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Oxazolochlorins. 9. *meso*-Tetraphenyl-2-oxabacteriochlorins and *meso*-Tetraphenyl-2,12/13-dioxabacteriochlorins[1]

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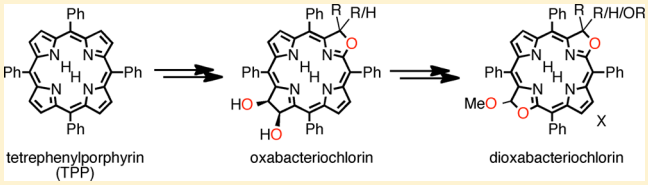
Supporting Information

ABSTRACT: The formal replacement of one or two pyrrole groups in *meso*-tetraphenylporphyrin by oxazole moieties is described, generating inter alia the bacteriochlorin-type chromophores oxazolobacteriochlorins (oxabacteriochlorins) and bisoxazolobacteriochlorins (dioxabacteriochlorins). The key step is the conversion of a *β*,*β*′-dihydroxy-functionalized pyrroline group into an oxazolone or (substituted) oxazole. Depending on the substitution pattern on the oxazole or oxazoline moieties, mono- and dioxabacteriochlorins may have chlorin- or bacteriochlorin-like spectra. The optical properties (as measured by UV−vis and fluorescence spectroscopies) of the novel oxa- and dioxabacteriochlorins are described and contrasted against benchmark chlorins and bacteriochlorins. The conformations of a representative number of mono- and dioxabacteriochlorins, as their free bases or Zn^{II} complexes, were determined by single-crystal X-ray diffractometry. They proved to be essentially planar, showing that the modulation of their optical properties is primarily due to their intrinsic electronic structures and electronic substituent effects and are not largely affected by conformational effects. The mono- and bisoxazolobacteriochlorins are a novel class of readily prepared and oxidatively stable chlorin and bacteriochlorin analogues with tunable optical spectra that, in part, reach into the NIR.

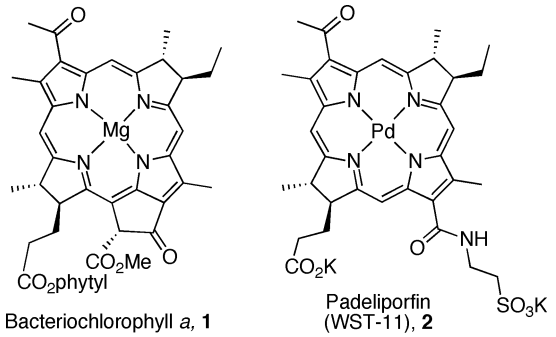


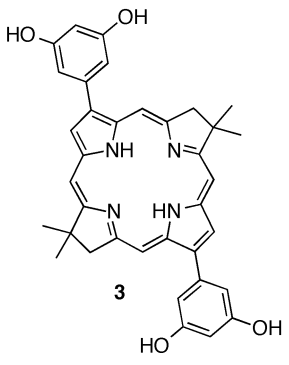
INTRODUCTION

Bacteriochlorins, 2,3,12,13-tetrahydroporphyrins, such as bacteriochlorophyll *a* (**1**), are the chromophores of the photosynthetic pigments of anoxygenic photoautotrophic purple and green bacteria and are the light antenna and electron-transfer pigments in strictly anaerobic heliobacteria.[2] Bacteriochlorins are characterized by UV−vis spectra with intense λ_{max} absorption bands in the near-infrared (NIR) region (>720 nm).[3] This property allows photosynthesis to take place deep in the water column beneath the green, chlorophyll-carrying algae (that typically possess λ_{max} values between 660 and 700 nm).[4]

The long wavelength UV−vis absorbance bands of bacteriochlorins also lie within the "optical window" of tissue (the range between 600 and 1300 nm; the wavelength of maximum penetration of breast tissue is ∼725 nm).[5] Thus, the NIR absorbing, emitting, and singlet oxygen sensitizing properties make bacteriochlorins suitable chromophores to be used as phototags, in photodynamic therapy,[6−9] as photoantimicrobials,[10] or as artificial light-harvesting pigments.[11]

Historically, the main approaches toward synthetic bacteriochlorins have been semisyntheses,[3,7,9,12,13] even though the isolation of naturally occurring chlorins and bacteriochlorins is nontrivial.[14] The commercially available photochemotherapeutic Pd^{II} complex WST-11 (**2**) is an example of a semisynthetic bacteriochlorin, prepared from bacteriochlorophyll **1**.[9] One difficulty in handling bacteriochlorins is generally caused by their sensitivity toward (light-induced) oxidations.





This prompted the total syntheses of chemically more stable bacteriochlorins. Chief among them are the bacteriochlorins

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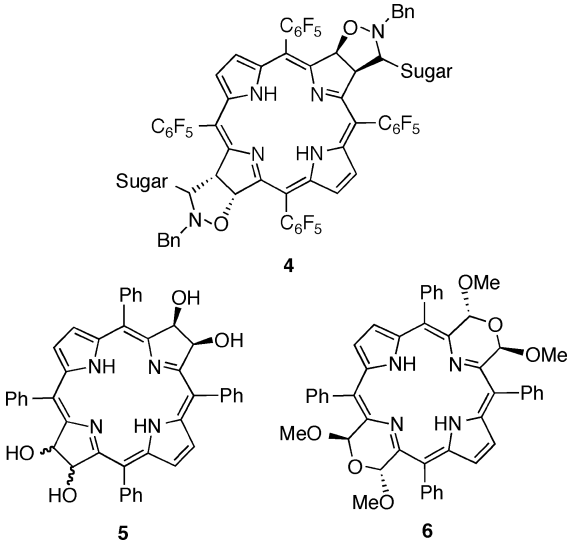
introduced by the group of Lindsey.[15−17] Bacteriochlorin **3** is one member of this family.[7] This macrocycle was shown to possess high biological activity as a photodynamic therapeutic agent against melanoma cells, which are deeply pigmented cells that are impervious to agents that require shorter wavelengths of activation.[8,18] Moreover, the stability of these bacteriochlorins against oxidation was also assured by virtue of the presence of the geminal-dimethyl moieties. Studies in which the chromophore substituents were systematically varied delineated the structural requirements that resulted in high extinction coefficients in these chromophores.[16] Overall, their scalable syntheses, their plasticity with respect to further chemical manipulations and the accompanying physical studies by the groups of Lindsey, Bocian, and Holten shifted the paradigm with respect to the access of bacteriochlorins, their utilization, and the understanding of their optical properties.[15−17]

An alternative approach toward bacteriochlorins is the conversion of a preformed synthetic porphyrin.[3,19] Multiple examples of these reactions were reported, ranging from simple reductions (using diimide)[20] to more sophisticated cycloadditions.[21] For instance, reaction of *meso*-tetrakis(pentafluorophenyl)porphyrin with excess sugar nitrones affords sugar-containing bacteriochlorins, such as **4**.[22] Multiple other analogous approaches were reported, primarily by the group of Cavaleiro.[21]

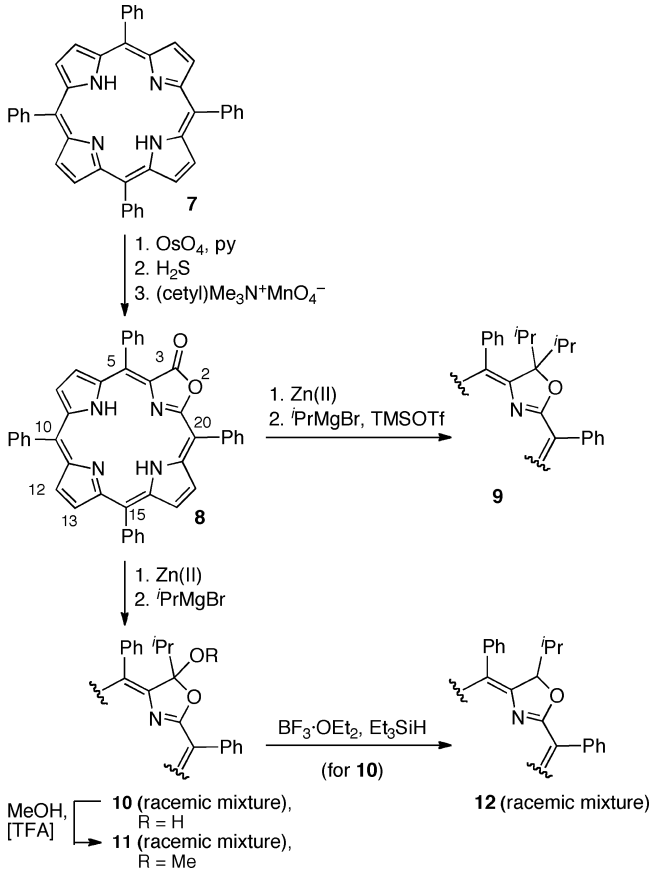
We,[23] and others,[24] reported the reaction of *meso*-arylporphyrins with 2 equiv of OsO_4 to form tetrahydroxybacteriochlorins such as **5**. Using our "breaking-and-mending of porphyrins" approach,[25] these tetraols were then subjected to conversion to bacteriochlorin analogues, such as bismorpholinobacteriochlorin **6** in which the parent bacteriochlorin chromophore was expanded by two oxygen atoms.[26]



4 **5** **6**

A similar approach was also applied to the replacement of one of the β-carbon atoms of a porphyrin with an oxygen atom, thus formally replacing the pyrrole moiety with an oxazole. The first compound that featured such a replacement was based on octaethylporphyrin.[27] *meso*-Tetrakis(pentafluorophenyl)porpholactone (2-oxa-3-oxoporphyrin), synthesized fortuitously by a one-step oxidation of the corresponding porphyrin, was the first such *meso*-tetraaryl-based system.[28,29] Porpholactones can also be made by oxidations of other porphyrins,[30] such as tetraphenylporphyrin **7** (Scheme 1).[31,32]

Scheme 1. Synthesis of 3-Alkyl-2-oxachlorins by Stepwise Conversion of Porphyrin 7[33]



Porpholactones are porphyrinoids with porphyrin-like optical properties. We recently demonstrated that the reduction, as well as alkyl-Grignard addition, to porpholactones resulted in the formation of chlorin analogues, such as alkyloxazolochlorins **9**−**12**.[31,33,34] The reductions, mono- and dialkylations, and hydrodehydroxylation significantly modulated their optical properties.[31,33,34] Importantly, the hyperchromic effect of the presence of the ring-oxygen could be computationally rationalized.[31]

We presented in a preliminary report that it was possible to generate oxazolobacteriochlorins by dihydroxylation of oxazolochlorin **9**.[34] We also showed a single example in which we replaced two pyrroles of a porphyrin with two oxazoles. This macrocycle possessed, however, chlorin-like optical properties, raising the question whether bacteriochlorin-like bisoxazolobacteriochlorins can be generated. Additionally, can the option to modulate the optical properties of the oxazolochlorins by variation of the substituents on the oxazoline moiety also be extended to the mono- and bisoxazolobacteriochlorins? In this paper, we provide answers to these questions. We report the systematic evaluation of the scopes and limits of the synthesis of bacteriochlorin-type chromophores possessing a single or double carbon-to-oxygen replacement at opposite ring positions, their optical properties, and the crystal structures of select members of this group of compounds.

RESULTS AND DISCUSSION

Nomenclature Conventions. There is no firmly established trivial nomenclature for most porphyrinoids. Thus, we

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define oxazolochlorins (2-oxachlorins) to be porphyrinoids in which a single pyrrole is replaced by an oxazole moiety and that possess chlorin-like optical spectra and oxazolobacteriochlorins (2-oxabacteriochlorins) to be bacteriochlorin-like porphyrinoids in which a single pyrrole is replaced by an oxazole moiety. Correspondingly, bisoxazolochlorins (2,12- or 2,13-dioxachlorins) are chlorin-type porphyrinoids in which two pyrroles are replaced by oxazole moieties. This double replacement can also result in the formation of bacteriochlorin-like chromophores; consequently, they are named bisoxazolobacteriochlorins (2,12/13-dioxabacteriochlorins). The numbering scheme used here is shown for compound **8** (Scheme 1).[35]

In cases in which two oxygen atoms are present in the backbone of bisoxazolochlorins and -bacteriochlorins, two regioisomers are possible, designated *cis* (2,13-isomer) and *trans* (2,12-isomer) (Figure 1). If a mixture of isomers is present, the compound is designated as a 3,12/13 isomeric mixture.

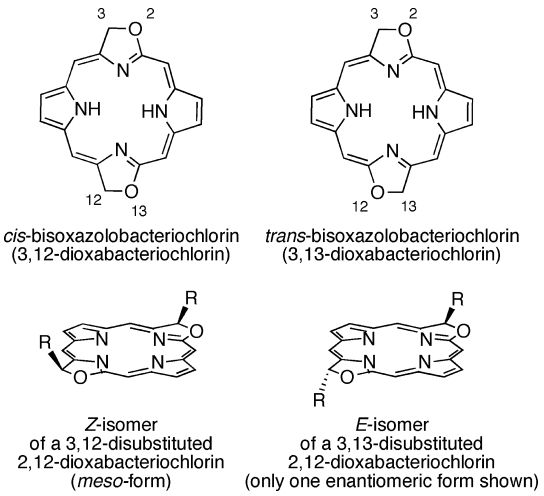
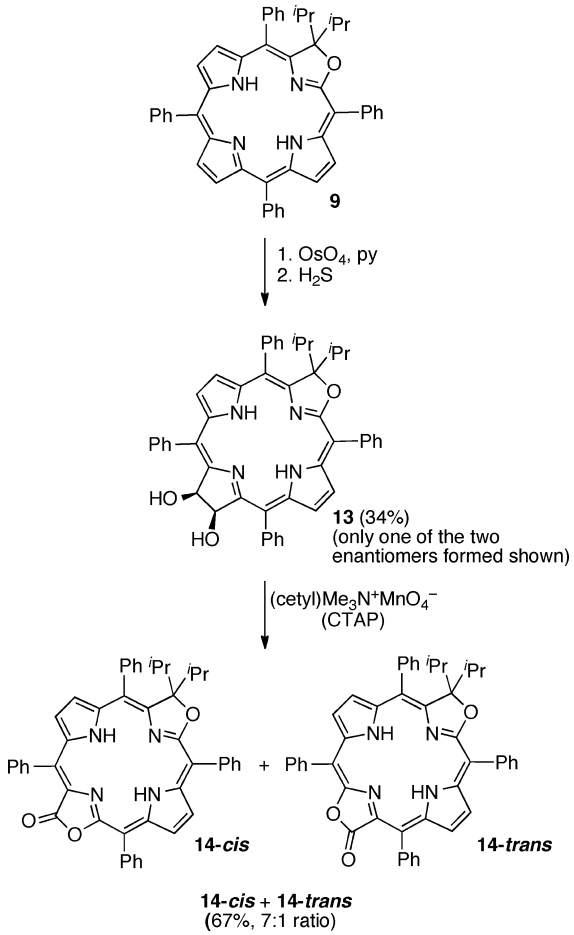


Figure 1. Nomenclature conventions for the regio- and stereoisomeric bisoxazole-substituted porphyrinoid chromophores.

The sp^3-hybridized carbon atoms of the pyrroline or oxazoline moieties may be chiral centers. Moreover, the substituents on these centers can be positioned relative to each other on opposite sides defined by the macrocycle mean plane, or on the same side (Figure 1). Following the nomenclature chosen for these type of stereoisomers that are also observed in the tetrahydroxybacteriochlorins, we name them *E* and *Z* isomers, respectively.[23] For identical substituents, the *Z*-isomer is a *meso*-compound; the *E*-isomer is chiral.

Syntheses of Oxazolobacteriochlorins. The highly regioselective OsO_4-mediated conversion of free base chlorins to form *β*,*β*′-dihydroxylated bacteriochlorins is well established for *β*-octaalkyl- as well as *meso*-di- and tetraarylchlorins.[23,24,36] This reaction can also be applied to the green, nonpolar 3,3-diisopropyloxazolochlorin **9**. Thus, dihydroxylation, followed by H_2S-reductive cleavage of the intermediate osmate ester, produced a single major purple-pink product in overall 34% isolated yield (with ∼50% recovered starting material). The reaction was much slower than observed for the oxidation of dihydroxychlorins, but neither extended reaction times nor an excess of oxidant improved the yield significantly. Based on the composition ($C_{49}H_{45}N_4O_3$ for MH^+ as per ESI^+ HR-MS) and diagnostic bacteriochlorin spectrum (with a λ_{max} of 750 nm; see Figure 5 and below for a more detailed description of the UV–vis spectra of all chromophores prepared) of the reaction product, it was identified as 12,13-dihydroxy-2-oxabacteriochlorin **13** (Scheme 2). The ^1H NMR spectrum of **13** showed

Scheme 2. Syntheses of Oxazolobacteriochlorin 13 and Bisoxazolochlorins 14



inter alia the presence of two nonequivalent pyrrole hydrogen atoms (the NMR spectra of all compounds are reproduced in the Supporting Information). The compound is chiral and is presumably formed as a racemate.

Synthesis of Bisoxazolochlorins. The oxidative conversion of a *β*,*β*′-diol to a lactone functionality in a number of chlorins, chlorin derivatives, and chlorin analogues is known.[31,37] This reaction could also be applied to dihydroxyoxazolobacteriochlorin **13**. Thus, oxidation of **13** using MnO_4^- (in the form of CTAP) converted the diol functionality into a lactone moiety, as indicated by the appearance of a carbonyl stretch at 1724 cm^{-1} in the IR spectrum of product **14**. In comparison, the corresponding stretching frequency for the parent porpholactone **8** is 1742 cm^{-1}.[31] The shift in the IR spectrum to lower wavenumbers for **14** likely reflects the higher HOMO energy level for hydroporphyrins compared to porphyrins.[3,38] The bacteriochlorin-type spectrum of the pink, polar starting material was replaced by a (bathochromic) chlorin-like spectrum of the much less polar gray-colored product **14** (Figure 3).

The ^1H NMR spectrum of the product **14** indicated the presence of two regioisomers in a 7:1 ratio (see the Supporting

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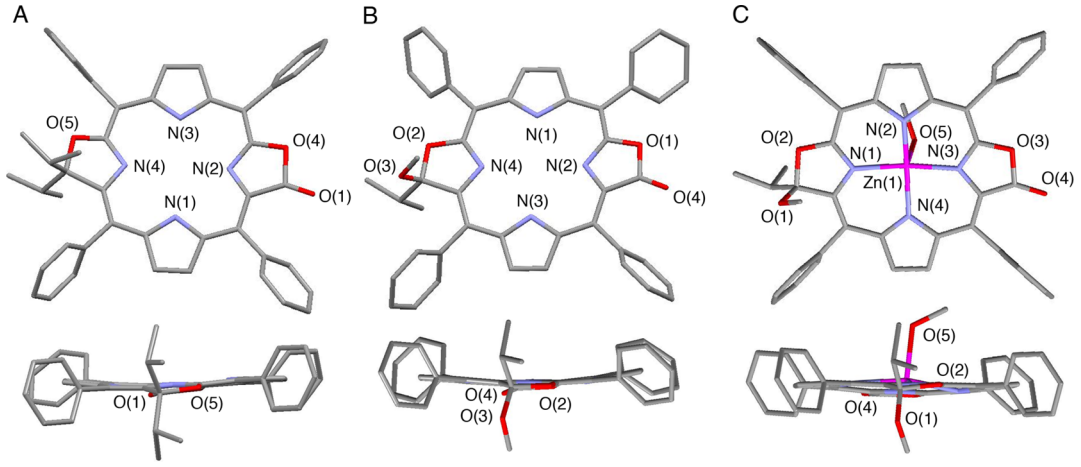

Figure 2. Representation of the molecular structures of **14-*cis*** (A), **16-*cis*** (B), and **16Zn-*cis*** (C) (top and side views). All hydrogen atoms and the minor disorder contributions have been omitted for clarity.

Information), assigned to the two isomers **14-*cis*** and **14-*trans*** that differ in their relative orientation of the lactone moiety. The absorption spectrum of this mixture possessed equally intense λ_{max} peaks at 695 and 705 nm. No flash column or preparative plate chromatographic separation methods were found to completely separate the two isomers at preparatively useful scales, but repeated column chromatography (50% hexane/CH_2Cl_2 on silica gel) enriched the mixture to a ~10:1 isomer ratio. Crystallization of this mixture resulted in the formation of a crystal of the slightly less polar majority product that was suitable for investigation by single-crystal X-ray diffractometry. The structure of the compounds was determined to be of type **14**, though due to disorder in the crystal, the *cis*-regiochemistry could not be assigned with absolute certainty (Figure 2). However, the crystal structure of the related compound **19-*cis*** (derived from **16-*cis***, to be described below) was unambiguous in the assignment of the *cis*-configuration. Interestingly, the *cis*- and *trans*-isomers of **14** and **16** (and similar regioisomers) possess different UV−vis spectra from each other. Since the UV−vis spectra of **14** and **19-*cis*** are very similar to each other and clearly differentiated from the *trans*-isomers, we infer that the majority compound in the isomer mixture of **14** is the *cis*-regioisomer.

Analytical samples of the isomers could be separated, allowing us to assess their surprisingly different UV−vis spectra. Isomer **14-*cis*** possesses a λ_{max} peak at 695 nm, while **14-*trans*** possessed a much more intense λ_{max} peak at 705 nm. Thus, the nonaxial symmetric electron distributions within each oxazole moiety affect significantly the frontier orbitals of the porphyrinoid with respect to energy, symmetry and associated transition dipole moments. Moreover, a strong influence of the β-carbonyl group on the (nonsymmetric) chromophore can be traced as the UV−vis spectra of the *cis*/*trans* isomers of bisoxazolobacteriochlorins **22** and **23** lacking a carbonyl group are very similar to each other (see below).

The dihydroxylation/oxidative diol cleavage reaction sequence applied to bisalkyloxazolochlorin **9** (to form bisoxazolochlorin **14**) can also be applied to both the hydroxy-substituted alkyloxazolochlorin **10** and its alkoxy derivative **11** to generate, via the purple-pink intermediates **17** and **15**, the greenish gray bisoxazolochlorins **18** and **16**, respectively (Scheme 3). However, the presence of a chiral center in these starting materials increased the complexity of the product isomer mixtures: each *cis*/*trans* isomer is formed as a racemic mixture.

All products possessed the expected spectroscopic and analytical properties (see the Supporting Information) with some notable features. Intermediate bacteriochlorin diols **15** and **17** formed as a separable mixture of *E*/*Z* isomers. However, since NMR spectroscopy does not allow an assignment of the isomers, their assignment remained speculative. In a related problem, the assignment of the tetrahydroxybacteriochlorin *E*/*Z* isomers was performed with the help of single-crystal diffractometry.[23] The tetrahydroxybacteriochlorin *E*-isomer was less polar than the *Z*-isomer, and it is likely that a similar rationale will also hold for the assignment of the *E*/*Z* isomers of the bacteriochlorin **15**. The UV−vis spectra of the intermediate diols **15** and **17** are identical and ~30 nm blue-shifted (λ_{max} = 720 nm) when compared to the spectrum of the corresponding dihydroxydialkyloxazolobacteriochlorin **13**. Thus, the α-hydroxy/methoxy-induced blue-shifts that were observed in the monooxazolochlorins (shifts of ~20 nm) are also present in the oxazolobacteriochlorin series, though the shifts are somewhat more pronounced.

The MnO_4^--mediated oxidation of either isomer of dihydroxybacteriochlorin **15** converts the bacteriochlorin-like chromophore into a regioisomeric mixture of **16-*cis*** and **16-*trans***. As expected, the sp^2-hybridized lactone carbon mimics the effect of a β,β'-double bond;[28,31] thus, the bacteriochlorin-type chromophore **15** is converted to chlorin-type bisoxazole chromophore **16** that is, however, significantly bathochromic compared to that of the corresponding mono-oxazolochlorin **11** (Figure 3).

As per the ^{1}H NMR spectrum of the isomeric mixture of **16-*cis*/*trans***, the formation of the 2,13-dioxachlorin **16-*cis*** isomer was slightly favored (*cis*/*trans* regioisomeric ratio as determined by NMR spectroscopy was 5:2). Again, the majority diastereomer could be enriched to ~10:1 by column chromatography and purified by fractional crystallization. The UV−vis spectrum of **16-*cis*** (10:1 mixture) exhibited a λ_{max} peak at 675 nm while the 5:2 *cis*/*trans* diasteromeric mixture possessed equally intense λ_{max} peaks at 675 and 695 nm. Thus, the latter band was assigned to the 2,12-dioxa-substituted *trans*-isomer **16-*trans***. The structure and regiochemistry of **16-*cis*** was confirmed using single-crystal X-ray diffractometry (Figure 2). In contrast to compound **14**, the *cis* geometry could thus be unambiguously established (see below).

Zinc insertion into the regioisomeric mixture of gray nonpolar **16** proceeded smoothly to form the more polar

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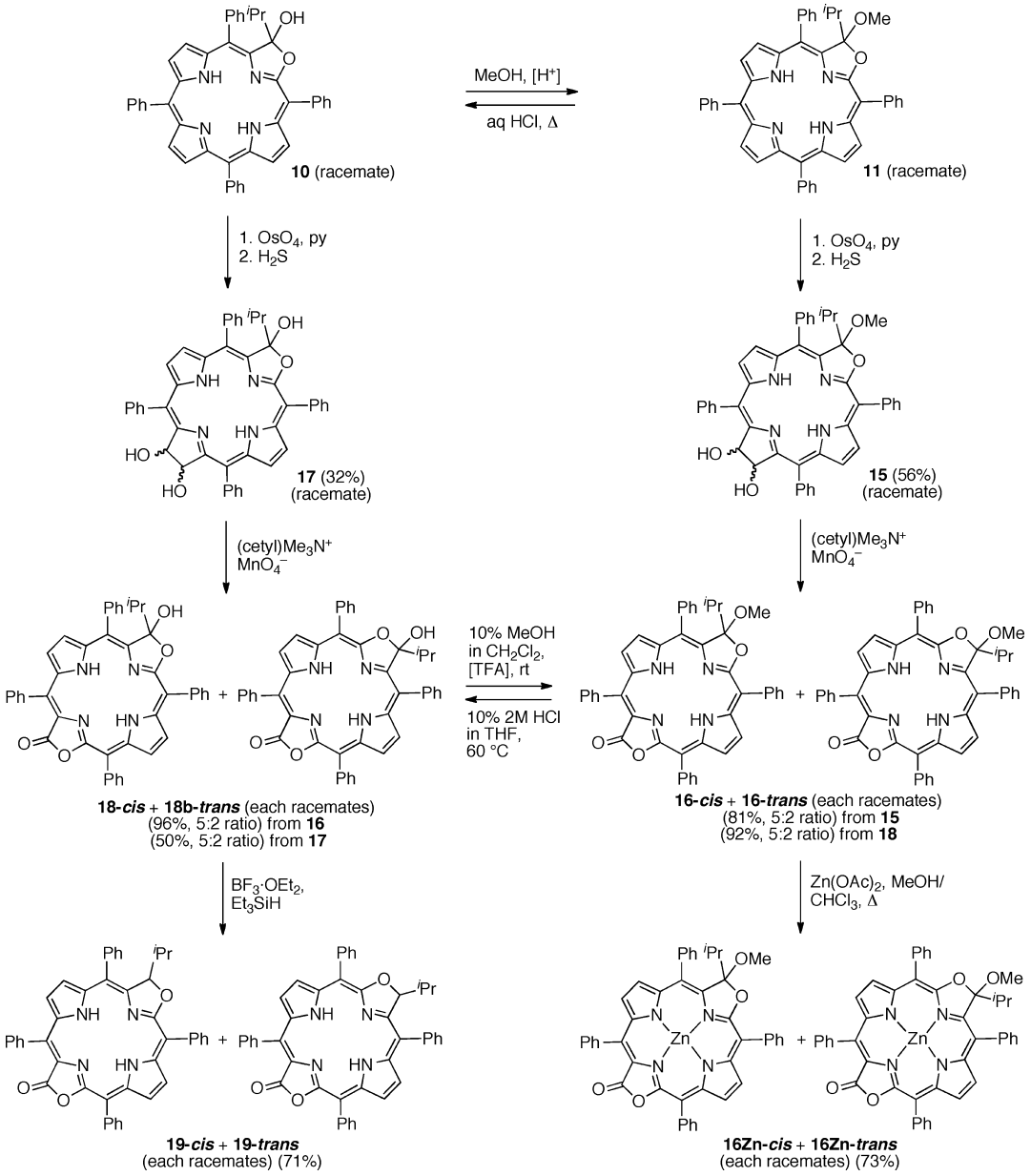
Scheme 3. Syntheses of Alkylbisoxazolochlorins 16, 16Zn, 18, and 19



green product **16Zn** of identical regioisomeric ratio. The product showed, as expected, a metallochlorin-type spectrum (see the Supporting Information). Compound **16-Zn-*cis*** was also elucidated by single-crystal X-ray methods. Thus, as for its free base **16-*cis***, the regiochemistry of this metallochlorin analogue could also be clearly determined (Figure 2).

Treatment of **16** with 2 M aqueous HCl in THF hydrolyzed its ketal moiety to form hemiketal **18** in near-quantitative yield. The replacement of the methoxy proton peak (at 3.1 ppm) in the ^{1}H NMR spectrum of the reactant with a hydroxy peak at 3.9 ppm (exchangeable with D_2O) in the ^{1}H NMR spectrum of the product, with no further significant differences in their spectra, confirmed the transformation. This reaction is reversible. Thus, hemiacetal **18** is swiftly converted back into **16** in the presence of methanol with catalytic amount of TFA at ambient temperature (see Scheme 3).[31,39] The UV−vis spectra of **16** and **18** are nearly identical (see the Supporting Information). The pathway toward **18** (**8** → **11** → **15** → **16** → **18**) proved to be overall higher yielding compared to the shorter alternative sequence (**8** → **10** → **17** → **18**) previously communicated.[34] This is because the presence of the acetal moiety in **11** significantly improved the yield of the dihydroxylation reaction as well as the MnO_4^--mediated oxidation step.

Hemiketals of type **10** could be hydro-dehydroxylated to the corresponding oxazolochlorin **12** (Scheme 1).[31] Likewise, treatment of **18** with $Et_3SiH/BF_3{\cdot}OEt_2$ produces the less polar grayish-green bisoxazolochlorin **19** in acceptable yield (Scheme 3). This transformation was expressed in the ^{1}H NMR spectrum of the product by the replacement of the hydroxy peak in spectrum of **18** by a diagnostic singlet for the oxazoline hydrogen (at 6.7 ppm). Once again, the removal of the α-hydroxy group caused a bathochromic shift in the UV−vis spectrum of **19** when compared to the spectrum of **18** and, not surprisingly, its spectrum is very similar to that of **14** (Figure 3).[31]

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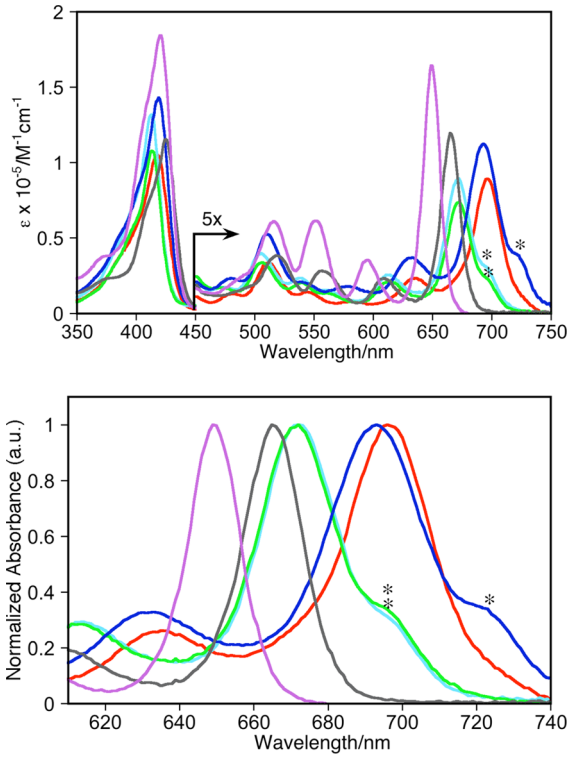


Figure 3. (A) UV−vis spectra (CH_2Cl_2) and (B) normalized λ_{max} bands of chlorins **9** (gray), **11** (purple), **14-*cis*** (blue), **16-*cis*** (lime green), **18-*cis*** (light blue), and **19-*cis*** (red). The asterisks on the shoulder features of the spectra of indicate the chlorins **14-*cis*** (blue), **16-*cis*** (lime green), and **18-*cis*** (light blue) result from a contribution from the corresponding *trans*-configured isomers that remained even after repeated crystallizations (*cis*/*trans* ratio ~10:1).

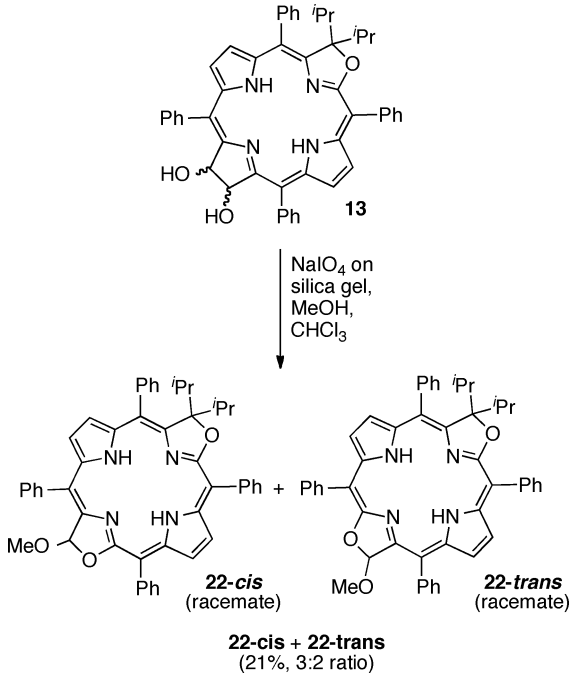
Much to our disappointment, none of the bisoxazolochlorins **16** (as its free base or zinc complex **16Zn**), **18**, or **19** were susceptible to an alkylation of the lactone moiety using Grignard reagents under a variety of reaction conditions without extensive decomposition. Likewise, the double-alkylation of bisporpholactone **20**[28,40,32] failed to provide any isolable product (Scheme 4). Thus, alkylation pathways did not allow the generation of bisoxazolobacteriochlorins.

An exhaustive hydride reduction (using DIBAl-H or Et_3SiH) of **20** appeared to reduce both lactones of **20** to methylene groups as the crude mixture showed a strongly red-shifted bacteriochlorin-type spectrum (λ_{max} = ~815 nm), and the HR-MS indicated the presence of a product of the desired composition (signal indicative of a MH^+ of the composition $C_{42}H_{31}N_4O_2$). However, the product appeared to be extremely light- and acid sensitive and could not be isolated in a quantity allowing an unequivocal characterization. We observed the sensitivity of unsubstituted oxazolochlorins or bis-pyrrole-modified chromophores previously.[26,31] Nonetheless, the discovery of a fortuitous transformation eventually led to the isolation of (partially alkylated) bisoxazolobacteriochlorins.

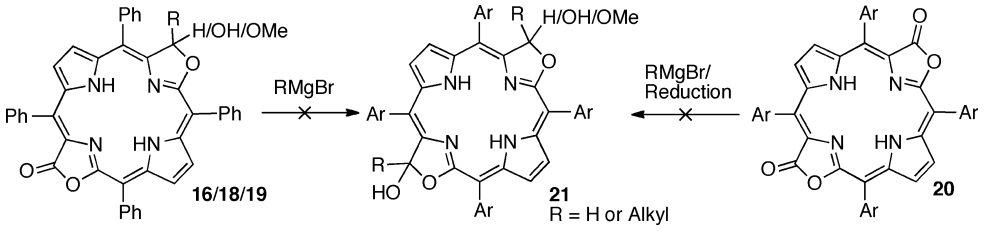
Synthesis of Bisoxazolobacteriochlorins. We previously established that the oxidative cleavage of a diol functionality of a dihydroxychlorin with $NaIO_4$/silica gel[41] generates the corresponding secochlorin bisaldehyde.[42] Performed in ROH/$CHCl_3$, this bisaldehyde is converted in situ to a dialkoxymorpholinochlorin.[43] Thus, for example, bismorpholinobacteriochlorin **6** is formed from tetraol **5**.[26]

When we submitted polar dihydroxyoxazolobacteriochlorin **13** to these reaction conditions, the resulting nonpolar product **22** showed the expected bathochromic UV−vis spectrum (λ_{max} = 770 nm), but it possessed a composition (as per ESI^+-HRMS) of $C_{49}H_{45}N_4O_3$ (for MH^+), i.e., short of a C_2H_4O fragment to the composition of the expected morpholinooxazolobacteriochlorin. Further, the ^1H NMR spectrum of this purple-pink product confirmed the loss of the diagnostic pyrroline hydrogen peaks of the *β*,*β*′-dihydroxy moiety but revealed the appearance of a new signal for only a single methoxy group (3.1 ppm, s, 3H) in a compound that appeared as a 3:2 mixture of two regioisomers (that could not be separated by plate or column chromatography), each occurring as a racemate. These findings are consistent with the formation of bisoxazolobacteriochlorin **22** (Scheme 5). A similar trans-

Scheme 5. Syntheses of Dialkylbisoxazolobacteriochlorins 22



Scheme 4. Failed Routes toward Dioxazolobacteriochlorins 21



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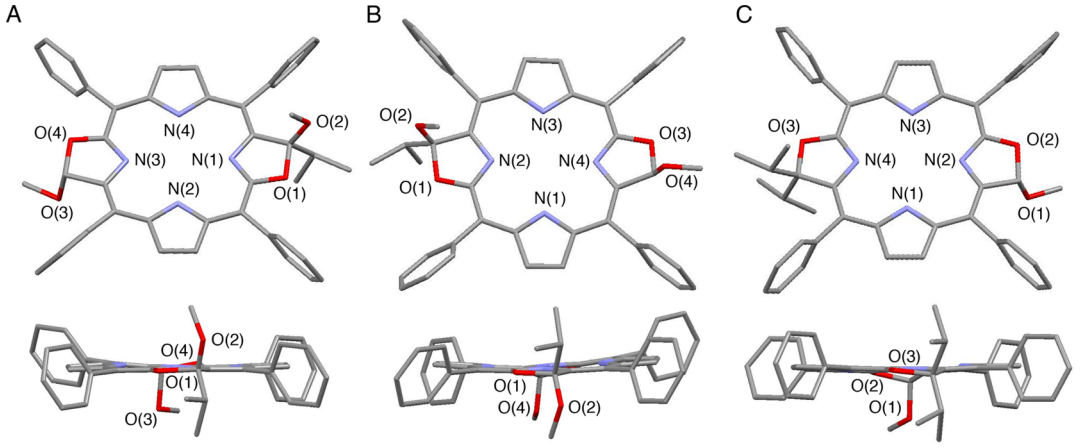
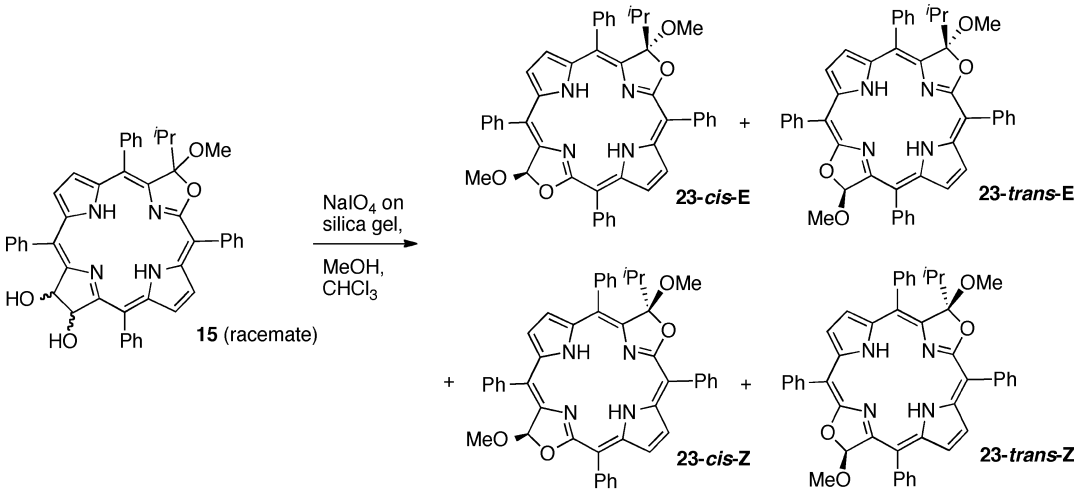


Figure 4. Representation of the molecular structures of **23-*trans*-*E*** (A), **23-*trans*-*Z*** (B), and **22-*cis*** (C) (top and side views). All hydrogen atoms attached to carbon positions and the minor disorder contributions have been omitted for clarity.

Scheme 6. Syntheses of Monoalkylbisoxazolobacteriochlorin Isomers 23



only one enantiomer of all regio- and stereo-isomers of **23** shown;
23, all isomers (31%) + recovered **15** (25%)

formation was utilized in the synthesis of oxazolochlorins.[1] Based on the findings reported above, we surmise that the *cis*-isomer is the majority isomer. Although the crystal structure of **22** shown in Figure 4 represents a *cis*-bisoxazolobacteriochlorin, this could not be clearly determined via X-ray structural analysis because of disorder in the asymmetric unit.

The one-step β,β'-dihydroxypyrroline to α-methoxyoxazoline conversion can also be applied to bacteriochlorin diol **15**. However, the spectroscopic analysis of the resulting bisoxazolobacteriochlorin **23** is complicated by the presence of several regio- and stereoisomers (Scheme 6). The molecule contains two chiral α-oxazoline carbons. Their relative orientations to each other gives rise to *E*/*Z* regioisomers. In addition, the second oxazole can be arranged such that the ring oxygen atoms are on the same side (*cis*) or on opposite sides (*trans*). All isomers are formed with little to no regioselectivity (as per ^{1}H NMR spectrum of the crude mixture). The regioisomeric mixture of **23** can be purified into the *E*- and *Z*-isomers using an automated flash chromatography system (on high performance silica gel, 50% hexane/CH_2Cl_2) though this process also causes substantial decomposition of products on the stationary phase (alumina did not allow any separation). Both fractions, bright pink in color, possess identical UV–vis absorption spectra and compositions ($C_{47}H_{41}N_4O_4$ as per ESI$^+$-HRMS). Based on the relative polarity of the *E*/*Z* isomers of the tetrahydroxybacteriochlorins,[23] we presumed that the less polar fraction contains the *E*-isomers while the more polar fraction contains the *Z*-isomers (vide infra). This could be confirmed by single-crystal X-ray structural elucidation. The nonpolar fraction contained the **23-cis**/***trans*-*E*** isomers while the more polar fraction contained **23-cis**/***trans*-*Z*** isomers. Because of disorder problems in the asymmetric unit, however, we could not unequivocally determine their regiochemistry (Figure 4; the *trans*-isomers are shown).

The UV–vis spectra of the starting oxazolobacteriochlorin diols (**13** and **15**) and the bisoxazolobacteriochlorins are typical bacteriochlorin-type spectra (Figure 5). Once again, the trend that the λ_{max} of a given chlorin or bacteriochlorin red-shifts upon replacement of a pyrroline by an oxazoline is maintained.[31]

The above findings demonstrate that the α,α-dialkylbisoxazolobacteriochlorins, such as **22**, are chemically more robust than their monoalkyl/alkoxy analogues. This suggested to us a renewed attempt at reducing a bisoxazolochlorin (such as **16**/**18**/**19**/**20**) to the corresponding bisoxazolobacteriochlorin. Indeed, reduction of α,α-dialkyloxazole-substituted lactone **14**

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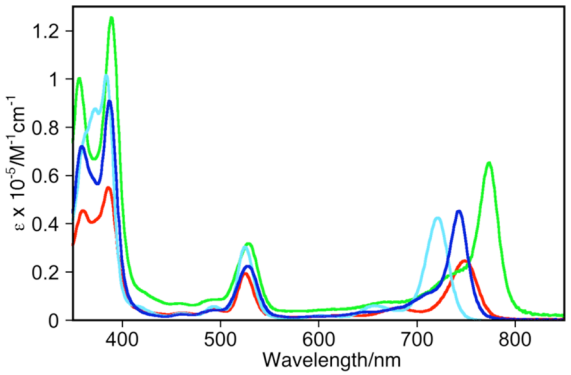
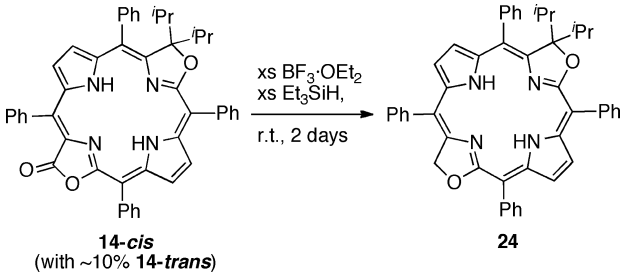


Figure 5. UV−vis spectra of **13** (red), **15** (light blue), **22** (*cis*/*trans* mixture, lime green), and **23** (mixture of all isomers, blue) in CH_2Cl_2 at ambient temperature.

could be achieved using a ∼30-fold large excess of Et_3SiH/BF_3·OEt_2. The reaction was slow, full conversion (determined by the development of the diagnostic product λ_{max} peak at 815 nm) to form bisoxazolobacteriochlorin **24** took nearly 48 h at room temperature, and the isolated yield was relatively low (**18**) (Scheme 7).

Scheme 7. Synthesis of Dialkylbisoxazolobacteriochlorins 24



The disappearance of the carbonyl $\nu_{C=O}$ in the IR spectrum of the product, the composition of $C_{48}H_{43}N_4O_2$ (as per ESI^+-HRMS), and the presence of the diagnostic oxazoline ^1H NMR peak (6.4 ppm, s, 2H) confirmed the dialkylbisoxazolobacteriochlorins structure of **24**. Product **24** was isomerically pure when a **14-*cis*** isomer-enriched (∼10:1) mixture was used as the starting material. In addition, the lack of chiral centers in **24** also greatly simplified its ^1H NMR spectrum. As expected, the UV−vis spectrum for **24** is a bathochromic shifted bacteriochlorin-type spectrum (Figure 6).

In part, the low yield of product **24** is because of a pronounced (light-induced) oxidation sensitivity of the non-alkylated oxazole moiety, forming the lactol derivative (indicated by the presence of the parent mass of the MH^+ ion at m/z 737 and a hypsochromic UV−vis spectrum, λ_{max} = 770 nm), or even regenerating the starting material.[31] The stability of alkylbisoxazolobacteriochlorin **24** on silica gel was also limited (and alumina proved unsuitable to separate the product from the reactant). Thus, we resorted to a fractional crystallization method (solvent exchange from CH_2Cl_2 to MeOH, at ambient temperatures, or below, and rigorously shielded from light) to isolate product **24**.

Fluorescence Emission Spectra of the Oxazolochlorins and Oxazolobacteriochlorins. The fluorescence emission spectra of the dioxazolochlorins **14**, **16**, and **18** are all chlorin-type (Figure 7) with the small Stoke's shift typical for porphyrinoids and with fluorescence quantum yields ranging between 0.11 to 0.19. The dihydroxyoxazolobacteriochlorins **13** and **15** exhibited fluorescence emission spectra with quantum yields in the range of 0.07 to 0.14, i.e., unusually high yields for bacteriochlorin-type chromophores.[8,17,44] The dioxazolobacteriochlorins show much lower fluorescence yields (in the range between 7% and under 1%; see the Supporting Information for details), values that at are more typical for regular bacteriochlorins.[8,17,44] Thus, as far as the fluorescence properties of the oxazole-derived chromophores is concerned, the effects of a replacement of one and two carbon atoms in the chromophore framework is largely comparable to the effects a reduction of the β,β'-bond, although the high emission yields of the mono-oxazole-based bacteriochlorins are remarkable. A detailed photophysical characterization of the oxazolobacteriochlorins is in preparation.

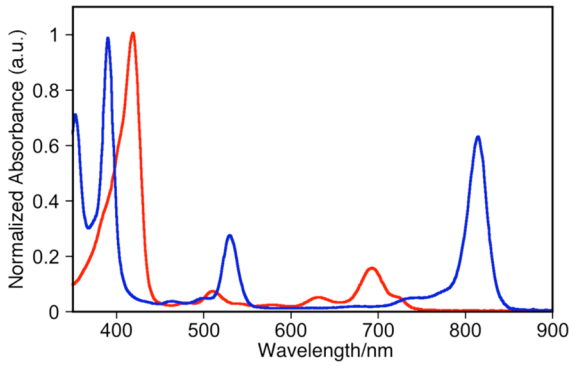


Figure 6. Comparison of the UV−vis spectra (CH_2Cl_2; normalized at λ_{Soret}) of α,α-dialkyloxazole-substituted lactone **14** (red) and its reduction product, dialkylbisoxazolobacteriochlorins **24** (blue).

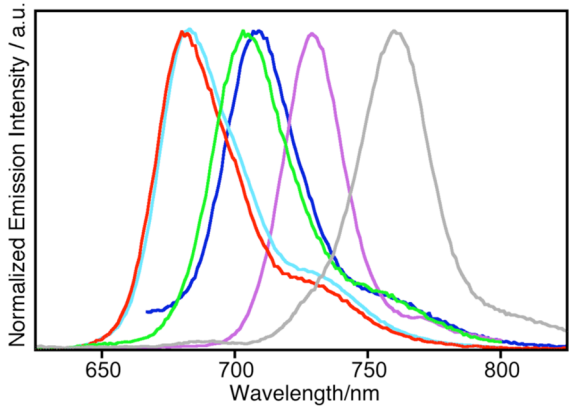


Figure 7. Normalized fluorescence spectra of **13** (gray), **14** (lime green), **15** (purple), **16** (light blue), **18** (red), and **19** (blue) (all in CH_2Cl_2 at ambient temperature $\lambda_{excitation} = \lambda_{soret}$).

■ CONCLUSIONS

We demonstrated the stepwise replacement of a pyrroline moiety in a bacteriochlorin chromophore by one or two oxazolone or oxazoline moieties. Depending on the presence of an oxazolone or oxazoline moiety, the resulting chromophores possess chlorin (when one oxazolone moiety is present) or bacteriochlorin characteristics (when either one pyrroline and oxazoline or two oxazoline moieties are present) (Figure 8). The chromophores possess UV−vis spectra that are predictably tuned based on the regioisomer and the number and position of the substituents. Thus, a stepwise modification of the porphyrin chromophore with oxazolines (variously substituted)

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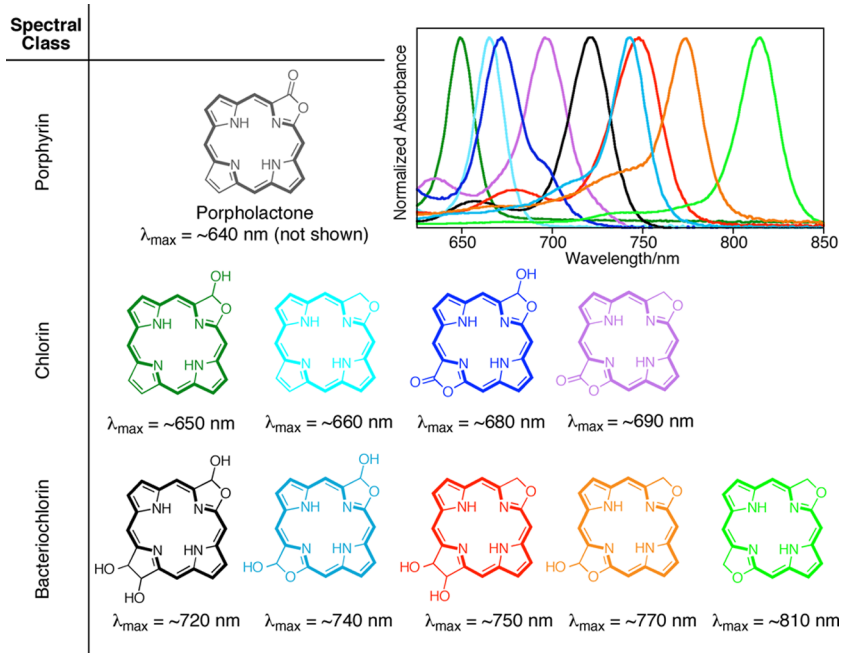

Figure 8. Oxazole-based chromophores sorted according to chromophore class and plot of their normalized λ_{max} band, delineating their structure–optical properties (λ_{max}) relationships.

in combination with oxazolines, oxazolones and (dihydroxy-substituted) pyrrolines allows a fine-tuning of their λ_{max} from 650 to 810 nm in small increments. Thus this study defines the structure-optical property relationships in oxazole-derived chlorins and bacteriochlorins.

A number of crystal structures of the bisoxazole-based chromophores demonstrate that the replacement of one or two β-carbons by oxygen atoms does not change the overall planarity of the macrocycle. In fact, most chromophores are more planar than, for instance, the chromophore of the parent tetrahydroxybacteriochlorin **5**,[23] implying that the observed tuning of the UV–vis spectra is an electronic substituent effect that is minimally, if at all, affected by conformational effects. Thus, the results we derived earlier for mono-oxazolochlorins can be transferred to the mono- and bis-oxazolobacteriochlorin series, except that the bacteriochlorins are more sensitive to substituent-induced shifts of their optical spectra.[31,33]

The relatively facile preparation of the novel bacteriochlorin analogues alkyloxazolobacteriochlorins, the oxidative stability of select members of this compound class, and the ability to tune their optical spectra suggests their further study with respect to their applicability as PDT agents, fluorescence tags, or in light-harvesting systems. Studies along these lines are currently ongoing in our laboratories.

EXPERIMENTAL SECTION

X-ray Single-Crystal Diffractometry. X-ray crystallographic analysis: Single crystals of **14-*cis***, **16-*cis***, **16Zn-*cis***, **22-cis**, **23-*trans*-E**, and **23-*trans*-Z** and were coated in Fomblin oil, mounted on a pin, and placed on a goniometer head under a stream of nitrogen cooled to 100 K. The data were collected on an APEX2 CCD diffractometer with Cu source Kα radiation (λ = 1.54178 Å). The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. Data were corrected for absorption effects using the multiscan method (SADABS), and the structure was solved and refined using the Bruker SHELXTL software package until the final anisotropic full-matrix, least-squares refinement of F2 converged. Data collection and structural parameters for the structure elucidations of **14-*cis***, **16-*cis***, **16Zn-*cis***, **22-*cis***, **23-*trans*-E**, and **23-*trans*-Z** can be found in the Supporting Information.

Materials and Instrumentation. *meso*-Tetraphenyl-2-oxachlorins **9**–**11** were synthesized as reported in the literature.[33] Flash column chromatography was performed manually in glass columns or on an automated flash chromatography system, on normal-phase silica (solvents used are indicated; isochratic elution modes). The fluorescence quantum yields (ϕ) were determined relative to those of *meso*-tetraphenylporphyrin (ϕ = 0.11 in benzene, calculated to be 0.09 in CH_2Cl_2);[45] $\lambda_{excitiation} = \lambda_{Soret}$.

***meso*-Tetraphenyl-12,13-*cis*-dihydroxy-3,3-diisopropyl-2-oxabacteriochlorin (13). General Procedure for the Conversion of 2-Oxachlorins to 2-Oxabacteriochlorins.** To a solution of **9** (1.1 g, 1.57 mmol) dissolved in $CHCl_3$ was added a solution of OsO_4 in pyridine (2 equiv, 796 mg). CAUTION: OsO_4 is volatile and extremely toxic, use with care; perform in fume hood and wear protective gear at all times! Reaction progress was monitored by TLC and UV–vis spectroscopy. The conversion of starting material to product can be identified by the formation of a sharp peak at ~750 nm in the UV–vis spectrum of an aliquot of the reaction mixture. The reaction was allowed to stir until no further reaction was detectable (2–3 days). The reaction vessel was then purged with gaseous H_2S for 5 min. CAUTION: fume hood; use of a bleach-filled H_2S scrubber is recommended. The reaction was stirred for approximately 15–30 min under an H_2S atmosphere. The excess H_2S was purged out using N_2 overnight, and the remaining solvent (if any) was evaporated by rotary evaporation. Product **13** was isolated by column chromatography (silica, 1% MeOH/CH_2Cl_2) as a dark purple solid in 34% yield (550 mg of the starting material **9** was also recovered): MW = 736.3 g/mol; R_f = 0.10 (silica, CH_2Cl_2); UV–vis (CH_2Cl_2) λ_{max} (log ε) 360 (4.65), 386 (4.74), 462 (3.49), 492 (3.66), 526 (4.28), 619 (3.31), 680 (3.69), 750 (4.39) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} 385 nm) 687, 760 nm, ϕ = 0.07; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.07 (m, 2H), 7.95–8.00 (m, 2H), 7.86–7.87 (m, 5H), 7.51–7.64 (m, 15H), 6.03 (d, ^3J = 7.1 Hz, 1H), 5.91 (d, ^3J = 7.1 Hz, 1H), 2.46–2.49 (m, 2H), 1.06 (d, ^3J = 6.6 Hz, 3H), 0.96 (d, ^3J = 6.6 Hz, 3H), 0.74 (d, ^3J = 6.8 Hz, 3H), 0.60 (d, ^3J = 6.8 Hz, 3H), 0.36 (s, 1H), −0.21 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 165.3, 161.9, 154.2, 152.9, 149.8, 141.6, 141.1, 140.5, 140.4, 140.1, 139.6, 138.2, 133.9, 133.6, 133.3, 133.1, 131.9, 131.6, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5, 127.4, 126.5, 126.5, 126.4, 125.6, 123.9, 120.3, 119.0, 118.6, 113.9, 112.1, 102.6, 100.1,

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74.5, 72.8, 70.7, 36.7, 36.6, 32.1, 29.8, 29.5, 29.4, 24.9, 22.8, 19.0, 18.9, 18.5, 14.3 ppm; HR-MS (ESI$^+$ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{49}H_{45}N_4O_3$ 737.3492, found 737.3490.

***meso*-Tetraphenyl-12,13-*cis*-dihydroxy-3-isopropyl-3-methoxy-2-oxabacteriochlorin (15).** A diastereomeric mixture of **15** (178 mg) was prepared as dark purple powder in 56% yield from *meso*-tetraphenyl-3-isopropyl-3-methoxy-2-oxachlorin (**11**) (300 mg, 0.44 mmol) according to the general procedure described for the formation of **13**. The two diastereomers were separated using automated chromatography (silica, CH_2Cl_2): MW = 724.84 g/mol; R_f = 0.30 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 374 (4.94), 383 (5.00), 494 (3.74), 525 (4.48), 657 (3.77), 722 (4.63) nm; fluorescence λ_{max} ($CHCl_3$, λ_{exc} = 385 nm): 729 nm, ϕ = 0.12; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.26 (dd, ^3J = 4.9, ^4J = 1.4 Hz, 1H), 8.12 (dd, ^3J = 4.7, ^4J = 1.4 Hz, 1H), 8.12−7.69 (m, 8H), 7.66−7.51 (m, 14H), 6.08 (m, 2H), 3.05 (s, 3H), 2.07 (m, 1H), 1.11 (d, ^3J = 6.5 Hz, 3H), 0.58 (d, ^3J = 6.8 Hz, 3H), −0.38 (s, 1H), −0.88 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 162.1, 161.9, 154.5, 145.1, 141.4, 140.8, 140.7, 139.9, 138.9, 138.8, 137.1, 134.7, 133.7, 133.5, 133.4, 133.2, 132.7, 132.1, 131.7, 128.2, 128.1, 127.8, 126.7, 126.1, 125.8, 120.9, 120.4, 118.2, 116.9, 114.8, 114.5, 102.9, 74.6, 73.2, 70.8, 50.7, 35.6, 31.8, 22.9, 17.4, 16.3, 14.3 ppm; HR-MS (ESI+ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{47}H_{41}N_4O_4$ 725.3128, found 725.3126.

***meso*-Tetraphenyl-12,13-*cis*-dihydroxy-3-hydroxy-3-isopropyl-2-oxabacteriochlorin (17).** A diastereomeric mixture (1:3) of **17** was prepared as dark purple solid in 32% yield from *meso*-tetraphenyl-3-hydroxy-3-isopropyl-2-oxachlorin (**10**) (300 mg, 0.44 mmol) according to the general procedure described for the synthesis of **13**. The diagnostic peak of product **17** was observed at ∼720 nm: MW = 710.80 g/mol; R_f = 0.10 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 371 (4.94), 383 (5.01), 460 (3.66), 491 (3.84), 524 (4.50), 597 (3.46), 654 (3.85), 719 (4.60) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 383 nm) 663, 731 nm, ϕ = 0.14; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.26 (d, ^3J = 4.0 Hz, 0.33H), 8.23 (d, ^3J = 4.2 Hz, 1H), 8.16 (d, ^3J = 7.5 Hz, 1H), 8.11 (m, 1.33H), 8.01−8.06 (m, 2.3H), 7.94 (m, 4H), 7.76−7.78 (m, 3.33H), 7.50−7.78 (m, 16H), 6.14 (d, ^3J = 6.9 Hz, 1H), 5.99 (d, ^3J = 6.9 Hz, 1H), 2.31 (m, 0.33H), 2.07 (m, 1H), 1.22 (d, ^3J = 6.5 Hz, 3H), 0.74 (d, ^3J = 6.7 Hz, 3H), −0.31 (s, 1H), −0.38 (s, 0.33H), −0.79 (s, 1H), −0.85 (s, 0.33H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 162.3, 161.9, 161.3, 161.3, 154.6, 154.0, 148.0, 141.5, 141.4, 140.8, 140.8, 140.8, 140.7, 140.1, 139.9, 138.9, 138.9, 138.9, 137.1, 137.0, 134.7, 134.7, 134.3, 134.3, 133.8, 133.6, 133.5, 133.4, 133.2, 133.2, 132.1, 132.0, 131.8, 131.7, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 126.8, 126.8, 126.7, 126.7, 126.2, 126.1, 125.8, 121.0, 120.9, 120.3, 120.2, 118.5, 114.7, 114.7, 114.5, 114.3, 113.1, 113.0, 103.2, 103.2, 102.9, 75.1, 75.1, 74.6, 73.2, 72.8, 70.8, 51.1, 36.2, 36.1, 32.2, 29.9, 29.9, 22.9, 17.9, 17.7, 15.9, 14.3 ppm; HR-MS (ESI$^+$ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{46}H_{39}N_4O_4$ 711.2971, found 711.2968.

***meso*-Tetraphenyl-3,3-diisopropyl-2,12-dioxa-13-oxochlorin (14-*trans*) and *meso*-Tetraphenyl-3,3-diisopropyl-2,13-dioxa-12-oxochlorin (14-*cis*). General Procedure for the Conversion of Diolbacteriochlorin to Bisoxazolochlorin.** Into a stirring solution of *meso*-tetraphenyl-12,13-*cis*-dihydroxy-3,3-diisopropyl-2-oxabacteriochlorin (**13**, 350 mg) in $CHCl_3$ (20 mL) was added 3 equiv of cetyltrimethylammonium permanganate (CTAP). The reaction was allowed to stir for ∼4 h. Reaction progress was monitored using UV−vis spectroscopy and TLC. The bacteriochlorin spectrum of **13** disappeared as the formation of a chlorin spectrum (λ_{max} ∼695 nm) was observed. Product **14** was isolated as diasteromeric mixture of gray-green powder-like solid in 67% yield (231 mg) using column chromatography (silica, CH_2Cl_2). ^{1}H NMR indicated a regioisomeric ratio of 7:1 favoring the formation of *meso*-tetraphenyl-3,3-diisopropyl-2,13-dioxa-12-oxochlorin. Repeated chromatography (silica, 50% hexane/CH_2Cl_2) enriched the regioisomeric mixture to about ∼10:1: MW = 720.86 g/mol; R_f = 0.95 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 419 (5.15), 510 (4.02), 632 (3.87), 693 (4.35) nm; Fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 409 nm): 703 nm, ϕ = 0.11; ^{1}H NMR (300 MHz, $CDCl_3$, δ, minority product peaks not listed) 8.23 (dd, ^3J = 5.2, ^4J = 1.7 Hz, 1H), 8.09 (dd, ^3J = 5.2, ^4J = 1.8 Hz, 1H), 7.90 −7.92 (m, 2H), 7.78−7.87 (m, 7H), 7.55−7.71 (m, 10H), 7.53−7.57 (m, 2H), 7.19 (dd, ^3J = 4.6, ^4J = 2.1 Hz, 1H), 2.486 (m, 2H), 1.57 (s, 1H), 1.03 (d, ^3J = 6.6 Hz, 6H), 0.71 (d, ^3J = 6.9 Hz, 6H), 0.69 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 167.9, 167.3, 157.6, 154.2, 143.9, 141.6, 141.5, 139.7, 138.4, 136.7, 133.6, 133.6, 133.2, 132.9, 131.7, 129.4, 128.6, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 126.9, 126.5, 125.0, 123.5, 120.1, 112.1, 104.4, 103.3, 100.8, 36.7, 19.1, 18.7 ppm; HR-MS (ESI+ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{48}H_{41}N_4O_3$ 721.3179, found 721.3161.

meso*-Tetraphenyl-3-isopropyl-3-methoxy-2,13-dioxa-12-oxochlorin (16-*cis*) and *meso*-Tetraphenyl-3-isopropyl-3-methoxy-2,12-dioxa-13-oxochlorin (16-*trans*).** A regioisomeric mixture of **16** (237 mg) was prepared as gray, powder-like solid in 81% yield from **15** (300 mg, 0.41 mmol) according to the general procedure described for the synthesis of **14**. ^{1}H NMR of the crude reaction mixture indicated the product to be in 5:2 regioisomeric ratio favoring the isomer **16-*cis. The major isomer **16-*cis*** can be further purified (up to ∼10:1 d.r.) by repeated column chromatography (50% hexane in CH_2Cl_2): MW = 708.8 g/mol; R_f = 0.90 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 414 (5.12), 505 (3.89), 538 (3.67), 614 (3.71), 672 (4.26) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 415 nm) 683 nm, ϕ = 0.19; ^{1}H NMR (300 MHz, $CDCl_3$, δ, peaks corresponding to the minority product are not listed) 8.38 (dd, ^3J = 5.2, ^4J = 1.5 Hz, 1H), 8.28 (dd, ^3J = 5.2, ^4J = 1.6 Hz, 1H), 8.01−7.87 (m, 8H), 7.72−7.60 (m, 14 H), 3.08 (m, 3H), 2.05 (m, 1H), 1.13 (d, ^3J = 6.6 Hz, 3H), 0.89 (s, 1H), 0.69 (d, ^3J = 6.8 Hz, 3H), 0.05 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 167.2, 164.8, 162.6, 154.4, 152.5, 147.8, 143.7, 141.8, 141.3, 140.4, 139.9, 138.1, 138.0, 137.9, 137.5, 136.8, 136.7, 136.6, 133.9, 133.8, 133.7, 133.3, 133.1, 133.0, 132.8, 132.5, 131.8, 131.7, 131.1, 129.5, 129.0, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.9, 127.8, 127.0, 126.9, 126.3, 126.0, 125.1, 124.6, 124.3, 120.8, 117.7, 117.2, 115.1, 107.3, 104.8, 103.4, 102.7, 50.8, 35.8, 35.6, 31.1. 17.4, 17.4, 16.4, 16.3 ppm; HR-MS (ESI+ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{46}H_{37}N_4O_4$ 709.2815, found 709.2825.

[*meso*-Tetraphenyl-3-isopropyl-3-methoxy-2,13-dioxa-12-oxochlorinate]Zn(II) (16Zn-*cis*). Free base **16** (100 mg of 10:1 mixture, 0.14 mol) was dissolved in 30% MeOH/$CHCl_3$ (v/v, 30 mL) and heated to reflux. A solution of $Zn(OAc)_2{\cdot}H_2O$ (∼3−5 equiv, 90−150 mg) in warm MeOH (∼5 mL) was added, and the mixture was heated to gentle reflux overnight. The reaction progress was monitored by TLC. Upon completion, the product was isolated by rotary evaporation, followed by flash chromatography (silica−CH_2Cl_2). The material was obtained as a green crystalline solid by crystallization using a slow solvent exchange from CH_2Cl_2 to MeOH or pentane (73%, 79 mg): MW = 772.17 g/mol; R_f = 0.45 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 424 (458), 520 (3.73), 572 (3.65), 613 (3.81), 663 (4.33) nm; Fluorescence λ_{max} ($CHCl_3$, λ_{exc} = 414 nm): 677 nm, ϕ = 0.08; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.38 (m, 1H), 8.27 (m, 1H), 8.04 (m, 1H), 7.82−7.98 (m, 6 H), 7.47−7.77 (m, 16H), 2.99 (s, 3H), 2.00 (m, 1H), 1.09 (m, 3H), 0.88 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 166.7, 162.5, 156.5, 153.3, 151.9, 151.3, 144.7, 144.4, 140.4, 139.4, 139.3, 139.1, 137.9, 137.6, 134.1, 134.0, 133.9, 133.3, 133.2, 132.5, 132.0, 131.9, 131.5, 128.6, 127.9, 127.8, 127.7, 127.5, 127.34, 127.32, 127.30, 126.8, 126.1, 124.5, 123.7, 118.3, 117.8, 116.3, 104.7, 101.4, 50.5, 35.7, 17.1, 17.0, 16.1; HR-MS (ESI+ of MH$^+$, 100% CH_3CN, TOF) m/z calcd for $C_{46}H_{35}N_4O_4Zn$ 771.1945, found 771.1950.

***meso*-Tetraphenyl-3-hydroxy-3-isopropyl-2,13-dioxa-12-oxochlorin (18-*cis*) and *meso*-Tetraphenyl-3-hydroxy-3-isopropyl-2,12-dioxa-13-oxochlorin (18-*trans*).** A 10:1 regioisomeric mixture of **16** (0.08 mmol, 57 mg) was dissolved in 10% 2 M HCl in THF (25 mL) and stirred overnight at 45 °C. The reaction progress was monitored using TLC, and the product was isolated through column chromatography (silica, CH_2Cl_2) to give **17** in powder form (gray-green in color) in 96% yield (53 mg): MW = 694.78 g/mol; R_f = 0.60 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 413 (5.03), 506 (3.83), 540 (3.60), 613 (3.63), 672 (4.16) nm; Fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 414 nm) 680 nm, ϕ = 0.19; ^{1}H NMR (300 MHz, $CDCl_3$, δ, the peaks corresponding to the minority product are not listed) 8.36−8.34 (dd, ^3J = 5.2, ^4J = 1.9 Hz, 1H), 8.25−8.26 (dd, ^3J =

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5.2, ^4J = 1.9 Hz, 1H), 7.88−8.00 (m, 6H), 7.54−7.77 (m, 16H), 3.93 (s, 1H), 2.05 (m, 1H), 1.17 (d, ^3J = 6.8 Hz, 3H), 0.71 (m, 4H), −0.12 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 167.2, 164.2, 154.2, 150.7, 143.7, 141.3, 140.1, 138.1, 138.0, 136.7, 134.4, 133.9, 133.9, 133.8, 133.2, 131.9, 131.7, 129.6, 128.6, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.1, 126.4, 125.9, 125.0, 124.4, 120.8, 115.0, 113.1, 104.7, 103.8, 35.9, 17.8, 17.7, 15.8 ppm; HR-MS (ESI+ of MH^+, 100% CH_3CN, TOF) m/z calcd for $C_{45}H_{35}N_4O_4$ 695.2658, found 695.2645.

meso-Tetraphenyl-3-isopropyl-2,13-dioxa-12-oxochlorin (19-*cis*) and _meso_-Tetraphenyl-3-isopropyl-2,12-dioxa-13-oxochlorin (19-*trans*). A 10:1 regioisomeric mixture of *meso*-tetraphenyl-3-hydroxy-3-isopropyl-2,13-dioxa-12-oxochlorin and *meso*-tetraphenyl-3-hydroxy-3-isopropyl-2,12-dioxa-13-oxochlorin (**18**, 100 mg,) was dissolved in CH_2Cl_2 (30 mL) and stirred at room temperature. To this solution were slowly added excess $BF_3{\cdot}OEt_2$ (10 equiv, 0.17 mL of 98%+ solution) and Et_3SiH (10 equiv, 0.23 mL). Reaction progress was monitored using UV−vis spectroscopy (formation of the diagnostic peak at ∼695 nm in a neutralized aliquot). Upon completion (∼2−3 h reaction time), the reaction mixture was quenched by addition of a satd aq $NaHCO_3$ solution. The mixture was transferred to a separatory funnel. The aqueous $NaHCO_3$ wash was repeated until all acids were removed. The organic layer was isolated and dried using Na_2SO_4, and the solvent was evaporated by rotary evaporation. The crude product was purified by flash chromatography (silica-CH_2Cl_2) to afford the product **19** as an powder like gray solid in 71% yield (69 mg). The product was isolated as a regioisomeric mixture (10:1 based on ^{1}H NMR) reflecting the diastereomeric mixture of the starting material. For the sake of simplicity, only the spectroscopic data of **19-*cis*** are listed here: MW = 678.78 g/mol; R_f = 0.95 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 418 (5.02), 483 (3.41), 510 (3.82), 544 (3.45), 633 (3.66), 695 (4.25) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} 414 nm) 709 nm, ϕ = 0.13; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 8.27 (dd, ^3J = 5.2, ^4J = 1.9 Hz, 1H), 8.14 (dd, ^3J = 5.2, ^4J = 1.9 Hz, 1H), 8.93−7.78 (m, 8H), 7.69−7.62 (m, 14 H), 6.73 (d, ^3J = 2.6 Hz, 1H), 1.92 (m, 1H), 1.44 (s, 1H), 1.05 (d, ^3J = 6.8 Hz, 3H), 0.68 (s, 1H), 0.59 (d, ^3J = 6.7 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 169.4, 169.2, 154.5, 154.1, 144.4, 144.1, 139.9, 139.8, 138.3, 138.2, 137.9, 136.8, 133.9, 133.6, 133.5, 133.3, 132.9, 132.4, 132.0, 131.8, 131.7, 130.4, 129.9, 129.6, 129.2, 128.6, 128.4, 128.3, 128.0, 127.7, 127.7, 127.7, 127.5, 126.4, 125.3, 124.1, 123.8, 123.1, 118.9, 112.1, 105.1, 102.9, 90.5, 90.5, 33.1, 32.7, 20.3, 20.1, 20.0, 14.4, 14.3 ppm; HR-MS (ESI+ of MH^+, 100% CH_3CN, TOF) m/z calcd for $C_{45}H_{35}N_4O_3$ 679.2709, found 679.2689.

meso-Tetraphenyl-3,3-diisopropyl-12-methoxy-2,13-dioxabacteriochlorin (22-*cis*) and _meso_-Tetraphenyl-3,3-diisopropyl-13-methoxy-2,12-dioxabacteriochlorin (22-*trans*). Prepared from diolbacteriochlorin **13** (48 mg) in 21% yield (10 mg, with ∼25% of **13** recovered) according to the general procedure described for the synthesis of **22**. The diagnostic peak of **23** in UV−vis spectroscopy was observed at ∼770 nm: MW = 736.89 g/mol; R_f = 0.85 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 390 (5.09), 356 (5.00), 528 (4.50), 774 (4.81) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 380 nm) 776 nm, ϕ = 0.03; ^{1}H NMR (300 MHz, $CDCl_3$, δ, contains **22-*cis*** and **22-*trans*** at a 3:2 ratio) 8.12 (m, 1H), 8.05 (m, 3H), 7.78−8.02 (m, 15H), 7.53−7.71 (m, 23H), 3.22 (s, 3H), 3.20 (s, 2H) 2.51 (m, 2H), 2.38 (m, 1H), 1.08 (m, 3H), 1.03 (m, 3H), 0.99 (m, 2H), 0.96 (m, 2H), 0.73 (m, 2H), 0.70 (m, 3H), 0.67 (m, 2H), 0.60 (m, 3H) −0.76(s, 1H), −0.92 (s, 1H) ppm;^{13}C NMR (100 MHz, $CDCl_3$, δ) 166.0, 164.1, 163.5, 160.2, 157.7, 152.2, 146.6, 143.1, 142.7, 140.9, 140.4, 140.3, 139.9, 139.6, 139.42, 139.36, 139.1, 137.9, 137.8, 137.4, 137.1, 136.5, 134.2, 133.9, 133.79, 133.78, 133.6, 133.4, 133.3, 133.2, 133.1, 132.8, 131.2, 130.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.79, 127.76, 127.68, 127.6, 127.5, 127.4, 127.3, 126.6, 126.5, 126.4, 122.98, 122.94, 122.4, 122.1, 117.7, 117.3, 117.1, 113.8, 113.2, 111.3, 105.9, 105.4, 103.7, 103.4, 102.9, 102.3, 100.6, 99.6, 54.25, 54.1, 37.0, 36.6, 36.5, 29.9, 19.4, 19.3, 19.1, 19.0, 18.9, 18.59, 18.57; HR-MS (ESI+ of MH^+, 100% CH_3CN, TOF) m/z calcd for $C_{49}H_{45}N_4O_3$ 737.3492, found 737.3504.

meso-Tetraphenyl-3-isopropyl-3,12/13-dimethoxy-2,12/13-dioxabacteriochlorin (23-*cis*/*trans*-E/Z). General Procedure for Conversion of Diolbacteriochlorins to Dioxazolobacteriochlorins. The starting compound (56 mg, 0.77 mmol) was dissolved in $CHCl_3$ (7 mL) at rt in a round-bottom flask equipped with a magnetic stirring bar, a N_2 inlet, and bubbler and shielded from ambient light with aluminum foil. Excess MeOH (3 mL) was added to the solution which then was purged with N_2. $NaIO_4$−silica[41] (∼ 0.5 g) was added to the stirring reaction mixture and allowed to react for ∼16 h. The reaction progress was monitored using UV−vis spectroscopy (product peak ∼740 nm). A full conversion of the starting material was never observed, and ∼25−30% recovery of starting material was generally observed. The mixture was then filtered (glass frit M), and the filter cake washed with CH_2Cl_2. The filtrate was evaporated to dryness by rotary evaporation. The bright pink products (in solution) were isolated by automated flash chromatography (silica, CH_2Cl_2). The nonpolar red-pink product was isolated in as an amorphous solid in 31% yield (17.5 mg, adjusted yield =45%) as a diastereomeric mixture: MW = 724.84 g/mol; R_f = 0.85 (silica, CH_2Cl_2); UV−vis (CH_2Cl_2) λ_{max} (log ε) 348 (4.86), 377 (4.96), 518 (4.34), 743 (4.37) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 377 nm) 747 nm, ϕ = 0.07; ^{1}H NMR (300 MHz, $CDCl_3$, δ, mixture of **23-*cis*/*trans*-E/Z**) 8.28 (m, 2H), 8.23 (m, 2H), 8.17 (m, 2H), 7.77−8.11 (m, 33H), 7.51−7.72 (m, 44H), 3.26 (s, 3H) 3.25 (s, 3H), 3.25 (s, 2H), 3.24 (s, 2H), 3.06 (s, 2H), 3.02 (s, 2H), 3.01 (s, 3H), 2.94 (s, 3H), 2.08 (m, 2H), 1.94 (m, 2H), 1.06 (m, 5H), 0.99 (m, 2H), 0.71 (m, 2H), 0.68 (m, 6H), 0.61 (m, 3H), −1.22 (m, 2H), −1.34 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 162.7, 163.0, 161.0, 160.9, 160.6, 160.5, 147.9, 147.8, 147.3, 147.1, 143.0, 142.9, 142.7, 142.3, 142.2, 139.7, 139.6, 139.5, 139.4, 139.10, 139.09, 138.8, 138.63 138.60, 138.5, 138.4, 137.94, 137.91, 137.6, 137.46, 137.45, 137.16, 137.14, 135.7, 135.6, 134.4, 134.3, 143.1, 133.9, 133.8, 133.6, 133.54, 133.52, 133.3, 133.20, 133.19, 133.0, 132.8, 132.6, 132.5, 131.2, 131.1, 130.6, 130.4, 128.1, 128.0, 127.96, 127.90, 127.74, 127.69, 127.6, 127.51, 127.49, 127.40, 127.38, 126.9, 126.8, 126.7, 126.1, 126.0, 123.7, 123.6, 123.2, 123.1, 122.64, 122.62, 118.4, 117.9, 117.8, 117.4, 117.20, 117.19, 116.6, 116.5, 116.3, 116.2, 113.97, 113.94, 113.44, 113.38, 106.24, 106.19, 105.6, 103.7, 103.6, 103.34, 103.33, 103.30, 103.27, 103.09, 103.05, 54.66, 54.5, 54.42, 54.38, 35.75, 35.73, 35.49, 35.42, 34.88, 34.73, 32.14, 25.5, 20.9, 17.6, 17.5, 16.5, 16.4, 16.3, 16.2 ppm; HR-MS (ESI+ of MH^+, 100% CH_3CN, TOF) m/z calcd for $C_{47}H_{41}N_4O_4$ 725.3128, found 725.3145.

meso-Tetraphenyl-3,3-diisopropyl-12,12-dihydro-2,13-dioxabacteriochlorin (24). In the dark or low light environment (important to avoid adventitious oxidation), a 10:1 diastereomeric mixture of *meso*-tetraphenyl-3,3-diisopropyl-2,12-dioxa-13-oxochlorin and *meso*-tetraphenyl-3,3-diisopropyl-2,13-dioxa-12-oxochlorin (**14-*cis*/*trans***, 80 mg, 0.11 mmol) was dissolved in CH_2Cl_2 and stirred at room temperature. To this solution was added slowly excess $BF_3{\cdot}OEt_2$ (30 equiv, 0.4 mL of 98+% solution) followed by Et_3SiH (30 equiv, 0.53 mL). Reaction progress was monitored using UV−vis spectroscopy (a band ∼820 nm in a neutralized aliquot, indicated the appearance of the product). The reaction was allowed to stir until all starting materials were consumed, and additional reductants were added as necessary until the UV−vis spectrum of the reaction mixture only displayed a the bacteriochlorin spectrum with a λ_{max} of ∼820 nm. Upon completion, the reaction mixture was quenched by addition of a satd aq $NaHCO_3$ solution. The mixture was transferred to a separatory funnel. The aq $NaHCO_3$ wash was repeated until all acids were removed. The organic layer was isolated and dried using Na_2SO_4, and the solvent was evaporated by rotary evaporation. The dark residue was redissolved in minimal CH_2Cl_2 and crystallized via slow solvent exchange with MeOH to give **24** as a thin, needle-like dark-purple crystalline solid in 18% yield (14 mg): MW = 706.87 g/mol; UV−vis (CH_2Cl_2) λ_{max} (log ε) 353 (4.65), 389 (4.79), 529 (4.24), 815 (4.6) nm; fluorescence λ_{max} (CH_2Cl_2, λ_{exc} = 379 nm) 819 nm, ϕ = <1%; ^{1}H NMR (500 MHz, $CDCl_3$, δ) 8.02 (dd, ^3J = 4.7, ^4J = 2.0 Hz, 1H), 7.87−7.93 (m, 6H), 7.82 (dd, ^3J = 4.5, ^4J = 2.0 Hz, 1H), 7.76−7.78 (m, 2H), 7.41−7.68 (m, 14H), 6.4 (s, 2H), 2.47 (m, 2H), 1.04 (d, ^3J = 6.6 Hz, 6H), 0.67 (d, ^3J = 6.9 Hz, 6H), −0.33 (s, 1H), −0.48 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, δ) 164.9, 163.6, 156.0, 152.4, 140.4, 140.2, 140.1, 139.4, 138.5, 137.9, 137.7, 136.8, 133.7, 133.2, 132.9, 131.6, 128.8, 128.2, 128.1, 127.8, 127.6, 127.5, 127.2, 126.4,

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122.8, 122.2, 121.8, 120.1, 111.8, 109.8, 102.8, 101.9, 100.1, 36.9, 19.3, 18.8; HR-MS (ESI+ of MH^+, 100% CH_3CN, TOF) m/z calcd for $C_{48}H_{43}N_4O_2$ 707.3386, found 707.3402.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR and IR spectra of all obtained compounds and experimental details for the crystal structure determination of **14-*cis***, **16-*cis***, **16-Zn-*cis***, **22-*cis***, **23-*cis*-E**, and **23-*trans*-Z**, including X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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