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Synthesis and photophysical characteristics of 2,3,12,13-tetraalkylbacteriochlorins†

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Bacteriochlorins absorb strongly in the near-infrared spectral region and hence are of great interest across the field of photochemistry. The established *de novo* self-condensation of a dihydrodipyrrin-acetal has afforded stable bacteriochlorins bearing a variety of β-pyrrolic substituents, but the route was incompatible with the presence of two alkyl groups. The lacuna stemmed from the instability of the dialkyl-substituted dihydrodipyrrin-acetal. Here, two dihydrodipyrrin-carboxaldehydes, each bearing a *tert*-butoxycarbonyl group at the pyrrole α-position, were prepared and found to be stable to routine handling. Each ester-substituted dihydrodipyrrin-carboxaldehyde in acid underwent *in situ* ester cleavage and ensuing self-condensation to provide the corresponding 2,3,12,13-tetraalkylbacteriochlorin. The alkyl groups examined include methyl and methyl acetate. Such synthetic bacteriochlorins, while previously unknown, provide valuable models of the natural chromophores. The absorption and fluorescence characteristics of the tetraalkylbacteriochlorins are generally typical for this genre of macrocycle. The X-ray structure of the tetramethylbacteriochlorin reveals that the pyrrolinic (reduced) rings are modestly more twisted out-of-plane (torsional angle ~11°) than those of the nearly planar (torsional angle ~1°) parent bacteriochlorin that lacks pyrrolic tetraalkyl groups. The resonance Raman spectrum of the tetramethylbacteriochlorin is also far richer in the low- to mid-frequency region than that of the unsubstituted analogue, but like the unsubstituted counterpart, is far sparser in the high-frequency region than that of native bacteriochlorophyll. Access to tetraalkylbacteriochlorins constitutes one step on the path from the most simple, fully unsubstituted bacteriochlorin to the fully decorated, natural bacteriochlorophylls.

Introduction

Bacteriochlorophylls are Nature's chosen chromophores for light-harvesting in the near-infrared (NIR) spectral region.[1,2] The bacteriochlorin chromophore of bacteriochlorophylls is a tetrahydroporphyrin wherein two reduced pyrrole rings are located at the opposite sides of the macrocycle. The structure of bacteriochlorophylls *a*, *b* and *g* are shown in Chart 1. Bacteriochlorins

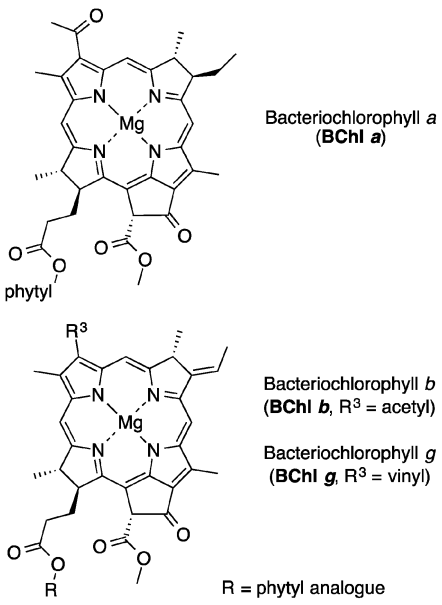

Chart 1 Natural bacteriochlorophylls.

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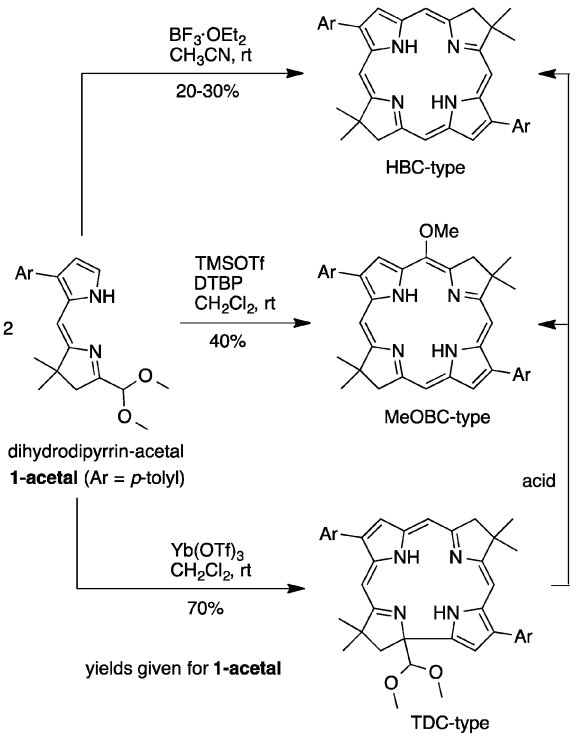
† Electronic supplementary information (ESI) available: Acid catalysis survey of the self-condensation of a dihydrodipyrrin-carboxaldehyde; X-ray structural data table for **BC-MM**; absorption spectra for **10-Me** and **10-CHO**; and characterization data for all new compounds. CCDC 1453311. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6nj00517a



Scheme 1 Self-condensation of a dihydrodipyrrin-acetal.

characteristically exhibit a strong ($\varepsilon \sim 10^5$ M^{-1} cm^{-1}) long-wavelength absorption band (Q_y band) located around 700–900 nm.[3] The strong NIR absorption makes bacteriochlorins attractive for fundamental studies as well as applications in solar-energy conversion and in photomedicine.[4–9]

Over some years now, a *de novo* synthesis route has been developed to gain access to diverse substituted bacteriochlorins.[10–13] The synthetic method relies on the self-condensation of a dihydrodipyrrin-acetal (**1-acetal**), which contains a dimethyl group integral to the reduced, pyrroline ring and an acetal unit located at the pyrroline α-position (Scheme 1). The gem-dimethyl group secures the pyrroline ring from adventitious oxidation that would lead to unsaturated products (*i.e.*, chlorins and porphyrins). By modification of the substituents attached to the pyrrolic units and/or the *meso*-positions, the bacteriochlorins can be tailored with regards to the position of the long-wavelength absorption band (ranging from 690 nm to 900 nm),[14–17] the polarity (hydrophobic, amphiphilic, or hydrophilic[18]) and the presence of derivatizable groups for bioconjugation or building-block applications.[8,9,15,17,19–21]

A key aspect of the self-condensation of a dihydrodipyrrin-acetal is that different acidic conditions (acid composition and concentration) and dihydrodipyrrin-acetal concentrations can lead to distinct outcomes with regards to the macrocycles formed: a free base 5-unsubstituted bacteriochlorin (HBC-type macrocycle), a free base 5-methoxybacteriochlorin (MeOBC-type macrocycle), a free base *B,D*-tetradehydrocorrin (TDC-type macrocycle).[10,11,22] As a general rule, the use of $BF_3{\cdot}OEt_2$ at modest concentrations in CH_3CN typically provides a mixture of two if not all three macrocycles, but with 140 mM $BF_3{\cdot}OEt_2$ and 18 mM dihydrodipyrrin-acetal, the HBC-type macrocycle is the dominant macrocyclic product (20–30% yield).[10] On the other hand, TMSOTf and 2,6-di-*tert*-butylpyridine (DTBP) in CH_2Cl_2 exclusively give the MeOBC-type macrocycle (40% yield),[11] whereas $Yb(OTf)_3$ in CH_2Cl_2 exclusively gives the corresponding TDC-type macrocycle in high yield (70%).[22]

One of our research objectives has been to install architectural features about the bacteriochlorin for wavelength tuning, water-solubilization, and bioconjugation. An opposite thrust has been to create sparsely substituted macrocycles, in particular to systematically "build up" the substituent pattern of bacteriochlorophylls beginning with the fully unsubstituted bacteriochlorin. A progression of such synthetic, free base bacteriochlorins is shown in Fig. 1. The progression begins with the fully unsubstituted HBC-type bacteriochlorin **BC0** and would add in (i) β-pyrrole substitution without potent auxochromes (four methyl groups, **BC-MM**), (ii) a single auxochrome (acetyl, **BC-A**^{3}), (iii) the isocyclic ring, which contains a single auxochrome in the bacteriooxophorbine (**BOP**),

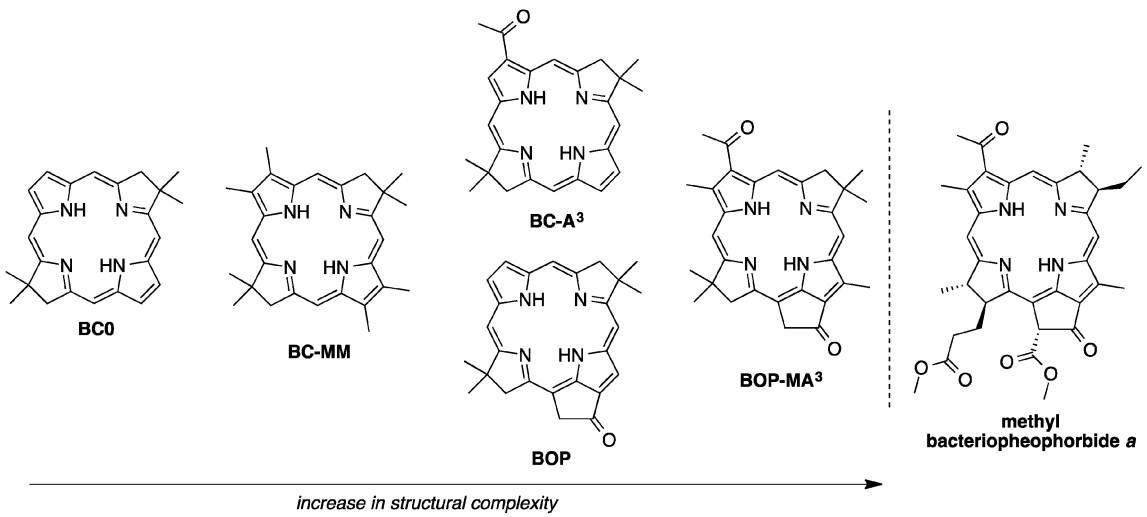
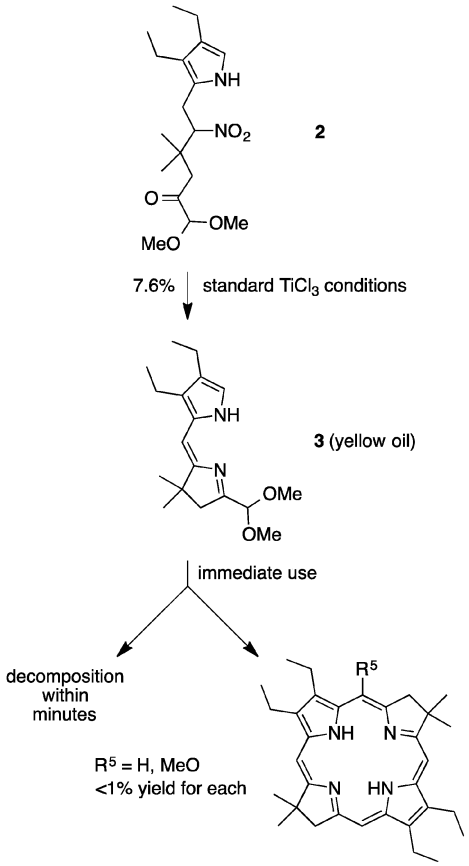


Fig. 1 Progression of structural complexity along the path to a free base derivative of **BChl *a***.

(iv) perhaps other structures of intermediate complexity, and finally (v) a structure (**BOP-MA**[3]) that contains two methyl groups, one acetyl group, and the isocyclic ring as in methyl bacteriopheophorbide *a*, the free base analogue of **BChl *a*** where the phytyl group has been transesterified. While access to **BC0** was achieved *via* the *de novo* route, we were unsuccessful in preparing the tetraethyl analogue of the next compound in the progression, the seemingly simple tetramethylbacteriochlorin.[11] We felt the origin of the failure stemmed from the instability of the diethyldihydrodipyrrin-acetal under the acidic reaction conditions. Thus, the synthesis of the seemingly simple tetraalkylbacteriochlorins, paradoxically, has proved more difficult than constructing architecturally elaborate bacteriochlorins.

In this paper, we report the synthesis of new β-dialkyldihydrodipyrrins and their conversion to tetraalkylbacteriochlorins. The β-dialkyldihydrodipyrrins differ from the dihydrodipyrrin-acetals used previously in two regards: (1) the acetal is replaced with a carboxaldehyde, and (2) the pyrrole is stabilized at the α-position with an acid-cleavable ester unit. The new β-dialkyldihydrodipyrrins have provided access to two new 2,3,12,13-tetraalkylbacteriochlorins (as well as one copper chelate), including **BC-MM** as desired in a step along the progression of structural complexity. The electronic spectral, vibrational, and excited-state properties of the bacteriochlorins have been investigated. In all, the present work should provide a convenient route to a variety of 2,3,12,13-tetraalkylbacteriochlorins that heretofore have been inaccessible.



Scheme 2 Failed access to tetraalkylbacteriochlorins.

Results and discussion

(I) Synthesis

(A) Reconnaisance. In our prior attempt to prepare tetraalkylbacteriochlorins,[11] pyrrole-nitrohexanone **2**, which bears two ethyl groups at the β-pyrrole positions, was subjected to the standard conditions for cyclization (*via* $TiCl_3$) to form the dihydrodipyrrin-acetal **3** (Scheme 2). The yield of the latter was 7.6%, to be compared with typical yields of 20–50% for diverse substrates; but even worse, the product began decomposing within minutes. Dihydrodipyrrin-acetal **3** was quickly purified (with limited characterization) and submitted to the bacteriochlorin-forming process under a handful of acid-catalysis conditions. In the best condition, only a slim signature (absorption bands, molecular ion peak) of the HBC- and MeOBC-type bacteriochlorins was observed, and the yield of each on the basis of absorption spectroscopy was $<1\%$. From this result we surmised that a viable synthesis of tetraalkylbacteriochlorins would require a strategy for stabilizing the dialkyl-substituted precursors.

The synthesis of porphyrins bearing an alkyl group at each β-pyrrole position has been known since the first half of the 20th century.[23] One general synthetic approach has employed pyrroles, dipyrrins or dipyrromethanes that are stabilized by the presence of ester substituents at the α-position(s). The electron-withdrawing effect of the esters counterbalances the electron-releasing effect of the β-alkyl groups. The same approach has been employed in rational routes to chlorins.[24] Battersby incorporated an α-ester to stabilize the β-alkyl-substituted dihydrodipyrrin **I** Western half precursor,[25] and Jacobi similarly incorporated an α-ester with the β-alkyl-substituted dihydrodipyrrin **II** for use as a Southern half precursor[26] (Chart 2). Note that **II** differs subtly from the dihydrodipyrrins employed in Schemes 1 and 2 in the position of the gem-dimethyl group in the pyrroline ring.

The general approach shown in Scheme 2 has provided access to diverse bacteriochlorins from the corresponding dihydrodipyrrin-acetals, none of which contained pyrrole α-ester stabilization. Two strategies for preparing such dihydrodipyrrin-acetals (**III**) have been developed (Scheme 3). The original method employs Michael addition of a 2-(2-nitroethyl)pyrrole and an α,β-unsaturated ketone-acetal (**4-acetal**) following by reductive cyclization. A more recent method relies on Michael addition of a 2-(2-nitroethyl)pyrrole (**IV**) and mesityl oxide (**4-Me**) to form

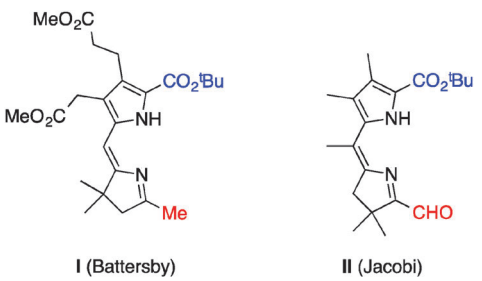
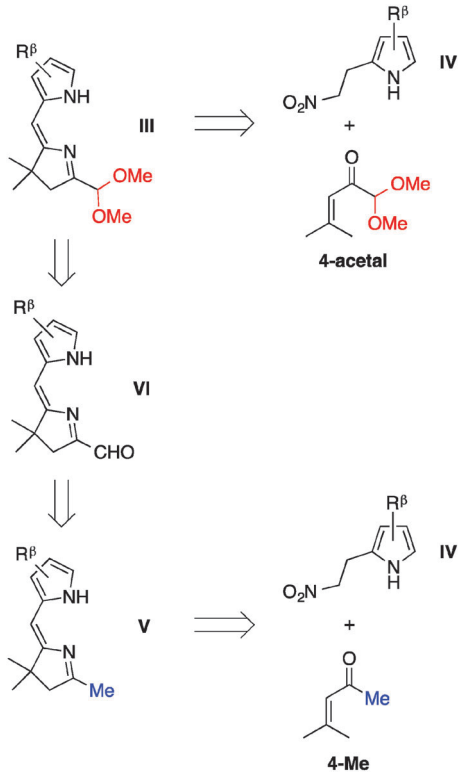


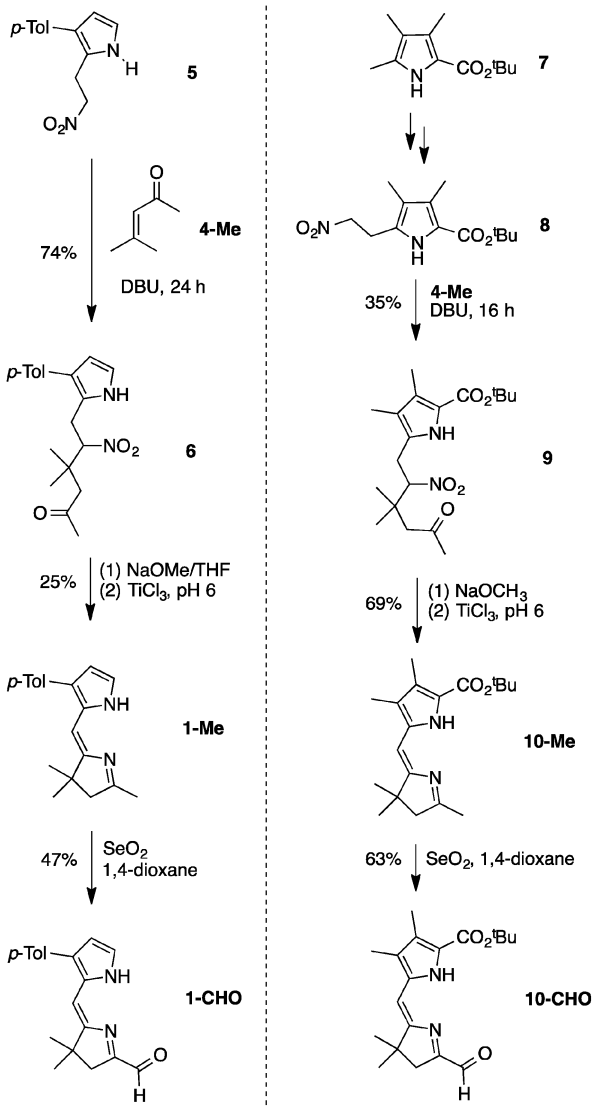
Chart 2 Dihydrodipyrrins used in chlorin syntheses.



Scheme 3 Retrosynthesis of dihydrodipyrrin-acetals.

the dihydrodipyrrin-Me (**V**). Subsequent oxidation (SeO_2) gives the dihydrodipyrrin-carboxaldehyde (**VI**), which is finally converted to the dihydrodipyrrin-acetal (**III**).[13] In prior examples of the second route (for β-pyrrole substituents = ethyl and carboethoxy), the intermediate dihydrodipyrrin-carboxaldehyde was not isolated or purified but instead converted to the desired target, the dihydrodipyrrin-acetal.[13] Here, we adopted the latter route to prepare and utilize two α-ester stabilized dihydrodipyrrin-carboxaldehydes.

(B) Preparation of dihydrodipyrrin-carboxaldehydes. We began the methodology studies with a substrate for which data were in hand concerning synthesis of the dihydrodipyrrin and conversion to a bacteriochlorin. Thus, the known *p*-tolyl-substituted nitroethylpyrrole **5**[11] was used in the synthesis of a dihydrodipyrrin-carboxaldehyde and the corresponding bacteriochlorin. Michael addition[27] of nitroethylpyrrole **5** with mesityl oxide (**4-Me**) in the presence of DBU gave γ-nitrohexanone **6** in 74% yield. Subsequent treatment of **6** with NaOMe followed by a buffered $TiCl_3$ solution to achieve reductive cyclization[10] afforded dihydrodipyrrin **1-Me** as a yellow solid in 25% yield. Oxidation of dihydrodipyrrin **1-Me** with SeO_2 in 1,4-dioxane at room temperature, a procedure first reported by Jacobi and coworkers,[13,28] gave the corresponding dihydrodipyrrin-carboxaldehyde **1-CHO** in 47% yield (Scheme 4). The conversion of **5** to **1-CHO** was reported earlier.[29] The formation of the carboxaldehyde is readily observed by absorption spectroscopy given the bathochromic shift into the visible region of the dihydrodipyrrin chromophore,[13] as well as by visual inspection (**1-Me** is light yellow whereas **1-CHO** is orange-red). Dihydrodipyrrin-carboxaldehyde **1-CHO** was prone to decomposition



Scheme 4 Preparation of dihydrodipyrrin-carboxaldehydes.

in chlorinated solvents and during silica column chromatography, but was stable for several days upon storage in solid form at −20 °C. Compound **1-CHO** was characterized by ^{1}H NMR spectroscopy and ESI-MS; however, a satisfactory ^{13}C NMR spectrum was not obtained. The ^{1}H NMR spectrum of the purified product indicated the presence of a minor impurity.

For the synthesis of the analogous dimethyldihydrodipyrrin-carboxaldehyde, a *tert*-butyl ester was introduced to the α-position in the dihydrodipyrrin. Prior synthetic work in this area had resulted in transformations along the series of known compounds **7**–**9** and **10-Me** for use in the formation of chlorins, where the dihydrodipyrrin-methyl compound **10-Me** suffices, but not for bacteriochlorins. Thus, **8**[30] was prepared beginning with acyclic precursors to **7**[31] following the literature, whereas **9**[32] and **10-Me**[32] were prepared *via* modified literature methods.[11,27] Treatment of the ester-substituted dimethyldihydrodipyrrin **10-Me** with SeO_2 in *p*-dioxane at room temperature afforded the corresponding dihydrodipyrrin-carboxaldehyde **10-CHO** in

63% yield (Scheme 4). The absorption spectra maxima in dichloromethane changed from 350 nm to 468 nm upon conversion of **10-Me** to **10-CHO**. Unlike dihydrodipyrrin-carboxaldehyde **1-CHO**, **10-CHO** was relatively stable in a variety of solvents (including CH_2Cl_2 and $CHCl_3$) as well as during silica column chromatography.

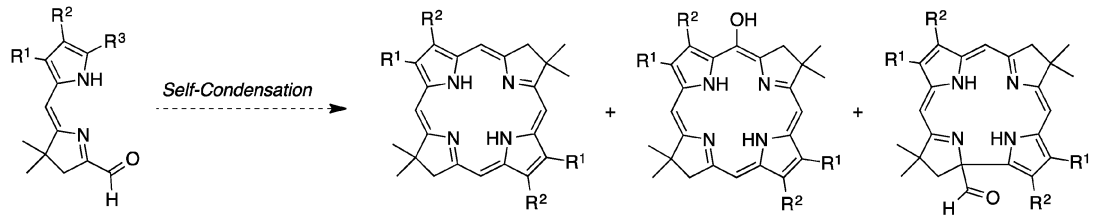
(C) Self-condensation study of dihydrodipyrrin-carboxaldehydes. The typical conditions for the self-condensation of dihydrodipyrrin-acetals were used for the reactions with the dihydrodipyrrin-carboxaldehydes **1-CHO** and **10-CHO**. The two acidic conditions chosen for the self-condensation study with 18 mM dihydrodipyrrin-carboxaldehyde were as follows: (1) 140 mM $BF_3{\cdot}OEt_2$, or (2) 72 mM TMSOTf/144 mM DTBP (Table 1, entries 1 and 2). A survey of other acidic conditions for the self-condensation is provided in the ESI.†

The self-condensation of **1-CHO** in CH_3CN containing $BF_3{\cdot}OEt_2$ gave **BC-T** in 12% yield, but little or no product was obtained with the other two acids (entries 1–3). No other macrocycles, including the HOBC-type or TDC-type species, were reliably observed by TLC analysis or laser-desorption mass spectrometry (LD-MS) of the crude sample from entry 1. The self-condensation of **10-CHO** gave nearly identical results in $BF_3{\cdot}OEt_2$ in CH_3CN, with 11% yield for **BC-MM** (entry 4). TMSOTf/DTBP gave no product but resulted in recovery of starting material, indicating the stability of the dihydrodipyrrin-carboxaldehyde (entry 5). On the other hand, the use of neat TFA gave **BC-MM** in 24% yield (entry 6). No other macrocycles were detected on the basis of TLC analysis or attempted isolation. A convenient feature of this latter result is that reaction occurred in 1 h rather than 19 h for $BF_3{\cdot}OEt_2$. The disparity in yield of bacteriochlorin (0.2% *versus* 24%) in neat TFA despite identical reacting motifs for **1-CHO** and **10-CHO** is striking (entries 3 and 6). Regardless of mechanistic origin, the acid survey confirmed the viability of the ester-substituted dihydrodipyrrin-carboxaldehyde as a means to access a tetraalkylbacteriochlorin.

(D) Preparation of a 2,3,12,13-tetramethylbacteriochlorin. The self-condensation of dihydrodipyrrin-carboxaldehyde **10-CHO** at ~10-fold increased scale (0.21 mmol) afforded **BC-MM** in 29% yield (Scheme 5). Again, no other macrocycles were observed or isolated. The copper chelate was of particular interest for examination by resonance Raman spectroscopy, given the absence of fluorescence from copper tetrapyrroles. Following a standard procedure for metalation of bacteriochlorins,[33] treatment of **BC-MM** with a large excess of sodium hydride and $Cu(OAc)_2$ in THF at 60 °C for 16 h under argon afforded **CuBC-MM**. Prolonging the reaction caused extensive byproducts. **CuBC-MM** was unstable on silica column chromatography (due to conversion to Cu(II)oxobacteriochlorins as found upon LD-MS analysis, or other decomposition) but could be purified on a short column, albeit in low yield. Given that NMR spectroscopy is not readily employed with copper tetrapyrroles, characterization relied on absorption spectroscopy, mass spectrometry, and absence of fluorescence, all of which are diagnostic for conversion of a free base tetrapyrrole to the copper chelate. The small quantity of **CuBC-MM** obtained was more than ample for resonance Raman spectroscopic characterization (*vide infra*).

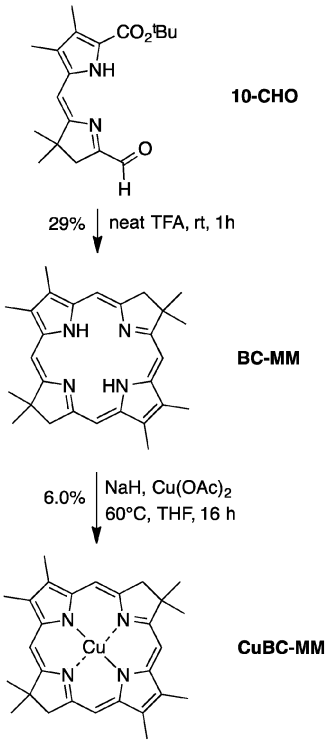
The bacteriochlorin **BC-MM** was characterized by ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, high-resolution mass spectrometry (ESI-MS) and absorption spectroscopy. The structure of **BC-MM** also was determined by single-crystal X-ray analysis (Fig. 2). Comparison of the structure of **BC-MM** with that of **BC0**[33] leads to the following findings. (1) The average nitrogen–centroid distance of **BC-MM** is 2.099 Å, which is slightly longer than that of **BC** (2.096 Å), indicating that the core size is slightly larger. (2) The torsion angle of the four carbons in the pyrroline ring (C6–C7–C8–C9; C16–C17–C18–C19) in **BC-MM** is 11.60°, which is much larger than that of **BC0** (1.11°). The out-of-plane twists of the two pyrroline rings in **BC-MM** are in opposite directions with respect to the macrocycle plane, imparting overall C_i symmetry.

Table 1 Acid survey for the self-condensation of dihydrodipyrrin-carboxaldehydes[a]



Entry	Reactant	R^1	R^2	R^3	Acidic condition	Time (h)	Bacteriochlorin	Yield (%)
1	**1-CHO**	*p*-tolyl	H	H	$BF_3{\cdot}OEt_2$ in CH_3CN	19	**BC-T**	12%
2	**1-CHO**	*p*-tolyl	H	H	TMSOTf/DTBP in CH_2Cl_2	19	**BC-T**	—[b]
3	**1-CHO**	*p*-tolyl	H	H	Neat TFA	1	**BC-T**	0.2%
4	**10-CHO**	Me	Me	$CO_2{}^t$Bu	$BF_3{\cdot}OEt_2$ in CH_3CN	19	**BC-MM**	11%
5	**10-CHO**	Me	Me	$CO_2{}^t$Bu	TMSOTf/DTBP in CH_2Cl_2	19	**BC-MM**	—[c]
6	**10-CHO**	Me	Me	$CO_2{}^t$Bu	Neat TFA[d]	1	**BC-MM**	24%

[a] All reactions were carried out (1.0 mL scale) with 18 mM dihydrodipyrrin-carboxaldehyde at room temperature. Concentrations of acid were 140 mM $BF_3{\cdot}OEt_2$ or 72 mM TMSOTf/144 mM DTBP. Yields were determined by absorption spectroscopy of samples isolated by chromatography. [b] Not detected. [c] Unreacted dihydrodipyrrin-carboxaldehyde remained. [d] The same reaction in TFA-*d* (0.068 mmol **10-CHO**) also gave **BC-MM** in comparable yield with no isotopic incorporation.



Scheme 5 Preparation of **BC-MM** and **CuBC-MM**.

(E) A bacteriochlorin with acetate side-chains. The successful synthesis of **BC-MM** prompted exploration of the synthesis of more elaborate alkyl substituents. Thus, the bacteriochlorin **BC-AmAm** was synthesized following the strategy reported above (Scheme 6). Compounds **11**,[34] **12**[35] and **13**[36] are known but **12** and **13** were prepared here *via* alternative routes. Thus, a rapid transesterification[37] of pyrrole **11** at 220 °C gave the tri-benzyl ester **12** in 68% yield, following by a selective base-catalyzed transesterification[37] at room temperature to give the dimethyl monobenzyl ester **13**. Next, hydrogenolysis followed by esterification[38] of the resulting carboxylic acid with *tert*-butyl alcohol and DCC along with 4-(*N,N*-dimethylamino)pyridine (DMAP) gave the new pyrrole **14**. Treatment of the latter with thionyl chloride followed by hydrolysis[32] caused oxidation of the α-methyl group in the presence of the three alkyl esters to give the corresponding pyrrole-carboxaldehyde **15**. Subsequent nitro-aldol condensation[11] and reduction by $NaBH_4$ afforded nitroethyl-pyrrole **16** in 39% yield. The Michael addition of **16** and mesityl oxide (**4-Me**) in the presence of TBAF at room temperature[39]

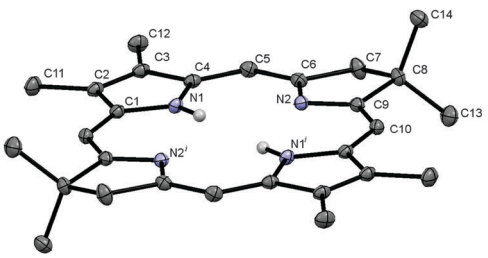
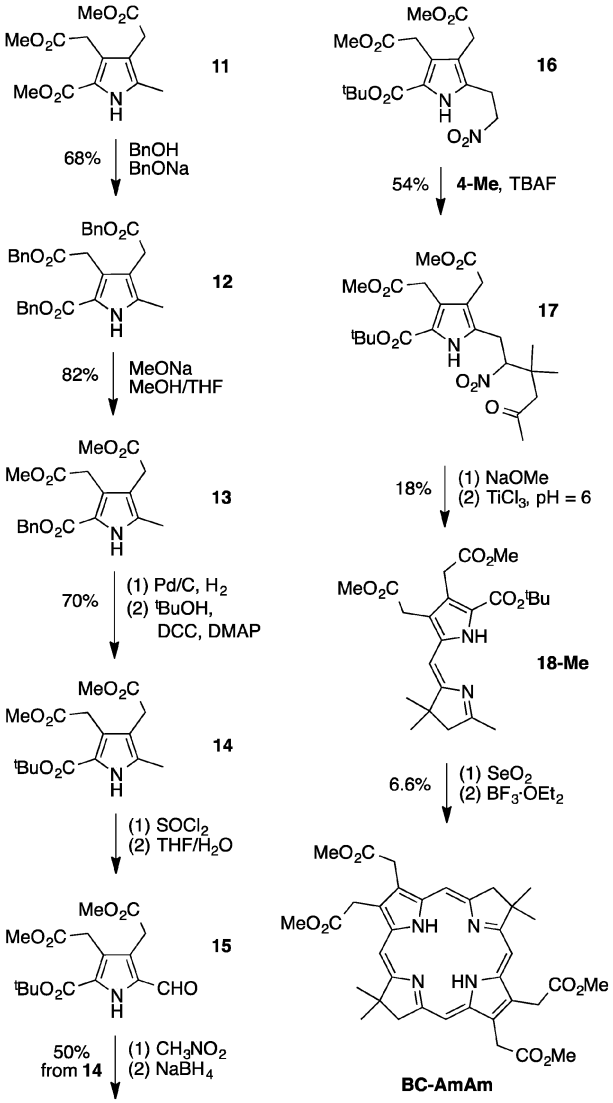


Fig. 2 ORTEP drawing of **BC-MM**. Ellipsoids are at the 50% probability level and hydrogen atoms (except N–H) are omitted for clarity.



Scheme 6 Synthesis of **BC-AmAm**.

afforded **17** in 54% yield. Reductive cyclization of **17** gave the desired dihydrodipyrrin **18-Me** in 18% yield. Finally, oxidation[13,28] of dihydrodipyrrin **18-Me** gave the resulting dihydrodipyrrin-carboxaldehyde **18-CHO** (not shown), which was sufficiently pure for direct use in the next step. To our surprise, treatment with neat TFA only afforded a trace amount of **BC-AmAm**. On the other hand, $BF_3{\cdot}OEt_2$-mediated self-condensation gave **BC-AmAm** in 6.6% yield for the two steps from **18-Me**. The bacteriochlorin was characterized by absorption spectroscopy, ^{1}H NMR spectroscopy, and mass spectrometry (ESI-MS). We note that established chemistry exists for the preparation of related dialkylpyrroles with substituents such as 3-Me/4-Et,[40] 3-Et/4-Me,[41] 3-Me/4-CH_2CH_2-CO_2Me,[42] and 3-$CH_2CH_2CO_2$Me/4-Me,[43] all of which may be potential starting materials to make tetraalkylbacteriochlorins.

(II) Photophysical characterization

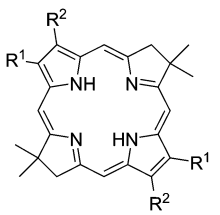
The photophysical data obtained upon characterization of the new bacteriochlorins were compared with three benchmark

bacteriochlorins (Chart 3). One benchmark is the fully unsubstituted bacteriochlorin **BC0**. Two others (**BC-MEs** and **BC-EEs**) have alkyl (methyl or ethyl) groups at the 2,12-positions and carboethoxy groups attached directly to the 3,13-positions of the macrocycle. Note that the four carbomethoxy groups of **BC-AmAm** are each removed from the macrocycle by a methylene group and thus do not directly interact with the bacteriochlorin π-system.

(A) Absorption and fluorescence spectra. Electronic ground-state absorption spectra of parent **BC0**, new tetraalkyl derivatives **BC-MM** and **BC-AmAm**, and copper chelate **CuBC-MM** are shown in Fig. 3 (solid lines). The figure also shows fluorescence spectra of the free base bacteriochlorins (dashed lines). Table 2 lists the spectral characteristics of the free base compounds along with those of additional benchmarks **BC-MEs** and **BC-EEs** studied previously.[14] The new tetraalkylbacteriochlorins **BC-MM** and **BC-AmAm** are quite soluble in toluene and remain stable even upon prolonged illumination without noticeable photo-aggregation, an adverse phenomenon that has occurred with other bacteriochlorins.[44,45]

The absorption spectrum of each bacteriochlorin consists of four major bands: B_y, B_x in the near ultraviolet, Q_x in the green-yellow and Q_y in the NIR region. Each origin, or (0,0), feature is accompanied by at least one weaker vibronic satellite band to higher energy. The Q_y band of **BC-AmAm** (732 nm) and **BC-MM** (721 nm) is bathochromically shifted from parent **BC0** (714 nm) but is hypsochromically shifted from benchmarks **BC-MEs** (760 nm) and **BC-EEs** (761 nm), which contain 2,3-dimethyl or 2,3-diethyl plus 3,13-dicarboethoxy groups (Table 2). Similar trends are observed for the wavelength (nm) positions of the Q_x origin bands: **BC0** (489) < **BC-MM** (490) < **BC-AmAm** (495) < **BC-MEs** (520) < **BC-EEs** (521). Like the Q_y feature, the Soret (B_y, B_x) bands (in nm) of **BC-AmAm** (347, 373) and **BC-MM** (346, 374) are bathochromically shifted from parent **BC0** (340, 365) and hypsochromically shifted from benchmarks **BC-MEs** (354, 384) and **BC-EEs** (354, 383). These trends thus reflect a general shift in the center of gravity of the spectrum among the compounds.

Several additional spectral characteristics are noteworthy: (1) the full-width-at-half-maximum (FWHM) of the Q_y absorption band of **BC-AmAm** and **BC-MM** is small and comparable to benchmark **BC0**, being in the range 12–13 nm or 229–243 cm^{-1} (Table 2). These features are about 30% narrower than for benchmarks **BC-MEs** and **BC-EEs** (19–20 nm, 337–343 cm^{-1}) and bacteriochlorins with substituents that impart an even longer wavelength Q_y band.[14] (2) The ratio of the Q_y and Soret



BC-MM	$R^1 = R^2 = Me$
BC-AmAm	$R^1 = R^2 = CH_2CO_2Me$
BC0	$R^1 = R^2 = H$
BC-MEs	$R^1 = Me$, $R^2 = CO_2Et$
BC-EEs	$R^1 = Et$, $R^2 = CO_2Et$

Chart 3 New and benchmark bacteriochlorins.

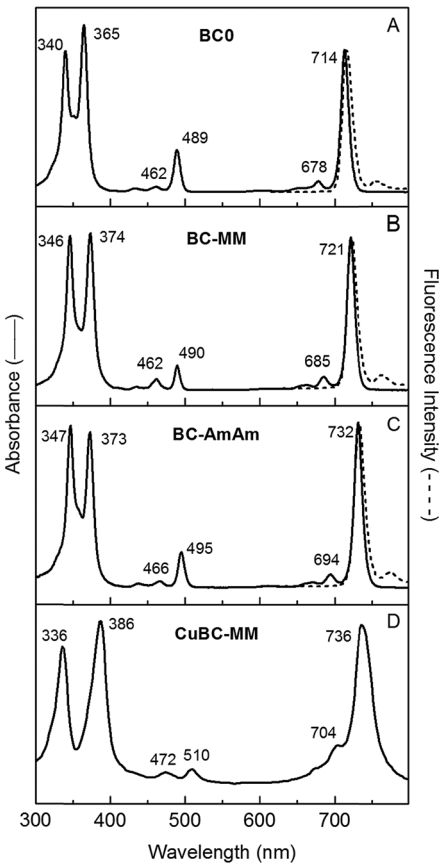


Fig. 3 Absorption (solid) and fluorescence (dashed) spectra of bacteriochlorins in toluene.

(B) maximum for the new tetra-substituted bacteriochlorins are comparable to the benchmarks (0.85–1.1). Compared to the parent and benchmarks, the $Q_x(1,0)$ vibronic satellite band of **BC-MM** and **BC-AmAm** has gained considerable intensity relative to the $Q_x(0,0)$ origin band. The $Q_x(0,0)/Q_x(1,0)$ peak-intensity ratio follows the trend **BC-MM** (1.9) < **BC-AmAm** (4.8) < **BC0** (7.9). Thus, the 2,3,12,13-tetraalkyl substituent pattern tends to turn on vibronic activity, whether Franck–Condon or Herzberg–Teller in origin.

The fluorescence spectra of **BC-MM** and **BC-AmAm** and parent **BC0** are shown in Fig. 3 (dashed lines). The fluorescence spectrum of each bacteriochlorin is dominated by the $Q_y(0,0)$ feature, which is positioned only 1–2 nm (19–29 cm^{-1}) to longer wavelength than the corresponding Q(0,0) absorption maximum. Such 'Stokes shift' is smaller than for **BC-MEs** or **BC-EEs** (Table 2) or other bacteriochlorins bearing simple substituents (*e.g.*, methyl, ethyl, phenyl, ester, acetyl, ethynyl) at the 2,3,12,13-positions, which give an average shift of ~4 nm (~90 cm^{-1}).[14] The FWHM (in cm^{-1}) of the Q_y emission feature of **BC-MM** and **BC-AmAm** (296–308) is small, even slightly reduced from parent **BC0** (312) and smaller still *versus* benchmarks **BC-MEs** and **BC-EEs** (350 and 368) (Table 2) and other bacteriochlorins bearing simple β-pyrrole substituents.[14]

(B) Resonance Raman studies of CuBC-MM. Resonance Raman (RR) measurements round out the static studies of

Table 2 Spectral characteristics of bacteriochlorins in toluene at room temperature

Compound	$B_y(0,0)$ abs (nm)	$B_x(0,0)$ abs (nm)	$Q_x(1,0)$ abs (nm)	$Q_x(0,0)$ abs (nm)	$I_{Q_x}(0,0)/I_{Q_x}(1,0)$	$Q_y(1,0)$ abs (nm)	$Q_y(0,0)$ abs (nm)	$Q_y(0,0)$ abs FWHM (nm)	$Q_y(0,0)$ abs FWHM (cm^{-1})	$Q_y(0,0)$ em (nm)	$Q_y(0,0)$ em FWHM (nm)	$Q_y(0,0)$ em FWHM (cm^{-1})	$I_{Q_y}/I_{B_{max}}$
BC-MM	346	374	462	490	1.9	685	721	11.9	229	723	15.5	296	0.97
BC-AmAm	347	373	466	495	4.8	694	732	13.0	243	733	16.7	308	1.08
BC0	340	365	462	489	7.9	678	714	12.0	236	716	16.0	312	0.85
BC-MEs[a]	354	384	488	520	17.0	719	760	19.0	337	764	20.0	350	0.98
BC-EEs[a]	354	383	489	521	8.3	721	761	20.0	343	775	21.0	368	0.94

[a] Data are from ref. 14.

the ground-state properties of the new tetraalkylbacteriochlorin constructs. The low- and mid-frequency regions (150–1700 cm^{-1}) of the Q_y-excitation RR spectrum of **CuBC-MM** (λ_{ex} = 737 nm) is compared with that previously reported[46] for **CuBC0** (λ_{ex} = 730 nm) in Fig. 4. For **CuBC-MM**, more noise is evident in the low-frequency than mid-frequency region of the spectrum owing to the fact that a weak fluorescence background underlies the low-frequency region (see Experimental section). The striking aspect of the Q_y-excitation RR spectrum of **CuBC0** is that it is extremely sparse in both the low- and mid-frequency regions and is dominated by a single strong band at 727 cm^{-1}. The mid-frequency region (800–1700 cm^{-1}) of the RR spectrum of **CuBC-MM** is similar to that of **CuBC0** in the exhibition of relatively few weak bands. In contrast, the low-frequency region (150–800 cm^{-1}) of the RR spectrum of **CuBC-MM** is much richer than that of **CuBC0**, exhibiting relatively strong bands at 359, 482, 602, 612, and 736 cm^{-1} and somewhat weaker bands at 219, 652, 692, and 768 cm^{-1}. The 736 cm^{-1} band of **CuBC-MM** is likely the analogue of the 727 cm^{-1} band of **CuBC0**. However, the 736 cm^{-1} band of **CuBC-MM** is not the strongest feature in the spectrum, being less intense than either the 482 or 612 cm^{-1} bands.

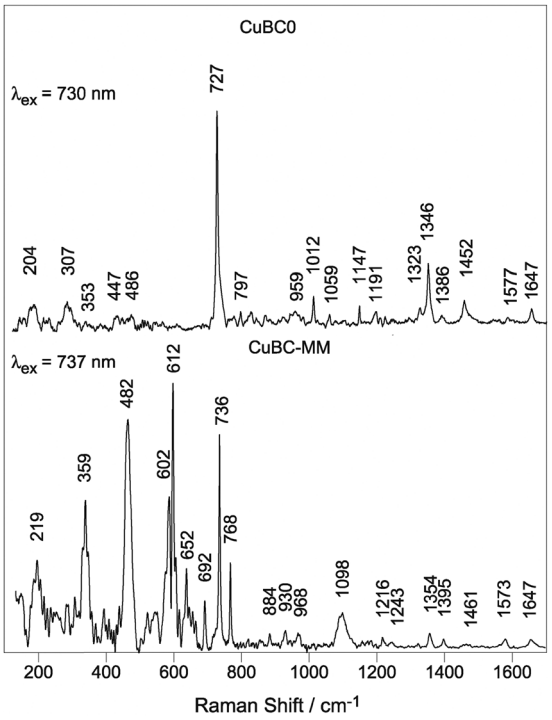


Fig. 4 Low- and mid-frequency regions of the Q_y-excitation RR spectra of **CuBC0** (λ_{ex} = 730 nm; CH_2Cl_2 solution) and **CuBC-MM** (λ_{ex} = 737 nm; benzene solution).

The rationale for examining the Q_y-excitation RR spectrum of **CuBC-MM** was to determine whether addition of the four methyl substituents at the β-pyrrolic positions of the macrocycle would substantially alter the general characteristics of the spectrum from that observed for **CuBC0**. As was previously noted, the Q_y-excitation RR spectrum is quite unusual, exhibiting only a single strong band at 727 cm^{-1} plus a few other weak features in both the low- and mid-frequency regions. These characteristics of the Q_y-excitation RR spectrum of **CuBC0** are strikingly different from those of the Q_y-excitation RR spectra of natural bacteriochlorophylls, both in solution and in proteins,[47–52] and a Cu–bacteriochlorophyll model complex,[53] all of which exhibit dozens of bands that span the low- and mid-frequency regions of the spectra. The **BChl *a*** macrocycle differs from that of **CuBC0** in that the former contains four β-pyrrolic substituents, including two methyl groups, an acetyl group, and a keto group embedded in the five-membered, isocyclic ring. The isocyclic ring spans the 13- and 15-positions and also contains a carbomethoxy substituent (Chart 1). Accordingly, addition of four β-pyrrolic substituents to **CuBC0**, yielding **CuBC-MM**, was viewed as one step in increasing the complexity of the macrocycle towards that found in **BChl *a***.

The results reported herein reveal that addition of the four β-pyrrolic substituents does indeed increase the richness of the RR spectra, but only in the low-frequency region. Thus, other structural characteristic of the natural pigment must also come into play in ultimately determining the overall RR spectral pattern. The detailed analysis of the RR spectrum of **CuBC-MM** is beyond the scope of this paper; however, the data acquired for this complex serve as a starting point for our program aimed at examining the RR spectra of a series of model complexes wherein the substituents present in **BChl *a*** are systematically added to the parent bacteriochlorin macrocycle.

(C) Excited-state properties. The S_1 lifetime (τ_S) and yields of $S_1 \rightarrow S_0$ fluorescence (Φ_f) and $S_1 \rightarrow T_1$ intersystem crossing (Φ_f), the triplet yield, were measured to fully characterize the decay properties of the S_1 (Q_y) excited state. The yield of $S_1 \rightarrow S_0$ internal conversion (Φ_{ic}) is obtained by the simple calculation $\Phi_{ic} = 1 - \Phi_f - \Phi_{isc}$. The rate constants for the three processes are then obtained using the expression $k_i = \Phi_i/\tau_S$, where i = f, isc,

Table 3 Photophysical properties of bacteriochlorins[a]

Compound	Q_y[b] (eV)	τ_S (ns)	Φ_f	Φ_{isc}	Φ_{ic}	k_f^{-1} (ns)	k_{isc}^{-1} (ns)	k_{ic}^{-1} (ns)	$\Sigma Q_y/\Sigma_{tot}$[c]
BC-MM	1.72	2.9	0.10	0.58	0.32	26	5	9	0.11
BC-AmAm	1.69	3.2	0.16	0.52	0.32	22	7	11	0.13
BC0	1.74	4.0	0.14	0.62	0.24	29	7	17	0.09
BC-MEs	1.63	3.0	0.13	0.52	0.35	23	6	9	0.15
BC-EEs	1.61	3.3	0.14	0.55	0.31	24	6	11	0.13

[a] All measurements were made in toluene at room temperature. Data for **BC-MEs** and **BC-EEs** are from ref. 14. The typical errors (percent of value) of the photophysical properties are as follows: τ_S (±7%), Φ_f (±5%), Φ_{isc} (±15%), Φ_{ic} (±20%), k_f (±10%), k_{isc} (±20%), k_{ic} (±25%). The error bars for τ_S, Φ_f, and Φ_{isc} were determined from select repeat measurements, and those for the Φ_{ic}, k_f, k_{isc} and k_{ic} were obtained from propagation of errors. [b] Average energy of the Q_y absorption and fluorescence bands. [c] Integrated intensity of the Q_y absorption manifold [$Q_y(0,0)$ and $Q_y(1,0)$] *versus* that of the total spectrum (300–900 nm) when plotted in wavenumbers.

and ic. The values of the photophysical properties are collected in Table 3.

The Φ_f values for **BC-MM** (0.10) and **BC-AmAm** (0.16) are comparable to those of parent **BC0** (0.14) and benchmarks **BC-MEs** (0.13) and **BC-EEs** (0.14). The τ_S values (in ns) for **BC-MM** and **BC-AmAm** (2.9 and 3.2 ns) are modestly shorter than those of parent **BC0** (4.0 ns) and more similar to benchmarks **BC-MEs** and **BC-EEs** (3.0 and 3.3 ns). The intersystem-crossing (triplet) yield values of **BC-MM** and **BC-AmAm** (0.58, 0.52) are comparable to those for the parent and benchmarks (0.62, 0.52, 0.55). The internal-conversion yields for **BC-MM** and **BC-AmAm** (both 0.32) are slightly higher than that for parent **BC0** (0.24) but comparable to benchmarks **BC-MEs** and **BC-EEs** (0.35, 0.31).

Although the internal-conversion yields carry large (cumulative) error because they derive from a series of measurements, the differences appear to be significant and contribute to the above-noted τ_S values. In general, as the Q_y band of bacteriochlorins bearing simple substituents (mostly at the 2,3,12,13-positions) moves to lower energy (longer wavelength), the τ_S values are progressively reduced.[3,16] The S_1 lifetime and energy are **BC-MM** (2.9 ns, 1.72 eV), **BC-AmAm** (3.2 ns, 1.69 eV), **BC-MEs** (3.0 ns, 1.63 eV) and **BC-EEs** (3.3 ns, 1.61 eV). The τ_S values for **BC-MM** and **BC-AmAm** are shorter than expected and should be intermediate between those of the two benchmarks and that of the parent **BC0**.

Although this result could reflect in part differences (or errors) in radiative rate constant (k_f), those values (derived from τ_S and Φ_f) are consistent with the integrated intensity of the Q_y band relative to the total spectrum (Fig. 5), as expected from the relationship of the Einstein coefficients.[54] The differences do not appear to reflect changes in intersystem-crossing rate constants (Table 3). The apparent origin is that **BC-MM** and **BC-AmAm** have more facile internal conversion than expected on the basis of the S_1 (Q_y) energy. It is interesting to speculate whether the more facile internal conversion of the two new 2,3,12,13-tetraalkylbacteriochlorins is connected with the increased vibronic activity manifest in the absorption spectrum and RR spectrum of **CuBC-MM** *versus* **CuBC0** (*vide supra*).

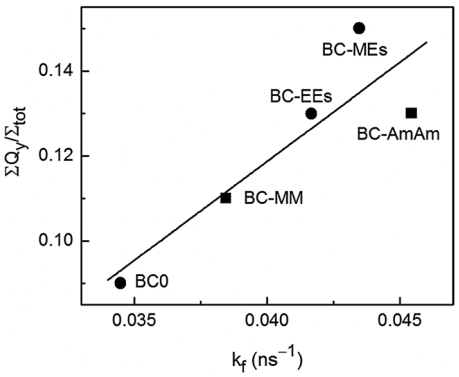


Fig. 5 Integrated intensity of the Q_y absorption manifold [$Q_y(0,0)$ and $Q_y(1,0)$] *versus* that of the total spectrum (300–900 nm) when plotted in wavenumbers (vertical axis) *versus* the radiative rate constant k_f obtained from the τ_S and Φ_f values (x-axis). The overall linear relationship reflects the consistency of the measurements and analysis.

Conclusions

The use of a deactivating group at the α-position of the pyrrole unit of a dihydrodipyrrin-acetal has enabled (1) the incorporation of two alkyl groups at the pyrrole β-positions, and (2) the smooth oxidation of the 9-methyl group to the corresponding aldehyde. This synthetic approach blends features of longstanding routes to natural porphyrins, where dialkylpyrrole-α-esters are commonplace, with gem-dimethyl-substituted dihydrodipyrrins to prepare tetraalkylbacteriochlorins. The tetraalkylbacteriochlorins are accessible, albeit in small quantities, *via* a relatively concise synthesis. The tetraalkylbacteriochlorins constitute macrocycles of intermediate complexity along the progression from the fully unsubstituted parent bacteriochlorin **BC0** to the native bacteriochlorophylls.

Experimental section

General methods

^{1}H NMR (300 MHz) and ^{13}C NMR (100 MHz) spectra were collected at room temperature in $CDCl_3$ unless noted otherwise. Absorption spectra were obtained in toluene at room temperature unless noted otherwise. Electrospray ionization mass spectrometry (ESI-MS) data are reported for the molecular ion or protonated molecular ion. THF used in all reactions was freshly distilled from Na/benzophenone ketyl. Compounds **5**,[11] **7**,[31] **8**[30] and **11**[34] were prepared as described in the literature.

Self-condensation study of dihydrodipyrrin-carboxaldehydes

Each reaction (1.0 mL) was carried out in a microreaction vial equipped with a stir bar and cap; the latter was sealed with Teflon tape to limit solvent evaporation. Reactions were done on a 0.018 mmol scale of dihydrodipyrrin-carboxaldehyde. Anhydrous solvents (CH_2Cl_2, CH_3CN) were reagent grade and were used as received.

The acids used were (1) $BF_3{\cdot}OEt_2$ in CH_3CN, (2) TMSOTf/DTBP in CH_2Cl_2, and (3) neat TFA. The procedures for each condition are as following: (i) the dihydrodipyrrin-carboxaldehyde

(0.018 mmol) in CH_3CN (1.0 mL) was treated with $BF_3{\cdot}OEt_2$ (17 μL, 140 μmol) under argon using a microsyringe. The reaction mixture was stirred at room temperature for 19 h. TEA (60 μL, 0.043 mmol) was added to the reaction mixture. Then the reaction mixture was concentrated. (ii) The dihydrodipyrrin-carboxaldehyde (0.018 mmol) in CH_2Cl_2 (1.0 mL) was treated with DTBP (33 μL, 144 μmol, 8 molar equiv.) followed by TMSOTf (13 μL, 72 μmol, 4 molar equiv.) under argon. The reaction mixture was stirred at room temperature for 19 h. The reaction mixture was concentrated. (iii) The dihydrodipyrrin-carboxaldehyde (0.018 mmol) was dissolved in TFA (1.0 mL) under argon. The resulting solution was stirred at room temperature for 1 h. Then the reaction mixture was poured into saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The extract was washed (brine), dried (Na_2SO_4) and concentrated.

The crude samples were checked by TLC, UV-vis spectroscopy and LD-MS. For TLC analysis, a tiny amount of the crude sample in CH_2Cl_2 was spotted directly onto the TLC plate [silica, hexanes/CH_2Cl_2 (1 : 1)]. TLC showed the consumption of starting material, and the formation of HBC-type and/or other macrocycles (if any). The diagnostic feature in the absorption spectrum was the characteristic bacteriochlorin Q_y absorption band. If present, the bacteriochlorin was isolated by column chromatography [silica, hexanes/CH_2Cl_2 (1 : 1)]. The fractions containing bacteriochlorins were collected, concentrated and the yield was determined spectroscopically. The assumed value of ε_{Q_y} = 120 000 M^{-1} cm^{-1} for HBC-type bacteriochlorins[10] was identical to that for **BC-MM** upon experimental determination.

6-[3-(4-Methylphenyl)pyrrol-2-yl]-4,4-dimethyl-5-nitro-2-hexanone (6)

Following a standard procedure,[27] a mixture of **5** (460 mg, 2.00 mmol) and mesityl oxide (458 μL, 4.00 mmol) in CH_3CN (4.0 mL) was treated with DBU (897 μL, 6.00 mmol). The reaction mixture was stirred for 24 h at room temperature, diluted with ethyl acetate (15.0 mL) and washed with water and brine. The organic layer was dried (Na_2SO_4) and concentrated. Excess mesityl oxide was removed under high vacuum. The resulting oil was chromatographed [silica, hexanes/ethyl acetate (2 : 1)] to afford a light brown oil (486 mg, 74%): ^{1}H NMR (400 MHz) δ 1.08 (s, 3H), 1.19 (s, 3H), 2.10 (s, 3H), 2.37 (s, 3H), 2.55 (AB, ^2J = 17.6 Hz, 2H), 3.21 (ABX, ^3J = 2.6 Hz, ^2J = 15.6 Hz, 1H), 3.38 (ABX, ^3J = 11.6 Hz, ^2J = 15.6 Hz, 1H), 5.18 (ABX, ^3J = 2.6 Hz, ^3J = 11.6 Hz, 1H), 6.22–6.24 (m, 1H), 6.67–6.69 (m, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 8.05–8.20 (br, 1H); ^{13}C NMR δ 21.0, 23.7, 23.9, 25.1, 31.4, 36.7, 50.8, 94.4, 109.1, 117.5, 121.8, 123.1, 128.0, 129.1, 133.4, 135.3, 206.9; ESI-MS obsd 329.1852, calcd 329.1860 [$(M + H)^+$, M = $C_{19}H_{24}N_2O_3$].

1,3,3-Trimethyl-7-(4-methylphenyl)-2,3-dihydrodipyrrin (1-Me)

Following a standard procedure,[10] a solution of **6** (256 mg, 0.780 mmol) in anhydrous THF (7.8 mL) under argon was treated with NaOMe (210 mg, 3.90 mmol). The mixture was bubbled with argon for 10 min and then was stirred under argon for 1 h at room temperature (first flask). In a second flask, $TiCl_3$ [8.6 wt% $TiCl_3$ in 28 wt% HCl (d = 1.2), 5.83 mL, 3.90 mmol, 5.0 mol equiv.] and H_2O (31 mL) were combined. The solution was bubbled with argon for 10 min. NH_4OAc (22.9 g, 297 mmol) was slowly added to buffer the solution to pH 6.0; and then THF (2.2 mL) was added under argon bubbling (~20 min). The solution in the first flask containing the nitronate anion of **6** 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 slowly poured into a stirred mixture of saturated aqueous $NaHCO_3$ solution (120 mL) and ethyl acetate (40 mL). After 10 min, the mixture was extracted with ethyl acetate. The combined organic extract was washed with water and then dried (Na_2SO_4). The solvent was removed under reduced pressure at room temperature. The crude product was passed through a short column [alumina, hexanes/ethyl acetate (2 : 1)] to afford a yellow solid (55 mg, 25%): mp 112–113 °C; ^{1}H NMR δ 1.18 (s, 6H), 2.21 (s, 3H), 2.38 (s, 3H), 2.51 (s, 2H), 5.97 (s, 1H), 6.27–6.28 (m, 1H), 6.84–6.86 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 10.99–11.10 (br, 1H); ^{13}C NMR (75 MHz) δ 20.7, 21.2, 29.1, 41.2, 53.7, 102.9, 108.9, 118.3, 123.3, 127.2, 128.5, 129.2, 134.4, 134.9, 161.2, 176.6; ESI-MS obsd 279.1853, calcd 279.1856 [$(M + H)^+$, M = $C_{19}H_{22}N_2$].

1-Formyl-3,3-dimethyl-7-(4-methylphenyl)-2,3-dihydrodipyrrin (1-CHO)

Following a general procedure,[13,28] a solution of **1-Me** (45 mg, 0.16 mmol) in 1,4-dioxane (3.2 mL) was treated with SeO_2 (27 mg, 0.24 mmol) under argon. The mixture was stirred for 1.5 h at room temperature. The reaction mixture was treated with saturated aqueous $NaHCO_3$ solution (4.0 mL) and extracted with ethyl acetate. The organic extract was washed with water, dried (Na_2SO_4), and chromatographed [silica, hexanes/ethyl acetate (3 : 1)] to give a dark orange solid (22 mg, 47%): ^{1}H NMR δ 1.22 (s, 6H), 2.41 (s, 3H), 2.72 (s, 2H), 6.34–6.35 (m, 1H), 6.38 (s, 1H), 7.00–7.02 (m, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 10.0 (s, 1H), 10.71–10.82 (br, 1H); FAB-MS obsd 293.1654, calcd 293.1654 [$(M + H)^+$, M = $C_{19}H_{20}N_2O$].

4,4-Dimethyl-6-(5-*tert*-butoxycarbonyl-3,4-dimethylpyrrol-2-yl)-5-nitrohexan-2-one (9)

Following a standard procedure[27] with modification, a mixture of **8** (4.02 g, 15.0 mmol) and mesityl oxide (**4-Me**, 4.40 g, 45.0 mmol) was treated with DBU (6.7 mL, 45.0 mmol) at room temperature. After 16 h, the reaction mixture was diluted with ethyl acetate and washed with HCl (0.5 M), saturated aqueous $NaHCO_3$ solution and brine. The organic layer was dried and filtered. The filtrate was concentrated. The residue was crystallized from hexane (20 mL) to give a light brown solid (1.95 g, 35%): mp 118–119 °C; ^{1}H NMR (400 MHz) δ 1.13 (s, 3H), 1.27 (s, 3H), 1.55 (s, 9H), 1.91 (s, 3H), 2.15 (s, 3H), 2.18 (s, 3H), 2.38–2.64 (AB, ^2J = 18.3 Hz, 2H), 2.94 (ABX, ^3J = 2.4 Hz, ^2J = 13.2 Hz, 1H), 3.26 (ABX, ^3J = 11.4 Hz, ^2J = 15.3 Hz, 1H), 5.08 (ABX, ^3J = 3.3 Hz, ^2J = 14.1 Hz, 1H), 8.40–8.50 (brs, 1H); ^{13}C NMR δ 8.9, 10.7, 24.3, 24.6, 25.2, 28.7, 32.1, 37.0, 51.6, 80.6, 93.7, 118.4, 119.8, 126.3, 161.2, 207.0; ESI-MS obsd 367.2221, calcd 367.2228 [$(M + H)^+$, M = $C_{19}H_{30}N_2O_5$]. Compound **9** has been prepared *via* an earlier route.[32]

2,3-Dihydro-1,3,3,7,8-pentamethyl-9-*tert*-butoxycarbonyldipyrrin (10-Me)

Following a general procedure[11] with modification, a solution of **9** (1.95 g, 5.33 mmol) in THF/methanol (10 : 1, 10 mL) under argon was treated with NaOMe (0.86 g, 15.9 mmol). The mixture was stirred at room temperature for 30 min. In a second flask, NH_4OAc (20.0 g, 266 mmol) in distilled THF (72 mL) was bubbled with argon for 15 min. Then $TiCl_3$ (27 mL, 20 wt% in 3% HCl solution) was added, and the mixture was degassed by bubbling with argon for 30 min. Then, the contents of the first flask mixture were transferred *via* cannula to the buffered $TiCl_3$ solution. The resulting mixture was stirred at room temperature for 20 h under argon. The mixture was then filtered through a pad of Celite, which was washed with ethyl acetate. The filtrate was washed with saturated aqueous $NaHCO_3$ solution, brine and water. The organic layer was dried and filtered. The filtrate was concentrated. Column chromatography (silica, CH_2Cl_2) afforded a light yellow solid (1.17 g, 69%): mp 143–144 °C; ^{1}H NMR δ 1.21 (s, 6H), 1.58 (s, 9H), 2.02 (s, 3H), 2.22 (s, 3H), 2.26 (s, 3H), 2.52 (s, 2H), 5.67 (s, 1H), 11.10 (brs, 1H); ^{13}C NMR δ 8.89, 10.4, 20.9, 28.6, 29.2, 41.5, 53.8, 79.6, 101.3, 118.3, 119.6, 126.2, 130.6, 161.2, 163.5, 178.4; ESI-MS obsd 317.2218, calcd 317.2223 [$(M + H)^+$, M = $C_{19}H_{28}N_2O_2$]; λ_{abs} (CH_2Cl_2) = 350 nm. Compound **10-Me** has been prepared *via* an earlier route.[32]

9-*tert*-Butoxycarbonyl-1-formyl-2,3-dihydro-3,3,7,8-pentamethyldipyrrin (10-CHO)

Following a general procedure,[13,28] a solution of dihydrodipyrrin **10-Me** (95 mg, 0.30 mmol) in 6.0 mL of 1,4-dioxane was treated with SeO_2 (100 mg, 0.90 mmol) under argon. The reaction mixture was stirred at room temperature and monitored *via* absorption spectroscopy for the characteristic bathochromic shift that accompanies oxidation of the pyrroline α-methyl group to the carboxaldehyde.[13] After 90 min, ethyl acetate was added. The reaction mixture was washed with aqueous $NaHCO_3$ solution and then brine. The organic layer was dried, concentrated and chromatographed (silica, CH_2Cl_2) to give an orange oil (63 mg, 63%): ^{1}H NMR δ 1.26 (s, 6H), 1.59 (s, 9 H), 2.09 (s, 3H), 2.26 (s, 3H), 2.73 (s, 2H), 6.14 (s, 1H), 9.98 (s, 1H), 10.81 (brs, 1H); ^{13}C NMR δ 9.2, 10.4, 28.6, 29.3, 41.3, 46.2, 80.6, 111.0, 122.8, 126.2, 129.6, 160.9, 162.4, 170.2, 190.3; ESI-MS obsd 331.2011, calcd 331.2016 [$(M + H)^+$, M = $C_{19}H_{26}N_2O_3$]; λ_{abs}(CH_2Cl_2) = 468 nm.

2,3,8,8,12,13,18,18-Octamethylbacteriochlorin (BC-MM)

A sample of **10-CHO** (69.0 mg, 0.208 mmol) was dissolved in TFA (10.0 mL) under argon and stirred for 1 h at room temperature. Then the reaction mixture was poured into saturated aqueous $NaHCO_3$ solution (200 mL). The resulting mixture was extracted with CH_2Cl_2 (200 mL). The organic extract was washed with brine and water, dried (Na_2SO_4), and concentrated. Column chromatography [silica, hexanes/CH_2Cl_2 (1 : 1)] afforded a green solid (13.0 mg, 29%): ^{1}H NMR (400 MHz) δ −2.43 (brs, 2H), 1.96 (s, 12H), 3.31 (s, 6H), 3.34 (s, 6H), 4.45 (brs, 4H), 8.57 (s, 2H), 8.71 (s, 2H); ^{13}C NMR δ 11.3, 11.4, 29.9, 31.3, 46.1, 51.9, 92.6, 95.1, 127.8, 133.7, 134.5, 156.4, 168.7; ESI-MS obsd 427.2850, calcd 427.2856 [$(M + H)^+$, M = $C_{28}H_{34}N_4$]; λ_{abs}(toluene) 347, 374, 490, 722 nm; $\varepsilon_{772\,nm}$ = 120 000 M^{-1} cm^{-1}.

Benzyl 3,4-bis(benzyloxycarbonylmethyl)-5-methylpyrrole-2-carboxylate (12)

Following a reported procedure,[37] a solution of the trimethyl ester **11** (7.32 g, 25.9 mmol) in benzyl alcohol (40 mL) in a 100 mL round-bottom flask was stirred under an argon stream and heated to reflux. After a few minutes, a solution of sodium (0.52 g) in benzyl alcohol (10.0 mL) was added dropwise; heating was continued throughout and a few minutes later (20 min from start of process) the hot solution was poured into a mixture of water (50 mL), acetic acid (1.0 mL) and methanol (100 mL). The solid product was collected, washed with water and then dissolved in CH_2Cl_2 (100 mL). After washing with water, the organic phase was dried (Na_2SO_4) and filtered. The filtrate was concentrated to a yellow oil. The oil was treated with hexanes/diethyl ether/CH_2Cl_2 (140 mL, 5 : 1 : 1), and the resulting mixture was refluxed whereupon a homogeneous solution was obtained. Upon allowing to cool to room temperature, white crystals formed. The mixture was cooled overnight at −10 °C to promote further crystallization. Filtration afforded a white solid (9.03 g, 68%): mp 84–85 °C; ^{1}H NMR δ 2.19 (s, 3H), 3.43 (s, 2H), 3.91 (s, 2H), 5.01 (s, 2H), 5.05 (s, 2H), 5.21 (s, 2H), 7.24–7.31 (m, 15H), 9.07 (br, 1H); ^{13}C NMR (75 MHz) δ 11.9, 30.5, 31.2, 66.1, 66.6, 66.8, 115.2, 118.0, 123.8, 128.3, 128.4, 128.7, 128.9, 131.9, 136.1, 136.3, 136.4, 161.1, 171.5, 200.6; ESI-MS obsd 512.2054, calcd 512.2068 [$(M + H)^+$, M = $C_{31}H_{29}NO_6$]. Compound **12** has been prepared *via* an earlier route.[35]

Benzyl 3,4-bis(methoxycarbonylmethyl)-5-methylpyrrole-2-carboxylate (13)

Following a reported procedure,[37] the triester **12** (12.78 g, 25.0 mmol) in THF (40 mL) and dry methanol (80 mL) was treated with sodium methoxide (1.08 g, 20.0 mmol). The reaction was monitored by TLC analysis. After 3 h, glacial acetic acid (3.0 mL) was added and the solution was concentrated. Then, water (200 mL) was added, and the mixture was extracted with CH_2Cl_2 (200 mL). The organic layer was washed, dried (Na_2SO_4) and concentrated. The crude product was recrystallized from hexanes/ether (100 mL/50 mL) to give white crystals (7.73 g, 82%): mp 90–91 °C; ^{1}H NMR (400 MHz) δ 2.21 (s, 3H), 3.40 (s, 2H), 3.58 (s, 3H), 3.64 (s, 3H), 3.86 (s, 2H), 5.26 (s, 2H), 7.35 (m, 5H), 9.38 (br, 1H); ^{13}C NMR δ 11.6, 30.1, 30.9, 51.9, 52.0, 65.9, 114.9, 117.7, 123.7, 128.2, 128.3, 128.6, 131.9, 136.2, 161.0, 171.9, 172.0; ESI-MS obsd 360.1428, calcd 360.1442 [$(M + H)^+$, M = $C_{19}H_{21}NO_6$]. Compound **13** has been prepared *via* an earlier route.[36]

***tert*-Butyl 3,4-bis(methoxycarbonylmethyl)-5-methylpyrrole-2-carboxylate (14)**

Following a reported procedure,[38] a solution of **13** (0.825 g, 2.30 mmol) in 20 mL of methanol was reduced overnight with hydrogen (balloon pressure) over 83 mg of 10% Pd/C. The catalyst was removed by filtration, and the filtrate was concentrated to dryness. The resulting residue was dissolved in 10 mL of dry

tert-butyl alcohol and 10 mL of dry THF. DCC (0.473 g, 2.30 mmol) and a catalytic amount of DMAP were added, and the mixture was stirred for 18 h at room temperature. The precipitate was removed by filtration. The filtrate was concentrated and chromatographed (silica, CH_2Cl_2) to afford a light yellow solid (522 mg, 70%): mp 130–131 °C; ^{1}H NMR (400 MHz) δ 1.54 (s, 9H), 2.25 (s, 3H), 3.41 (s, 2H), 3.65 (s, 3H), 3.67 (s, 3H), 3.84 (s, 2H), 9.65 (br, 1H); ^{13}C NMR δ 11.7, 28.6, 30.3, 31.1, 52.1, 56.0, 81.1, 114.5, 120.0, 122.2, 131.2, 161.3, 172.2, 172.3; ESI-MS obsd 348.1405, calcd 348.1418 [$(M + Na)^+$, M = $C_{16}H_{23}NO_6$].

tert-Butyl 3,4-bis(methoxycarbonylmethyl)-5-(2-nitroethyl)pyrrole-2-carboxylate (16)

Following a reported procedure,[32] a solution of **14** (0.975 g, 3.00 mmol) in CH_2Cl_2 (30 mL) was stirred vigorously at 0 °C with K_2CO_3 (4.55 g, 33.0 mmol) during dropwise addition of $SOCl_2$ (510 μL, 6.3 mmol). The mixture was stirred for 10 min at 0 °C and 10 min at 20 °C before filtration through Celite. The filtrate was concentrated to yield the crude dichloromethylpyrrole. A solution of this product in acetone (30 mL) and water (15 mL) was kept for 1 h before dilution with water (30 mL) and extraction with CH_2Cl_2 (50 mL). The combined organic extract was washed with saturated aqueous $NaHCO_3$ solution, dried (Na_2SO_4) and concentrated to give the crude formylpyrrole **15**, which was used in the next step without further purification: ^{1}H NMR (400 MHz) δ 1.56 (s, 9H), 3.69 (s, 3H), 3.70 (s, 3H), 3.82 (s, 2H), 3.87 (s, 2H), 9.80 (s, 1H), 10.22 (br, 1H); ^{13}C NMR δ 28.2, 29.5, 30.0, 52.0, 52.4, 83.0, 122.6, 125.6, 126.6, 130.2, 160.0, 170.7, 171.2, 179.8; ESI-MS obsd 362.1199, calcd 362.1210 [$(M + Na)^+$, M = $C_{16}H_{21}NO_7$].

Following a standard procedure,[11] the crude formylpyrrole **15**, nitromethane (0.48 mL, 9.0 mmol), potassium acetate (0.35 g, 3.6 mmol) and methylamine hydrochloride (0.24 g, 3.6 mmol) were stirred together in methanol (10.0 mL) for 5 h. Then the mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extract was washed with water, dried (Na_2SO_4) and concentrated to give the crude (2-nitrovinyl)pyrrole. The residue was dissolved in methanol (40 mL) and DMF (4 mL) containing acetic acid (0.18 g, 3.0 mmol). The solution was treated with sodium borohydride (0.37 g, 10. mmol) in one portion. Then the mixture was cooled to 0 °C, acidified to pH 2 with HCl solution (2 M), diluted with water (200 mL) and extracted with ether (2 × 100 mL). The combined organic extract was washed [saturated aqueous $NaHCO_3$ solution and brine (50 mL)], dried and concentrated. Chromatography [silica, hexanes/ethyl acetate (1 : 1)] gave a yellow oil (0.580 g, 50%): ^{1}H NMR (400 MHz) δ 1.53 (s, 9H), 3.30 (t, J = 7.2 Hz, 2H), 3.45 (s, 2H), 3.66 (s, 3H), 3.68 (s, 3H), 3.82 (s, 2H), 4.61 (t, J = 7.2 Hz, 2H), 10.06 (br, 1H); ^{13}C NMR δ 23.7, 28.3, 29.9, 30.7, 51.8, 52.1, 73.9, 81.5, 115.8, 121.2, 121.8, 128.5, 160.9, 171.8, 171.9; ESI-MS obsd 407.1415, calcd 407.1425 [$(M + Na)^+$, M = $C_{17}H_{24}N_2O_8$].

4,4-Dimethyl-6-(5-*tert*-butoxycarbonyl-3,4-bis(methoxycarbonylmethyl)pyrrol–2-yl)-5-nitro-hexan-2-one (17)

Following a standard procedure,[39] samples of **16** (0.580 g, 1.51 mmol), mesityl oxide (0.740 g, 7.50 mmol), TBAF (1.0 M in THF, 1.51 mL, 1.51 mmol) and 4 Å molecular sieves (1.5 g) were stirred together in DMF (30 mL) for 3 h. The mixture was then diluted with water (120 mL) and extracted with ether (4 × 30 mL). The combined organic extract was washed [HCl solution (2 M, 20 mL), saturated aqueous $NaHCO_3$ solution (20 mL) and brine (20 mL)], dried (Na_2SO_4) and concentrated. Chromatography [silica, CH_2Cl_2, then CH_2Cl_2/ethyl acetate (1 : 1)] afforded a yellow oil (393 mg, 54%): ^{1}H NMR (400 MHz) δ 1.13 (s, 3H), 1.25 (s, 3H), 1.53 (s, 9H), 2.17 (s, 3H), 2.43, 2.60 (AB, ^2J = 17.6 Hz, 2H), 3.07 (ABX, ^3J = 2.0 Hz, ^2J = 15.2 Hz, 1H), 3.33 (ABX, ^3J = 12.4 Hz, ^2J = 16.0 Hz, 1H), 3.41 (s, 2H), 3.66 (s, 3H), 3.67 (s, 3H), 3.80 (s, 2H), 5.19 (ABX, ^3J = 2.6 Hz, ^3J = 12.0 Hz, 1H), 8.93 (br, 1H); ^{13}C NMR δ 24.0, 24.1, 24.7, 28.3, 29.8, 30.6, 31.8, 36.8, 51.2, 51.7, 52.0, 81.1, 93.5, 115.8, 121.2, 121.6, 128.2, 160.3, 171.7, 171.8, 207.0; ESI-MS obsd 505.2144, calcd 505.2157 [$(M + Na)^+$, M = $C_{23}H_{34}N_2O_9$].

9-*tert*-Butoxycarbonyl-2,3-dihydro-7,8-bis(methoxycarbonylmethyl)-1,3,3-trimethyldipyrrin (18-Me)

Following a standard procedure,[11] a solution of **17** (393 mg, 0.815 mmol) in THF/methanol (2.0 mL/0.20 mL) under argon was treated with sodium methoxide (221 mg, 4.08 mmol). The mixture was stirred at room temperature for 30 min. In a second flask, ammonium acetate (6.13 g, 81.5 mmol) in distilled THF (20 mL) was bubbled with argon for 15 min before $TiCl_3$ solution (8.37 g of 12 wt% in 5–10% HCl solution) was added. The mixture was degassed by bubbling with argon for 30 min. Then, the solution in the first flask was transferred *via* cannula to the buffered $TiCl_3$ solution. The resulting mixture was stirred for 20 h at room temperature under argon. The mixture was poured into 200 mL of saturated aqueous $NaHCO_3$ solution and extracted with ethyl acetate (2 × 200 mL). The organic extract was filtered through Celite. The filtrate was washed with brine, dried (Na_2SO_4) and concentrated. Chromatography [silica, CH_2Cl_2/ethyl acetate (3 : 1)] gave a yellow oil (65 mg, 18%): ^{1}H NMR (400 MHz) δ 1.21 (s, 6H), 1.55 (s, 9H), 2.23 (s, 3H), 2.53 (s, 2H), 3.52 (s, 2H), 3.64 (s, 3H), 3.66 (s, 3H), 3.90 (s, 2H), 5.71 (s, 1H), 11.46 (br, 1H); ^{13}C NMR δ 21.0, 28.5, 29.1, 30.2, 30.7, 41.6, 51.9, 52.1, 53.9, 80.5, 100.8, 115.0, 120.9, 131.9, 165.0, 172.1, 172.2, 179.5; ESI-MS obsd 433.2327, calcd 433.2333 [$(M + H)^+$, M = $C_{23}H_{32}N_2O_6$].

2,3,12,13-Tetrakis(methoxycarbonylmethyl)-8,8,18,18-tetramethylbacteriochlorin (BC-AmAm)

Following a standard procedure,[13,28] a solution of **18-Me** (20 mg, 0.046 mmol) in 1,4-dioxane (1.0 mL) was treated with SeO_2 (15 mg, 0.139 mmol) with vigorous stirring at room temperature. After 2 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (100 mL). The organic extract was washed with brine, dried (Na_2SO_4) and concentrated. The residue was passed through a short silica column [hexanes/ethyl acetate (3 : 1)] to give **18-CHO** as a yellow-orange oil. The oil was dissolved in dry CH_3CN (2.50 mL) and treated with $BF_3{\cdot}OEt_2$ (45 μL, 0.37 mmol) under argon. The vial was sealed with Parafilm and stirred at room temperature for 20 h. Then trimethylamine (50 μL) was added to quench the reaction. The mixture was concentrated and chromatographed

[silica, hexanes/CH_2Cl_2 (3 : 1)] to give a green solid (1.0 mg, 6.6%): ^{1}H NMR (400 MHz) δ −2.13 (br, 2H), 1.95 (s, 12H), 3.73 (s, 6H), 3.75 (s, 6H), 4.44 (s, 4H), 4.89 (s, 2H), 4.91 (s, 2H), 8.67 (s, 2H), 8.76 (s, 2H); λ_{abs}(toluene) 347, 373, 495, 732 nm; ESI-MS obsd 659.3052, calcd 659.3075 [$(M + H)^+$, M = $C_{36}H_{42}N_4O_8$].

Cu(II)-2,3,8,8,12,13,18,18-Octamethylbacteriochlorin (CuBC-MM)

Following a reported procedure,[33] **BC-MM** (2.0 mg, 4.7 μmol), sodium hydride (24 mg, 0.94 mmol, 60% dispersion in mineral oil) and copper(II) acetate (43 mg, 0.24 mmol) were placed in a Schlenk tube and flushed with argon. Freshly distilled THF (1.2 mL) was added, and the reaction mixture was heated at 60 °C under argon for 16 h. Then the mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ solution. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated. Flash chromatography [silica, hexanes/CH_2Cl_2 (2 : 1), with 1% triethylamine] afforded a green solid (6.0%, determined by absorption spectroscopy assuming equal molar absorptivity of the respective free base and metallobacteriochlorins at the Q_y(0,0) band): λ_{abs}(toluene) 336, 385, 506, 736 nm; LD-MS obsd 488.6; ESI-MS obsd 487.1900, calcd 487.1918 [M^+, M = $C_{28}H_{32}CuN_4$].

X-ray structure determination

A single-crystal X-ray analysis of **BC-MM** was made on a Bruker-Nonius X8 Apex2 CCD diffractometer at 110 K. The frame integration was performed using SAINT+.[55] The resulting raw data were scaled and absorption-corrected by multiscan averaging of symmetry equivalent data using SADABS.[56] The structure was solved using direct methods from SIR92[57] and refined using the NRCVAX[58] crystallographic suite. The structure was refined using the SHELXL program from the SHELX2013[59] package, and graphic plots were produced using Mercury 3.5.

RR spectroscopy

The RR spectrum of **CuBC-MM** was obtained at room temperature on a sample (~0.2 mM) in deoxygenated benzene solution contained in a 5 mm diameter NMR tube which had been cut to a length of ~4 cm. The NMR tube was spun to mitigate photodamage. Spectra were initially acquired in CH_2Cl_2 solution; however, **CuBC-MM** was quite photolabile in this solvent and tended to demetalate, resulting in severe interference from fluorescence emission from the free base. **CuBC-MM** was much less prone to demetalation in benzene, albeit a small amount of demetalation occurred during the course of data acquisition, as was evidenced by increasing fluorescence emission.

The RR spectrum was acquired with a red-optimized triple spectrograph (Spex 1877) equipped with a holographically etched 1200 groove per mm grating in the third state. A back-illuminated (CCD) was used as the detector (Princeton Instruments LN/CCD equipped with a Tektronix chip). The excitation wavelength was provided by the discrete output of a Ti:sapphire laser (Coherent 890), pumped by a diode-pumped solid-state laser (Coherent Verdi-V6). The laser powers were typically in the 6–7 mW range; the beam diameter was ~0.5 mm. The scattered light was collected in a 90° configuration by using a 50 mm, f/1.2 camera lens. The spectra were acquired with 2 h of signal averaging (60 × 120 s or 120 × 60 s scans, depending on the spectral window). The spectral resolution was ~2 cm^{-1} at a Raman shift of 200 cm^{-1}. The spectral data were calibrated using the known frequencies of indene[60] and fenchone.[61]

Photophysical measurements

Static absorption (Shimadzu UV-1800), fluorescence (Horiba Nanolog), and time-resolved measurements were performed at room temperature. Measurement of the fluorescence quantum yield (Φ_f) and singlet excited-state lifetime (τ_S) utilized dilute (μM) Ar-purged toluene solutions. Static emission measurements employed 2–4 nm excitation and detection bandwidths. Emission spectra were corrected for detection-system spectral response. Samples for Φ_f measurements generally had an absorbance of <0.05 for **BC-MM** and **BC-AmAm** in the Q_y band to minimize inner-filter effects associated with the very small (1–2 nm) fluorescence-absorption (Stokes) shifts. For analogues with larger (up to 6 nm) Stokes shifts, the Q_y absorbance could be increased somewhat but was never >0.15. The Φ_f measurements employed an integrating sphere in which the ratio of excitation and emission bands were compared for a blank and a sample to calculate the absolute fluorescence quantum yield (Horiba, Quanti-Phi). Fluorescence lifetimes were obtained using several methods and then averaged. The first method utilized a stroboscopic fluorescence decay technique on an apparatus with an approximately Gaussian instrument response function with a FWHM of ~1 ns (Photon Technology International, LaserStrobe TM-3). Samples were excited in the blue to green spectral regions by a dye laser pumped by a nitrogen laser at 337 nm. The second method utilized transient absorption decay measurements in which difference spectra (450–750 nm) were measured as a function of time following a 130 fs excitation flash in the Q_x or Q_y band. One setup utilized 130 fs white-light probe pulses and delay times to 8 ns (Ultrafast Systems, Helios). The second method used a continuum probe laser with a pulse width of ~1 ns and data acquisition in 100 ps bins to a delay time of ~0.5 ms (Ultrafast Systems, EOS). The values from the various measurements were in good agreement with those obtained previously[14] for benchmarks using a fluorescence modulation technique (Spex Tau2). The EOS system was also used for measurements of the yield of $S_1 \rightarrow T_1$ intersystem crossing (*i.e.*, the triplet yield). In particular, from the transient absorption difference spectra, time profiles for bleaching of the ground-state Q bands relative to the basically featureless excited-state absorption were fit to an exponential (the excited-state lifetime) and the amplitude at the asymptote of the decay (due to T_1) was compared to the value at t = 0 (due to S_1).

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