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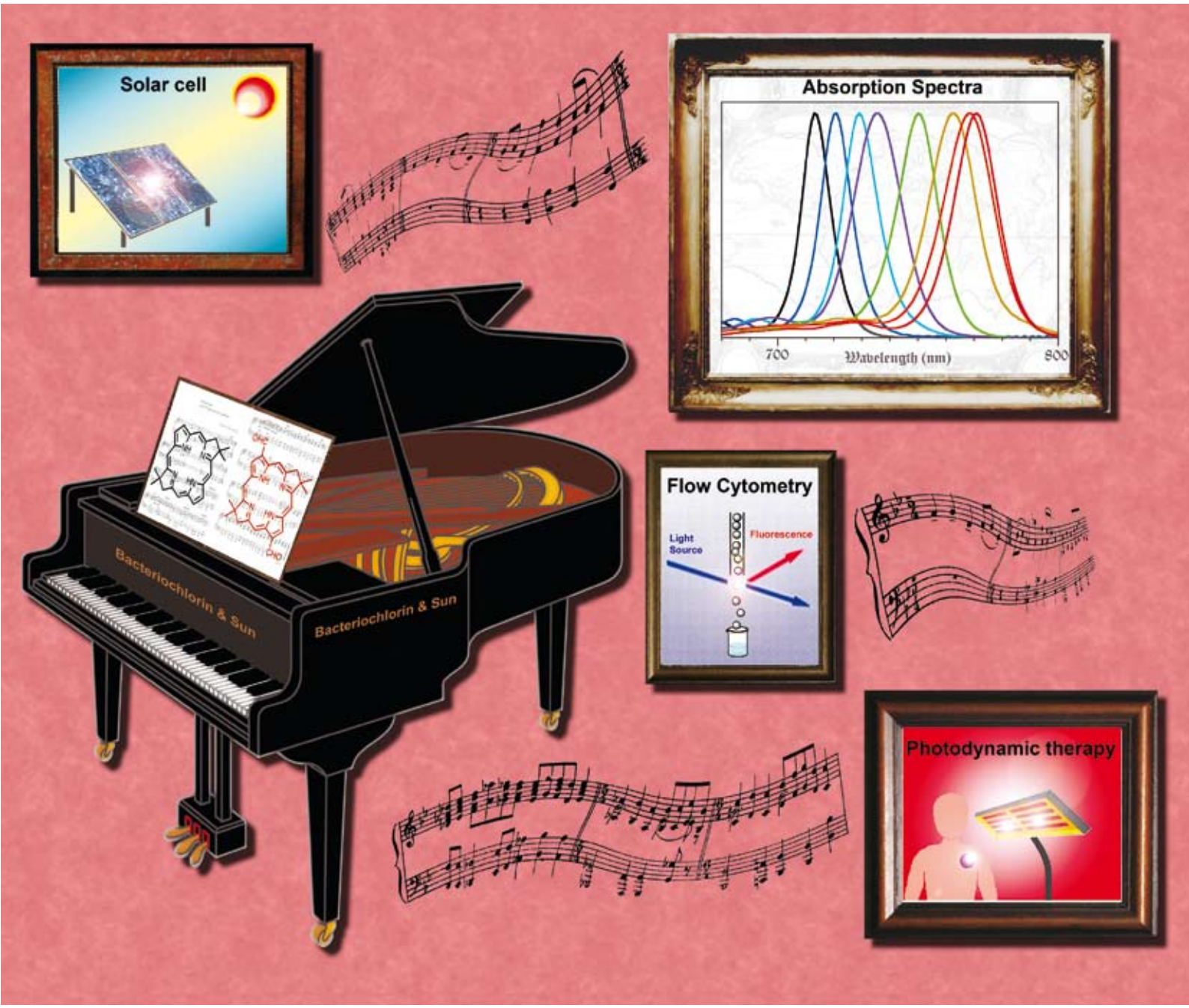

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PAPER

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Accessing the near-infrared spectral region with stable, synthetic, wavelength-tunable bacteriochlorins

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Accessing the near-infrared spectral region with stable, synthetic, wavelength-tunable bacteriochlorins

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The near-infrared (NIR) spectral region has been comparatively under-utilized for diverse materials and medical applications owing to the lack of chromophores that afford stability, solubility, synthetic malleability, and tunable photophysical features. Bacteriochlorins are attractive candidates in this regard; however, preparation *via* modification of naturally occurring bacteriochlorophylls or reduction of porphyrins or chlorins has proved cumbersome. To overcome such limitations, a dibromobacteriochlorin (**BC-Br^{3}Br^{13}**) was prepared *de novo* by the acid-catalyzed condensation of an 8-bromodihydrodipyrrin-acetal. **BC-Br^{3}Br^{13}** bears (1) a geminal dimethyl group in each reduced ring to block adventitious dehydrogenation, and (2) bromo groups at the 3- and 13-positions for further chemical modifications. **BC-Br^{3}Br^{13}** was subjected to four types of Pd-mediated coupling reaction (Suzuki, Stille, Sonogashira, dehalogenation) to give bacteriochlorins bearing substituents at the 3- and 13-positions (phenyl, vinyl, acetyl, phenylethynyl), and a benchmark bacteriochlorin lacking such substituents. The 3,13-divinylbacteriochlorin was transformed to the 3,13-diformylbacteriochlorin. Depending on the substituents at the 3- and 13-positions, the position of the long-wavelength absorption maximum (Q_y(0,0) band) lies between 713 and 771 nm, the fluorescence emission maximum lies between 717 and 777 nm, and the fluorescence quantum yield ranges from 0.15 to 0.070. The ability to introduce a wide variety of functional groups *via* Pd-mediated coupling reactions and the tunable absorption and emission spectral properties suggest that synthetic bacteriochlorins are viable candidates for a wide variety of photochemical applications.

Introduction

Photosynthetic systems make extensive use of photons in the red and near-infrared (NIR) spectral regions (600–700 nm and 700–1000 nm, respectively),[1] yet these spectral regions have been relatively under-utilized for photochemical applications.[2] Photons in the red and NIR regions are sufficiently energetic (1.2–2 eV) to drive a variety of molecular/electronic transitions. The ability to capture red and NIR light is essential for efficient solar-energy conversion schemes given the large fraction of solar flux in this spectral region.[3] A number of applications in photomedicine, such as photodynamic therapy (PDT) or optical imaging, are best carried out with NIR light owing to the deep penetration of soft tissue afforded by light of these wavelengths.[4] In addition, for biolabeling applications in which a large number of spectrally distinct chromophores are desired (*i.e.*, polychromatic flow cytometry[5,6] or combinatorial barcoding[7,8]), access to the NIR would be very attractive when the UV and visible regions are effectively filled to capacity.

In applications such as PDT, the presence of a strong absorption band in the NIR is desired, whereas in biolabeling the ability to tune the absorption band across a spectral range is essential. Multicolor biolabeling also requires fairly narrow absorption bands to selectively access and detect a given label. Biolabeling for flow cytometry or optical imaging[9] typically relies on the detection of fluorescence emission following excitation. Although a significant number of NIR absorbers are known, most have quite broad absorption bands, and far fewer exhibit significant fluorescence emission.[10] The availability of a series of chromophores with sharp, tunable long-wavelength transitions would also be desirable for the design of energy-cascade architectures,[11] which funnel excitation energy down a gradient. The irreversible flow enables excitation energy to be delivered to a designated site, similar to the manner in which natural light-harvesting antennae feed a reaction center.

We previously prepared a series of synthetic free base or zinc chlorins (analogues of chlorophylls) and found that the introduction of auxochromes enabled the long-wavelength absorption band to be tuned from 603 nm to 686 nm.[12–22] The auxochromes were located at the 3- and 13-positions, which lie along the axis that gives rise to the long-wavelength transition (Q_y band), as is shown in Chart 1. The absorption

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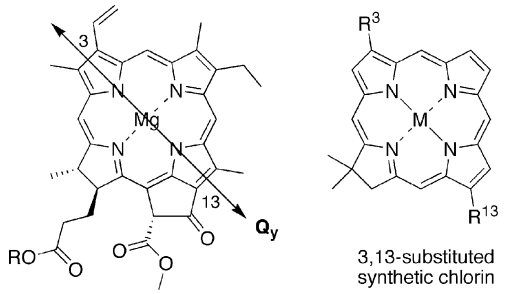


Chart 1

and emission bands were quite sharp (15–20 nm full-width-at-half-maximum, fwhm), suggesting amenability of the chlorins for use in multicolor or energy-cascade applications but not ideal for optical imaging or PDT owing to the position of the long-wavelength transition in the red rather than the NIR spectral region.

Bacteriochlorins absorb at longer wavelengths than chlorins (*i.e.*, NIR *versus* red region)[23] owing to the presence of two reduced pyrrole rings rather than one as in chlorins. The prototypical bacteriochlorin is bacteriochlorophyll *a* (Chart 2). Studies of wavelength tunability in bacteriochlorins have previously been somewhat hampered by the limited stability of the naturally occurring compounds,[24] as well as their poor malleability owing to the presence of multiple substituents about the perimeter of the macrocycle. However, Sasaki and Tamiaki were able to convert the 3-acetyl substituent of methyl bacteriopheophorbide *a* (a free base analogue of bacteriochlorophyll *a*, Chart 2) to the α-hydroxyethyl, vinyl, carboxy, formyl, or 2,2-dicyanovinyl group. Such modifications caused the long-wavelength maximum to be shifted from 717 to 790 nm.[25]

To expand beyond the limitations of semisynthetic approaches with naturally occurring bacteriochlorins requires reliable methods of synthesis from simple precursors to give stable products. Reduction of porphyrins typically affords regioisomeric mixtures of oxidation-sensitive bacteriochlorins.[26] Brückner and Dolphin and Boyle *et al.* have employed vicinal dihydroxylation of porphyrins or chlorins to form tetrahydroxybacteriochlorins, which are quite stable.[27] A complementary approach that we developed entails a *de novo* synthesis of bacteriochlorins.[28] In this approach, the condensation of a 7-*p*-tolyl-substituted dihydrodipyrrin-acetal afforded the corresponding 2,12-di-*p*-tolylbacteriochlorins

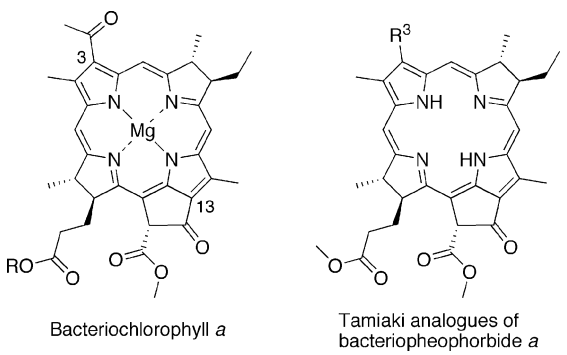


Chart 2

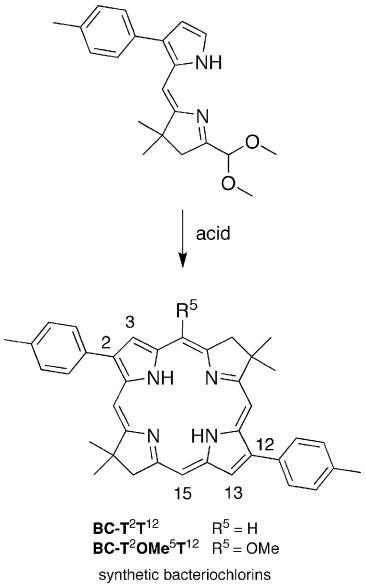


Chart 3

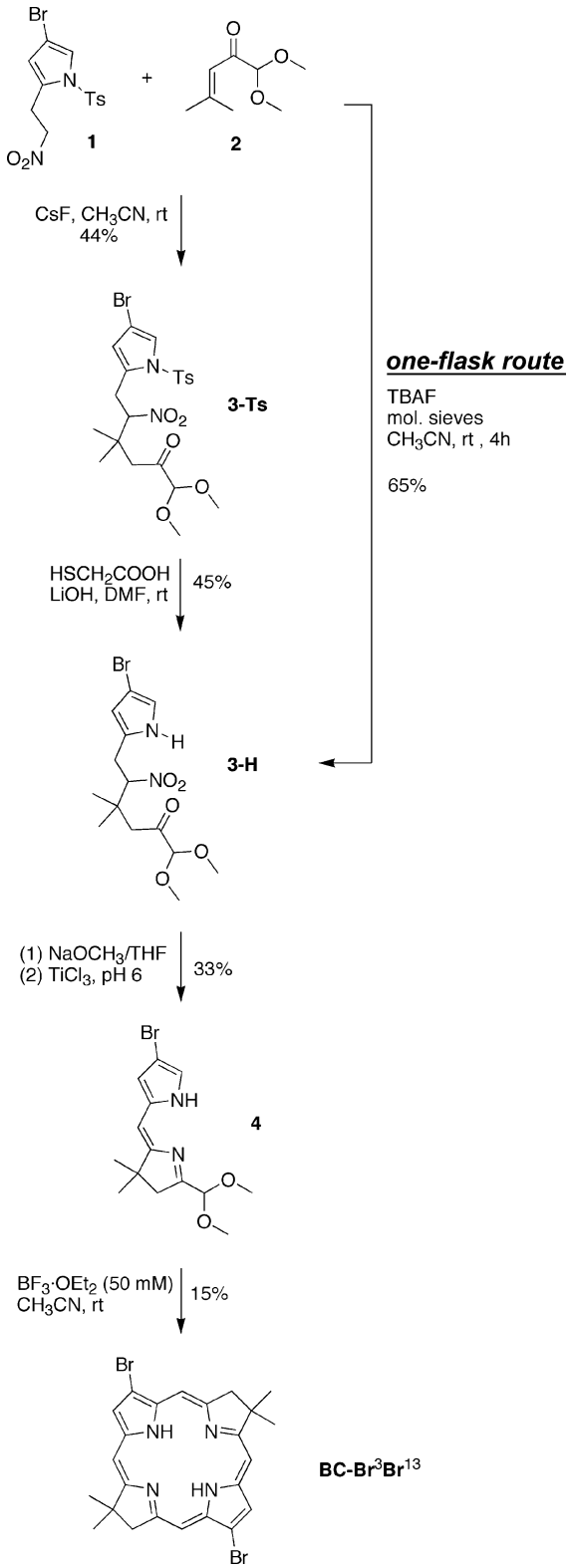
BC-T^{2}T^{12} and **BC-T^{2}OMe^{5}T^{12}** (Chart 3).[28] Further functionalization was achieved by regioselective 15-bromination of **BC-T^{2}OMe^{5}T^{12}**; subsequent Pd-mediated coupling reactions enabled introduction of diverse functional groups at the bacteriochlorin 15-position.[29] The synthetic bacteriochlorins are sufficiently stable for handling on the bench-top owing to the presence of a geminal dimethyl group in each reduced pyrrole ring, which blocks adventitious dehydrogenation to give porphyrins or chlorins. Moreover, the synthetic bacteriochlorins exhibit general photochemical features similar to those of the naturally occurring counterparts.[28–32] The characteristics of **BC-T^{2}OMe^{5}T^{12}** are illustrative in this respect, namely a strong, sharp NIR absorption (λ_{abs} = 732 nm, ε = 120 000 M^{-1} cm^{-1}, fwhm = 20 nm), a sharp emission (λ_{em} = 739 nm, fwhm = 22 nm) with a small Stokes shift (130 cm^{-1}), a long-lived singlet excited state (4.8 ns), and a significant fluorescence quantum yield (Φ_f = 0.18).[28,32]

Given the success in achieving wavelength tunability with synthetic chlorins, we embarked on a program to prepare a set of wavelength-tunable bacteriochlorins. As in the chlorins, the 3- and 13-positions are of most interest in order to accentuate the intensity of the long-wavelength Q_y absorption band. Herein, we report the synthesis of a 3,13-dibromobacteriochlorin by self-condensation of an 8-bromo-substituted dihydrodipyrrin-acetal. The 3,13-dibromobacteriochlorin provides a stable and versatile substrate for a wide variety of Pd-mediated coupling reactions, which enable introduction of diverse auxochromes at both the 3- and 13-positions. The absorption and fluorescence properties of the resulting series of wavelength-tunable bacteriochlorins have been compared with those of several classes of NIR dyes.

Results and discussion

1. Synthesis

A. Precursors to the bacteriochlorin. The synthesis of the bacteriochlorin building block **BC-Br^{3}Br^{13}** is shown in



Scheme 1

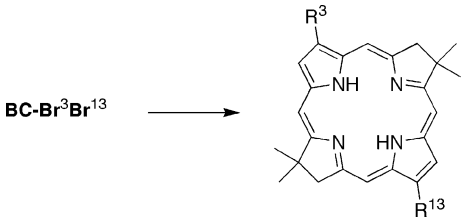
Scheme 1. A key step entails the Michael addition reaction of two advanced precursors, 4-bromo-2-(2-nitroethyl)-*N*-tosylpyrrole (**1**)[16] and 1,1-dimethoxy-4-methyl-3-penten-2-one (**2**).[28] The Michael addition of a 2-nitroethylpyrrole and mesityl oxide (or analogue thereof) is an essential step in the syntheses of chlorins and bacteriochlorins. To date we have employed CsF,[12] tetrabutylammonium fluoride (TBAF),[12] and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[33] for this type of Michael addition. Thus, the Michael addition of **1** and **2** using CsF in CH_3CN at room temperature gave the desired product **3-Ts** in 44% yield. Following a known procedure,[16,34] cleavage of the *N*-tosyl group with LiOH–$HSCH_2COOH$ in DMF at room temperature afforded **3-H** in 45% yield.

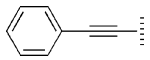
Studies of the Michael addition of **1** and **2** revealed the following: (1) the reaction typically gives a mixture of **3-Ts**, **3-H**, and several side products; (2) the side products derive from **3-H** rather than the starting material or **3-Ts**; and (3) **3-H** is somewhat unstable in solution, especially under heat (although **3-H** can be stored at −10 °C for several months in solid form without showing any sign of decomposition). Accordingly, the Michael addition and detosylation also were performed in one flask by treatment of **1** and **2** with TBAF and molecular sieves in acetonitrile at room temperature, which afforded **3-H** in 65% yield. Cyclization of **3-H** by treatment with NaOMe followed by a buffered (∼pH 6) solution of $TiCl_3$ afforded 8-bromodihydrodipyrrin-acetal **4** in 33% yield.

B. 3,13-Dibromobacteriochlorin. Our previous study of acid-catalyzed bacteriochlorin formation showed that the reaction gives a mixture of bacteriochlorin, 5-methoxy-substituted bacteriochlorin, and a tetradehydrocorrin.[28] The product distribution is dependent on the concentration of acid and the concentration of the dihydrodipyrrin-acetal. A preliminary microscale study of $BF_3{\cdot}OEt_2$ (50 mM) catalyzed condensation of **4** (5 mM) gave the 5-unsubstituted bacteriochlorin selectively. In a larger scale reaction, **BC-Br^3Br^{13}** was obtained in 15% yield (120 mg) without any sign of the 5-methoxy-substituted bacteriochlorin. In some cases, a trace of dibromochlorin also was observed and was readily separated upon chromatography or recrystallization. The structure and origin of the chlorin will be described elsewhere.

C. Other 3,13-disubstituted bacteriochlorins. The 3,13-dibromobacteriochlorin provided a versatile substrate for a variety of Pd-mediated coupling reactions. This strategy mirrors that we have recently employed with 3-bromo, 13-bromo, or 3,13-dibromo chlorins to obtain a series of the corresponding 3- and/or 13-substituted chlorins.[16] The Pd-mediated coupling reactions and 3,13-disubstituted bacteriochlorins derived from the 3,13-dibromobacteriochlorin (**BC-Br^3Br^{13}**) are shown in Table 1. The Suzuki coupling with 2-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, carried out under standard conditions for use with porphyrins,[35,36] chlorins,[15,18] and bacteriochlorins,[29] afforded **BC-Ph^3Ph^{13}** in 94% yield. The Sonogashira coupling with phenylacetylene was carried out under conditions that have been used with porphyrins,[37] chlorins,[15] and bacteriochlorins,[29] affording **BC-PE^3PE^{13}** in 30% yield. Stille coupling with tributyl(vinyl)tin was carried out under conditions that have been employed with porphyrins[38] and chlorins[16] to afford **BC-V^3V^{13}** in 28% yield. The Stille coupling with tributyl(1-ethoxyvinyl)tin followed by acidic hydrolysis unveiled the acetyl group[16,39] to give the 3,13-diacetylbacteriochlorin **BC-A^3A^{13}** in 55% yield.

Table 1 Pd-mediated substitution of **BC-Br^{3}Br^{13}**[a]

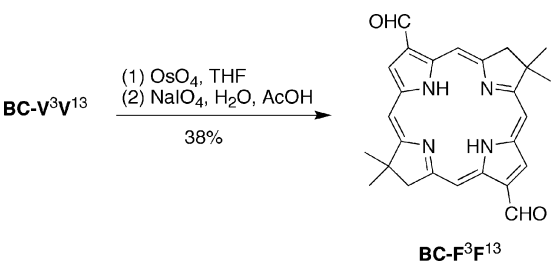


Entry	R^3, R^{13}	Condition	Product	Yield (%)
1		A	**BC-Ph^{3}Ph^{13}**	94
2		B	**BC-PE^{3}PE^{13}**	30
3		C	**BC-V^{3}V^{13}**	28
4		D	**BC-A^{3}A^{13}**	55

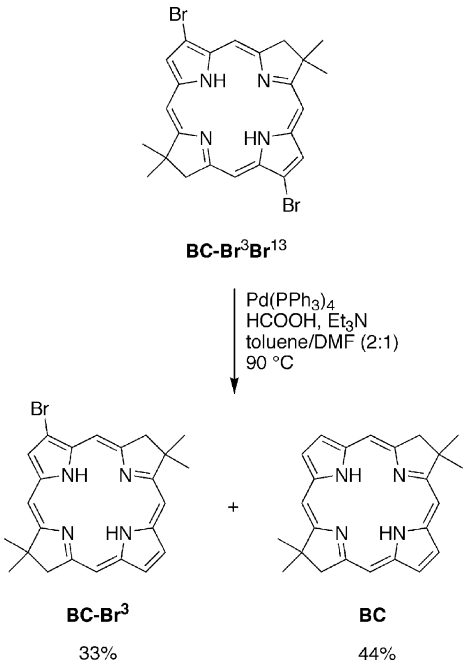
[a] Conditions: (A) 2-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, $Pd(PPh_3)_4$, K_2CO_3, toluene–DMF (2 : 1), Ar, 90 °C, 12 h; (B) phenylacetylene, $Pd_2(dba)_3$, P(*o*-tol)$_3$, toluene–TEA (5 : 1), Ar, 60 °C, 16 h; (C) $Bu_3SnCH{=}CH_2$, $(PPh_3)_2PdCl_2$, THF, reflux, 16 h; (D) (1) tributyl(1-ethoxyvinyl)tin, $(PPh_3)_2PdCl_2$, THF, reflux, 23 h, (2) 10% aq. HCl.

Divinylbacteriochlorin **BC-V^{3}V^{13}** was treated with osmium tetroxide followed by sodium periodate under conditions similar to those reported for porphyrins[40] and chlorins.[41] In this manner, the two vinyl groups were oxidatively cleaved to give the diformylbacteriochlorin **BC-F^{3}F^{13}** in 38% yield (Scheme 2).

D. Benchmark bacteriochlorin. The recent synthesis of sparsely substituted chlorins[17–19] provided the foundation for a series of fundamental spectroscopic studies of these molecules.[20,21] A key element of this study entailed gaining access to the chlorin lacking any *meso*- or β-pyrrole substituents. The analogous bacteriochlorin would also be a valuable benchmark for comparison of its spectral properties with substituent-elaborated bacteriochlorin derivatives, including the naturally occurring bacteriochlorophylls. The synthesis of the benchmark bacteriochlorin was stymied previously in our hands by the apparent limited stability of the unsubstituted dihydrodipyrrin-acetal precursor (*i.e.*, the de-bromo analogue of **4**). An alternative approach to unsubstituted



Scheme 2



Scheme 3

porphyrinic macrocycles entails preparation of a substituted macrocycle followed by removal of the substituent(s). For example, Neya and Funasaki reported that porphine can be synthesized *via* dealkylation of *meso*-tetra(*tert*-butyl)porphyrin.[42] It is known that bromoporphyrins or bromochlorins can undergo debromination under Pd-mediated coupling reaction conditions.[43,44] Treatment of **BC-Br^{3}Br^{13}** under such conditions using formic acid and triethylamine (TEA) afforded partially debrominated bacteriochlorin **BC-Br^3** in 33% yield, and the di-debrominated bacteriochlorin **BC** in 44% yield (Scheme 3).

The benchmark bacteriochlorin **BC** bears a geminal dimethyl group in each reduced ring, and lacks any *meso*- or β-pyrrole substituents. By contrast, the fully unsubstituted bacteriochlorin lacking *gem*-dimethyl groups (**u-BC**, Chart 4) has been prepared by self-condensation of 2-(*N*,*N*-dimethylaminomethyl)pyrrole, or by reduction of chlorin, itself prepared by self-condensation of 2-(*N*,*N*-dimethylaminomethyl)-pyrrole.[45] Only a handful of reports have appeared concerning the photophysical properties of bacteriochlorin **u-BC**,[46–48] perhaps due to the awkward purification and its susceptibility to dehydrogenation yielding chlorin or porphine. The presence of the geminal dimethyl groups in the benchmark **BC** are not expected to alter significantly the electronic or photophysical features, analogous to what we have found for chlorins.[21,22]

All bacteriochlorins prepared herein were characterized by ^{1}H NMR spectroscopy, laser-desorption mass spectrometry in the absence of a matrix,[49] and absorption and fluorescence spectroscopy. The absorption and fluorescence spectroscopic results are described in the next section.

2. Electronic spectra of 3,13-disubstituted bacteriochlorins

A. Absorption spectra. The absorption spectra of the synthetic bacteriochlorins were measured in toluene at room temperature and are shown in Fig. 1. For comparison

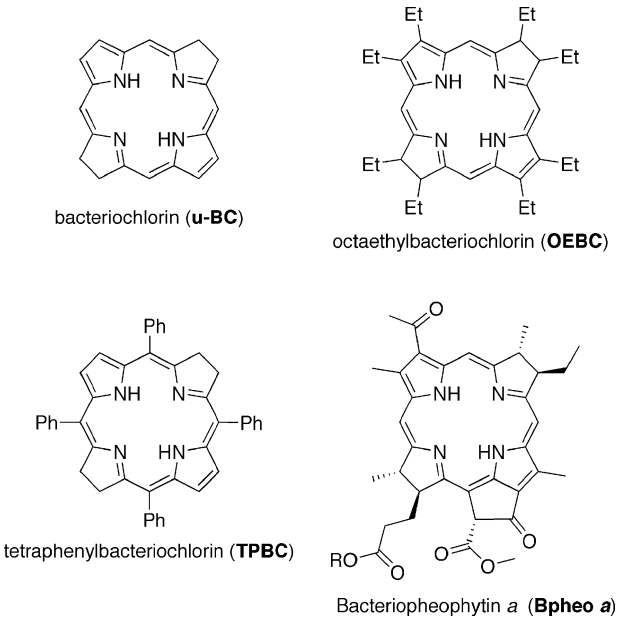


Chart 4

purposes, spectra were normalized to the maximum intensity of the $Q_y(0,0)$ band, which is the prominent, longest-wavelength feature in the spectrum. The assignment of the bands from lowest to highest energy (Q_y, Q_x, B_x, B_y) follows the standard convention.[23] In general, the absorption spectra of bacteriochlorins exhibit a strong dependence on the substituents at the 3- and 13-positions. For example, for the benchmark **BC**, the absorption maxima of the $Q_y(0,0)$, $B_x(0,0)$, and $B_y(0,0)$ bands are 713, 365, and 340 nm, respectively. For the diformyl analogue (**BC-F^{3}F^{13}**) the analogous bands are 771, 393, and 363 nm, respectively.

The spectral properties of the series of 3,13-disubstituted bacteriochlorins prepared herein are listed in Table 2. Also included in the table are data for the 2,12-di-*p*-tolylbacteriochlorin **BC-T^{2}T^{12}** prepared previously,[28] two traditional synthetic bacteriochlorins [octaethylbacteriochlorin (**OEBC**) and tetraphenylbacteriochlorin (**TPBC**)],[50] and the free base derivative of bacteriochlorophyll *a*, bacteriopheophytin *a* (**BPheo *a***).[51,52] The structures are shown in Charts 3 and 4. Note that the latter compound contains the isocyclic ring wherein the keto group is coplanar with the bacteriochlorin macrocycle.[1] The shifts of each transition ($B_y(0,0)$, $B_x(0,0)$, $Q_x(0,0)$, and $Q_y(0,0)$) from those of the benchmark bacteriochlorin **BC** are

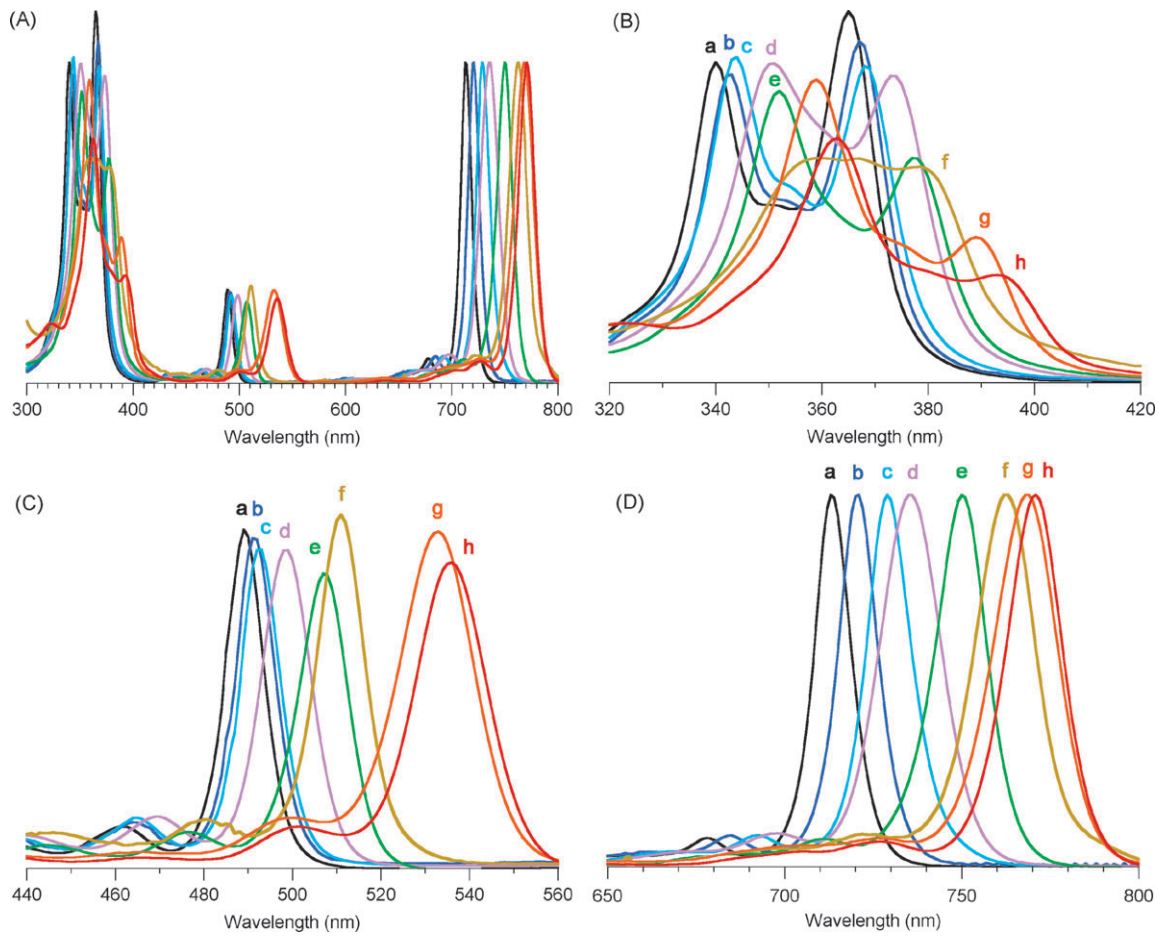


Fig. 1 Absorption spectra in toluene at room temperature of bacteriochlorins (normalized at the Q_y bands). (A) Entire spectra, (B) magnification of B_y and B_x region, (C) magnification of Q_x region, and (D) magnification of Q_y region. The labels and the colors in the graph are as follows: **BC** (a, black), **BC-Br^3** (b, blue), **BC-Br^{3}Br^{13}** (c, light blue), **BC-Ph^{3}Ph^{13}** (d, purple), **BC-V^{3}V^{13}** (e, lime), **BC-PE^{3}PE^{13}** (f, light brown), **BC-A^{3}A^{13}** (g, orange), and **BC-F^{3}F^{13}** (h, red).

Table 2 Absorption spectral properties of bacteriochlorins[a]

Compound	$\lambda B_y(0,0)$/ nm	$\Delta B_y(0,0)$/ cm^{-1}[b]	$\lambda B_x(0,0)$/ nm	$\Delta B_x(0,0)$/ cm^{-1}[b]	$\lambda Q_x(0,0)$ (fwhm)/nm	$\Delta Q_x(0,0)$/ cm^{-1}[b]	$\lambda Q_y(0,0)$ (fwhm)/nm	$\Delta Q_y(0,0)$/ cm^{-1}[b]	$I_{Q_y(0,0)}/I_{B_x(0,0)}$[c]	$I_{Q_y(0,0)}/I_{B_y(0,0)}$[d]	Σ_{Q_y}/Σ_B[e]
BC	340	0	365	0	489 (10)	0	713 (12)	0	1.0	0.86	0.46
BC-Br^3	343	250	367	150	491 (11)	−80	721 (13)	−150	1.04	0.94	0.51
BC-Br^{3}Br^{13}	344	350	368	200	493 (11)	−150	729 (15)	−300	0.98	1.01	0.55
BC-T^{2}T^{12}[f]	351	920	374	650	499 (13)	−400	737 (20)	−460	1.02	1.06	0.59
BC-Ph^{3}Ph^{13}	351	920	373	600	499 (13)	−400	736 (20)	−440	1.00	1.04	0.60
BC-V^{3}V^{13}	352	1000	377	870	507 (13)	−730	750 (17)	−690	1.10	1.43	0.65
BC-PE^{3}PE^{13}	360[g]	1600	378	940	511 (13)	−880	763 (20)	−920	1.43	1.48	0.65
BC-A^{3}A^{13}	359	1550	389	1700	533 (20)	−1700	768 (21)	−1000	1.06	2.20	0.72
BC-F^{3}F^{13}	363	1850	393	1950	536 (19)	−1800	771 (19)	−1050	1.31	2.97	0.71
OEBC[h]	346	500	375	730	490 (9)	−40	724 (12)	−210	0.92	0.86	0.39
TPBC[h]	356[i]	1300	378	950	522 (15)	−1300	742 (14)	−550	1.12	0.87	0.45
BPheo *a*[j]	356	1300	383	1300	525 (22[k])	−1400	750 (30[k])	−690	0.59	1.08	0.59[k]

[a] In toluene at room temperature unless noted otherwise. [b] The shift of the band relative to that of the parent bacteriochlorin (**BC**). [c] Ratio of the intensities of the $B_y(0,0)$ and $Q_y(0,0)$ bands. [d] Ratio of the intensities of the $B_x(0,0)$ and $Q_y(0,0)$ bands. [e] Ratio of the integrated intensities of the B (B_y and B_x; 320–420 nm) and Q_y [$Q_y(0,0)$ and vibrational progression including $Q_y(1,0)$; 660–800 nm] bands. [f] Absorption data from ref. 28. [g] Shoulder at 367 nm. [h] Absorption data from ref. 50 (in benzene). [i] Shoulder at 368 nm. [j] Absorption data from ref. 51 (in diethyl ether). [k] Data from ref. 52 (in diethyl ether).

tabulated to evaluate the effect of the substituents. Several observations are noteworthy:

(1) The spectral range covered by the $Q_y(0,0)$ band of the synthetic bacteriochlorins (λ = 713–771 nm) spans a larger range than that of the traditional synthetic benchmarks (**OEBC**, **TPBC**) and the naturally occurring **BPheo *a***, which together encompass 724–750 nm.

(2) The benchmark bacteriochlorin **BC** generally exhibits the sharpest absorption features [$Q_y(0,0)$, fwhm = 12 nm; $Q_x(0,0)$, fwhm = 10 nm]. The widths of the $Q_y(0,0)$ and $Q_x(0,0)$ bands tend to increase as these transitions shift toward longer wavelengths. For example, **BC-A^{3}A^{13}** and **BC-F^{3}F^{13}** exhibit $Q_y(0,0)$ and $Q_x(0,0)$ bands with fwhm ~20 nm. **BPheo *a*** has the broadest absorption features with $Q_y(0,0)$ and $Q_x(0,0)$ exhibiting fwhm = 30 and 22 nm, respectively.

(3) The 2,12-diaryl-substituted bacteriochlorin **BC-T^{2}T^{12}** and the 3,13-diphenyl-substituted bacteriochlorin **BC-Ph^{3}Ph^{13}** exhibit nearly identical spectra. The similarity of the spectra for **BC-T^{2}T^{12}** and **BC-Ph^{3}Ph^{13}** suggests that the *gem*-dimethyl groups at the reduced pyrrole ring cause no significant steric or electronic effects on the photophysical features. Note, that in the absence of the geminal dimethyl groups, the 2,12- and 3,13-positions in the otherwise unsubstituted bacteriochlorin would be equivalent. The equivalence stems from the symmetry of the bacteriochlorin chromophore, wherein positions 2 and 3 are symmetrically disposed on opposite sides of the *x*-axis, as is also the case for the 12- and 13-positions.

(4) The absorption characteristics of **OEBC** and **TPBC** exhibit different trends when compared with those of **BC**. The $Q_x(0,0)$ band of **OEBC** is shifted by 40 cm^{-1} *versus* **BC**, a shift much smaller than that exhibited by the $B_y(0,0)$, $B_x(0,0)$, or $Q_y(0,0)$ bands. In contrast, the $Q_x(0,0)$ band of **TPBC** shifts 1300 cm^{-1} compared to that of **BC**, a shift much larger than that exhibited by the $B_y(0,0)$, $B_x(0,0)$, or $Q_y(0,0)$ bands. Relatively little room-temperature solution spectral data has been reported for bacteriochlorin (**u-BC**), for which the $Q_y(0,0)$ band appears at ~720 nm in *n*-hexane[46] or 722.5 nm in *n*-octane.[48]

(5) Introduction of the 3,13-substituents causes the position of all absorption bands [$B_y(0,0)$, $B_x(0,0)$, $Q_x(0,0)$, and $Q_y(0,0)$] to shift in the same direction (bathochromically or hypsochromically). The magnitude of the shift [$\Delta B_y(0,0)$, $\Delta B_x(0,0)$, $\Delta Q_x(0,0)$, and $\Delta Q_y(0,0)$] relative to the benchmark **BC** is listed in Table 2. Plots of $\Delta B_y(0,0)$, $\Delta B_x(0,0)$, and $\Delta Q_x(0,0)$ *versus* $\Delta Q_y(0,0)$ for the series of seven 3,13-substituted bacteriochlorins are shown in Fig. 2. The correlation of shifts is fairly linear across the series of bacteriochlorins. In other words, among the five substituents examined, the substituent (formyl) that causes the largest effect on one band does so for all bands, whereas the substituent (bromo) that causes the smallest effect on one band also has the smallest effect on all other bands. The magnitude of the shift across the series of 3,13-substituted bacteriochlorins is large for $B_y(0,0)$ ~1850 cm^{-1}, $B_x(0,0)$ ~1950 cm^{-1}, and $Q_x(0,0)$ ~1800 cm^{-1}, but less for $Q_y(0,0)$ ~1050 cm^{-1}.

(6) For chlorophylls, the ratio of the peak intensities of the B and Q_y bands (*e.g.*, I_B/I_{Q_y} ratio) has traditionally been employed as an indicator of the intensification of the Q_y band as a function of the presence of different substituents. This

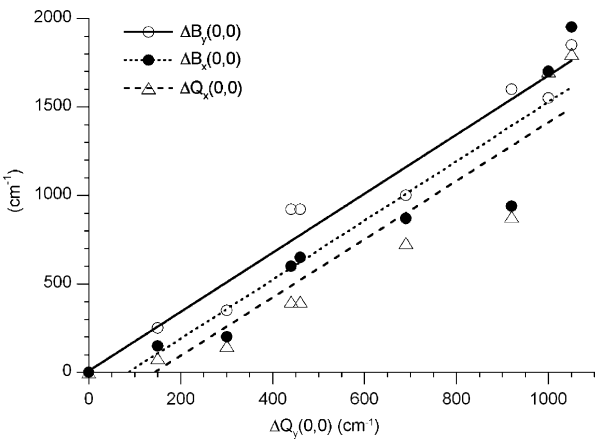


Fig. 2 Correlation between the spectral shift for the long-wavelength transition [$\Delta Q_y(0,0)$] and any other transition [$\Delta B_y(0,0)$, $\Delta B_x(0,0)$, $\Delta Q_x(0,0)$], given for synthetic bacteriochlorins *versus* the benchmark bacteriochlorin **BC**.

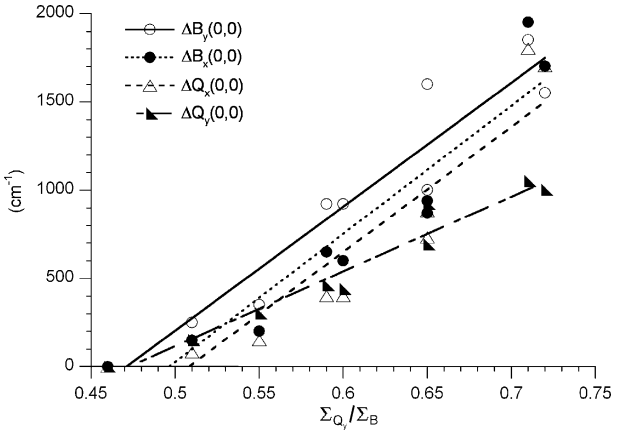


Fig. 3 Correlation between the ratio of the integration of the Q_y and B band regions (Σ_{Q_y}/Σ_B) and the shift of each transition [$\Delta B_y(0,0)$, $\Delta B_x(0,0)$, $\Delta Q_x(0,0)$, and $\Delta Q_y(0,0)$], given for synthetic bacteriochlorins *versus* the benchmark bacteriochlorin **BC**.

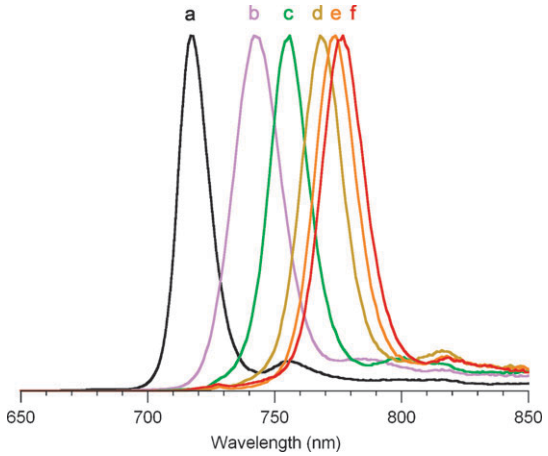


Fig. 4 Emission spectra in toluene at room temperature of bacteriochlorins (normalized). The labels and the colors in the graph are as follows: **BC** (a, black), **BC-Ph^{3}Ph^{13}** (b, purple), **BC-V^{3}V^{13}** (c, lime), **BC-PE^{3}PE^{13}** (d, light brown), **BC-A^{3}A^{13}** (e, orange), and **BC-F^{3}F^{13}** (f, red).

ratio has been used in lieu of direct comparison of molar absorption coefficients, owing to the unreliability of molar absorption coefficients encountered upon handling small quantities of materials.[53] For the bacteriochlorins, similar comparisons can be made for the ratios of the B and Q_y bands. The ratio of Q_y to the individual B bands of the bacteriochlorins ($I_{Q_y(0,0)}/I_{B_y(0,0)}$ or $I_{Q_y(0,0)}/I_{B_x(0,0)}$) is not entirely accessible owing to the overlap of the $B_y(0,0)$ and $B_x(0,0)$ bands. Accordingly, we evaluated the ratio of the integrated B and Q_y band region (Σ_{Q_y}/Σ_B). A plot of the shift of each band from that of the benchmark bacteriochlorin transition [$\Delta B_y(0,0)$, $\Delta B_x(0,0)$, $\Delta Q_x(0,0)$, and $\Delta Q_y(0,0)$] *versus* the Σ_{Q_y}/Σ_B for the series of 3,13-substituted bacteriochlorins is shown in Fig. 3. A reasonably linear correlation is observed, which indicates that the shift of the transition toward longer wavelength is accompanied by a relative increase in the intensity of the Q_y band. The increase is predominantly in the $Q_y(0,0)$ transition since there is relatively little intensity in the vibronic satellite bands.

B. Fluorescence properties. The fluorescence properties of the synthetic bacteriochlorins were examined in toluene at room temperature. The fluorescence spectra are displayed in Fig. 4. In each case, the fluorescence spectrum mirrors the long-wavelength absorption band, exhibiting a strong $Q_y(0,0)$ transition and a much weaker, almost negligible $Q_y(0,1)$ transition. The fwhm of the $Q_y(0,0)$ transition is 14 to 22 nm; the Stokes shift ($\Delta\nu$) between absorption and emission origin transitions ranges from 70 to 130 cm^{-1}. The fluorescence spectral properties are summarized in Table 3.

The fluorescence quantum yields (Φ_f) were measured in deaerated toluene at room temperature using excitation in the $B_y(0,0)$ band at 363 nm (Table 3). The same results were obtained using excitation in the $Q_x(0,0)$ band (489 to 536 nm). The bromobacteriochlorins exhibit quite weak fluorescence, as expected due to the heavy atom effect. Otherwise, the fluorescence quantum yields ranged from 0.15 for bis(phenylethynyl)bacteriochlorin **BC-PE^{3}PE^{13}** to 0.070 for the diformylbacteriochlorin **BC-F^{3}F^{13}**, to be compared with 0.14 for **BC-T^{2}T^{12}**. The decrease in fluorescence quantum yield generally parallels the bathochromic shift of the $Q_y(0,0)$ band.

The fluorescence quantum yield of **BC-F^{3}F^{13}** is of particular interest given that several formylhydroporphyrins have been reported to exhibit very low fluorescence quantum yields. For example, introduction of a *meso*-formyl substituent in a chlorin e_6 derivative suppressed the fluorescence quantum yield ~20 fold,[54] and a series of *meso*-formylbacteriochlorin derivatives exhibited very low fluorescence quantum yields (~0.002).[55] On the other hand, the fluorescence quantum yield of **BC-F^{3}F^{13}** is lower by only ~60% compared to that of the benchmark bacteriochlorin **BC**. Further study is required to probe the origin of such disparate fluorescence properties owing to the presence of *meso- versus* β-formyl groups.

C. Comparison with other NIR dyes. The NIR spectral and photophysical attributes of the series of 3,13-disubstituted bacteriochlorins (*e.g.*, Fig. 5B) can be compared with those of other NIR dyes[2,11] such as cyanine dyes, quantum dots, and expanded porphyrins (Fig. 5A, C and D).

Table 3 Fluorescence spectral properties of bacteriochlorins

Compound	λ_{em} (fwhm)/nm[a]	$\Delta\nu$/cm^{-1}[b]	Φ_f[c]
BC	717 (14)	80	0.11
BC-Br^3	725 (15)	80	<0.02[d]
BC-Br^{3}Br^{13}	733 (16)	70	<0.002[d]
BC-T^{2}T^{12}	744 (21)	130	0.14
BC-Ph^{3}Ph^{13}	742 (22)	110	0.12
BC-V^{3}V^{13}	756 (20)	110	0.10
BC-PE^{3}PE^{13}	768 (20)	90	0.15
BC-A^{3}A^{13}	774 (20)	100	0.088
BC-F^{3}F^{13}	777 (20)	100	0.070

[a] Excitation was performed at the λ_{max} of 363 nm. [b] Stokes shift. [c] Determined in toluene at room temperature with λ_{exc} at 363 nm using chlorophyll *a* as a standard unless otherwise noted. See ref. 16 and 20 for methods. [d] Determined in toluene at room temperature with λ_{exc} at the Q_x band (491 or 493 nm) using **BC-T^{2}T^{12}** as a standard.[28]

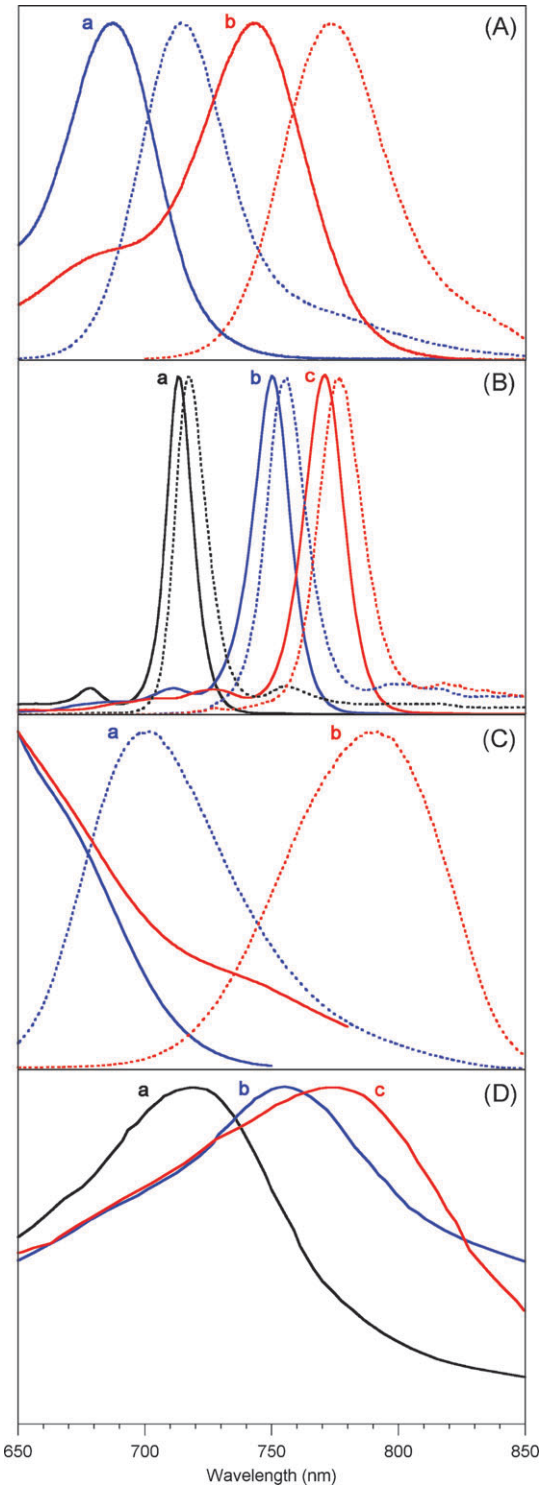
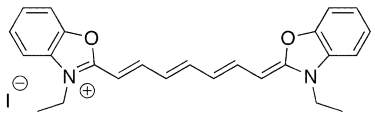
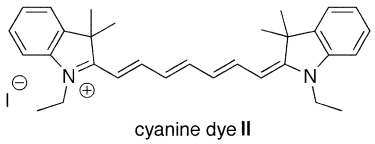


Fig. 5 Absorption (—) and emission (--) spectra of known dyes and new bacteriochlorins. Intensity is normalized. The labels and colors are as follows: (A) tricarbocyanine dyes **I** (a, blue) and **II** (b, red).[57–59] (B) Bacteriochlorins **BC** (a, black), **BC-V^{3}V^{13}** (b, blue), and **BC-F^{3}F^{13}** (c, red). (C) Quantum dots QDot 705 (a, blue) and QDot 800 (b, red).[6,62] (D) Expanded porphyrins containing 9 (a, black), 10 (b, blue), or 11 (c, red) pyrrole units.[63]





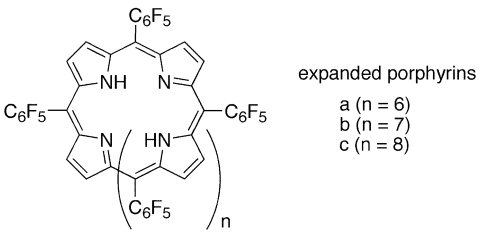


Chart 5

The spectral features of cyanine dyes can be tuned from the near-UV across the visible into the NIR by lengthening the polyene chain and/or by alteration of the terminal heterocyclic units.[56] Common NIR cyanine dyes include 1,1′-diethylbenzoxatricarbocyanine **I**[57] and 1,1′-diethyl-3,3,3′,3′-tetramethylindotricarbocyanine **II**;[57,58] the latter is an analogue of the widely used fluorescent standard 1,1′,3,3,3′,3′-hexamethylindotricarbocyanine (HITC).[59] The structures of such dyes are shown in Chart 5, and the absorption and emission spectra[60] are shown in Fig. 5A. The fwhm of the absorption/emission bands are 45/44 nm and 53/49 nm for **I** and **II**, respectively, and the Stokes shift is $\sim$500 cm^{-1} in each case.

Quantum dots also can be tuned by alteration of size and elemental composition.[61] The emission spectra of quantum dots in the visible range typically are rather sharp, but, at least for the materials in common use, the spectra in the NIR range are rather broad. Typical spectra are shown in Fig. 5C for Qdot 705 and Qdot 800.[6,62] The fwhm of the emission band is 66 or 74 nm for Qdot 705 or Qdot 800, respectively.

A more recent example of tunable chromophores entails a series of expanded porphyrins.[63] The absorption spectra of three expanded porphyrins are shown in Fig. 5D. The fwhm is 122, 185, and 182 nm along the series of expanded porphyrins containing 9–11 pyrrole units.

For all of the systems shown in Fig. 5A, C and D, wavelength tunability is achieved; however, the absorption spectra and emission spectra (where available) are quite broad. The broad absorption and emission bands limit the number of distinct components that can be incorporated in the NIR spectral window. Other classes of dyes of potential interest include derivatives of dipyrrinatoboron-difluoride, perylene, and phthalocyanine.[11] In the case of dipyrrinatoboron-difluoride and perylene dyes, substantial structural modification is required to shift the absorption into the NIR.[64,65] In the case of phthalocyanines, simple annulation or substitution does afford absorption in the NIR.[66] Regardless, the phthalocyanines in general exhibit rather limited synthetic malleability.[67] These compounds also exhibit a pronounced tendency to

aggregate, even for the neutral phthalocyanines in organic solutions. Finally, we note that many dyes are charged (*e.g.*, cyanines, triarylmethanes, oxazines/thiazines), which can significantly complicate the synthetic chemistry and purification.[68] By contrast, the bacteriochlorins exhibit sharp absorption and emission spectra (<20 nm fwhm), can be readily tuned *via* systematic synthesis (absorption 713–771 nm; emission 717–777 nm), bear no intrinsic charge (yet in principle can be derivatized with cationic or anionic substituents if desired), and are stable on routine handling.

Outlook

A concise *de novo* route to a stable 3,13-dibromobacteriochlorin **BC-Br^{3}Br^{13}** has been developed. The 3,13-dibromobacteriochlorin **BC-Br^{3}Br^{13}** can be tailored with a wide variety of groups by Pd-mediated coupling reactions including Sonogashira, Suzuki, and Stille coupling reactions. The sparsely substituted bacteriochlorin **BC**, obtained by debromination of **BC-Br^{3}Br^{13}**, provides a valuable benchmark for spectroscopic comparison with more elaborate bacteriochlorins. A stable bacteriochlorin lacking β-pyrrole and *meso*-substituents has heretofore not been available.

The absorption spectra of bacteriochlorins can be manipulated by substitution at the 3- and 13-positions. Indeed, a family of chromophores with ~10 nm increments in absorption or emission spectra can now be obtained. The bathochromic shift of the $Q_y(0,0)$ band imparted by 3,13-diformyl or 3,13-diacetyl substitution is substantial (~1000 cm^{-1}) and is accompanied by intensification of the $Q_y(0,0)$ band. On the other hand, the fluorescence yield decreases by as much as ~60% upon 3,13-diformyl or 3,13-diacetyl substitution. The extent to which the long-wavelength transition of bacteriochlorins can be further shifted into the NIR region while retaining the desired photochemical attributes (sharp spectral bands, reasonably long-lived excited singlet-state, relatively high fluorescence yield) remains to be determined.

For extension to biological applications, provisions for water solubilization and bioconjugation may be necessary. In this regard, high aqueous solubility of tetrapyrrole macrocycles has recently been achieved through use of a diphosphonate- or diphosphate-terminated branched alkyl group appended to the tetrapyrrole macrocycle.[69] The availability of the 3,13-dibromobacteriochlorin **BC-Br^{3}Br^{13}** should enable a much broader examination of substituents for tuning the spectral and photochemical properties of bacteriochlorins, and for tailoring the molecular structure as desired for extension to a number of photochemical applications.

Experimental

General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were collected at room temperature in $CDCl_3$. Bacteriochlorins were analyzed by laser desorption mass spectrometry without a matrix (LD-MS).[49] Fast atom bombardment mass spectrometry (FAB-MS) or electrospray ionization mass spectrometry (ESI-MS) data are reported for the molecule ion or protonated molecule ion. Chromatography was performed with flash silica (80–200 mesh).

Absorption and fluorescence spectra were obtained in toluene (spectroscopic grade) at room temperature as described previously.[16,20] The bacteriochlorins were excited at 363 nm, a wavelength where each bacteriochlorin shows sufficient absorption intensity: each bacteriochlorin exhibited an absorption of at least 0.060 at the wavelength of excitation when the most intense absorption band exhibited an absorption of 0.10. The wavelength 363 nm was the λB_x maximum for **BC-F^{3}F^{13}**, which was the least emissive bacteriochlorin with the exception of the bromobacteriochlorins.

Fluorescence quantum yields (Φ_f) were measured as described previously[16,22] for de-aerated toluene solutions of the bacteriochlorins using chlorophyll *a* (Φ_f = 0.325)[70] as a standard. All samples were excited at the same wavelength (363 nm; A = 0.060–0.10). The same results to within ±15% were obtained using excitation in the $Q_x(0,0)$ band (489 to 536 nm).

All commercially available materials including the molecular sieves were used as received. 4-Bromo-2-(2-nitroethyl)-*N*-tosylpyrrole (**1**)[16] and 1,1-dimethoxy-4-methyl-3-penten-2-one (**2**)[28,71] were prepared following literature procedures.

All of the palladium-mediated coupling reactions were performed under argon using a Schlenk line technique.[37] The Schlenk flask equipped with reflux condenser was attached, *via* thick-walled Tygon tubing, to a dual manifold. The flask containing all solid materials was evacuated *via* a vacuum pump for 3 min and after the evacuation period the flask was back-flushed with argon for 3 min. The process of evacuation and flushing was performed a total of 5 times. De-aerated solvents were introduced by syringe, while argon flow was increased and the threaded stopcock was removed. The threaded stopcock was replaced and Pd-mediated coupling reactions were carried out under each condition described below.

6-(4-Bromo-*N*-tosylpyrrol-2-yl)-1,1-dimethoxy-4,4-dimethyl-5-nitrohexanone (3-Ts). Following a general procedure[16,28] for Michael addition of 2-(2-nitroethyl)pyrrole with slight modification, a mixture of **1** (3.73 g 10.0 mmol) and **2** (1.47 g, 11.0 mmol) in dry acetonitrile (100 mL) was transferred by syringe to a flask containing CsF (7.60 g, 50.0 mmol, 5 mol equiv., freshly dried by heating to 100 °C under vacuum for 1 h prior to the reaction) and stirred under argon for 24 h at room temperature. The reaction mixture was poured into water and extracted with ethyl acetate. The organic extract was dried (Na_2SO_4) and filtered. The filtrate was concentrated to dryness. The residue was chromatographed [silica, hexanes–ethyl acetate (4 : 1)] to give a brown oil, which solidified on standing at −10 °C to a light brown solid (2.32 g, 44%): mp 73–75 °C; ^{1}H NMR δ 1.14 (s, 3H), 1.23 (s, 3H), 2.44 (s, 3H), 2.60, 2.69 (AB, ^{2}J = 18.6 Hz, 2H), 3.19 (ABX, $^{2}J_{AB}$ = 15.7 Hz, $^{3}J_{BX}$ = 2.0 Hz, 1H), 3.37 (ABX, $^{2}J_{AB}$ = 15.7 Hz, $^{3}J_{AX}$ = 11.7 Hz, 1H), 3.42 (s, 6H), 4.36 (s, 1H), 5.19 (ABX, $^{3}J_{AX}$ = 11.7 Hz, $^{3}J_{BX}$ = 2.0 Hz, 1H), 6.02 (s, 1H), 7.27 (s, 1H), 7.35 (AA′XX′, 2H), 8.32 (AA′XX′, 2H); ^{13}C NMR δ 21.9, 23.97, 24.20, 26.5, 36.7, 44.7, 55.31, 55.34, 93.5, 101.0, 104.9, 117.1, 122.5, 126.9, 130.25, 130.63, 135.6, 146.0, 203.3. Anal calcd for

$C_{21}H_{27}BrN_2O_7S$: C, 47.46; H, 5.12; N, 5.27. Found: C, 47.18; H, 5.09; N, 5.28%.

6-(4-Bromo-1*H*-pyrrol-2-yl)-1,1-dimethoxy-4,4-dimethyl-5-nitrohexanone (3-H). Following a reported procedure for cleavage of the tosyl group,[16,34] a stirred suspension of **3-Ts** (1.86 g, 3.50 mmol) and LiOH (393 mg, 16.4 mmol) in anhydrous DMF (17.5 mL) was treated with $HSCH_2COOH$ (490 μL, 7.00 mmol) at room temperature under argon. The reaction was monitored by ^{1}H NMR spectroscopy to confirm the deprotection of the tosyl group. To force the reaction to completion, after 15 h additional LiOH (393 mg, 16.4 mmol) and $HSCH_2COOH$ (490 μL, 7.00 mmol) were added to the reaction mixture. After stirring for 3 h, the reaction mixture was poured into water and extracted with ethyl acetate. The organic extract was dried (Na_2SO_4) and filtered. The filtrate was concentrated to dryness. The residue was chromatographed [silica, hexanes–CH_2Cl_2 (1 : 1)] to give a white solid (592 mg, 45%): mp 77–81 °C; ^{1}H NMR δ 1.09 (s, 3H), 1.18 (s, 3H), 2.57, 2.68 (AB, ^2J = 18.8 Hz, 2H), 2.95 (ABX, $^2J_{AB}$ = 15.4 Hz, $^3J_{BX}$ = 2.2 Hz, 1H), 3.27 (ABX, $^2J_{AB}$ = 15.4 Hz, $^3J_{AX}$ = 11.8 Hz, 1H), 3.40 (s, 6H), 4.34 (s, 1H), 5.11 (ABX, $^3J_{AX}$ = 11.8 Hz, $^3J_{BX}$ = 2.2 Hz, 1H), 5.93 (s, 1H), 6.58 (s, 1H), 8.43–8.58 (br, 1H); ^{13}C NMR δ 24.34, 24.43, 26.9, 36.6, 45.3, 55.4, 94.6, 96.2, 104.8, 110.0, 117.8, 127.3, 204.0. Anal calcd for $C_{14}H_{21}BrN_2O_5$: C, 44.57; H, 5.61; N, 7.43. Found: C, 44.77; H, 5.44; N, 7.36%.

Direct synthesis of 3-H. A solution of **1** (11.2 g, 30.0 mmol) and **2** (5.69 g, 36.0 mmol) in dry CH_3CN (53.3 mL) was treated with 3 Å molecular sieves (6.67 g) for 30 min at room temperature under argon. The reaction mixture was treated with TBAF·$3H_2O$ (39.2 g, 150 mmol) for 3 h at room temperature under argon, then additional TBAF·$3H_2O$ (15.7 g, 60 mmol) was added as deemed necessary upon monitoring by ^{1}H NMR spectroscopy. After 1 h, the reaction mixture was filtered. The filtrate was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate. The organic solution was washed with water, dried (Na_2SO_4), and chromatographed [silica, CH_2Cl_2] to give a brown oil which solidified upon storing at −10 °C (7.31 g, 65%). The characterization data were consistent with the data described above.

8-Bromo-2,3-dihydro-1-(1,1-dimethoxymethyl)-3,3-dimethyldipyrrin (4). Following a general procedure for dihydrodipyrrin synthesis,[12,28] a solution of **3-H** (4.90 g, 13.0 mmol) in distilled THF (70 mL) was treated with NaOMe (3.54 g, 64.8 mmol), and the mixture was stirred for 1 h at room temperature under argon (first flask). In a second flask, $TiCl_3$ (10.0 g, 64.8 mmol), aqueous HCl (13 mL) and H_2O (175 mL) were combined; NH_4OAc (326 g, 2.93 mol) was added to buffer the solution to pH 6, and then THF (18 mL) was added. The buffered mixture was degassed with argon for 1 h. The solution in the first flask containing the nitronate anion of **3-H** was transferred *via* cannula to the buffered $TiCl_3$ solution in the second flask. The resulting mixture was stirred at room temperature for 16 h under argon. A saturated aqueous solution of $NaHCO_3$ (200 mL) was added to the reaction mixture, which was then extracted with ethyl acetate. The organic extract was dried (Na_2SO_4) and concentrated at reduced pressure. The residue was chromatographed [alumina, hexanes–ethyl acetate (3 : 1)] to give a light brown oil which solidified upon standing at room temperature (1.39 g, 33%): mp 101–103 °C; ^{1}H NMR δ 1.20 (s, 3H), 1.25 (s, 3H), 2.61 (s, 2H), 3.44 (s, 6H), 5.01 (s, 1H), 5.77 (s, 1H), 6.12 (s, 1H), 6.78 (s, 1H), 10.62–10.74 (br, 1H); ^{13}C NMR δ 29.2, 29.9, 40.3, 48.4, 54.80, 54.84, 96.7, 102.8, 106.6, 111.1, 119.0, 131.5, 161.0, 175.4. Anal calcd for $C_{14}H_{19}BrN_2O_2$: C, 51.39; H, 5.58; N, 8.56. Found: C, 51.51; H, 5.91; N, 8.37%.

3,13-Dibromo-8,8,18,18-tetramethylbacteriochlorin (BC-Br^{3}Br^{13}). Following a general procedure for bacteriochlorin synthesis,[28] a solution of **4** (982 mg, 3.00 mmol, 5.0 mM) in HPLC-grade CH_3CN (600 mL) was treated with neat BF_3·OEt_2 (3.77 mL, 30.0 mmol, 50 mM) dropwise over 3 min at room temperature. The reaction was allowed to proceed at room temperature for 17 h. TEA was added (4.20 mL) to the reaction mixture. The reaction mixture was then concentrated. Note that the title compound has poor solubility in organic solvents such as hexanes and CH_2Cl_2; hence, the mixture was not concentrated to dryness. Chromatography of the crude product over a short column [silica, hexanes–CH_2Cl_2 (2 : 1)] afforded a single band, which upon isolation and concentration gave a green solid (120 mg, 15%): ^{1}H NMR δ −2.17 to −2.13 (br, 2H), 1.95 (s, 12H), 4.46 (s, 4H), 8.60 (s, 2H), 8.77 (d, J = 2.0 Hz, 2H), 8.90 (s, 2H); LD-MS obsd 526.9; FAB-MS obsd 526.0355, calcd 526.0368 ($C_{24}H_{24}Br_2N_4$); λ_{abs} 344, 369, 493, 729 nm.

Functionalization of bacteriochlorins

3,13-Bis(phenylethynyl)-8,8,18,18-tetramethylbacteriochlorin (BC-PE^{3}PE^{13}). Following a procedure for Sonogashira coupling with chlorins,[15] a mixture of **BC-Br^{3}Br^{13}** (10.5 mg, 20.0 μmol), phenylacetylene (6.6 μL, 60 μmol), $Pd_2(dba)_3$ (2.7 mg, 3.0 μmol), and P(o-tol)$_3$ (7.3 mg, 24 μmol) was heated at 60 °C in toluene–TEA (5 : 1, 10 mL) in a Schlenk flask. After 8 h, phenylacetylene (6.6 μL, 60 μmol), $Pd_2(dba)_3$ (2.7 mg, 3.0 μmol), and P(o-tol)$_3$ (7.3 mg, 24 μmol) were added to the reaction mixture. After 8 h, the reaction mixture was concentrated to dryness. The residue was chromatographed [silica, hexanes–CH_2Cl_2 (3 : 1)] to afford a green solid (3.4 mg, 30%): ^{1}H NMR δ −1.83 to −1.77 (br, 2H), 1.97 (s, 12H), 4.48 (s, 4H), 7.43–7.55 (m, 6H), 7.88–7.92 (m, 4H), 8.61 (s, 2H), 8.82 (d, J = 1.7 Hz, 2H), 9.06 (s, 2H); LD-MS obsd 570.9; FAB-MS obsd 570.2808, calcd 570.2783 ($C_{40}H_{34}N_2$); λ_{abs} 360, 378, 511, 763 nm.

3,13-Diacetyl-8,8,18,18-tetramethylbacteriochlorin (BC-A^{3}A^{13}). Following a procedure for replacement of a bromo group with an acetyl group on a chlorin,[16] a mixture of **BC-Br^{3}Br^{13}** (8.4 mg, 16 μmol), tributyl(1-ethoxyvinyl)tin (22 μL, 64 μmol) and $(PPh_3)_2PdCl_2$ (4.5 mg, 6.4 μmol) was refluxed in THF (1.6 mL) for 23 h in a Schlenk flask. The reaction mixture was treated with 10% aqueous HCl (5 mL) at room temperature for 2 h. The reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ and extracted with dichloromethane. The organic extract was dried (Na_2SO_4) and filtered. The filtrate was concentrated to dryness. The residue was

chromatographed (silica, CH_2Cl_2) to give a green solid (4.0 mg, 55%): ^{1}H NMR δ −1.24 to −1.20 (br, 2H), 1.93 (s, 12H), 3.17 (s, 6H), 4.41 (s, 4H), 8.60 (s, 2H), 9.08 (d, J = 2.1 Hz, 2H), 9.81 (s, 2H); LD-MS obsd 454.1; FAB-MS obsd 454.2387, calcd 454.2369 ($C_{28}H_{30}N_4O_2$); λ_{abs} 359, 389, 533, 768 nm.

3,13-Divinyl-8,8,18,18-tetramethylbacteriochlorin (BC-V^{3}V^{13}). Following a procedure for replacement of a bromo group with a vinyl group on a chlorin,[16] a mixture of **BC-Br^{3}Br^{13}** (52.8 mg, 0.100 mmol), $Bu_3SnCH{=}CH_2$ (100 μL, 0.293 mmol) and $(PPh_3)_2PdCl_2$ (10.5 mg, 15.0 μmol) was refluxed in THF (10 mL) for 16 h in a Schlenk flask. The reaction mixture was concentrated and chromatographed [silica, hexanes–CH_2Cl_2 (3 : 1)] to afford a green solid (12.0 mg, 28%): ^{1}H NMR δ −1.95 to −1.91 (br, 2H), 1.95 (s, 12H), 4.43 (s, 4H), 5.79 (d, J = 10.7 Hz, 2H), 6.42 (d, J = 17.6 Hz, 2H), 8.08 (dd, J = 17.6, 10.7 Hz, 2H), 8.62 (s, 2H), 8.82 (s, 2H), 8.85 (s, 2H); LD-MS obsd 421.8; ESI-MS obsd 423.2542, calcd 423.2543 [(M + H)$^+$, M = $C_{28}H_{30}N_4$]; λ_{abs} 352, 377, 507, 750 nm.

3,13-Diphenyl-8,8,18,18-tetramethylbacteriochlorin (BC-Ph^{3}Ph^{13}). Following a procedure for Suzuki coupling with chlorins,[14] a mixture of **BC-Br^{3}Br^{13}** (21.1 mg, 40.0 μmol), 2-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (65.3 mg, 0.320 mmol), $Pd(PPh_3)_4$ (27.7 mg, 24.0 μmol), and K_2CO_3 (177 mg, 1.28 mmol) was heated in toluene and DMF (2:1, 8 mL) at 90 °C for 12 h in a Schlenk flask. The reaction mixture was concentrated and chromatographed [silica, hexanes–CH_2Cl_2 (3 : 1)] to afford a green solid (19.6 mg, 94%): ^{1}H NMR δ −2.01 to −1.97 (br, 2H), 1.98 (s, 12H), 4.44 (s, 4H), 7.59–7.64 (m, 2H), 7.70–7.79 (m, 4H), 8.19–8.23 (m, 4H), 8.72 (s, 2H), 8.80 (d, J = 1.5 Hz, 2H), 8.94 (s, 2H); LD-MS obsd 522.8; ESI-MS obsd 523.2852, calcd 523.2856 [(M + H)$^+$, M = $C_{36}H_{34}N_4$]; λ_{abs} 351, 373, 499, 736 nm.

3,13-Diformyl-8,8,18,18-tetramethylbacteriochlorin (BC-F^{3}F^{13}). Following a procedure for oxidation with OsO_4 of a vinyl group on a porphyrin,[40,41] a solution of **BC-V^{3}V^{13}** (8.4 mg, 20 μmol) in THF (10 mL) was treated with OsO_4 (42.4 mg, 0.166 mmol) at 0 °C for 5 min. The reaction mixture was allowed to warm to room temperature (for 10 min), then treated with a solution of $NaIO_4$ (87.8 mg, 0.410 mmol) in 1.5% aqueous acetic acid (2 mL) for 8 h at room temperature. The reaction mixture was treated with water (20 mL) and CH_2Cl_2 (20 mL). The organic extract was washed with a saturated aqueous solution of $NaHCO_3$ and brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated at reduced pressure at room temperature. The residue was chromatographed [silica, hexanes–CH_2Cl_2 (1 : 1), then CH_2Cl_2] to give a reddish purple solid (3.2 mg, 38%): ^{1}H NMR δ −1.18 to −1.14 (br, 2H), 1.95 (s, 12H), 4.41 (s, 4H), 8.65 (s, 2H), 9.12 (s, 2H), 9.58 (s, 2H), 11.14 (s, 2H); LD-MS obsd 426.5; ESI-MS obsd 427.2133, calcd 427.2129 [(M + H)$^+$, M = $C_{26}H_{26}N_4O_2$]; λ_{abs} 363, 393, 536, 771 nm.

8,8,18,18-Tetramethylbacteriochlorin (BC) and 3-bromo-8,8,18,18-tetramethylbacteriochlorin (BC-Br^3). Following a procedure for debromination of porphyrins,[43] a mixture of **BC-Br^{3}Br^{13}** (10.6 mg, 20.0 μmol), $Pd(PPh_3)_4$ (27.7 mg, 24.0 μmol), formic acid (15 μL, 0.40 mmol), and TEA (55 μL, 0.40 mmol) was heated in toluene (20 mL) at 100 °C for 15 h in a Schlenk flask. The reaction mixture was concentrated and chromatographed [silica, hexanes–CH_2Cl_2 (3 : 1)] to afford a fast-moving component (**BC-Br^3**, 3.0 mg, 33%, a green solid) and a slow-moving component (**BC**, 3.3 mg, 44%, a green solid). Data for **BC**: ^{1}H NMR δ −2.40 to −2.36 (br, 2H), 1.98 (s, 12H), 4.48 (s, 4H), 8.72–8.75 (m, 2H), 8.74 (s, 2H), 8.75–8.80 (m, 2H), 8.84 (s, 2H); LD-MS obsd 369.8; ESI-MS obsd 371.2227, calcd 371.2230 [(M + H)$^+$, M = $C_{24}H_{26}N_4$]; λ_{abs} 340, 365, 489, 713 nm. Data for **BC-Br^3**: ^{1}H NMR ($CDCl_3$) δ −2.22 to −2.18 (br, 2H), 1.95 (s, 6H), 1.97 (s, 6H), 4.45 (s, 2H), 4.48 (s, 2H), 8.61 (s, 1H), 8.69 (s, 1H), 8.72–8.78 (m, 3H), 8.79 (s, 1H), 8.92 (s, 1H); LD-MS obsd 447.8; ESI-MS obsd 449.1330, calcd 449.1335 [(M + H)$^+$, M = $C_{24}H_{25}BrN_4$]; λ_{abs} 343, 367, 491, 721 nm.

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