band with peaks at 356 and 374 nm, a weak $Q_x(0,0)$ band at 511 nm, and a strong $Q_y(0,0)$ band at 732 nm. The overall absorption spectra of **H**−**BC** and **MeO**−**BC** resemble those of bacteriopheophytin *a* (the free base analogue of bacteriochlorophyll *a*) as well as synthetic, meso-substituted bacteriochlorins such as 5,15-diphenylbacteriochlorin[43] and 5,10,15,20-tetraphenylbacteriochlorin (λ_{abs} 356, 378, 520, and 742 nm; $\epsilon_{742\ nm}$ = 130 000 M^{-1} cm^{-1}).[7,44] The bacteriochlorins exhibit a light green appearance in dilute solution in CH_2Cl_2 or toluene.

Fluorescence Properties. The fluorescence spectra and fluorescence quantum yields of **H**−**BC** and **MeO**−**BC** were collected in toluene at room temperature. The fluorescence spectrum of each bacteriochlorin is dominated by a $Q_y(0,0)$ band with Stokes shift of ∼7−9 nm (Figure 4). Measurements of the fluorescence quantum yield (Φ_f) using chlorophyll *a* (Φ_f = 0.325)[45] as a reference gave a value of 0.14 or 0.18 for **H**−**BC** or **MeO**−**BC**, respectively, upon illumination in the B-band region (see Supporting Information).

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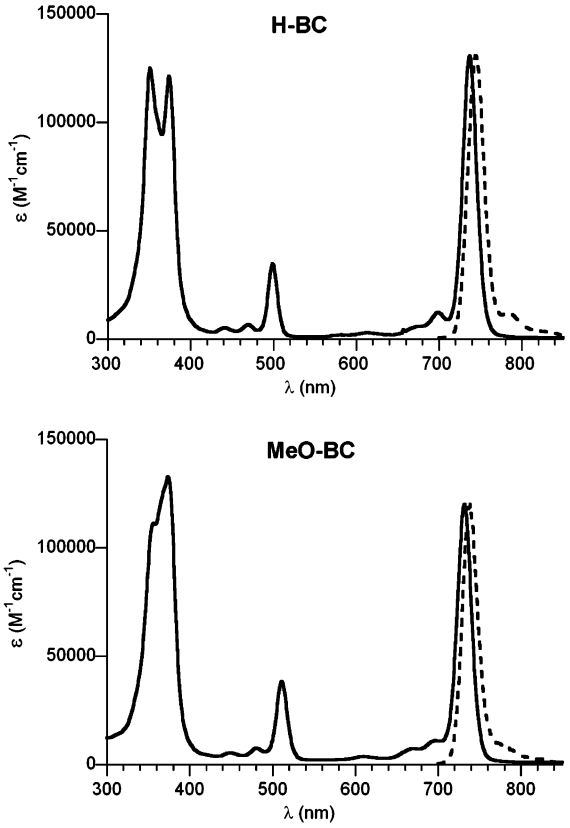

FIGURE 4. Electronic spectra of **H**−**BC** and **MeO**−**BC** in toluene at room temperature. Absorption (solid line); emission (dashed line).

The few data available concerning the fluorescence quantum yields of free base bacteriochlorins are quite varied. The free base analogue of the naturally occurring bacteriochlorophyll *a* (bacteriopheophytin *a*) has Φ_f estimated to be 0.12[46] or 0.094,[47] whereas a 13[1]-deoxo-20-formyl-pyropheophorbide derivative gave $\Phi_f \sim 0.002$.[10] Synthetic bacteriochlorins such as *meso*-tetrakis(3-hydroxyphenyl)bacteriochlorin[48] or 5,15-diphenylbacteriochlorin[43] gave Φ_f values of 0.11 or 0.14, respectively. A series of halogenated *meso*-tetraarylbacteriochlorins gave $\Phi_f = 0.068$ (Ar = 2,6-difluorophenyl), 0.048 (Ar = 2-chlorophenyl), and 0.012 (Ar = 2,6-dichlorophenyl).[49] On the other hand, the dioxobacteriochlorin derived from octaethylporphyrin was reported to have Φ_f of 0.48.[50] A deeper understanding of the effects of substituents on the fluorescence properties of bacteriochlorins will require the examination of a larger and more systematic collection of bacteriochlorins, the preparation of which may be enabled by the new synthesis described herein.

Laser Desorption Mass Spectrometry (LD-MS). Porphyrins typically give a strong molecule ion peak upon LD-MS analysis without requirement for use of a matrix.[51] LD-MS analysis of **H**−**BC** or **MeO**−**BC** gave a molecule ion peak (m/z = 580.1 or 550.0) consistent with the proposed structures. The mass difference (∼30) between **H**−**BC** and **MeO**−**BC** is consistent with the presence of the methoxy group in the former compound.

^{1}H NMR Spectra. The ^{1}H NMR spectra of **H**−**BC** and **MeO**−**BC** were readily assigned by NOESY and COSY measurements (see Supporting Information). In the case of **H**−**BC**, which nominally has C_{2h} symmetry, a relatively simple ^{1}H NMR spectrum is observed. Noteworthy features include a broad upfield peak (δ −1.96 ppm), a singlet at δ 1.93 ppm, and a singlet at δ 4.46 ppm, which are attributed to the two NH protons, the pair of geminal dimethyl groups, and the CH_2 groups of the pyrroline rings, respectively. A doublet (J = 2.0 Hz) at δ 8.73 ppm and two singlets at δ 8.81 and 8.86 ppm stem from the six protons (3-, 5-, 10-, 13-, 15-, and 20-positions) about the perimeter of the bacteriochlorin. Bacteriochlorin **MeO**−**BC** has generally similar features, but the presence of the 5-methoxy group nominally results in C_s symmetry and more complex splittings (see Supporting Information). Taken together, the absorption, fluorescence, LD-MS, and ^{1}H NMR spectroscopic data support the structures proposed for bacteriochlorins **H**−**BC** and **MeO**−**BC**. The structure of **MeO**−**BC** has been confirmed by single-crystal X-ray analysis, the results of which will be presented elsewhere.

6. Stability. The synthetic tetrahydroporphyrinic macrocycles (**H**−**BC**, **MeO**−**BC**, and **TDC**) are quite robust. For example, each compound was stable upon standing on the benchtop in solution exposed to air for more than 10 days, chromatography on silica in air in the presence of ambient lighting, dissolution in a variety of solvents (CH_2Cl_2, $CHCl_3$, THF, hexanes, toluene, DMF), or treatment with mild bases. Unlike bacteriochlorins derived from photosynthetic bacteria,[3−6] the synthetic bacteriochlorins do not undergo adventitious dehydrogenation upon routine handling.

Conclusion

A straightforward eight-step synthesis from simple precursors has been developed that affords free base tetrahydroporphyrinic macrocycles, including two bacteriochlorins and a B,D-tetradehydrocorrin. The macrocycles are stable toward dehydrogenation due to the presence of a geminal dimethyl group in each of the pyrroline rings. The synthesis entails self-condensation of dihydrodipyrrin-acetal **1** under mild acid catalysis at room temperature without requirement for an oxidant. The formation of the tetradehydrocorrin is understood in part by the recognition that a tetradehydrocorrin is to a bacteriochlorin what an octadehydrocorrin (a corrole tautomer) is to a porphyrin. The tetradehydrocorrin and bacteriochlorins lie at the same oxidation state ($4e^-/4H^+$ reduced) relative to the fully unsaturated corrinoid and porphyrinoid macrocycles. One key difference, however, is that the tetradehydrocorrin is not aromatic whereas the bacteriochlorins are aromatic macrocycles. Mere

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adjustment of the concentrations of **1** and $BF_3{\cdot}OEt_2$ enables a given macrocycle (**H**−**BC**, **MeO**−**BC**, **TDC**) to be obtained in reasonable yield. The bacteriochlorins exhibit characteristic absorption and fluorescence properties and are stable to a variety of reaction conditions. The synthesis described herein should provide ready access to tetrahydroporphyrinic macrocycles bearing a variety of substituents, which are essential for fundamental studies and diverse applications.

Experimental Section

Survey of Conditions for Bacteriochlorin-Forming Reactions. The condensations were carried out in 4 mL vials containing magnetic stir bars. A freshly prepared sample of **1** (0.85−1.7 mg) was dissolved in a specific amount (0.50−2.0 mL) of a solvent. The condensation was initiated by adding the desired acid to the stirred reaction mixture at room temperature. The progress of the reaction was monitored by taking aliquots periodically from the reaction mixture via syringe and neutralizing with TEA, followed by absorption spectroscopy. In particular, for 5 mM reactions of **1**, 10 μL aliquots were removed from the reaction vessel and diluted with 3 mL of CH_2Cl_2. The diluted solution was treated with one drop of TEA, and the visible absorption spectrum was recorded. [In cases where the acid yielded a heterogeneous mixture (e.g., $InCl_3$, $Yb(OTf)_3$), or broadened absorption in the Q_y region, the 10 μL aliquots were passed through a 2 cm long pipet column (CH_2Cl_2/ethyl acetate). The first collected sample (green; eluted with CH_2Cl_2) and the second collected sample (pink; eluted with ethyl acetate) were separately concentrated and then diluted with 3 mL of CH_2Cl_2. The visible absorption spectrum was recorded with the diluted solutions.] The yield of bacteriochlorins was determined by the intensity of the Q_y band (above 700 nm, $\epsilon = 120\,000\ M^{-1}\ cm^{-1}$) measured from the apex to the middle point of the baseline, established across the blue to red edge of the band. This eliminated the contribution of any other components that may absorb in the region >700 nm. In the case of insoluble acids, **1** and the insoluble acids were preweighed in the vial followed by addition of a microstir bar and the desired solvent.

Examination of Effects of Concentration (1, $BF_3{\cdot}OEt_2$). Stock solutions of **1** (100 mM, ∼2 mL, ∼50 mg of **1**) and $BF_3{\cdot}OEt_2$ (1.0 M, 2 mL, 253 μL of $BF_3{\cdot}OEt_2$) in acetonitrile were prepared immediately before the reactions were carried out. Solutions of **1** (5.0, 14, 22, 36, and 100 mM) in 0.5 mL of acetonitrile were prepared by taking a specific volume from the stock solution of **1**. Similarly, the $BF_3{\cdot}OEt_2$ solutions (20, 74, 140, 280, and 1000 mM) in 0.5 mL of acetonitrile were prepared by taking specific volumes from the stock solution. Each condensation was carried out in a 4 mL vial containing **1** and $BF_3{\cdot}OEt_2$ in acetonitrile with stirring and exposure to air. The condensation was initiated by adding the acid solution (0.50 mL) to the stirred acetal solution (0.50 mL) at room temperature, giving a total reaction volume of 1.0 mL. The progress of the reaction was monitored for 23 h by taking aliquots (5 μL) periodically from the reaction mixture. The aliquot was diluted into CH_2Cl_2 (3 mL). The diluted solution was neutralized with TEA (2−3 μL) and examined by absorption spectroscopy. The total yield of bacteriochlorins (**H**−**BC** + **MeO**−**BC**) was determined by the intensity of the Q_y band (733−737 nm, $\epsilon = 120\,000\ M^{-1}\ cm^{-1}$) as described above.

After stirring for 23 h, the reaction vials were treated with TEA (1−3 drops). The solvent was removed, and the residue was chromatographed (silica). Elution with CH_2Cl_2/hexanes (1:1) gave two bacteriochlorins. The first product, **H**−**BC**, was nonpolar ($R_f = 0.70$). The second product, **MeO**−**BC**, was slightly more polar ($R_f = 0.54$). Subsequent elution of the column with CH_2Cl_2 gave **TDC**. Each isolated product was relatively pure. In each case, the isolated yield was determined by concentrating the product to dryness and then dissolving the resulting residue in a known volume of solvent (typically 3 mL). A sample from this solution was then analyzed by absorption spectroscopy using the measured molar absorption coefficients for each species: **H**−**BC** ($\epsilon_{737\ nm} = 130\,000\ M^{-1}\ cm^{-1}$); **MeO**−**BC** ($\epsilon_{732\ nm} = 120\,000\ M^{-1}\ cm^{-1}$); **TDC** ($\epsilon_{431\ nm} = 24\,000\ M^{-1}\ cm^{-1}$).

Alternatively, absorption spectroscopy of the isolated bacteriochlorins was used to determine the relative amount of product; the actual amount of bacteriochlorin produced was calculated on the basis of the spectroscopic yield of the mixture of bacteriochlorins (as described in the preceding paragraph) and the relative ratios of the two species. No such correction was possible for **TDC**; the yields of **TDC** refer to isolated material.

1-(1,1-Dimethoxymethyl)-3,3-dimethyl-7-(4-methylphenyl)-2,3-dihydrodipyrrin (1). Following the procedure for preparing a β-substituted pyrrole,[16] a solution of **8** (237 mg, 0.610 mmol) in anhydrous THF (3.00 mL) under argon was treated with NaOMe (165 mg, 3.05 mmol), and the mixture was stirred for 1 h at room temperature (first flask). In a second flask, $TiCl_3$ (8.6 wt % $TiCl_3$ in 28 wt % HCl, 4.56 mL, 3.05 mmol, 5.0 mol equiv) and H_2O (24 mL) were combined; NH_4OAc (18.8 g, 244 mmol) was added to buffer the solution to pH 6.0, and then THF (1.60 mL) was added. The solution in the first flask containing the nitronate anion of **8** was transferred via a cannula to the buffered $TiCl_3$ solution in the second flask. The resulting mixture was stirred at room temperature for 6 h under argon. Then, the mixture was extracted with ethyl acetate. The organic extract was washed with 5% aqueous $NaHCO_3$ and water, dried ($NaSO_4$), and concentrated under reduced pressure at room temperature. The crude product was passed through a short column [alumina, hexanes/ethyl acetate (2:1)] to afford a light yellow solid (57 mg, 28%): mp 104−105 °C; ^{1}H NMR δ 1.19 (s, 6H), 2.38 (s, 3H), 2.62 (s, 2H), 3.45 (s, 6H), 5.03 (s, 1H), 6.11 (s, 1H), 6.28−6.30 (m, 1H), 6.86−6.88 (m, 1H), 7.22 (d, $J = 8.0$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 10.80−10.90 (br, 1H); ^{13}C NMR δ 21.3, 29.3, 40.5, 48.3, 54.8, 103.0, 106.2, 109.3, 119.2, 124.7, 126.9, 128.7, 129.4, 134.2, 135.4, 160.1, 174.2; FAB-MS obsd 338.2020, calcd 338.1994. Anal. Calcd for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74; N, 8.28. Found: C, 74.46; H, 7.79; N, 8.08. λ_{abs} (CH_2Cl_2) 358 nm.

Ethyl-3-(4-methylphenyl)prop-2-enoate (2).[19] A solution of ethyl malonate potassium salt (27.0 g, 158 mmol) in water (20.0 mL) was treated with concentrated HCl (∼35%, 15.0 mL), and the resulting mixture was stirred for 10 min at room temperature. The mixture was extracted with ether. The extract was washed with water, dried (Na_2SO_4), and concentrated to give a colorless oil (16.7 g, 79%), which was used without characterization.[18] A solution of *p*-tolualdehyde (11.6 g, 96.9 mmol) and monoethyl malonate (16.7 g, 126 mmol) in pyridine (39.2 mL, 485 mmol) containing piperidine (958 μL, 9.69 mmol) was refluxed for 8 h under argon. The reaction mixture was cooled to room temperature, quenched with 2 N HCl (∼250 mL), and extracted with ether. The extracts were washed with water, base ($NaHCO_3$), and water. The organic solution was dried (Na_2SO_4), concentrated, and chromatographed (silica, CH_2Cl_2) to give a colorless oil (14.6 g, 79%): ^{1}H NMR δ 1.33 (t, $J = 7.2$ Hz, 3H), 2.37 (s, 3H), 4.26 (q, $J = 7.2$ Hz, 2H), 6.39 (d, $J = 15.8$ Hz, 1H), 7.18 (d, $J = 8.2$ Hz, 2H), 7.42 (d, $J = 8.2$ Hz, 2H), 7.66 (d, $J = 15.8$ Hz, 1H); ^{13}C NMR δ 14.5, 21.6, 60.6, 117.4, 128.2, 129.8, 131.9, 140.8, 144.8, 167.4. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.76; H, 7.44.

3-(Ethoxycarbonyl)-4-(4-methylphenyl)pyrrole (3).[20] A suspension of TosMIC (15.7 g, 80.5 mmol) and **2** (14.6 g, 76.7 mmol) in dry ether/DMSO (2:1) (154 mL) was added dropwise under argon to a stirred suspension of NaH (2.39 g, 99.7 mmol) in ether (70 mL). The mixture started to reflux due to the exothermic reaction. After 3 h, water (200 mL) was cautiously added to the mixture, and the aqueous phase was extracted with ether and CH_2Cl_2. The combined organic extracts were

dried (Na_2SO_4), concentrated, and chromatographed [silica, CH_2Cl_2/ethyl acetate (9:1)] to give a light brown solid (13.1 g, 74%): mp 154−155 °C (lit.[20] mp 135−137 °C); ^{1}H NMR δ 1.25 (t, J = 7.2 Hz, 3H), 2.36 (s, 3H), 4.22 (q, J = 7.2 Hz, 2H), 6.75−6.77 (m, 1H), 7.16 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 7.46−7.48 (m, 1H), 8.38−8.54 (br, 1H); ^{13}C NMR δ 14.5, 21.4, 59.8, 113.9, 118.3, 125.4, 126.8, 128.6, 129.4, 132.0, 136.3, 165.2. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.11; H, 6.59; N, 6.12.

3-(4-Methylphenyl)pyrrole (4).[21−23] Following a standard procedure,[16] a mixture of **3** (6.81 g, 29.7 mmol) and ethylene glycol (76.0 mL) in a 250 mL Claisen flask was flushed with argon for 10 min, and then powdered NaOH (3.05 g, 76.2 mmol) was added. The flask was placed in an oil bath at 120 °C, and the temperature was raised to 160 °C. After 2.5 h, the flask was cooled to room temperature, and 10% aqueous NaCl (150 mL) was added. The aqueous layer was extracted with CH_2Cl_2. The organic extract was washed with 10% aqueous NaCl, dried (Na_2SO_4), concentrated, and chromatographed (silica, CH_2Cl_2) to give a light brown solid (3.33 g, 71%): mp 92−93 °C (lit.[21] mp 93−95 °C; lit.[22] mp 80−82 °C; lit.[23] mp 85−87 °C); ^{1}H NMR δ 2.34 (s, 3H), 6.51−6.54 (m, 1H), 6.82−6.84 (m, 1H), 7.05−7.08 (m, 1H), 7.15 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 7.8 Hz, 2H), 8.15−8.32 (br, 1H); ^{13}C NMR δ 21.3, 106.7, 114.4, 119.0, 125.1, 125.4, 129.5, 133.1, 135.2; FAB-MS obsd 157.0885, calcd 157.0891 ($C_{11}H_{11}N$).

2-Formyl-3-(4-methylphenyl)pyrrole (5). Following a standard procedure,[16] a solution of **4** (472 mg, 3.00 mmol) in DMF (0.96 mL) and CH_2Cl_2 (30 mL) under argon was cooled to 0 °C, and then $POCl_3$ (340 μL, 3.60 mmol) was added dropwise. After 1 h, the flask was warmed to room temperature and stirred overnight (∼18 h). The reaction was quenched at 0 °C with 2.5 M aqueous NaOH (25 mL). The mixture was poured into water (50 mL) and extracted with CH_2Cl_2. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, CH_2Cl_2/ethyl acetate (9:1)] to give a brown solid. ^{1}H NMR spectroscopy showed two regioisomers in a ca. 13:1 ratio. Cooling of the solution (ethyl acetate/hexanes) at ca. −16 °C resulted in precipitation of an orange solid, which proved to be a single regioisomer (354 mg, 64%): mp 149−150 °C; ^{1}H NMR δ 2.41 (s, 3H), 6.42−6.44 (m, 1H), 7.10−7.13 (m, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 9.63−9.64 (m, 1H), 9.52−9.78 (br, 1H); ^{13}C NMR δ 21.4, 111.6, 126.2, 128.9, 129.3, 129.7, 130.9, 137.7, 137.9, 180.2; FAB-MS obsd 186.0907, calcd 186.0919 ($C_{12}H_{11}NO$).

3-(4-Methylphenyl)-2-(2-nitroethyl)pyrrole (6). Following a standard procedure,[16] a mixture of **5** (3.93 g, 21.2 mmol), KOAc (2.29 g, 23.3 mmol), methylamine hydrochloride (1.72 g, 25.4 mmol), and nitromethane (190 mL) under argon was stirred at room temperature. The mixture slowly yielded an orange-red precipitate. After the mixture was stirred for 2.5 h, TLC showed the appearance of a new component and the disappearance of **5**. The reaction was quenched with brine and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated. The residue was dissolved in THF/MeOH (210 mL, 3:7) at 0 °C. $NaBH_4$ (2.41 g, 63.6 mmol) was added in portions at 0 °C. Then, the mixture was stirred for 0.5 h at room temperature. The reaction mixture was neutralized with acetic acid (pH = 7); then, water (150 mL) was added, and the mixture was extracted with ethyl acetate. The organic extract was washed with water and brine, dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (3:1)] to give a light brown solid (3.61 g, 74%): mp 81−82 °C; ^{1}H NMR δ 2.37 (s, 3H), 3.44 (t, J = 6.8 Hz, 2H), 4.54 (t, J = 6.8 Hz, 2H), 6.27−6.29 (m, 1H), 6.73−6.75 (m, 1H), 7.18−7.25 (m, 4H), 8.19−8.36 (br, 1H); ^{13}C NMR δ 21.2, 24.4, 75.2, 109.6, 117.7, 121.9, 123.2, 128.0, 129.5, 133.4, 135.8; FAB-MS obsd 230.1060, calcd 230.1055 ($C_{13}H_{14}N_2O_2$).

1,1-Dimethoxy-4-methyl-3-penten-2-one (7). The following procedure employs the approach of Tiecco et al.[25] but at 80-times larger scale and with altered workup. A mixture of mesityl oxide (18.0 mL, 160 mmol), diphenyl diselenide (5.00 g, 16.0 mmol), and ammonium peroxydisulfate (109 g, 480 mmol) in anhydrous MeOH (1.20 L) was refluxed for 4 h under argon. The progress of the reaction was monitored by TLC. The reaction mixture was poured into water (1.20 L) and extracted with $CHCl_3$. The organic layer was washed with water, dried (Na_2SO_4), and concentrated to give a dark brown oil. Bulb-to-bulb distillation of the oil at 50 °C/0.04−0.05 mmHg gave a yellow oil. The ^{1}H NMR spectrum of the oil showed the presence of unknown impurities. The oil was chromatographed [silica, hexanes/ethyl acetate (3:1)] to give a pale yellow oil (7.37 g, 29%). Characterization data were consistent with the literature[25] for the title compound: ^{1}H NMR δ 1.96 (d, J = 1.2 Hz, 3H), 2.21 (d, J = 1.2 Hz, 3H), 3.42 (s, 6H), 4.49 (s, 1H), 6.36−6.38 (m, 1H); ^{13}C NMR δ 21.3, 28.2, 54.5, 104.5, 119.1, 160.2, 194.2; FAB-MS obsd 159.1020, calcd 159.1021 ($C_8H_{14}O_3$) $[M + H]^+$. Note: The use of reagent-grade methanol resulted in a slow reaction (>26 h for completion) in comparison to the relatively fast reaction (<4 h) when anhydrous methanol was used.

1,1-Dimethoxy-4,4-dimethyl-6-[3-(4-methylphenyl)pyrrol-2-yl]-5-nitro-2-hexanone (8). Following a general procedure,[15,16] CsF (1.82 g, 12.0 mmol, 3.00 mol equiv, freshly dried by heating to 100 °C under vacuum for 1 h) was placed in a flask under argon. A mixture of **6** (921 mg, 4.00 mmol) and **7** (6.33 g, 40.0 mmol, 10 mol equiv) in dry acetonitrile (40 mL) was transferred by cannula to the flask containing CsF. The mixture was heated at 65 °C for 1.2 h, whereupon TLC analysis showed the reaction to be complete. The reaction mixture was filtered through a bed of silica (ethyl acetate), and the filtrate was concentrated. The resulting oil was subjected to bulb-to-bulb distillation at room temperature/0.04−0.05 mmHg for 3 h, affording recovery of the acetal **7** (∼2 g) as the distillate and the desired product in the crude undistilled residue. Purification of the residue by column chromatography [alumina, ethyl acetate/hexanes (1:3)] gave a light brown solid (626 mg, 40%): mp 98−100 °C; ^{1}H NMR δ 1.09 (s, 3H), 1.19 (s, 3H), 2.37 (s, 3H), 2.53, 2.71 (AB, ^2J = 18.8 Hz, 2H), 3.21 (ABX, ^3J = 2.4 Hz, ^2J = 15.4 Hz, 1H), 3.39 (ABX, ^3J = 11.6 Hz, ^2J = 15.4 Hz, 1H), 3.41 (s, 6H), 4.34 (s, 1H), 5.22 (ABX, ^3J = 2.4 Hz, ^3J = 11.6 Hz, 1H), 6.22−6.24 (m, 1H), 6.66−6.68 (m, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 8.06−8.14 (br, 1H); ^{13}C NMR δ 21.3, 24.1, 24.3, 25.3, 36.8, 45.1, 55.20, 55.22, 95.0, 104.7, 109.5, 117.7, 122.1, 123.7, 128.4, 129.4, 133.5, 135.6, 203.7. Anal. Calcd for $C_{21}H_{28}N_2O_5$: C, 64.93; H, 7.27; N, 7.21. Found: C, 65.02; H, 7.34; N, 7.14.

Conversion of 1 → Tetrahydroporphyrinic Macrocycles: Preparation to Obtain MeO−BC (5 mM 1 and 50 mM BF_3·OEt_2). A solution of **1** (93 mg, 0.27 mmol) in CH_3CN (54 mL) was treated with neat BF_3·OEt_2 (350 μL, 2.7 mmol, 50 mM). The reaction mixture was stirred at room temperature without deaeration for 15 h. The reaction was monitored by absorption spectroscopy. TEA (1.0 mL) was added to the reaction mixture. The reaction mixture was concentrated, and the residue was dissolved in CH_2Cl_2. The solution was washed (water), dried (Na_2SO_4), concentrated, and chromatographed [silica, CH_2Cl_2/hexanes (1:1)]. The first band (green) was collected (**H−BC**, 8.1 mg, 11%), and then the second band (green) was collected (**MeO−BC**, 24 mg, 30%).

Preparation to Obtain TDC (11 mM 1 and 10 mM BF_3·OEt_2). BF_3·OEt_2 (18 μL, 0.14 mmol) in CH_3CN (1.6 mL) was slowly added to a solution of **1** (50. mg, 0.15 mmol) in CH_3CN (12 mL). The reaction mixture was stirred at room temperature without deaeration for 24 h. TEA (20 μL, 0.14 mmol) was added to the reaction mixture. The reaction mixture was concentrated, and the residue was chromatographed [silica, CH_2Cl_2/hexanes (1:1)]. The first green band was collected (**H−BC**, ≪0.1 mg, ≪0.1%). Some pinkish material then eluted (not identified). The second green band was collected (**MeO−BC**, 2.7 mg, 6.3%). Further elution with CH_2Cl_2 afforded the third green band (**TDC**, 30. mg, 66%).

Preparation to Obtain H−BC (18 mM 1 and 140 mM BF_3·OEt_2). A solution of **1** (50. mg, 0.15 mmol) in CH_3CN (8.3 mL) was treated with BF_3·OEt_2 (150 μL, 1.2 mmol). The reaction mixture was stirred at room temperature without deaeration for 24 h. TEA (167 μL, 1.2 mmol) was added to the reaction mixture. The reaction mixture was concentrated, and the residue was chromatographed [silica, CH_2Cl_2/hexanes (1:1)]. The first green band was collected (**H−BC**, 20. mg, 49%). The second green band was collected (**MeO−BC**, 0.80 mg, 1.9%). Further elution with CH_2Cl_2 did not afford any **TDC**.

Data for 8,8,18,18-Tetramethyl-2,12-bis(4-methylphenyl)bacteriochlorin (H−BC): ^{1}H NMR δ −2.00 (br, 2H), 1.93 (s, 12H), 2.61 (s, 6H), 4.56 (s, 4H), 7.59 (d, J = 8.0 Hz, 4H), 8.13 (d, J = 8.0 Hz, 4H), 8.73 (d, J = 2.0 Hz, 2H), 8.81 (s, 2H), 8.86 (s, 2H); λ_{abs} (toluene)/nm 351 (ϵ = 130 000 M^{-1} cm^{-1}), 374 (120 000), 499 (35 000), 737 (130 000, fwhm 20 nm); λ_{em} (λ_{exc} 499 nm) 744 nm (fwhm 21 nm), Φ_f = 0.14; LD-MS obsd 550.0; FAB-MS obsd 550.3068, calcd 550.3096 ($C_{38}H_{38}N_4$).

Data for 5-Methoxy-8,8,18,18-tetramethyl-2,12-bis(4-methylphenyl)bacteriochlorin (MeO−BC): ^{1}H NMR δ −1.90 (br, 1H), −1.78 (br, 1H), 1.91 (s, 6H), 1.92 (s, 6H), 2.61 (s, 6H), 4.40 (s, 2H), 4.41 (s, 2H), 4.49 (s, 3H), 7.58 (two d, J = 8.0 Hz, 4H), 8.10 (d, J = 8.0 Hz, 2H), 8.14 (d, J = 8.0 Hz, 2H), 8.66−8.69 (m, 2H), 8.78 (s, 1H), 8.81 (s, 1H), 8.95 (d, J = 2.0 Hz, 1H); λ_{abs} (toluene)/nm 356 (ϵ = 110 000 M^{-1} cm^{-1}), 374 (130 000), 511 (39 000), 732 (120 000); λ_{em} (λ_{exc} 511 nm) 739 nm, Φ_f = 0.18; LD-MS obsd 580.1; FAB-MS obsd 580.3232, calcd 580.3202 ($C_{39}H_{40}N_4O$).

Data for 1*H*,22*H*,24*H*-7,8,17,18-Tetradehydro-1-(1,1-dimethoxymethyl)-3,3,13,13-tetramethyl-7,17-bis(4-methylphenyl)corrin (TDC): ^{1}H NMR δ 1.04 (s, 3H), 1.24 (s, 3H), 1.26 (s, 3H), 1.33 (s, 3H), 1.82 (d, ^2J = 13.2 Hz, 1H), 2.38 (s, 3H), 2.42 (s, 3H), 2.49 (d, ^2J = 13.2 Hz, 1H), 2.65, 2.71 (AB, ^2J = 18.8 Hz, 2H), 3.37 (s, 3H), 3.40 (s, 3H), 4.26 (s, 1H), 5.42 (s, 1H), 5.43 (s, 1H), 6.02 (s, 1H), 6.25 (d, J = 2.8 Hz, 1H), 6.57 (d, J = 1.6 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 8.42 (d, J = 8.0 Hz, 2H), 11.34−11.40 (br, 1H), 11.89−11.96 (br, 1H); λ_{abs} (toluene)/nm 343 (ϵ = 24 000 M^{-1} cm^{-1}), 437 (7400), 640 (4300), 703 (5400); LD-MS obsd 612.7; FAB-MS obsd 612.3447, calcd 612.3464 ($C_{40}H_{44}N_4O_2$).

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Supporting Information Available: Experimental procedure for determination of fluorescence quantum yields of bacteriochlorins; NMR data and assignments for **H−BC**, **MeO−BC**, and **TDC**; spectral data for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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