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Synthesis and self-assembly of amphiphilic zinc chlorins possessing a 3^1-hydroxy group

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Abstract—Amphiphilic zinc chlorins possessing a 3^1-hydroxy group were prepared. Non-ionic (oligo)oxyethylene group, anionic sulfonate and cationic quaternary ammonium groups were introduced on the 17-position of a zinc chlorin moiety. All the three kinds of amphiphilic chlorophyll derivatives self-assembled in an aqueous medium to favor a formation of the anti-parallel dimeric structure. In contrast, the amphiphilic zinc chlorins formed large aggregates in non-polar organic solvent. These studies showed self-assemblies of amphiphilic zinc chlorin chromophores were controlled in environments.

1. Introduction

Generally, light-harvesting (LH) antenna of photosynthetic organisms consist of chlorophyll–protein complexes, in which antenna chlorophyll molecules are adequately arranged for effective energy transfer within a protein scaffold.[1] Green photosynthetic bacteria, however, have unique LH systems called chlorosomes, in which a number of bacteriochlorophyll(BChl)-*c*, *d* and *e* molecules (Fig. 1) self-aggregate to give rod-like oligomers.[2–4] The light energy absorbed at the aggregated BChls is efficiently transferred into a baseplate of BChl-*a*–protein complex, indicating that the chlorosomal aggregate acts as a supramolecular light-harvesting device without any participation of proteins.[5] BChls-*c*, *d* and *e* are characteristic in possessing the 3^1-hydroxy group, which plays important roles in the self-assembly. The C=O···H–O···Mg bonding among the 13^1-keto and 3^1-hydroxy groups and central magnesium is found in the self-aggregate.[6] Interestingly, BChl molecules isolated from natural chlorosomes self-aggregate in vitro to reproduce the supramolecular aggregates.[7] The strong excitonic interaction among BChl molecules results in red-shifted absorption bands and the intense CD signals in both in vivo and in vitro aggregates.[7–9] Natural chlorosomal BChls have a hydrophobic large alkyl chain such as farnesyl, stearyl, phytyl etc. at the 17^4-position.[10] The lipophilic BChls are organized within a hydrophobic region by monolayer of galactolipids. Although the precise suprastructure of the rod-like chlorosomal aggregate is not clarified, one of the proposed models suggested that the alkyl chain at the 17^4-position is oriented to outside the rod-structure.[3]

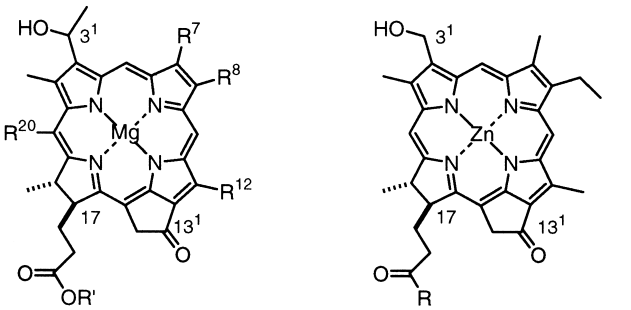

Figure 1. Structures of chlorosomal BChls and synthetic zinc chlorins **1**–**4**.

The synthetic zinc chlorins with 3^1-hydroxy group such as **1** (Fig. 1) similarly form chlorosome-type aggregates in vitro.[11] Moreover, the artificial model of chlorosomal aggregate acts as light-harvesting device as well as natural BChls-*c*, *d* and *e* do in a chlorosome.[12,13] The synthetic chlorophyll derivative is relatively stable compared to the natural pigments and the substituents are readily modified to

Keywords: amphiphilic molecule; chlorophyll; photosynthesis; self-aggregate.

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produce novel synthetic chlorophylls.[14,15] The synthetic zinc chlorin **1** is monomeric in a polar organic solvent, such as methanol, tetrahydrofuran (THF), pyridine, etc. When the monomeric solution was diluted with an excess amount of non-polar organic solvent[11] or water,[13] zinc chlorin **1** immediately self-aggregated to form their precipitates in the new environment. In contrast, the zinc chlorin **1** formed stable aqueous aggregates within a microheterogeneous medium produced by the added surfactants such as phosphatidyl choline or Triton X-100.[13,16]

Self-assembly of the amphiphilic molecules in an aqueous medium gives unique aggregates with a micellar, hexagonal or lamellar suprastructure. The structure of the hydrophilic and hydrophobic parts in the amphiphilic molecule strongly affects the suprastructure. The (metallo)porphyrin possessing hydrophilic groups self-aggregates to give fibriform suprastructure in an aqueous medium, in which strong exciton coupling among porphyrin chromophore was observed.[17] On the other hand, a free-base pyropheophorbide-*a* derivative possessing a cationic ammonium group formed dimeric aggregate in an aqueous medium.[18] The unique supramolecular architecture of the aggregated amphiphilic tetrapyrroles was probably induced by the strong π−π interaction between the tetrapyrrole macrocycles.

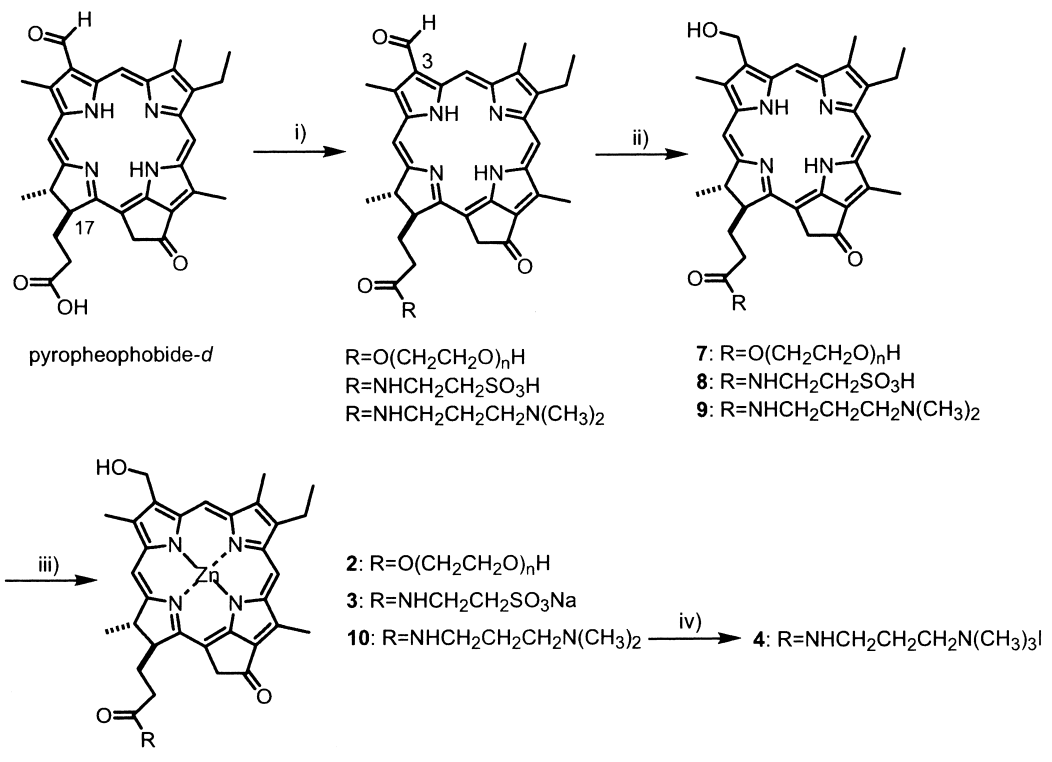
Here, we report that syntheses and self-assemblies of novel amphiphilic zinc analogues of chlorosomal BChls possessing a hydrophilic group. The cationic, anionic and non-ionic hydrophilic groups were introduced on the 17-substituent of zinc 3[1]-hydroxy-chlorins. The amphiphilic pigments self-assembled to form dimeric or large aggregates in aqueous or non-polar organic media, respectively.

2. Results and discussion

2.1. Synthesis of amphiphilic zinc chlorins possessing 3[1]-hydroxy group

The non-ionic hydrophilic groups were introduced into chlorins as follows (Scheme 1). The propionic acid chain at the 17-position of pyropheophorbide-*d* was esterified with glycol by using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP).[19] Mono- (a), di- (b), tri- (c) and tetraethylene glycol (d), and polyethylene glycol (PEG) 300 (e), 400 (f), 600 (g), 1000 (h), 1540 (i) and 2000 (j) were used for the esterification. The average number of oxyethylene group of PEG 300, 400, 600, 1000, 1540 and 2000 (*n* in Scheme 1) were 6.4, 8.7, 13.3, 22.6, 34.0 and 44.1, respectively. The 3-formyl group of the esterified chlorin was selectively reduced into the 3-hydroxymethyl group as in **7** and the following zinc metallation[11] gave corresponding zinc chlorins **2** containing monoesterified (oligo)ethylene glycols and PEGs, 17[2]-$COO(CH_2CH_2O)_nH$; **2a** (*n*=1), **2b** (2), **2c** (3), **2d** (4), **2e** (6.4), **2f** (8.7), **2g** (13.3), **2h** (22.6), **2i** (34.0) and **2j** (44.1).

The anionic zinc chlorin **3** (sodium salt form) was prepared by condensation of pyropheophorbide-*d* with 2-aminoethanesulfonic acid (taurine),[19] followed by reduction of 3-formyl group (**8**), zinc metallation and neutralization. The cationic chlorin possessing a quaternary ammonium group was prepared as follows. Pyropheophorbide-*d* was reacted with *N*,*N*-dimethyl-1,3-propanediamine to give the corresponding amide. After reduction of 3-formyl group, the free-base chlorin **9** was zinc-metallated. The tertiary amino group of **10** was methylated to the quaternary ammonium



Scheme 1. Synthesis of amphiphilic zinc 3-hydroxymethyl-chlorins **2**–**4**. (i) $HO(CH_2CH_2O)_nH$, $H_2NCH_2CH_2SO_3H$ or $H_2NCH_2CH_2CH_2N(CH_3)_2$, EDC·HCl, DMAP/$CH_2Cl_2$, (ii) *t*$BuNH_2$·$BH_3$/$CH_2Cl_2$, (iii) $Zn(OAc)_2$·$2H_2O$/MeOH, CH_2Cl_2 and aq. $NaHCO_3$, (iv) MeI/MeOH, CH_2Cl_2.

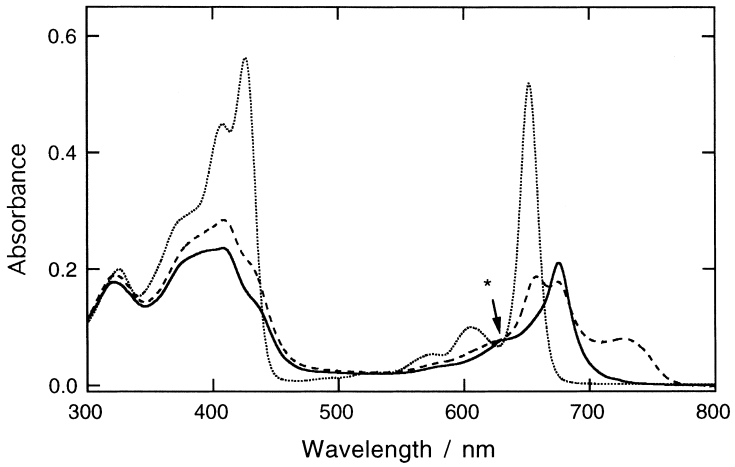


Figure 2. Visible absorption spectra of non-ionic zinc chlorin **2g** (ca. 10 μM); ··· in methanol, - - - in 1% MeOH–water immediately after aggregation (20 min), — in 1% MeOH–water after standing for 2 days.

group by the addition of methyl iodide to give cationic zinc chlorin **4** (iodide form). The solubility of the amphiphilic zinc chlorins **2**–**4** in an aqueous media was dependent upon the structure of the hydrophilic group. Ionic zinc chlorins (**3**, **4**) and some non-ionic zinc chlorins **2g**–**j** ($n \geq 13.3$) were well soluble in water. In contrast, the other non-ionic zinc chlorins **2a**–**f** possessing a shorter (oligo)oxyethylene group (≤ 8.7) were sparingly soluble in water.

2.2. Amphiphilic zinc chlorins in an aqueous medium

Zinc chlorin **2g** possessing PEG 600 ($n=13.3$) gave absorption maxima at 425 and 652 nm in methanol showing the zinc chlorin as its monomeric form (the dotted line of Fig. 2). The other amphiphilic zinc chlorins **2**–**4** also gave similar visible spectra, indicating that a hydrophilic part of the 17^2-position did not affect the optical properties of monomeric zinc chlorin. When the methanol solution of **2g** was diluted with 99-fold volume of water, the absorption spectrum was red-shifted due to the self-aggregation. Non-ionic zinc chlorin **2g** gave Qy bands at 652, 675 and 730 nm in 1% MeOH–H_2O (the dashed line of Fig. 2). Compared to the previous studies on aggregation of zinc chlorins,[11,15] the absorption bands were ascribable to monomer, dimer and large aggregate of **2g**, respectively. The spectrum was, however, gradually changed at room temperature. After standing for 2 days, both the 652- and 730-nm bands decreased concomitantly with increase in 675-nm band (the solid line of Fig. 2). This result suggested that both the monomeric and large aggregate species of **2g** were relatively unstable and changed to stable dimeric species. That is, the hydrophilic polyoxyethylene (POE) chain disturbed the formation of a large aggregate. In addition, the slight increase in a 640-nm band (* on Fig. 2) was accompanied by dimerization of **2g**, which might be due to the other vibrational transition of dimer.

The other non-ionic zinc chlorins also gave the stable dimer in an aqueous medium. Fig. 3 shows the absorption spectra of zinc chlorins **2a**–**j** in 1% MeOH–water after standing for 3 days at room temperature. In zinc chlorins **2a**–**h** ($n \leq 22.6$), the 675 nm band of dimer was preferentially observed at the Qy region. Although the absorption band around 720 nm of large aggregates was slightly observed in **2a**–**d** ($n \leq 4$), the red-shifted band gradually decreased during standing the solution. The zinc chlorins **2i** and **2j** with a longer POE chain ($n \geq 34.0$) showed the 657 nm band concomitant with a small band at 675 nm. The 675 nm band was enhanced with an increase of the concentration of zinc chlorin, aqueous 640 μM solution of **2j** gave the dimer as a major component. These results indicated that the non-ionic zinc chlorin **2** preferentially formed the dimeric structure in an aqueous medium, regardless of the length of POE chain.

The zinc chlorins possessing a long POE chain **2g**–**j** ($n \geq 13.3$) were soluble in water and showed an absorption maximum at 675 nm without addition of methanol. Thus, the presence of methanol was independent upon the formation of dimer. Similarly, both the anionic and cationic zinc chlorins **3** and **4** gave an absorption maximum at 675 nm in 1% MeOH–water (Fig. 4) and in only water.

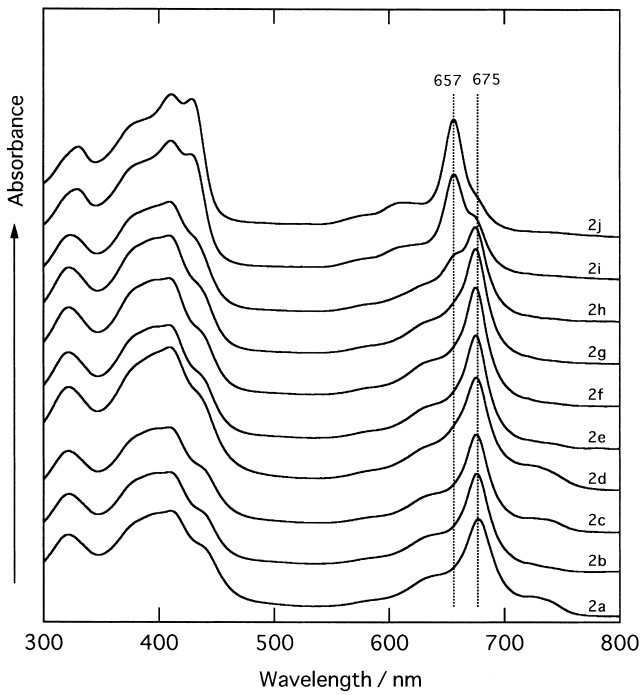


Figure 3. Visible absorption spectra of non-ionic zinc chlorins **2a**–**j** (ca. 10 μM) in 1% MeOH–water after standing for 3 days.

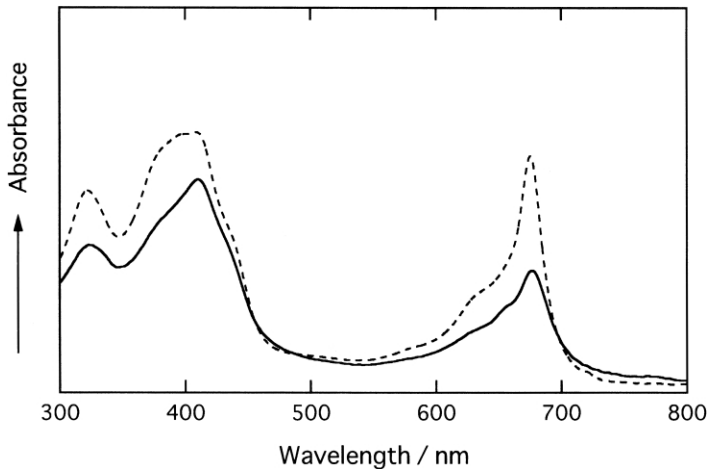


Figure 4. Visible absorption spectra of ionic zinc chlorins **3** and **4** (ca. 10 μM) in 1% MeOH–water after standing for 3 days; - - - **3**, — **4**.

These results indicated that zinc chlorins possessing a hydrophilic group at the 17^2-position self-aggregate to give the dimeric species in an aqueous medium, regardless of the structure of hydrophilic part.

Fluorescence emission and fluorescence excitation spectra of the non-ionic zinc chlorins **2** are measured as shown in Fig. 5. The emission spectrum of dimeric aggregates of amphiphilic zinc chlorin **2g** (the solid line of Fig. 5) gave an emission peak at 666-nm and a broad band around 700–750 nm, which was independent of excitation wavelength. The fluorescence excitation spectra measured at 710-nm (the dashed line of Fig. 5) was identical with absorption spectrum of the monomeric zinc chlorin measured in methanol. The spectral features showed that the dimeric zinc chlorin species was non- or much less fluorescent. Similar phenomena was reported in the other dimeric species of chlorophyll derivatives.[18,20]

2.3. Suprastructure of dimeric species of amphiphilic zinc chlorins

The amphiphilic zinc chlorins possessing a 3^1-hydroxy group favored formation of dimeric species in an aqueous medium, which was accompanied by a red-shift of the Qy band from 652 to 675 nm. Fig. 6A showed visible absorption spectra of amphiphilic zinc chlorin **5** lacking the 3^1-hydroxy group in an aqueous medium. Zinc 3-ethyl-chlorin **5** showed absorption maxima at 424, 647 nm in methanol (the dotted line of Fig. 6A) which were slightly red-shifted to 425, 652 nm in 1% methanol–water (the solid line of Fig. 6A). The small spectral changes were considered to solvent effect, thus **5** was monomeric in an aqueous medium. On the other hand, the free-base cationic 3^1-hydroxy-chlorin **6** showed absorption maxima at 406 and 660 nm in methanol, and 376 and 666 nm in an aqueous medium. The blue shift in Soret band ($\Delta\lambda$=30 nm) suggested that the free-base chlorins aggregated in an aqueous medium. Similar spectral feature was reported in another dimerization of the cationic pyropheophorbide-*a* derivatives in an aqueous medium.[18] The π–π interaction between the chlorin chromophores should induce the dimerization of free-base **6** without any assistance of the 3^1-hydroxy groups. In the aqueous zinc chlorin **5**, the surrounding methanol or water might coordinate to central zinc. The solvation disturbed the π–π interaction, which resulted in formation of monomeric zinc chlorin **5** in an aqueous medium. These spectral studies showed that both

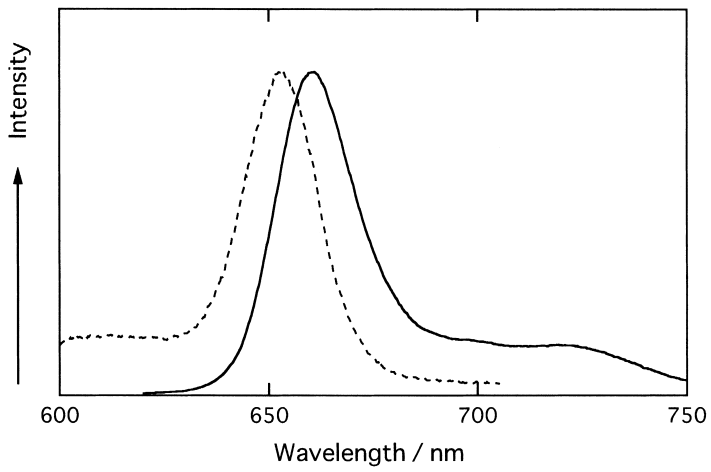


Figure 5. Fluorescence emission (excited at 450 nm: —) and fluorescence excitation (measured at 710 nm: - - -) of non-ionic zinc chlorin **2g** (ca. 10 μM) in 1% MeOH–water after standing for 3 days.

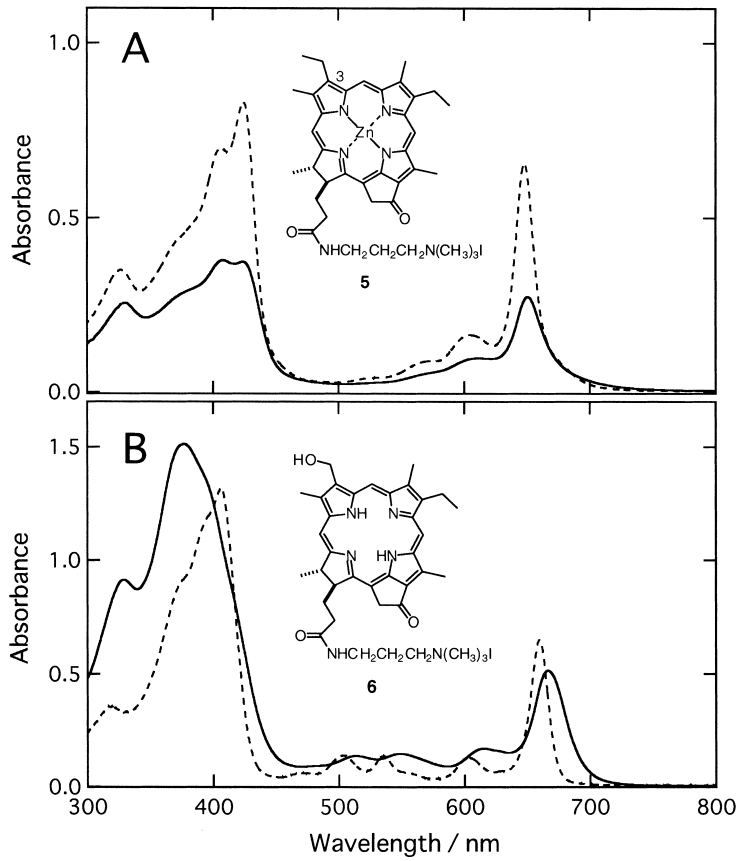


Figure 6. Visible absorption spectra of zinc 3-ethyl-chlorin **5** (A) and free-base chlorin **6** (B) in MeOH (- - -) and in 1% MeOH–water (—).

the central zinc and 3^1-hydroxy group were necessary for formation of the dimeric species characterized by 675 nm absorption band shown in Figs. 2–4.

As a result, the oxygen atom of the 3^1-hydroxy group was coordinated to the central zinc in the dimer of **2**–**4**. In addition, the resonance Raman spectrum of the dimeric aggregate of zinc chlorin **2i** showed maxima at 1563 and 1621 cm^{-1}. The two peaks were assigned to C–C or C–N stretchings of five coordinated zinc chlorin moiety.[6] The two structural models are available for the dimeric structure of amphiphilic zinc chlorins, the parallel structure I and the anti-parallel structure II (Fig. 7). The visible absorption spectra of the mixed aggregate of zinc 3^1-hydroxy-chlorin **4** and zinc 3-ethyl-chlorin **5** in an aqueous medium was similar to the linear combination of that of pure **4** and **5** (data not shown). Thus, the dimerization of amphiphilic zinc 3^1-hydroxy-chlorin **4** was not disturbed by addition of **5**. This result indicated that the anti-parallel structure II was favorable for dimeric species of the amphiphilic zinc chlorins, in which the 3^1-hydroxy group of both zinc chlorins were coordinated to the central zinc each other.

2.4. Amphiphilic zinc chlorins in a non-polar organic solvent

The amphiphilic zinc chlorins **2**–**4** were dissolved in a small amount of tetrahydrofuran (THF) and diluted with a large volume of hexane. The Qy absorption maximum of the non-ionic zinc chlorin **2g** showed a red-shifted and broadened band at around 740 nm with a 710-nm shoulder, which was not shifted after standing for a long period (the solid line of Fig. 8). In addition, the precipitate of the aggregated **2g** was immediately appeared in hexane solution. Similar results were observed in the other non-ionic zinc chlorins **2a**–**j** in 1% THF–hexane. These results indicated that the non-ionic **2** did not form dimeric species but several large aggregates in a non-polar organic medium. The hydrophilic oxyethylene group probably oriented to inside the large aggregate. On the other hand, in the anionic and cationic

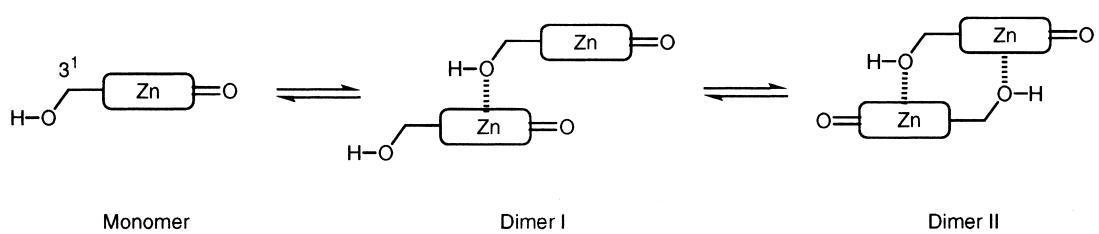


Figure 7. Proposed suprastructures of dimeric aggregate of amphiphilic zinc chlorin.

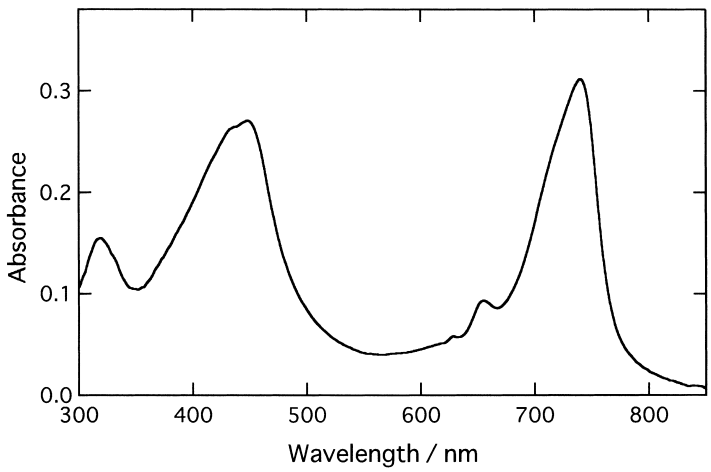


Figure 8. Visible absorption spectrum of non-ionic zinc chlorin **2g** (ca. 10 μM) in 1% THF–hexane.

zinc chlorins **3** and **4**, the formation of precipitate was too rapid to measure the absorption spectrum.

2.5. Self-assembly processes of amphiphilic zinc chlorins

In an aqueous medium, amphiphilic zinc chlorins formed a large aggregate immediately after dilution with water. The previous studies showed the hydrophobic zinc chlorin **1** self-aggregate to give precipitate in an aqueous media.[13] Thus, the aggregation of the hydrophobic zinc chlorin continuously proceeded until the precipitate was formed. In contrast, the large aggregate of the amphiphilic zinc chlorin was formed without any precipitate, indicating that the hydrophilic group of zinc chlorin disturbed the further aggregation. The hydrophilic group at the 17^2-position should be oriented to the bulk water to surround the core aggregated zinc chlorin moieties. In a non-polar medium, the hydrophilic part of the amphiphilic zinc chlorins, however, did not cover the aggregated zinc chlorins, which resulted in formation of precipitate in hexane.

The temporarily formed micelle-like aggregate in an aqueous media was, however, thermodynamically unstable, thus it gradually disaggregated to the dimeric species. The suprastructure of the aqueous assembly of amphiphilic molecules is, in general, affected by the structures of hydrophilic and hydrophobic parts. However, in all the amphiphilic zinc chlorins **2**–**4** examined here, the anti-parallel dimeric species should be the most favorable structure in aqueous self-assemblies.

3. Conclusion

Zinc 3^1-hydroxy-chlorins possessing a hydrophilic part on the 17-position were prepared. In an aqueous medium, the amphiphilic zinc chlorins formed a large aggregate as a kinetic product, which was thermodynamically unstable to change more favorable dimeric species with anti-parallel structure. In contrast, the amphiphilic zinc chlorins formed large aggregates in a non-polar organic medium. Thus, environments strongly affect the suprastructures of amphiphilic zinc chlorin aggregates; water molecules as a solvent interacted with the hydrophilic group to stabilize a compact dimer and hexane molecules repulsed them to make large self-aggregates through interaction among the hydrophilic group in a supramolecule.

4. Experimental

4.1. Apparatus

Visible absorption and fluorescence spectra were measured by Shimadzu UV-3100 spectrophotometer and Hitachi F-4500 fluorescence spectrophotometer, respectively. Resonance Raman spectra were measured with Jasco NR-1800 spectrophotometer using a 457.9 nm line of Ar^+ laser. ^1H NMR spectra were recorded with Bruker DPX-400 spectrophotometer with tetramethylsilane as internal standard. Fast atomic bombardment (FAB)-mass spectra (MS) were measured with a JEOL GCmate II spectrometer. FAB-MS samples were dissolved in CH_2Cl_2 and 3-nitrobenzyl alcohol or glycerol was used as a matrix. High performance liquid chromatography (HPLC) was performed with a Shimadzu LC-10AS pump and an SPD-M10AV diode array detector.

4.2. Materials

Pyropheophorbide-*d* was prepared according to the reported procedure.[12] Polyethylene glycol 300, 400, 600, 1000, 1540 and 2000 were purchased from Katayama Chemical Co. Ltd. (Japan). The average molecular weights of the PEG samples are 300, 402, 603, 1011, 1514, 2047, respectively. Flash column chromatography (FCC) was performed with silica gel (Merck, Kieselgel 60, 9385). HPLC was done with a packed ODS column (Gelpack GL-OP100, Hitachi Chemical Co., (Japan), 6.0ϕ×150 mm or Cosmosil $5C_{18}$-ARII, Nacalai tesque, (Japan), 6.0ϕ×250 mm).

4.3. General procedures

Reduction of the 3-formyl group of a chlorin to the 3-hydroxymethyl group and zinc metallation of a chlorin were performed according to the reported procedures.[11]

Condensation of pyropheophorbide-d with glycol or amine. Pyropheophorbide-*d* (0.025 mmol) was dissolved with dried dichloromethane (20 mL). EDC·HCl (0.15 mmol) and DMAP (0.3 mmol) were added to the solution with stirring at 0°C. The excess amount of glycol or amine (>0.5 mmol) was added to the solution and stirred for 5 h. The reaction mixture was poured into 2% HCl and CH_2Cl_2. The organic layer was separated and washed with 4% $NaHCO_3$, water and dried with Na_2SO_4. The product was purified with FCC or HPLC to give the corresponding glycol monoester or amide.

N-Methylation of tertiary amine. To a dry dichloromethane solution (3.0 mL) of tertiary amine compound (0.02 mmol) was added dry methanol (0.5 mL) and dry methyl iodide (0.5 mL). The reaction mixture was stirred for 20 h at room temperature under N_2 in the dark. After evaporation of the solvent, the residue was purified with HPLC to give the corresponding ammonium iodide.

4.4. Spectral data

4.4.1. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* ethylene glycol monoester (7a). Esterification of pyropheophorbide-*d* with ethylene glycol followed by reduction of 3-formyl group gave black solids of **7a**, 72% yield (FCC 2% MeOH–CH_2Cl_2). Mp 226–229°C; VIS (CH_2Cl_2) λ_{max} (relative intensity)=662 (0.46), 606 (0.07), 536 (0.09), 505 (0.09), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.41, 9.39, 8.53 (each 1H, s, 5-, 10-, 20-H), 5.87 (2H, s, 3-CH_2), 5.17, 5.04 (each 1H, d, J=20 Hz, 13^2-H_2), 4.43 (1H, dq, J=2, 7 Hz, 18-H), 4.24 (1H, dt, J=8, 2 Hz, 17-H), 4.02–4.13 (2H, m, $COOCH_2$), 3.65 (2H, q, J=7 Hz, 8-CH_2), 3.58–3.64 (2H, m, $COOCH_2CH_2$), 3.57, 3.40, 3.24 (each 3H, s, 2-, 7-, 12-CH_3), 2.47–2.65, 2.17–2.37 (each 2H, m, 17-CH_2CH_2), 1.77 (3H, d, J=7 Hz, 18-CH_3), 1.67 (3H, t, J=7 Hz, 8^1-CH_3), 0.20, −1.86 (each 1H, s, NH). MS (FAB) found: m/z=583. Calcd for $C_{34}H_{39}N_4O_5$: MH^+, 583.

4.4.2. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* diethylene glycol monoester (7b). Esterification of pyropheophorbide-*d* with diethylene glycol followed by reduction of 3-formyl group gave black solids of **7b**, 71% yield (FCC 2–3% MeOH–CH_2Cl_2). Mp 122–125°C; VIS (CH_2Cl_2) λ_{max}=662 (0.47), 606 (0.08), 536 (0.09), 506 (0.09), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.48, 9.44, 8.55 (each 1H, s, 5-, 10-, 20-H), 5.90 (2H, s, 3-CH_2), 5.25, 5.09 (each 1H, d, J=20 Hz, 13^2-H_2), 4.48 (1H, dq, J=2, 7 Hz, 18-H), 4.28 (1H, dt, J=8, 2 Hz, 17-H), 4.08–4.19 (2H, m, $COOCH_2$), 3.69 (2H, q, J=7 Hz, 8-CH_2), 3.43–3.67 (6H, m, $COOCH_2CH_2OCH_2CH_2OH$), 3.65, 3.42, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.52–2.74, 2.20–2.38 (each 2H, m, 17-CH_2CH_2), 1.80 (3H, d, J=7 Hz, 18-CH_3), 1.69 (3H, t, J=7 Hz, 8^1-CH_3), 0.32, −1.77 (each 1H, s, NH). MS (FAB) found: m/z=627. Calcd for $C_{36}H_{43}N_4O_6$: MH^+, 627.

4.4.3. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* triethylene glycol monoester (7c). Esterification of pyropheophorbide-*d* with triethylene glycol followed by reduction of 3-formyl group gave black solids of **7c**, 75% yield (FCC 4% MeOH–CH_2Cl_2). Mp 97–99°C; VIS (CH_2Cl_2) λ_{max}=662 (0.47), 606 (0.07), 536 (0.09), 504 (0.09), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.53, 9.47, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.87–5.97 (2H, m, 3-CH_2), 5.27, 5.12 (each 1H, d, J=20 Hz, 13^2-H_2), 4.49 (1H, dq, J=2, 7 Hz, 18-H), 4.33 (1H, dt, J=8, 2 Hz, 17-H), 3.98–4.12 (2H, m, $COOCH_2$), 3.71 (2H, q, J=7 Hz, 8-CH_2), 3.68, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 3.32–3.55 (10H, m, $COOCH_2CH_2O(CH_2CH_2O)_2$), 2.63–2.74, 2.46–2.57, 2.16–2.40 (1H+1H+2H, m, 17-CH_2CH_2), 1.80 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3), 0.34, −1.76 (each 1H, s, NH). MS (FAB) found: m/z=671. Calcd for $C_{38}H_{47}N_4O_7$: MH^+, 671.

4.4.4. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* tetraethylene glycol monoester (7d). Esterification of pyropheophorbide-*d* with tetraethylene glycol followed by reduction of 3-formyl group gave black solids of **7d**, 69% yield (FCC 5% MeOH–CH_2Cl_2). Mp 89–92°C; VIS (CH_2Cl_2) λ_{max}=663 (0.47), 606 (0.08), 536 (0.09), 505 (0.10), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.44, 9.41, 8.55 (each 1H, s, 5-, 10-, 20-H), 5.89, 5.84 (each 1H, d, J=13 Hz, 3-CH_2), 5.21, 5.07 (each 1H, d, J=20 Hz, 13^2-H_2), 4.46 (1H, dq, J=2, 7 Hz, 18-H), 4.28 (1H, dt, J=8, 2 Hz, 17-H), 4.03–4.11, 3.93–4.00 (each 1H, m, $COOCH_2$), 3.66 (2H, q, J=7 Hz, 8-CH_2), 3.62, 3.43, 3.24 (each 3H, s, 2-, 7-, 12-CH_3), 3.32–3.59 (14H, m, $COOCH_2CH_2O(CH_2CH_2O)_3$), 2.43–2.74, 2.11–2.34 (each 2H, m, 17-CH_2CH_2), 1.78 (3H, d, J=7 Hz, 18-CH_3), 1.68 (3H, t, J=7 Hz, 8^1-CH_3), 0.23, −1.84 (each 1H, s, NH). MS (FAB) found: m/z=715 (MH^+). Calcd for $C_{40}H_{51}N_4O_8$: MH^+, 715.

4.4.5. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 300 monoester (7e). Esterification of pyropheophorbide-*d* with polyethylene glycol 300 (n=6.4) followed by reduction of 3-formyl group gave black solids of **7e**, 72% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 5.0 min). Mp 60–69°C; VIS (CH_2Cl_2) λ_{max}=663 (0.44), 606 (0.07), 536 (0.09), 505 (0.10), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.46, 9.44, 8.55 (each 1H, s, 5-, 10-, 20-H), 5.90, 5.86 (each 1H, d, J=14 Hz, 3-CH_2), 5.23, 5.09 (each 1H, d, J=20 Hz, 13^2-H_2), 4.47 (1H, dq, J=2, 7 Hz, 18-H), 4.29 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.19 (2H, m, $COOCH_2$), 3.68 (2H, q, J=7 Hz, 8-CH_2), 3.28–3.68 (24H, m, $COOCH_2CH_2O(CH_2CH_2O)_{5.4}$), 3.63, 3.41, 3.25 (each 3H, s, 2-, 7-, 12-CH_3), 2.45–2.72, 2.19–2.34 (each 2H, m, 17-CH_2CH_2), 1.79 (3H, d, J=7 Hz, 18-CH_3), 1.68 (3H, t, J=7 Hz, 8^1-CH_3), 0.26, −1.82 (each 1H, s, NH). MS (FAB) found: m/z=671, 715, 759, 803, 847, 891, 935, 979. Calcd for $C_{38}H_{47}N_4O_7$: MH^+, 671 (n=3), $C_{40}H_{51}N_4O_8$: MH^+, 715 (n=4), $C_{42}H_{55}N_4O_9$: MH^+, 759 (n=5), $C_{44}H_{59}N_4O_{10}$: MH^+, 803 (n=6), $C_{46}H_{63}N_4O_{11}$: MH^+, 847 (n=7), $C_{48}H_{67}N_4O_{12}$: MH^+, 891 (n=8), $C_{50}H_{71}N_4O_{13}$: MH^+, 935 (n=9), $C_{52}H_{75}N_4O_{14}$: MH^+, 979 (n=10).

4.4.6. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 400 monoester (7f). Esterification of pyropheophorbide-*d* with polyethylene glycol 400 (n=8.7) followed by reduction of 3-formyl group gave black solids of **7f**, 83% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 4.8 min). Mp 57–64°C; VIS (CH_2Cl_2) λ_{max}=663 (0.44), 606 (0.08), 536 (0.09), 505 (0.10), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.48, 9.45, 8.56 (each 1H, s, 5-, 10-, 20-H), 5.91, 5.87 (each 1H, d, J=13 Hz, 3-CH_2), 5.24, 5.10 (each 1H, d, J=20 Hz, 13^2-H_2), 4.48 (1H,

dq, J=2, 7 Hz, 18-H), 4.30 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.17 (2H, m, $COOCH_2$), 3.69 (2H, q, J=7 Hz, 8-CH_2), 3.29–3.68 (33H, m, $COOCH_2CH_2O(CH_2CH_2O)_{7.7}$), 3.65, 3.42, 3.25 (each 3H, s, 2-, 7-, 12-CH_3), 2.48–2.72, 2.20–2.35 (each 2H, m, 17-CH_2CH_2), 1.80 (3H, d, J=7 Hz, 18-CH_3), 1.69 (3H, t, J=7 Hz, 8^1-CH_3), 0.27, −1.80 (each 1H, s, NH). MS (FAB) found: m/z=715, 759, 803, 847, 891, 935, 979, 1023, 1067. Calcd for $C_{40}H_{51}N_4O_8$: MH^+, 715 (n=4), $C_{42}H_{55}N_4O_9$: MH^+, 759 (n=5), $C_{44}H_{59}N_4O_{10}$: MH^+, 803 (n=6), $C_{46}H_{63}N_4O_{11}$: MH^+, 847 (n=7), $C_{48}H_{67}N_4O_{12}$: MH^+, 891 (n=8), $C_{50}H_{71}N_4O_{13}$: MH^+, 935 (n=9), $C_{52}H_{75}N_4O_{14}$: MH^+, 979 (n=10), $C_{54}H_{79}N_4O_{15}$: MH^+, 1023 (n=11), $C_{56}H_{83}N_4O_{16}$: MH^+, 1067 (n=12).

4.4.7. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 600 monoester (7g). Esterification of pyropheophorbide-*d* with polyethylene glycol 600 (n=13.3) followed by reduction of 3-formyl group gave black solids of **7g**, 76% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 13.8 min). Mp 52–55°C; VIS (CH_2Cl_2) λ_{max}=662 (0.47), 605 (0.08), 536 (0.09), 505 (0.10), 410 nm (1.00); ^1H NMR ($CDCl_3$) δ=9.52, 9.48, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.93, 5.90 (each 1H, d, J=13 Hz, 3-CH_2), 5.26, 5.12 (each 1H, d, J=20 Hz, 13^2-H_2), 4.49 (1H, dq, J=2, 7 Hz, 18-H), 4.32 (1H, dt, J=8, 2 Hz, 17-H), 4.03–4.16 (2H, m, $COOCH_2$), 3.71 (2H, q, J=7 Hz, 8-CH_2), 3.36–3.71 (51H, m, $COOCH_2CH_2O(CH_2CH_2O)_{12.3}$), 3.67, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.51–2.75, 2.23–2.37 (each 2H, m, 17-CH_2CH_2), 1.81 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3), 0.34, −1.76 (each 1H, s, NH). MS (FAB) found: m/z=847, 891, 935, 979, 1023, 1067, 1111, 1155, 1199, 1243, 1287. Calcd for $C_{46}H_{63}N_4O_{11}$: MH^+, 847 (n=7), $C_{48}H_{67}N_4O_{12}$: MH^+, 891 (n=8), $C_{50}H_{71}N_4O_{13}$: MH^+, 935 (n=9), $C_{52}H_{75}N_4O_{14}$: MH^+, 979 (n=10), $C_{54}H_{79}N_4O_{15}$: MH^+, 1023 (n=11), $C_{56}H_{83}N_4O_{16}$: MH^+, 1067 (n=12), $C_{58}H_{87}N_4O_{17}$: MH^+, 1111 (n=13), $C_{60}H_{91}N_4O_{18}$: MH^+, 1155 (n=14), $C_{62}H_{95}N_4O_{19}$: MH^+, 1199 (n=15), $C_{64}H_{99}N_4O_{20}$: MH^+, 1243 (n=16), $C_{66}H_{103}N_4O_{21}$: MH^+, 1287 (n=17).

4.4.8. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 1000 monoester (7h). Esterification of pyropheophorbide-*d* with polyethylene glycol 1000 (n=22.6) followed by reduction of 3-formyl group gave black solids of **7h**, 76% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 12.6 min). Mp <30°C; VIS (CH_2Cl_2) λ_{max}=662 (0.48), 605 (0.08), 535 (0.09), 505 (0.10), 410 nm (1.00); ^1H NMR ($CDCl_3$) δ=9.48, 9.46, 8.56 (each 1H, s, 5-, 10-, 20-H), 5.91, 5.88 (2H, d, J=13 Hz, 3-CH_2), 5.24, 5.10 (each 1H, d, J=20 Hz, 13^2-H_2), 4.48 (1H, dq, J=2, 7 Hz, 18-H), 4.30 (1H, dt, J=8, 2 Hz, 17-H), 4.03–4.17 (2H, m, $COOCH_2$), 3.38–3.73 (88H, m, $COOCH_2CH_2O(CH_2CH_2O)_{21.6}$), 3.69 (2H, q, J=7 Hz, 8-CH_2), 3.65, 3.42, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.63–2.73, 2.50–2.61, 2.23–2.34 (1H+1H+2H, m, 17-CH_2CH_2), 1.80 (3H, d, J=7 Hz, 18-CH_3), 1.69 (3H, t, J=7 Hz, 8^1-CH_3), 0.30, −1.79 (each 1H, s, NH). MS (FAB) found: m/z=1111, 1155, 1199, 1243, 1287, 1331, 1375, 1419, 1463, 1507, 1551, 1595, 1639, 1683, 1727, 1771, 1815, 1859. Calcd for $C_{58}H_{87}N_4O_{17}$: MH^+, 1111 (n=13), $C_{60}H_{91}N_4O_{18}$: MH^+, 1155 (n=14), $C_{62}H_{95}N_4O_{19}$: MH^+, 1199 (n=15), $C_{64}H_{99}N_4O_{20}$: MH^+, 1243 (n=16), $C_{66}H_{103}N_4O_{21}$: MH^+, 1287 (n=17), $C_{68}H_{107}N_4O_{22}$: MH^+, 1331 (n=18), $C_{70}H_{111}N_4O_{23}$: MH^+, 1375 (n=19), $C_{72}H_{115}N_4O_{24}$: MH^+, 1419 (n=20), $C_{74}H_{119}N_4O_{25}$: MH^+, 1463 (n=21), $C_{76}H_{123}N_4O_{26}$: MH^+, 1507 (n=22), $C_{78}H_{127}N_4O_{27}$: MH^+, 1551 (n=23), $C_{80}H_{131}N_4O_{28}$: MH^+, 1595 (n=24), $C_{82}H_{135}N_4O_{29}$: MH^+, 1639 (n=25), $C_{84}H_{139}N_4O_{30}$: MH^+, 1683 (n=26), $C_{86}H_{143}N_4O_{31}$: MH^+, 1727 (n=27), $C_{88}H_{147}N_4O_{32}$: MH^+, 1771 (n=28), $C_{90}H_{151}N_4O_{33}$: MH^+, 1815 (n=29), $C_{92}H_{155}N_4O_{34}$: MH^+, 1859 (n=30).

4.4.9. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 1540 monoester (7i). Esterification of pyropheophorbide-*d* with polyethylene glycol 1540 (n=34.0) followed by reduction of 3-formyl group gave black solids of **7i**, 72% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 11.5 min). Mp 40–43°C; VIS (CH_2Cl_2) λ_{max}=662 (0.46), 605 (0.08), 536 (0.09), 505 (0.10), 411 nm (1.00); ^1H NMR ($CDCl_3$) δ=9.51, 9.48, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.92, 5.89 (2H, d, J=13 Hz, 3-CH_2), 5.26, 5.11 (each 1H, d, J=20 Hz, 13^2-H_2), 4.49 (1H, dq, J=2, 7 Hz, 18-H), 4.31 (1H, dt, J=8, 2 Hz, 17-H), 4.03–4.17 (2H, m, $COOCH_2$), 3.39–3.73 (134H, m, $COOCH_2CH_2O(CH_2CH_2O)_{33}$), 3.70 (2H, q, J=7 Hz, 8-CH_2), 3.67, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.64–2.74, 2.51–2.61, 2.23–2.36 (1H+1H+2H, m, 17-CH_2CH_2), 1.81 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3), 0.33, −1.77 (each 1H, s, NH). MS (FAB) found: m/z=1595, 1639, 1683, 1727, 1771, 1815, 1859, 1903, 1947, 1991, 2035, 2079, 2123, 2167, 2211, 2255, 2299, 2343, 2387. Calcd for $C_{80}H_{131}N_4O_{28}$: MH^+, 1595 (n=24), $C_{82}H_{135}N_4O_{29}$: MH^+, 1639 (n=25), $C_{84}H_{139}N_4O_{30}$: MH^+, 1683 (n=26), $C_{86}H_{143}N_4O_{31}$: MH^+, 1727 (n=27), $C_{88}H_{147}N_4O_{32}$: MH^+, 1771 (n=28), $C_{90}H_{151}N_4O_{33}$: MH^+, 1815 (n=29), $C_{92}H_{155}N_4O_{34}$: MH^+, 1859 (n=30), $C_{94}H_{159}N_4O_{35}$: MH^+, 1903 (n=31), $C_{96}H_{163}N_4O_{36}$: MH^+, 1947 (n=32), $C_{98}H_{167}N_4O_{37}$: MH^+, 1991 (n=33), $C_{100}H_{171}N_4O_{38}$: MH^+, 2035 (n=34), $C_{102}H_{175}N_4O_{39}$: MH^+, 2079 (n=35), $C_{104}H_{179}N_4O_{40}$: MH^+, 2123 (n=36), $C_{106}H_{183}N_4O_{41}$: MH^+, 2167 (n=37), $C_{108}H_{187}N_4O_{42}$: MH^+, 2211 (n=38), $C_{110}H_{191}N_4O_{43}$: MH^+, 2255 (n=39), $C_{112}H_{195}N_4O_{44}$: MH^+, 2299 (n=40), $C_{114}H_{199}N_4O_{45}$: MH^+, 2343 (n=41), $C_{116}H_{203}N_4O_{46}$: MH^+, 2387 (n=42).

4.4.10. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 2000 monoester (7j). Esterification of pyropheophorbide-*d* with polyethylene glycol 2000 (n=44.1) followed by reduction of 3-formyl group gave black solids of **7j**, 68% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 10.7 min). Mp 46–49°C; VIS (CH_2Cl_2) λ_{max}=662 (0.48), 605 (0.08), 536 (0.09), 505 (0.10), 410 nm (1.00); ^1H NMR ($CDCl_3$) δ=9.54, 9.49, 8.58 (each 1H, s, 5-, 10-, 20-H), 5.92 (2H, s, 3-CH_2), 5.27, 5.12 (each 1H, d, J=20 Hz, 13^2-H_2), 4.50 (1H, dq, J=2, 7 Hz, 18-H), 4.33 (1H, dt, J=8, 2 Hz, 17-H), 4.03–4.17 (2H, m, $COOCH_2$), 3.39–3.83 (182H, m, $COOCH_2CH_2O(CH_2CH_2O)_{43.1}$), 3.71 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.44, 3.28 (each 3H, s, 2-, 7-, 12-CH_3), 2.65–2.75, 2.52–2.62, 2.24–2.37 (1H+1H+2H, m, 17-CH_2CH_2), 1.81 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3), 0.36, −1.75 (each 1H, s, NH). MS (FAB) found: m/z=1947, 1991, 2035, 2079, 2123, 2167, 2211, 2255, 2299, 2343,

2387, 2431, 2475, 2519, 2563, 2607, 2651, 2695, 2739, 2783, 2827. Calcd for $C_{96}H_{163}N_4O_{36}$: MH^+, 1947 (n=32), $C_{98}H_{167}N_4O_{37}$: MH^+, 1991 (n=33), $C_{100}H_{171}N_4O_{38}$: MH^+, 2035 (n=34), $C_{102}H_{175}N_4O_{39}$: MH^+, 2079 (n=35), $C_{104}H_{179}N_4O_{40}$: MH^+, 2123 (n=36), $C_{106}H_{183}N_4O_{41}$: MH^+, 2167 (n=37), $C_{108}H_{187}N_4O_{42}$: MH^+, 2211 (n=38), $C_{110}H_{191}N_4O_{43}$: MH^+, 2255 (n=39), $C_{112}H_{195}N_4O_{44}$: MH^+, 2299 (n=40), $C_{114}H_{199}N_4O_{45}$: MH^+, 2343 (n=41), $C_{116}H_{203}N_4O_{46}$: MH^+, 2387 (n=42), $C_{118}H_{207}N_4O_{47}$: MH^+, 2431, (n=43), $C_{120}H_{211}N_4O_{48}$: MH^+, 2475 (n=44), $C_{122}H_{215}N_4O_{49}$: MH^+, 2519 (n=45), $C_{124}H_{219}N_4O_{50}$: MH^+, 2563 (n=46), $C_{126}H_{223}N_4O_{51}$: MH^+, 2607 (n=47), $C_{128}H_{227}N_4O_{52}$: MH^+, 2651 (n=48), $C_{130}H_{231}N_4O_{53}$: MH^+, 2695 (n=49), $C_{132}H_{235}N_4O_{54}$: MH^+, 2739 (n=50), $C_{134}H_{239}N_4O_{55}$: MH^+, 2783 (n=51), $C_{136}H_{243}N_4O_{56}$: MH^+, 2827 (n=52).

4.4.11. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* ethylene glycol monoester (2a). Zinc metallation of **7a** gave dark green solids of **2a**, 92% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 9.4 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.75), 601 (0.10), 567 (0.05), 521 (0.03), 424 (1.00), 405 nm (0.55); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.31, 8.35 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.18, 5.07 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.09 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.62–3.67 (2H, m, $COOCH_2CH_2OH$), 2.22–2.59 (4H, m, 17-CH_2CH_2), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=644. Calcd for $C_{34}H_{36}N_4O_5Zn$: M^+, 644.

4.4.12. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* diethylene glycol monoester (2b). Zinc metallation of **7b** gave dark green solids of **2b**, 90% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 9.3 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.75), 601 (0.10), 566 (0.06), 523 (0.04), 424 (1.00), 404 nm (0.56); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.56, 9.31, 8.35 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.20, 5.07 (each 1H, d, J=20 Hz, 13^2-H_2), 4.41 (1H, dq, J=2, 7 Hz, 18-H), 4.21 (1H, dt, J=8, 2 Hz, 17-H), 4.06–4.16 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.64–3.67, 3.45–3.58 (2H+4H, m, $COOCH_2CH_2OCH_2CH_2OH$), 2.22–2.64 (4H, m, 17-CH_2CH_2), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=688. Calcd for $C_{36}H_{40}N_4O_6Zn$: M^+, 688.

4.4.13. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* triethylene glycol monoester (2c). Zinc metallation of **7c** gave dark green solids of **2c**, 89% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 9.2 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.74), 602 (0.10), 568 (0.06), 521 (0.04), 424 (1.00), 405 nm (0.59); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.32, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.85, 5.81 (each 1H, d, J=13 Hz, 3-CH_2), 5.18, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 3.96–4.09 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.36–3.53 (10H, m, $COOCH_2CH_2O(CH_2CH_2O)_2H$), 2.20–2.59 (4H, m, 17-$CH_2CH_2$), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=732. Calcd for $C_{38}H_{44}N_4O_7Zn$: M^+, 732.

4.4.14. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* tetraethylene glycol monoester (2d). Zinc metallation of **7d** gave dark green solids of **2d**, 93% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 9.1 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.73), 603 (0.10), 567 (0.05), 521 (0.03), 424 (1.00), 405 nm (0.56); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.32, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.84, 5.81 (each 1H, d, J=13 Hz, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 3.93–4.09 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.33–3.51 (14H, m, $COOCH_2CH_2O(CH_2CH_2O)_3H$), 2.26–2.60 (4H, m, 17-$CH_2CH_2$), 1.71 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=776. Calcd for $C_{40}H_{48}N_4O_8Zn$: M^+, 776.

4.4.15. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 300 monoester (2e). Zinc metallation of **7e** gave dark green solids of **2e**, 92% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 8.3 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.73), 602 (0.10), 566 (0.05), 521 (0.03), 424 (1.00), 405 nm (0.56); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.33, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.85, 5.81 (each 1H, d, J=13 Hz, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 3.96–4.13 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.33–3.68 (24H, m, $COOCH_2CH_2O(CH_2CH_2O)_{5.4}$), 2.24–2.59 (4H, m, 17-$CH_2CH_2$), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=732, 776, 820, 864, 908, 952, 996, 1040. Calcd for $C_{38}H_{44}N_4O_7Zn$: M^+, 732 (n=3), $C_{40}H_{48}N_4O_8Zn$: M^+, 776 (n=4), $C_{42}H_{52}N_4O_9Zn$: M^+, 820 (n=5), $C_{44}H_{56}N_4O_{10}Zn$: M^+, 864 (n=6), $C_{46}H_{60}N_4O_{11}Zn$: M^+, 908 (n=7), $C_{48}H_{64}N_4O_{12}Zn$: M^+, 952 (n=8), $C_{50}H_{68}N_4O_{13}Zn$: M^+, 996 (n=9), $C_{52}H_{72}N_4O_{14}Zn$: M^+, 1040 (n=10).

4.4.16. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 400 monoester (2f). Zinc metallation of **7f** gave dark green solids of **2f**, 88% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 8.1 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.75), 601 (0.10), 567 (0.05), 520 (0.03), 424 (1.00), 405 nm (0.56); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.33, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.84, 5.81 (each 1H, d, J=13 Hz, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.14 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.36–3.69 (33H, m, $COOCH_2CH_2O(CH_2CH_2O)_{7.7}$), 2.25–2.60 (4H, m, 17-$CH_2CH_2$), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=776, 820, 864, 908, 952, 996, 1040, 1084, 1128. Calcd for $C_{40}H_{48}N_4O_8Zn$: M^+, 776 (n=4), $C_{42}H_{52}N_4O_9Zn$: M^+, 820 (n=5), $C_{44}H_{56}N_4O_{10}Zn$: M^+, 864

(n=6), $C_{46}H_{60}N_4O_{11}Zn$: M^+, 908 (n=7), $C_{48}H_{64}N_4O_{12}Zn$: M^+, 952 (n=8), $C_{50}H_{68}N_4O_{13}Zn$: M^+, 996 (n=9), $C_{52}H_{72}N_4O_{14}Zn$: M^+, 1040 (n=10), $C_{54}H_{76}N_4O_{15}Zn$: M^+, 1084 (n=11), $C_{56}H_{80}N_4O_{16}Zn$: M^+, 1128 (n=12).

4.4.17. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 600 monoester (2g). Zinc metallation of **7g** gave dark green solids of **2g**, 93% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 7.8 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.75), 602 (0.10), 567 (0.05), 522 (0.03), 424 (1.00), 405 nm (0.56); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.32, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.39 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.13 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.39–3.73 (51H, m, $COOCH_2CH_2O(CH_2CH_2O)_{12.3}$), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.23–2.61 (4H, m, 17-CH_2CH_2), 1.71 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=908, 952, 996, 1040, 1084, 1128, 1172, 1216, 1260, 1304, 1348. Calcd for $C_{46}H_{60}N_4O_{11}Zn$: M^+, 908 (n=7), $C_{48}H_{64}N_4O_{12}Zn$: M^+, 952 (n=8), $C_{50}H_{68}N_4O_{13}Zn$: M^+, 996 (n=9), $C_{52}H_{72}N_4O_{14}Zn$: M^+, 1040 (n=10), $C_{54}H_{76}N_4O_{15}Zn$: M^+, 1084 (n=11), $C_{56}H_{80}N_4O_{16}Zn$: M^+, 1128 (n=12), $C_{58}H_{84}N_4O_{17}Zn$: M^+, 1172 (n=13), $C_{60}H_{88}N_4O_{18}Zn$: M^+, 1216 (n=14), $C_{62}H_{92}N_4O_{19}Zn$: M^+, 1260 (n=15), $C_{64}H_{96}N_4O_{20}Zn$: M^+, 1304 (n=16), $C_{66}H_{100}N_4O_{21}Zn$: M^+, 1348 (n=17).

4.4.18. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 1000 monoester (2h). Zinc metallation of **7h** gave dark green solids of **2h**, 87% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 7.4 min). Mp >300°C; VIS (THF) λ_{max}=647 (0.75), 602 (0.10), 566 (0.05), 521 (0.03), 424 (1.00), 405 nm (0.55); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.33, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.00–4.14 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.41–3.73 (88H, m, $COOCH_2CH_2O(CH_2CH_2O)_{21.6}$), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.20–2.61 (4H, m, 17-CH_2CH_2), 1.71 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=1172, 1216, 1260, 1304, 1348, 1392, 1436, 1480, 1524, 1568, 1612, 1656, 1700, 1744, 1788, 1832, 1876, 1920. Calcd for $C_{58}H_{84}N_4O_{17}Zn$: M^+, 1172 (n=13), $C_{60}H_{88}N_4O_{18}Zn$: M^+, 1216 (n=14), $C_{62}H_{92}N_4O_{19}Zn$: M^+, 1260 (n=15), $C_{64}H_{96}N_4O_{20}Zn$: M^+, 1304 (n=16), $C_{66}H_{100}N_4O_{21}Zn$: M^+, 1348 (n=17), $C_{68}H_{104}N_4O_{22}Zn$: M^+, 1392 (n=18), $C_{70}H_{108}N_4O_{23}Zn$: M^+, 1436 (n=19), $C_{72}H_{112}N_4O_{24}Zn$: M^+, 1480 (n=20), $C_{74}H_{116}N_4O_{25}Zn$: M^+, 1524 (n=21), $C_{76}H_{120}N_4O_{26}Zn$: M^+, 1568 (n=22), $C_{78}H_{124}N_4O_{27}Zn$: M^+, 1612 (n=23), $C_{80}H_{128}N_4O_{28}Zn$: M^+, 1656 (n=24), $C_{82}H_{132}N_4O_{29}Zn$: M^+, 1700 (n=25), $C_{84}H_{136}N_4O_{30}Zn$: M^+, 1744 (n=26), $C_{86}H_{140}N_4O_{31}Zn$: M^+, 1788 (n=27), $C_{88}H_{144}N_4O_{32}Zn$: M^+, 1832 (n=28), $C_{90}H_{148}N_4O_{33}Zn$: M^+, 1876 (n=29), $C_{92}H_{152}N_4O_{34}Zn$: M^+, 1920 (n=30).

4.4.19. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 1540 monoester (2i). Zinc metallation of **7i** gave dark green solids of **2i**, 89% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 6.9 min). Mp 221–224°C; VIS (THF) λ_{max}=647 (0.75), 603 (0.10), 566 (0.05), 520 (0.03), 424 (1.00), 404 nm (0.55); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.33, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.01–4.14 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.41–3.83 (134H, m, $COOCH_2CH_2O(CH_2CH_2O)_{33}$), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.25–2.60 (4H, m, 17-CH_2CH_2), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=1656, 1700, 1744, 1788, 1832, 1876, 1920, 1964, 2008, 2052, 2096, 2140, 2184, 2228, 2272, 2316, 2360, 2404, 2448. Calcd for $C_{80}H_{128}N_4O_{28}Zn$: M^+, 1656 (n=24), $C_{82}H_{132}N_4O_{29}Zn$: M^+, 1700 (n=25), $C_{84}H_{136}N_4O_{30}Zn$: M^+, 1744 (n=26), $C_{86}H_{140}N_4O_{31}Zn$: M^+, 1788 (n=27), $C_{88}H_{144}N_4O_{32}Zn$: M^+, 1832 (n=28), $C_{90}H_{148}N_4O_{33}Zn$: M^+, 1876 (n=29), $C_{92}H_{152}N_4O_{34}Zn$: M^+, 1920 (n=30), $C_{94}H_{156}N_4O_{35}Zn$: M^+, 1964 (n=31), $C_{96}H_{160}N_4O_{36}Zn$: M^+, 2008 (n=32), $C_{98}H_{164}N_4O_{37}Zn$: M^+, 2052 (n=33), $C_{100}H_{168}N_4O_{38}Zn$: M^+, 2096 (n=34), $C_{102}H_{172}N_4O_{39}Zn$: M^+, 2140 (n=35), $C_{104}H_{176}N_4O_{40}Zn$: M^+, 2184 (n=36), $C_{106}H_{180}N_4O_{41}Zn$: M^+, 2228 (n=37), $C_{108}H_{184}N_4O_{42}Zn$: M^+, 2272 (n=38), $C_{110}H_{188}N_4O_{43}Zn$: M^+, 2316 (n=39), $C_{112}H_{192}N_4O_{44}Zn$: M^+, 2360 (n=40), $C_{114}H_{196}N_4O_{45}Zn$: M^+, 2404 (n=41), $C_{116}H_{200}N_4O_{46}Zn$: M^+, 2448 (n=42).

4.4.20. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* polyethylene glycol 2000 monoester (2j). Zinc metallation of **7j** gave dark green solids of **2j**, 84% yield (HPLC, Cosmosil with 10% H_2O/MeOH 1.0 mL/min, the retention time was 6.6 min). Mp 208–212°C; VIS (THF) λ_{max}=647 (0.76), 600 (0.10), 568 (0.05), 522 (0.03), 424 (1.00), 404 nm (0.55); ^{1}H NMR (0.2% C_5D_5N/$CDCl_3$) δ=9.57, 9.33, 8.36 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.17, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 4.01–4.13 (2H, m, $COOCH_2$), 3.76 (2H, q, J=7 Hz, 8-CH_2), 3.41–3.83 (182H, m, $COOCH_2CH_2O(CH_2CH_2O)_{43.1}$), 3.69, 3.35, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.23–2.60 (4H, m, 17-CH_2CH_2), 1.72 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=2008, 2052, 2096, 2140, 2184, 2228, 2272, 2316, 2360, 2404, 2448, 2492, 2536, 2580, 2624, 2668, 2712, 2756, 2800, 2844, 2888. Calcd for $C_{96}H_{160}N_4O_{36}Zn$: M^+, 2008 (n=32), $C_{98}H_{164}N_4O_{37}Zn$: M^+, 2052 (n=33), $C_{100}H_{168}N_4O_{38}Zn$: M^+, 2096 (n=34), $C_{102}H_{172}N_4O_{39}Zn$: M^+, 2140 (n=35), $C_{104}H_{176}N_4O_{40}Zn$: M^+, 2184 (n=36), $C_{106}H_{180}N_4O_{41}Zn$: M^+, 2228 (n=37), $C_{108}H_{184}N_4O_{42}Zn$: M^+, 2272 (n=38), $C_{110}H_{188}N_4O_{43}Zn$: M^+, 2316 (n=39), $C_{112}H_{192}N_4O_{44}Zn$: M^+, 2360 (n=40), $C_{114}H_{196}N_4O_{45}Zn$: M^+, 2404 (n=41), $C_{116}H_{200}N_4O_{46}Zn$: M^+, 2448 (n=42), $C_{118}H_{204}N_4O_{47}Zn$: M^+, 2492 (n=43), $C_{120}H_{208}N_4O_{48}Zn$: M^+, 2536 (n=44), $C_{122}H_{212}N_4O_{49}Zn$: M^+, 2580 (n=45), $C_{124}H_{216}N_4O_{50}Zn$: M^+, 2624 (n=46), $C_{126}H_{220}N_4O_{51}Zn$: M^+, 2668 (n=47), $C_{128}H_{224}N_4O_{52}Zn$: M^+, 2712 (n=48), $C_{130}H_{228}N_4O_{53}Zn$: M^+, 2756 (n=49), $C_{132}H_{232}N_4O_{54}Zn$: M^+, 2800 (n=50), $C_{134}H_{236}N_4O_{55}Zn$: M^+, 2844 (n=51), $C_{136}H_{240}N_4O_{56}Zn$: M^+, 2888 (n=52).

4.4.21. 3-Devinyl-3-hyroxymethyl-pyropheophorbide-*a* 2-sulfoethyl amide (8). Amidation of pyropheophorbide-*d*

with taurine followed by reduction of 3-formyl group gave black solids of **8**, 59% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 5.0 min). Mp >300°C; VIS (MeOH) λ_{max}=660 (0.46), 604 (0.10), 536 (0.11), 504 (0.11), 406 nm (1.00); ^{1}H NMR ($CDCl_3/CD_3OD$=2/1) δ=9.48, 9.44, 8.60 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 3-CH_2), 5.31, 5.11 (each 1H, d, J=20 Hz, 13^2-H_2), 4.49 (1H, dq, J=2, 7 Hz, 18-H), 4.29 (1H, dt, J=8, 2 Hz, 17-H), 3.69 (2H, q, J=7 Hz, 8-CH_2), 3.64, 3.42, 3.25 (each 3H, s, 2-, 7-, 12-CH_3), 3.58 (2H, t, J=6.4 Hz, CONHCH_2), 2.91 (2H, t, J=6.4 Hz, CONHCH$_2$CH_2), 2.63–2.77, 2.40–2.52, 2.16–2.33 (1H+1H+2H, m, 17-CH_2CH_2), 1.81 (3H, d, J=7 Hz, 18-CH_3), 1.70 (3H, t, J=7 Hz, 8^1-CH_3), 0.14, −1.58 (each 1H, s, NH). MS (FAB) found: m/z=646. Calcd for $C_{34}H_{40}N_5O_6S$: MH^+, 646.

4.4.22. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* 2-sulfoethyl amide sodium salt (3). Zinc metallation of **8** gave dark green solids of **3**, 88% yield (HPLC, Cosmosil with 25% H_2O/MeOH 1.0 mL/min, the retention time was 9.5 min). Mp >300°C; VIS (MeOH) λ_{max}=653 (0.87), 607 (0.17), 575 (0.09), 427 (1.00), 408 nm (0.78); ^{1}H NMR ($CDCl_3/CD_3OD$=2/1) δ=9.49, 9.26, 8.34 (each 1H, s, 5-, 10-, 20-H), 5.76, 5.72 (each 1H, d, J=13 Hz, 3-CH_2), 5.23, 5.06 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 3.74 (2H, q, J=7 Hz, 8-CH_2), 3.63, 3.30, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 3.43–3.49 (2H, m, CONHCH_2), 2.79 (2H, t, J=6 Hz, CONHCH$_2$CH_2), 2.58–2.68, 2.01–2.43, (1H+3H, m, 17-CH_2CH_2), 1.78 (3H, d, J=7 Hz, 18-CH_3), 1.71 (3H, t, J=7 Hz, 8^1-CH_3). MS (FAB) found: m/z=752. Calcd for $C_{34}H_{36}N_5O_6SZnNa_2$: $(M-H+Na)^+$, 752.

4.4.23. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* 3-*N*,*N*-dimethylaminopropyl amide (9). Amidation of pyropheophorbide-*d* with *N*,*N*-dimethyl-1,3-propanediamine followed by reduction of 3-formyl group gave black solids of **9**, 63% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 8.8 min). Mp >300°C; VIS (CH_2Cl_2) λ_{max}=662 (0.42), 605 (0.07), 536 (0.08), 504 (0.09), 410 nm (1.00); ^{1}H NMR ($CDCl_3$) δ=9.44, 9.39, 8.52 (each 1H, s, 5-, 10-, 20-H), 5.98–6.10 (1H , m, 17-CONH), 5.85, 5.79 (each 1H, d, J=13 Hz, 3-CH_2), 5.17, 5.05 (each 1H, d, J=20 Hz, 13^2-H_2), 4.49 (1H, dq, J=2, 7 Hz, 18-H), 4.29 (1H, dt, J=8, 2 Hz, 17-H), 3.67 (2H, q, J=7 Hz, 8-CH_2), 3.62, 3.38, 3.22 (each 3H, s, 2-, 7-, 12-CH_3), 2.88–3.17 (2H, m, CONHCH_2), 2.53–2.73, 2.25–2.44, 2.04–2.20 (4H, m, 17-CH_2CH_2), 1.76 (3H, d, J=7 Hz, 18-CH_3), 1.68 (3H, t, J=7 Hz, 8^1-CH_3), 1.08–1.24 (2H, m, CONHCH$_2$CH_2), 0.27, −1.81 (each 1H, s, NH). MS (FAB) found: m/z=623. Calcd for $C_{37}H_{47}N_6O_3$: MH^+, 623.

4.4.24. 3-Devinyl-3-hydroxymethyl-pyropheophorbide-*a* 3-*N*,*N*,*N*-trimethylamonio-propyl amide iodide (6). N-methylation of **9** gave black solids of **6**, 72% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 4.8 min). Mp >300°C; VIS (MeOH) λ_{max}=659 (0.48), 603 (0.09), 535 (0.09), 503 (0.09), 405 nm (1.00); ^{1}H NMR ($CDCl_3/CD_3OD$=2/1) δ=9.37, 9.36, 8.59 (each 1H, s, 5-, 10-, 20-H), 7.27 (1H, br, 17-CONH), 5.77, 5.72 (each 1H, d, J=13 Hz, 3-CH_2), 5.23, 5.03 (each 1H, d, J=20 Hz, 13^2-H_2), 4.55 (1H, dq, J=2, 7 Hz, 18-H), 4.24 (1H, dt, J=8, 2 Hz, 17-H), 3.64 (2H, q, J=7 Hz, 8-CH_2), 3.54, 3.37, 3.22 (each 3H, s, 2-, 7-, 12-CH_3), 3.09–3.18 (2H, m, CONHCH$_2$-CH$_2$CH_2), 2.81–2.99 (2H, m, CONHCH_2), 2.50–2.61, 2.39–2.50, 2.12–2.32 (1H+1H+2H, m, 17-CH_2CH_2), 1.77 (3H, d, J=7 Hz, 18-CH_3), 1.66 (3H, t, J=7 Hz, 8^1-CH_3), 1.41–1.56 (2H, m, CONHCH$_2$CH_2), 0.88, −1.80 (each 1H, s, NH). MS (FAB) found: m/z=637. Calcd for $C_{38}H_{49}N_6O_3$: $[M-I]^+$, 637.

4.4.25. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* 3-*N*,*N*-dimethylamino-propyl amide (10). Zinc metallation of **9** gave dark green solids of **10**, 89% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 3.5 min). Mp >300°C; VIS (CH_2Cl_2) λ_{max}=654 (0.64), 612 (0.10), 575 (0.06), 524 (0.03), 428 nm (1.00); ^{1}H NMR ($CDCl_3/CD_3OD$=2/1) δ=9.56, 9.34, 8.34 (each 1H, s, 5-, 10-, 20-H), 5.84 (2H, s, 3-CH_2), 5.18, 5.05 (each 1H, d, J=20 Hz, 13^2-H_2), 4.45 (1H, dq, J=2, 7 Hz, 18-H), 4.21 (1H, dt, J=8, 2 Hz, 17-H), 3.75 (2H, q, J=7 Hz, 8-CH_2), 3.68, 3.32, 3.23 (each 3H, s, 2-, 7-, 12-CH_3), 2.86–3.16 (2H, m, CONHCH_2), 2.52–2.71, 2.23–2.41, 2.02–2.16 (4H, m, 17-CH_2CH_2), 2.16 (6H, s, N$(CH_3)_2$), 1.71 (3H, d, J=7 Hz, 18-CH_3), 1.69 (3H, t, J=7 Hz, 8^1-CH_3), 1.07–1.22 (2H, m, CONHCH$_2$CH_2). MS (FAB) found: m/z=685. Calcd for $C_{37}H_{45}N_6O_3Zn$: MH^+, 685.

4.4.26. Zinc 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* 3-*N*,*N*,*N*-trimethyl-amoniopropyl amide iodide (4). *N*-Methylation of **10** gave dark green solids of **4**, 75% yield (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 4.4 min). Mp >300°C; VIS (MeOH) λ_{max}=652 (0.69), 609 (0.16), 571 (0.08), 426 nm (1.00); ^{1}H NMR ($CDCl_3/CD_3OD$=2/1) δ=9.46, 9.21, 8.34 (each 1H, s, 5-, 10-, 20-H), 7.27 (1H, m, 17-CONH), 5.71, 5.66 (each 1H, d, J=13 Hz, 3-CH_2), 5.18, 5.04 (each 1H, d, J=20 Hz, 13^2-H_2), 4.40 (1H, dq, J=2, 7 Hz, 18-H), 4.22 (1H, dt, J=8, 2 Hz, 17-H), 3.70 (2H, q, J=7 Hz, 8-CH_2), 3.60, 3.27, 3.23 (each 3H, s, 2-, 7-, 12-CH_3), 2.95–3.02 (2H, m, CONHCH_2), 2.87 (2H, t, J=6.4 Hz, CONHCH$_2$CH$_2$CH_2-N$(CH_3)_3$), 2.80 (9H, s, N$(CH_3)_3$), 2.55–2.65, 2.36–2.47, 2.18–2.29, 1.97–2.09 (each 1H, m, 17-CH_2CH_2), 1.78 (3H, d, J=7 Hz, 18-CH_3), 1.69 (3H, t, J=7 Hz, 8^1-CH_3), 1.37–1.49 (2H, m, CONHCH$_2$CH_2). MS (FAB) found: m/z=699. Calcd for $C_{38}H_{47}N_6O_3Zn$: $[M-I]^+$, 699.

4.4.27. Zinc mesopyropheophorbide-*a* 3-*N*,*N*,*N*-trimethylamoniopropyl iodide (5). Amidation of mesopyropheophorbide-*a* (the 3-ethyl chlorin) with *N*,*N*-dimethyl-1,3-propanediamine followed by zinc metallation and *N*-methylation gave dark green solids of **5** (HPLC, Gelpack with MeOH 1.0 mL/min, the retention time was 5.2 min). Mp >300°C; VIS (MeOH) λ_{max}=647 (0.81), 602 (0.18), 571 (0.10), 424 nm (1.00); ^{1}H NMR (0.4% $C_5D_5N/CDCl_3$) δ=9.46, 9.05, 8.26 (each 1H, s, 5-, 10-, 20-H), 6.55 (1H, m, 17-CONH), 5.20, 5.00 (each 1H, d, J=20 Hz, 13^2-H_2), 4.42 (1H, dq, J=2, 7 Hz, 18-H), 4.15 (1H, dt, J=8, 2 Hz, 17-H), 3.71 (4H, q, J=7 Hz, 3-, 8-CH_2), 3.62, 3.23, 3.19 (each 3H, s, 2-, 7-, 12-CH_3), 3.23–3.29 (2H, m, CONHCH$_2$), 3.16 (2H, t, J=6.4 Hz, CONHCH$_2$CH$_2$CH_2N$(CH_3)_3$), 2.32 (9H, s, N$(CH_3)_3$), 2.05–2.40 (4H, m, 17-CH_2CH_2), 1.69 (3H, d, J=7 Hz, 18-CH_3), 1.673, 1.667 (each 3H, t, J=7 Hz, 3^1-, 8^1-CH_3), 1.53–1.66 (2H, m, CONHCH$_2$CH_2). MS (FAB) found: m/z=697. Calcd for $C_{39}H_{49}N_6O_2Zn$: $[M-I]^+$, 697.

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