Syntheses, structures, modification, and optical properties of *meso*-tetraaryl-2,3-dimethoxychlorin, and two isomeric *meso*-tetraaryl-2,3,12,13-tetrahydroxybacteriochlorins†

Lalith P. Samankumara,[a] Matthias Zeller,[b] Jeanette A. Krause[c] and Christian Brückner*[a]

Received 2nd December 2009, Accepted 22nd January 2010
First published as an Advance Article on the web 22nd February 2010
DOI: 10.1039/b924539a

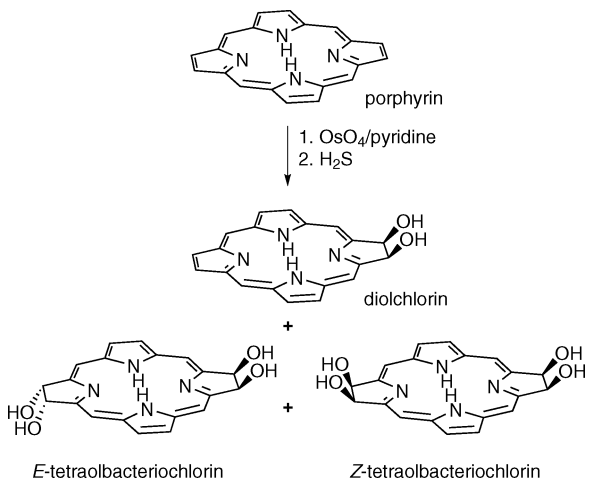
The refined syntheses, modification, and first X-ray structural characterization of *meso*-tetraarylporphyrin-derived β-tetraolbacteriochlorins are described. These investigations assign the relative stereochemistry of their two isomers (both *cis*-*vic*-diol pairs on the same or opposite sides of the porphyrin plane), an assignment that could not be provided by NMR, UV-vis or fluorescence spectroscopy, or mass spectrometry. Moreover, the first crystal structures of a 2-hydroxychlorin and a 2,3-dihydroxychlorin, as its dimethylether, are reported. Dihydroxylation and diimide reduction of the dimethoxychlorin result in the formation of stable mixed-functionality bacteriochlorins. The photophysical properties (UV-vis absorption and fluorescence emission) of all chromophores are contrasted against each other, delineating the electronic effects of diol substitution and conformational modulation. Lastly, the acid-induced dehydration/demethoxylation of the tetraol-, dioldimethoxy-, and tetramethoxybacteriochlorins to provide chlorins is delineated.

Introduction

The synthesis and study of chlorins (2,3-dihydroporphyrins) and bacteriochlorins (2,3,12,13-tetrahydroporphyrins) are key interests in current porphyrin-related research.[1] Photomedical and light-harvesting applications are two areas that drive the research. Two principle pathways are available towards their synthesis: total synthesis from monopyrrolic building blocks or the conversion of a porphyrin.[2,3]

A host of addition or reduction reactions are known that convert porphyrins to chlorins and bacteriochlorins though most require an appropriately β-substituted porphyrin.[4,5] However, two methods for the conversion of porphyrins to chlorins and bacteriochlorins have emerged as being fairly general: one is the diimide reduction of porphyrins,[5–7] the other their OsO_4-mediated β,β′-dihydroxylation.[8,9,10–15] Though the latter reaction is formally an oxidation reaction, it also generates chlorin chromophores.

Reaction of a porphyrin with one equivalent of OsO_4, followed by reductive cleavage of the osmate ester (commonly performed with H_2S) produces a 2,3-*cis*-diolchlorin. Reaction of the porphyrin with two equivalents of OsO_4 and subsequent reduction generates two isomeric 2,3,12,13-bis-(*cis*-diol)-bacteriochlorins (Scheme 1).[13-16] The two bacteriochlorin isomers vary in the relative orientation of their two diol functionalities. They can be on the same side of the mean plane defined by the porphyrin framework—we will refer to this isomer as the *Z*-tetraolbacteriochlorin (point group symmetry C_S), or they can be on opposite sides—we will refer to this isomer as the *E*-tetraolbacteriochlorin (C_{2h}).[17]



Scheme 1

Using octaalkylporphyrins, this osmylation reaction was first described by Hans Fischer in the early days of synthetic porphyrin chemistry,[8] and it proved of wide utility in the further derivatization of octaalkylporphyrins.[18–20] The corresponding reaction for *meso*-tetraaryl-porphyrins and -chlorin was first communicated in 1995.[21,22] While the *meso*-aryldiolchlorins have since found use as photosensitizers,[11–13,15] or synthetic intermediates towards the generation of pyrrole-modified porphyrins,[10,23,24] the corresponding

[a]*Department of Chemistry, University of Connecticut, Unit 3060, Storrs, CT 06269-3060, USA. E-mail: c.bruckner@uconn.edu; Fax: +860-486-2981; Tel: +860-486-2743*
[b]*Department of Chemistry, Youngstown State University, One University Plaza, Youngstown, OH 44555-3663, USA*
[c]*Department of Chemistry, The Richard C. Elder X-ray Crystallography Facility, University of Cincinnati, P.O. Box 210172, Cincinnati, OH 45221-0172, USA*

† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR, and UV-vis/fluorescence spectra of all novel compounds obtained; 2D-NMR spectra and (tandem) ESI(+) spectra for selected compounds, and experimental details for the crystal structure determination of **4b-*E***, **4d-*Z***, **5a** and **7d-*E***. CCDC reference numbers 756648–756652. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b924539a

tetraolbacteriochlorins were used much less frequently.[13–15,21] In part, this may be due to their high polarity and limited solubility. They are generally harder to prepare, purify, and to handle than the diolchlorins.

The stereochemistry of the *E*/*Z*-isomers has never been unequivocally assigned for the tetraaryltetrahydroxybacteriochlorins (although an educated guess predicts the correct assignment, see below).[14,21,25] Also, derivatives of the tetraols that preserve their bacteriochlorin chromophore have not been reported. Furthermore, it was previously observed that the longest wavelength of absorbance in the tetraolbacteriochlorins is significantly blue-shifted compared to that of the tetrahydrobacteriochlorins but a rationalization on the basis of either electronics or sterics was not provided.[21] Single crystal X-ray structures of the tetraolbacteriochlorins or the precursor *meso*-tetraaryldiolchlorin have not been determined to aid in answering these questions. In fact, only four other *meso*-arylbacteriochlorin crystal structures have been reported to date.[26]

We report here the synthesis, separation and unambiguous assignment of the two isomeric tetraolbacteriochlorins. Together with the structure of a dimethoxychlorin also reported here, the questions regarding the conformational effects of the dihydroxylation and methylation of the diol functionalities can be answered. We also present full NMR spectroscopic assignments of representative *meso*-tetraarylbacteriochlorins, report on some mixed functionality derivatives, and their reaction in acid. In so doing, we contribute to the understanding of these readily available, long wavelength absorbing and emitting, relatively stable, and potentially highly versatile chromophores, thus making them accessible for a number of applications.

Results and discussion

Synthesis of chlorins 2, 3, and tetraolbacteriochlorins 4

The osmylation of free base *meso*-tetraarylporphyrins **1** was principally performed as previously described,[10] with the implementation of two modifications that were found to significantly improve the reaction yields. Firstly, the reaction was run in $CHCl_3$/30% pyridine (instead of 10% pyridine). Secondly, the porphyrin was completely dissolved in the least amount of slightly warmed solvent before adding the solid OsO_4; porphyrin suspensions should be avoided (the amount of solvent required depended on the solubility of the particular aryl derivative). These measures assure the highest possible porphyrin concentration in solution. This translates into higher reaction rates (from up to 6 days down to 1–3 days at ambient temperature). In turn, we find fast reactions tend to increase the chlorin yields.

Traditionally, the reactions are run until no further change in the UV-vis of the crude reaction mixture is detectable, whereupon the reaction mixture is, after the replacement of all pyridine by $CHCl_3$–10% MeOH, quenched by gaseous H_2S (Scheme 2).[10] Column and plate chromatographies then isolate diol chlorin **3** and the two isomeric tetraolbacteriochlorins **4**.[14,21]

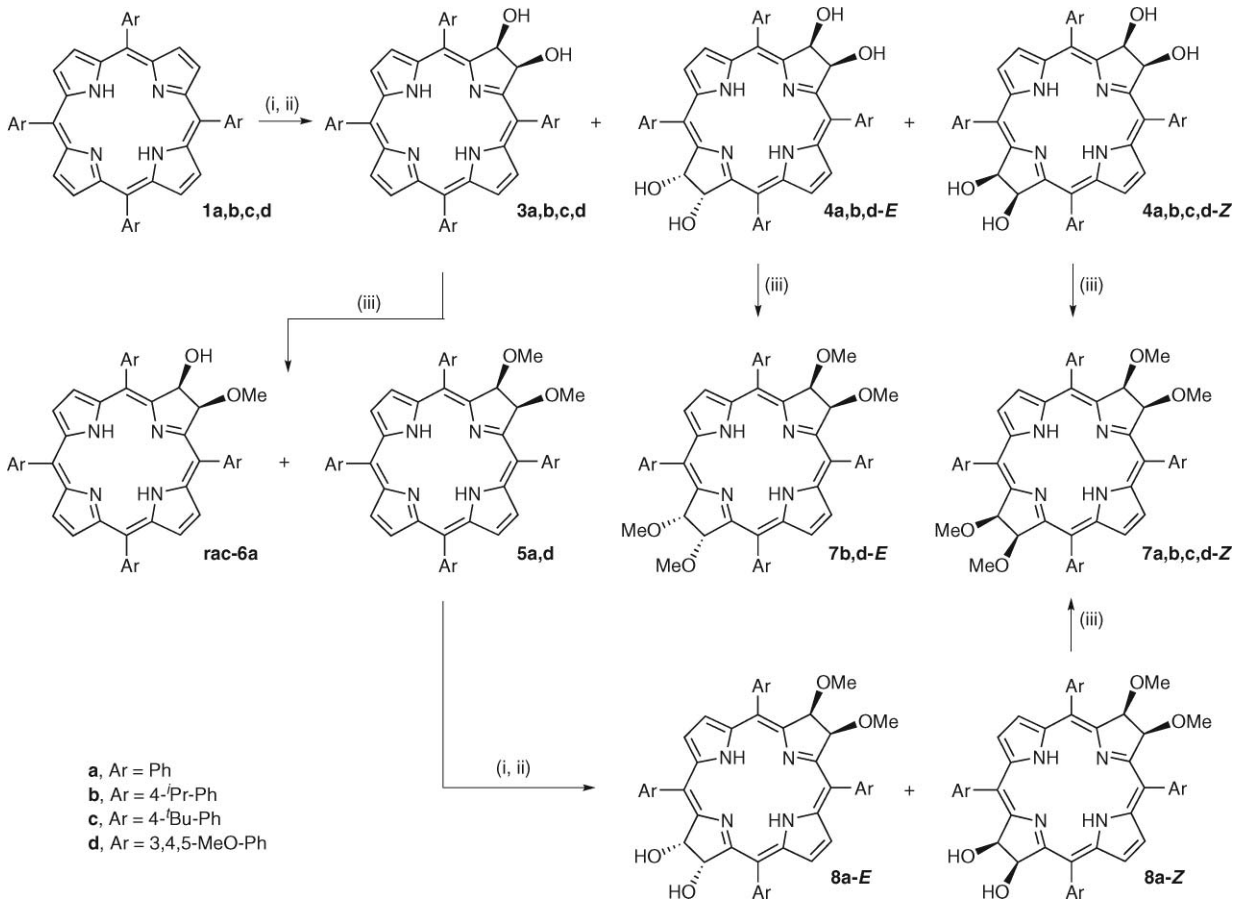
We have found that it is, in many instances, easier to evaporate the crude mixture to dryness and to first separate the osmate esters by column chromatography (silica, gradient CH_2Cl_2 to CH_2Cl_2–5% MeOH, depending on the polarity of the products). The isolated chlorin and bacteriochlorin osmate ester fractions are then reduced with H_2S and purified by filtration through a plug of Celite and/or short column chromatography.

The tetraolbacteriochlorin osmate esters are stable. In some cases, and depending on the aryl substituents, the stereoisomers of the osmate esters can be readily separated by plate or column chromatography but in many other cases, both bacteriochlorin osmate ester isomers are best isolated together. While we will describe the diolchlorin osmate ester below in detail, we elected to reduce the bacteriochlorin osmate esters without further characterization, and to focus on the separation and characterization of the resulting tetraolbacteriochlorins.

Depending on the stoichiometric ratio of OsO_4 and porphyrin used, ranging from 0.7 : 1 to 2.5 : 1, diol chlorin **3** is formed concurrently with less or more of the bacteriochlorins **4**, respectively. Even using very small ratios, some bacteriochlorins form, indicating that the dihydroxylation of the chlorin is much faster than the dihydroxylation of the porphyrin. This circumstance is readily rationalized by the comparably larger activation energy required to remove the first pseudoolefinic β,β′-double bond from the fully conjugated porphyrinoid π-system when contrasted against the energy required to dihydroxylate a second pseudoolefinic double bond of a chlorin. This is because the presence of one reduced β,β′-double bond 'fixes' the conjugation pathway of the 18 π-electron core and 'activates' the pseudoolefinic double bond opposite of the pyrrolidine moiety toward further addition reactions in the free base chlorins. This (and the metal-directing effect resulting in the formation of metalloisobacteriochlorins upon osmylation of metallochlorins—not studied here) is a well documented observation in porphyrin chemistry.[27,28] Very large OsO_4 to porphyrin ratios (>3 : 1) tend to over-oxidize the porphyrin, as judged by the larger quantities of unidentified baseline material that is formed.

The absolute yields of chlorins and bacteriochlorins vary greatly. On one hand, the yields are strongly dependent on the purity and solubility of the porphyrin and the purity of the solvents as even small amounts of double-bond containing fractions greatly diminish the OsO_4 available for porphyrin modification. On the other hand, some bacteriochlorins (such as those of the *meso*-phenyl-series **4a**) are characterized by a high affinity for silica gel and tend to 'streak'. They require large quantities of ~30% MeOH in CH_2Cl_2 or $CHCl_3$ or pure THF to elute though these solvents are unsuitable to separate the bacteriochlorin isomers or to affect any chlorin/bacteriochlorin separations. Thus, it is best to first isolate the chlorin fraction and then elute the bacteriochlorin fractions from the column with large quantities of solvent, and to subject them (perhaps, after the cleavage of the osmate esters) to plate chromatography separations. Alternatively, the mixture can be *O*-methylated to reduce their polarity (see below). Once the bacteriochlorins have been isolated, they freely dissolve in $CHCl_3$/$CDCl_3$/mixtures of halogenated solvents and alcohols or more polar organic solvents (DMF, DMSO, THF).

In contrast to our preliminary report that the two bacteriochlorin isomers (we shall refer here to these isomers as the high and low polarity isomers; for their assignment, see below) form in about 1 : 1 ratio (by reaction of **3a** with OsO_4),[21] they are isolated from the reaction of **1a** with OsO_4 in ~1 : 4 ratio of low polarity : high polarity isomer. The low polarity fraction is generally characterized by a significantly lower chemical stability compared to the high polarity fraction, further skewing the yields. Again, a large influence of the nature of the aryl groups is noted.



Scheme 2 *Reaction conditions*: (i) 1. 0.7–2.5 eq OsO_4, $CHCl_3$–30% pyridine, r.t., 4–7 d; optional column chromatography. (ii) H_2S, $CHCl_3$–10% MeOH, r.t., 15 min, followed by column chromatography (silica, gradient 100% CH_2Cl_2 to CH_2Cl_2–5% MeOH. (iii) ~5 eq per OH group NaH (60.8% NaH in mineral oil), THF, r.t., 30–45 min, anhydrous conditions (N_2), followed by >6 eq per OH group MeI, r.t., 2–3 h.

The NMR spectra for the high and low polarity bacteriochlorins are very similar to each other and diagnostic for their connectivity, but not their relative stereochemistry (see also Fig. 9). While it appears reasonable to assume that the tetraol carrying all four hydroxy groups on one side of the plane defined by the porphyrin (*Z*-isomer) is more polar compared to the *E*-isomer presenting one *cis*-diol on each side, we could not prove this by NMR spectroscopy.[14,21,25] To complicate matters, neither the tetraphenyldiolchlorins nor the tetraphenyltetraolbacteriochlorins showed any propensity to crystallize. Thus, we were seeking diol/tetraol and *meso*-aryl derivatives of higher crystallinity.

X-Ray single crystal structures of 4d-*Z* and 4b-*E*

We improved the crystallinity of the tetraolbacteriochlorins by varying the aryl group from phenyl to 4-^{i}Pr-phenyl, 4-^{t}Bu-phenyl, and 3,4,5-MeO-phenyl (Scheme 2), though their crystallization proved generally difficult. The high polarity isomer of the 3,4,5-trimethoxyphenyl-derived bacteriochlorin **4d-*Z*** eventually provided high quality crystals (Fig. 1). Indeed, the structure proves our projection that the high polarity isomer is the isomer carrying all hydroxy groups on the same side of the macrocycle plane.

A planar porphyrinoid framework with coplanar *cis*-dihydroxylated β,β′-bonds would place the –OH groups in each diol functionality into an eclipsed conformation. This potential steric clash is alleviated by a asymmetric distortion of each pyrrolidine—one β-carbon is located significantly above the mean plane defined by the porphyrin, thus resulting in a 30° dihedral angle between the hydroxy groups. The distortion of each pyrrolidine is transmitted to a reduced degree to the macrocycle. The two pyrrole moieties are nearly co-planar to each other. All other metric parameters (such as the C–C bond lengths in the macrocycle and the dihedral angles between the aryl groups and the porphyrin mean plane) are as expected.

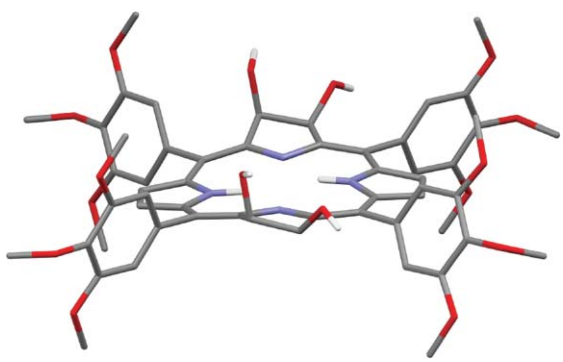


Fig. 1 Capped stick model of the crystal structure of **4d-*Z***; disordered solvate molecules ($CHCl_3$) and all CH hydrogens removed for clarity.

We were also able to crystallize the low polarity isomer of the 4-^{i}Pr-phenyl-substituted derivative **4b-*E*** (Fig. 2). The structure confirms that this compound is, as presumed, the isomer carrying the two *vic*-diol functionalities on opposite sides of the porphyrinoid plane. The distortion modes observed for each individual pyrrolidine moiety are very similar to those observed in **4d-*Z***, with dihedral angles between the hydroxy groups of 29°. However, while both pyrrolidines in **4b-*E*** are related by a (crystallographic) inversion centre, those in **4d-*Z*** are related by an (idealized) mirror plane. For the detailed conformational analysis of both macrocycles, see below.

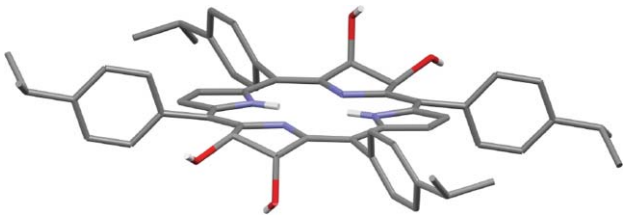


Fig. 2 Capped stick model of the crystal structure of **4b-*E***; solvate molecules (two molecules of MeOH) and all CH hydrogens removed for clarity.

Synthesis, spectroscopic and structural characterization of dimethoxychlorin 5a

To reduce the polarity of the diol functionality, we converted the diol chlorins to their corresponding dimethoxy derivative using classic methylation conditions (Scheme 2). Thus, reaction of diol chlorin **3a** with excess NaH, followed by a stoichiometric excess of MeI, led to exhaustive *O*-methylation and the corresponding dimethoxychlorin was isolated in 60% yield in crystalline form. We never observed *N*-methylated products under these reaction conditions,[29] thus avoiding the use of Zn(II) as a protecting group.[24] The formation of monomethoxymonohydroxychlorin **6a** is observed during the course of the reaction and, particularly when using shorter reaction times or lower quantities of methylating agent, **6a** can also be isolated (as a racemic mixture, ***rac*-6a**). Both methylated products show the expected gain in mass (+14 and 28 amu, respectively), and the ^{1}H and ^{13}C NMR spectra demonstrate the replacement of the OH signal by a methoxy signal and the pyrrolidine β-carbon shifts about 10 ppm downfield (see the ESI†). No other significant shifts are observed. The UV-vis and fluorescence spectra of **3a**, **5a** and **6a** are typical chlorin-type spectra and essentially indistinguishable from each other (see the ESI†), indicating that methylation does not alter the electronic properties of chlorin **3a** due to, for instance, steric effects.

The crystal structure of **5a** is shown in Fig. 3. As observed in the tetraolbacteriochlorins, the eclipsed conformation of the two methoxy groups is avoided by means of a distortion of the pyrrolidine moiety but presumably the larger overall rigidity of the chlorin framework, when compared to that of the bacteriochlorins, allows only a 17° dihedral angle between the methoxygroups. A similar conformation is also observed for β-octaethyl-2,3-dihydroxychlorin.[30]

Compared to the parent diols **3**, dimethoxyderivatives **5** are much less susceptible to oxidation or dehydration,[22,31] thus providing an excellent, stable chlorin model compound. The alkylation

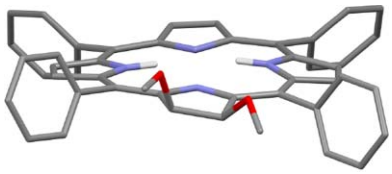
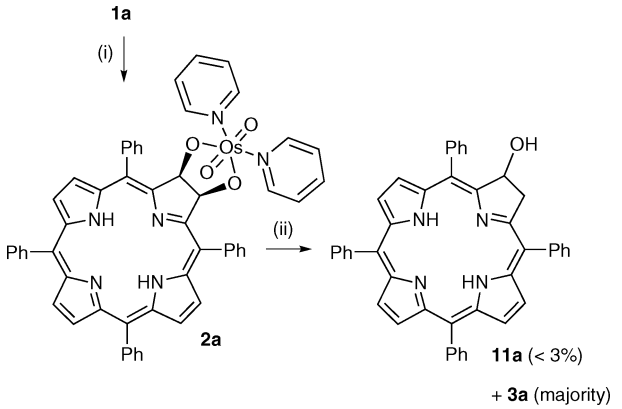


Fig. 3 Capped stick model of the crystal structure of **5a**; all CH hydrogens removed for clarity.

reaction is also readily applicable to the tetraolbacteriochlorins **4**, as detailed below.

Monohydroxychlorin 11a

As alluded to above, the diolchlorin osmate esters are stable. For instance, the osmate ester of *meso*-tetraphenyl-2,3-diolchlorin **3a** can be identified as the 2-fold symmetric bispyridine complex **2a** (Scheme 3).



Scheme 3 *Reaction conditions*: (i) 1. ~1.0 eq OsO_4, $CHCl_3$–30% pyridine, r.t., 4–7 d; optional column chromatography. (ii) H_2S, $CHCl_3$–10% MeOH, r.t., 15 min, followed by column chromatography (silica, gradient 100% CH_2Cl_2 to CH_2Cl_2–5% MeOH).

Only one type of pyridine is detectable by NMR (see spectra in the ESI†), suggestive of their *cis*-arrangement opposite of the *cis*-alkoxides about an octahedral Os(VI) centre. This further implies a *trans*-arrangement of the oxo ligands. This coordination geometry around the osmium centre is also consistent with the findings of a range of crystallographically characterized osmate esters.[32]

The reduction of osmate ester **2a** with gaseous H_2S is generally a clean reaction but particularly in larger scale reactions (500 mg of **2a**, and above), we noticed the formation of a slightly less polar side product that possesses a near-identical UV-vis spectrum to that of diol chlorin **3a**.[10] However, its ^{1}H NMR spectrum showed a lack of two-fold symmetry, three types of sp^{3}-hydrogens, plus a typical, albeit complex, pyrrolidine proton signal that resolves into a doublet upon washing with D_2O (see the ESI†). The HR-MS of this compound indicated that it contains one oxygen less than **3a**. Thus, we assigned this compound the monohydroxychlorin structure **11a**, an assignment confirmed by single crystal diffractometry (Fig. 4).

In contrast to the structures of **4b-*E***, **4d-*Z***, **5a** and **7d-*E*** (see below), which have the molecules located at positions that agree with the molecular symmetry and that do not exhibit any major disorder of their chromophores, the structure of **11a** is complicated

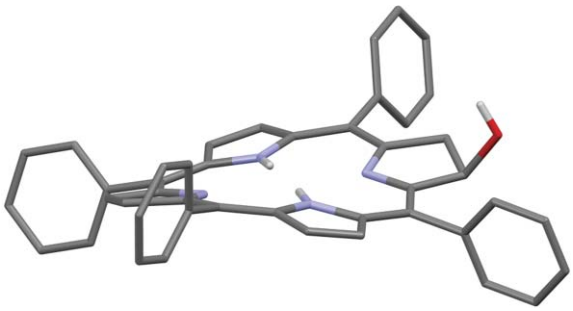


Fig. 4 Capped stick model of the crystal structure of **11a**; disorder and all CH hydrogens removed for clarity.

by being located on a crystallographic four fold axis that renders all pyrrole rings equivalent and has them disordered in a 3 : 1 ratio with respect to the 2-hydroxy pyrrolidine. The hydroxyl group is also disordered over two alternative positions at neighboring pyrrolidine carbon atoms, further complicating the analysis of the structure (see the ESI† for a detailed description of the solid state disorder in **11a**). However, the quality of the single crystal data of **11a** is exceptionally good. Thus, irrespective of the disorder, the assignment of the molecular structure of **11a** is well founded. The chromophore is slightly ruffled but, in the absence of any steric crowding of the hydroxy group, essentially planar. For a more detailed conformational analysis, see below.

Dihydroxylation of dimethoxychlorin 5a. Synthesis and optical properties of the dimethoxydihydroxybacteriochlorin 8a

Dimethoxychlorin **5a** is susceptible to β,β′-dihydroxylation using the standard porphyrin osmylation conditions.[10] This reaction generates, after the reduction with H_2S, two isomeric bacteriochlorin-type chromophores in a 4 : 1 high : low polarity ratio (50% combined yield). The high polarity fraction (R_f 0.42, silica, CH_2Cl_2–2% MeOH) we assign to be dimethoxydiolbacteriochlorin **8a-*Z*** while we assign the low polarity fraction (R_f 0.73, silica, CH_2Cl_2–2% MeOH) to be **8a-*E*** (Scheme 2). Both products are of significantly lower polarity than the corresponding tetraols **4a-*E*/*Z*** (R_f 0.71 and 0.40, respectively, silica, CH_2Cl_2–5% MeOH) and they do not display the extraordinary affinity of the tetraols to silica gel. The ^{1}H and ^{13}C NMR spectra of **8a-*E*/*Z*** reflect the introduction of a second pyrrolidine moiety into **5a** that is indicated by an additional β-sp^3 hydrogen and carbon and the splitting of the remaining non-equivalent β-H into two sets of doublet of doublets. It is noteworthy that, using NOESY spectra, all hydrogen atoms of the dihydroxydimethoxybacteriochlorins **8a-*E*** can be fully assigned, with no apparent differences between the NMR spectra seen in both isomers (see the ESI† and *cf.* Fig. 9).

The UV-vis absorption and fluorescence emission spectra of **8a-*E*/*Z*** are shown in Fig. 5. Their spectra are typical for bacteriochlorins, and essentially indistinguishable for those of the parent tetraols (see the ESI†), and from each other. Both isomers also possess identical relative fluorescence yields. The single-band fluorescence spectra are characterized by a small (< 7 nm) Stokes shift. These observations can be generalized for all bacteriochlorins described here (for further discussion, see below).

As in the direct bis-dihydroxylation of porphyrin **1**, the *E*/*Z* isomers in the dihydroxylation of **5a** do not form in equal amounts.

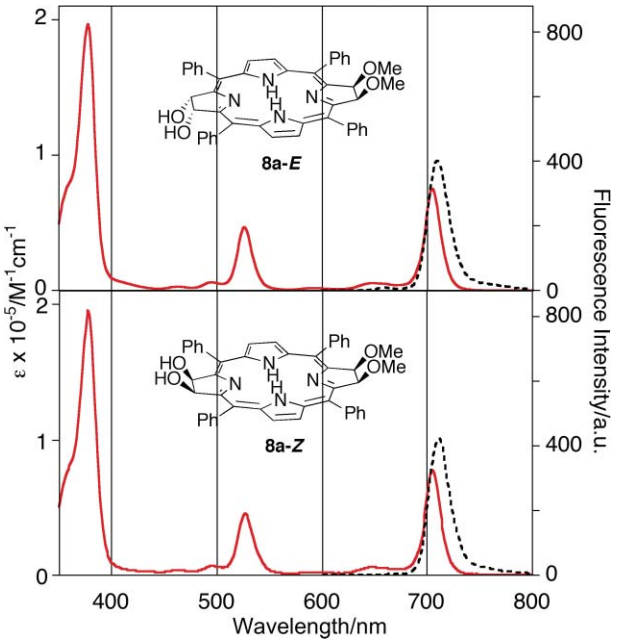


Fig. 5 UV-vis (solid red trace) and fluorescence spectra (dashed black trace) of **8a-*E*** and **8a-*Z*** in CH_2Cl_2.

The minor isomer formed is always the *E*-bacteriochlorin. Should any steric influences between the osmate ester/dimethoxy groups and the second approaching OsO_4–pyridine adduct play any role in the stereoselectivity, a preference for the *Z*-isomer would have been predicted. Also, the *E*-isomers are generally chemically much less stable than the corresponding *Z*-isomers. For example, **8a-*E***, tends to decompose within hours in $CDCl_3$ that was not rigorously dried and deacidified but **8a-*Z*** is stable in untreated $CDCl_3$. Both compounds are stable in the solid phase. The stability of the bacteriochlorins also varied greatly with the aryl substituents.

Diimide reduction of chlorins 3a and 5d. Synthesis and optical properties of the dimethoxy/dihydroxybacteriochlorins 9a and 10d

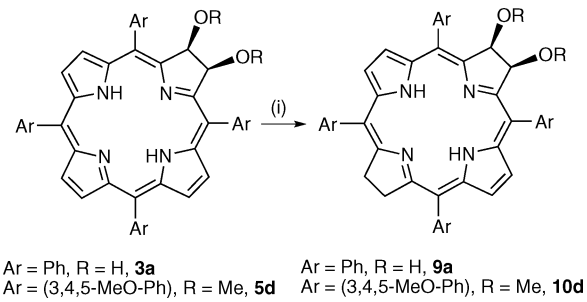
The established Whitlock procedure for the diimide reductions of porphyrins and chlorin (*p*-toluenesulfonylhydrazide/K_2CO_3/pyridine, reflux)[33] can be applied to diolchlorin **3a** or dimethoxychlorin **5d**, thus generating bacteriochlorins **9a** and **10d**, respectively (Scheme 4). The isolation of these chromophores from their starting materials is, due to their very similar polarities, difficult and consequently the isolated yields are marginal (less than 12%). The ^{1}H NMR spectra of these compounds confirm their connectivity. The pyrrolidine β-hydrogens opposite of the dihydroxylated pyrrolidine moiety are, by virtue of the face differentiation brought about by the diol functionality, diastereotopic. Thus, they exhibit the diagnostic AA′BB′-coupling pattern shown in Fig. 6.

The UV-vis of diol/dimethoxybacteriochlorins **9a** and **10d** are typical bacteriochlorin spectra (see the ESI†). A notable trend is apparent. With increasing number of β-hydroxy groups, λ_{max} hypsochromically shifts of up to 34 nm compared to the parent tetrahydrobacteriochlorins are recorded (Table 1). A corresponding shift can be observed for the chlorin series. This highlights the fact that the MOs of chlorins and bacteriochlorins possess some

Table 1 Select UV-vis data delineating the hypsochromic shift with increasing β-OH substitution. Directly comparable compounds are arranged in blocks

Compound	λ_{max} (solvent)[a]	Reference
meso-Tetraphenylchlorin	652 (benzene)	6
Tetraphenyl-2-hydroxychlorin (**11a**)	644 (CH_2Cl_2)	This work
Tetraphenyl-2,3-dihydroxychlorin (**3a**) or dimethoxy derivative **5a**	644 (CH_2Cl_2)	10, this work
meso-Tetraphenylbacteriochlorin	742 (benzene)	6
Tetraphenyl-2,3-dihydroxybacteriochlorin (**9a**)	724 (CH_2Cl_2)	21, this work
Tetraphenyl-2,3,12,13-tetrahydroxybacteriochlorin (**4a**) or tetramethoxy derivative **7a**	708 (CH_2Cl_2)	21, this work
5,10-Diphenylchlorin	645 (C_6H_6)	37
5,10-Diphenyl-2,3-dihydroxychlorin	638 (CH_2Cl_2)	38
5,10-Diphenylbacteriochlorin	734 (C_6H_6)	37
5,10-Di(3,4,5-MeO-Ph)-2,3,12,13-tetrahydroxybacteriochlorin	702 (CH_2Cl_2)	13
Octaethylchlorin	646 (C_6H_6)	6, 39
Octaethyl-2,3-dihydroxychlorin	643 (CH_2Cl_2)	19, 40
Octaethylbacteriochlorin	724 (C_6H_6)	39
Octaethyl-2,3-12,13-tetrahydroxybacteriochlorin	715 ($CHCl_3$)	5

[a] The UV-vis spectra of these compound show generally only small (< 2 nm) solvatochromic shifts



Scheme 4 *Reaction condition*: (i) K_2CO_3, excess *p*-toluenesulfonylhydrazide, pyridine, 105 °C, ~6–8 h.

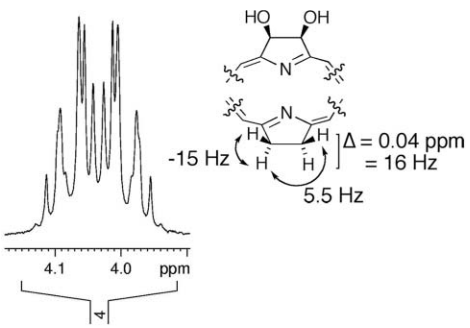


Fig. 6 Interpretation of the pyrrolidine region of the ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **9a**. The *J*-coupling values were determined based on a simulation of the second-order peak pattern using WinDNMR.[34]

electron density on the pyrrolidine β-carbons though they are formally not part of the chromophore.[35] Accordingly, even one hydroxy substituent at these positions modulates the electronic properties of the chromophore, as the spectrum of **11a** and a literature precedent demonstrate.[36] This substituent-induced shift is also noticeable in moderated form in the β-octaethylchlorin series. On the other hand, hydroxy groups at benzylic positions attached to the β- or *meso*-groups show no or only minimal electronic effects (see the ESI†).

Methylation of the bacteriochlorin derivatives 4 and 8

Smooth exhaustive methylation of the tetraolbacteriochlorins **4** can be achieved using the method described for the diolchlorins **3** but using twice the reagent quantities. Methylation of the high polarity tetraolbacteriochlorins **4-*Z*** generates the higher polarity tetramethoxyderivative **7-*Z***, and accordingly, the lower polarity bacteriochlorins **4-*E*** form the lower polarity tetramethoxybacteriochlorins **7-*E***. Likewise, the high polarity fraction of the dioldimethoxybacteriochlorin **8a-*Z*** forms **7a-*Z*** upon methylation. Based on the crystallographically characterized bacteriochlorins, this assigns conclusively the relative (and absolute) stereochemistry of all bacteriochlorin derivatives.

In all instances, the tetramethoxy derivatives are, by column or plate chromatography, much more readily separated from each other (and the corresponding dimethoxychlorin) than their corresponding hydroxy derivatives. Thus, the exhaustive methylation of the alcohol fractions of a crude reaction mixture, followed by the separation of the derivatives **5** and **7-*E*/*Z*** is a convenient and efficient way of preparing the derivatives in high purity and yields up to 40%. We thus focus in our further spectroscopic characterization on the methoxy derivatives.

Structural characterization of the tetramethoxybacteriochlorin 7d-*E*

Similarly to the diol case, methylation of the hydroxy groups does not change the UV-vis spectra of the bacteriochlorins (*cf.* also Fig. 5 and 10), suggesting that the conformation and conformational flexibility of the macrocycles in solution are not fundamentally affected by the *O*,*O*′-dialkylation reaction. The solid state conformation of tetramethoxybacteriochlorin **7d-*E*** is shown in Fig. 7. It is comparable to that of the *E*-tetraol **4b-*E*** (Fig. 2), albeit the dihedral angle between the methoxy groups on

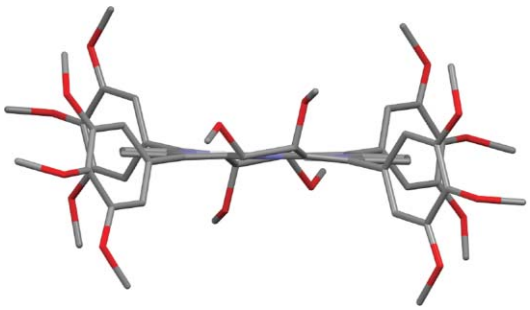


Fig. 7 Capped stick model, side view along an N–N axis, of the crystal structure of **7d-*E***; solvent molecules (CH_2Cl_2) and all CH hydrogens removed for clarity.

each pyrrolidine are slightly reduced to 24°. Since the molecules lies on a crystallographic inversion centre, the conformations of both pyrrolins are identical.

NSD analysis of all structurally characterized chromophores

The lowest-frequency normal-coordinate structural decomposition (NSD) analysis of a porphyrinic $C_{20}N_4$ macrocycle allows a breakdown of its conformation into six lowest energy out-of-plane distortion modes.[41] Applying this algorithm to all crystallographically characterized chlorin or bacteriochlorin chromophores will generate results that are certainly not directly comparable to porphyrins, as the lowest energy distortion modes of the more flexible and lower molecular symmetry chlorins/bacteriochlorins are different from those of porphyrins. Nonetheless, an NSD analysis of a number of related chlorins/bacteriochlorins will allow a relative comparison of their conformation.

Fig. 8 shows the results of this NSD analysis. All five compounds are only slightly distorted from planarity. Two compounds do, however, deviate more strongly from planarity than the others. One is the tetraolbacteriochlorin **4d-*Z***, the only *Z*-isomer investigated, that is mainly saddled. The other is the mainly ruffled monohydroxychlorin **11a**. However, all chlorin and bacteriochlorin chromophores have identical UV-vis spectra, respectively. We

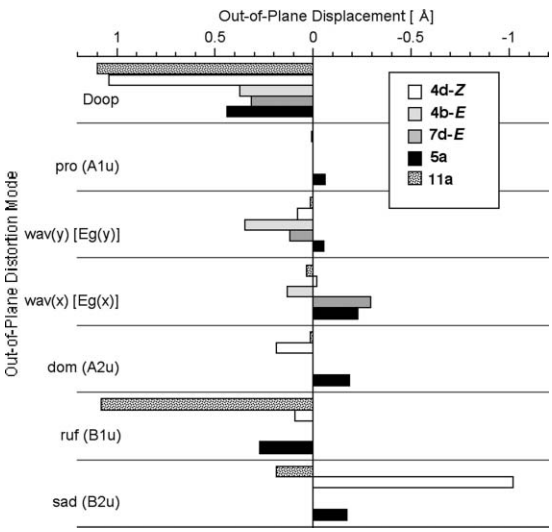
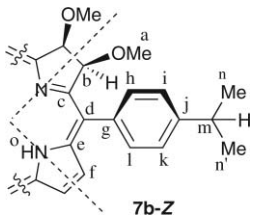


Fig. 8 Lowest frequency normal-coordinate structural decomposition (NSD) results for all crystallographically characterized chromophores.

Table 2 ^1H and ^{13}C NMR (400/100 MHz, $CDCl_3$) assignments of **7b-*Z***



Position	δ_H/ppm	δ_C/ppm
a	s, 2.96	58.27
b	s, 5.93	81.83
c		157.08
d		116.27
e		137.18
f	d, 8.15	123.77
m	h, 3.18	34.29
n, n′	two overlapping d, 1.47 and 1.48	24.49
g		139.37
h	d, 8.01	134.13
i	d, 7.57	125.37
j		147.90
k	d, 7.46	125.15
l	d, 7.74	131.19
o	br s, -1.78, exchangeable with D_2O	—

conclude from this that the conformational flexibility of all the chlorin/bacteriochlorins are similar such that they all show the similar averaged conformation in solution. Ultimately, the observed differences in their solid state conformations are likely more a reflection of differing packing effects and a testimonial to their conformational flexibility, rather than a measure of their native conformation.

NMR spectroscopic characterization of the tetramethoxybacteriochlorins

The ^1H and ^{13}C NMR spectra of the tetramethoxybacteriochlorins are very similar to those of the corresponding tetraols and are generally well resolved and readily interpreted. Next to the low-field signals for the inner NH protons (in the range between –1.8 to –2.0 ppm), diagnostic peaks are the low-field signals for the β-protons (s at 8.1 to 8.3 ppm) together with the dihydroxylated/dimethoxylated pyrrolidine signals (s at ~5.9 ppm, and the signals for the MeO group from 2.9–3.2 ppm).

Fig. 9 shows a representative example of the near-identical spectra for the two *E*/*Z* isomers of **7d**. In this particular case, the appearance of two *o*-phenyl hydrogens (s at 7.02 and 7.36 ppm) signify the face differentiation by the dimethoxy groups, combined with a slow rotation of the *meso*-aryl group around the *meso*-*ipso*-bond. The down field signal is assigned to hydrogen located on the same side as the neighbouring methoxy groups. Low temperature (–40 °C) NOE, HMBC, HSQC, and H,H-COSY spectra allow the assignment of all hydrogens and all carbons (Table 2, also see the ESI†).

Optical properties of the tetramethoxybacteriochlorins

The UV-vis and fluorescence spectra of both isomers of the tetramethoxy derivatives **7** are identical to those of the dimethoxy-**8** and tetrahydroxybacteriochlorins **4** (Fig. 10; *cf.* to Fig. 5 and the ESI†). The spectra of the two isomers **7d-*E*** and **7d-*Z*** are essentially

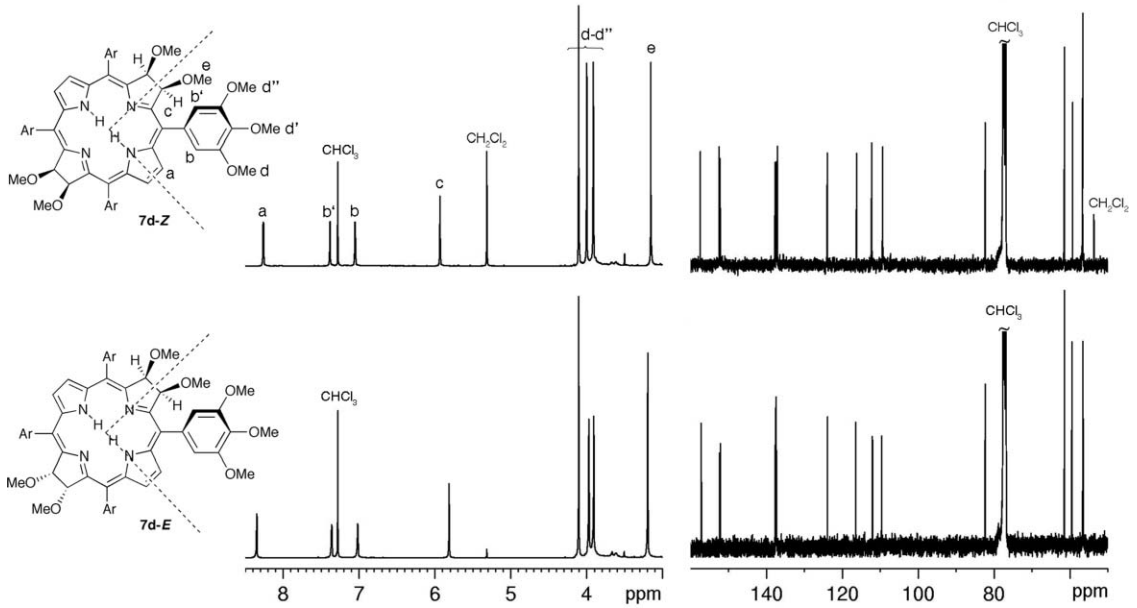


Fig. 9 Comparison of the ^{1}H and ^{13}C NMR spectra ($CDCl_3$, 400/100 MHz) of **7d-*Z*** and **7d-*E***. The dotted line indicates the quadrant of the molecule that is the NMR-spectroscopic repeat unit.

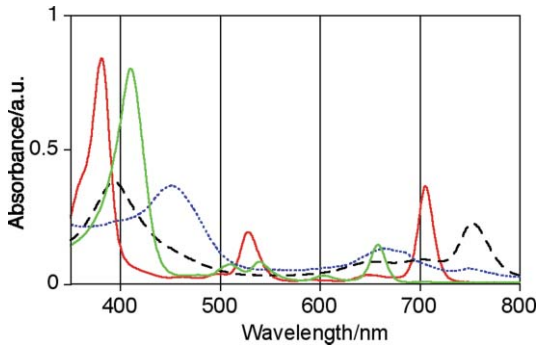


Fig. 10 UV-vis spectra of **7d-*Z*** in CH_2Cl_2 before the addition of 2% TFA (solid red trace), after the addition of 2% TFA, recorded directly after the addition (dashed black trace), and after 15 min. at r.t. (dotted blue trace); [**7d-*Z***] within 2% identical. UV-vis of isolated product (**15d**) after neutralization with NH_4OH and extraction (solid green trace).

identical to each other, as are their fluorescence yields. In CH_2Cl_2, the fluorescence yield ϕ is 0.21, *i.e.* approximately twice as high as for porphyrin **1a**.[42]

ESI-MS spectrometry of the bacteriochlorins

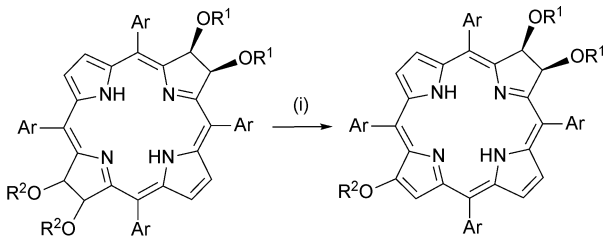
All free base bacteriochlorins investigated showed clear ESI+ mass spectra (100% CH_3CN). The (protonated) molecular ion peaks were the prominent signals. Minor fragmentation patterns included the loss of one, and to a much lesser extent, two molecules of H_2O (for the tetraol species) or the loss of MeOH (for the dimethoxy species) from the parent MH^+ ions. This fragmentation pattern mirrors the reactivity of the bacteriochlorins in solution (see below). Collision-induced tandem mass spectra (ESI+, 100% CH_3CN) have been used in the past to differentiate isomeric porphyrins.[43] However, the isomers **7b-*Z*** and **7b-*E*** did not show any differences that would have allowed any conclusion on their absolute stereochemistry (see the ESI†).

Protonation of the bacteriochlorins

Porphyrinoids can be protonated, displaying characteristic spectra for their protonated chromophores.[44] Bacteriochlorins are less basic than chlorins and porphyrins, a property that was utilized in their separation.[6] Comparably little is known about the spectral signatures of protonated bacteriochlorins. Moreover, it is known that octaalkyl-β-hydroxychlorins and bacteriochlorins undergo an acid-catalyzed pinacole–pinacolone rearrangement.[45–48] Fig. 10 shows the unprotonated and protonated UV-vis spectra of the tetramethoxybacteriochlorin **7d-*Z***. Upon protonation, the number of bands are reduced, and the Soret band broadens and shifts to 394 nm, whilst λ_{max} red-shifts to 753 nm. The fluorescence of the protonated species is quenched to less than 1% of the fluorescence intensity of the neutral chromophore (not shown).

Upon standing of the bacteriochlorins in acidic solution (2% TFA in CH_2Cl_2), the spectrum converts within 15 min to that of a protonated chlorin (Fig. 10). Upon neutralization, the UV-spectrum of the resulting species possesses typical free base chlorin spectrum character,[10] with a λ_{max} of 658 nm (for the reaction of tetramethoxybacteriochlorins **7d-*E*/*Z***). Dioldimethoxybacteriochlorins **8** and the tetrahydroxybacteriochlorins **4** showed the same behaviour.

The reaction can be scaled to a preparative scale. For instance, isolation of product **15d** of the reaction of **7d-*Z*** in 2% TFA–CH_2Cl_2 after neutralization was straight forward as the reactant converted quantitatively within 1.5 h. Mass spectrometry (ESI+, 100% MeCN) showed the formal loss of MeOH (*m*/*z* 1067.4263 for MH^+). The ^{1}H NMR spectrum is diagnostic for the assignment of the 2,3,12-trimethoxychlorin structure **15d** (Scheme 5, Fig. 11).



$R^1 = R^2 = H$, **4b-*Z***
$R^1 = H$, $R^2 = Me$, **8a-*Z***
$R^1 = Me$, $R^2 = Me$, **7d-*Z***, **7d-*E***

$R^1 = R^2 = H$, **12b**
$R^1 = H$, $R^2 = Me$, **13a** (major product)
+ $R^1 = Me$, $R^2 = H$, **14a** (minor product),
$R^1 = Me$, $R^2 = Me$, **15d**

a, Ar = Ph
b, Ar = 4-^{i}Pr-Ph
d, Ar = 3,4,5-MeO-Ph

Scheme 5 *Reaction conditions*: 1–2% TFA in CH_2Cl_2, r.t., up to 1.5 h.

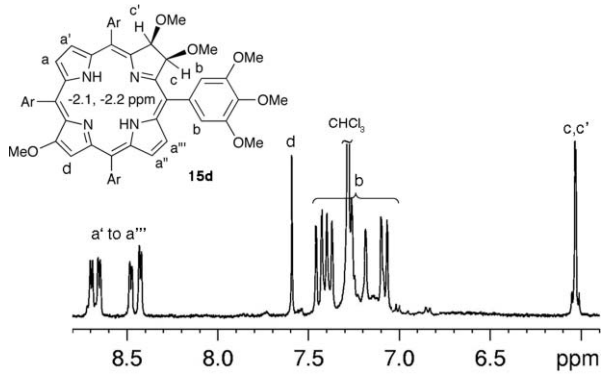


Fig. 11 Partial ^1H spectrum ($CDCl_3$, 400 MHz) of **15d**.

The loss of two-fold symmetry in **15d** is clearly reflected in the coupling patterns and chemical shift differences of the β-protons, and the appearance of a signal at 7.59 ppm (s, 1H), assigned to the pyrrole β-position adjacent to the methoxy group. The remaining pair of pyrrolidine protons are surprisingly only slightly shifted with respect to each other. The signal for the inner NH protons in **7d-*Z*** (br s, –1.90 ppm, 2H) is split into two signals (br s, –2.11 and –2.25 ppm, 1H each). Most significantly, the reaction of both *E*- and *Z*-isomers of **7d** produced the same product, **15d**.

Mass spectrometry confirmed that the tetraolbacteriochlorins **4b** lost H_2O upon exposure to the acidic conditions, forming 2,3,12-trihydroxychlorin **12b**. This is the chlorin analogue to Crossley's 2-hydroxyporphyrin.[49] An interesting case is the reaction of the dioldimethoxybacteriochlorin **8a-*Z*** as it could lose H_2O or MeOH. Mass spectrometry on the acid reaction product mixture (ESI+, 100% CH_3CN) shows it to be mostly (> 90%) the product resulting from the loss of MeOH (**13a**), with the remainder the product resulting from the loss of H_2O (9%, **14a**).

Experimental

Materials and instruments

All solvents and reagents (Aldrich, Acros) were used as received. Analytical (aluminium backed, silica gel 60, 250 μm thickness), preparative (20 × 20 cm, glass backed, silica gel 60, 500 or 1000 μm thickness) TLC plates, and the flash column silica gel (standard grade, 60 Å, 32-63 μm) used were provided by Sorbent Technologies, Atlanta, GA. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX400 or a Varian 500 MHz instrument. High and low resolution mass spectra were provided by the Mass Spectrometry Facilities at the Department of Chemistry, University of Connecticut. UV-vis spectra were recorded on a Cary 50, and the fluorescence spectra on a Cary Eclipse spectrophotometer, both Varian Inc. IR spectra were recorded on a JASCO FT-IR-410 using a diffuse reflectance unit. Fluorescence quantum yields were determined relative to *meso*-tetraphenylporphyrin **1a** ($\phi = 0.11$ in benzene, calculated to be 0.09 in CH_2Cl_2).[42]

The tetraarylporphyrins **1a–d** were all prepared using the method of Adler *et al*.[50]

meso-Tetraphenyl-2,3-dihydroxychlorin osmate ester bispyridine adduct (2a). General procedure for the osmylation of *meso*-tetraarylporphyrins 1

1a (3.00 g, 4.88 mmol) was dissolved in a minimum amount of $CHCl_3$–30% pyridine (350 ml) in a 500 ml round bottom flask equipped with a magnetic stir bar. The dissolution of **1a** was facilitated by the occasional warming of the mixture using a heat gun, suspensions should be avoided. To the cool solution was added OsO_4 (1.00 g, 3.94 mmol, 0.81 equiv; it is advantageous to break an ampule and add the entire ampule immediately to the reaction flask) (Caution: fume hood and eye protection!). The reaction mixture was stoppered and covered from ambient light (aluminium foil), and stirred for 3–4 days at ambient conditions. The progress of the reaction was monitored by TLC with respect to the appearance of the polar products. When the UV-vis spectrum of the reaction mixture indicated no further change, the reaction mixture was evaporated to dryness on a rotary evaporator (a gentle stream of air/nitrogen through the flask containing the crude material removes all remaining traces of pyridine). Column chromatography (silica, gradient of 100% CH_2Cl_2 to CH_2Cl_2–5% MeOH) recovers **1a** in ~15% (0.48 g, 0.78 mmol) and the osmate ester chlorin **2a** is isolated in 55% yield (2.36 g, 2.87 mmol). Extensive flushing (CH_2Cl_2–10-20% MeOH) of the column yields ~20% of E/Z bacteriochlorin fractions. The same procedure was extended toward the preferential formation of bacteriochlorin osmate esters by doubling the amount of OsO_4 and allowing longer reaction times (controlled by TLC and UV-vis spectroscopy). The high polarity bacteriochlorin osmate esters are isolated in about 30-40% yields by column chromatography (silica, CH_2Cl_2–5-10% MeOH) as a mixture of two regioisomers (*Z* and *E*) and they were directly used to react with gaseous H_2S, without further purification, to obtain the corresponding tetraol bacteriochlorins **4**. **2a**: R_f 0.22 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$) 8.59 and 8.62 (3H, two overlapping doublets, J 4.89 Hz and 5.14 Hz), 8.47 (1H, s), 8.30 (1H, d, $J_{1,4}$ 4.84 Hz), 8.13 (2H, br d, J 5.68 Hz), 8.08 (1H, br d, J 7.11), 8.01 (1H, br d, J 6.67 Hz), 7.53–7.79 (6H, m), 7.36 (3H, t, J 6.77 Hz), 7.02 (1H, s); δ_C(100 MHz, $CDCl_3$): 163.2, 152.9, 150.1, 142.5, 142.4, 141.2, 140.0, 135.7, 134.4, 134.1, 132.5, 132.4, 127.7, 127.7, 127.3, 127.1, 126.8, 126.4, 125.0, 124.6, 122.2, 114.3, 96.8; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 420 (5.26), 519 (4.19), 547 (4.15), 594 (3.89), 647 (4.33); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 648 (1.00), 711 (0.12).

meso-Tetraphenyl-2,3-dihydroxychlorin (3a). General procedure for the reductive cleavage of diolchlorin and tetraolbacteriochlorin osmate esters

meso-Tetraphenyl-2,3-dihydroxychlorin osmate ester **2a** (1.00 g, 0.97 mmol) was dissolved in $CHCl_3$–10% MeOH (200 ml) in a 500 ml round bottom flask equipped with a magnetic stir bar. Gaseous H_2S was allowed to flow into the flask for ~5 min (bubbling through the solution is not necessary, and requires a liquid trap between the H_2S gas bottle and the reaction flask) (Caution: fume hood!). Once TLC control has indicated the consumption of the starting material, the reaction mixture is thoroughly purged with air or nitrogen (fume hood!), and evaporated into dryness. The crude product was dissolved in CH_2Cl_2 and the black osmium sulfide was removed by filtration through a plug of Celite. The resulting mixture was concentrated and loaded onto a flash chromatography column (silica, 100% CH_2Cl_2 to CH_2Cl_2–2% MeOH) to obtain diol chlorin **3a**, after crystallization by slow solvent exchange on the rotary evaporator from $CHCl_3$ to EtOH (or CH_2Cl_2–MeOH) and air drying, as a purple, microcrystalline solid in >80% yields (0.517 g, 0.80 mmol). For the isolation and identification of the side product **11a**, see below.

Bacteriochlorin osmate esters are susceptible to the same procedure and the corresponding tetraolbacteriochlorins **4-*Z*/*E*** are isolated in up to 80% yields.

meso-Tetraphenyl-2(*R*),3(*S*),12(*S*),13(*R*)-tetrahydroxybacteriochlorin (4a-*E*) and *meso*-tetraphenyl-2(*R*),3(*S*),12(*R*),13(*S*)-tetrahydroxybacteriochlorin (4a-*Z*)

4a-*E*/*Z* were prepared as a mixture from **1a** according to the general procedures. The isomers were separated by preparative TLC (silica, CH_2Cl_2–5% MeOH, several developments) as the higher (**4a-*Z***) and lower (**4a-*E***) polarity tetraolbacteriochlorin isomers. Minimal loadings of the preparative plate lead to better separation. **4a-*E***: MW = 682.8; mp = d > 150 °C; R_f 0.71 (silica, CH_2Cl_2–5% MeOH); δ_H(400 MHz, DMSO-d_6): 8.09 (2H, s), 7.93 (2H, br s), 7.65 (6H, br s), 5.95 (2H, s), 5.05 (2H, br s), -1.75 (1H, s); UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 376 (5.40), 528 (5.01), 708 (4.86); LR-MS (+FAB, 3-NBA) *m*/*z* 682 (19.4, M^+), 665 (7.4, M^+-OH), 649 (9.4), 648 (7.5, M^+-2OH), 613 (1.5, M^+-4OH -H); HR-MS (+FAB, 3-NBA) *m*/*z* calculated for $C_{44}H_{34}N_4O_4$: 682.25797, found: 682.25518. **4a-*Z***: MW = 682.8; mp = d > 150 °C; R_f 0.40 (silica, CH_2Cl_2–5.0% MeOH); δ_H (300 MHz, DMSO-d_6): 7.96 (4H, overlapping s and broad s), 7.86 (2H, br s), 7.60 (6H, br m), 5.87 (2H, d, *J* 4.9 Hz), 4.99 (2H, d, *J* 4.9 Hz), -1.65 (1H, s); δ_C(75 MHz, DMSO-d_6): 73.1, 115.6, 122.9, 127.1, 131.5, 133.9, 136.2, 141.2, 160.1; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 376 (5.42), 528 (5.08), 708 (4.89); LR-MS (+ FAB, 3-NBA) *m*/*z* 682 (100, M^+), 665 (31.1, M^+ - OH), 648 (5.8, M^+-2OH), 613 (6.4, M^+-4OH -H); HR-MS (+FAB, 3-NBA) *m*/*z* calculated for $C_{44}H_{34}N_4O_4$: 682.25801, found: 682.25470.

meso-Tetra(4-isopropylphenyl)-2(*R*),3(*S*),12(*S*),13(*R*)-tetrahydroxybacteriochlorin (4b-*E*) and *meso*-tetra(4-isopropylphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetrahydroxybacteriochlorin (4b-*Z*)

4b-*E*/*Z* were prepared as a mixture according to the general procedure. The isomers were separated by preparative TLC (silica, CH_2Cl_2–5% MeOH) as the higher (**4b-*Z***) and lower (**4b-*E***) polarity bacteriochlorin isomers, as described for **4a-*E*/*Z***. The osmate esters of **4a-*E*/*Z*** (crude mixture, not further characterized) can also be readily separated (silica, CH_2Cl_2–5% MeOH), followed by the reduction with gaseous H_2S and short column chromatography (silica, gradient of CH_2Cl_2–1% MeOH to CH_2Cl_2–3% MeOH). **4b-*E***: R_f 0.20 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.41 (2H, s), 8.19 (2H, br s), 8.01 (2H, br s), 7.55 (4H, br s), 6.21 (2H, s), 3.16-3.23 (4H, m), 1.49 (12H, d, $J_{1,3}$ 6.92 Hz), -1.78 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.1, 148.6, 138.5, 137.6, 133.3, 132.3, 126.2, 125.8, 123.7, 116.0, 74.3, 34.2, 29.9, 24.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 378 (5.07), 530 (4.42), 707 (4.65); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712, ϕ = 0.20; HR-MS (ESI+, 100% CH_3CN) *m*/*z* calculated for $C_{56}H_{59}N_4O_4$ (MH^+): 851.4536, found: 851.4485. **4b-*Z***: R_f 0.40 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.15 (2H, d, $J_{1,4}$ 1.9 Hz), 8.03 (2H, d, $J_{1,3}$ 7.2 Hz), 7.82 (2H, d, $J_{1,3}$ 7.5 Hz), 7.58 (2H, d, $J_{1,3}$ 7.5 Hz), 7.53 (2H, d, $J_{1,3}$ 7.5 Hz), 6.30 (2H, s), 3.19 (2H, h, $J_{1,3}$ 6.9 Hz), 3.14 (2H, s), 1.49 (12H, d, $J_{1,3}$ 6.9 Hz), -1.70 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.5, 148.6, 138.5, 137.5, 133.7, 131.9, 126.1, 125.9, 123.5, 115.9, 74.2, 34.2, 24.4, 24.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 379 (5.20), 530 (4.54), 708 (4.80); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712, ϕ = 0.24; HR-MS (ESI+, 100% CH_3CN) *m*/*z* calculated for $C_{56}H_{59}N_4O_4$ (MH^+): 851.4536, found: 851.4497.

meso-Tetra(4-*tert*-butylphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetrahydroxybacteriochlorin (4c-*Z*)

4c-*Z* was prepared from **1c** according to the general procedures. Isolated by column chromatography (silica, gradient of CH_2Cl_2–1% MeOH to CH_2Cl_2–3% MeOH) as the higher polarity isomer (only traces of the lower polarity isomer were found). **4c-*Z***: R_f 0.45 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.15 (2H, s), 8.04 (2H, d, $J_{1,3}$ 6.55 Hz), 7.83 (2H, d, $J_{1,3}$ 6.82 Hz), 7.74 (2H, d, $J_{1,3}$ 6.82 Hz), 7.70 (2H, br), 6.31 (2H, s), 3.12 (2H, br s), 1.65 (18H,s), -1.69 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.4, 151.0, 138.1, 137.5, 133.5, 131.7, 125.0, 124.7, 123.7, 115.8, 74.3, 35.1, 31.8; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 379 (5.07), 530 (4.42), 707 (4.65); Fluorescence λ_{max}(CH_2Cl_2)/nm: 713; HR-MS (ESI+, 100% CH_3CN) *m*/*z* calculated for $C_{60}H_{67}N_4O_4$ (MH^+): 907.5162, found: 907.5185.

meso-Tetra(3,4,5-trimethoxyphenyl)-2(*R*),3(*S*),12(*S*),13(*R*)-tetrahydroxybacteriochlorin (4b-*E*) and *meso*-tetra(3,4,5-trimethoxyphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetrahydroxybacteriochlorin (4b-*Z*)

4d-*E* and **4d-*Z*** were prepared from **1d** according to the general procedures and isolated by column chromatography (silica, CH_2Cl_2–4-5% MeOH). **4d-*E***: R_f 0.24 (silica, CH_2Cl_2–3% MeOH); δ_H(400 MHz, $CDCl_3$–10% MeOD-d_4): 8.32 (2H, d, $J_{1,4}$ 1.69 Hz), 7.39 (2H, s), 7.07 (2H, s), 6.21 (2H, s), 4.11 (6H, s), 3.96 (6H, s), 3.91 (6H, s), -1.90 (1H, s); δ_H(400 MHz, DMSO-d_6): 8.25 (2H, d, $J_{1,4}$ 1.69 Hz), 7.39 (2H, s), 7.06 (2H, s), 5.98 (2H, d, $J_{1,4}$ 2.52 Hz), 5.17 (2H, s, exchangeable with D_2O), -1.89 (1H, s); UV-vis λ_{max}(CH_2Cl_2)/nm (rel. intensity): 379 (1.00), 529 (0.24), 709 (0.47); Fluorescence λ_{max}(CH_2Cl_2)/nm: 713. The ^{13}C NMR spectrum of **4d-*E*** could not be acquired due to the instability of the compound; HR-MS (ESI+, 100% CH_3CN) *m*/*z* calculated for

$C_{56}H_{59}N_4O_{16}$ (MH^+): 1043.3926, found: 1043.4047. **4d-*Z***: R_f 0.10 (silica, CH_2Cl_2–3% MeOH); δ_H(400 MHz, $CDCl_3$): 8.30 (2H, s), 7.41 (2H, s), 7.11 (2H, s), 6.33 (2H, s), 4.13 (6H, s), 4.00 (6H, s), 3.92 (6H, s), 3.21 (2H, s), -1.78 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.5, 152.7, 152.6, 138.1, 137.4, 136.3, 123.8, 115.8, 111.7, 109.8, 74.5, 61.7, 56.6, 56.6; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 379 (5.51), 530 (4.84), 710 (5.16); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712; HR-MS (ESI+, 100% CH_3CN) *m/z* calculated for $C_{56}H_{59}N_4O_{16}$ (MH^+): 1043.3926, found: 1043.3883.

meso-Tetraphenyl-2-hydroxychlorin (11a)

Formed as a minor (<3%) product during the synthesis of **3a** according to the general procedure. R_f 0.28 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.67 (2H, br s, resolves into a dd, *J* 4.5 Hz, upon D_2O wash), 8.51 (2H, two overlapping d, *J* 4.5 Hz), 8.33 (1H, d, *J* 4.77 Hz), 8.29 (1H, d, *J* 4.96 Hz), 8.03-8.25 (8H, m), 7.66-7.82 (12H, m), 6.47 (1H, m, resolves into a d, *J* 8.00 Hz, upon D_2O wash), 4.46 (1H, dd, *J* 18.00 and 7.75 Hz), 4.47 (1H, d, *J* 18.02 Hz), 2.30 (1H, d, *J* 3.5 Hz, exchangeable with D_2O), -1.75 (2H, s, exchangeable with D_2O); δ_C(100 MHz, $CDCl_3$): 164.5, 163.2, 153.4, 152.6, 142.6, 142.0, 141.4, 140.7, 140.6, 135.8, 135.2, 134.0, 133.6, 132.9, 132.7, 132.3, 132.3, 132.2, 128.3, 128.2, 128.0, 127.8, 127.7, 127.7, 127.6, 126.7, 126.7, 124.4, 123.5, 123.4, 122.3, 112.8, 73.5, 44.1; λ_{max}(CH_2Cl_2)/nm (log ε): 416 (5.20), 517 (4.11), 543 (4.06), 691 (3.25), 644 (4.37); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 647 (1.00), 712 (0.06); HR-MS (ESI+, 100% CH_3CN) *m/z* calculated for $C_{44}H_{33}N_4O$ (MH^+): 633.2654, found: 633.2674.

meso-Tetraaryl-2,3-*cis*-dimethoxychlorins 5 and *meso*-tetraphenyl-2,3-*cis*-hydroxymethoxychlorin (6a). General procedure for the methylation of diolchlorins and tetraolbacteriochlorins

meso-Tetraphenyl-2,3-*cis*-dihydroxychlorin (**3a**) (200 mg, 3.08×10^{-1} mmol) was, under N_2, dissolved in THF in a 250 ml round bottom flask equipped with a magnetic stir bar (500.0 ml) and excess (~125 mg) NaH (60% emulsion in oil) was added in portions. After stirring 30–45 min at ambient temperature, the reaction mixture turned from purple to dark green (time and colour change depend on the amount of NaH added). After this time, CH_3I (0.25 mL, 12-fold molar excess per OH group to make up for evaporative losses) was added by syringe and the reaction mixture was allowed to stir for ~2 h at ambient temperature (Caution: gloves and fume hood!). The completion of the reaction was monitored by TLC. After all the starting material was consumed, the reaction was quenched by the slow addition of water and the product was extracted into $CHCl_3$. The organic phase was evaporated to dryness and the residue was purified by column chromatography (silica, CH_2Cl_2) to provide **5a**, after recrystallization by slow solvent exchange of $CHCl_3$ to EtOH on the rotary evaporator, as purple, crystalline material in 60% yield (120 mg, 1.8×10^{-1} mmol). A minor, higher polarity fraction formed, depending on the amount of MeI added and the reaction time, in variable amounts, and was identified as the monohydroxymonomethoxychlorin **6a**. **5a**: R_f 0.29 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.67 (1H, d, $J_{1,3}$ 4.87 Hz), 8.53 (1H, s), 8.38 (1H, d, $J_{1,3}$ 4.82 Hz), 8.18 (2H, br d, $J_{1,3}$ 7.12 Hz), 8.12 (1H, d, $J_{1,3}$ 6.54 Hz), 7.88 (1H, d, $J_{1,3}$ 6.75 Hz), 7.65-7.78 (6H, m), 6.07 (1H, s), 3.03 (3H, s), -1.86 (1H, s); δ_C(100 MHz, $CDCl_3$): 160.4, 153.16, 142.0, 141.9, 140.6, 135.7, 134.2, 134.0, 132.67, 131.6, 128.0, 127.7, 127.4, 127.2, 127.1, 126.7, 124.6, 122.7, 114.0, 81.8, 58.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 414 (5.15), 517 (4.08), 544 (4.05), 593 (3.75), 644 (4.27); UV-vis (CH_2Cl_2/2% TFA λ_{max}(CH_2Cl_2)/nm (log ε): 433 (5.09), 584 (3.97), 639 (4.23); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 647 (1.00), 714 (0.07); MS (CI) *m/z* 676 (M^+), 645 (M^+-OCH_3), 629 (M^+-OC_2H_7), 614 (M^+-$O_2C_2H_6$), 601. HR-MS (ESI+, 100% CH_3CN) *m/z* calculated for $C_{46}H_{37}N_4O_2$ (MH^+): 677.2911, found: 677.2903. **6a**: Isolated as side-product as described. Its relative quantity can be increased by following the procedure for **5a** but using shorter reaction times (less than 1 h) and less than half the stoichiometric excess of MeI. Purified by preparative TLC (silica, 15-25% petroleum ether 30-60–EtOAc). R_f 0.42 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.68 (2H, d, $J_{1,3}$ 4.76 Hz), 8.53 (2H, s), 8.38 (2H, d, $J_{1,3}$ 4.79 Hz), 8.15-8.24 (6H, m), 7.95 (1H, br d, $J_{1,3}$ 6.62 Hz), 7.90 (1H, d, $J_{1,3}$ 4.45 Hz), 7.73-7.79 (12H, br m), 6.33 (1H, t, $J_{1,3}$ 6.90 Hz), 6.02 (1H, d, $J_{1,3}$ 7.19 Hz), 3.53 (1H, d, $J_{1,3}$ 6.72 Hz), 3.13 (3H, s), -1.84 (2H, s); δ_C(100 MHz, $CDCl_3$): 142.0, 141.9, 141.5, 140.8, 140.6, 135.7, 134.5, 134.4, 134.2, 134.0, 132.7, 132.2, 131.4, 128.0, 127.7, 127.7, 127.4, 127.4, 127.3, 127.1, 126.7, 124.6, 124.4, 122.9, 122.8, 114.0, 113.8, 83.1, 72.2, 60.3; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 414 (5.21), 515 (4.13), 543 (4.12), 591 (3.84), 643 (4.33); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 648 (1.00), 711 (0.07); HR-MS (ESI+, 100% CH_3CN) *m/z* calculated for $C_{45}H_{35}N_4O_2$ (MH^+): 663.2760, found: 663.2839.

meso-Tetra(3,4,5-trimethoxyphenyl)-2,3-*cis*-dimethoxychlorin (5d)

Synthesized from **3d** in 40% yields according to the general procedure. **5d**: R_f 0.33 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.80 (1H, d, $J_{1,4}$ 4.80 Hz), 8.63 (1H, s), 8.50 (1H, d, $J_{1,4}$ 4.85 Hz) 7.44-7.46 (3H, three overlapping s), 7.39 (1H, s), 7.10 (1H, s), 6.05 (1H, s), 4.18 (3H, s), 4.14 (3H, s), 4.03 (3H, s), 3.94-3.98 (8H, three overlapping s), 3.23 (3H, s) -1.91 (1H, s); δ_C(100 MHz, $CDCl_3$): 160.6, 153.3, 152.3, 152.1, 151.7, 140.8, 138.1, 137.8, 137.5, 137.4, 135.9, 132.8, 128.2, 124.9, 122.8, 114.1, 112.5, 112.4, 109.9, 82.5, 61.5, 59.5, 56.7, 56.6, 56.5; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 419 (5.29), 518 (4.16), 546 (4.12), 593 (3.83), 646 (4.37); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 649 (1.00), 713 (0.06); HR-MS (ESI+, 100% CH_3CN) *m/z* calculated for $C_{58}H_{61}N_4O_{14}$ (MH^+): 1037.4184, found: 1037.4271.

meso-Tetraphenyl-2(*R*),3(*S*),12(*R*),13(*S*)-tetramethoxybacteriochlorin (7a-*Z*)

The crude mixture containing **4a-*E*** and **4a-*Z*** was reacted with excess MeI (estimated to be 4 eq of MeI per OH group) according to the general procedure described to **5a** to obtain **7a-*Z*** in 40-50% yields (5.2 mg, 7.04×10^{-3} mmol). **7a-*Z*** was also synthesized, using the same procedure, form **8a-*Z*** in 50% yields. The formation of **7a-*E*** was not observed. **7a-*Z***: R_f 0.63 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.12 (2H, d, $J_{1,4}$ 1.86 Hz), 8.10 (2H, br s), 7.82 (2H, br d, $J_{1,3}$ 6.8 Hz), 7.71 (2H, br t, 6.4 Hz) 7.63-7.66 (4H, m), 5.94 (2H, s), 2.99 (6H, s), -1.80 (1H, s); δ_C(100 MHz, $CDCl_3$): 157.4, 142.0, 137.1, 134.2, 131.3, 127.5, 127.3, 123.8, 116.4, 81.8, 58.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 379 (5.14), 527 (4.50), 704 (4.71); Fluorescence λ_{max}(CH_2Cl_2)/nm: 710; HR-MS (ESI+, 100%

CH_3CN) m/z calculated for $C_{48}H_{43}N_4O_4$ (MH^+): 739.3284, found: 739.3236.

meso-Tetra(4-isopropylphenyl)-2(*R*),3(*S*),12(*S*),13(*R*)-tetramethoxybacteriochlorin (7b-*E*) and *meso*-tetra(4-isopropylphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetramethoxybacteriochlorin (7b-*Z*)

The tetramethoxyderivatives **7b-*E*/*Z*** were synthesized from the tetraols **4b-*E*/*Z*** in 40–50% yields according to the general procedure described for **5a**. **7b-*E***: R_f 0.43 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.22 (2H, d, $J_{1,4}$ 1.82 Hz), 7.97 (2H, br s), 7.69 (2H, br s), 7.51 (4H, s), 5.80 (2H, s), 3.12-3.22 (2H, h, $J_{1,3}$ 6.92 Hz), 2.97 (6H, s), 1.47 and 1.46 (12H, two overlapping d, $J_{1,3}$ 7 Hz), -1.91 (1H, s); δ_C(100 MHz, $CDCl_3$): 156.8, 147.8, 139.5, 137.4, 133.6, 131.5, 125.1, 123.7, 116.5, 58.3, 34.3, 24.5, 24.5; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 380 (5.08), 528 (4.43), 703 (4.63); Fluorescence λ_{max}(CH_2Cl_2)/nm: 711, $\phi = 0.21$; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{60}H_{67}N_4O_4$ (MH^+): 907.5162, found: 907.5187. **7b-*Z***: R_f 0.78 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.15 (2H, d, $J_{1,4}$ 1.80 Hz), 8.01 (2H, d, $J_{1,3}$ 7.46 Hz), 7.74 (2H, d, $J_{1,3}$ 7.58 Hz), 7.57 (2H, d, $J_{1,3}$ 7.46 Hz), 7.46 (2H, d, $J_{1,3}$ 7.74 Hz), 5.93 (2H, s), 3.18 (2H, h, $J_{1,3}$ 6.8 Hz), 2.96 (6H, s), 1.48 and 1.47 (12H, two overlapping doublets, $J_{1,3}$ 6.9 Hz), -1.78 (1H, s); δ_C(100 MHz, $CDCl_3$): 157.1, 147.9, 139.4, 137.2, 134.1, 131.2, 125.4, 125.1, 123.8, 116.3, 81.8, 58.3, 34.3, 24.5; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 381 (5.45), 531 (4.78), 705 (5.01); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712; $\phi = 0.22$; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{60}H_{67}N_4O_4$ (MH^+): 907.5162, found: 907.5085.

meso-Tetra(4-*tert*-butylphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetramethoxybacteriochlorin (7c-*Z*)

Synthesized from **4c-*Z*** according to the procedure, in 40-50% yields (4.1 mg). **7c-*Z***: R_f 0.74 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.14 (2H, d, $J_{1,4}$ 1.76 Hz), 8.02 (2H, br d, $J_{1,3}$ 7.79 Hz) 7.73 (4H, two overlapped doublets, $J_{1,3}$ 7.79 Hz), 7.63 (2H, br d, $J_{1,3}$ 7.79 Hz), 5.92 (2H, s), 2.94 (2H, s), 1.54 (18H, s), -1.76 (1H, s); δ_C(100 MHz, $CDCl_3$): 157.0, 150.2, 139.0, 137.2, 133.9, 130.9, 124.2, 124.0, 123.8, 116.2, 81.9, 58.2, 35.0, 31.8; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 381 (5.40), 530 (4.73), 704 (4.96); Fluorescence λ_{max}(CH_2Cl_2)/nm: 708; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{64}H_{75}N_4O_4$ (MH^+): 963.5788, found: 963.5718.

meso-Tetra(3,4,5-trimethoxyphenyl)-2(*R*),3(*S*),12(*S*),13(*R*)-tetramethoxybacteriochlorin (7d-*E*) and *meso*-tetra(3,4,5-trimethoxyphenyl)-2(*R*),3(*S*),12(*R*),13(*S*)-tetramethoxybacteriochlorin (7d-*Z*)

7d-*E*/*Z* were synthesized from **4d-*E*/*Z*** according to the general procedure in 50–65% yields. **7d-*E***: R_f 0.34 (silica, CH_2Cl_2–3% MeOH); δ_H(400 MHz, $CDCl_3$): 8.34 (2H, d, $J_{1,4}$ 1.93 Hz), 7.37 (2H, s), 7.02 (2H, s), 5.82 (2H, s), 4.11 (6H, s), 3.98 (6H, s), 3.91 (6H, s), 3.20 (6H, s), -2.05 (1H, s); δ_C(100 MHz, $CDCl_3$): 157.0, 152.2, 152.0, 137.6, 137.5, 137.4, 124.0, 116.4, 112.0, 109.6, 82.3, 61.4, 59.5, 56.6, 56.5; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 380 (4.93), 527 (4.30), 705 (4.55); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712, $\phi = 0.19$; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{60}H_{67}N_4O_{16}$ (MH^+): 1099.4552, found: 1099.4480. **7d-*Z***: R_f 0.28 (silica, CH_2Cl_2–3% MeOH); δ_H(400 MHz, $CDCl_3$): 8.26 (2H, d, $J_{1,4}$ 1.55 Hz), 7.39 (2H, d, $J_{1,4}$ 1.35 Hz), 7.05 (2H, d, $J_{1,4}$ 1.36 Hz), 5.94 (2H, s), 4.11 (6H, s), 4.00 (6H, s), 3.92 (6H, s), 3.16 (6H, s), -1.90 (1H, s); δ_C(100 MHz, $CDCl_3$): 157.3, 152.3, 152.0, 137.7, 137.3, 137.1, 123.9, 116.2, 112.2, 109.3, 82.3, 61.6, 59.3, 56.6, 56.6; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 381 (5.18), 528 (4.54), 706 (4.83); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712, $\phi = 0.20$; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{60}H_{67}N_4O_{16}$ (MH^+): 1099.4552, found: 1099.4513

meso-Tetraphenyl-2(*R*),3(*S*)-dihydroxy-12(*S*),13(*R*)-dimethoxybacteriochlorin (8a-*E*) and *meso*-tetraphenyl-2(*R*),3(*S*)-dihydroxy-12(*R*),13(*S*)-dimethoxybacteriochlorin (8a-*Z*)

8a-*E* (5 mg, 7.0×10^{-3} mmol) and **8a-*Z*** (20 mg, 2.8×10^{-2} mmol) were synthesized from **5a** according to the general procedures and isolated by preparative TLC (silica, CH_2Cl_2–2% MeOH) in 40% combined yields with ~1 : 4 ratio of ***E*** and ***Z*** isomers. **8a-*E***: R_f 0.73 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$) 8.20 (2H, br d, $J_{1,4}$ 2 Hz), 8.08 (2H, br s), 7.89 (1H, br s), 7.80 (1H, br s), 7.69 and 7.64 (6H, two overlapped singlets), 6.18 (1H, s), 5.84 (1H, s), 3.10 (1H, br s), 3.00 (3H, s), -1.85 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.0, 157.0, 142.0, 141.4, 137.5, 137.3, 133.8, 133.5, 131.5, 128.0, 127.6, 127.4, 127.3, 127.2, 124.0, 123.5, 177.0, 115.7, 81.7, 74.2, 58.5; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 378 (5.29), 526 (4.67), 705 (4.87); Fluorescence λ_{max}(CH_2Cl_2)/nm: 709; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{46}H_{39}N_4O_4$ (MH^+): 711.2971, found: 711.2957. **8a-*Z***: R_f 0.42 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.10-8.17 (4H, overlapped two dd and d), 7.91 (1H, br d, $J_{1,3}$ 6.18 Hz), 7.83 (1H, br d, $J_{1,3}$ 6.61 Hz), 7.63–7.74 (6H, m), 6.29 (1H, s), 5.95 (1H, s), 2.99 (4H, overlapped br s and s), -1.75 (1H, s); δ_C(100 MHz, $CDCl_3$): 158.4, 157.3, 141.9, 141.3, 137.4, 137.2, 134.2, 134.0, 132.0, 131.3, 128.0, 127.7, 127.6, 127.3, 124.0, 123.6, 116.9, 115.6, 81.7, 74.1, 58.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 378 (5.29), 527 (4.65), 705 (4.89); Fluorescence λ_{max}(CH_2Cl_2)/nm: 712; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{46}H_{39}N_4O_4$ (MH^+): 711.2971, found: 711.3024.

meso-Tetraphenyl-2,3-*vic*-dihydroxybacteriochlorin (9a) and *meso*-tetra(3,4,5-trimethoxyphenyl)-2,3-*vic*-dimethoxybacteriochlorin (10d)

meso-Tetraphenylchlorin (20 mg, 3.1×10^{-2} mmol) **3a** was dissolved in a suspension of anhydrous K_2CO_3 (40 mg) in dry pyridine (10 ml) in a 50 ml round bottom flask equipped with a magnetic stir bar. The mixture was refluxed, under N_2, at 105 °C. *p*-Toluenesulfonylhydrazide (30 mg) was added in two portions to the mixture and refluxing was continued for 6–8 h (TLC control). The mixture was cooled, filtered, the filtrate was evaporated to dryness and the residue was separated on a preparative TLC (silica, CH_2Cl_2–1.5% MeOH) plate. The pink band of **9a** separating from the brown band was isolated, after recrystallization from CH_2Cl_2–CCl_4, in 12% yield. **10d** was prepared from **5d** according to the same procedure and isolated by preparative TLC (silica, CH_2Cl_2–2% MeOH). **9a**: R_f 0.17 (silica, CH_2Cl_2); δ_H(400 MHz, $CDCl_3$): 8.08-8.11 (2H, overlapping dd and s), 8.02 (1H, dd, *J* 4.7 and 1.9 Hz), 7.90 (1H, br s), 7.84 (2H, br t, *J* 6.7 Hz), 7.65-7.71 (6H, m), 6.21 (1H, s), 3.96-4.11 (2H, m), 3.00 (1H,

Table 3 Crystal data

Compound	**4b-*E*** · 4 MeOH	**4d-*Z*** · 4.62 $CHCl_3$	**5a**	**7d-*E*** · 4 CH_2Cl_2	**11a**
Formula	$C_{60}H_{74}N_4O_8$	$C_{60.62}H_{62.62}Cl_{13.86}N_4O_{16}$	$C_{46}H_{36}N_4O_2$	$C_{64}H_{74}Cl_8N_4O_{16}$	$C_{44}H_{32}N_4O$
M/g mol^{-1}	979.23	1594.67	676.79	1438.87	632.74
Crystal system	Triclinic	Triclinic	Monoclinic	Triclinic	Tetragonal
a, b, c/Å	8.1709(10), 11.1196(14), 15.653(2)	11.6873(9), 15.6713(12), 22.2525(17)	14.3828(4), 10.2429(3), 24.0675(7)	10.8723(15), 12.237(3), 14.380(2)	15.0677(9), 15.0677(9), 13.8543(17)
α, β, γ (°)	76.5000(17), 84.6620(19), 79.0700(18)	69.9290(10), 82.0790(10), 72.1360(10)	90, 98.0890(10), 90	108.550(3), 111.400(2), 95.110(3)	90, 90, 90
U/Å^3	1356.0(3)	3641.2(5)	3510.38(17)	1642.5(5)	3145.4(5)
T/K	100(2)	100(2)	150(2)	100(2)	100(2)
Space group	$P\bar{1}$ (#2)	$P\bar{1}$ (#2)	$P2_1/n$ (#14)	$P\bar{1}$ (#2)	I-42d (#84)
Z	1	2	4	1	4
Reflections measured	6634	29 211	47 955	16 694	13 888
Unique (R_{int})	6634 (0.0336)	12 829 (0.0355)	8719 (0.0465)	8035 (0.0265)	13 888 (0.0301)
Data/restraints/parameters	6634/0/335	12829/0/896	8719/0/469	8035/0/423	1089/26/136
Goodness-of-fit on F^2	1.054	1.087	1.003	1.031	1.061
$R(F)$ [$I > 2\sigma(I)$]	0.0459	0.0920	0.0424	0.0509	0.0402
$R(F)$ [all data]	0.0613	0.1140	0.0761	0.0688	0.0473
w$R(F_2)$ [$I > 2\sigma(I)$]	0.1147	0.2307	0.0990	0.1108	0.1117
w$R(F_2)$ [all data]	0.1214	0.2518	0.1179	0.1216	0.1191

br s), -1.53 (1H, s); δ_C(100 MHz, $CDCl_3$): 163.4, 157.4, 143.2, 141.5, 137.4, 136.8, 133.7, 132.4, 132.1, 131.9, 128.1, 128.1, 128.0, 128.0, 127.6, 123.4, 122.5, 115.6, 115.2, 74.1, 35.4; UV-vis λ_{max}(CH_2Cl_2)/nm (log ε): 378 (4.96), 524 (4.49), 724 (4.71); Fluorescence λ_{max}(CH_2Cl_2)/nm: 726; LR-MS (+FAB, 3NBA) m/z 650 (100, M$^+$), 633 (19.2, M$^+$-OH); HR-MS (+FAB, 3-NBA) m/z calculated for $C_{44}H_{34}N_4O_2$: 650.26818, found 650.27118. **10d**: R_f 0.2 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.25, 8.16 (1H, d, J 4.12 Hz), 7.37 (1H, s), 7.04 and 7.06 (3H, two overlapped s), 5.85 (1H, s), 3.8-4.3 (21H, m), 3.17 (3H, s), -1.68 (1H, s): UV-vis λ_{max}(CH_2Cl_2)/nm (rel. intensity): 380 (1.00), 524 (0.3), 724 (0.65); Fluorescence λ_{max}(CH_2Cl_2)/nm: 726; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{58}H_{62}N_4O_{14}$ (MH$^+$): 1038.4263, found: 1038.4287

meso-Tetra(3,4,5-trimethoxyphenyl)-2,3,12-trimethoxychlorin (15d). General procedure for the acid-induced dehydration/demethoxylation of 2,3,12,13-tetraol/tetramethoxybacteriochlorins

Bacteriochlorin **7d-*Z*** (4.0 mg, 3.6 × 10^{-3} mmol) was dissolved in CH_2Cl_2 (50 ml) in a 100 ml round bottom flask equipped with a magnetic stir bar. To this solution was added 10% TFA–CH_2Cl_2 (1.00 ml, using a glass pipette) and the reaction mixture was stoppered and covered from ambient light (aluminium foil) and stirred for 1.5 h at ambient conditions. The progress of the transformation was monitored by UV-vis spectroscopy. After the reaction was completed, the mixture was neutralized by the slow addition of NH_4OH (1.0 ml of an aqueous 2.8–3.0 wt% solution). The product was extracted into CH_2Cl_2 (>90% yield). **15d**: R_f 0.24 (silica, CH_2Cl_2–2% MeOH); δ_H(400 MHz, $CDCl_3$): 8.69 (1H, d, J 5.29 Hz), 8.65 (1H, d, J 5.09 Hz), 8.48 (1H, d, J 4.43 Hz), 8.42 (1H, d, J 4.78 Hz), 7.59 (1H, s), 7.37-7.46 (4H, m), 7.26 (1H, s), 7.19 (1H, s), 7.10 (1H, s), 7.07 (1H, s), 6.03 (2H, two overlapping d, J 7.17 Hz), 3.90–4.18 (39H, m), 3.20 and 3.22 (6H, two overlapping s), -2.11 (1H, br s), -2.25 (1H, br s); λ_{max}(CH_2Cl_2)/nm (rel. intensity): 410 (1.00), 510 (0.09), 540 (0.10), 603 (0.04), 658 (0.18); Fluorescence λ_{max}(CH_2Cl_2)/nm: 663; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{59}H_{63}N_4O_{15}$ (MH$^+$): 1067.4290, found: 1067.4263.

meso-Tetra(4-isopropylphenyl)-2,3,12-trihydroxychlorin (12b)

Synthesized from **4b-*Z*** according to the procedure described for **15d**. **12b**: R_f 0.51 (silica, CH_2Cl_2–2% MeOH) UV-vis λ_{max}(CH_2Cl_2)/nm (rel. intensity): 413 (1.00), 515 (0.11), 543 (0.12), 599 (0.04), 654 (0.10), 690 (0.11); Fluorescence λ_{max}(CH_2Cl_2)/nm (rel. intensity): 658 (1.00) 696 (0.39); HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{56}H_{57}N_4O_3$ (MH$^+$): 833.4431, found: 833.4462.

meso-Tetraphenyl-2,3-*vic*-dihydroxy-12-methoxychlorin (13a)

Synthesized from **8a-*Z*** according to the procedure described for **15d**. **13a**: UV-vis λ_{max}(CH_2Cl_2)/nm (rel. intensity): 408 (1.00), 512 (0.09), 540 (0.10), 603 (0.03), 658 (0.16), 692 (0.06); Fluorescence λ_{max}(CH_2Cl_2)/nm: 662; HR-MS (ESI+, 100% CH_3CN) m/z calculated for $C_{45}H_{35}N_4O_3$ (MH$^+$): 679.2709, found: 679.2683.

Crystal structure determinations

Single crystals of **4b-*E*** (CH_2Cl_2–MeOH), **4d-*Z*** ($CHCl_3$–petroleum ether 30-60), **5a** ($CHCl_3$–MeOH), **7d-*E*** (CH_2Cl_2–petroleum ether 30-60), and **11a** ($CHCl_3$–MeOH) were grown by vapour phase diffusion of a non-solvent into dilute solutions of the compounds using the solvent combinations indicated in parentheses (solvent–non-solvent). The crystals were mounted in inert oil on a glass fibre or Mitegen micromesh mount and transferred to the cold gas stream of the diffractometer. Crystal data are listed in Table 3. For additional information, see the ESI.†

Conclusions

The double dihydroxylation of *meso*-tetraarylporphyrins allows the preparation of two isomeric and stable bacteriochlorins. The

O-methylation of the diol functionalities is facile and assists in the isolation and separation of the isomers, and further stabilizes the bacteriochlorins. Structural characterization of the two isomeric tetrahydroxybacteriochlorins assigns unambiguously their relative stereochemistry. Thus, this work makes these bacteriochlorins available for further study. It also paves the way toward bacteriochlorin-derived pyrrole-modified porphyrins, as either dimethoxydiolbacteriochlorins **8** or diolbacteriochlorins **9** might be susceptible to similar functional group transformation sequences that we demonstrated for the diolchlorins. Experiments toward this end are currently ongoing in our laboratories.

Acknowledgements

We thank Michelle Dean who first noticed the formation of **11a**. We also thank Heather Daniel, Christopher Arntsen (supported through a Pfizer-CBIA summer research grant), Doug Mooney (supported through NSF-REU grant CHE-0754580), and Renee Rubenstein for expert experimental support, and Claudia Ryppa for the compilation of Table ESI-1. This work was supported by the US National Science Foundation under Grant Numbers CHE-0517782 and CMMI-0730826 (to CB). The APEX diffractometer was funded by NSF grant 0087210, by the Ohio Board of Regents grant CAP-491, and by YSU. The SMART6000 diffractometer (University of Cincinnati) was funded by NSF-MRI grant CHE-0215950.

Notes and references

1 (*a*) *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, 2003; (*b*) H. Scheer and H. H. Inhoffen, in *The Porphyrins*, ed. D. Dolphin, Academic Press, New York, San Francisco, London, 1978, pp. 45-90; (*c*) E. D. Sternberg, D. Dolphin and C. Brückner, *Tetrahedron*, 1998, **54**, 4151; (*d*) S. Shanmugathasan, C. Edwards and R. W. Boyle, *Tetrahedron*, 2000, **56**, 1025; (*e*) F.-P. Montforts, B. Gerlach and F. Höper, *Chem. Rev.*, 1994, **94**, 327; (*f*) Y. Chen, G. Li and R. K. Pandey, *Curr. Org. Chem.*, 2004, **8**, 1105.

2 For representative examples of the total synthesis of bacteriochlorins, see, *e.g.*: (*a*) W. G. O'Neal and P. A. Jacobi, *J. Am. Chem. Soc.*, 2008, **130**, 1102; (*b*) C. L. Gibson, M. J. Doyle, P. R. Raithby and A. R. Battersby, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1893; (*c*) K. E. Borbas, C. Ruzié and J. S. Lindsey, *Org. Lett.*, 2008, **10**, 1931; (*d*) H.-J. Kim and J. S. Lindsey, *J. Org. Chem.*, 2005, **70**, 5475; (*e*) M. Taniguchi, D. L. Cramer, A. D. Bhise, H. L. Kee, D. F. Bocian, D. Holten and J. S. Lindsey, *New J. Chem.*, 2008, **32**, 947.

3 D. H. Burns, T. M. Caldwell and M. W. Burden, *Tetrahedron Lett.*, 1993, **34**, 2883.

4 (*a*) P. Yon-Hin, T. P. Wijesekera and D. Dolphin, *Tetrahedron Lett.*, 1991, **32**, 2875; (*b*) A. M. G. Silva, A. C. Tome, M. G. P. M. S. Neves, A. M. S. Silva and J. A. S. Cavaleiro, *J. Org. Chem.*, 2005, **70**, 2306; (*c*) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, A. M. S. Silva, J. A. S. Cavaleiro, D. Perrone and A. Dondoni, *Tetrahedron Lett.*, 2002, **43**, 603; (*d*) A. M. G. Silva, A. C. Tome, M. G. P. M. S. Neves, J. A. S. Cavaleiro and C. O. Kappe, *Tetrahedron Lett.*, 2005, **46**, 4723; (*e*) A. M. G. Silva, A. C. Tome, M. G. P. M. S. Neves, A. M. S. Silva and J. A. S. Cavaleiro, *Chem. Commun.*, 1999, 1767; (*f*) D. Kusch, E. Töllner, A. Lincke and F.-P. Montforts, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 784; (*g*) A. C. Tomé, P. S. S. Lacerda, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Chem. Commun.*, 1997, 1199.

5 K. R. Adams, M. C. Berenbaum, R. Bonnett, A. N. Nizhnik, A. Salgado and M. A. Valles, *J. Chem. Soc., Perkin Trans. 1*, 1992, 1465.

6 H. W. Whitlock Jr., R. Hanamer, M. Y. Oester and B. K. Bower, *J. Am. Chem. Soc.*, 1969, **91**, 7485.

7 M. C. Berenbaum, S. L. Akande, R. Bonnett, H. Kaur, S. Ioannou, R. D. White and U.-J. Winfield, *Br. J. Cancer*, 1986, **54**, 717.

8 (*a*) H. Fischer and H. Eckoldt, *Justus Liebigs Ann. Chem.*, 1940, **544**, 138–162; (*b*) H. Fischer and H. Pfeiffer, *Justus Liebigs Ann. Chem.*, 1944, **556**, 131–153.

9 (*a*) H. H. Inhoffen, J. Ullrich, H. A. Hoffmann and G. Klinzmann, *Tetrahedron Lett.*, 1969, **10**, 613; (*b*) R. Bonnett, A. N. Nizhnik and M. C. Berenbaum, *J. Chem. Soc., Chem. Commun.*, 1989, 1822; (*c*) I. Meunier, R. K. Pandey, M. M. Walker, M. O. Senge, T. J. Dougherty and K. M. Smith, *Bioorg. Med. Chem. Lett.*, 1992, **2**, 1575; (*d*) K. R. Gerzevske, R. K. Pandey and K. M. Smith, *Heterocycles*, 1994, **39**, 439; (*e*) R. K. Pandey, F. Y. Shiau, A. B. Sumlin, T. J. Dougherty and K. M. Smith, *Bioorg. Med. Chem. Lett.*, 1994, **4**, 1263; (*f*) G. Zheng, T. J. Dougherty and R. K. Pandey, *J. Org. Chem.*, 1999, **64**, 3751.

10 C. Brückner, S. J. Rettig and D. Dolphin, *J. Org. Chem.*, 1998, **63**, 2094.

11 A. Wiehe, H. Stollberg, S. Runge, A. Paul, M. O. Senge and B. Röder, *J. Porphyrins Phthalocyanines*, 2001, **5**, 853.

12 J. K. MacAlpine, R. Boch and D. Dolphin, *J. Porphyrins Phthalocyanines*, 2002, **6**, 146.

13 J. M. Sutton, N. Fernandez and R. W. Boyle, *J. Porphyrins Phthalocyanines*, 2000, **4**, 655.

14 S. D. Starnes, D. M. Rudkevich and J. Rebek Jr., *J. Am. Chem. Soc.*, 2001, **123**, 4659.

15 J. M. Sutton, O. J. Clarke, N. Fernandez and R. W. Boyle, *Bioconjugate Chem.*, 2002, **13**, 249.

16 R. Bonnett, A. N. Nizhnik and M. C. Berenbaum, *J. Chem. Soc., Chem. Commun.*, 1989, 1822.

17 In the experimental section, we are using the absolute stereochemical nomenclature for the compounds to be described but for sake of simplicity, the discussion will use the more informal and relative stereochemical *E*/*Z* nomenclature.

18 (*a*) H. H. Inhoffen and W. Nolte, *Justus Liebigs Ann. Chem.*, 1969, **725**, 167; C. G. Chang and C. Sotiriou, *J. Org. Chem.*, 1987, **52**, 926; (*b*) L. A. Anderson, C. Sotiriou, C. K. Chenag and T. M. Loehr, *J. Am. Chem. Soc.*, 1987, **109**, 258; (*c*) K. R. Adams, R. Bonnett, P. J. Burke, A. Salgado and M. A. Vallés, *J. Chem. Soc., Chem. Commun.*, 1993, 1860; (*d*) K. R. Adams, R. Bonnett, P. J. Burke, A. Salgado and M. A. Vallés, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1769.

19 C. G. Chang and C. Sotiriou, *J. Org. Chem.*, 1987, **52**, 926.

20 C. Ryppa, D. Niedzwiedzki, N. L. Morozowich, R. Srikanth, M. Zeller, H. A. Frank and C. Brückner, *Chem.–Eur. J.*, 2009, **15**, 5749.

21 C. Brückner and D. Dolphin, *Tetrahedron Lett.*, 1995, **36**, 9425.

22 C. Brückner and D. Dolphin, *Tetrahedron Lett.*, 1995, **36**, 3295.

23 (*a*) C. Brückner, E. D. Sternberg, J. K. MacAlpine, S. J. Rettig and D. Dolphin, *J. Am. Chem. Soc.*, 1999, **121**, 2609; (*b*) C. J. Campbell, J. F. Rusling and C. Brückner, *J. Am. Chem. Soc.*, 2000, **122**, 6679; (*c*) J. R. McCarthy, H. A. Jenkins and C. Brückner, *Org. Lett.*, 2003, **5**, 19; (*d*) H. W. Daniell and C. Brückner, *Angew. Chem., Int. Ed.*, 2004, **43**, 1688; (*e*) J. R. McCarthy, M. A. Hyland and C. Brückner, *Org. Biomol. Chem.*, 2004, **2**, 1484; (*f*) C. Brückner, M. A. Hyland, E. D. Sternberg, J. MacAlpine, S. J. Rettig, B. O. Patrick and D. Dolphin, *Inorg. Chim. Acta*, 2005, **358**, 2943; (*g*) M. J. Perez, J. R. McCarthy, C. Brückner and R. Weissleder, *Nano Lett.*, 2005, **5**, 2552; (*h*) J. Akhigbe, C. Ryppa, M. Zeller and C. Brückner, *J. Org. Chem.*, 2009, **74**, 4927.

24 S. Banerjee, M. Zeller and C. Brückner, *J. Org. Chem.*, 2009, **74**, 4283.

25 K. K. Lara, C. K. Rinaldo and C. Brückner, *Tetrahedron*, 2005, **61**, 2529.

26 CCSD Code VIXGEO–5,10,15,20-tetrakisphenylbacteriochlorinato]-Zn(II) pyridine solvate, K. M. Barkigia, M. Miura, M. A. Thompson and J. Fajer, *Inorg. Chem.*, 1991, **30**, 2233. RAPTOR–bis[μ2-5-(2-pyridyl)-10,15,20-tris(3,5-difluorophenyl) porphyrinato]Zn(II) *p*-xylene solvate,; J. Vasudevan, R. T. Stibrany, J. Bumby, S. Knapp, J. A. Potenza, T. J. Emge and H. J. Schugar, *J. Am. Chem. Soc.*, 1996, **118**, 11676. FUBJIV–*trans*-2,3-*cis*-12,13-tetrahydro-2,3-bis(dicyanomethyl)-(12:13)-(di(methoxycarbonyl)methano)-5,10,15,20-tetraphenylporphyrin $CHCl_3$ solvate,; K. M. Shea, L. Jaquinod, R. G. Khoury and K. M. Smith, *Tetrahedron*, 2000, **56**, 3139. YAJYAK–5,10,15,20-tetrakis(4-chlorophenyl)-3′,3″-bis(2,6-dichlorophenyl)-(4′,5′-g;4″,5″-q)bis(isoxazolo)bacteriochlorin CH_2Cl_2 $CHCl_3$ solvate,; X. Li, J. Zhuang, Y. Li, H. Liu, S. Wang and D. Zhu, *Tetrahedron Lett.*, 2005, **46**, 1555.

27 C. G. Chang, C. Sotiriou and W. Weishih, *J. Chem. Soc., Chem. Commun.*, 1986, 1213.

28 A. N. Kozyrev, T. J. Dougherty and R. K. Pandey, *Tetrahedron Lett.*, 1996, **37**, 3781.

29 D. K. Lavallee, *The Chemistry and Biochemistry of N-substituted Porphyrins*, VCH, Weinheim, New York, 1987.

30 K. M. Barkigia, C. K. Chang and J. Fajer, *J. Am. Chem. Soc.*, 1991, **113**, 7445.
31 H. W. Daniell, S. C. Williams, H. A. Jenkins and C. Brückner, *Tetrahedron Lett.*, 2003, **44**, 4045.
32 (*a*) J. M. Hawkins, A. Meyer, T. A. Lewis, S. Loren and F. J. Hollander, *Science*, 1991, **252**, 312; (*b*) L. R. Subbaramn, J. Subbaraman and E. J. Behrman, *Inorg. Chem.*, 1972, **11**, 2621; (*c*) J. M. Wallis and J. K. Kochi, *J. Am. Chem. Soc.*, 1988, **110**, 8207; (*d*) W. A. Herrman, S. J. Eder and W. Scherer, *Chem. Ber.*, 1993, **126**, 39–43.
33 J. W. Whitlock and M. Y. Oester, *J. Am. Chem. Soc.*, 1973, **95**, 5738.
34 H. J. Reich, WinDNMR: Dynamic NMR Spectra for Windows *J. Chem. Educ.* Software 3D2.
35 C. Brückner, J. R. McCarthy, H. W. Daniell, Z. D. Pendon, R. P. Ilagan, T. M. Francis, L. Ren, R. R. Birge and H. A. Frank, *Chem. Phys.*, 2003, **294**, 285.
36 D. H. Burns, Y. H. Li, D. C. Shi and M. O. Delaney, *Chem. Commun.*, 1998, 1677.
37 T. Y. Wang, J. R. Chen and J. S. Ma, *Dyes Pigm.*, 2002, **52**, 199.
38 T. Y. Wang, H. L. Liu, J. R. Chen, F. G. Liu, Y. Gu and J. S. Ma, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 2049.
39 J. D. Keegan, A. M. Stolzenberg, Y. C. Lu, R. E. Linder, G. Barth, A. Moscowitz, E. Bunnenberg and C. Djerassi, *J. Am. Chem. Soc.*, 1982, **104**, 4305.
40 H. Tamiaki, S. Kimura and T. Kimura, *Tetrahedron*, 2003, **59**, 7423.
41 (*a*) J. A. Shelnutt, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, 7, 167; (*b*) W. Jentzen, X.-Z. Song and J. A. Shelnutt, *J. Phys. Chem. B*, 1997, **101**, 1684; (*c*) L. Song, J. A. Shelnutt, NSD Engine Version 3.0 (http://jasheln.unm.edu/jasheln/content/nsd/NSDengine/start.htm).
42 (*a*) P. G. Seybold and M. Gouterman, *J. Mol. Spectrosc.*, 1969, **31**, 1; (*b*) T. Y. Wang, J. R. Chen Jin and S. Ma, *Dyes Pigm.*, 2002, **52**, 199.
43 M. R. M. Domingues, M. G. O. S. -Marques, P. Domingues, M. Graça Neves, J. A. S. Cavaleiro and A. J. Ferrer-Correia, *J. Am. Soc. Mass Spectrom.*, 2001, **12**, 381.
44 C. Brückner, P. C. D. Foss, J. O. Sullivan, R. Pelto, M. Zeller, R. R. Birge and G. Crundwell, *Phys. Chem. Chem. Phys.*, 2006, **8**, 2402.
45 C. G. Chang and C. Sotiriou, *J. Heterocycl. Chem.*, 1985, **22**, 1739.
46 A. Osuka, S. Marumo and K. Maruyama, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 3837.
47 K. R. Pandey, F. Y. Shiau, M. Isaac, S. Ramaprasad, T. J. Dougherty and K. M. Smith, *Tetrahedron Lett.*, 1992, **33**, 7815.
48 R. K. Pandey, M. Isaac, I. MacDonald, C. J. Medforth, M. O. Senge, T. J. Dougherty and K. M. Smith, *J. Org. Chem.*, 1997, **62**, 1463.
49 (*a*) M. M. Catalano, M. J. Crossley and L. G. King, *J. Chem. Soc., Chem. Commun.*, 1984, 1537; (*b*) M. J. Crossley, L. G. King and S. M. Pyke, *Tetrahedron*, 1987, **43**, 4569; (*c*) M. J. Crossley, M. M. Harding and S. Sternhell, *J. Org. Chem.*, 1988, **53**, 1132.
50 A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour and L. Korsakoff, *J. Org. Chem.*, 1967, **32**, 476.