Tetrahedron Letters 55 (2014) 2825-2828

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Self-aggregation of a synthetic zinc chlorophyll derivative possessing a 13¹-dicyanomethylene group as a light-harvesting antenna model

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ARTICLE INFO

Article history: Received 14 February 2014 Revised 13 March 2014 Accepted 17 March 2014 Available online 21 March 2014

Keywords: Bacteriochlorophyll Chlorosome J-aggregate Photosynthesis

ABSTRACT

Zinc methyl 3-hydroxymethyl-13¹-dicyanomethylene-pyropheophorbide-*a*, one of the bacteriochlorophyll-*d* analogs, was prepared by modifying chlorophyll-*a*. The semi-synthetic compound self-aggregated in an aqueous Triton X-100 solution to give large oligomers with red-shifted and broadened electronic absorption bands. The J-aggregates were similar to self-aggregates of bacteriochlorophyll-*d* molecules in natural light-harvesting antennas of green photosynthetic bacteria. The strongly electron-withdrawing dicyanomethylene group was an alternative functional moiety of the hydrogen-bond accepting 13¹-oxo group which had been necessary for such self-aggregation.

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Light-harvesting antenna systems are essential for natural photosynthesis.¹ Most of the systems are constructed by specific interaction of pigments with peptides and some models using chlorophyll pigments and helical peptides have been already reported.² In contrast, self-aggregates of chlorophylls are available in the main antenna complexes of green photosynthetic bacteria, called chlorosomes.³ Self-assemblies of chlorosomal chlorophylls and their model compounds have been reported and are promising for artificial antenna systems.⁴ Bacteriochlorophyll(BChl)-d is one of the naturally occurring chlorosomal chlorophylls (see the left drawing of Fig. 1)⁵ and zinc chlorophyll derivatives 4a/4a' (right drawing of Fig. 1) were effective for their synthetic models.^{6,7} Almost all the self-aggregative models reported to date are coordinatable metal complexes of cyclic tetrapyrroles bearing 3¹-hydroxy and 13¹-oxo groups and the three linearly situated moieties were specifically interacted to form chlorosomal J-aggregates: $M \cdots O - H \cdots O = C$. Zinc 3¹-hydroxy-chlorins 4a/4a' possessing the 13¹-oxo moiety aggregated in a non-polar organic solvent, an aqueous micelle solution, and the solid thin film to form large oligomers with red-shifted and broadened electronic absorption bands, but the analog 5a/5a' lacking the 13¹-oxo moiety could not self-aggregate under the same conditions.^{6,8} In the supramolecular structures of chlorosomal self-aggregates, the 13¹-oxo group of a molecule was hydrogen-bonded with the 3¹-hydroxy group of another molecule (vide supra). The 13¹-hydroxylated analogs including 6a have been reported to be partially effective

Figure 1. Molecular structures of one of the chlorosomal chlorophyll homologs, farnesylated 8-ethyl-12-methyl-bacteriochlorophyll-*d* (left), and its synthetic analogs, zinc methyl 3¹-hydroxy-pyropheophorbide-*a* derivatives (right).

for the alternative models of chlorosomal chlorophylls due to the hydrogen-bond accepting ability of the 13¹-O moiety.⁹

The central metal of porphyrinoids was coordinated with the oxygen atom of the 3¹-hydroxy group to form the chlorosomal self-aggregates mentioned above. The electron-withdrawing carbonyl group at the 13-position enhanced the coordinated ability of the metals including zinc.¹⁰ Therefore, the 13-C=O provides dual functions for chlorosomal self-aggregation. Here, a dicyanomethylene group was introduced at the 13¹-position of **4a** to give **1a** and





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its self-aggregation was examined in an aqueous micelle solution and the solid film by visible, near infrared, and infrared absorption as well as circular dichroism (CD) spectroscopies. The dicyanomethylene moiety is a strongly electron-withdrawing functional group but has less ability as a hydrogen-bonding acceptor. It is discussed whether the dicyanomethylene could be an alternative functional group of the 13¹-oxo moiety in chlorosomal chlorophylls.

According to reported procedures,¹¹ the 13¹-oxo group of methyl pyropheophorbide-*a* (**3c**) prepared by modifying chlorophyll-*a* was transformed into a dicyanomethylene group as in **2c** by Knoevenagel reaction with malononitrile and the 3-vinyl group of **2c** was converted to a formyl group as in **2d** by Lemieux–Johnson oxidation [see steps (i) and (ii) in Scheme 1]. The 3-formyl group of **2d** was selectively reduced by *tert*-butylamine borane complex⁶ to give 3-hydroxymethyl-13¹-dicyanomethylene-chlorin **2a** in an excellent yield [93%, step (iii)].¹² The resulting free base **2a** was treated with zinc acetate to afford the corresponding zinc complex **1a** in an excellent yield [92%, step (iv)].¹² The 3-ethyl analog of **1a** as in **1b** was produced by the following sequential steps:¹² hydrogenation of 3-vinyl to ethyl group [**3c** \rightarrow **3b**, step



Scheme 1. Synthesis of zinc methyl 13¹-dicyanomethylene-pyropheophorbides **1a/b** from methyl pyropheophorbide-*a* (**3c**): (i) CH₂(CN)₂, Et₃N/THF, reflux; (ii) OSO₄, NaIO₄/aq AcOH–THF; (iii) (CH₃)₃CNH₂·BH₃/CH₂Cl₂; (iv) Zn(OAc)₂·2H₂O/CHCl₃– pyridine, reflux for **1a** and /CH₂Cl₂–MeOH, rt for **1b**; (v) H₂, Pd-C/acetone.

(v)], Knoevenagel reaction of 13^1 -oxo to dicyanomethylene group [**3b** \rightarrow **2b**, step (i)], and zinc-metallation of **2b** to **1b** [step (iv)].

When zinc 3¹-hydroxy-13¹-dicyanomethylene-chlorin **1a** was dissolved in THF, a bright-green colored solution was obtained. The diluted THF solution (10 μ M) gave an intense absorption band at 696 nm and four peaks at 455, 436, 386, and 348 nm (see the blue broken line of Fig. 2A): the former and latter are called Qy and Soret bands, respectively. The solution showed small CD bands (see the blue broken line of Fig. 2B), and especially a weak negative peak was observed at the Qy position. Compared to reported data of the related compounds,^{6,11} **1a** was axially coordinated to a THF molecule to be a monomeric species in the solution. A THF solution of **1a** containing Triton X-100 was diluted with 99-fold water at room temperature to give a pale-green colored solution: the final concentrations of 1a, THF, and Triton X-100 were 10 µM, 1% (v/v), and 0.025% (wt/v), respectively. The aqueous solution showed red-shifted and broadened bands compared with the monomeric THF solution (Fig. 2A). The Qy band was shifted from 696 to 804 nm and the full width at half maximum increased from 530 to 860 cm⁻¹ (see also Table 1). The red-shift value Δ was 1920 cm⁻¹ and the bandwidth was 1.6 times wider. In the Soret bands, similar changes were obtained. In the aqueous solution, large CD bands were observed and particularly an intense S-shaped signal was measured at the red-shifted Qy region.

The spectral changes in **1a** were similar to those by chlorosomal self-aggregation of **4a** reported earlier^{6,13} (see Fig. 3A and Table 1; Δ = 1980 cm⁻¹ and 1.8 times broadening), so **1a** self-aggregated in the aqueous micelle solution to give large oligomers with π - π stacking of chlorin chromophores. Zinc 3-ethyl-13¹-dicyanomethylene-chlorin **1b** afforded less red-shifted bands in the aqueous solution (Fig. 3B), while both **1a** and **1b** showed almost the same absorption bands in THF. The Δ -value of **1b** was estimated to be 190 cm⁻¹ and 10 times smaller than that of **1a**. The small but apparent shift could be due to the environmental effect. Therefore no chlorosomal aggregation of **1b** was observed under the present conditions. Metal-free form **2a** of **1a** also showed slight red-shifts (Fig. 3C) and could not give chlorosomal self-aggregates. Lack of the 3¹-hydroxy group or the central zinc metal completely



Figure 2. Electronic absorption (A) and CD spectra (B) of zinc 3-hydroxymethyl- 13^1 -dicyanomethylene-pyropheophorbide-*a* (**1a**) in THF (blue broken line) and an aqueous 1% (v/v) THF solution containing 0.025% (wt/v) Triton X-100 (red solid line): [**1a**] = 10 μ M.

Table 1 Electronic absorption maxima λ of (zinc) methyl pyropheophorbides in a solution^a and red-shift values Δ of Qy maxima^b

Compound		λ (nm)			
	In THF		In aq micelle ^c		
	Soret	Qy	Soret	Qy	
1a [Zn/3 ¹ -OH/13 ¹ =C(CN) ₂]	436	696 (530)	462	804 (860)	1920
1b [Zn/3 ¹ -CH ₃ /13 ¹ =C(CN) ₂]	436	694 (520)	440	703	190
2a [2H/3 ¹ -OH/13 ¹ =C(CN) ₂]	448	696 (430)	455 (sh)	703	150
4a [Zn/3 ¹ -OH/13 ¹ =O]	424	646 (320)	450	741 (560)	1980

^a The values in parentheses show a full width at half maximum (cm⁻¹).

^b $\Delta = [1/\lambda(\text{in THF}) - 1/\lambda(\text{in aq micelle})] \times 10^7.$

In an aqueous solution containing 1% (v/v) THF and 0.025% (wt/v) Triton X-100.



Figure 3. Electronic absorption spectra of (zinc) methyl pyropheophorbides **4a** (A), **1b** (B), and **2a** (C) in THF (blue broken line) and an aqueous 1% (v/v) THF solution containing 0.025% (wt/v) Triton X-100 (red solid line): **[4a]** = **[1b]** = **[2a]** = 10 μ M.

suppressed the formation of large self-aggregates. Coordination of the 3^1 -OH to Zn in a supramolecule was necessary for the chlorosomal self-aggregation. It was reported that hydrogen-bond of the 3^1 -OH with 13^1 =O was an additional requisite for chlorosomal aggregation of **4a** and specific bonds of Zn···O-H···O=C were conserved.^{6,13} In the present system, such a hydrogen-bond seemed to be unnecessary for the chlorosomal aggregation.

In the solid thin film, each 13^1 -dicyanomethylene-chlorin **1a**, **1b**, or **2a** gave a similar electronic absorption spectrum as in aqueous micelle solution (Fig. 4), so **1a** self-aggregated in the solid states but neither **1b** nor **2a** afforded chlorosomal self-aggregates. In all three solids, almost the same vibrational bands of $C \equiv N$ stretching were measured as shown in Fig. 5B: $v(C \equiv N) = 2218$ (for **1a**), 2215 (for **1b**), and 2217 cm⁻¹ (for **2a**). The bands were consistent with those in THF: $v(C \equiv N) = 2215$ (**1a**), 2215 (**1b**), and



Figure 4. Electronic absorption spectra of (zinc) methyl pyropheophorbides **1a** (red solid line), **1b** (blue broken line), and **2a** (black dotted line) in solid thin films. The spectra were normalized at the Qy peaks.



Figure 5. Infrared absorption spectra of (zinc) methyl pyropheophorbides **1a** (red solid line), **1b** (blue broken line), and **2a** (black dotted line) in solid thin films: in vibrational regions of hydroxy (A), cyano (B), and ester carbonyl groups (C). The spectra were normalized at the cyano peaks and the spectra in (A) were enlarged three times. The broad bands at around 3500 cm^{-1} may be ascribable to moisture in the solid films. An about 60-cm^{-1} lower shift of the $3^{1}\text{-}O\text{-H}$ band in the top to bottom spectra of (A) might be ascribable to the coordination of OH to Zn in (**1a**)_n.

2218 cm⁻¹ (**2a**). Their ester carbonyl stretching peaks in the solid states were also situated at almost the same position (Fig. 5C): v(C=O) = 1732 (**1a**), 1737 (**1b**), and 1735 cm⁻¹ (**2a**). A relatively sharp O–H vibrational band was observed at 3340 cm⁻¹ in the solid



Figure 6. Electronic absorption spectral changes of zinc methyl 3-hydroxymethylpyropheophorbides **1a** (A) and **4a** (B) in an aqueous 1% (v/v) THF by addition of Triton X-100: [**1a**] = [**4a**] = 10 μ M and [Triton X-100] = 0.025 (red solid line), 0.1. 0.2, 0.4, 0.6, 0.8 (black to gray broken lines), and 1.0% (wt/v) (blue solid line).

self-aggregated **1a** (see the red solid line of Fig. 5A), while a broad O–H band was reported at around 3200 cm^{-1} for chlorosomal aggregates of **4a**.⁶ Therefore, the absence of hydrogen bonding of 3^1 -OH with any functional groups including the C=N was confirmed in self-aggregates of **1a**.

Deaggregation of self-aggregates of **1a** in an aqueous micelle solution was examined by addition of Triton X-100. Successive addition of Triton X-100 to the aqueous micelle solution gradually decreased the Qy peak of self-aggregated 1a at 804 nm and concomitantly exposed its monomeric Qy band at 706 nm (Fig 6A). At 1.0% (wt/v) concentration of Triton X-100, the aggregated Qy peak was primary and its monomeric peak was less intense. In contrast, self-aggregated 4a completely changed to the monomeric species at the same concentration (Fig. 6B). In spite of the absence of a hydrogen-bond in self-aggregated 1a, a stronger aggregation of 1a was observed than of 4a. This was ascribable to the stronger coordination of 3¹-O to Zn and tighter π -stacking of chlorin chromophores, since the strongly electron-withdrawing 13¹-dicyanomethylene group produced a more electron-deficient zinc site and further extended a π -conjugated system. Its strongly electron-withdrawing effect may reinforce polarization of the macrocycle, and the polarization may facilitate stacking of the macrocycles.

In conclusion, zinc 3-hydroxymethyl-13¹-dicyanomethylenechlorophyll derivative **1a** self-aggregated in a J-type fashion to give chlorosomal self-aggregates inside an aqueous micelle. The synthetic compound was not hydrogen-bonded in the J-aggregates, which had been a requisite for chlorosomal self-aggregation, but did produce more tightly stacked supramolecules with powerful coordination. A strongly electron-withdrawing dicyanomethylene group at the 13¹-position was recognized to be an alternative functional moiety to the oxo moiety used usually. It was reported that the 3¹-methoxy analogs of **4a** possessing long chains at the 17-propionate residue self-aggregated in a specific environment to give models of chlorosomal aggregates and hydrogen bonding was not always necessary for such J-aggregation.¹⁴ The present system is consistent with the previous ones utilizing no hydrogen-bond donating moiety at the 3¹-position, and **1a** was the first model of chlorosomal chlorophylls which no longer performed hydrogen-bond accepting role at the 13¹-position.

Acknowledgements

This work was partially supported by Grants-in-Aid for Scientific Research (A) (No. 22245030) as well as on Innovative Areas 'Artificial Photosynthesis (AnApple)' (No. 24107002) from the Japan Society for the Promotion of Science (JSPS).

Supplementary data

Supplementary data (synthesis of Chl derivatives **1/2a,b** and their spectral data as well as preparation procedures of aqueous Chl solutions) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.03.071.

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