Step-wise Reduction of Octaethyl-β,β'-dioxochlorin Isomers: Access to Structurally and Electronically Diverse Hydroporphyrins

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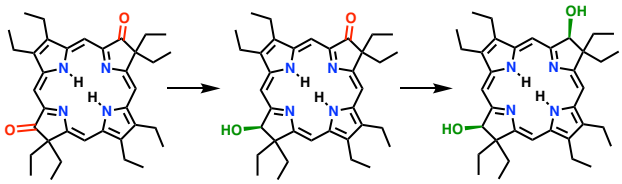


ABSTRACT: Di-and tetrahydroporphyrins (chlorins, bacteriochlorins and isobacteriochlorins, respectively) are key 'pigments of life'. They have been a major focus of attention in synthetic tetrapyrrole chemistry. A long-known one-pot epoxidation/epoxide ring opening/pinacol-pinacolone rearrangement of octaethylporphyrin (**OEP**) generates a β-ketochlorin and all five β,β'-diketone isomers. We present herein the single and double reductions of all isomers of the β,β'-diketones, generating hydroxychlorin and β-hydroxy-β-ketodihydroporphyrin isomers, generally in regioselective manner, and sets of separable stereoisomeric dihydroxytetrahydroporphyrin regioisomers. The connectivity of the regio- and stereoisomers were determined spectroscopically and, in many cases, using single crystal X-ray crystallography. The optical properties of the chlorin, bacteriochlorin-, and isobacteriochlorin-type chromophores are described. They highlight general observations on the regiochemical effects of the β-oxo-auxochrome. This contribution thus delineates the formation of a range of regio- and stereo-isomers of a family of chromophores with broadly varying optical properties from a single and readily available starting material (**OEP**) in two straight-forward steps, albeit requiring extensive chromatography.

INTRODUCTION

All of nature's hydroporphyrins carry alkyl substituents at their pyrrolic β-positions, including nature's archetype chlorins (e.g., chlorophyll *a*), bacteriochlorins (e.g., bacteriopheophytin), or isobacteriochlorins (e.g., heme *d*) (Chart 1).[1]

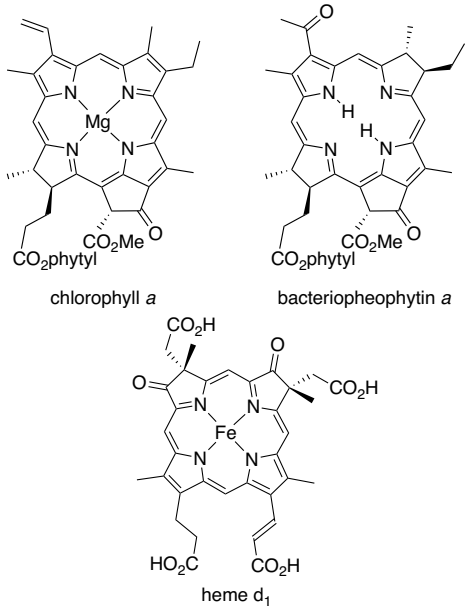
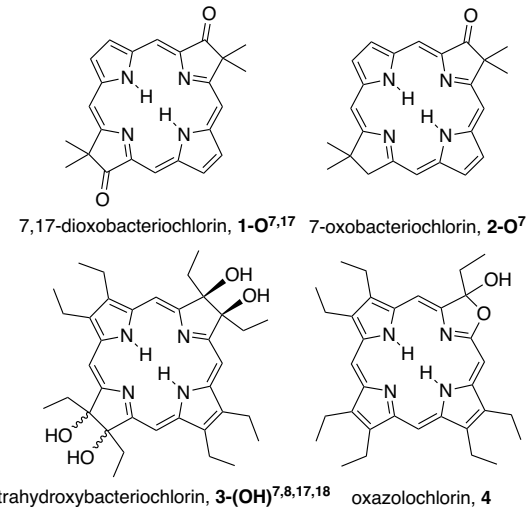


Chart 1. Example structures of naturally occurring chlorins, bacteriochlorins, and isobacteriochlorins.

Synthetic or naturally derived (hydro)porphyrins found many uses in technical and biomedical applications.[2] While chlorins are present in bulk quantities in plant materials,[3] their isolation is hampered by their chemical instability and their derivatization is met with regioselectivity problems.[2a,4] The total syntheses of a range of variously functionalized β-alkylhydroporphyrins, such as β,β'-dioxo- and oxo-bacteriochlorin **1-O**^{7,17} and **2-O**^{7} (Chart 2), were made possible by the paradigm-shifting work of Lindsey and coworkers,[2c,2d,5] but it nonetheless remains non-trivial.[2,5a] The synthetic and spectroscopic work by the groups of Bocian, Holten, and Lindsey also clearly delineated the electronic effects of the number and placement of β-oxo functionalities on the tetrapyrrolic macrocycle.[6] Robust octaethylporphyrin (**OEP**) is the most readily accessible synthetic β-alkylporphyrin.[7] Facilitated by its high symmetry, many methods toward the functionalization of its *meso*- and β-positions and ethyl side chains were described.[8] Its reduction and functionalization to chlorins and bacteriochlorins (e.g., tetraol **3-(OH)**^{7,8,17,18}) or chlorin analogues (e.g., oxazolochlorin **4**), are representative examples.[8e,8h]



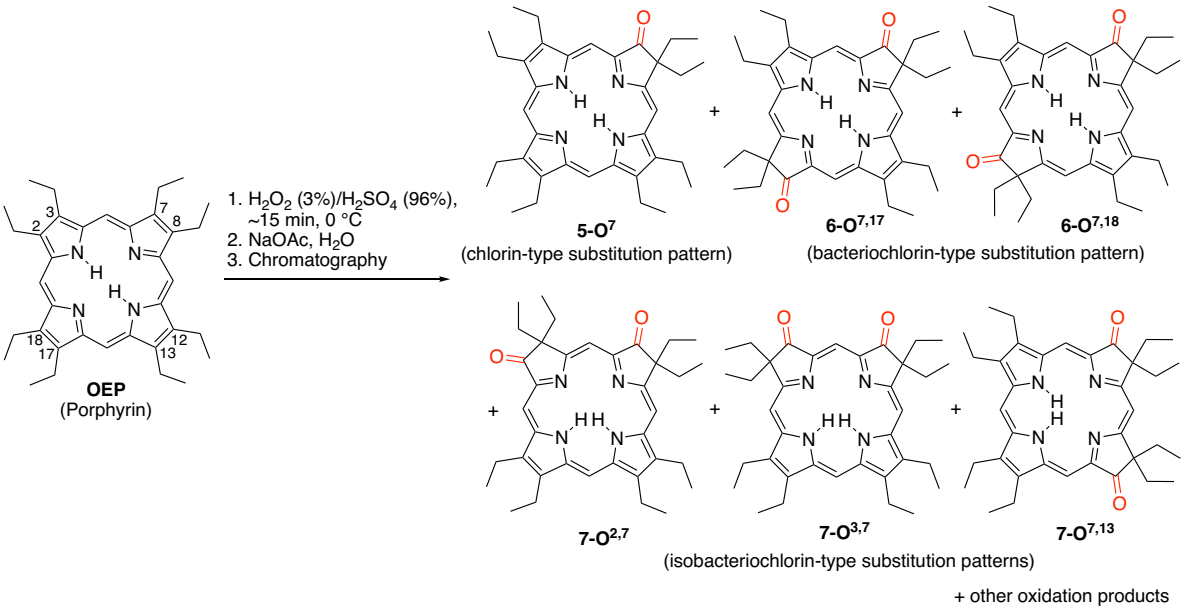
7,17-dioxobacteriochlorin, **1-O**^{7,17} 7-oxobacteriochlorin, **2-O**^{7}

tetrahydroxybacteriochlorin, **3-(OH)**^{7,8,17,18} oxazolochlorin, **4**

Chart 2. Example structures of synthetic oxo- and hydroxy-bacteriochlorins and a β-hydroxyoxazolochorin.

A simple method to introduce β-oxo functionalities into **OEP** is its treatment with H_2O_2 in conc. H_2SO_4 (Scheme 1).[9] The reaction originated in the 1930's (using β-alkylporphyrins other than **OEP**),[10] though the connectivity of the β-oxo products were not identified until 34 years later.[9c,11] This one-pot epoxidation/epoxide ring opening/pinacol-pinacolone rearrangement reaction was expanded to **OEP** and the chromatographic separation of all products formed in this rather non-specific oxidation reaction allowed the isolation and identification of oxochlorin **5-O**^{7} and all isomers of the diketones: the two possible isomers of the bacteriochlorin series (**6-O**^{7,17} and **6-O**^{7,18}), the three isomers of the isobacteriochlorin series (**7-O**^{2,7}, **7-O**^{3,7}, and **7-O**^{7,13}), as well as triketone pyrrocorphins, *meso*-oxo-substituted phlorins, and ring-opened products (not shown).[9] The introduction of β-oxo auxochromes into β-alkylporphyrins influences their chromophore electronic properties in profound ways.[6,12] It also changes the basicity of the chromophore and its ability to act as a ligand.[12e,13] Most importantly in the current context, the oxo-functionality can also act as a synthetic handle for further chemical manipulations of the chromophore.

Scheme 1. Literature known oxidation of OEP to corresponding monooxo- and dioxochlorins; OEP also shows the numbering system used for naming of oxochlorins.



The reactivity of the **OEP**-derived oxochlorins – primarily that of oxochlorin **5-O⁷** – with respect to reduction,[14] carbonyl *C*-methylation,[9d] thionation[15], *N*-methylation,[16] *N*-oxidation,[8g] *meso*-deuteration,[17] *meso*-chlorination,[8c] *meso*-hydroxylation,[8g] and β,β'-osmylation[18] reactions was studied. We also found oxochlorin **5-O⁷** to be a suitable starting material for the preparation of a pyrrole-modified porphyrinoid.[8b,19] However, the structures and reactivity of the β,β'-dioxochlorins,[15] outside of their coordination chemistry,[12e,13,20] was much less studied.

We describe here the systematic stepwise reduction of all β,β'-dioxochlorin isomers to a range of chromophores, ranging from regioisomeric β-hydroxy-β-oxo-bacteriochlorins and -isobacteriochlorins and regio- and stereo-isomeric β,β'-dihydroxy-bacteriochlorins and -isobacteriochlorins. We contrast their optical properties and, where available, their structures to those of the parent chromophores. The findings also provide experimental evidence to support recent hypotheses put forward to explain how different substitution patterns result in regioisomers with different optical properties. In so doing, we provide access to a host of β-hydroxylated β-alkylhydroporphyrins using porphyrin modification strategies as an alternative to total syntheses.[2c,2d,5a] We thusly encourage their further study of their applicability in biological and technical applications.

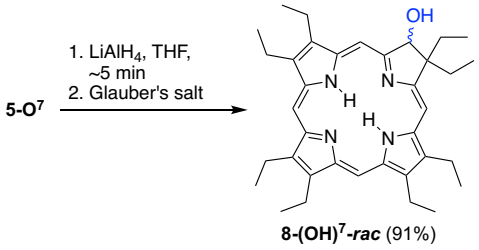
RESULTS AND DISCUSSION

Synthesis

Preparation of Oxochlorins. Octaethyl-7-oxochlorin **5-O⁷** (15% yield) and all possible five isomers of dioxochlorin bacteriochlorin series **6-O** (between 0.3 and 2.5%) and dioxochlorin isobacteriochlorin series **7-O** (between 1 and 2.5%) were synthesized using the classic procedure reported by Inhoffen and Nolte (and later Chang)[9d] using 3% H_2O_2 in 96% H_2SO_4 applied to 2-4 g batches of **OEP** (Scheme 1).[9b]

Reduction of *β*-Oxochlorin 5-O⁷. The reduction of *β*-oxochlorin **5-O⁷** using Li[BEt_3H], generating *β*-hydroxychlorin **8-(OH)⁷**, is known.[14a] We found the use of $LiAlH_4$ to be simpler and equally satisfying, reducing brown-colored oxochlorin **5-O⁷** rapidly (~5 min at 0 °C) to blue-green **8-(OH)⁷** in high isolated yield (91%) (Scheme 2). The appearance of the diagnostic pyrroline hydrogen signal in the ^{1}H NMR in the product, in combination with the absence of the carbonyl carbon in its ^{13}C NMR spectrum (at 210 ppm for **5-O⁷**), was used to evaluate the success and location of this reduction. These benchmarks were also used to assess the reductions of the dioxochlorins described below.

Scheme 2. Reduction of oxochlorin 5-O⁷ to hydroxychlorin 8-(OH)⁷-*rac*.



Upon reduction, the chlorin-type optical spectrum of oxochlorin **5-O⁷** turned to the chlorin-type spectrum of **8-(OH)⁷** in which the Soret band is hypsochromically shifted by 10 nm and some Q-bands are intensified and shifted, but the position of the band of longest wavelength absorption (λ_{max} band) remained unchanged at 642 nm (Figure 1).[14a]

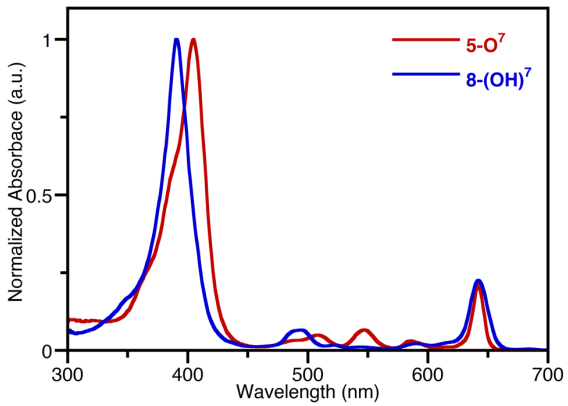


Figure 1. Normalized UV-vis spectra (CH_2Cl_2) of the compounds indicated.

Monoreduction of Bacteriochlorin-Type β,β'-Dioxochlorins Isomers 6-O^{7,17} and 6-O^{7,18}. All dioxochromophores possess the option for the sequential reduction of one or two oxo-groups. The selective reduction of the bacteriochlorin-type dioxobacteriochlorins **6-O^{7,17}** and **6-O^{7,18}** to their corresponding mono-reduced 17-hydroxy-7-oxo (**9-O^{7}(OH)^{17}**) and 18-hydroxy-7-oxobacteriochlorin (**9-O^{7}(OH)^{18}**) derivatives was achieved using 5 equiv of $NaBH_4$ at ambient temperature over the course of 24 h (Scheme 3). The isolated yields of the mono-hydroxylated species were in excess of 75%, with a small fraction (~8-10%) of unreacted reactant recovered. Importantly, under these conditions, no bis-reduced compound was observed, even after the increase of the molar equivalents of $NaBH_4$ to speed up the reaction. In either case, the starting materials are two-fold symmetric (**6-O^{7,17}** contains a C_2-axis vertical to the mean plane of the chromophore and **6-O^{7,18}** contains a mirror plane σ), rendering both oxo-groups to be equivalent in either cases. Consequently, the reduction of one group does not generate any regioisomers, but simply a racemic mixture of one regioisomerically pure product.

Diagnostic for the reduction of the oxo-groups are the appearance of a more polar product and the emergence of a pyrroline signal in their ^{1}H NMR spectra. Mono-reduction was clearly indicated by the breaking of the two-fold symmetries of the diketones **6-O^{7,17}** and **6-O^{7,18}**, as seen in their ^{1}H and ^{13}C NMR spectra (see Supporting Information for a reproduction of the key spectra) and the retention of one carbonyl moiety in the ^{13}C NMR spectra of the products **9-O^{7}(OH)^{17}** and **9-O^{7}(OH)^{18}** (at 210 ppm) and the presence of a carbonyl stretching frequency ($\nu_{C=O}$, at ~1670 cm^{-1}) in their FT-IR spectra. The UV-vis and fluorescence emission spectra of the mono- (and bis-) reduced diketones are described below.

The reduction of each carbonyl group of **9-O^{7,17}** and **9-O^{7,18}** generates a chiral center. We did not attempt the separation of the enantiomers. The connectivity and (solid state) conformation of the mono-reduction products **9-O^{7}(OH)^{17}-*rac*** and **9-O^{7}(OH)^{18}-*rac***, as their racemates, was determined by single crystal X-ray diffractometry (Figure 2).

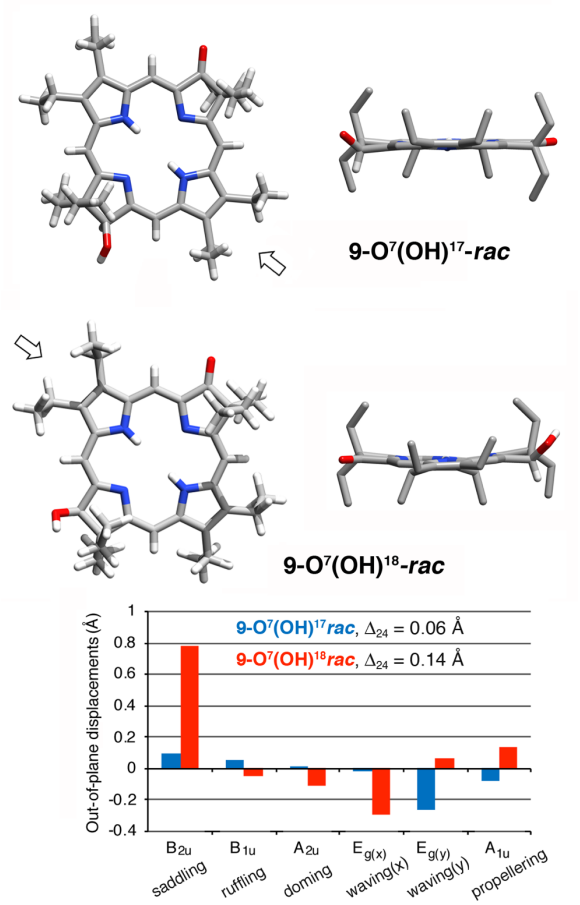
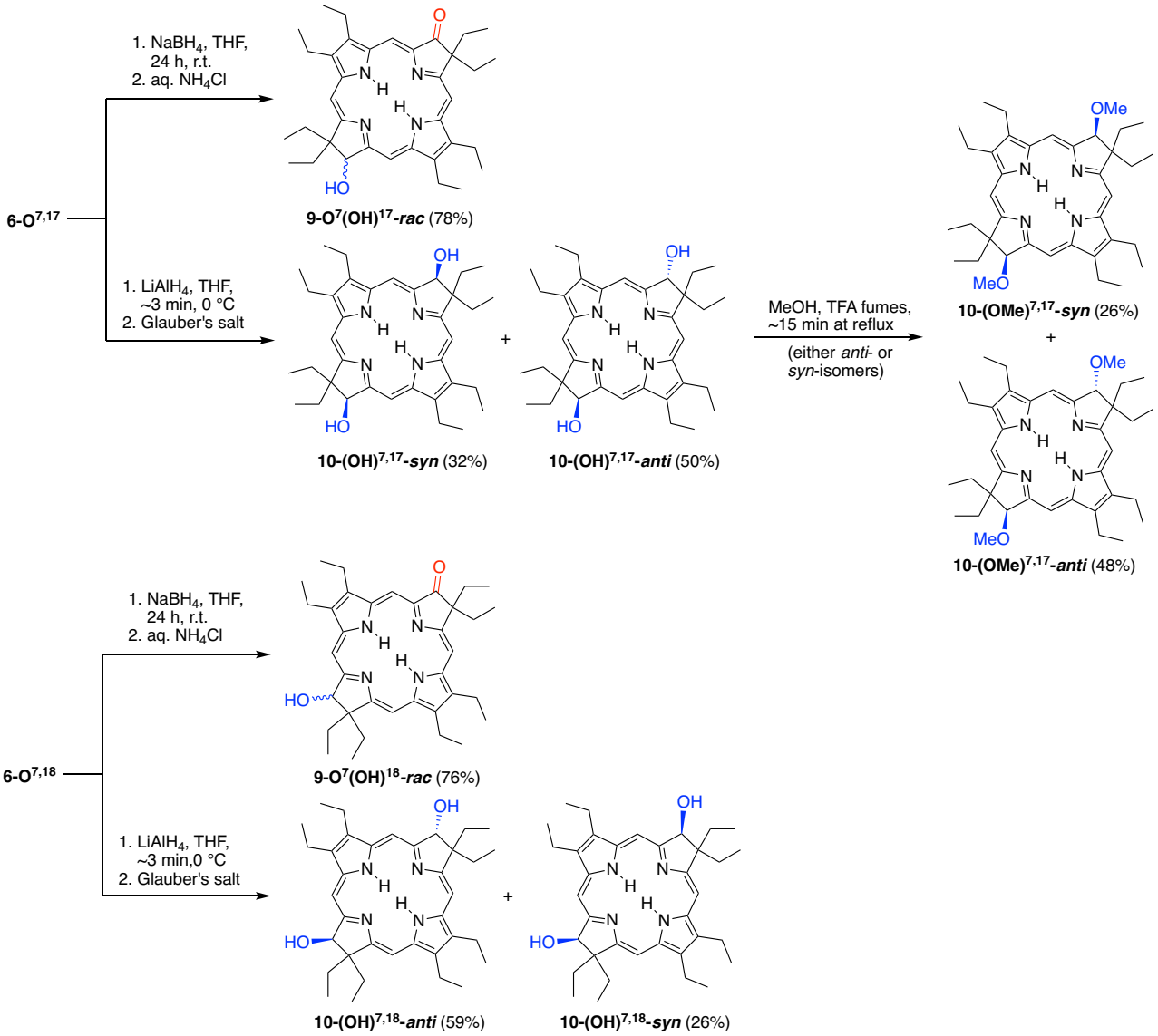


Figure 2. Stick representation of the X-ray single crystal structures of the compounds indicated, top and side views; the arrow in the top view images shows the point of view of the corresponding side view. All disorder and solvents (if present) are removed for clarity; only one enantiomer of the racemic mixture present in the non-chiral unit cell shown. In the side views, all *meso*- and ethyl-hydrogen atoms were removed for clarity. NSD analysis[21] as implemented by Kingsbury and Senge.[22] For details to the structural determinations and structural analyses, see Supporting Information.

The conformations of the chromophores of the isomeric mono-reduced products **9-O^{7}(OH)^{17}-*rac*** and **9-O^{7}(OH)^{18}-*rac*** are both show only small but clear deviations from planarity. Whereas **9-O^{7}(OH)^{17}-*rac*** shows a minor waving distortion, **9-O^{7}(OH)^{18}-*rac*** shows a more significant saddling distortion in addition to a minor waving component.

Scheme 3. Mono- and bis-reductions of the bacteriochlorin-type dioxochlorin isomers 6-O^{7,17} and 6-O^{7,18}.



Bis-reduction of Bacteriochlorin-Type β,β'-Dioxochlorins Isomers. Bisreduction of both β-oxo-groups in bacteriochlorins type diketones (**6-O^{7,17}** and **6-O^{7,18}**) could be achieved within minutes at 0 °C using $LiAlH_4$ as the reducing agent (Scheme 3). The reactions cleanly generated for each starting material two readily separable fractions of polar materials in unequal amounts, both with near-identical bacteriochlorin-type optical spectra (for a discussion of the optical spectra, see below). All products possessed identical compositions ($C_{36}H_{50}N_4O_2$ for M^+, as per HR-MS), corresponding to the expected composition of the diols of **10-(OH)^{7,17}** and **10-(OH)^{7,18}**. Bis-reduction did not change the two-fold symmetry of the reactants (even though it changes, depending in the stereoisomer considered, specific symmetry elements). The presence of the diagnostic pyrroline hydrogen signals in their ^{1}H NMR spectra (at ~6.2 ppm) clearly indicated the sites of reduction. Whereas the two regioisomeric sets possess similar, albeit distinctly different ^{1}H NMR spectra (with the number of NH proton signals being the strongest distinguishing feature between the **10-(OH)^{7,17}** and **10-(OH)^{7,18}** isomers), the spectra of the two *anti/syn*-configurational pairs in each set are near-identical (Figure 3). D_2O exchange confirmed the identity of two exchangeable (OH) protons (see Supporting Information). Notably, the low acidity of the bacteriochlorins inner NH protons is expressed in a slow D_2O exchange rate;[12e,23] non-exchanged NH protons are present in the ^{1}H NMR spectrum (in DMSO-d_6) even after days in contact with D_2O, whereas the more acidic NH protons in the other chlorins and isobacteriochlorins (see below) exchange much more rapidly.

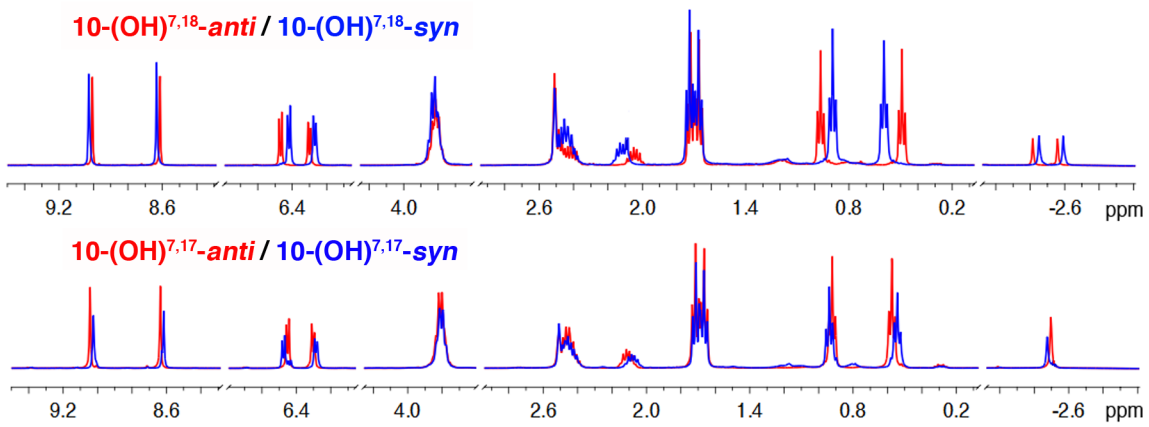


Figure 3. ^{1}H NMR spectra of the *anti* (Red) and *syn* (blue) stereoisomers of the bacteriochlorin diol regioisomers **10-(OH)^{7,17}** and **10-(OH)^{7,18}**.

Despite the presence of two chiral centers on **10-(OH)^{7,17}** and **10-(OH)^{7,18}**, the two-fold constitutional symmetry of the products (**10-(OH)^{7,18}-*syn***, for example, is a *meso*-compound) reduces the number of possible stereoisomers to two. They are distinguished based on the relative orientation of the two alcohols with respect to the hemispheres defined by the plane of the porphyrin; they are designated as the *anti*- (alcohols pointing into different hemispheres) and *syn*-isomers (alcohol functionalities point into the same hemisphere).[8e,24] Because both alcohol groups in the *syn*-isomer can simultaneously interact with a surface, it is more polar than the corresponding *anti*-isomer. This allowed a tentative assignment of the two bacteriochlorin diol stereoisomers. These assignments could be indirectly verified by the single crystal X-ray crystallographical analysis of the corresponding dimethoxy derivatives **10-(OMe)^{7,17}**-*anti* and -*syn* (Figure 4).

When we crystallized **10-(OH)^{7,17}**-*anti* from CH_2Cl_2/MeOH, we were surprised to obtain crystals that proved to be the dimethylated derivative **10-(OMe)^{7,17}**-*anti*. The biggest surprise was the stereo-pure *anti*-configuration of the product. Under the (inherently acidic) crystallization conditions, both an alkylation of the bacteriochlorin alcohol functionality or an S_N1-type exchange of the alcohols under retention of their configuration seemed highly unlikely. Instead, an (acid-catalyzed) S_N1-type exchange of the alcohol with concomitant racemization and formation of the *anti*- and *syn*-isomers of the dimethylated product would have been expected. Some minor degree of stereo-selection might be operative as the reductions also show some preference for the *anti*-isomer. Nonetheless, we deemed the exclusive formation of one isomer to be unlikely.

We thus performed the acid-catalyzed methylation reaction (MeOH, catalytic amounts of TFA, reflux) individually with both the *anti*-and -*syn* stereoisomers of **10-(OH)^{7,17}** (Scheme 3). Within 10 min reaction time, the dimethylated products **10-(OMe)^{7,17}** began to precipitate from the solutions. TLC analysis of the precipitates indicated the presence of two products in unequal amounts; all of identical composition ($C_{38}H_{54}N_4O_2$ for M^+, as per HR-MS) and bacteriochlorins-type UV-vis spectra (see Supporting Information). The low polarity methylated product **10-(OMe)^{7,17}** confirmed to identical to the *anti*-isomer determined by X-ray diffractometry. Likewise, crystals of the high polarity isomer confirm it to be the *syn*-isomer (Figure 4). We can thus conclude that the formal alkylations of **10-(OH)^{7,17}**-*anti* and -*syn* each forming **10-(OMe)^{7,17}**-*anti* and -*syn* proceeded, as expected, via an S_N1-type exchange of the alcohol functionalities.

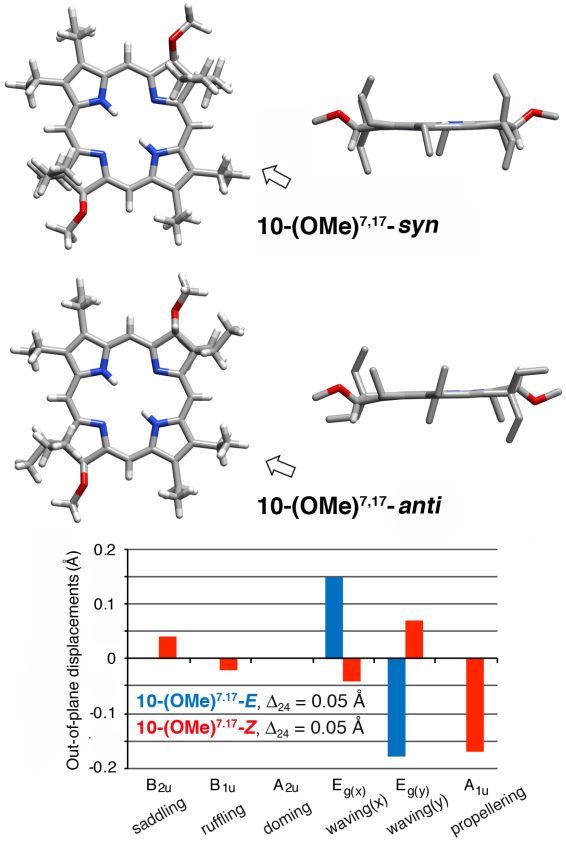


Figure 4. Stick representation of the X-ray single crystal structures of the compounds indicated, top and side views; the arrow in the top view images shows the point of view of the corresponding side view. All disorder removed for clarity. In side views, all *meso*- and ethyl-hydrogen atoms were removed for clarity. NSD analysis[21] as implemented

by Kingsbury and Senge.[22] For details to the structural determinations and analyses, see Supporting Information.

Why then was only one isomer found during the inadvertent methylation under the crystallization conditions? We believe both isomers show very different solubilities and the *anti*-isomer just happened to form good crystals, while the *syn*-isomer was left behind in the mother liquor; we did not find any crystals containing the *syn*-isomer (the mother liquor was already discarded).

This solubility hypothesis is supported by the unusual and very different solubilities of the **10-(OMe)^{7,17}-*anti*** and **-*syn*** isomers that affected our ability to record well-resolved ^{1}H NMR spectra. While both **10-(OMe)^{7,17}-*anti*** and **-*syn*** stereoisomers were soluble in $CDCl_3$ and CD_2Cl_2, we could not detect their *meso*-H atom signals or see well-resolved signals for the ethyl protons. The high polarity *syn*-isomer was only sparingly soluble in acetone-d_6 but the NMR spectra were well-resolved.

Optical Spectra of the Reduction Products of the Bacteriochlorin-type β,β'-Diketones. The UV-vis spectra of the mono-reduced compounds **9-O^7(OH)^{17}** and **9-O^7(OH)^{18}** are more chlorin- than bacteriochlorin-like when considering the position of the (split) Soret band and the number and relative intensities of the Q-bands (Figure 5). The two regioisomers show optical differences as expressed in the relative intensities of their Soret and Q-bands. The λ_{max} bands ($Q_{y(0,0)}$) are at 694 nm and 690 nm, respectively, i.e, much red-shifted (49-53 nm) compared to the spectrum of regular chlorin **8-(OH)^7**. The fluorescence emission spectra of the mono-reduced compounds **9-O^7(OH)^{17}** and **9-O^7(OH)^{18}** show the small Stokes shift typical for porphyrinoids, with a two-band spectrum that resembles that of chlorins.

Bisreduction of the dioxochlorins **6-O^{7,17}** and **6-O^{7,18}** generated chromophores with typical bacteriochlorin-type spectra, with λ_{max} bands ($Q_{y(0,0)}$) at 714 nm, whereby the spectra of the *anti*- and *syn*-isomers as well as of both regioisomers are essentially identical (see Supporting Information). The optical differences between the regioisomers of the two dioxo-isomers **6-O^{7,17}** and **6-O^{7,18}** ($\Delta\lambda_{max}$ = 14 nm) diminish with increasing reduction ($\Delta\lambda_{max}$ for **9-O^7(OH)^{17}** and **9-O^7(OH)^{18}** = 4 nm; $\Delta\lambda_{max}$ for **10-(OH)^{7,17}** and **10-(OH)^{7,18}** = 0 nm) (for overlays of the regioisomer spectra, see Supporting Information). We will discuss the implications of this observation in more detail below in the context of the regioisomeric differences observed for the isobacteriochlorin series. The fluorescence emission spectra follow this trend and all are bacteriochlorin-type single band spectra.

The strong auxochromic influence of β-oxo groups was described before.[6b-d] The electronic peculiarities of bacteriochlorins with zero, one, or two oxo-groups have been investigated and discussed in depths by Lindsey, Dewey, Holten, and coworkers,[6] and we can confirm that all trends described also hold our series of compounds, such as the hypsochromic shift in the Q_y band absorption upon introduction of one or two oxo-groups versus the parent bacteriochlorin. In fact, even the band positions for our diketones (**6-O^{7,17}** and **6-O^{7,18}**), hydroxyoxo- (**9-O^7(OH)^{17}** and **9-O^7(OH)^{18}**) and the dihydroxybacteriochlorins (**10-(OH)^{7,17}** and **10-(OH)^{7,18}**) closely match with corresponding Lindsey compounds. We also note their similarity with respect to the presence of *gem*-dialkly groups next to the ketone/alcohols (cf. to compounds **1-O^{7,17}** and **2-O^7**).

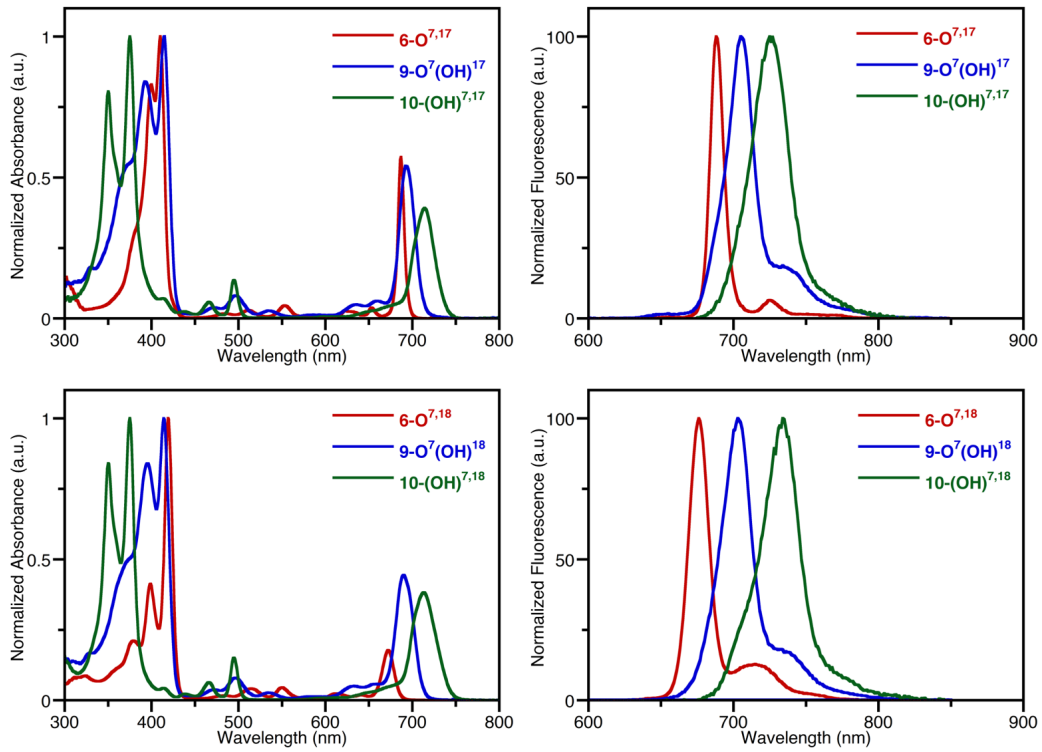
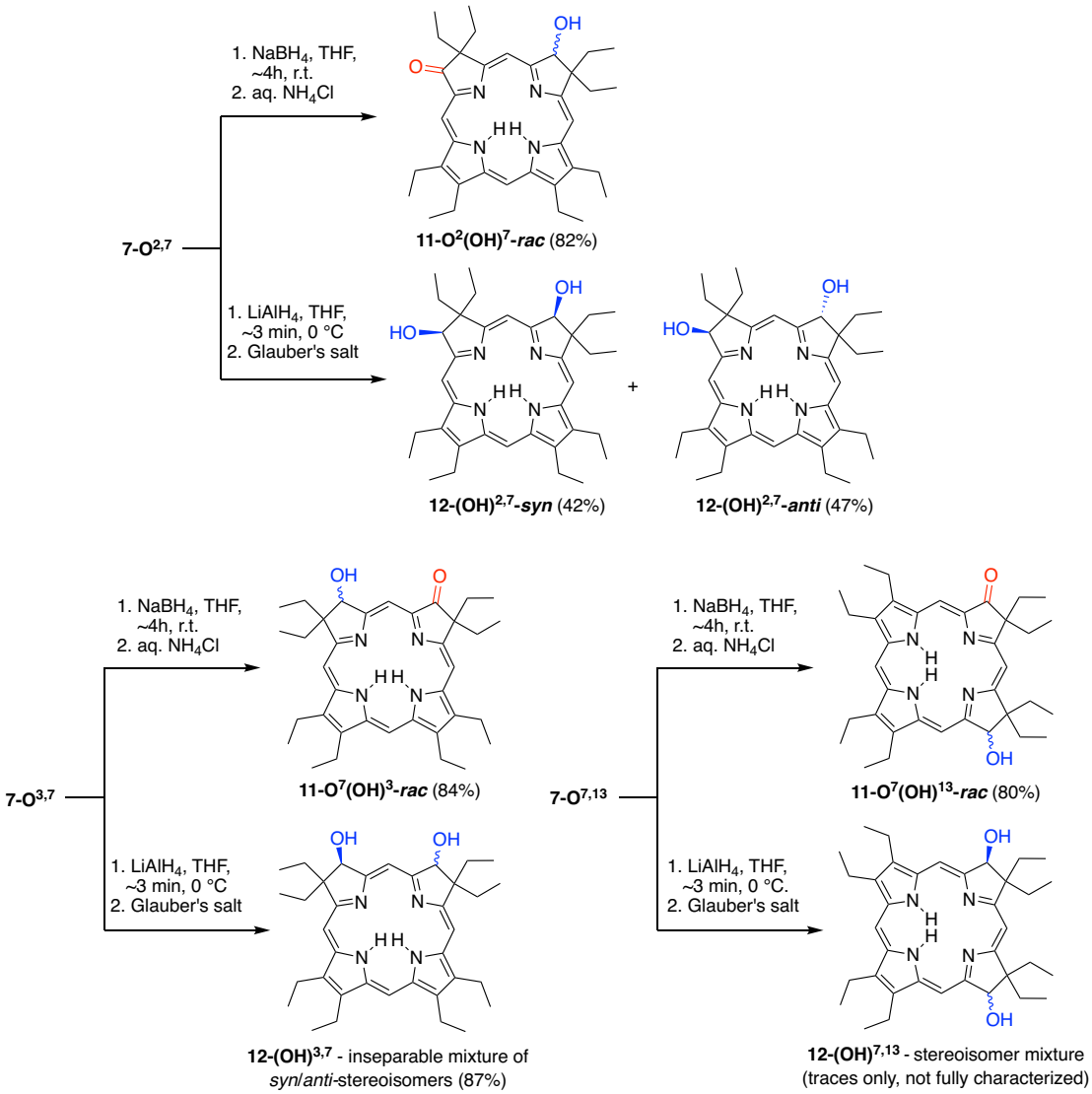


Figure 5. (Left) UV-vis and (right) fluorescence emission spectra (both CH_2Cl_2) of dioxochlorins **6-O^{7,17}** (top) and **6-O^{7,18}** (bottom) and their corresponding mono- and bis-reduced derivatives (*anti*-isomers) ($\lambda_{excitation} = \lambda_{Soret}$).

Mono-reduction of Isobacteriochlorin-Type β,β'-Dioxochlorin Isomers. The dioxoisobacteriochlorin-type isomers **7-O^{2,7}**, **7-O^{3,7}**, and **7-O^{7,13}** could each also be selectively mono-reduced to their corresponding hydroxyoxo-derivatives **11** using the methodologies described for the dioxobacteriochlorins series (Scheme 4), but with some notable differences: Mono-reduction of the dioxoisobacteriochlorins was generally significantly faster (completion within 3-4 h) than the corresponding dioxobacteriochlorin reduction (completion requiring 24 h). This more facile reduction also led to the formation of small amounts of the 'over-reduced' dihydroxyisobacteriochlorins **12** (described below).

The two isobacteriochlorin-type diones **7-O^{3,7}**, and **7-O^{7,13}** contain a mirror plane. Their mono-reduction breaks this two-fold symmetry (for example, four *meso*-CH proton signals can be distinguished in the corresponding products **11**). The diagnostic pyrroline signals appeared in their ^{1}H NMR spectra, they possess the expected composition (as per HR-MS), and a ketone functionality is retained (as per FT-IR and ^{13}C NMR). The optical spectra of all isobacteriochlorin-type chromophores will be discussed below.

Scheme 4. Mono- and bis-reductions of the dioxoisobacteriochlorin-type isomers 7-O^{2,7}, 7-O^{3,7}, 7-O^{7,13}.



The single crystal X-ray analysis of **11-O^7(OH)^3** shows that the reduction of one ketone of **7-O^{3,7}** returns a largely planar chromophore, with only minor saddling distortions (Figure 6). The NH proton tautomer observed in the solid state is that with the NH protons located on opposite nitrogen atoms (the hydrogen atoms were located in the electron density map; for details see Supporting Information). The expected should have adjacent-tautomers ofisobacteriochlorin-type isomers with the NH protons located on adjacent nitrogen atoms as shown in Scheme 4. While the opposite-tautomer is sterically more favorable than the alternative tautomer, it does not maintain the typical aromatic 18 π-electron conjugation pathway of (hydro)porphyrins.[25] The opposite-tautomers of the isobacteriochlorins have been observed and studied before in octaalkylisobacteriochlorins.[9d,25-26]

Mono-reduction of non-axially symmetric **7-O**[2,7] can result in the formation of two distinct regioisomeric products but we find that only one product is formed regioselectively, hydroxyoxochlorin **11-O**[2]**(OH)**[7], as a racemic mixture. The reduction of any oxo-functionality affects the chemical shift of the neighboring *meso*-CH proton the most, and in case of the reduction of **7-O**[2,7] we find this *meso*-position to be also next to a *gem*-diethyl functionality. This spectroscopically assigns the connectivity of the mono-reduction product to be **11-O**[2]**(OH)**[7], confirmed also by single crystal X-ray diffractometry (Figure 6). Mono-oxo-mono-hydroxy compound **11-O**[2]**(OH)**[7] deviates significantly from planarity, adopting, next to saddling, also a considerable ruffling deformation; it also exhibits the opposite-NH tautomer.[25] We will report on the computational assessment of the stabilities of the possible isobacteriochlorin isomers of these compound series and their influence on their optical properties in due course.

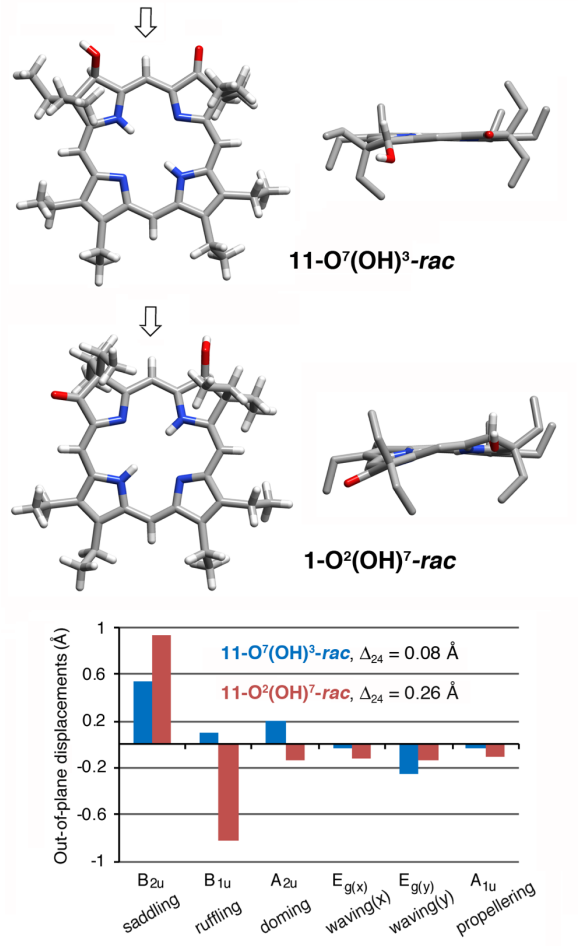


Figure 6. Stick representation of the X-ray single crystal structures of the compound indicated, top and side views; the arrow in the top view image shows the point of view of the corresponding side view. Disorder removed for clarity; only one enantiomer of the racemic mixture present in the non-chiral unit cell shown. In the side views, all *meso*- and ethyl-hydrogen atoms were removed for clarity. NSD analysis [21] as implemented by Kingsbury and Senge.[22] For details to the structural determinations and structural analyses, see Supporting Information.

Any regioselective reduction of diketone **7-O**[2,7] could be controlled by either sterics or electronics, or a combination of both effects. The formation of product **11-O**[7]**(OH)**[2] seems not likely to be controlled by sterics since the ketone functionality that actually gets reduced is flanked by two sets of *gem*-diethyl groups. We therefore surmise that an electronic control is at play.

Bis-reduction of Isobacteriochlorin-Type β,β'-Dioxochlorins Isomers.

Bis-reduction of each of the three dioxoisobacteriochlorins **7-O** using $LiAlH_4$ theoretically also provides separable *anti*- and *syn*-stereoisomers of the diols **12-(OH)**. In practice, the diols **12-(OH)**[2,7]-*anti* and -*syn* form smoothly and separate well. Isomer **12-(OH)**[2,7]-*anti* could also be crystallographically characterized (Figure 7) also proving the confirmation that the low polarity isomer has the *anti*-configuration; we thus assign the higher polarity isomer the *syn*-configuration. The conformation of this isobacteriochlorin diol macrocycle is significantly ruffled. Thus, the reduction of the formal precursor **11-O**[2]**(OH)**[7] led to a significant planarization of the macrocycle, with the release of essentially all saddling contributions to the deformation modes. The diol also shows the opposite NH tautomer of its precursor.

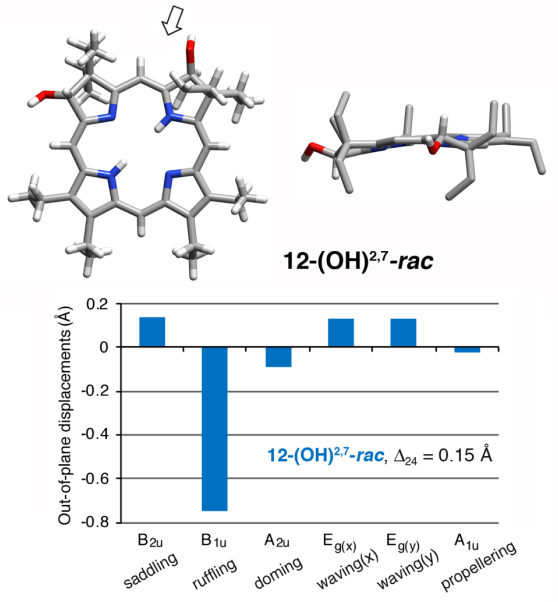


Figure 7. Stick representation of the X-ray single crystal structures of the compound indicated, top and side view; the arrow in the top view image shows the point of view of the corresponding side view. Disorder removed for clarity. In the side views, all *meso*- and ethyl-hydrogen atoms and pyrrole ethyl groups were removed for clarity. NSD analysis [21] as implemented by Kingsbury and Senge.[22] For details to the structural determinations and structural analyses, see Supporting Information.

The *anti*- and *syn*-isomers of the diol reduction product of **11-O**[7]**(OH)**[3], diol **12-(OH)**[3,7], however, could not be separated. The ^{1}H NMR spectrum of the product mixture indicates the presence of a 1:0.7 ratio of isomers.

In case of the third isobacteriochlorin isomer, only the more prevalent low polarity (*anti*-) isomer of **12-(OH)**[7,13]

could be isolated and characterized. This is primarily because of the scarcity of its precursor **7-O^{7,13}**, the most rare of the diones (formed in only 0.3% yield from **OEP**), forcing us to do the downstream reactions at minimal scales.[9]

All isobacteriochlorins diols possess the same expected composition (as per HR-MS) and similar ^{1}H and ^{13}C NMR spectra (see Supporting Information). Diagnostic signals in the ^{1}H NMR spectra for the bis-reduced products are, for example for **12-(OH)^{2,7}**, the presence of two doublets in the chemical shift range for pyrroline protons (~5.6 ppm) and the presence of two -OH protons that readily exchange with D_2O (see Supporting Information).

Optical Spectra of the Reduction Products of the Isobacteriochlorin-type β,β'-Diketones. The UV-vis absorption spectra of the three dioxoisobacteriochlorin isomers vary significantly from each other (as also expressed in their widely varying λ_{max} values: $\Delta\lambda_{max}$ for **7-O^{2,7}**, **7-O^{3,7}**, and **7-O^{7,13}** range from 16 to 66 nm).[9b,9d] These differences translate to the corresponding isobacteriochlorin-type spectra of the mono-reduced products, the hydroxyoxoisobacteriochlorins **11-O^{2}(OH)^{7}**, **11-O^{7}(OH)^{3}**, and **11-O^{7}(OH)^{13}** in different ways (Figure 8). The Soret band wavelengths for **11-O^{2}(OH)^{7}** and **11-O^{7}(OH)^{13}** are similar and significantly blue-shifted compared to the corresponding spectra of their parent dioxocompounds, but the spectrum of **11-O^{7}(OH)^{3}** does not significantly differ from that of its parent dione. Again, these findings show the very large and regiochemically distinct influence of the β-oxo substituents.[6b-d,27] Again, once the electronic influence of all β-oxo substituents was removed, the optical spectra of all dihydroxyisobacteriochlorins **12** are very similar ($\Delta\lambda_{max}$ for **12-(OH)^{2,7}**, **12-(OH)^{3,7}**, and **12-(OH)^{7,13}** = 0 nm) and are typical isobacteriochlorin-type spectra.

The fluorescence emission spectra follow the trends of the UV-vis spectra. The one-band emission spectra of the diones give way to clear isobacteriochlorin-like two band spectra at almost identical positions.

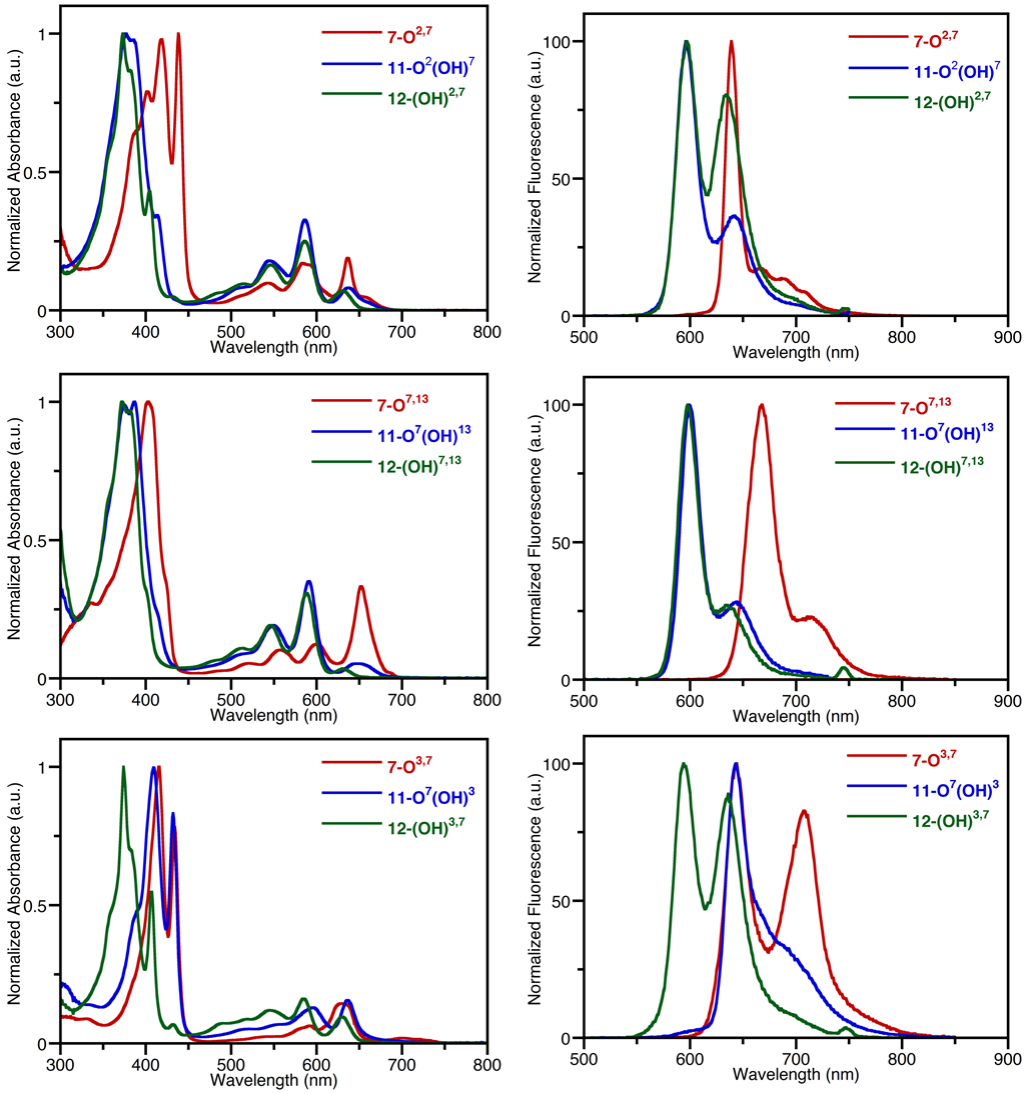


Figure 8. (Left) UV-vis spectra and (right) emission spectra (both CH_2Cl_2) of dioxochlorins **7-O^{2,7}** (top), **7-O^{7,13}** (middle) and **7-O^{3,7}** (bottom) and their corresponding mono- and di-reduced derivatives (*anti*-isomers); ($\lambda_{excitation} = \lambda_{Soret}$).

Intramolecular Interactions in the Crystals of Select Reduced β,β'-Dioxochromophores

In some of the β-hydroxy-substituted isobacteriochlorins (**11-O²(OH)⁷** and **12-(OH)⁷,¹⁷**), the β-hydroxy group expresses an inter molecular H-bond to the inner imine-nitrogen of a neighboring macrocycle, forming dimers in the solid state (Figure 9). As a result, one molecule sits nearly perpendicular onto the other. The dimers are linked in the same fashion to other dimers forming infinite chains. We do not believe this H-bonding scheme contributes to the opposite NH tautomers observed since hydroxyoxoisobacteriochlorin isomer **11-O⁷(OH)³** also shows the same tautomer but without the intermolecular H-bonding interaction to the inner nitrogen atoms. Instead, the H-bond donor and -acceptor functionalities on **11-O⁷(OH)³** located on the same side of the molecule face each other, suitable to form a self-complimentary dimer. In cases in which the H-bond donor and -acceptor functionalities are on opposite sides of the macrocyles, as in the hydroxyoxobacteriochlorins **9-O⁷(OH)¹⁷** and **9-O⁷(OH)¹⁸** (not shown), they form infinite chains. Generally, the infinite chains or dimers are slip-stacked in the solid state well outside of any π-π stacking distances – and as is common for octaethylporphyrin derivatives (for details, see Supporting Information).[28]

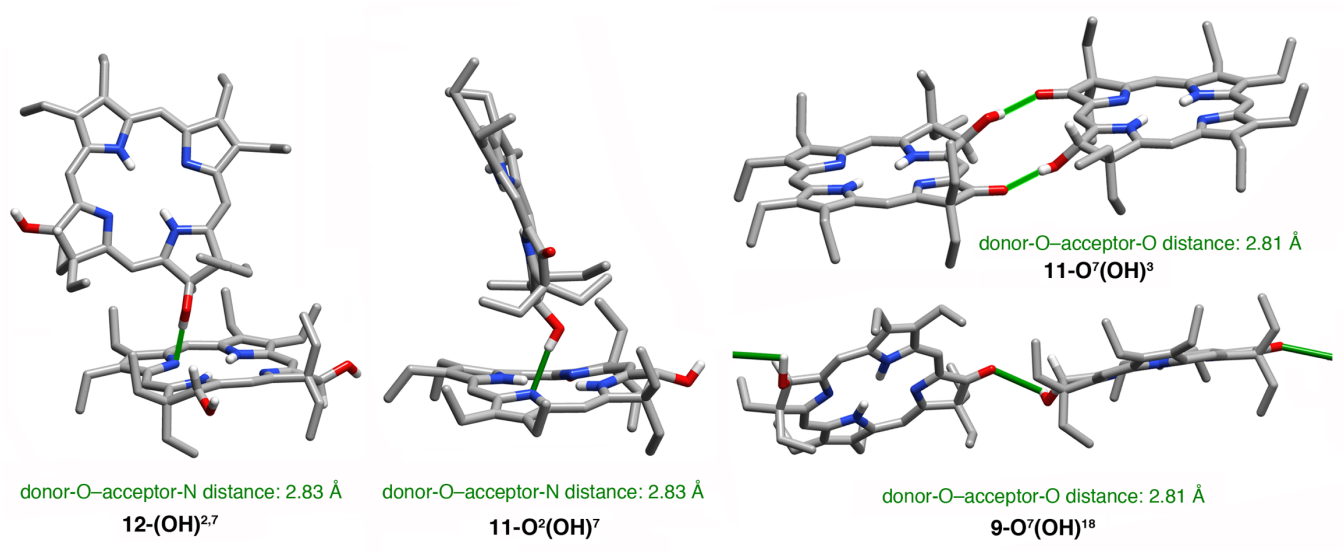


Figure 9. Stick presentations of the molecular structures of compounds indicated, highlighting their interactions in the crystal. Solvents, disorder and all ethyl and *meso*-H atoms removed for clarity; when present, only one of the symmetry-related pairs in the crystal shown. For details, see Supporting Information.

CONCLUSIONS

In conclusions, a variety of chromophores, ranging from regioisomeric β-hydroxy-β-oxo-bacteriochlorins and -isobacteriochlorins and regio- and stereo-isomeric β-dihydroxy-bacteriochlorins and –isobacteriochlorins were synthesized using stepwise reductions of the corresponding diketones. Thus, we introduced pathways to access a range of bacterio- and isobacteriochlorins from known β-oxo porphyrins along a porphyrin modification strategy as an alternative approach to total syntheses. Because of their NIR absorbance, particularly the bacteriochlorins are attractive chromophores for a number of technical and biological applications. The β-hydroxy- and β-oxo-substituents were shown to be capable of organizing the chromophores in the solid state. A number of isobacteriochlorins – generally much less studies than all other hydroporphyrins – have also been described. This study also provided further experimental evidence to recent hypotheses put forward which types of substituents result in electronically distinct regioisomeric chromophores within the bacterio- and isobacteriochlorin series.[27] We hope that the relatively straight-forward access to a range of related hydroporphyrin chromophores encourages their further study.

EXPERIMENTAL SECTION

Materials. Solvents and reagents were used as received. OEP was converted to oxochlorin and β,β'-dioxochlorins using the procedure described Inhoffen and Nolte or later Chang.[9] Aluminum-backed, silica gel 60, 250 μm thickness analytical plates, 20 × 20 cm, glass-backed, silica gel 60, 500 μm thickness preparative TLC plates, and standard grade, 60 Å, 32-63 μm flash column silica gel were used. Alternatively, flash column chromatography was performed manually or on an automated flash chromatography system using normal-phase silica gel columns.

Octaethyl-7-hydroxychlorin 8-(OH)⁷. Prepared from 7-oxochlorin **5-O⁷** (50 mg, 9.07×10^{-5} mol) and $LiAlH_4$ (10 mg, 2.7×10^{-4} mol, 3 equiv.) in THF (2 mL) as described by us previously. The product was isolated as dark solid in 91% yield (46 mg, 8.32×10^{-5} mol). Data for this known compound are included for comparison. MW = 552.8 g/mol; R_f = 0.19 (silica-CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.78 (d, *J* = 3.5 Hz, 2H, *meso*-H), 9.20 (s, 1H, *meso*-H), 8.79 (s, 1H, *meso*-H), 6.53 (s, 1H, pyrroline-H), 4.07-3.87 (m, 12H, -CH_2), 2.71-2.52 (m, 4H, -CH_2), 2.35-2.30 (m, 1H, -OH),

1.89-1.79 (m, 18H, -CH_3), 0.97 (t, *J* = 7.0 Hz, 3H, -CH_3), 0.74 (t, *J* = 7.0 Hz, 3H, -CH_3), 2.55 (s, 2H, -NH). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 167.1, 162.5, 150.1, 149.8, 142.9, 142.7, 139.4, 137.6, 137.5, 135.1, 134.9, 132.5, 99.4, 99.0, 92.5, 92.2, 84.1, 57.4, 31.9, 28.3, 19.9, 19.7, 19.5, 19.4, 18.8, 18.5, 18.4, 18.2, 18.1, 10.1, 9.4. UV-vis (CH_2Cl_2) λ_{max} (log ε): 390 (5.02), 493 (3.85), 521 (3.25), 588 (3.31), 611 (3.26), 642 (4.38) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 390 nm) λ_{max} = 647 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{49}N_4O$, 553.3901 (for $M+H^+$); found, 553.3936.

General Synthetic Procedure for the Preparation of Hydroxyoxochromophores 9 and 11 by Mono-Reduction of β,β'-Diketones 6 and 7, Respectively. A solution of octaethyldioxochlorins **6-O** or **7-O** in THF was stirred under N_2 on an ice bath for several minutes. To the chilled solution, 5 equiv. of $NaBH_4$ was added and the reaction mixture was stirred at ambient temperature for variable time periods. Generally, the isobacteriochlorins took ~3-4 h, whereas bacteriochlorins were stirred for 24 h. The reaction progress was monitored by TLC. After completion, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with a sat'd aqueous solution of NH_4Cl. The organic layer was separated, dried over anhydrous Na_2SO_4, and filtered. The filtrate was reduced to dryness using rotatory evaporation. The crude mixture was purified by silica-gel column chromatography.

17-Hydroxy-7-oxo-bacteriochlorin 9-O⁷(OH)¹⁷. Prepared according to the general procedure from **6-O**[7,17] (50 mg, 8.82×10^{-5} mol) in 3 mL THF and $NaBH_4$ (17 mg, 4.4×10^{-4} mol, 5 equiv.). The product was isolated as greenish gray solid in 78% yield (39 mg, 6.86×10^{-5} mol). Chromatography condition: hexanes-CH_2Cl_2 (20:80 v/v) followed by 100% CH_2Cl_2. MW = 568.7919 g/mol. R_f = 0.53 (silica-1% acetone in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) *δ*: 9.60 (s, 1H, *meso*-H), 9.05 (s, 1H, *meso*-H), 8.81 (s, 1H, *meso*-H), 8.67 (s, 1H, *meso*-H), 6.40 (d, *J* = 8.5 Hz, 1H, pyrroline-H), 3.90 (dt, *J* = 16.5, 8.0 Hz, 8H, -CH_2), 2.68-2.45 (m, 8H, -CH_2), 2.27 (td, *J* = 14.5, 7.0 Hz, 1H, -OH), 1.79-1.73 (m, 12H, -CH_3), 1.00 (t, *J* = 7.0 Hz, 3H, -CH_3), 0.82 (t, *J* = 7.0 Hz, 3H, -CH_3), 0.39 (dd, *J* = 18.5, 7.5 Hz, 6H, -CH_3), -2.14 (s, 1H, -NH), -2.22 (s, 1H, -NH) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ:* 210.6, 164.1, 162.9, 161.1, 144.0, 138.3, 138.2, 137.6, 136.3, 135.4, 134.8, 134.2, 130.6, 95.2, 95.1, 93.3, 92.9, 83.9, 60.3, 56.4, 31.4, 31.2, 27.9, 19.3, 19.2, 19.1, 18.1, 18.0, 17.8, 9.9, 9.2, 8.5, 8.4 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 392 (4.84), 414 (4.91), 497 (3.83), 534 (3.35), 632 (3.59), 660 (3.70), 693 (4.65) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 414 nm) λ_{max} = 705 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{48}N_4O_2$, 568.3777 (for M^+); found, 568.3747.

18-Hydroxy-7-oxo-bacteriochlorin 9-O⁷(OH)¹⁸. Prepared according to the general procedure from **6-O**[7,18] (50 mg, 8.82×10^{-5} mol) in 3 mL THF and $NaBH_4$ (17 mg, 4.4×10^{-4} mol, 5 equiv.). The product was isolated as greenish-gray solid in 76% yield (38 mg, 6.68×10^{-5} mol). Chromatography condition: CH_2Cl_2. MW = 568.79 g/mol. R_f = 0.30 (silica-1% acetone in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) *δ*: 9.58 (s, 1H, *meso*-H), 9.05 (s, 1H, *meso*-H), 8.77 (s, 1H, *meso*-H), 8.61 (s, 1H, *meso*-H), 6.38 (d, *J* = 8.5 Hz, 1H, pyrroline-H), 3.96-3.80 (m, 8H, -CH_2), 2.68-2.54 (m, 6H, -CH_2), 2.53-2.44 (m, 2H,-CH_2), 2.35-2.25 (m, 1H, -OH), 1.81-1.72 (m, 12H, -CH_3), 0.98 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.83 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.40 (dt, *J* = 11.5, 7.5 Hz, 6H, -CH_3), -2.02 (s, 2H, -NH) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ:* 210.6, 168.3, 161.7, 159.8, 143.7, 138.3, 138.1, 137.7, 136.6, 135.9, 134.6, 134.0, 130.4, 95.6, 95.1, 93.5, 92.6, 83.1, 60.4, 57.4, 31.3, 31.1, 27.6, 19.2, 19.1, 19.0, 18.2, 18.0, 17.8, 9.9, 9.1, 8.4 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 394 (4.83), 414 (4.90), 496 (3.81), 534 (3.34), 633 (3.62), 661 (3.67), 690 (4.55) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 414 nm) λ_{max} = 702 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{48}N_4O_2$, 568.3777 (for M^+); found, 568.3800.

7-Hydroxy-2-oxoisobacteriochlorin 11-O²(OH)⁷. Prepared according to the general procedure from **7-O**[2,7] (50 mg, 8.82×10^{-5} mol) in 3 mL THF and $NaBH_4$ (17 mg, 4.4×10^{-4} mol, 5 equiv.) in 82% yield (41 mg, 7.21×10^{-5} mol) as burgundy solid. Chromatography condition: CH_2Cl_2 followed by 1% acetone in CH_2Cl_2. MW = 568.79 g/mol; R_f = 0.55 (silica-5% acetone in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) *δ:* 8.62 (s, 1H, *meso*-H), 8.58 (s, 1H, *meso*-H), 7.39 (s, 1H, *meso*-H), 7.30 (s, 1H, *meso*-H), 5.95 (s, 1H, pyrroline-H), 3.53-3.38 (m, 6H, -CH_2), 3.30 (q, *J* = 7.5 Hz, 2H, -CH_2), 2.97 (s, 1H, -NH), 2.53 (s, 1H, -NH), 2.29 (dtd, *J* = 21.0, 14.0, 7.0 Hz, 7H, -CH_2), 2.05 (dt, *J* = 14.5, 7.5 Hz, 1H, -CH_2), 1.61-1.49 (m, 12H, -CH_3), 1.13 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.86 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.44 (t, *J* = 7.0 Hz, 6H, -CH_3) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ:* 209.7, 169.0, 156.5, 154.0, 153.1, 144.9, 144.6, 143.1, 137.9, 136.4, 135.3, 133.4, 131.7, 104.3, 98.5, 91.9, 88.0, 80.9, 60.5, 53.8, 30.4, 30.3, 28.9, 26.2, 19.0, 18.8, 18.7, 18.5, 17.9, 17.7, 17.2, 9.0, 8.9, 8.6, 8.5 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 377 (4.91), 543 (4.16), 586 (4.42), 638 (3.82) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 377 nm) λ_{max} = 596, 642 (sh) nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{49}N_4O_2$, 569.3850 (for $M+H^+$); found, 569.3799.

13-Hydroxy-7-oxoisobacteriochlorin 11-O⁷(OH)¹³. Prepared according to the general procedure from **7-O**[7,13] (15 mg, 2.65×10^{-5} mol) in 2 mL THF and $NaBH_4$ (5 mg, 1.33×10^{-4} mol, 5 equiv.) in 80% yield (12 mg, 2.11×10^{-5} mol). The product was isolated as purple solid. Chromatographic condition: CH_2Cl_2. MW = 568.79 g/mol; R_f = 0.58 (silica-3% acetone in CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) *δ*: 8.59 (s, 1H, *meso*-H), 8.53 (s, 1H, *meso*-H), 7.75 (s, 1H, *meso*-H), 6.86 (s, 1H, *meso*-H), 5.89 (s, 1H, pyrroline-H), 3.43 (ddt, *J* = 28.0, 15.0, 7.5 Hz, 6H, -CH_2), 3.33-3.25 (m, 2H, -CH_2), 3.07 (s, 1H, -NH), 2.41 (s, 1H, -NH), 2.33 (dd, *J* = 14.0, 7.0 Hz, 2H, -CH_2), 2.28-2.18 (m, 4H, -CH_2), 2.15-2.04 (m, 2H, -CH_2), 1.58-1.49 (m, 12H, -CH_3), 1.02 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.88 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.44 (dt, *J* = 12.5, 7.5 Hz, 6H, -CH_3) ppm. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) *δ*: 209.6, 168.5, 157.4, 157.4, 149.7, 144.9, 142.7, 140.1, 138.1, 136.9, 135.7, 132.7, 105.6, 98.6, 92.0, 88.6, 80.0, 60.4, 55.0, 30.7, 29.4, 26.1, 19.2, 18.9, 18.6, 18.1, 17.9, 17.4, 9.3, 9.0, 8.7, 8.6 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 373 (4.80), 386 (4.81), 548 (4.09), 590 (4.35), 647 (3.54) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 373 nm) λ_{max} = 599, 644 (sh) nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{49}N_4O_2$, 569.3850 (for $M+H^+$); found, 569.3849.

3-Hydroxy-7-oxoisobacteriochlorin 11-O⁷(OH)³. Prepared according to the general procedure from **7-O**[3,7] (50 mg, 8.82 × 10^{-5} mol) in 3 mL THF and $NaBH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.). The product was isolated as purple crystalline solid in 84% yield (42 mg, 7.38 × 10^{-5} mol). Chromatography condition: CH_2Cl_2 followed by 1% acetone in CH_2Cl_2. MW = 568.79 g/mol. R_f = 0.60 (silica-2% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.39 (s, 1H, *meso*-H), 8.71 (s, 1H, *meso*-H), 8.45 (s, 1H, *meso*-H), 8.25 (s, 1H, *meso*-H), 6.23 (s, 1H, pyrroline-H), 3.76 (ddt, *J* = 24.5, 15.5, 7.5 Hz, 8H, -CH_2), 2.54 (qd, *J* = 7.5, 2.5 Hz, 4H, -CH_2), 2.48-2.22 (m, 4H,), 1.80 – 1.62 (m, 12H), 1.04 (t, *J* = 7.5 Hz, 3H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.50 (dt, *J* = 10.0, 7.5 Hz, 6H), -0.11 (s, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) *δ:* 211.0, 163.5, 161.2, 160.3, 150.6, 143.6, 140.8, 138.5, 138.1, 134.4, 133.5, 132.6, 129.2, 97.7, 93.4, 92.6, 90.1, 83.5, 57.8, 55.4, 31.4, 31.3, 30.3, 26.6, 19.4, 19.3, 19.0, 18.1, 17.9, 17.7, 9.7, 9.1, 8.7, 8.6 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 409 (4.90), 432 (4.82), 597 (4.02), 636 (4.09) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 409 nm) λ_{max} = 643 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{49}N_4O_2$, 569.3850 (for $M+H^+$); found, 569.3793.

General Synthetic Procedure for the Preparation of Dihydroxychromophores 10 and 12 by Bis-Reduction of β,β'-Diketones 6 and 7, Respectively:

Octaethyldioxochlorin **6-O** or **7-O** was dissolved in dry THF and stirred on an ice bath under N_2. To the chilled solution was added a suspension of $LiAlH_4$ (5 equiv.) in THF and the mixture was stirred for ~3-5 minutes at 0 °C. The reaction was monitored by TLC and UV-vis spectroscopy. After completion of the reaction, the reaction mixture was quenched by slurrying with Glauber's salt (Na_2SO_4·10 H_2O, ~1.5 g). The resulting mixture was filtered through a pad of Celite and the pad was washed with CH_2Cl_2. The combined filtrates were passed through anhydrous Na_2SO_4 and reduced to dryness by rotatory evaporation. The crude solid was purified by either column chromatography (silica gel) or using preparative TLC (silica gel).

7,17-Dihydroxybacteriochlorin 10-(OH)⁷,¹⁷-anti. Prepared according to the general procedure from **6-O**[7,17] (50 mg, 8.82 × 10^{-5} mol) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.) in dry THF (1.5 mL). The product was isolated as green colored crystalline solid in 50% yield (25 mg, 4.38 × 10^{-5} mol). Chromatography condition: separation on preparative TLC plate with CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.47 (silica-1% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.03 (s, 2H, *meso*-H), 8.62 (s, 2H, *meso*-H), 6.44 (d, *J* = 6.0 Hz, 2H, -OH), 6.29 (d, *J* = 6.0 Hz, 2H, pyrroline-H), 3.80 (dd, *J* = 13.0, 5.5 Hz, 8H, -CH_2), 2.47-2.38 (m, 6H, -CH_2), 2.10 (dq, *J* = 14.5, 7.0 Hz, 2H, -CH_2), 1.68 (dt, *J* = 20.0, 7.5 Hz, 12H, -CH_3), 0.91 (t, *J* = 7.5 Hz, 6H, -CH_3), 0.56 (t, *J* = 7.0 Hz, 6H, -CH_3), -2.51 (s, 2H, -NH) ppm. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) *δ:* 163.3, 160.6, 133.9, 133.6, 132.4, 132.4, 94.3, 93.9, 81.1, 56.1, 31.2, 28.6, 18.5, 18.1, 17.9, 9.6, 9.3 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (4.72), 375 (4.79), 464 (3.56), 496 (3.96), 713 (4.42) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 375 nm) λ_{max} = 726 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 570.3934 (for M^+); found, 570.3893.

7,17-Dihydroxybacteriochlorin 10-(OH)⁷,¹⁷-syn. Prepared according to the general procedure from **6-O**[7,17] (50 mg, 8.82 × 10^{-5} mol) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.) in dry THF (1.5 mL). The product was isolated as green colored crystalline solid in 32% yield (16 mg, 2.80 × 10^{-5} mol). Chromatographic condition: separation on preparative TLC plate with CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.43 (silica-1% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.02 (s, 2H, *meso*-H), 8.61 (s, 2H, *meso*-H), 6.46 (d, *J* = 4 Hz, 2H,-OH), 6.28 (d, *J* = 8.0 Hz, 2H, pyrroline-H), 3.80 (dd, *J* = 14.5, 7.0 Hz, 8H, -CH_2), 2.49–2.37 (m, 6H, -CH_2), 2.12–2.03 (m, 2H, -CH_2), 1.68 (dt, *J* = 18.0, 7.5 Hz, 12H, -CH_3), 0.93 (t, *J* = 7.5 Hz, 6H, -CH_3), 0.53 (t, *J* = 7.5 Hz, 6H, -CH_3), -2.48 (s, 2H, -CH_2) ppm. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ: 163.0, 160.7, 133.8, 133.6, 132.4, 94.1, 93.9, 81.0, 56.2, 31.2, 28.7, 18.5, 18.1, 17.9, 9.5, 9.3 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (4.73), 375 (4.81), 465 (3.58), 495 (3.98), 714 (4.40) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 374 nm) λ_{max} = 730 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 570.3934 (for M^+); found, 570.3840.

7,18-dihydroxy-bacteriochlorin 10-(OH)⁷,¹⁸-anti. Prepared according to the general procedure from **6-O**[7,18] (50 mg, 8.82 × 10^{-5} mol) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.) in dry THF (1.5 mL). The product was isolated as green colored solid in 59% yield (30 mg, 5.26 × 10^{-5} mol). Chromatographic condition: separation on preparative TLC plate with 1% acetone in CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.24 (silica-1% acetone in CH_2Cl_2).^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 9.00 (s, 2H, *meso*-H), 8.60 (s, 2H, *meso*-H), 6.46 (d, *J* = 6.0 Hz, 2H, -OH), 6.29 (d, *J* = 6.0 Hz, 2H, pyrroline-H), 3.85-3.74 (m, 8H, -CH_2), 2.49-2.35 (m, 6H, -CH_2), 2.10-1.97 (m, 2H, -CH_2), 1.68 (dt, *J* = 19.0, 7.5 Hz, 12H, -CH_3), 0.95 (t, *J* = 7.5 Hz, 6H, -CH_3), 0.48 (t, *J* = 7.5 Hz, 6H, CH_3), -2.42 (s, 1H, -NH), -2.57 (s, 1H, -NH) ppm. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) *δ:* 163.2, 160.6, 133.9, 133.5, 132.4, 132.3, 94.1, 93.9, 80.9, 56.3, 31.2, 28.8, 18.6, 18.5, 18.1, 18.0, 9.5, 9.3 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (4.85), 375 (4.92), 466 (3.73), 495 (4.10), 714 (4.51) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 374 nm) λ_{max} = 733 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 570.3934 (for M^+); found, 570.3939.

7,18-Dihydroxybacteriochlorin 10-(OH)⁷,¹⁸-syn. Prepared according to the general procedure from **6-O**[7,18] (50 mg, 8.82 × 10^{-5} mol) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.) in dry THF (1.5 mL). The product was isolated as green colored crystalline solid in 26% yield (13 mg, 2.28 × 10^{-5} mol). Chromatography condition: separation on preparative TLC plate with 1% acetone in CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.18 (silica-1% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 9.02 (s, 2H, *meso*-H), 8.62 (s, 2H, *meso*-H), 6.41 (d, *J* = 6.0 Hz, 2H, -OH), 6.26 (d, *J* = 6.0 Hz, 2H, pyrroline-H), 3.87-3.76 (m, 8H, -CH_2), 2.49-2.35 (m, 6H, -CH_2), 2.13 (dd, *J* = 14.0, 6.5 Hz, 2H, -CH_2), 1.69 (dt, *J* = 21.0, 7.5 Hz, 12H, -CH_3), 0.89 (t, *J* = 7.5 Hz, 6H, -CH_3), 0.59 (t, *J* = 7.0 Hz, 6H, -CH_3), -2.46 (s, 1H, -NH), -2.60 (s, 1H, -NH) ppm. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) *δ:* 163.4, 160.4,

133.9, 133.5, 132.4, 132.3, 94.3, 93.9, 80.9, 56.2, 31.2, 28.6, 18.6, 18.5, 18.1, 17.9, 9.6, 9.2 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (4.87), 375 (4.95), 466 (3.75), 494 (4.11), 714 (4.57) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 374 nm) λ_{max} = 729 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 570.3934 (for M^+); found, 570.3809.

7,17-Dimethoxybacteriochlorins 10-(OMe)^{7,17}-anti and 10-(OMe)^{7,17}-syn. Either bacteriochlorin diol **10-(OH)^{7,17}-*anti*** or **10-(OH)^{7,17}-*syn*** (70 mg, 1.23 × 10^{-4} mol) were dissolved in 15 mL MeOH and TFA fumes from a TFA bottle head space were delivered by pipette and the mixture was heated to reflux for 15 min. A green-colored compound precipitated. The mixture was cooled to room temperature and the solid was filtered (glass frit F or micro-filtration setup). The crude solid was separated by preparative TLC (silica gel) using (40:60 V/V) hexanes:CH_2Cl_2 mixture as eluent. TLC gave two main products, **10-(OMe)^{7,17}-*anti*** in 48% yield (35 mg, 5.84 × 10^{-5} mol), and **10-(OMe)^{7,17}-*syn*** in 26% yield (19 mg, 3.17 × 10^{-5} mol). **10-(OMe)^{7,17}-*anti*:** The product was isolated as sparkling green colored crystalline solid. MW = 598.86 g/mol. R_f = 0.60 (silica-1:1 CH_2Cl_2:hexanes). UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (5.00), 375 (5.09), 438 (3.39), 465 (3.86), 495 (4.24), 714 (4.74) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 375) λ_{max} = 728 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{38}H_{54}N_4O_2$, 598.4247 (for M^+); found, 598.4248. **10-(OMe)^{7,17}-*syn*:** The product was isolated as sparkling green colored crystalline solid. MW = 598.86 g/mol; R_f = 0.48 (silica-1:1 CH_2Cl_2:hexanes). ^{1}H NMR (400 MHz, acetone-d_6) *δ*: 9.07 (s, 2H, *meso*-H), 8.74 (s, 2H, *meso*-H), 6.03 (s, 2H, pyrroline-H), 4.04 (s, 6H, -OCH_3), 3.89 (qd, *J* = 7.5, 3.5 Hz, 8H, -CH_2), 2.61 (ddd, *J* = 14.5, 7.5, 3.0 Hz, 4H, -CH_2), 2.40 (dd, *J* = 14.5, 7.5 Hz, 2H, -CH_2), 2.30 (dd, *J* = 14.0, 7.5 Hz, 2H, -CH_2), 1.75 (q, *J* = 7.5 Hz, 12H, -CH_3), 0.86 (t, *J* = 7.5 Hz, 6H, -CH_3), 0.71 (t, *J* = 7.5 Hz, 6H, -CH_3), -2.44 (s, 2H, -NH) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 350 (4.83), 375 (4.92), 438 (3.28), 465 (3.70), 495 (4.08), 714 (4.55) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 375 nm) λ_{max} = 729 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 598.4247 (for M^+); found, 598.4138.

2,7-Dihydroxy-isobacteriochlorin 12-(OH)^{2,7}-anti. Prepared according to the general procedure from **7-O^{2,7}** (50 mg, 8.82 × 10^{-5} mol) in dry THF (1.5 mL) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.). The product was isolated as burgundy solid in 47% yield (24 mg, 4.20 × 10^{-5} mol). Chromatography condition: CH_2Cl_2 followed by 2% acetone in CH_2Cl_2. MW = 570.81 g/mol. R_f = 0.44 (silica-5% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.35 (s, 1H, *meso*-H), 7.56 (s, 1H, *meso*-H), 7.15 (s, 1H, *meso*-H), 6.92 (s, 1H, *meso*-H), 6.34 (d, *J* = 6.5 Hz, 1H, -OH), 6.20 (d, *J* = 6.0 Hz, 1H, -OH), 5.68-5.62 (m, 2H, pyrroline-H), 3.50 (s, 2H, -NH), 3.33-3.26 (m, 4H, -CH_2), 3.24-3.12 (m, 4H, -CH_2), 2.20-2.01 (m, 6H, -CH_2), 1.74 (td, *J* = 14.5, 7.5 Hz, 2H, -CH_2), 1.47-1.38 (m, 12H, -CH_3), 1.03 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.94 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.56 (dt, *J* = 14.5, 7.5 Hz, 6H, -CH_3) ppm. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) *δ:* 166.7, 161.6, 154.5, 154.0, 146.6, 143.4, 140.1, 138.8, 136.3, 133.9, 132.7, 131.3, 105.4, 93.0, 92.7, 88.2, 78.9, 77.3, 55.6, 53.4, 29.7, 28.9, 27.9, 27.6, 18.1, 17.9, 17.5, 17.4, 9.1, 9.0, 8.9 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 373 (5.02), 404 (4.65), 546 (4.24), 586 (4.42), 631 (3.87) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 373 nm) λ_{max} = 596, 634 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{51}N_4O_2$, 571.4007 (for $M+H^+$); found, 571.3966.

2,7-Dihydroxy-isobacteriochlorin 12-(OH)^{2,7}-syn. Prepared according to the general procedure from **3^{2,7}** (50 mg, 8.82 × 10^{-5} mol) in dry THF (1.5 mL) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.). The product was isolated as burgundy crystalline solid in 42% yield (21 mg, 3.68 × 10^{-5} mol). Chromatography condition: CH_2Cl_2 followed by 4% acetone in CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.28 (silica-5% acetone in CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): *d* 8.40 (s, 1H, *meso*-H), 7.63 (s, 1H, *meso*-H), 7.22 (s, 1H, *meso*-H), 7.02 (s, 1H, *meso*-H), 6.31 (d, *J* = 6.5 Hz, 1H, -OH), 6.15 (d, *J* = 6.0 Hz, 1H, -OH), 5.63 (d, *J* = 5.5 Hz, 2H, pyrroline-H), 3.38 – 3.32 (m, 4H, -CH_2), 3.26 – 3.18 (m, 4H, -CH_2), 2.17 – 2.05 (m, 6H, -CH_2), 1.82 (dd, *J* = 21.0, 10.0 Hz, 2H, -CH_2), 1.49 – 1.39 (m, 12H, -CH_3), 0.99 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.90 (t, *J* = 7.5 Hz, 3H, -CH_3), 0.64 (dd, *J* = 13.0, 7.0 Hz, 6H, -CH_3) ppm. ^{13}C NMR{^{1}H} (126 MHz, DMSO-d_6) *δ:* 166.9, 161.1, 154.9, 154.1, 146.3, 143.6, 140.0, 139.0, 136.2, 134.2, 132.7, 131.5, 105.3, 93.5, 92.7, 88.3, 79.5, 77.5, 55.7, 54.9, 52.9, 29.6, 29.2, 27.6, 27.0, 18.1, 17.9, 17.5, 17.4, 9.3, 9.1, 8.9 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 373 (4.72), 404 (4.38), 546 (3.93), 586 (4.10), 630 (3.61) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 373 nm) λ_{max} = 596, 636 (sh) nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{51}N_4O_2$, 571.4007 (for $M+H^+$); found, 571.3949.

7,13-Dihydroxyisobacteriochlorin 12-(OH)^{7,13}-anti (low polarity isomer). Prepared according to the general procedure from **7-O^{7,13}** (15 mg, 2.65 × 10^{-5} mol) in dry THF (1 mL) and $LiAlH_4$ (17 mg, 1.32 × 10^{-4} mol, 5 equiv.); not sufficient material for the full characterization of the low-polarity isomer of ***12-(OH)^{7,13}*** could be obtained. ***12-(OH)^{7,13}-anti***: The product was isolated as dark purple solid in 54% yield (8.2 mg, 1.44 × 10^{-5} mol). MW = 570.8078 g/mol; R_f = 0.27 (silica-3% acetone in CH_2Cl_2). Chromatographic condition: CH_2Cl_2 followed by 4% acetone in CH_2Cl_2. ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: δ 8.38 (s, 1H, *meso*-H), 7.60 (s, 2H, *meso*-H), 6.65 (s, 1H, *meso*-H), 6.16 (d, *J* = 6.0 Hz, 2H, -OH), 5.58 (d, *J* = 5.5 Hz, 2H, pyrroline-H), 3.50 - 3.46 (m, 4H, -CH_2), 3.21 (dd, *J* = 14.5, 7.0 Hz, 4H, -CH_2), 2.19 – 2.08 (m, 4H, -CH_2), 1.99 (dd, *J* = 14.0, 7.0 Hz, 2H, -CH_2), 1.85 (dd, *J* = 13.5, 7.0 Hz, 2H, -CH_2), 1.49 – 1.43 (m, 12H, -CH_3), 1.23 (s, 2H, -NH), 0.86 (d, *J* = 7.5 Hz, 6H, -CH_3), 0.67 (t, *J* = 7.0 Hz, 6H, -CH_3) ppm. ^{13}C NMR{^{1}H} (101 MHz, DMSO-d_6) *δ:* 165.2, 152.9, 145.00, 139.6, 135.6, 132.2, 105.5, 93.2, 88.8, 77.4, 72.3, 69.9, 69.8, 69.5, 69.2, 65.5, 60.2, 55.6, 31.3, 29.2, 26.7, 18.8, 18.1, 17.9, 17.3, 15.1, 13.7, 9.2, 8.8 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 372 (4.80), 382 (4.78), 509 (3.84), 547 (4.08), 589 (4.29), 631 (3.35) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 372 nm) λ_{max} = 598, 636 (sh) nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{50}N_4O_2$, 570.3934 (for M^+); found, 570.3847.

3,7-Dihydroxy-isobacteriochlorin 12-(OH)^{3,7} (stereoisomeric mixture). Prepared according to the general procedure from **7-O^{3,7}** (50 mg, 8.82 × 10^{-5} mol) and $LiAlH_4$ (17 mg, 4.4 × 10^{-4} mol, 5 equiv.) in dry THF (1.5 mL). The

product was isolated as dark purple crystalline solid in 87% yield (44 mg, 7.70×10^{-5} mol). Chromatography condition: CH_2Cl_2 followed by 1% acetone in CH_2Cl_2. MW = 570.81 g/mol; R_f = 0.17 (silica-2% acetone in CH_2Cl_2). ^{1}H NMR (for one isomer) (400 MHz, DMSO-d_6) δ: 8.44 (s, 1H, *meso*-H), 7.38 (s, 1H, *meso*-H), 7.28 (s, 2H, *meso*-H), 3.25-3.21 (m, 8H, -CH_2), 2.19-2.00 (m, 8H, -CH_2), 1.50-1.41 (m, 12, -CH_3), 1.03-0.97 (m, 6H, -CH_3), 0.64-0.62 (m, 6H, -CH_3), 0.44-0.34 (2H, -NH) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε): 373 (4.95), 406 (4.69), 544 (4.03), 584 (4.16), 630 (3.93) nm. Fluorescence (CH_2Cl_2, $\lambda_{excitation}$ = 373 nm) λ_{max} = 594, 635 nm. HR-MS (ESI+, 100% CH_3CN, TOF): *m/z* calc'd for $C_{36}H_{51}N_4O_2$, 571.4007 (for $M+H^+$); found, 571.3944.

NOTE

The authors declare no competing financial interest.

Associated Content

Supporting Information. Reproduction of the UV-vis, fluorescence, IR and ^{1}H and ^{13}C NMR spectra of all hydroporphyrins;. FAIR data for publication including primary NMR FID files for compounds **8-(OH)^7-*rac***, **9-O^7-(OH)^{17}-*rac***, **9-O^7-(OH)^{18}-*rac***, **10-(OH)^{7,17}-***syn*/*anti*, **10-(OMe)^{7,17}-***syn*, **10-(OH)^{7,18}-***syn*/*anti*, **11-O^2-(OH)^7-*rac***, **11-O^7-(OH)^{13}-*rac***, **11-O^7-(OH)^3-*rac***, **12-(OH)^{2,7}-***syn*/*anti*, **12-(OH)^{3,7}**, and **12-(OH)^{7,13}-*anti*.** Experimental details for the crystal structure determinations of **9-O^7-(OH)^{17}-*rac*** (CCDC # 2022993), **9-O^7-(OH)^{18}-*rac*** (CCDC # 2022998), **10-(OMe)^{7,17}-***syn* (CCDC # 2022995), **10-(OMe)^{7,17}-***anti* (CCDC # 2022992), **11-O^7-(OH)^3-*rac*** (CCDC # 2022994), **11-O^7-(OH)^2-*rac*** (CCDC # 2022996), and **12-(OH)^{2,7}-*rac*** (CCDC # 2022997), including the .cif files. This material is available free of charge via the Internet at http://pubs.acs.org. The cif files can also be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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