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Porphyrinoids

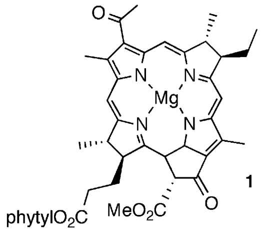
Expanded Bacteriochlorins**

*Lalith P. Samankumara, Sarah Wells, Matthias Zeller, Alonso M. Acuña, Beate Röder, and Christian Brückner**

The Mg^{2+} complexes of bacteriochlorins (7,8,17,18-tetrahydroporphyrins), such as bacteriochlorophyll *a* (**1**), are used by phototrophic purple bacteria, heliobacteria, and green sulfur bacteria as light-harvesting chromophores in anoxygenic photosynthesis.[1] Bacteriochlorins absorb light at wavelengths that are not absorbed by the chlorophylls (Mg^{2+} complexes of chlorins, 7,8-dihydroporphyrins), the chromophores of the green plants and cyanobacteria. Bacteriochlorins strongly absorb light in the near-IR region, allowing photosynthesis to take place deep in the water column. The near-IR-absorbing, -emitting, and singlet-oxygen-sensitizing properties make bacteriochlorins intriguing targets for synthetic chromophores to be used as phototags, in photomedicine, and as artificial light-harvesting pigments.[2,3]

Relatively few methods are known that generate synthetic bacteriochlorins. One approach is the modification of naturally occurring bacteriochlorins.[4] The groups of Lindsey, Holton, and Bocian presented recently total syntheses of chemically robust bacteriochlorins, such as **2**.[5] Their work represented a quantum leap in the synthesis, fundamental photophysical understanding, and application of bacteriochlorins.[3,6]

Demonstrating an alternative approach toward synthetic bacteriochlorins, we[7] and others offered methods to convert synthetic porphyrins by stepwise removal of two β,β double bonds.[8] A representative example is tetrahydroxybacteriochlorin **3a**, synthesized by the OsO_4-mediated dihydroxylation of *meso*-tetraphenylporphyrin.[7] Furthermore, we demonstrated the formal expansion of the dihydroxypyrrolidine moiety in chlorins by an oxygen atom to form morpholinochlorins **4**.[9–12] These chromophores display chlorin-like optical spectra that are red-shifted compared to those of the starting dihydroxychlorin.



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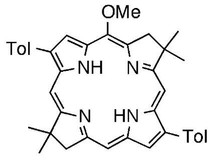

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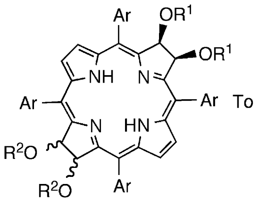
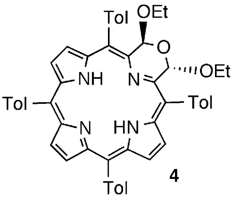


3a, Ar = Ph, $R^1 = R^2 = H$
3b, Ar = Ph, $R^1 = H$, $R^2 = Me$
3c, Ar = Ph, $R^1 = R^2 = Me$, *E/Z* isomer mix
3d, Ar = 3,4,5-$(MeO)_3C_6H_2$,
$R^1 = R^2 = Me$, *E* isomer



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A number of porphyrin-modification strategies were used by us[13] and others[14,15] to prepare other chlorin and porphyrin analogues containing nonpyrrolic moieties. However, practically nothing is known about the preparation of such bacteriochlorin analogues. In cases in which the expansion of two opposite pyrrole moieties within a tetrapyrrolic macrocycle was accomplished, all ring carbons remained sp^2-hydridized.[15] Consequently, the chromophores did not display bacteriochlorin-like spectra. The fundamental question thus arises: Can the synthetic principles established to generate *meso*-tetraphenylchlorin analogues be extended to form bacteriochlorin analogues? This contribution answers this question in the affirmative by presenting the synthesis of *meso*-tetraarylmorpholinobacteriochlorins of unprecedented nonplanarity and intriguing stereostructure that are characterized by extremely red-shifted and tunable bacteriochlorin-type optical spectra.

Dimethoxydihydroxybacteriochlorin **3b** is derived from the parent tetraol **3a** by protection of one of the two diol functionalities.[7] We subjected this bacteriochlorin diol to the mildest oxidation conditions ($NaIO_4$ heterogenized on silica gel, $CHCl_3$, alcohol, ambient temperature) that are known to, in one pot, cleave the diol functionality to generate a secochlorin bisaldehyde. This undergoes an alcohol-induced ring closure to form a dialkoxy-substituted morpholine moiety, leading to a single product in satisfying yields (Scheme 1).[10] Based on the diagnostic NMR signals for the morpholino

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[*] L. P. Samankumara, S. Wells, Prof. Dr. C. Brückner
University of Connecticut, Department of Chemistry, Unit 3060
Storrs, CT 06269-3060 (USA)
E-mail: c.bruckner@uconn.edu
Homepage: http://bruckner.chem.uconn.edu

Dr. M. Zeller
Youngstown State University
One University Plaza, Youngstown OH 44555-3663 (USA)

A. M. Acuña, Prof. Dr. B. Röder
Humboldt-Universität zu Berlin
Institut für Physik, AG Photobiophysik
Newtonstrasse 15, 12489 Berlin (Germany)

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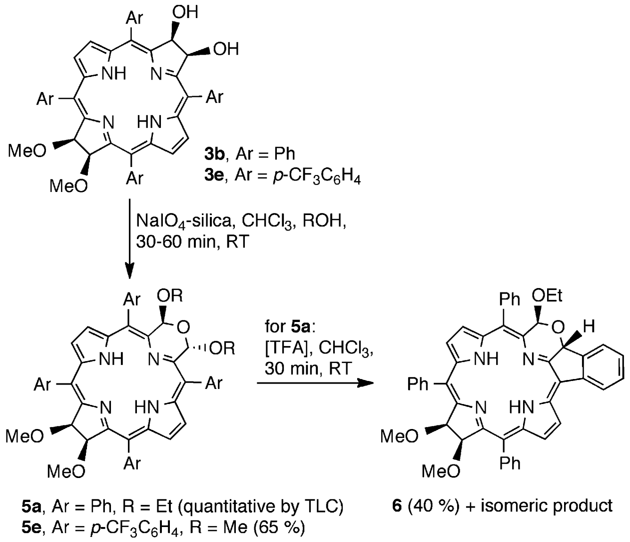


Scheme 1. Synthesis of the morpholinobacteriochlorins **5** and **6** (see the Supporting Information for details).

moiety,[10] it could be characterized as morpholinobacteriochlorin **5**, an assignment supported by X-ray diffractometry.[16]

The UV/Vis spectrum of morpholinobacteriochlorin **5e** is bacteriochlorin-like but more than 40 nm red-shifted (for λ_{max}) and significantly broadened compared to the spectrum of the starting material (Figure 1 A).[17] The solid-state conformation provides a possible explanation for the shift of the optical properties (Figure 2).[18] In stark contrast to the near-planar conformations of dimethoxychlorin,[7] morpholinochlorin **4**,[10,11] or tetramethoxybacteriochlorin **3d** (shown as comparison),[7] the conformation of morpholinobacteriochlorin **5e** is severely ruffled. Evidently, the bacteriochlorin chromophore is significantly more flexible than the chlorin chromophore and therefore responds much more strongly to the strain introduced by the insertion of the oxygen atom between the two sp^3-hybridized pyrrolidone β carbons.[19]

Acid treatment of morpholinochlorins leads to the establishment of an intramolecular β-to-*o*-phenyl linkage.[11,12] This reaction is also applicable to morpholinobacteriochlorin **5a**, forming the monofused bacteriochlorin **6**. For most porphyrins that incorporate such linkages, their optical spectra are red-shifted compared to the parent chromophore.[20] This is rationalized by the extended π conjugation of the porphyrinic chromophore that includes the idealized coplanar *meso*-aryl group(s). Contrary to this trend, the UV/Vis spectrum of **6** is 32 nm blue-shifted compared to the parent bacteriochlorin **5a** (Figure 1 A). The spectrum of **6** is also much less broadened than that of **5e**, inferring an increased conformational rigidity.

The crystal structure of **6** shows that the fusion of the *meso*-phenyl group to the morpholine moiety leads to a partial planarization of the chromophore and the introduction of nonruffled conformational modes (some doming and saddling can be made out; Figure 2).[21] We conclude that the observed modulations of the bacteriochlorin-type spectra of **5** and **6** are dominated by conformational effects.[22]

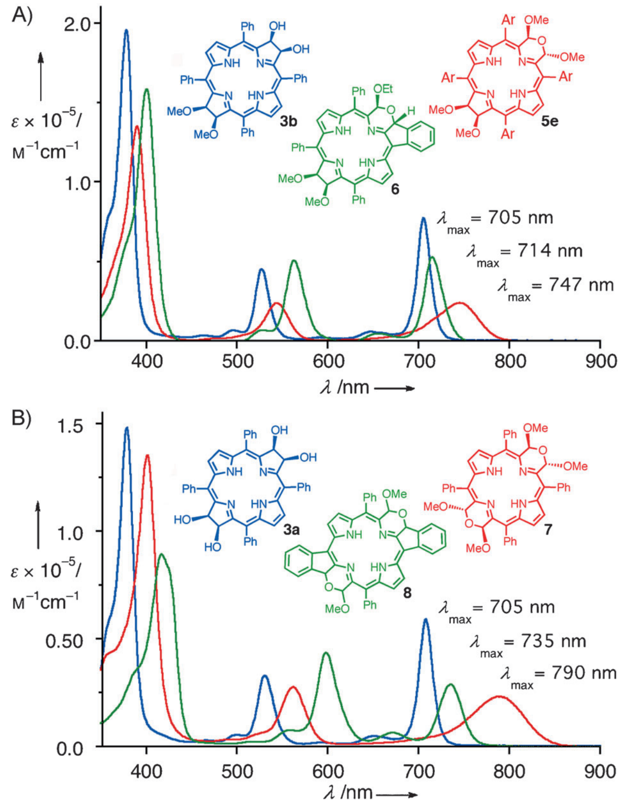


Figure 1. UV/Vis absorption spectra of: A) dihydroxydimethoxybacteriochlorin **3b** (blue trace), morpholinobacteriochlorin **5e** (red trace), and β-*o*-phenyl-linked morpholinobacteriochchlorin **6** (green trace); B) tetrahydroxybacteriochlorin **3a** (blue trace), bismorpholinobacteriochlorin **7** (red trace), and twofold β-*o*-phenyl-linked bismorpholinobacteriochlorin **8** (green trace), all in deacidified CH$_2$Cl$_2$.

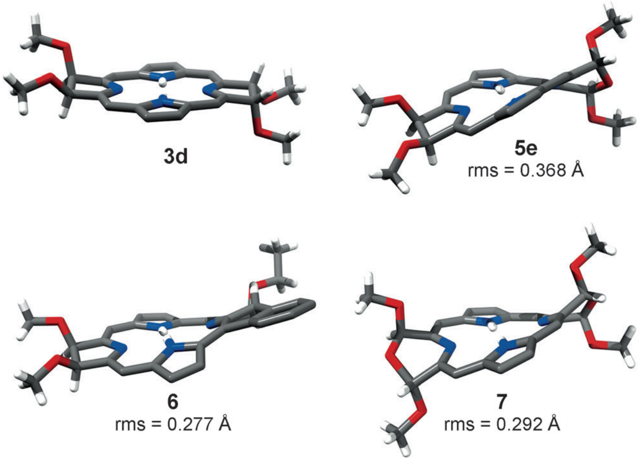


Figure 2. Capped stick models of the molecular structures of **3d**, **5e**, **6**, and **7**;[23] oblique views chosen such that the distant pyrrole moiety is viewed approximately from the same perspective. Disorder and solvent molecules, all *meso*-aryl groups and hydrogen atoms attached to sp^2 CH groups omitted for clarity. The rms values are computed based on deviation of the C$_{16}$N$_4$ macrocycle (excluding the pyrrolidine/morpholine β-carbon atoms) from planarity.[18]

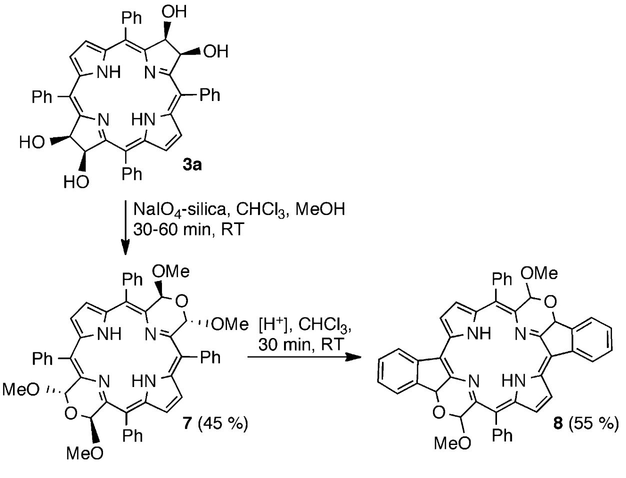
Other photophysical parameters underline this interpretation.[24] For instance, benchmark tetramethoxybacteriochlorin **3c** has a fluorescence yield Φ_{Fl} of 17% and a fluorescence lifetime τ_{Fl} of 5.13 ns (Table 1). The corresponding intersystem crossing (ISC) quantum yield Φ_{ISC} is 45%, with a singlet-state lifetime τ_{S1} of 5.40 ns. The introduction of the morpholine moiety results in a drastic erosion of Φ_{Fl} to 3%, reduction of τ_{Fl} to 3.73 ns, and an increase in the ISC quantum yield Φ_{ISC} to 85% but with concomitant reduction of τ_{S1} to 3.77 ns. Establishment of the β-to-*o*-phenyl linkage in **6** somewhat rigidifies the chromophore but does not planarize it. The Φ_{Fl} recovers to 8% with a slightly longer τ_{Fl} of 3.90 ns. The corresponding Φ_{ISC} is reduced to 54%, with a slightly longer τ_{S1} of 3.99 ns.

Table 1: Photophysical parameters of the bacteriochlorin-like chromophores.[a]

Parameter	3c	5e	6	7	8
Φ_{Fl} ($\pm$0.03)	0.17	0.03	0.08	$<$0.01	0.18
τ_{Fl} [ns] ($\pm$0.02)	5.13	3.73	3.90	0.32	3.45
Φ_{ISC} ($\pm$3%)	0.45	0.85	0.54	0.87	0.38
τ_{S1} [ns] ($\pm$10%)	5.40	3.77	3.99	0.45	4.07

[a] For experimental details, see the Supporting Information.

Once we gathered experience with the formation of monomorpholinobacteriochlorins of types **5** and **6**, we treated tetrahydroxybacteriochlorin **3a** under the mild oxidation conditions described in Scheme 1 in the presence of methanol (Scheme 2). The major product formed displays dramatically simplified ^{1}H and ^{13}C NMR spectra (only one signal in the β-region at $\delta = 7.78$ ppm (d, $^{4}J = 2.0$ Hz), one phenyl group, one H and sp^{3} carbon assigned to the morpholino moiety, at $\delta =$ 6.14 and 95.8 ppm, respectively, and one methoxy group) that reflect the high symmetry of **7**. X-ray diffractometry provided the ultimate proof for the bismorpholinobacteriochlorin connectivity of **7** (Figure 2).



Scheme 2. Synthesis of the bismorpholinobacteriochlorins **7** and **8** (see the Supporting Information for details).

The conformation of bismorpholinobacteriochlorin **7** is extremely nonplanar, with the twist inherent to both morpholino groups acting in concert to introduce a large degree of ruffling into the chromophore. Irrespective of the presence of five stereocenters in this molecule (four sp^{3} carbons at the morpholine rings and the helicity of the molecule),[11] no indications for the presence of diastereomers are observed. Thus, the coupling of the stereocenters to the helicity of the macrocycle, as observed for the morpholinochlorins, is also preserved in the morpholinobacteriochlorins.[11] Likewise, this compound crystallizes as a racemic mixture.[17]

The UV/Vis spectrum of **7** is, no doubt a result of its strongly twisted conformation, 85 nm (for $\lambda_{\max}$) red-shifted compared to that of the parent tetrahydroxybacteriochlorin **3a** (Figure 1B). The spectrum is also significantly broadened, again suggestive of a conformationally dynamic structure. As a consequence of the nonplanar conformation and conformational flexibility, Φ_{Fl} collapses to under 1%, with a very short τ_{Fl} of 0.32 ns (Table 1).[24] The intersystem crossing quantum yield Φ_{ISC} is, as expected for the very nonplanar and flexible chromophore, high (87%), albeit not much higher than that of the monomorpholinobacteriochlorin **5e**, but with an τ_{S1} of 0.45 ns that is almost an order of magnitude shorter than that found for **5e**.

Treatment of bismorpholinobacteriochlorin **7** with traces of TFA vapors generated a new compound (Scheme 2). The high-resolution mass spectrum of this compound **8** indicated a composition derived from **7** that underwent a loss of two molecules of MeOH ($C_{46}H_{35}N_4O_4$ for MH^{+}). The ^{1}H and ^{13}C NMR spectra of **8** show the formation of a twofold symmetric molecule (two signals at $\delta = 9.13$ ppm and $\delta =$ 7.96 ppm (each dd, $^{3}J = 4.8$ and $^{4}J = 1.8$ Hz) assigned to β-H) containing one type of β-to-*o*-phenyl linkage. Its bacteriochlorin-like UV/Vis spectrum is significantly sharpened and hypsochromically shifted relative to that of the starting material **7**, but still 30 nm ($\lambda_{\max}$) red-shifted relative to the spectrum of tetrahydroxybacteriochlorin **3a** (Figure 1B). Based on the observed spectroscopic effects of the introduction of the β-to-*o*-phenyl linkage in **6**, we conclude that compound **8** possesses a doubly fused bismorpholinochlorin structure. The absence of detectable diastereomers and the symmetry of the molecule implied by the NMR spectra allowed us to predict that **8** is the result of a unidirectional β-to-*o*-phenyl fusion reaction,[25] but the relative stereostructure of the linkage and the methoxy group on each morpholino moiety remains to be determined. While a *trans* arrangement such as that in morpholinobacteriochlorin **6** (and an analogous morpholinochlorin) is likely, the extreme twist and flexibility of **7** may also make a *cis* arrangement possible.[11]

The introduction of two β-to-*o*-phenyl linkages rigidifies the (projected nonplanar) chromophore, thus Φ_{Fl} increases to 18% with a lengthened τ_{Fl} of 3.90 ns (Table 1).[24] The associated Φ_{ISC} (of 54%), with a τ_{S1} of 3.99 ns, are relatively close to those of the regular bacteriochlorin **3c**, highlighting the strong rigidifying effect of the β-to-*o*-phenyl linkage and the resulting strong similarity of the two chromophores.

In conclusion, we demonstrated how to expand one and two pyrrolidine moieties in *meso*-tetraaryl-7,8,17,18-tetrahydroxybacteriochlorins to morpholine rings, resulting in the formation of the first bacteriochlorin-like porphyrinoid containing two nonpyrrolic heterocycles. Owing to their nonplanar conformations, they display dramatically broadened and red-shifted optical spectra relative to the spectra of regular, planar bacteriochlorins. Furthermore, the introduction of β-to-*o*-phenyl linkages into these chromophores tunes their solution-state photophysical properties, highlighting the interplay between bacteriochlorin chromophore, conformation, and conformational flexibility.

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[18] CCDC 855681 (**5e**), 855679 (**6**), and 855680 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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