Facile Synthesis of Self-aggregative Zinc Bacteriochlorins by Modifying Naturally Occurring Chlorophyll-*a*

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We prepared zinc 7,8-*cis*-dihydroxy-3-hydroxymethyl-13^1-oxo-bacteriochlorin **1** by modifying naturally occurring chlorophyll-*a* and examined its self-aggregation mimicking self-aggregates of natural bacteriochlorophylls-*c*/*d*/*e* in the main light-harvesting antenna system of green photosynthetic bacteria. Bacteriochlorin **1** has interactive hydroxy groups not only at the 3^1-position but also at the 7,8-positions, and the latter two hydroxy groups did not disturb its self-aggregation process.

It is well known that the presence of 3^1-hydroxy and 13^1-oxo groups and a central axial-coordinative metal on a cyclic tetrapyrrole induces self-aggregation of the dye molecules, similarly to the self-aggregates of naturally occurring bacteriochlorophyll(BChl)s-*c*/*d*/*e* (see molecular structures of left in Figure 1) in the main light-harvesting antenna system of green photosynthetic bacteria (called chlorosomes).[1] For such a chlorosomal self-aggregation, the presence of the above three moieties situated along the Qy axis in a cyclic tetrapyrrole (a line between N21 and N23 in Figure 1) is important. Recently, some reports demonstrated that a bacteriochlorin π-conjugate system (both C7–C8 and C17–C18 single bonds, typically **2** at the right in Figure 1) was acceptable for making chlorosomal self-aggregation, as true of the chlorin π system (C7=C8 and C17–C18, as in BChls of Figure 1).[2] Change of the double to single C7–C8 bond greatly affects the optical properties of self-aggregates as well as monomers: the longest-wavelength absorption band (Qy band) of bacteriochlorin self-aggregates was situated around the near-infrared region. Thus, chlorosomal self-aggregation of bacteriochlorin molecules was interesting, but most of their starting materials were limited to natural BChl-*a* possessing a bacteriochlorin π-conjugate system, which was obtained from cultured purple photosynthetic bacteria. Methyl 7,8-*cis*-dihydroxy-pyropheophorbide-*d* (**3**, see Scheme S1 in Supporting Information (SI)),[3] easily available from naturally occurring chlorophyll(Chl)-*a*, has a bacteriochlorin π system and is, therefore, suitable as a starting material of such a self-aggregative bacteriochlorin. Here, we report synthesis of zinc 7,8-*cis*-dihydroxy-3-hydroxymethyl-13^1-oxo-bacteriochlorin **1** (see center drawing in Figure 1) and its self-aggregation in aqueous micellar solutions.

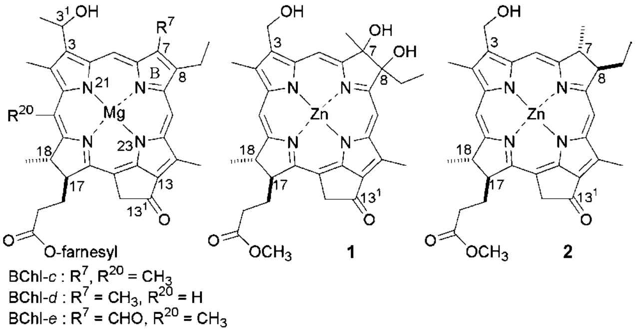

Figure 1. Molecular structures of chlorosomal BChls (left), 7,8-*cis*-dihydroxy-**1** (center) and 7,8-*trans*-dihydro-**2** (right).

Table 1. Electronic absorption maxima (λ_{max}/nm) of **1** (a 6:5 mixture of **1a** and **1b**), **1a**, **1b** and **2** in THF and aqueous TX-100 solution, and red-shift values (Δ/cm^{-1}) of Qy band by self-aggregation

Compound	λ_{max} in THF (in aq. 0.025v/v% TX-100)			Δ
	Soret	Qx	Qy	
1	349, 384 (390)	551 (560)	721 (878)	2480
1a	349, 384 (390)	551 (555)	721 (931)	3130
1b	349, 384 (385)	552 (559)	723 (893)	2630
2	346, 386 (369)	548 (558)	727 (860)	2130

Self-aggregative zinc bacteriochlorin **1** was synthesized according to Scheme S1.[3] 3-Formyl-7,8-*cis*-dihyroxy-bacteriochlorin **3** (a 5:6 mixture of 7*R*,8*S*/7*S*,8*R*-diols) was prepared from Chl-*a* according to the reported procedure.[4] The resulting free base **3** was refluxed in chloroform–pyridine solution (6:1) of zinc acetate, affording the corresponding zinc complex **4** in 85% yield. Selectively, the 3-formyl group in **4** was reduced by sodium borohydride to give desired **1** (a 5:6 stereochemical mixture of 7,8-*cis*-diols) in 75% yield, in which even an excess amount of the reductant could not reduce the 13^1-oxo group, confirming the previous reports.[2a,5] Molecular structures of synthetic compounds were determined by ^1H, $^1H–^1H$ COSY/NOESY NMR, and FAB-MS spectra.

The electronic absorption spectrum of **1** in neat THF showed sharp absorption bands, characteristic of a bacteriochlorin π system: Soret, Qx, and Qy bands from blue to red (solid line in Figure 2 upper). The 7,8-*cis*-dihydroxy moiety in **1** did not affect the electronic absorption spectrum because the absorption maxima of **1** in THF were nearly equal to those of zinc methyl 3-hydroxymethyl-bacteriopyropheophorbide-*a* (**2**)[2c] synthesized recently (Table 1). The circular dichroism (CD) spectrum of **1** (solid line in Figure 2 lower with left scale) showed weak signals in the regions of the three electronic absorption bands. The above results indicated that **1** was monomeric in THF. When a THF solution of **1** containing Triton X-100 (a nonionic surfactant, TX-100) was diluted with water (the final concentrations of THF and TX-100 were 1.0 and 0.025 v/v%), the solution was changed from purple to dark blue. Electronic and CD absorption spectra of **1** in the aqueous solution (dotted lines in Figure 2) showed significant differences from those of monomeric **1** in THF. The electronic absorption spectrum of **1** in the aqueous solution (dotted line in Figure 2 upper) was broadened and showed a large red shift in the Qy band (721 to 878 nm),

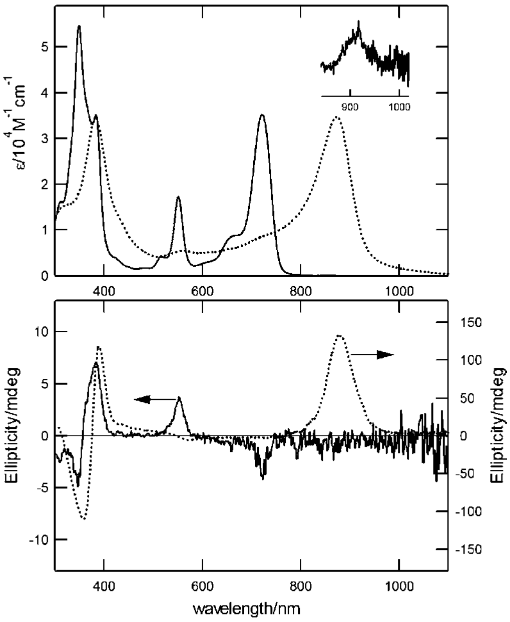

Figure 2. Electronic (upper) and CD absorption spectra (lower) of **1** in THF (solid) and 0.025 v/v% aqueous TX-100 solution (dotted). Inset of the upper figure shows fluorescent emission spectrum of **1** in 0.025 v/v% aq. TX-100 excited at 390 nm.

similar to the self-aggregation of **2** (727 to 860 nm, Table 1). CD spectrum of **1** in the aqueous solution (dotted line in Figure 2 lower with right scale) showed intense CD signals around the newly appeared absorption peak positions, which were characteristic of strong π–π interactions in well-ordered supramolecules.[6] These mean that **1** self-aggregated in the aqueous micellar solution to form chlorosome-like oligomers as did natural BChls[1a,1b,7] and synthetic models.[6,8] The red-shift value (Δ) by self-aggregation of **1** in the solution was 2480 cm^{-1}, which was larger than that of 7,8-*trans*-dihydro-form **2** (2130 cm^{-1}). Typically, Δs of Qy band by self-aggregation of bacteriochlorins are larger (2000–2500 cm^{-1})[2] than those of chlorins (1000–2000 cm^{-1}),[8] so that the present observed value ($\Delta = 2480$ cm^{-1}) was acceptable. Despite the presence of two additional hydroxy groups at the 7,8-positions on the B ring, chlorosomal self-aggregation of **1** occurred and the exciton couplings among the composite molecules in the supramolecule were stronger than those of **2**, as observed by the larger Δ value (2130 → 2480 cm^{-1}). The fluorescent emission peak in oligomeric **1** (inset in Figure 2 upper) was observed at around 910 nm, indicating the potential for use of the photoactive nanodevice driving in near-infrared region.

Electronic and CD absorption spectra of 7,8-stereochemically pure forms of **1** were also examined. The stereoisomers of zinc bacteriochlorin **4** were easily separated on preparative reverse-phase HPLC (pyridine/H_2O/MeOH = 1/9/90) to give the first (**4a**) and second elutions (**4b**), respectively, whose diastereomeric ratio was 6:5. 3-Formyl-bacteriochlorins **4a** and **4b** were reduced to stereochemically pure **1a** and **1b** (vide supra); their stereochemistry could not be determined from NMR spectral analyses. Electronic and CD absorption spectra of **1a** and **1b** in THF showed small differences; Soret, Qx and Qy absorption maxima in **1b** were shifted to a slightly longer wavelength than those of **1a**, in which a difference in the Qy maxima of **1a** and **1b** was denoted (see Table 1). Similar spectral difference was observed between 3-formyl-**4a** and **4b** (see spectral data in SI),[3] indicating that these differences were induced from the different 7,8-configurations. In an aqueous 0.025 v/v% TX-100 solution, electronic and CD absorption spectra of **1a** and **1b** (see Figure S1)[3] showed red-shifted Qy absorption bands with intense induced CD signals, similar to its 6:5 mixture as described above, indicating that both **1a** and **1b** formed chlorosomal self-aggregation in the aqueous micellar solution. The Qy absorption maximum of self-aggregated **1a** was situated at 931 nm and the Δ value was 3130 cm^{-1}, which is the largest value in the chlorosomal self-aggregation.

The present zinc bacteriochlorin **1** has two additional hydroxy groups on the B ring, which have potential to disturb chlorosomal self-aggregation by forming coordination and hydrogen bonding with a zinc atom and/or 13-C=O moiety of another molecule, respectively. From X-ray crystallographic data reported previously,[9] β,β'-*cis*-dihydroxy groups on a cyclic tetrapyrrole caused hydrogen bonding between both the intra- and intermolecules in the crystal packages. The large red-shift values of Qy band by self-aggregation of the present zinc bacteriochlorins **1** are distinct proof of the strong π–π interactions among the well-ordered Qy dipole moments in the supramolecule, so that the 7,8-*cis*-dihydroxy moieties in **1** did not disturb the self-aggregation but strengthened the π–π stacking through any intermolecular interaction of the 7,8-substituents.[1b] The sterically less-hindered primary 3^1-OH exclusively coordinated with a zinc atom of another molecule rather than the secondary 7- and 8-OH groups on the B ring.

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3 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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