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Methyl pyropheophorbide-*a* (MPPa) (**1**) was converted to two aldehydes, methyl 2-formylmethyl-2-devinylpyropheophorbide-*a* (**2**) and methyl 2-formyl-2-devinylpyropheophorbide-*a* (**3**). The former **2** reacted with active methylene compounds having a cyano function in the presence of sulfur to afford thiophene-substituted chlorins **5a-c** and reacted with arylhydrazines to yield indole-substituted chlorins **6a-d**. From the latter **3**, a α-diketo chlorin **7** was obtained *via* Wittig reaction and oxidation. Compound **7** reacted with *o*-phenylenediamine to afford 2-quinoxalyl-substituted pyropheophorbide-*a* **8**. The reaction of MPPa (**1**) with anthranilamide to give a spiro-substituted compound **9**.

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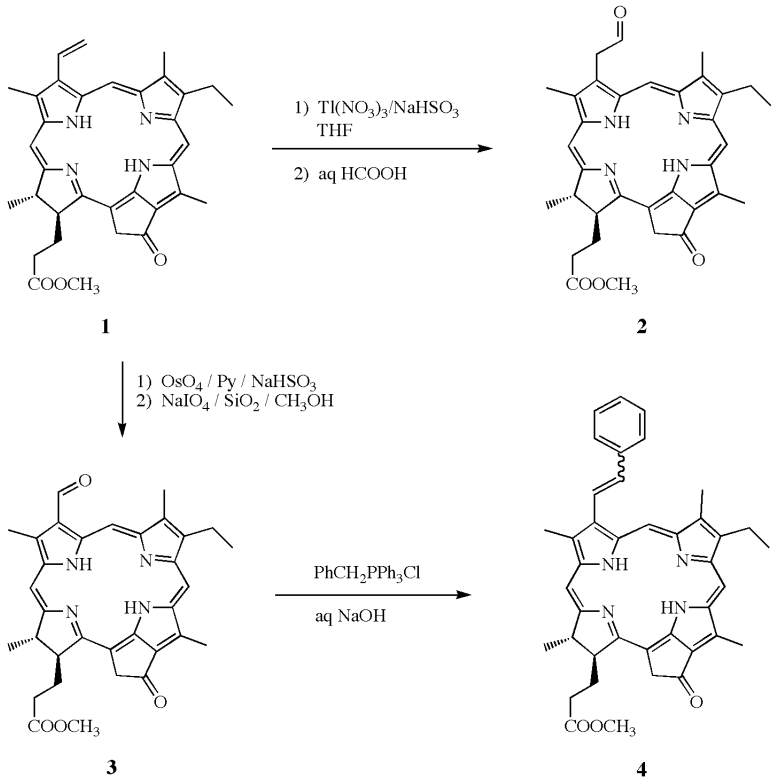
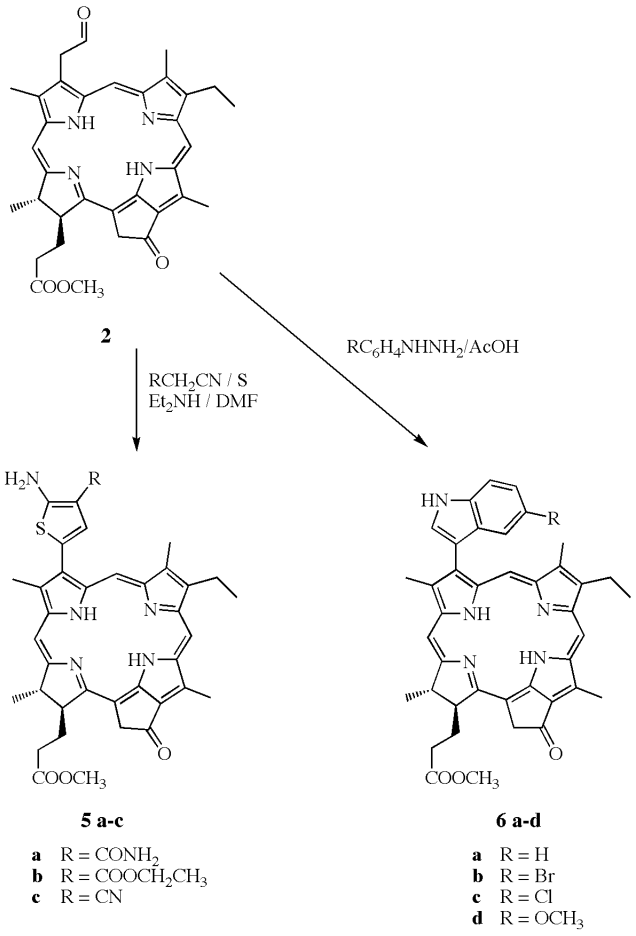
Photodynamic therapy (PDT) is a promising cancer treatment that involves the combination of light, photosensitizer, and oxygen [1]. The emphasis for development of new anticancer drugs in PTD has been concentrated on molecular design, chemical synthesis, and biological evaluation for porphyrin derivatives. Recently, a variety of

Scheme 1



Scheme 2



photosensitizers related to chlorins, bacteriochlorins, porphycenes, phthalocyanines, naphthalocyanines, and porphyrins have been synthesized and evaluated for PDT efficacy. From many earlier works about various chlorin- and bacteriochlorin-related compounds, it has been shown that the presence and position of the substituents in the parent molecule make a remarkable difference in biological activity [2]. In this respect, the studies on *in vivo* quantitative structure-activity relationship (QSAR) of a variety of compounds were carried out [3]. These works suggested that introduction of some heterocyclic function on chlorin should provide valuable information for developing new photosensitizer in photodynamic therapy. However, only a few studies address the synthesis of heterocycle-substituted chlorins. We wish to report herein the synthesis of the pyropheophorbide derivatives bearing some heterocyclic ring on the chlorin chromophores.

Treatment of methyl pyropheophorbide-*a* (MPPa) (**1**) with thallium(III) nitrate in tetrahydrofuran gave the bisdimethylacetal, which was stirred in 88% formic acid at room temperature to yield methyl 2-formylmethyl-2-devinylpyropeophorbide-*a* (**2**) [4]. According to the Gewald synthesis [5], thiophene-substituted chlorins **5a-c** were obtained by the condensation of the aldehyde **2** with cyano-substituted active methylene compounds in the presence of sulfur in 53-65% yields. By using Fischer indole synthesis, the aldehyde **2** reacted with arylhydrazines in boiling glacial acetic acid to afford the indole-substituted chlorins **6a-d**.

MPPa **1** was oxidized with osmium(IV) oxide in tetrahydrofuran containing a catalytic amount of pyridine at 0 °C for 1 hour to give vicinal alcohol, which was treated with sodium periodate in aqueous tetrahydrofuran to give methyl 2-formyl-2-devinylpyropheophorbide-*d* (MPPd) (**3**) [6]. This formylchlorin **3** reacted with benzyltriphenylphosphonium chloride in the presence of sodium hydroxide to give methyl 2b-phenylpyropheophorbide-*a* (**4**) as a mixture of *cis*- (25%) and *trans*-isomer (64%) [6]. The compound **4** was treated with osmium(IV) oxide to give dialcohol, which was oxidized with tetrapropylammonium perruthenate and *N*-methylmorpholine *N*-oxide to afford an α-diketo product **7** in 61% yield. This diketo compound **7** is useful as a building block for the synthesis of heterocycle-substituted chlorins. Thus, compound **7** was treated with *o*-phenylenediamine in boiling dichloromethane in the presence of a catalytic amount of trifluoroacetic acid to give the quinazoline-substituted chlorin **8** in 78% yield.

The condensation of MPPa **1** with anthranilamide in benzene in the presence of *p*-toluenesulfonic acid to give a spiro-chlorin **9** bearing 4-oxo-1,2,3,4-tetrahydroquinazoline moiety in 42% yield.

EXPERIMENTAL

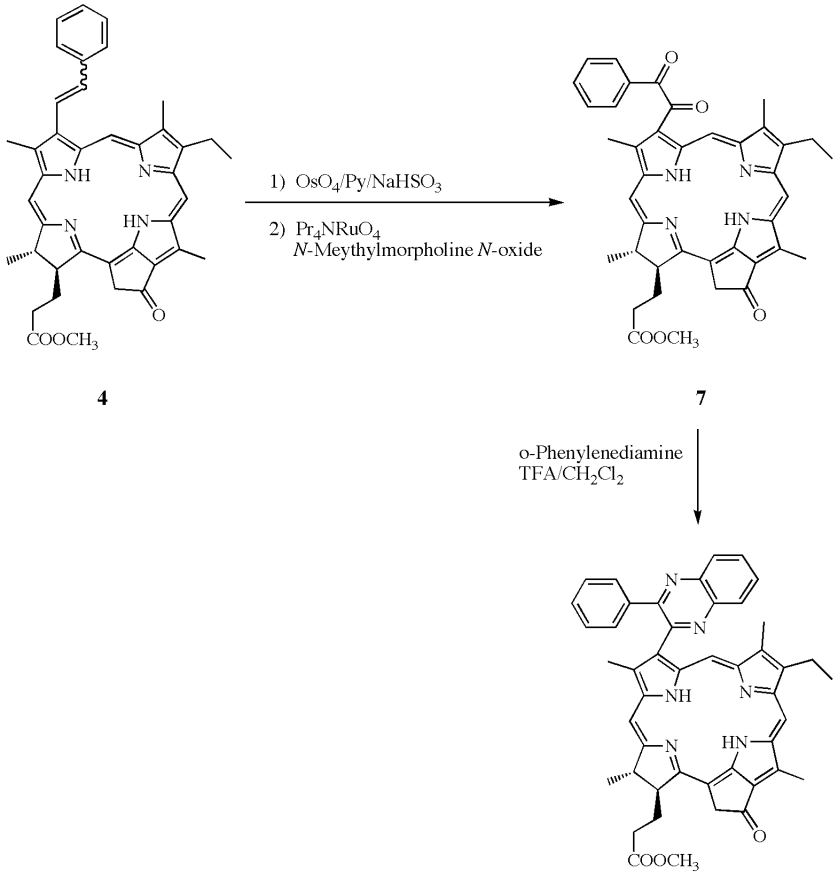
The ir spectra were measured with a Shimadzu FT IR 8300 spectrophotometer. The uv-vis spectra were taken with a Unicam SP 800 spectrophotometer. The ^{1}H nmr spectra were recorded with a Varian 300 spectrometer. The elemental analyses were performed on a Perkin-Elmer 240 microanalyzer. All chemical reagents were commercially available and purified with standard methods. Solvents were dried in routine ways and redistilled. Methyl pyropheophorbide-*a* (MPPa) (**1**) and methyl 2-formylmethyl-2-devinylpyropheophorbide-*a* (**2**) were obtained according to Smith's method [4], while methyl 2-formyl-2-devinylpyropheophorbide-*a* (**3**) was prepared by the Tamiaki's method [6].

Reactions of Formylchlorin **2** with Active Methylene Compounds in the Presence of Sulfur.

General Procedure.

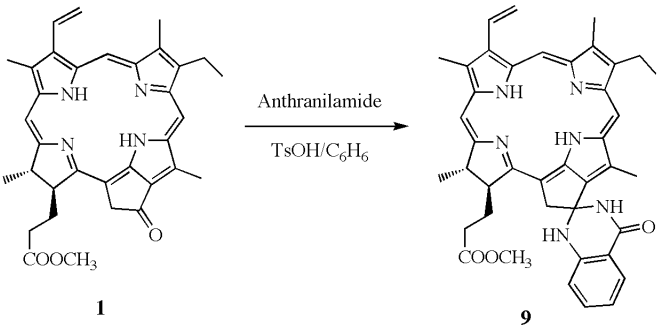
To a suspension of active methylene compound (0.500 mmol) and sulfur (16 mg, 0.500 mmol) in *N,N*-dimethylformamide (15 mL) was added triethylamine (5 mL). After addition of the aldehyde **2** (230 mg, 0.407 mmol), the mixed solution was stirred for 4 hours at room temperature. The mixture was poured into water (30 mL) and extracted with dichloromethane. The extract was washed with water (30 mL x 2) and dried over sodium sulfate. The evaporation residue was purified by using chromatography on a silica gel column with hexane-ethyl acetate (4:1) to give methyl 2-thienyl-2-devinylpyropheophorbide-*a*'s **5a-c**.

Scheme 3



4 **7** **8**

Scheme 4



1 **9**

Methyl 2-[5-(2-Amino-3-carbamoyl)thienyl]-2-devinylpyropheophorbide-*a* (**5a**).

This compound **5a** was obtained from the reaction using cyanoacetamide (42 mg, 0.500 mmol) as dark red solid (143 mg, 53%) (from chloroform-hexane); mp 274-277 °C; ir (potassium bromide): ν 1740 (C=O), 1734 (C=O), 1689 (C=O), 1617 (C=C), 1510 (chlorin skeleton), 1445, 1391, 1321, 1263, 1205, 1188, 1094 cm^{-1}; uv-vis (chloroform): λ (log ε) 319 (3.24), 414 (5.04), 510 (3.00), 540 (2.95), 612 (2.92), 670 nm (3.78); ^1H nmr (deuteriochloroform): δ -1.78 (1H, br.s, NH), 0.21 (1H, br.s, NH), 1.67 (3H, t, *J* = 7.4 Hz, 4b-CH_3), 1.81 (3H, d, *J* = 7.3 Hz, 8-CH_3), 2.18-2.53 (2H, m, 7b-CH_2), 2.52-2.88 (2H, m, 7a-CH_2), 3.20 (3H, s, CH_3), 3.45 (3H, s, CH_3), 3.62 (3H, s, CH_3), 3.64 (3H, s, $COOCH_3$), 3.65 (2H, q, *J* = 7.4 Hz, 4a-CH_2), 4.20-4.30 (1H, m, 8-H), 4.40-4.61 (1H, m, 7-H), 5.14 (1H, d, *J* = 18.6 Hz, 10-H_a), 5.23 (1H, d, *J* = 18.6 Hz, 10-H_b), 5.70 (2H, br.s, 2'-NH_2), 6.51 (2H, br.s, 3'-$CONH_2$), 8.02 (1H, s, 4'-H), 8.58 (1H, s, meso-H), 9.44 (1H, s, meso-H), 9.45 (1H, s, meso-H).

Anal. Calcd. for $C_{37}H_{38}N_6O_4S$: C, 67.05; H, 5.78; N, 12.68. Found: C, 66.85; H, 5.94; N, 12.88.

Methyl 2-[5-(2-Amino-3-ethoxycarbonyl)thienyl]-2-devinylpyropheophorbide-*a* (**5b**).

This compound **5b** was obtained from the reaction using ethyl cyanoacetate (50 mg, 0.500 mmol) as dark red solid (143 mg, 53%) (from chloroform-hexane); mp 251-254 °C; ir (potassium bromide): ν 1746 (C=O), 1730 (C=O), 1621 (C=C), 1514 (chlorin skeleton), 1446, 1390, 1321, 1266, 1205, 1191, 1088 cm^{-1}; uv-vis (chloroform): λ (log ε) 319 (3.37), 416 (5.10), 511 (3.06), 540 (3.06), 613 (2.98), 670 nm (3.98); ^1H nmr (deuteriochloroform): δ -1.74 (1H, br.s, NH), 0.22 (1H, br.s, NH), 1.42 (3H, t, *J* = 7.8 Hz, 3'-$COOCH_2CH_3$), 1.71 (3H, t, *J* = 7.5 Hz, 4b-CH_3), 1.83 (3H, d, *J* = 7.2 Hz, 8-CH_3), 2.12-2.43 (2H, m, 7b-CH_2), 2.52-2.81 (2H, m, 7a-CH_2), 3.21 (3H, s, CH_3), 3.44 (3H, s, CH_3), 3.61 (3H, s, CH_3), 3.68 (3H, s, $COOCH_3$), 3.70 (2H, q, *J* = 7.4 Hz, 4a-CH_2), 4.20-4.36 (1H, m, 8-H), 4.41 (2H, q, *J* = 7.8 Hz, 3'-$COOCH_2CH_3$), 4.40-4.68 (1H, m, 7-H), 5.16 (1H, d, *J* = 19.0

Hz, 10-H_a), 5.24 (1H, d, *J* = 19.0 Hz, 10-H_b), 6.30 (2H, br.s, 2'-NH_2), 7.63 (1H, s, 4'-H), 8.58 (1H, s, meso-H), 9.50 (1H, s, meso-H), 9.53 (1H, s, meso-H).

Anal. Calcd. for $C_{39}H_{41}N_5O_5S$: C, 67.70; H, 5.97; N, 10.12. Found: C, 67.91; H, 6.10; N, 10.44.

Methyl 2-[5-(2-Amino-3-cyano)thienyl]-2-devinylpyropheophorbide-*a* (**5c**).

This compound **5c** was obtained from the reaction using malononitrile (33 mg, 0.500 mmol) as dark red solid (171 mg, 65%) (from chloroform-hexane); mp 264-267 °C; ir (potassium bromide): ν 2264 (C≡N), 1741 (C=O), 1730 (C=O), 1620 (C=C), 1518 (chlorin skeleton), 1440, 1395, 1318, 1259, 1211, 1190, 1087 cm^{-1}; uv-vis (chloroform): λ (log ε) 320 (3.52), 415 (5.13), 468 (2.93), 509 (3.11), 539 (3.06), 562 (2.86), 613 (3.01), 670 nm (4.47); ^{1}H nmr (deuteriochloroform): δ -1.79 (1H, br.s, NH), 0.27 (1H, br.s, NH), 1.69 (3H, t, *J* = 7.5 Hz, 4b-CH_3), 1.81 (3H, d, *J* = 7.4 Hz, 8-CH_3), 2.18-2.38 (2H, m, 7b-CH_2), 2.45-2.72 (2H, m, 7a-CH_2), 3.19 (3H, s, CH_3), 3.42 (3H, s, CH_3), 3.61 (3H, s, CH_3), 3.67 (3H, s, $COOCH_3$), 3.69 (2H, q, *J* = 7.5 Hz, 4a-CH_2), 4.24-4.39 (1H, m, 8-H), 4.41-4.60 (1H, m, 7-H), 5.14 (1H, d, *J* = 19.0 Hz, 10-H_a), 5.19 (2H, br.s, 2'-NH_2), 5.23 (1H, d, *J* = 19.0 Hz, 10-H_b), 7.30 (1H, s, 4'-H), 8.61 (1H, s, meso-H), 9.39 (1H, s, meso-H), 9.52 (1H, s, meso-H).

Anal. Calcd. for $C_{37}H_{36}N_6O_5S$: C, 68.92; H, 5.63; N, 13.04. Found: C, 68.85; H, 5.84; N, 12.86.

Reactions of Formylchlorin **2** with Arylhydrazines.

General Procedure.

A solution of **2** (200 mg, 0.354 mmol) and arylylhydrazine (0.500 mmol) in glacial acetic acid (25 mL) was refluxed for 3 hours under nitrogen atmosphere. The reaction mixture was poured onto ice (150 g) and extracted with dichloromethane (25 mL x 2). The extract was washed with water and dried over sodium sulfate. The evaporation residue was purified by using chromatography on a silica gel column with hexane-ethyl acetate (4:1) to give methyl 2-(3-indolyl)-2-devinylpyropheophorbide-*a*'s **6a**-**d**.

Methyl 2-(3-Indolyl)-2-devinylpyropheophorbide-*a* (**6a**).

This compound **6a** was obtained from the reaction using phenylhydrazine (54 mg, 0.500 mmol) as dark red solid (158 mg, 70%) (from chloroform-hexane); mp 237-239 °C; ir (potassium bromide): ν 1741 (C=O), 1733 (C=O), 1620 (C=C), 1513 (chlorin skeleton), 1446, 1388, 1318, 1254, 1210, 1179, 1101 cm^{-1}; uv-vis (chloroform): λ (log ε) 320 (3.22), 413 (5.02), 507 (3.00), 538 (2.96), 607 (2.92), 663 nm (3.63); ^{1}H nmr (deuteriochloroform): δ -1.58 (1H, br.s, NH), 0.24 (1H, br.s, NH), 1.61 (3H, t, *J* = 7.6 Hz, 4b-CH_3), 1.78 (3H, d, *J* = 7.2 Hz , 8-CH_3), 2.10-2.39 (2H, m, 7b-CH_2), 2.44-2.82 (2H, m, 7a-CH_2), 3.26 (3H, s, CH_3), 3.54 (3H, s, CH_3), 3.61 (3H, s, CH_3), 3.61 (3H, s, $COOCH_3$), 3.67 (2H, q, *J* = 7.5 Hz, 4a-CH_2), 4.19-4.31 (1H, m, 8-H), 4.38-4.58 (1H, m, 7-H), 5.09 (1H, d, *J* = 19.1 Hz, 10-H_a), 5.18 (1H, d, *J* = 19.1 Hz, 10-H_b), 6.98 (1H, br.s, 1'-NH), 7.16-7.79 (4H, m, 4'-,5'-,6'-,7'-H), 8.52 (1H, s, meso-H), 8.86 (1H, s, 2'-H), 9.23 (1H, s, meso-H), 9.36 (1H, s, meso-H).

Anal. Calcd. for $C_{40}H_{39}N_5O_3$: C, 75.32; H, 6.16; N, 10.98. Found: C, 75.46; H, 6.32; N, 10.78.

Methyl 2-(5-Bromo-3-indolyl)-2-devinylpyropheophorbide-*a* (**6b**).

This compound **6b** was obtained from the reaction using 4-bromophenylhydrazine (94 mg, 0.500 mmol) as dark red solid (185 mg, 73%) (from chloroform-hexane); mp 222-225 °C; ir (potassium bromide): ν 1740 (C=O), 1734 (C=O), 1622 (C=C), 1511 (chlorin skeleton), 1438, 1386, 1319, 1254, 1210, 1154, 1109 cm^{-1}; uv-vis (chloroform): λ (log ε) 318 (3.28), 413 (5.25), 506 (3.03), 538 (3.16), 606 (3.13), 664 nm (3.97); ^{1}H nmr (deuteriochloroform): δ -1.69 (1H, br.s, NH), 0.26 (1H, br.s, NH), 1.60 (3H, t, *J* = 7.4 Hz, 4b-CH_3), 1.78 (3H, d, *J* = 7.5 Hz, 8-CH_3), 2.10-2.34 (2H, m, 7b-CH_2), 2.39-2.76 (2H, m, 7a-CH_2), 3.27 (3H, s, CH_3), 3.50 (3H, s, CH_3), 3.60 (3H, s, OCH_3), 3.63 (3H, s, $COOCH_3$), 3.70 (2H, q, *J* = 7.4 Hz, 4a-CH_2), 4.18-4.30 (1H, m, 8-H), 4.36-4.60 (1H, m, 7-H), 5.11 (1H, d, *J* = 19.0 Hz, 10-H_a), 5.18 (1H, d, *J* = 19.0 Hz, 10-H_b), 6.81 (1H, br.s, 1'-NH), 6.98 (1H, d, *J* = 8.0 Hz, 6'-H), 7.48 (1H, d, *J* = 8.0 Hz, 7'-H), 7.72 (1H, s, 4'-H), 8.53 (1H, s, meso-H), 8.66 (1H, s, 2'-H), 9.29 (1H, s, meso-H), 9.42 (1H, s, meso-H).

Anal. Calcd. for $C_{40}H_{38}N_5O_3Br$: C, 67.03; H, 5.34; N, 9.77. Found: C, 67.26; H, 5.42; N, 9.58.

Methyl 2-(5-Chloro-3-indolyl)-2-devinylpyropheophorbide-*a* (**6c**).

This compound **6c** was obtained from the reaction using 4-chlorophenylhydrazine (71 mg, 0.500 mmol) as dark red solid (186 mg, 78%) (from chloroform-hexane); mp 241-243 °C; ir (potassium bromide): ν 1741 (C=O), 1733 (C=O), 1626 (C=C), 1519 (chlorin skeleton), 1444, 1390, 1311, 1257, 1209, 1162, 1109 cm^{-1}; uv-vis (chloroform): λ (log ε) 318 (3.29), 413 (5.30), 508 (3.14), 538 (2.99), 605 (3.08), 663 nm (3.72); ^{1}H nmr (deuteriochloroform): δ -1.69 (1H, br.s, NH), 0.22 (1H, br.s, NH), 1.62 (3H, t, *J* = 7.5 Hz, 4b-CH_3), 1.79 (3H, d, *J* = 7.3 Hz, 8-CH_3), 2.10-2.39 (2H, m, 7b-CH_2), 2.40-2.81 (2H, m, 7a-CH_2), 3.29 (3H, s, CH_3), 3.50 (3H, s, CH_3), 3.62 (3H, s, CH_3), 3.65 (3H, s, $COOCH_3$), 3.69 (2H, q, *J* = 7.5 Hz, 4a-CH_2), 4.12-4.29 (1H, m, 8-H), 4.36-4.55 (1H, m, 7-H), 5.11 (1H, d, *J* = 18.4 Hz, 10-H_a), 5.18 (1H, d, *J* = 18.4 Hz, 10-H_b), 6.81 (1H, br.s, 1'-NH), 7.01 (1H, d, *J* = 8.5 Hz, 6'-H), 7.52 (1H, d, *J* = 8.5 Hz, 7'-H), 7.73 (1H, s, 4'-H), 8.56 (1H, s, meso-H), 8.69 (1H, s, 2'-H), 9.29 (1H, s, meso-H), 9.44 (1H, s, meso-H).

Anal. Calcd. for $C_{40}H_{38}N_5O_3Cl$: C, 71.49; H, 5.70; N, 10.42. Found: C, 71.56; H, 5.52; N, 10.28.

Methyl 2-(5-Methoxy-3-indolyl)-2-devinylpyropheophorbide-*a* (**5d**).

This compound **6d** was obtained from the reaction using 4-methoxyphenylhydrazine (69 mg, 0.500 mmol) as dark red solid (186 mg, 78%) (from chloroform-hexane); mp 241-243 °C; ir (potassium bromide): ν 1742 (C=O), 1731 (C=O), 1624 (C=C), 1513 (chlorin skeleton), 1440, 1394, 1310, 1255, 1207, 1168, 1111 cm^{-1}; uv-vis (chloroform): λ (log ε) 320 (3.45), 413 (5.18), 507 (3.14), 538 (3.11), 607 (3.08), 663 nm (3.77); ^{1}H nmr (deuteriochloroform): δ -1.65 (1H, br.s, NH), 0.25 (1H, br.s, NH), 1.59 (3H, t, *J* = 7.3 Hz, 4b-CH_3), 1.77 (3H, d, *J* = 7.2 Hz, 8-CH_3), 2.08-2.35 (2H, m, 7b-CH_2), 2.40-2.78 (2H, m, 7a-CH_2), 3.28 (3H, s, CH_3), 3.54 (3H, s, CH_3), 3.60 (3H, s, CH_3), 3.63 (3H, s, $COOCH_3$), 3.76 (2H, q, *J* = 7.5 Hz, 4a-CH_2), 3.77 (3H, s, 5'-OCH_3), 4.16-4.31 (1H, m, 8-H), 4.39-4.59 (1H, m, 7-H), 5.09 (1H, d, *J* = 18.9 Hz, 10-H_a), 5.17 (1H, d, *J* = 18.9 Hz, 10-H_b), 6.80 (1H, br.s, 1'-NH), 7.00 (1H, d, *J* = 8.9 Hz, 6'-H), 7.50 (1H, d, *J* = 8.9 Hz, 7'-H), 7.70 (1H, s, 4'-H), 8.54 (1H, s, meso-H), 8.76 (1H, s, 2'-H), 9.27 (1H, s, meso-H), 9.41 (1H, s, meso-H).

Anal. Calcd. for $C_{41}H_{41}N_5O_4$: C, 73.74; H, 6.19; N, 10.49. Found: C, 73.56; H, 6.42; N, 10.28.

Methyl 2-Phenyloxalyl-2-devinylpyropheophorbide-*a* (**7**).

To a solution of compound **4** (230 mg, 0.368 mmol) in tetrahydrofuran (35 mL) containing pyridine (0.3 mL) was added osmium(IV) oxide (93 mg, 0.336 mmol) at 0 °C. The mixed solution was stirred for 30 minutes at the same temperature in dark and stirred for additional 1 hour at room temperature. After adding a solution of sodium hydrogensulfite (15 g) in 50% aqueous methanol, the mixture was stirred for 20 minutes. The brown osmium(III) oxide precipitate was filtered off. The filtrate was diluted with water and extracted with dichloromethane. The extract was dried over sodium sulfate and the solvent was removed. To the solution of the residue in dichloromethane (25 mL), *N*-methylmorpholine *N*-oxide (60 mg) was added rapidly. After stirring for 20 minutes at room temperature under nitrogen atmosphere, tetrapropylammonium perruthenate (25 mg) was added to the solution and the stirring was continued for 1 hour. The reaction mixture was poured into water (20 mL) and stirred for 5 minutes. The organic layer was separated, washed with water, and dried over sodium sulfate. The evaporation residue was chromatographed on a silica gel column initially with dichloromethane to remove *N*-methylmorpholine *N*-oxide and with dichloromethane containing 1% methanol to give **7** (148 mg, 61%) as dark red solid (chloroform-hexane); mp 212-214 °C; ir (potassium bromide): ν 1740 (C=O), 1733 (C=O), 1715 (C=O), 1622 (C=C), 1516 (chlorin skeleton), 1444, 1381, 1311, 1247, 1198, 1158, 1112 cm^{-1}; uv-vis (chloroform): λ (log ε) 329 (3.21), 391 (3.83), 434 (3.77), 525 (2.98), 562 (3.00), 643 (2.93), 701 nm (3.65); ^{1}H nmr (deuteriochloroform): δ -2.15 (1H, br.s, NH), -0.23 (1H, br.s, NH), 1.58 (3H, t, *J* = 7.6 Hz, 4b-CH_3), 1.82 (3H, d, *J* = 7.2 Hz, 8-CH_3), 2.18-2.42 (2H, m, 7b-CH_2), 2.45-2.83 (2H, m, 7a-CH_2), 3.10 (3H, s, CH_3), 3.57 (3H, s, CH_3), 3.62 (3H, s, CH_3), 3.68 (3H, s, $COOCH_3$), 3.69 (2H, q, *J* = 7.6 Hz, 4a-CH_2), 4.25-4.42 (1H, m, 8-H), 4.47-4.64 (1H, m, 7-H), 5.18 (1H, d, *J* = 19.0 Hz, 10-H_a), 5.36 (1H, d, *J* = 19.0 Hz, 10-H_b), 7.58-7.82 (3H, m, 3'-, 4'-,5'-H), 8.25-8.50 (2H, m, 2'-,6'-H), 8.85 (1H, s, meso-H), 9.54 (1H, s, meso-H), 10.18 (1H, s, meso-H).

Anal. Calcd. for $C_{40}H_{38}N_4O_5$: C, 73.37; H, 5.85; N, 8.56. Found: C, 73.16; H, 6.02; N, 8.48.

Methyl 2-(3-Phenyl-2-quinoxalynyl)-2-devinylpyropheophorbide-*a* (**8**).

A solution of **7** (120 mg, 0.183 mmol), *o*-phenylenediamine (33 mg, 0.300 mmol), and trifluoroacetic acid (catalytic amount) in dichloromethane (30 mL) was refluxed for 5 hours under nitrogen atmosphere. The reaction mixture was poured onto ice (150 g) and extracted with dichloromethane (25 mL x 2). The extract was washed with water and dried over sodium sulfate. The evaporation residue was purified by using chromatography on a silica gel column with hexane-ethyl acetate (4:1) to give **8** (104 mg, 78%) as dark green solid (chloroform-hexane); mp 209-211 °C; ir (potassium bromide): ν 1742 (C=O), 1731 (C=O), 1624 (C=C), 1513 (chlorin skeleton), 1440, 1394, 1310, 1255, 1207, 1168, 1111 cm^{-1}; uv-vis (chloroform): λ (log ε) 319 (3.39), 410 (5.60), 471 (3.03), 510 (3.16), 539 (3.11), 612 (3.08), 670 nm (3.95); ^{1}H nmr (deuteriochloroform): δ -1.75 (1H, br.s, NH), 0.31 (1H, br.s, NH), 1.69 (3H, t, *J* = 7.4 Hz, 4b-CH_3), 1.82 (3H, d, *J* = 7.3 Hz, 8-CH_3), 2.14-2.45 (2H, m, 7b-CH_2), 2.47-2.84 (2H, m, 7a-CH_2), 2.96 (3H, s, CH_3), 3.06 (3H, s, CH_3), 3.65 (3H, s, CH_3), 3.67 (2H, q, *J* = 7.4 Hz, 4a-CH_2), 3.69 (3H, s, $COOCH_3$), 4.21-4.39 (1H, m, 8-H), 4.41-4.59 (1H, m, 7-H), 5.13 (1H, d, *J* = 19.7 Hz, 10-H_a), 5.31 (1H, d, *J* = 19.7 Hz, 10-H_b), 6.85-8.48 (9H, m, phenyl-H + quinoxalyl-H), 8.50 (1H, s, meso-H), 9.29 (1H, s, meso-H), 9.55 (1H, s, meso-H).

Anal. Calcd. for $C_{46}H_{42}N_6O_3$: C, 76.01; H, 5.83; N,11.56. Found: C, 76.26; H, 5.62; N, 11.48.

Methyl 9-Spiro-2'-[(4'-oxo-1',2',3',4'-tetrahydro)quinazolyl]-pyropheophorbide-*a* (**9**).

To a solution of 2-aminobenzamide (82 mg, 0.600 mmol) and MPPa (**1**) (220 mg, 0.401 mmol) in benzene (50 mL) was added *p*-toluenesulfonic acid (15 mg). The solution was refluxed for 24 hours while the water formed in the reaction was continuously removed using a Dean-Steak trap. After removal of the solvent, the residue was chromatogtraphed on a silica gel column with hexane-ethyl acetate (4:1) to give **9** (112 mg, 42%) as dark red solid (from chloroform-hexane); mp 267-269 °C; ir (potassium bromide): ν 1742 (C=O), 1731 (C=O), 1669 (C=O), 1623 (C=C), 1520 (chlorin skeleton), 1444, 1400, 1305, 1246, 1207, 1153, 1109 cm^{-1}; uv-vis (chloroform): λ (log ε) 400 (5.75), 500 (3.13), 549 (2.89), 599 (2.94), 654 nm (3.72); ^{1}H nmr (deuteriochloroform): δ -3.12 (1H, br.s, NH), 1.58 (3H, t, *J* = 7.7 Hz, 4b-CH_3), 1.74 (3H, d, *J* = 7.4 Hz, 8-CH_3), 1.98 (1H, br.s, NH), 2.08-2.72 (4H, m, 7a-CH_2 + 7b-CH_2), 3.02 (3H, s, CH_3), 3.37 (3H, s, CH_3), 3.38 (3H, s, CH_3), 3.54 (3H, s, $COOCH_3$), 3.68 (2H, q, *J* = 7.7 Hz, 4a-CH_b), 4.21-4.41 (1H, m, 8-H), 4.38-4.62 (1H, m, 7-H), 5.18 (1H, d, *J* = 19.5 Hz, 10-H_a), 5.25 (1H, d, *J* = 19.5 Hz, 10-H_b), 5.42 (1H, br.s, 1'-NH), 6.21 (2H, m, 2b-CH_2), 6.38 (1H, br.s, 3'-NH), 6.80-7.78 (4H, m, 4'-,6'-,7'-8'-H), 8.18 (1H, m, 2a-H), 8.81 (1H, s, meso-H), 9.61 (1H, s, meso-H), 9.80 (1H, s, meso-H).

Anal. Calcd for $C_{41}H_{42}N_6O_3$: C, 73.85; H, 6.35; N, 12.60. Found: C, 73.66; H, 6.49; N, 12.55.

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