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J-Aggregation of Zinc 3^1,13^1-Dihydroxychlorins by Exclusive Coordination Bonding between 3^1-Hydroxy Group and Central Zinc Atom

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Zinc 3^1,13^1-dihydroxychlorin lacking an exo-five-membered E-ring was prepared as a model of natural bacteriochlorophyll-*d* possessing 3^1-OH and 13-C=O groups. The synthetic zinc complex has the 13-CH_2OH instead of the 13-C=O and self-aggregated in a nonpolar organic solvent, giving slipped and π-overlapped molecular stackings (J-aggregates) with red-shifted and broadened electronic absorption bands. For the intermolecular interactions among the J-aggregates, coordination bonding of the 3^1-OH (not 13^1-OH) with the central Zn was utilized.

We have reported a series of synthetic chlorophyllous pigments which have potential to form J-aggregates by intermolecular coordination (3^1-O···M), hydrogen bonding (3^1-O–H···O=C-13), and π–π stacking of their cyclic tetrapyrrolic π-systems.[1–3] Molecular structures of the self-aggregative chlorophylls were designed from natural bacteriochlorophyll(BChl)s-*c*/*d*/*e* possessing 3^1-OH, central coordinative Mg and 13-C=O moieties in a straight (*y* axis) line (see upper of Figure 1 for BChls-*c* and -*d*), which self-aggregated to form excitonically well-delocalized J-aggregates in the light-harvesting antenna systems (chlorosomes) of green photosynthetic bacteria by use of the above intermolecular connections. Structural requirements for such chlorosomal J-aggregation are the above three moieties on a tetrapyrrolic macrocycle in the *y* axis, and these characters were present in a simple and stable model **1** (lower left of Figure 1).[4]

Removal of one of them resulted in no formation of J-aggregates,[4] but slight chemical modifications were acceptable. Substitution of the 3-C–OH with 3-C=O (CHO or $COCH_3$) led to little chlorosomal J-aggregation,[5] but zinc 3-methoxymethyl-chlorin was useful for chlorosomal J-aggregation because the oxygen atom of the methoxy group could coordinate to the central zinc of another molecule as did the hydroxy group in BChls and **1**.[6,7]

For another interaction site, the 13-keto-C=O group, various chemical modifications have been reported and have shown that ester,[8,9] imide,[10] anhydride,[9,10] and formyl groups,[11] all of which have the conjugated C=O group, could be alternatives to the original keto group for making J-aggregates. As mentioned above, removal of the 13-C=O group in zinc chlorin as in **2** (lower left of Figure 1) did not show any aggregated species in a nonpolar organic solvent, because the 13^1-oxo group connected the stepwise linear aggregates up to three-dimensional by a hydrogen-bonding network. As an alternative hydrogen bonding acceptor, the oxygen atom of the 13^1-OH had been preliminarily examined by Smith and his colleagues;[12] conversion of Mg to Zn and reduction of the 13-C=O group in the extracted BChls-*c* gave 3^1,13^1-epimeric and 8,12-homologous mixtures of Zn–13-CHOH-BChls-*c* which still showed similar J-aggregated species. However, self-aggregation of structurally confirmed model compounds possessing the 3^1,13^1-dihydroxy groups had not yet been examined in detail. Here we report self-aggregation properties of synthetic zinc 3^1,13^1-dihydroxychlorins **3** and **4** (lower of Figure 1) in a nonpolar organic solvent and clarify which OH group in dihydroxychlorins was useful for the coordination with the central Zn in a supramolecule.

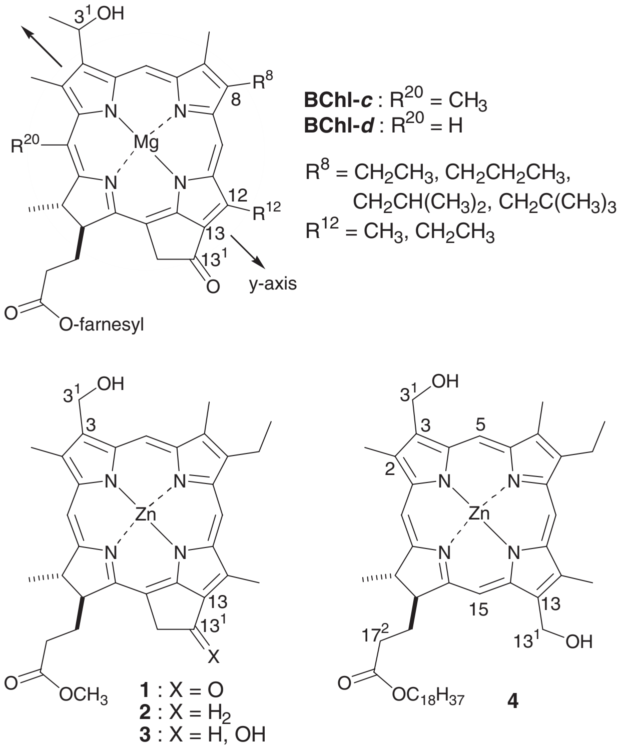

Figure 1. Molecular structures of natural BChls-*c* and -*d*, and synthetic zinc chlorins **1**–**4**.

First, we examined the self-aggregation behavior of 13^1-OH-chlorin **3** possessing the E-ring, which was easily prepared by reduction of the 13-C=O group in **1** with $NaBH_4$.[13] UV–vis and CD spectra of **3** were measured in polar (THF) and nonpolar (1% v/v CH_2Cl_2/hexane) organic solvents. A THF solution of **3** showed two intense absorption bands at 408 and 620 nm as Soret and Q_y maxima (dotted line in Figure 2A) and showed small positive and negative CD signals at the Soret and Q_y regions (dotted line in Figure 2B), indicating **3** to be monomeric. In contrast, **3** in 1% v/v CH_2Cl_2/hexane gave Soret and Q_y absorption bands at 445 and 667 nm (solid line in Figure 2A), which were shifted to a longer wavelength region than residual

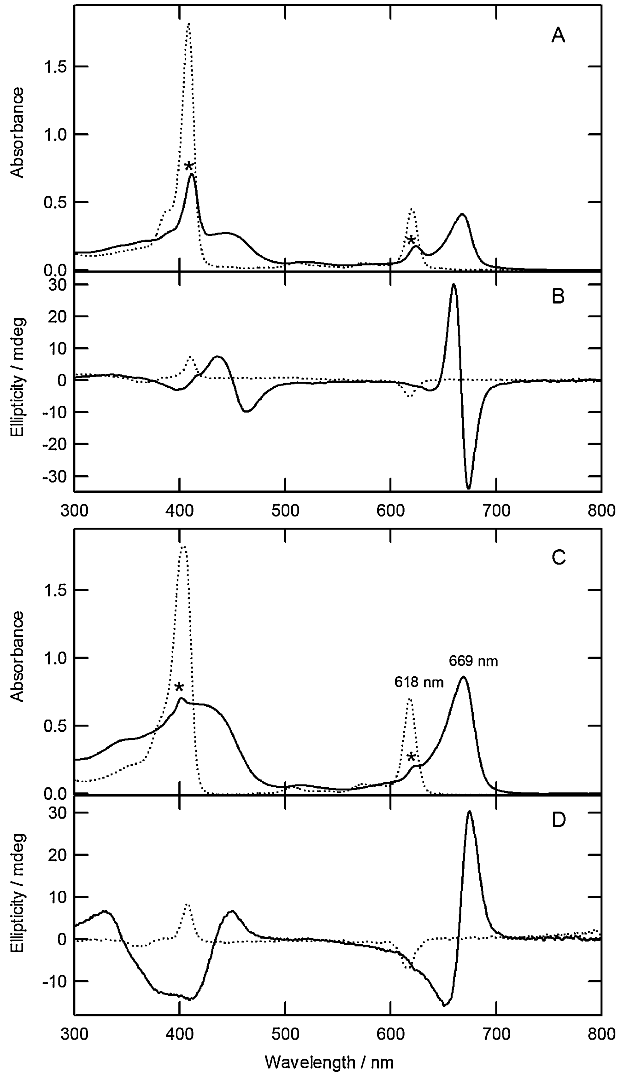

Figure 2. UV–vis (A/C) and CD spectra (B/D) of **3**/**4** (upper/lower) in THF (dotted lines) and 1% v/v CH_2Cl_2/hexane (solid lines). Asterisks in A/C indicate absorption bands derived from the residual monomeric species. Concentrations of all the samples were ca. 10 µM.

monomeric peaks (* shown in Figure 2A). Intense CD signals around the newly appeared peaks, a typical sign of the strong exciton coupling, were also observed (solid line in Figure 2B), showing that Zn–3^1,13^1-OH-**3** self-aggregated in the hydrophobic environment in a J-aggregated fashion. Red-shift values by self-aggregation of **1** and **3** were 2000 and 1140 cm^{-1}, respectively, suggesting that aggregation number in the supramolecule of **3** would be less than that of **1**.

Zn–3^1,13^1-OH-**4** was prepared in a similar manner to the synthesis of the corresponding methyl ester;[11] the methyl ester in 3,13-diformylchlorin was transesterified[14,15] to the corresponding octadecyl ester, and reduction of both the 3,13-diformyl groups with $NaBH_4$ followed by zinc insertion afforded zinc complex **4**.[16] Introduction of a longer oligomethylene chain increased the solubility of synthetic chlorophylls,[17,18] whose self-aggregates were successfully examined by solution-state ^{1}H NMR spectroscopy.

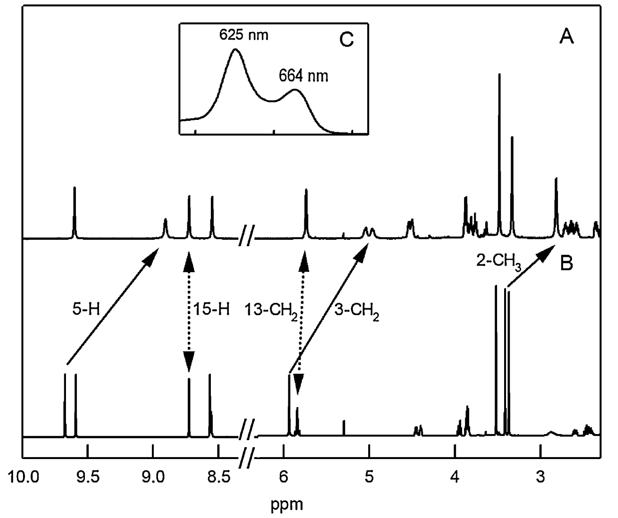

Figure 3. ^{1}H NMR spectra of **4** in $CDCl_3$ (A) and 3% v/v pyridine-d_5/$CDCl_3$ (B). Inset (C) showed UV–vis spectrum of **4** in $CDCl_3$ measured with 0.1-mm cell. Concentrations of all the samples were ca. 5 mM.

UV–vis and CD spectra of **4** in THF (a blue-colored solution) were characteristic of monomeric zinc chlorin (dotted lines in Figures 2C and 2D): Soret and Q_y bands at 404 and 618 nm with small positive and negative CD bands. UV–vis and CD spectra of **4** in nonpolar organic solvent (a green-colored solution) showed red-shifted and broadened Soret/Q_y bands and intense CD couplets (solid lines in Figures 2C and 2D), ascribable to J-aggregation of **4**. The red-shift value of Q_y maximum by self-aggregation of **4** was 1230 cm^{-1}, which was comparable to that of **3**.

^{1}H NMR spectra of **4** in $CDCl_3$ and 3% v/v pyridine-d_5/$CDCl_3$ (5 mM) were measured to confirm how a composite molecule associated with another molecule in a supramolecule (Figure 3). The colors of the former and latter solutions were green and blue, respectively, indicating that zinc chlorin **4** could intermolecularly interact in the concentrated $CDCl_3$ without pyridine-d_5 and that addition of 3% v/v pyridine-d_5 changed **4** to monomeric as in THF. UV–vis spectrum of **4** in $CDCl_3$ gave two Q_y bands at 625 and 664 nm (Figure 3C), whose positions were due to the monomer and oligomer as shown in Figure 2C. The ^{1}H NMR spectrum of **4** in 3% v/v pyridine-d_5/$CDCl_3$ (Figure 3B) was characteristic of a monomeric zinc complex: four *meso*-protons (5,10,15,20-H) appeared at a low field (8.5–10 ppm) and two CH_2OH were obtained at 5.9 and 5.8 ppm. Compared to the monomeric spectrum, high-field shifts were observed in the signals (near the 3^1-position) of **4** in $CDCl_3$ (Figure 3A): 5-H (9.7 → 8.9 ppm), 3-CH_2 (5.9 → 5.0 ppm), and 2-CH_3 (3.4 → 2.8 ppm) (three solid arrows in Figure 3). These shifts were ascribable to intermolecular overlapping of these protons over another chlorin π-system through 3^1-O···Zn coordination. Minimal shifts were observed at around the 13-CH_2OH (dotted arrows in Figure 3). Two proton signals of 3-CH_2 of **4** in $CDCl_3$ (5 ppm in Figure 3A) were not equivalent, indicating that the rotation around the C3–C3^1 was restricted, probably because of coordination bonding between 3^1-OH and Zn. Two Q_y bands were observed in the UV–vis spectrum as described above, but ^{1}H NMR spectrum of the solution afforded a single species, showing that the equilibrium between association (to oligomer) and dissociation (to monomer) occurred rapidly in solution. These results clearly indicated that the 3^1-OH group in **4** exclusively coordinated to a central Zn atom of another molecule in the aggregates: coordination ability of the 13-CH_2OH group was less than that of the 3-CH_2OH. Zn–3^1-OH-13^1-H_2-chlorin **2** gave no J-aggregated species, suggesting that the 13^1-OH in **4** (**3**) was significantly important and should intermolecularly interact.

To clarify the reason why the 13^1-OH in **4** could not coordinate, FT-IR spectroscopy was examined. The FT-IR spectrum of **4** in THF gave 17^2-C=O stretching at 1736 cm^{-1}, but that in $CDCl_3$ (5 mM) showed a 17^2-C=O signal at 1723 cm^{-1}, which was down-shifted by 13 cm^{-1}. The shift was ascribed to intramolecular hydrogen bonding between the 17^2-C=O with 13^1-OH, which had been observed in Zn–3-C=O-13^1-OH-chlorin in a previous report.[11]

In conclusion, Zn–3^1,13^1-OH-chlorins **3** and **4** self-aggregated in a nonpolar organic solvent, similarly to Zn–3^1-OH-13-C=O-chlorin **1**. Self-aggregates of **3** possessing secondary 13^1-OH showed a large amount of the residual monomeric species, due to its steric hindrance and inflexibility. Compound **4** possessing two primary alcoholic OH groups self-aggregated more stably, and a clear distinction was observed between the roles of 3^1- and 13^1-OH groups; intermolecular coordination bonding was preferentially formed by 3^1-OH and Zn, and intramolecular hydrogen bonding of 13^1-OH with 17^2-C=O was favorable. Additional intermolecular hydrogen bonding of 13^1-O with 3^1-OH and/or 13^1-OH with 3^1-O was necessary for chlorosomal J-aggregation.

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References and Notes

1 T. Miyatake, H. Tamiaki, *J. Photochem. Photobiol., C* **2005**, *6*, 89.

2 H. Tamiaki, R. Shibata, T. Mizoguchi, *Photochem. Photobiol.* **2007**, *83*, 152.

3 H. Tamiaki, Y. Kotegawa, S. Nitta, S. Sasaki, K. Mizutani, *Tetrahedron* **2009**, *65*, 628.

4 H. Tamiaki, M. Amakawa, Y. Shimono, R. Tanikaga, A. R. Holzwarth, K. Schaffner, *Photochem. Photobiol.* **1996**, *63*, 92.

5 H. Tamiaki, T. Miyatake, R. Tanikaga, *Tetrahedron Lett.* **1997**, *38*, 267.

6 T. Miyatake, S. Tanigawa, S. Kato, H. Tamiaki, *Tetrahedron Lett.* **2007**, *48*, 2251.

7 S. Ganapathy, S. Sengupta, P. K. Wawrzyniak, V. Huber, F. Buda, U. Baumeister, F. Würthner, H. J. M. de Groot, *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 11472.

8 M. Kunieda, H. Tamiaki, *Eur. J. Org. Chem.* **2006**, 2352.

9 H. Tamiaki, H. Yoshimura, Y. Shimamura, M. Kunieda, *Photosynth. Res.* **2008**, *95*, 223.

10 H. Tamiaki, Y. Shimamura, H. Yoshimura, S. K. Pandey, R. K. Pandey, *Chem. Lett.* **2005**, *34*, 1344.

11 M. Kunieda, H. Tamiaki, *J. Org. Chem.* **2007**, *72*, 2443.

12 K. M. Smith, L. A. Kehres, J. Fajer, *J. Am. Chem. Soc.* **1983**, *105*, 1387.

13 The 13-C=O group in **1** was reduced according to the reported procedure described in Ref. 5 to give a 1:1.4 13^1S- and 13^1R-epimeric mixture of **3** in a quantitative yield. We used the epimeric mixture of **3** because HPLC-separated pure samples did not show any significant difference in either the monomeric or oligomeric state. Data for **3**: λ_{max}(THF), nm: 620 (rel., 0.25), 573 (0.03), 509 (0.03), and 408 (1.00); HRMS (FAB) m/z: 616.2037 (M^+), calcd for $C_{33}H_{36}N_4O_4Zn$ 616.2028.

14 S. Sasaki, T. Mizoguchi, H. Tamiaki, *J. Org. Chem.* **2007**, *72*, 4566.

15 H. Tamiaki, T. Michitsuji, R. Shibata, *Photochem. Photobiol. Sci.* **2008**, *7*, 1225.

16 λ_{max}(THF), nm: 618 (rel., 0.31), 573 (0.05), 506 (0.03), and 404 (1.00); ^{1}H NMR (600 MHz; 3% v/v pyridine-d_5/$CDCl_3$) δ 9.67 (1H, s, 5-H), 9.59 (1H, s, 10-H), 8.73 (1H, s, 15-H), 8.57 (1H, s, 20-H), 5.94 (2H, s, 3-CH_2), 5.84, 5.82 (each 1H, d, $J = 12$ Hz, 13-CH_2), 4.46 (1H, m, 18-H), 4.39 (1H, m, 17-H), 3.90 (2H, m, $COOCH_2$), 3.84 (2H, q, $J = 8$ Hz, 8-CH_2), 3.52 (3H, s, 12-CH_3), 3.41 (3H, s, 2-CH_3), 3.37 (3H, s, 7-CH_3), 2.88 (2H, br, OH × 2), 2.60, 2.44, 2.11 (1H + 2H + 1H, m, 17-CH_2CH_2), 1.78 (3H, d, $J = 8$ Hz, 18-CH_3), 1.72 (3H, t, $J = 8$ Hz, 8^1-CH_3), 1.41 (2H, m, $COOCCH_2$), 1.31–1.13 (30H, m, $COOCCC_{15}H_{30}$), 0.87 (3H, t, $J = 8$ Hz, $COOC_{17}CH_3$); MS (FAB) m/z: 842 (M^+), calcd for $C_{49}H_{70}N_4O_4Zn$ 842.

17 P. Hildebrandt, H. Tamiaki, A. R. Holzwarth, K. Schaffner, *J. Phys. Chem.* **1994**, *98*, 2192.

18 V. Huber, M. Katterle, M. Lysetska, F. Würthner, *Angew. Chem., Int. Ed.* **2005**, *44*, 3147.