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Synthesis of Regioisomeric Bacteriochlorophyll-*d* Analogues Possessing a Hydroxy Group at the 2^1- or 3^1-Position: Their Chlorosome-Like Self-Aggregation in Solid Films

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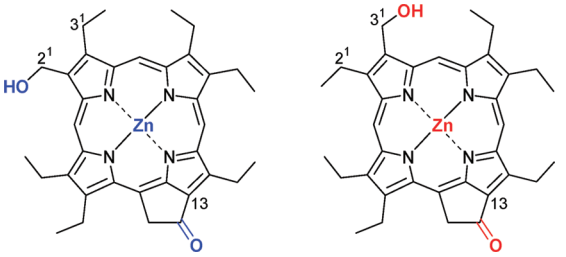

Zinc 2^1- and 3^1-hydroxy-13-carbonylhexaethylporphyrins **2** and **3** were synthesized by modifying easily available octaethylporphyrin, and the HPLC-separated regioisomers were fully characterized. The latter compound 3^1-OH-13-C=O-**3**, which structurally resembled naturally self-aggregative bacteriochlorophyll-*d* (3^1-OH/13-C=O), was preferable to make ordered *J*-aggregates in the solid film, compared to its regioisomeric 2^1-OH-13-C=O-**2**. In contrast, more ordered oligomers were obtained by self-aggregation of zinc porphyrin **1** possessing the interactive moieties (3^1-OH, Zn, 13-C=O) at the same positions, which was prepared by modifying natural chlorophyll-*a* molecule. The difference between self-aggregation of **1** and **3** was ascribable to the methyl and ethyl groups attached at the 2-position neighboring the 3^1-OH group which is requisite for self-aggregation; the steric environment around the interactive OH group is important to make highly ordered supramolecules through strong molecular packings.

Introduction

Chlorophyllous pigments in natural photosynthesis have a cyclic tetrapyrrole skeleton and are distinguished by the π-conjugate systems as in porphyrin (fully conjugated), chlorin (singly reduced, C17−C18), and bacteriochlorin (doubly reduced, C7−C8 and C17−C18).[1,2] Changing their π-systems generates large differences in their optical and chemical properties, while the peripheral substituents control them to a lesser degree. The latter moieties play a predominant role in intermolecular interactions for constructing photosynthetic apparatus; their hydrophilic and hydrophobic interactions with amino acid residues of protein scaffolds are found in most photosynthetic apparatuses, and specific intermolecular coordination and hydrogen-bondings of bacteriochlorophyll(BChl) molecules by themselves are found in major antenna systems of green photosynthetic bacteria, called chlorosomes.[2−4] Such chlorosomal self-aggregates are attractive for construction of molecular devices in a simple and well-ordered fashion.

BChl-*d* (upper left in Figure 1), one of the natural self-aggregative BChls, is characterized by the presence of OH, coordinative metal (Mg), and C=O moieties along the *y*-axis[3] (arrow in Figure 1), a major transition dipole moment of photoactive chlorophyllous pigments. Similarly to natural

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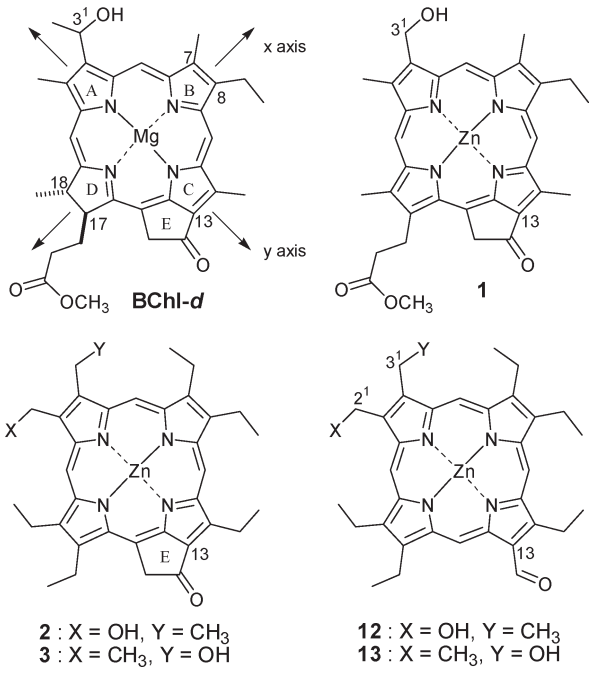

FIGURE 1. Molecular structures of natural BChl-*d*, model compound **1** derived from chlorophyll(Chl)-*a*, and their present (**2** and **3**) and previous analogues (**12** and **13**) derived from octaethylporphyrin (OEP).

BChl molecules,[5−12] their synthetic zinc porphyrin analogue **1** (upper right in Figure 1) self-aggregated in nonpolar[13] and/or aqueous micellar media[14] by coordination (3^1-O···M) and hydrogen-bondings (3^1-OH···O=C-13) as well as by their $\pi-\pi$ stackings. We previously reported chemical modification of fully synthesized octaethylporphyrin (OEP) to BChl-*d* analogues **12** and **13** (lower right in Figure 1).[15] The compound 3^1-OH-**13**, resembling natural BChl-*d*, self-aggregated in nonpolar organic solvent while its regioisomeric 2^1-OH-**12** hardly formed such a *J*-aggregate, indicating that a linear situation of OH, Zn, and C=O as in **13** was preferable for the self-aggregation, compared to the slightly bent order in **12**. These models **12** and **13** could have the interactive C=O group with freely rotational conformers, which might have more potential to reduce the strength of intermolecular interaction as in hydrogen bonding between C=O and OH groups than the conformationally fixed 13-C=O in natural BChl-*d*.[16] Introducing an exo-five-membered ring (called E-ring) with an interactive C=O group to synthetic porphyrin would be useful for the construction of models of natural chlorophylls.[17−19] Our recent report[19] described that a regioselective OsO_4-dihydroxylation of 13^2,15-cyclized OEP derivative **4** gave 2,3- and 12,13-dihydroxychlorins **5** and **6** (see Scheme 1) and that the latter **6** was a good precursor of phytoporphyrin analogue **15** possessing an exo-five-membered E-ring with a 13^1-oxo group (**4** → **6** → **14** → **15**, Scheme 1, bottom). Pandey's group previously reported that an electron-withdrawing group conjugated with the porphyrin π-system controlled the regioselectivity upon OsO_4 oxidation of the porphyrin to give the *cis*-diol on its opposite pyrrole ring.[20] According to the rule, porphyrin derivatives possessing a C=O group on the A- or C-rings, which can be prepared from **5** or **6**, would be modified at the $\beta-\beta'$ double bond on the diagonal C- and A-rings, respectively, along the *y*-axis.

Here we report synthesis and regioisomeric separation of BChl-*d* analogues **2** and **3** (lower left in Figure 1) whose molecular structures differ only at the position of the OH group; we also examined their self-aggregation behaviors taking particular note of the regioisomeric effect. The present models **2** and **3** are improved from previous **12** and **13** by introduction of the E-ring; conformationally fixed 13-C=O can interact with a hydroxy group of another porphyrin similarly to natural BChl-*d*. Chemical modifications of OEP described in this report might provide a series of OEP derivatives possessing functional groups at the A- and C(E)-rings, where important functional groups are found in the molecular structures of all the photosynthetically active chlorophyllous pigments.[1]

Results and Discussion

Synthesis of Zinc 2- and 3-Hydroxymethyl-13^1-oxoporphyrins 2 and 3. Modification of the Dihydroxy Moiety in Diol 5 to 2- and 3-Formylated Porphyrins 11. The 2,3-dihydroxy moiety of **5** was a useful starting point for modifying the β-positions on the A-ring as mentioned above[19] and was doubly dehydrated by refluxing a benzene solution containing concd HCl, affording 2- and 3-vinylporphyrins **7** (69% yield). The regioisomeric ratio (2:1) was the same as in the previously reported monodehydration of **5** giving 2- and 3-(1-hydroxyethyl)porphyrins,[19] which was reasonable because the present bis-dehydration proceeded via the monodehydrated intermediate. At this stage, it had not been determined which regioisomer was major, and the mixture of 2- and 3-vinylpoprhyrins was used for the next step. The 2- and 3-vinyl groups in **7** were easily converted to the formyl group by treatment with OsO_4 and $NaIO_4$ to give **8** (54%), whose regioisomeric ratio remained unchanged, indicating no difference in the reactivity between the 2- and 3-vinyl groups. To modify the pyrrole C-ring diagonal to the A-ring possessing an electron-withdrawing formyl group, **8** was treated by OsO_4-H_2S, as mentioned in the Introduction.

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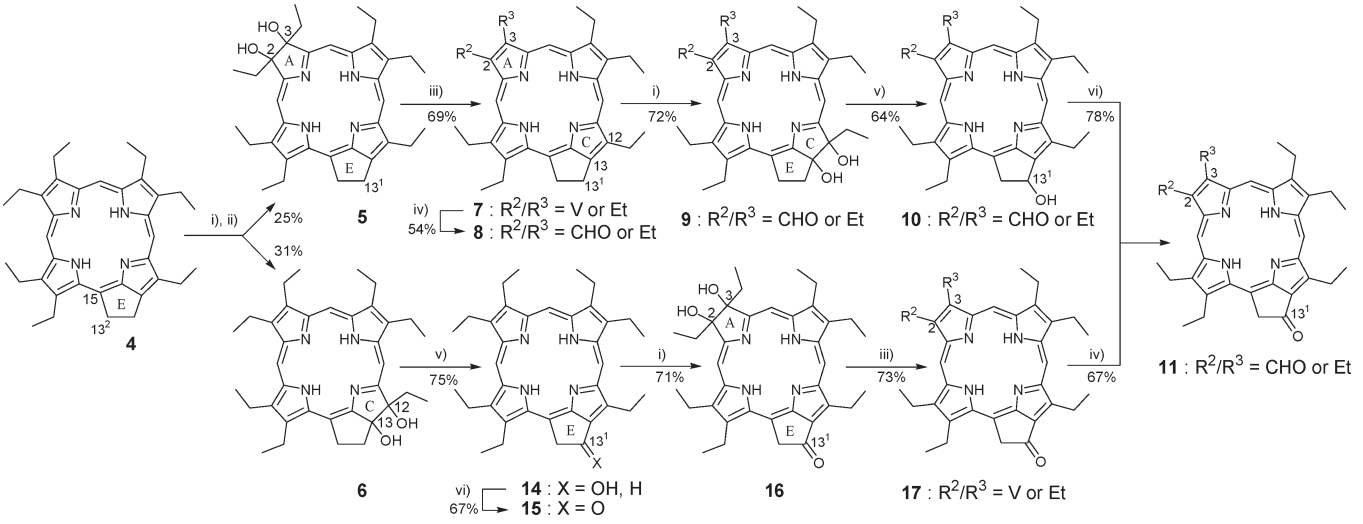
SCHEME 1. Chemical Modification of 13^2,15-Cyclized OEP (4) to 2- and 3-Formylated 13^1-Oxophytoporphyrin Analogues 11[a]



[a]Reagents and conditions: (i) OsO_4/pyridine, CH_2Cl_2, H_2S; (ii) FCC separation; (iii) concd HCl, benzene, reflux; (iv) cat. OsO_4, $NaIO_4$, THF−1,4-dioxane−H_2O; (v) dilute HCl, 1,4-dioxane, 50 °C; (vi) Pr_4NRuO_4, NMO, CH_2Cl_2. "V" indicates a vinyl group.

The oxidation of a mixture of 2- and 3-formylporphyrins **8** gave a mixture of two products, whose main mass spectral peak at the mass number of **8** plus 34 proved them to be dihydroxylated compounds. Bacteriochlorin (two reduced diagonal pyrrole rings) and isobacteriochlorin-like products (two reduced neighboring pyrrole rings) were not observed from mass spectral analysis, indicating that no further oxidation occurred after one $\beta-\beta'$ double bond on a pyrrole ring was reacted. In the ^{1}H NMR spectrum in $CDCl_3$, one triplet signal with three protons was observed at 0.9 ppm, showing that the dihydroxylation of **8** occurred at the C12═C13 on the C-ring where only one ethyl group was attached; the products were 2- and 3-formyl-12,13-dihydroxychlorins **9** (72%). The regioisomeric ratio of the product **9** was 2:1 which was the same as that of the starting material **8**, so the 2- and 3-formyl groups in **8** did not affect the yield of the 12,13-dihydroxylation. The dihydroxy moiety of **9** was also transformed to the 13^1-oxo group by the same procedures as reported (**6** → **14** → **15**),[19] affording 2- and 3-formylated phytoporphyrin analogues **11**. The initial step, monodehydration of the *cis*-diol **9** (v in Scheme 1), regioselectively gave 13^1-OH-**10** (64%), so change of the functional group at the A-ring (ethyl to formyl, **6** to **9**) still followed the reaction rule via a sole allyl-type carbocation at the 13^1-position as its intermediate.

Modification of Dihydroxy Moiety in Diol 6 to 2- and 3-Formylated Porphyrins 11. Alternatively, 12,13-dihydroxychlorin **6** was converted to phytoporphyrin analogue **15** in two steps according to the previous report,[19] in which the monodehydration of the 12,13-diol in **6** produced 13^1-OH-porphyrin **14** predominantly (vide supra). Treatment of **15** with OsO_4 and H_2S afforded a sole chlorin chromophore whose molecular structure was determined by 1D and 2D ^{1}H NMR and FAB-MS spectra as 2,3-dihydroxy-13^1-oxoporphyrin **16** (71%). The present chemical modification of porphyrin derivatives possessing the 13^1-oxo-E-ring is useful for introduction of the peripheral substituents at the A-ring, where important functional groups are attached in naturally occurring chlorophyll(Chl)s and BChls: 3-CH═CH_2 in Chls-*a*/*b*/*c* and BChl-*g*, 3-CHO in Chl-*d*, 3-$COCH_3$ in BChls-*a*/*b* and 3-CH(OH)CH_3 in BChls-*c*/*d*/*e*. Double dehydration of the 2,3-dihydroxy moiety in **16** also gave a mixture of 2- and 3-vinylporphyrins **17** (73%). However, the regioisomeric ratio of **17** was about 1:1, in contrast to the case of 2,3-dihydroxy-13^1-deoxo-**5** to 2- and 3-vinyl-13^1-deoxo-**7** (2:1). The presence or absence of the 13^1-oxo group slightly controlled the regioselectivity of the dehydration. Conversion of the 2- and 3-vinyl group in **17** was readily achieved to give 2- and 3-formylporphyrins **11** (67%), respectively. Here, a mixture of 2- and 3-formylporphyrins **11** derived from **5** and **6** were represented as **11a** (2:1) and **11b** (1:1), respectively.

Synthesis and HPLC Separation of Self-Aggregative Zinc Porphyrins 2 and 3 as Models of BChl-*d*. Reduction of the 2- and 3-formyl groups in **11a**/**b** was achieved by a mild reductant, tBuN$H_2\cdot BH_3$, to give 2- and 3-hydroxymethyl-**18a**/**b**, whose 13-keto-carbonyl group was not reduced, similarly to the previous reports.[14,21] In this case, no difference of reactivity between the 2- and 3-formyl groups was observed: the regioisomeric ratios were 2:1 and 1:1 for **18a** (from **5**) and **18b** (from **6**), respectively. Successive zinc metalation of **18a** and **18b** gave the corresponding mixtures of **2** and **3**. Separation of regioisomers **2** and **3** was carried out with normal-phase HPLC (1% pyridine−1,2-dichloroethane), and two bands were eluted at 18.5 and 20.9 min (see Figure S1 in the Supporting Information). HPLC chromatograms showed that **2**/**3** from **18a** gave a 1:2 mixture of the first and second elutions, while that derived from **18b** was a 1:1 mixture (Scheme 2).

The molecular structures of separated regioisomers were determined by their ^{1}H−^{1}H COSY and NOESY spectra (see the Supporting Information). The key NOE correlation is between the 20-H and the substituent at the 2-position: the 20-H of the first and second fraction were correlated with singlet (2H, 6.07 ppm) and quartet signals (2H, 4.09 ppm),

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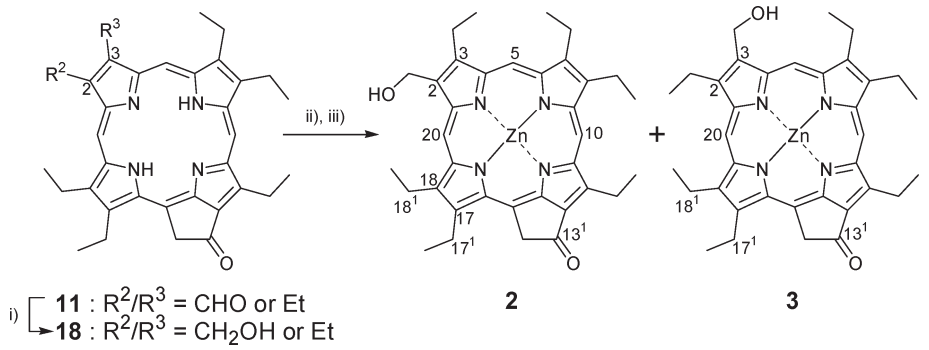
SCHEME 2. Synthesis of BChl-*d* analogues 2 and 3[a]



[a]Reagents and conditions: (i) $tBuNH_2 \cdot BH_3$, CH_2Cl_2; (ii) $Zn(OAc)_2 \cdot 2H_2O$, CH_2Cl_2−methanol; (iii) normal-phase HPLC (1% v/v pyridine−1,2-dichloroethane).

respectively. The former and latter 2-CH_2 are assigned to hydroxymethyl and β-ethyl groups, respectively. These 1D/2D ^{1}H NMR spectra clearly indicated that the first and second elutions were zinc 2-hydroxymethyl-13^1-oxoporphyrin **2** and zinc 3-hydroxymethyl-13^1-oxoporphyrin **3**. Both the important NOE and COSY correlations for **2** and **3** are summarized in Figure S2 (Supporting Information).

From the structural determinations of **2** and **3**, the major regioisomers of **7**, **8**, **9**, **10**, **11a**, and **18a** had substituents altered at the 2-position and a 3-ethyl group. During the bis-dehydration of **5** to **7**, allyl-type carbocation at the 3^1-position was produced as the intermediate in preference to that at the 2^1-position, which was ascribable to the presence of the exo-five-membered E-ring lacking a keto-carbonyl group. It is noteworthy that the introduction of 13^1-oxo group in the E-ring as in **5** → **16** suppressed the above regioselectivity: 2:1 → 1:1.

Self-Aggregation Behaviors of Zinc 2- and 3-Hydroxymethylporphyrins 2 and 3. Each THF solution of **2** and **3** showed the same UV−vis spectra (thin line in Figure 2). Their sharp absorption bands indicated that an oxygen atom of a THF molecule coordinated axially to the central zinc atom of **2** and **3** to be their monomers. Soret and Qy absorption maxima of **2** and **3** were 428 and 608 nm, respectively, which were significantly similar to those of the previously reported zinc porphyrin **1** (see ref 14 for the spectral data), derivatized from naturally occurring Chl-*a*. This indicated that UV−vis spectral properties of monomeric zinc porphyrins possessing the 13^1-oxo group on the E-ring were independent of the peripheral alkyl groups attached at the β-positions of the porphyrin π-system.

Self-aggregation behaviors of **2** and **3** were examined in nonpolar organic solvent (data not shown). In 1% v/v THF/hexane solution, UV−vis spectra of both **2** and **3** were nearly the same as those of THF solutions. After standing, some precipitation occurred and the solutions soon became colorless. Dilution of their THF solutions with 100-fold cyclohexane or heptane also resulted in the same situation. These results indicated that the present zinc porphyrins **2** and **3** were partially soluble as monomers in such media but their oligomers, probably *J*-aggregates, were insoluble in such solvents, in sharp contrast to the previously reported zinc porphyrin **1** which formed chlorosomal *J*-aggregates in the solutions.

Thin films of **2** and **3** were prepared by dropping their 1:1 dichloromethane and cyclohexane solutions onto a quartz glass plate and were characterized by electronic absorption (using an optical waveguide) and resonance Raman (RR) spectra. The UV−vis spectrum of 2^1-OH-**2** (bold dotted line in Figure 2) had broadened absorption bands, where two distinct peaks corresponding to the Soret and Qy transitions were observed at 437 and 617 nm, respectively. Both maxima were shifted to a 9-nm longer wavelength than the monomeric ones in THF. These spectral changes were rather similar to those of **19**[18] lacking the OH group at the 2^1- or 3^1-position (see Chart 1). The UV−vis spectrum of **19** in the solid state (see red line in Figure S3, Supporting Information) showed broadened absorption bands, but its Qy band moved slightly (606 nm in THF → 610 nm in the

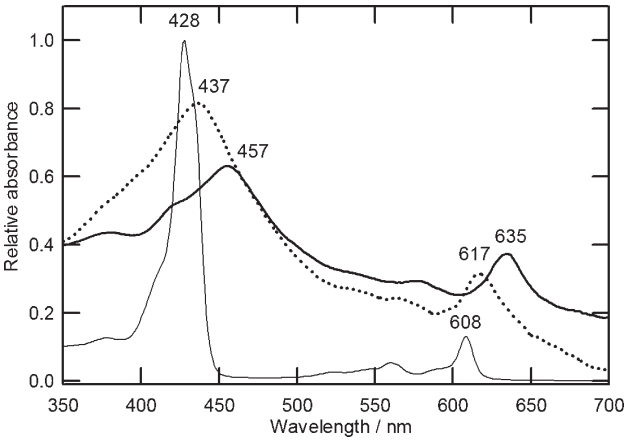
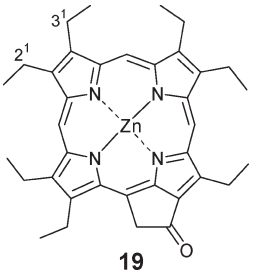


FIGURE 2. UV−vis spectra of zinc 2- or 3-hydroxymethylporphyrins **2** and **3** in THF (thin line) and solid state (bold dotted and solid lines for **2** and **3**). Since the THF solutions of **2** and **3** gave the same spectra, their thin lines were completely overlapped.

CHART 1



film); this spectral change would be ascribable to the simple $\pi-\pi$ stacking among the molecules, but their Qy transition dipole moments in the aggregates were randomly oriented. The spectral change observed in **2** was slightly larger than **19** but would be mainly due to their random $\pi-\pi$ stacking among the planar porphyrin π-systems. In the case of 3^1-OH-**3**, the Soret and Qy absorption bands in the thin film were situated at 457 and 635 nm, respectively (bold solid line in Figure 2), which moved to longer wavelengths compared to 2^1-OH-**2**. The spectral change of **3** from its THF solution to the thin film was closer to those from monomer of **1** in THF (428 and 608 nm) to its oligomer in a nonpolar organic solvent[13] (464 and 644 nm), an aqueous micellar solution[14] (465 and 655 nm) and the solid state (443 and 654 nm, black line in Figure S3, Supporting Information). Absorption maxima and spectral shapes of **2**, **3**, **19**, and **1** would be classified as two types, ordered *J*-aggregates (**1** and **3**) and randomly formed aggregates (**2** and **19**). These results indicated that zinc porphyrin **3** possessing the interactive moieties in a line (the *y*-axis) formed slipped overlapping *J*-aggregates in well ordered fashion, while **2** possessing those in a slightly bent line made amorphous aggregates even by introduction of the conformationally fixed 13-C=O.

RR spectra of **2** and **3** in THF (thin solid line in Figure 3) were measured by excitation at 405 nm and showed no apparent difference between them, similar to their monomeric visible spectra in THF (vide supra). From the previous report,[14] a vibrational band of the 13-C=O group was easily assigned as the intense signal at 1697 cm^{-1}, and the others appearing at around 1500 to 1600 cm^{-1} were assigned to skeletal C−C, C=C, C−N, and C=N stretchings. The thin films of **2** and **3** described above were also examined by RR spectra (bold dotted and solid lines in Figure 3 for films of **2** and **3**, respectively). All of the spectral shapes of both thin films were quite similar to those in monomer, except for a RR shift of the 13-C=O vibrational band in **3** at 1671 cm^{-1}. Such a down-shift (26 cm^{-1}) was a typical sign of the presence of its hydrogen bonding.[10,14,16,21] These results indicated that 3^1-OH-**3** aggregated to form a relatively ordered supramolecular structure driven by the intermolecular interaction observed in a motif of chlorosomal self-aggregates (coordination and hydrogen-bondings). No shift of 13-C=O by self-aggregation of 2^1-OH-**2** was consistent with its less red-shifted absorption bands: the slightly bent situation of the interactive moieties rarely formed well-ordered molecular alignments (vide supra). Conformationally fixed 13-carbonyl group in **2** and **3** would be preferable to bond with the 3^1-OH group of another molecule, compared to the freely rotatable 13-C=O in **12** and **13**, but no enhancement of hydrogen-bond ability was observed in the present study. Conformational fixation of the 13-C=O in ZnOEP-derivatives in **12** → **2** and **13** → **3** would have little influence on the chlorosomal self-aggregation.

Difference between *J*-Aggregates of 3^1-Hydroxy-13^1-oxoporphyrins 1 and 3: An Effect of the Peripheral Substituent Groups. The presence and situation of interactive OH, Zn, and C=O moieties in a molecule were the same in semi-natural **1** and fully synthetic **3**, but their self-aggregation behaviors in the solid states, especially their red-shift values of Qy band by forming their *J*-aggregates, were different as described above: Qy peaks = 608 → 654 and 608 → 635 nm for **1** and **3**, respectively, in a THF solution → in the film and

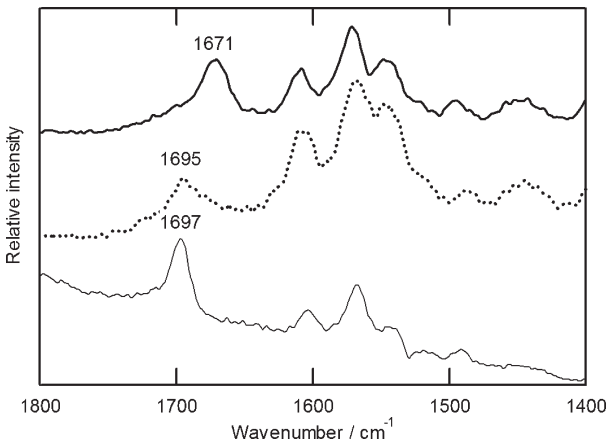


FIGURE 3. RR spectra of zinc 2- and 3-hydroxymethylporphyrins **2** and **3** in THF (thin solid) and in the solid state (bold dotted and solid lines for **2** and **3**). RR spectra of THF solutions of **2** and **3** were the same. All spectra were measured with excitation by a 405-nm laser.

the red-shift value by self-aggregation of **1** (1160 cm^{-1}) was about 1.7-fold larger than that in **3** (700 cm^{-1}). The reason they behaved differently is ascribable to their different peripheral substituents, especially the 2-methyl and 2-ethyl groups neighboring the 3^1-OH in **1** and **3**, respectively. We have reported that various substituents at the 7- and 8-positions on the B-ring in the natural and synthetic chlorosomal pigments did not greatly affect their self-aggregation;[22] modification of the 17-propionate residue also did to only a lesser degree.[2,23] Natural BChls have ethyl, propyl, isobutyl, and neopentyl groups at the 8-positions, and methyl and ethyl groups are attached at the 12-position.[2,11,12] It was noteworthy that the presence of the 12-ethyl group in natural BChls did not reduce their self-aggregativity. Therefore, the presence of the 12-ethyl group neighboring the interactive 13-C=O group in **3** would not be ascribable to disturbance of its *J*-aggregation, compared to **1** possessing the 12-methyl group. The 3^1-OH group in chlorosomal pigments has two roles, coordination with the central metal of another molecule and hydrogen bonding with the 13-C=O group of the third molecule. Sterically less hindrance around the 3^1-OH with the dual roles is important, compared to the 13-C=O with the sole role by forming a hydrogen bond. All of the naturally occurring BChls have various alkyl groups (by 8^2- and 12^1-methylation) in the right half of the molecules to tune their optical properties without loss of their self-aggregativity, but such methylation is not observed at the 2^1-position in natural chlorosomal BChls. To construct well-packed *J*-aggregates, green photosynthetic bacteria would take only a methyl group at the 2-position of the self-aggregative molecule, which avoids an increase of steric hindrance around the neighboring 3^1-OH.

Experimental Section

Synthesis of 2- and 3-Vinylporphyrins 7. To a benzene solution (20 mL) of 2,3-dihydroxychlorin **5**[19] (63.0 mg, 111 μmol) was added three drops of a concd HCl and the mixture refluxed for

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2 h under nitrogen. The reaction mixture was poured into water and extracted with dichloromethane until the aqueous layer was colorless. The combined extracts were washed with aq 4% $NaHCO_3$ and water, dried over Na_2SO_4, and evaporated to dryness. The residue was purified on FCC (dichloromethane) and recrystallized (dichloromethane−methanol) to give a 2:1 regioisomeric mixture of 2-vinyl-**7** and 3-vinyl-**7** as a red solid (41.0 mg, 69%): VIS (CH_2Cl_2) 617 (relative intensity, 0.03), 566 (0.05), 541 (0.04), 504 (0.09), 403 nm (1.0); ^{1}H NMR ($CDCl_3$, 2-vinyl-**7**/3-vinyl-**7** = 2/1) δ = 10.25/10.20, 10.09/10.13, 10.01 (each 1H, s, 5-, 10-, 20-H), 8.30−8.21 (1H, m, 2/3-CH═), 6.32−6.26, 6.15−6.08 (each 1H, m, 2/3-C═CH_2), 5.48−5.40 (2H, m, 13^1-CH_2), 4.21−4.08 (14H, m, 3/2-, 7-, 8-, 12-, 13-, 17-, 18-CH_2), 2.04−1.98, 1.97−1.89, 1.84−1.79 (3H + 12H + 3H, m, 3^1/2^1-, 7^1-, 8^1-, 12^1-, 17^1-, 18^1-CH_3), −2.95, −3.71 (each 1H, br s, NH×2); HRMS (FAB) *m*/*z* 530.3407 (M^+), calcd for $C_{36}H_{42}N_4$ 530.3409.

Synthesis of 2- and 3-Formylporphyrins 8. To a 2:1 mixture of 2- and 3-vinylporphyrins **7** (41.0 mg, 77 μmol) in THF solution (15 mL) was added OsO_4 (4.0 mg, 16 μmol) and the mixture stirred. After 10 min of stirring, an aq 25% v/v acetic acid solution (5 mL) of $NaIO_4$ (174 mg, 81 μmol) was added and the mixture stirred for 5 h under nitrogen. The reaction mixture was poured into aq 10% NaOAc and extracted with dichloromethane. The organic phase was washed with aq $NaHCO_3$ and water, dried over Na_2SO_4, and evaporated to dryness. The residue was purified on FCC (1% Et_2O−dichloromethane) and recrystallized (dichloromethane−hexane) to give a 2:1 regioisomeric mixture of 2-formyl-**8** and 3-formyl-**8** as a red solid (22.2 mg, 54%): VIS (CH_2Cl_2) 631 (relative intensity, 0.02), 577 (0.05), 559 (0.06), 518 (0.05), 417 nm (1.0); ^{1}H NMR ($CDCl_3$, 2-formyl-**8**/3-formyl-**8** = 2/1) δ = 11.51 (1H, s, 2/3-CHO), 11.10/10.19, 10.17/11.02 (each 1H, s, 5-, 20-H), 9.97/9.93 (1H, s, 10-H), 5.41 (2H, br-s, 13^1-CH_2), 4.50−4.42 (2H, m, 3/2-CH_2), 4.21−4.06 (12H, m, 7-, 8-, 12-, 13-, 17-, 18-CH_2), 2.03−1.90 (15H, m, 3^1/2^1-CH_3, 7^1-, 8^1-, 12^1-, 18^1-CH_3), 1.84−1.79 (3H, m, 17^1-CH_3), −2.77, −3.65/−3.44 (each 1H, br-s, NH × 2); HRMS (FAB) *m*/*z* 532.3203 (M^+), calcd for $C_{35}H_{40}N_4O$ 532.3202.

Synthesis of 2- and 3-Formyl-12,13-dihydroxychlorins 9. To a 2:1 mixture of 2- and 3-formylporphyrins **8** (22.2 mg, 42 μmol) in dichloromethane (30 mL) was added a pyridine solution (2 mL) of OsO_4 (13.9 mg, 55 μmol) and the mixture stirred for 1 day under nitrogen. After bubbling of H_2S, the resulting OsS_4 was removed by filtration on Celite. The filtrate was evaporated to dryness, and the residue was purified with FCC (3−5% Et_2O−dichloromethane) to give a 2:1 mixture of 2-formyl-**9** and 3-formyl-**9** as a dark red solid (17.2 mg, 72%): VIS (CH_2Cl_2) 645 (relative intensity, 0.11), 589 (0.07), 563 (0.07), 520 (0.06), 424 nm (1.0); ^{1}H NMR ($CDCl_3$, 2-formyl-**9**/3-formyl-**9** = 2/1) δ = 10.60/10.67 (1H, s, 2/3-CHO), 9.84/9.39, 9.38/9.85 (each 1H, s, 5-, 20-H), 8.90/8.84 (1H, s, 10-H), 5.01−4.91, 4.77−4.71 (each 1H, m, 13^1-CH_2), 4.60/4.58, 3.40−3.00 (each 1H, br + br, 12-, 13-OH), 3.92−3.57 (10H, m, 3/2-, 7-, 8-, 17-, 18-CH_2), 3.23−3.16, 2.87−2.79 (each 1H, m, 13-CH_2), 2.28−2.18, 2.16−2.08 (each 1H, m, 12-CH_2), 1.86−1.61 (15H, m, 3^1/2^1-, 7^1-, 8^1-, 17^1-, 18^1-CH_3), 0.91/0.89 (3H, m, 12^1-CH_3), −1.31/−1.41, −2.10/−1.74 (each 1H, br-s, NH×2); HRMS (FAB) *m*/*z* 566.3245 (M^+), calcd for $C_{35}H_{42}N_4O_3$ 566.3257.

Synthesis of 2- and 3-Formyl-13^1-hydroxyporphyrins 10. To a 2:1 mixture of 2-formyl-**9** and 3-formyl-**9** (17.2 mg, 30 μmol) in 1,4-dioxane (20 mL) was added aqueous 10% HCl (4 mL) and the mixture stirred for 1.5 h under nitrogen. The organic mixture was poured into water and extracted with dichloromethane twice. The organic phase was washed with water twice, dried over Na_2SO_4, and evaporated to dryness. The residue was purified on FCC (1% Et_2O−dichloromethane) and recrystallized (dichloromethane−hexane) to give a 2:1 mixture of 2-formyl-**10** and 3-formyl-**10** as a red solid (10.4 mg, 64%): VIS (CH_2Cl_2) 632 (relative intensity, 0.02), 579 (0.06), 561 (0.07), 519 (0.05), 416 nm (1.0); ^{1}H NMR ($CDCl_3$, 2-formyl-**10**/3-formyl-**10** = 2/1) δ = 11.46 (1H, s, 2/3-CHO), 11.03/10.12, 10.13/11.01 (each 1H, s, 5-, 20-H), 10.02/9.98 (1H, s, 10-H), 6.49, 5.96−5.88, 5.27−5.20 (each 1H, m, 13-CH, 13^1-CH_2), 4.45−4.38 (2H, m, 3/2-CH_2), 4.26−4.08 (8H, m, 7-, 8-, 12-, 18-CH_2), 4.08−4.00 (2H, m, 17-CH_2), 2.58−2.51 (1H, br, 13^1-OH), 2.09−2.05, 2.00−1.90 (3H+12H, m, 3^1/2^1-, 7^1-, 8^1-, 12^1-, 18^1-CH_3), 1.83−1.79 (3H, m, 17^1-CH_3), −2.82/−2.85, −3.77/−3.58 (each 1H, br-s, NH × 2); MS (FAB) *m*/*z* 548 (M^+), calcd for $C_{35}H_{40}N_4O_2$ 548.

Synthesis of 2,3-Dihydroxy-13^1-oxochlorin 16. Similarly to **8** → **9**, 13^1-oxoporphyrin **15**[19] (38.6 mg, 71 μmol) was dihydroxylated to give the titled compound **16** as a dark red solid (29.1 mg, 71%) after FCC (dichloromethane): VIS (CH_2Cl_2) 628 (relative intensity, 0.10), 579 (0.10), 544 (0.07), 441 (0.49), 419 nm (1.0); ^{1}H NMR ($CDCl_3$) δ = 9.07 (1H, s, 10-H), 8.94 (1H, s, 5-H), 8.78 (1H, s, 20-H), 4.77, 4.69 (each 1H, s, 2-, 3-OH), 4.19, 2.78−2.65 (each 1H, d and br, *J* = 19 Hz, 13^1-CH_2), 3.90 (4H, q, *J* = 8 Hz, 7-, 8-CH_2), 3.88, 3.60 (each 1H, dq, *J* = 15, 8 Hz, 18-CH_2), 3.40−3.31, 3.20−3.09 (each 1H, m, 12-CH_2), 3.07−2.98, 2.50−2.38 (each 1H, m, 17-CH_2), 2.67, 2.66 (each 1H, dq, *J* = 15, 7 Hz, 3-CH_2), 2.60, 2.56 (each 1H, dq, *J* = 15, 7 Hz, 2-CH_2), 1.86 (6H, t, *J* = 8 Hz, 7^1-, 8^1-CH_3), 1.70 (3H, t, *J* = 8 Hz, 18^1-CH_3), 1.46 (3H, t, *J* = 8 Hz, 12^1-CH_3), 1.14 (6H, t, *J* = 7 Hz, 3^1-, 17^1-CH_3), 1.03 (3H, t, *J* = 8 Hz, 2^1-CH_3), −0.79, −2.37 (each 1H, s, NH × 2); HRMS (FAB) *m*/*z* 580.3409 (M^+), calcd for $C_{36}H_{44}N_4O_3$ 580.3413.

Synthesis of 2- and 3-Vinyl-13^1-oxoporphyrins 17. Similarly to **5** → **7**, **16** (29.1 mg, 50 μmol) was doubly dehydrated to give a 1:1 mixture of 2-vinyl-**17** and 3-vinyl-**17** as a purple solid (19.9 mg, 73%) after FCC (dichloromethane) and recrystallization (dichloromethane−methanol): VIS (CH_2Cl_2) 639 (relative intensity, 0.02), 591 (0.08), 567 (0.10), 526 (0.05), 419 nm (1.0); ^{1}H NMR ($CDCl_3$, 1/1) δ = 10.15_0/10.14_6 (1H, s, 10-H), 10.09/10.03, 9.98/9.92 (each 1H, s, 5-, 20-H), 8.19−8.11 (1H, m, 2/3-CH═), 6.31−6.26, 6.17−6.04 (each 1H, m, 2/3-C═CH_2), 5.92/5.90 (2H, s, 13^1-CH_2), 4.33 (2H, m, 12-CH_2), 4.17−4.02 (8H, m, 3/2-, 7-, 8-, 18-CH_2), 4.00−3.92 (2H, m, 17-CH_2), 2.08 (3H, m, 12^1-CH_3), 1.96−1.87 (12H, m, 3^1/2^1-, 7^1-, 8^1-, 18^1-CH_3), 1.80−1.74 (3H, m, 17^1-CH_3), −2.48, −3.42 (each 1H, s, NH × 2); HRMS (FAB) *m*/*z* 544.3211 (M^+), calcd for $C_{36}H_{40}N_4O$ 544.3202.

Synthesis of 2- and 3-Formyl-13^1-oxoporphyrins 11. By Oxidation of 10 to 11a. To a 2:1 mixture of 2-formyl-**10** and 3-formyl-**10** (10.4 mg, 19 μmol) in dichloromethane (15 mL) was added NMO (34.6 mg, 0.30 mmol) and the mixture stirred under nitrogen. After 5 min of stirring, tetrapropylammonium perruthenate (10.3 mg, 29 μmol) was added to the solution and further stirred for 2 h under nitrogen. The reaction mixture was directly purified by FCC (dichloromethane) and then recrystallized (dichloromethane−methanol) to give a 2:1 mixture of 2-formyl-**11a** and 3-formyl-**11a** as a dark green solid (**11a**, 8.1 mg, 78%).

By Oxidation of 17 to 11b. Similarly to **7** → **8**, the 2- and 3-vinyl groups in **17** (a 1:1 mixture, 19.9 mg, 37 μmol) were oxidatively cleaved to the 2- and 3-formyl groups to give a 1:1 mixture of 2-formyl-**11b** and 3-formyl-**11b** as a dark green solid (**11b**, 13.3 mg, 67%) after FCC (dichloromethane) and recrystallization (dichloromethane−methanol): VIS (CH_2Cl_2) 653 (relative intensity, 0.04), 603 (0.08), 578 (0.11), 531 (0.04), 423 nm (1.0); ^{1}H NMR ($CDCl_3$, 1/1) δ = 11.40/11.38 (1H, s, 2/3-CHO), 10.85/9.91 (1H, s, 5-H), 10.67/9.73 (1H, s, 20-H), 9.95/9.89 (1H, s, 10-H), 5.60/5.54 (2H, s, 13^1-CH_2), 4.33/4.29 (2H, q, *J* = 8 Hz, 3/2-CH_2), 4.25−4.18 (2H, m, 12-CH_2), 4.13−4.00 (4H, m, 7-, 8-CH_2), 3.96−3.88 (2H, m, 18-CH_2), 3.75/3.66 (2H, q, *J* = 8 Hz, 17-CH_2), 2.04−1.87 (12H, m, 3^1/2^1-, 7^1-, 8^1-, 12^1-CH_3), 1.82/1.81

(3H, t, $J = 8$ Hz, 18^1-CH_3), 1.66/1.62 (3H, t, $J = 8$ Hz, 17^1-CH_3), −3.07/−3.17, −4.15/−4.30 (each 1H, s, NH × 2); HRMS (FAB) m/z 546.3003 (M^+), calcd for $C_{35}H_{38}N_4O_2$ 546.2995

Synthesis of 2- and 3-Hydroxymethyl-13^1-oxoporphyrins 18. To a 1:1 mixture of 2-formyl-**11** and 3-formyl-**11** (**11b**, 13.3 mg, 24 μmol) in dichloromethane (15 mL) was added tBuNH$_2\cdot$BH$_3$ (56 mg, 0.66 mmol) and the mixture stirred for 3 h under nitrogen. The reaction mixture was poured into aq 2% HCl, extracted with dichloromethane, washed with water, dried over Na_2SO_4, and evaporated to dryness. The residue was purified on FCC (5% Et_2O−dichloromethane) and recrystallized (dichloromethane−hexane) to give a 1:1 mixture of 2-hydroxymethyl-**18** and 3-hydroxymethyl-**18** as a dark green solid (**18b**, 11.0 mg, 83%): VIS (CH_2Cl_2) 639 (relative intensity, 0.02), 589 (0.06), 566 (0.08), 524 (0.04), 418 nm (1.0); ^{1}H NMR ($CDCl_3$, 1/1) δ = 10.17/9.88 (1H, s, 5-H), 10.02/10.00 (1H, s, 10-H), 9.86/9.65 (1H, s, 20-H), 6.05/6.01 (2H, s, 2/3-CH_2), 5.25/4.73 (2H, s, 13^1-CH_2), 4.33−4.07 (8H, m, 3/2-, 7-, 8-, 12-CH_2), 3.79/3.75 (2H, q, $J = 8$ Hz, 18-CH_2), 3.37/2.85 (2H, br, 17-CH_2), 2.93/2.76 (1H, br-s, 2^1/3^1-OH), 2.03−1.87 (12H, m, 3^1/2^1-, 7^1-, 8^1-, 12^1-CH_3), 1.75/1.67 (3H, t, $J = 8$ Hz, 18^1-CH_3), 1.49/1.30 (3H, t, $J = 8$ Hz, 17^1-CH_3), −2.96/-3.05, −4.41/-4.61 (each 1H, s, NH × 2); MS (FAB) m/z 548 (M^+), calcd for $C_{35}H_{40}N_4O_2$ 548.

Synthesis of Zinc 2- and 3-Hydroxymethyl-13^1-oxoporphyrins 2 and 3. To a 1:1 regioisomeric mixture of **18** (**18b**, 7.5 mg, 12 μmol) in dichloromethane (20 mL) was added a methanol solution (3 mL) saturated with $Zn(OAc)_2$ and the mixture stirred for 3 h under nitrogen. The organic mixture was poured into aq 4% $NaHCO_3$, extracted with 2% v/v pyridine and dichloromethane, washed with water, dried over Na_2SO_4, and evaporated to dryness. Normal-phase HPLC separation (Cosmosil 5SLII, 10 $\phi \times 250$ mm, 1% v/v pyridine−1,2-dichloroethane, 2 mL/min) gave regioisomerically pure **3** (18.5 min) and **2** (20.9 min). Recrystallization from 1% v/v pyridine−chloroform and hexane gave analytically pure samples as a green powder in quantitative yield.

2: VIS (THF) 608 (relative intensity, 0.13), 560 (0.05), 428 nm (1.0); ^{1}H NMR (3% pyridine-d_5−$CDCl_3$) δ = 10.06 (1H, s, 10-H), 9.95 (1H, s, 20-H), 9.78 (1H, s, 5-H), 6.07 (2H, s, 2-CH_2), 5.88 (2H, s, 13^1-CH_2), 4.35 (2H, q, $J = 8$ Hz, 12-CH_2), 4.09 (2H, q, $J = 8$ Hz, 3-CH_2), 4.01 (2H, q, $J = 8$ Hz, 8-CH_2), 3.97 (2H, q, $J = 8$ Hz, 7-CH_2), 3.94 (2H, q, $J = 8$ Hz, 18-CH_2), 3.84 (2H, q, $J = 8$ Hz, 17-CH_2), 2.08 (3H, t, $J = 8$ Hz, 12^1-CH_3), 1.90 (3H, t, $J = 8$ Hz, 8^1-CH_3), 1.88 (3H, t, $J = 8$ Hz, 3^1-CH_3), 1.87 (3H, t, $J = 8$ Hz, 7^1-CH_3), 1.84 (3H, t, $J = 8$ Hz, 18^1-CH_3), 1.72 (3H, t, $J = 8$ Hz, 17^1-CH_3); HRMS (FAB) m/z 610.2290 (M^+), calcd for $C_{35}H_{38}N_4O_2{}^{64}Zn$ 610.2286.

3: VIS (THF) 608 (relative intensity, 0.13), 560 (0.05), 428 nm (1.0); ^{1}H NMR (3% pyridine-d_5−$CDCl_3$) δ = 10.04 (1H, s, 10-H), 9.94 (1H, s, 5-H), 9.80 (1H, s, 20-H), 6.06 (2H, s, 3-CH_2), 5.92 (2H, s, 13^1-CH_2), 4.34 (2H, q, $J = 8$ Hz, 12-CH_2), 4.09 (2H, q, $J = 8$ Hz, 2-CH_2), 3.98 (2H+2H, q, $J = 8$ Hz, 8-, 18-CH_2), 3.94 (2H, q, $J = 8$ Hz, 7-CH_2), 3.89 (2H, q, $J = 8$ Hz, 17-CH_2), 2.09 (3H, t, $J = 8$ Hz, 12^1-CH_3), 1.88_2, 1.87_9 (each 3H, t, $J = 8$ Hz, 2^1-, 18^1-CH_3), 1.87 (3H, t, $J = 8$ Hz, 8^1-CH_3), 1.83 (3H, t, $J = 8$ Hz, 7^1-CH_3), 1.75 (3H, t, $J = 8$ Hz, 17^1-CH_3); HRMS (FAB) m/z 610.2289 (M^+), calcd for $C_{35}H_{38}N_4O_2{}^{64}Zn$ 610.2286.

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Supporting Information Available: HPLC chromatograms of **2** and **3**. Structural determination of **2** and **3** by 1D and 2D ^{1}H NMR spectra and the schematic representation for their selected 2D ^{1}H correlations. UV−vis spectra of **1** and **19** in films. 1D and 2D ^{1}H NMR spectra of synthetic compounds. This material is available free of charge via the Internet at http://pubs.acs.org.