Supplementary Material (ESI) for Photochemical & Photobiological Sciences

Synthesis of zinc bacteriochlorophyll-*d* analogues with various 17-substituents and their chlorosomal self-aggregates in non-polar organic solvents†

Hitoshi Tamiaki,* Tomotaka Michitsuji and Reiko Shibata

Department of Bioscience and Biotechnology, Faculty of Science and Engineering, Ritsumeikan University, Kusatsu, Shiga 525-8577, Japan.

E-mail: tamiaki@se.ritsumei.ac.jp; Fax: +81-77-561-2659

Synthetic procedures of novel chlorins and their spectral data

Ethyl pyropheophorbide-*d* (5a). Into a dry toluene solution (30 ml) of **4** (102 mg, 185 μmol), ethanol (8.73 g, 189 mmol) and bis(dibutylchlorotin)oxide (14.1 mg, 25 μmol) were added, stirred and refluxed for 27 h. After evaporating the solvent, the residue was purified by FCC (4% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane) to give **5a** (62.3 mg, 60%) as a black solid: mp 222-225 °C; VIS (CH_2Cl_2) λ_{max} = 694 (relative intensity, 0.80), 632 (0.09), 554 (0.16), 521 (0.15), 429 (1.00), 388 nm (0.84); ^{1}H-NMR ($CDCl_3$) δ = 11.55 (1H, s, 3-CHO), 10.30, 9.61, 8.84 (each 1H, s, 5-, 10-, 20-H), 5.34, 5.19 (each 1H, d, *J* = 20 Hz, 13^2-H_2), 4.58 (1H, q, *J* = 7 Hz, 18-H), 4.39 (1H, d, *J* = 7 Hz, 17-H), 4.13-4.02 (2H, m, 17^2-$COOCH_2$), 3.77, 3.72, 3.32 (each 3H, s, 2-, 7-, 12-CH_3), 3.72 (2H, q, *J* = 7 Hz, 8-CH_2), 2.75-2.70, 2.62-2.54, 2.35-2.26 (1H+1H+2H, m, 17-CH_2CH_2), 1.85 (3H, d, *J* = 7 Hz, 18-CH_3), 1.72 (3H, t, *J* = 7 Hz, 8^1-CH_3), 1.16 (3H, t, *J* = 7 Hz, 17^2-$COOCCH_3$), -0.13, -2.06 (each 1H, s, NH × 2); MS (APCI) found: *m/z* 565. Calcd. for $C_{34}H_{37}N_4O_4$: MH^+, 565.

Dodecyl pyropheophorbide-*d* (5b). Similarly to synthesis of **5a**, transesterification of **4** (101 mg, 183 μmol) with 1-dodecanol (293 mg, 1.85 mmol) in toluene (30 ml) of tin-catalyst (10.3 mg, 18.7 μmol) for 5 h gave **5b** (83.0 mg, 64%) as a black solid after FCC (3-4% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 125-130 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel., 0.80), 632 (0.09), 554 (0.17), 521 (0.15), 428 (1.00), 388 nm (0.84); ^{1}H-NMR ($CDCl_3$) δ = 11.57 (1H, s, 3-CHO), 10.33, 9.64, 8.85 (each 1H, s, 5-, 10-, 20-H), 5.35, 5.20 (each 1H, d, *J* = 20 Hz, 13^2-H_2), 4.58 (1H, dq, *J* = 2, 8 Hz, 18-H), 4.40 (1H, dt, *J* = 9, 2 Hz, 17-H), 4.00-3.91 (2H, m, 17^2-$COOCH_2$), 3.79, 3.73, 3.34 (each 3H, s, 2-, 7-, 12-CH_3), 3.74 (2H, q, *J* = 8 Hz, 8-CH_2), 2.76-2.69, 2.61-2.53, 2.37-2.24 (1H+1H+2H, m, 17-CH_2CH_2), 1.85 (3H, d, *J* = 8 Hz, 18-CH_3), 1.73 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.25-1.17 (20H, m, 17^2-$COOCC_{10}H_{20}$), 0.84 (3H, t, *J* = 7 Hz, 17^2-$COOC_{11}CH_3$), -0.11, -2.04 (each 1H, s, NH × 2); MS (APCI) found: *m/z* 705. Calcd. for $C_{44}H_{57}N_4O_4$: MH^+, 705.

Docosyl pyropheophorbide-*d* (5c). Similarly to synthesis of **5a**, transesterification of **4** (80 mg, 145 μmol) with 1-docosanol (469 mg, 1.44 mmol) in toluene (25 ml) of tin-catalyst (5.6 mg, 10.1 μmol) for 5 h gave **5c** (95.0 mg, 78%) as a black solid after FCC (3-4% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 110-114 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel., 0.80), 632 (0.09), 554 (0.17), 521 (0.15), 429 (1.00), 388 nm (0.84); ^{1}H-NMR ($CDCl_3$) δ = 11.58 (1H, s, 3-CHO), 10.35, 9.65, 8.86 (each 1H, s, 5-, 10-, 20-H), 5.34, 5.23 (each 1H, d, *J* = 20 Hz, 13^2-H_2), 4.59 (1H, dq, *J* = 2, 8 Hz, 18-H), 4.40 (1H, dt, *J* = 8, 2 Hz, 17-H), 4.01-3.90 (2H, m, 17^2-$COOCH_2$), 3.80, 3.74, 3.35 (each 3H, s, 2-, 7-, 12-CH_3), 3.75 (2H, q, *J* = 8 Hz, 8-CH_2), 2.77-2.69, 2.62-2.54, 2.37-2.27 (1H+1H+2H, m, 17-CH_2CH_2), 1.85 (3H, d, *J* = 8 Hz, 18-CH_3), 1.74 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.26-1.18 (40H, m, 17^2-$COOCC_{20}H_{40}$), 0.88 (3H, t, *J* = 7 Hz, 17^2-$COOC_{21}CH_3$), -0.10, -2.02 (each 1H, s, NH × 2); MS (APCI) found: *m/z* 845. Calcd. for $C_{54}H_{77}N_4O_4$: MH^+, 845.

Neopentyl pyropheophorbide-*d* (5d). Similarly to synthesis of **5a**, transesterification of **4** (85 mg, 154 μmol) with 2,2-dimethylpropanol (neopentyl alcohol, 133 mg, 1.51 mmol) in toluene (25 ml) of tin-catalyst (8.9 mg, 16.1 μmol) for 21 h gave **5d** (55.7 mg, 60%) as a black solid after FCC (4% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 175-180 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel., 0.81), 632 (0.09), 554 (0.17), 522 (0.15), 429 (1.00), 388 nm (0.84); ^{1}H-NMR ($CDCl_3$) δ = 11.55 (1H, s, 3-CHO), 10.29, 9.60, 8.85 (each 1H, s, 5-, 10-, 20-H), 5.34, 5.20 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.59 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.41 (1H, dt, *J* = 8, 2 Hz, 17-H), 3.78, 3.70 (each 1H, d, *J* = 10 Hz, 17^2-$COOCH_2$), 3.78, 3,72, 3.31 (each 3H, s, 2-, 7-, 12-CH_3), 3.72 (2H, q, *J* = 8 Hz, 8-CH_2), 2.78-2.72, 2.63-2.58, 2.37-2.29 (1H+1H+2H, m, 17-CH_2CH_2), 1.86 (3H, d, *J* = 7 Hz, 18-CH_3), 1.71 (3H, t, *J* = 8 Hz, 8^1-CH_3), 0.84 (9H, s, 17^2-$COOCC(CH_3)_3$), -0.15, -2.07 (each 1H, s, NH × 2); MS (APCI) found: *m/z* 607. Calcd. for $C_{37}H_{43}N_4O_4$: MH^+, 607.

Benzyl pyropheophorbide-*d* (5e). Similarly to synthesis of **5a**, transesterification of **4** (97 mg, 175 μmol) with benzyl alcohol (201 mg, 1.86 mmol) in toluene (30 ml) of tin-catalyst (30.0 mg, 54.2 μmol) for 6 h gave **5e** (77.0 mg, 70%) as a black solid after FCC (4-5% Et_2O/CH_2Cl_2) and

recrystallization (CH_2Cl_2/methanol): mp 98-102 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel., 0.80), 633 (0.09), 555 (0.17), 522 (0.15), 429 (1.00), 388 nm (0.83); ^{1}H-NMR ($CDCl_3$) δ = 11.55 (1H, s, 3-CHO), 10.31, 9.61, 8.82 (each 1H, s, 5-, 10-, 20-H), 7.26-7.25 (3H, m, 3-, 4-, 5-H of Ph), 7.21-7.19 (2H, m, 2-, 6-H of Ph), 5.31, 5.14 (each 1H, d, J = 20 Hz, 13^2-H_2), 5.05, 4.98 (each 1H, d, J = 12 Hz, 17^2-$COOCH_2$), 4.56 (1H, dq, J = 1, 7 Hz, 18-H), 4.37 (1H, br-d, J = 7 Hz, 17-H), 3.77, 3.72, 3.32 (each 3H, s, 2-, 7-, 12-CH_3), 3.73 (2H, q, J = 8 Hz, 8-CH_2), 2.77-2.71, 2.65-2.60, 2.36-2.29 (1H+1H+2H, m, 17-CH_2CH_2), 1.82 (3H, d, J = 7 Hz, 18-CH_3), 1.72 (3H, t, J = 8 Hz, 8^1-CH_3), -0.14, -2.08 (each 1H, s, NH × 2); MS (APCI) found: *m/z* 627. Calcd. for $C_{39}H_{39}N_4O_4$: MH^+, 627.

17^2-Acetoxymethyl-17^2-decarboxy-pyropheophorbide-*d* (9a). To a dry CH_2Cl_2 solution (70 ml) of **8** (100.0 mg, 191 μmol), acetic acid (45.2 mg, 764 μmol), 1-[3-(*N*,*N*-dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC·HCl, 220.0 mg, 1148 μmol) and DMAP (96.7 mg, 792 μmol) were added at 0 °C and stirred for 18 h under N_2 at room temperature. The reaction mixture was washed with aq. 2% HCl, aq. 4% $NaHCO_3$ and H_2O, dried over Na_2SO_4 and evaporated to dryness. The residue was purified by FCC (7% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane) to give **9a** (99.7 mg, 93%) as a black green solid: mp 250-252 °C; VIS (CH_2Cl_2) λ_{max} = 695 (rel., 0.81), 633 (0.09), 554 (0.16), 522 (0.15), 429 (1.00), 387 nm (0.85); ^{1}H-NMR ($CDCl_3$) δ = 11.56 (1H, s, 3-CHO), 10.31, 9.62, 8.85 (each 1H, s, 5-, 10-, 20-H), 5.29, 5.19 (each 1H, d, J = 19 Hz, 13^2-H_2), 4.60 (1H, dq, J = 2, 7 Hz, 18-H), 4.37 (1H, dt, J = 9, 2 Hz, 17-H), 4.12, 4.10 (each 1H, dt, J = 11, 7 Hz, 17^2-CH_2), 3.73 (2H, q, J = 8 Hz, 8-CH_2), 3.79, 3.73, 3.33 (each 3H, s, 2-, 7-, 12-CH_3), 2.45-2.40, 2.15-2.08, 1.95-1.88, 1.68-1.61 (each 1H, m, 17-CH_2CH_2), 2.01 (3H, s, 17^3-$OCOCH_3$), 1.87 (3H, d, J = 7 Hz, 18-CH_3), 1.72 (3H, t, J = 8 Hz, 8^1-CH_3), -0.10, -2.03 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 565. Calcd. for $C_{34}H_{37}N_4O_4$: MH^+, 565.

17^2-Decarboxy-17^2-dodecanoyloxymethyl-pyropheophorbide-*d* (9b). Similarly to synthesis of **9a**, esterification of **8** (100.0 mg, 191 μmol) with dodecanoic acid (lauric acid, 153.1 mg, 764 μmol) in CH_2Cl_2 (70 ml) of EDC·HCl (219.7 mg, 1146 μmol) and DMAP (93.3 mg, 764 μmol) for 23 h gave **9b** (105.0 mg, 78%) as a black solid after FCC (6% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 156-158 °C; VIS (CH_2Cl_2) λ_{max} = 695 (rel, 0.82), 633 (0.09), 555 (0.16), 522 (0.15), 429 (1.00), 387 nm (0.84); ^{1}H-NMR ($CDCl_3$) δ = 11.56 (1H, s, 3-CHO), 10.33, 9.63, 8.85 (each 1H, s, 5-, 10-, 20-H), 5.29, 5.19 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.60 (1H, dq, *J* = 2, 8 Hz, 18-H), 4.37 (1H, dt, *J* = 9, 2 Hz, 17-H), 4.12 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.74 (2H, q, *J* = 8 Hz, 8-CH_2), 3.79, 3.73, 3.33 (each 3H, s, 2-, 7-, 12-CH_3), 2.45-2.39, 2.14-2.08, 1.95-1.87, 1.69-1.63 (each 1H, m, 17-CH_2CH_2), 2.26, 2.23 (each 1H, dt, *J* = 15, 8 Hz, 17^3-$OCOCH_2$), 1.87 (3H, d, *J* = 8 Hz, 18-CH_3), 1.73 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.25-1.15 (18H, m, 17^3-$OCOC(CH_2)_9$), 0.84 (3H, t, *J* = 7 Hz, 17^3-$OCOC_{10}CH_3$), -0.09, -2.03 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 705. Calcd. for $C_{44}H_{57}N_4O_4$: MH^+, 705.

17^2-Decarboxy-17^2-docosanoyloxymethyl-pyropheophorbide-*d* (9c). Similarly to synthesis of **9a**, esterification of **8** (90.0 mg, 172 μmol) with docosanoic acid (behenic acid, 239.0 mg, 702 μmol) in CH_2Cl_2 (70 ml) of EDC·HCl (197.7 mg, 1031 μmol) and DMAP (84.0 mg, 688 μmol) for 21 h gave **9c** (114.5 mg, 79%) as a black solid after FCC (5% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 153-155 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel, 0.82), 633 (0.10), 554 (0.17), 522 (0.16), 429 (1.00), 387 nm (0.85); ^{1}H-NMR ($CDCl_3$) δ = 11.55 (1H, s, 3-CHO), 10.30, 9.60, 8.85 (each 1H, s, 5-, 10-, 20-H), 5.29, 5.18 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.60 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.37 (1H, dt, *J* = 9, 3 Hz, 17-H), 4.12 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.73 (2H, q, *J* = 8 Hz, 8-CH_2), 3.78, 3.72, 3.32 (each 3H, s, 2-, 7-, 12-CH_3), 2.44-2.40, 2.14-2.08, 1.95-1.89, 1.69-1.63 (each 1H, m, 17-CH_2CH_2), 2.25 (2H, t, *J* = 7 Hz, 17^3-$OCOCH_2$), 1.87 (3H, d, *J* = 7 Hz, 18-CH_3), 1.72 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.30-1.15 (38H, m, 17^3-$OCOC(CH_2)_{19}$), 0.87 (3H, t, *J* = 7 Hz, 17^3-$OCOC_{20}CH_3$), -0.12, -2.04 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 845. Calcd. for $C_{54}H_{77}N_4O_4$: MH^+, 845.

17^2-Decarboxy-17^2-pivaloyloxymethyl-pyropheophorbide-*d* (9d). Similarly to synthesis of **9a**, esterification of **8** (102.0 mg, 195 μmol) with 2,2-dimethylpropanoic acid (pivalic acid, 99.0 mg, 969 μmol) in CH_2Cl_2 (70 ml) of EDC·HCl (332.0 mg, 1732 μmol) and DMAP (156.7 mg, 1282 μmol) for 62 h to give **9d** (37.5 mg, 32%) as a black solid after FCC (5% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 253-257 °C; VIS (CH_2Cl_2) λ_{max} = 695 (rel, 0.81), 633 (0.10), 554 (0.17), 522 (0.16), 429 (1.00), 387 nm (0.85); ^{1}H-NMR ($CDCl_3$) δ = 11.57 (1H, s, 3-CHO), 10.34, 9.64, 8.86 (each 1H, s, 5-, 10-, 20-H), 5.27, 5.29 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.60 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.38 (1H, dt, *J* = 9, 3 Hz, 17-H), 4.10 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.75 (2H, q, *J* = 8 Hz, 8-CH_2), 3.79, 3.74, 3.34 (each 3H, s, 2-, 7-, 12-CH_3), 2.45-2.40, 2.15-2.09, 1.95-1.89, 1.69-1.61 (each 1H, m, 17-CH_2CH_2), 1.87 (3H, d, *J* = 7 Hz, 18-CH_3), 1.73 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.15 (9H, s, 17^3-$OCOC(CH_3)_3$), -0.08, -2.01 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 607. Calcd. for $C_{37}H_{43}N_4O_4$: MH^+, 607.

To a dry THF (2 ml) and CH_2Cl_2 solution (20 ml) of **8** (100.0 mg, 191 μmol) with stirring, a dry CH_2Cl_2 solution (20 ml) of pivaloyl chloride (1854 mg, 15.4 mmol) and triethylamine (956.0 mg, 9.45 mmol) at room temperature under N_2. After heating at 45 °C for 4 h, the reaction mixture was treated with the similar work-up as mentioned above to give **9d** (84.5 mg, 72%).

17^2-Benzoyloxymethyl-17^2-decarboxy-pyropheophorbide-*d* (9e). Similarly to synthesis of **9a**, esterification of **8** (69.0 mg, 132 μmol) with benzoic acid (71.4 mg, 855 μmol) in CH_2Cl_2 (60 ml) of EDC·HCl (185.5 mg, 968 μmol) and DMAP (68.5 mg, 561 μmol) gave **9e** (45.5 mg, 55%) as a black solid after FCC (4-5% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 95-99 °C; VIS (CH_2Cl_2) λ_{max} = 694 (rel, 0.80), 633 (0.10), 554 (0.17), 522 (0.16), 429 (1.00), 387 nm (0.85); ^{1}H-NMR ($CDCl_3$) δ = 11.55 (1H, s, 3-CHO), 10.31, 9.61, 8.86 (each 1H, s, 5-, 10-, 20-H), 7.96, 7.95 (2H, dd, *J* = 1, 8 Hz, 2-, 6-H of Ph), 7.53 (1H, tt, *J* = 1, 7 Hz, 4-H of Ph), 7.39 (2H, t, *J* = 8 Hz, 3-, 5-H of Ph), 5.30, 5.20 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.64 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.42 (1H, dt, *J* = 9, 3 Hz, 17-H), 4.36 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.73 (2H, q, *J* = 8 Hz, 8-CH_2), 3.78,

3.72, 3.32 (each 3H, s, 2-, 7-, 12-CH_3), 2.55-2.49, 2.26-2.19, 2.08-1.99, 1.78-1.74 (each 1H, m, 17-CH_2CH_2), 1.88 (3H, d, J = 7 Hz, 18-CH_3), 1.72 (3H, t, J = 8 Hz, 8^1-CH_3), -0.11, -2.04 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 627. Calcd. for $C_{39}H_{39}N_4O_4$: MH^+, 627.

Ethyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (6a). Borane *t*-butylamine complex (*t*$BuNH_2 \cdot BH_3$, 13.3 mg, 153 μmol) was added to a CH_2Cl_2 solution (10 ml) of **5a** (57.8 mg, 102 μmol) at room temperature. After stirring for 2 h, the reaction mixture was washed with aq. 2% HCl, aq. 4% $NaHCO_3$ and H_2O, dried over Na_2SO_4 and evaporated to dryness. The residue was purified by FCC (20-24% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane) to give **6a** (51.2 mg, 88%) as a black green solid: mp 227-232 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.48), 606 (0.08), 535 (0.09), 504 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.47, 9.43, 8.55 (each 1H, s, 5-, 10-, 20-H), 5.90 (2H, s, 3-CH_2), 5.22, 5.08 (each 1H, d, J = 19 Hz, 13^2-H_2), 4.47 (1H, dq, J = 2, 7 Hz, 18-H), 4.26 (1H, dt, J = 9, 2 Hz, 17-H), 4.14-4.04 (2H, m, 17^2-$COOCH_2$), 3.68 (2H, q, J = 8 Hz, 8-CH_2), 3.64, 3.42, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.69-2.64, 2.56-2.51, 2.28-2.22 (1H+1H+2H, m, 17-CH_2CH_2), 1.79 (3H, d, J = 7 Hz, 18-CH_3), 1.69 (3H, t, J = 8 Hz, 8^1-CH_3), 1.17 (3H, t, J = 7 Hz, 17^2-$COOCCH_3$), 0.25, -1.82 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 567. Calcd. for $C_{34}H_{39}N_4O_4$: MH^+, 567.

Dodecyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (6b). Similarly to synthesis of **6a**, reduction of **5b** (51.0 mg, 72 μmol) by *t*$BuNH_2 \cdot BH_3$ (9.4 mg, 108 μmol) in CH_2Cl_2 (10 ml) gave **6b** (37.7 mg, 74%) as a black solid after FCC (6-10% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 118-121 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 605 (0.08), 535 (0.09), 504 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.48, 9.44, 8.56 (each 1H, s, 5-, 10-, 20-H), 5.91 (2H, s, 3-CH_2), 5.24, 5.09 (each 1H, d, J = 19 Hz, 13^2-H_2), 4.48 (1H, dq, J = 2, 8 Hz, 18-H), 4.28 (1H, dt, J = 9, 2 Hz, 17-H), 4.02-3.92 (2H, m, 17^2-$COOCH_2$), 3.69 (2H, q, J = 8 Hz, 8-CH_2), 3.65, 3.42, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.70-2.64, 2.56-2.51, 2.31-2.23 (1H+1H+2H, m, 17-CH_2CH_2), 1.80 (3H, d, J = 8 Hz, 18-CH_3), 1.69 (3H, t, J = 8 Hz, 8^1-CH_3), 1.26-1.18 (20H, m,

17^2-$COOCC_{10}H_{20}$), 0.84 (3H, t, J = 7 Hz, 17^2-$COOC_{11}CH_3$), 0.27, -1.81 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 707. Calcd. for $C_{44}H_{59}N_4O_4$: MH^+, 707.

Docosyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (6c). Similarly to synthesis of **6a**, reduction of **5c** (85.3 mg, 101 μmol) by *t*$BuNH_2 \cdot BH_3$ (13.2 mg, 152 μmol) in CH_2Cl_2 (20 ml) gave **6c** (66.2 mg, 77%) as a dark green solid after FCC (4-6% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 130-132 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 605 (0.09), 536 (0.10), 505 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.49, 9.44, 8.56 (each 1H, s, 5-, 10-, 20-H), 5.91 (2H, s, 3-CH_2), 5.24, 5.09 (each 1H, d, J = 19 Hz, 13^2-H_2), 4.49 (1H, dq, J = 2, 7 Hz, 18-H), 4.28 (1H, br-d, J = 9 Hz, 17-H), 4.02-3.92 (2H, m, 17^2-$COOCH_2$), 3.69 (2H, q, J = 8 Hz, 8-CH_2), 3.65, 3.42, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.70-2.64, 2.56-2.51, 2.32-2.23 (1H+1H+2H, m, 17-CH_2CH_2), 1.80 (3H, d, J = 7 Hz, 18-CH_3), 1.69 (3H, t, J = 8 Hz, 8^1-CH_3), 1.30-1.18 (40H, m, 17^2-$COOCC_{20}H_{40}$), 0.87 (3H, t, J = 7 Hz, 17^2-$COOC_{21}CH_3$), 0.28, -1.80 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 847. Calcd. for $C_{54}H_{79}N_4O_4$: MH^+, 847.

Neopentyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (6d). Similarly to synthesis of **6a**, reduction of **5d** (46.3 mg, 76 μmol) by *t*$BuNH_2 \cdot BH_3$ (10.0 mg, 115 μmol) in CH_2Cl_2 (10 ml) gave **6d** (37.4 mg, 81%) as a black solid after FCC (5-7% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 205-207 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 605 (0.08), 535 (0.09), 504 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.50, 9.45, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.91 (2H, s, 3-CH_2), 5.23, 5.10 (each 1H, d, J = 20 Hz, 13^2-H_2), 4.50 (1H, dq, J = 2, 7 Hz, 18-H), 4.30 (1H, br-d, J = 8 Hz, 17-H), 3.77, 3.71 (each 1H, d, J = 11 Hz, 17^2-$COOCH_2$), 3.70 (2H, q, J = 8 Hz, 8-CH_2), 3.66, 3.43, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.72-2.66, 2.59-2.54, 2.36-2.27 (1H+1H+2H, m, 17-CH_2CH_2), 1.81 (3H, d, J = 7 Hz, 18-CH_3), 1.69 (3H, t, J = 8 Hz, 8^1-CH_3), 0.85 (9H, s, 17^2-$COOCC(CH_3)_3$), 0.28, -1.79 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 609. Calcd. for $C_{37}H_{45}N_4O_4$: MH^+, 609.

Benzyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (6e). Similarly to synthesis of **6a**, reduction of **5e** (72.6 mg, 116 μmol) by *t*BuNH$_2$·BH$_3$ (15.1 mg, 174 μmol) in CH_2Cl_2 (20 ml) gave **6e** (64.3 mg, 88%) as a black green solid after FCC (4-6% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 206-210 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.48), 606 (0.08), 535 (0.09), 504 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.52, 9.46, 8.55 (each 1H, s, 5-, 10-, 20-H), 7.26-7.24 (3H, m, 3-, 4-, 5-H of Ph), 7.22-7.21 (2H, m, 2-, 6-H of Ph), 5.92 (2H, s, 3-CH_2), 5.23, 5.06 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 5.05, 5.00 (each 1H, d, *J* = 12 Hz, 17^2-$COOCH_2$), 4.46 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.28 (1H, br-d, *J* = 8 Hz, 17-H), 3.70 (2H, q, *J* = 8 Hz, 8-CH_2), 3.67, 3.42, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.73-2.67, 2.61-2.56, 2.35-2.22 (1H+1H+2H, m, 17-CH_2CH_2), 1.77 (3H, d, *J* = 7 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 0.31, -1.79 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 629. Calcd. for $C_{39}H_{41}N_4O_4$: MH^+, 629.

17^2-Acetoxymethyl-17^2-decarboxy-3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (10a). Similarly to synthesis of **6a**, reduction of **9a** (89.5 mg, 159 μmol) by *t*BuNH$_2$·BH$_3$ (20.2 mg, 232 μmol) in CH_2Cl_2 (20 ml) gave **10a** (88.3 mg, 98%) as a black solid after FCC (15-23% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 226-231 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 605 (0.09), 535 (0.11), 504 (0.12), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.47, 9.44, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.91 (2H, s, 3-CH_2), 5.20, 5.09 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.50 (1H, dq, *J* = 2, 8 Hz, 18-H), 4.27 (1H, dt, *J* = 9, 3 Hz, 17-H), 4.10 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.69 (2H, q, *J* = 8 Hz, 8-CH_2), 3.66, 3.43, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.41-2.35, 2.12-2.04, 1.93-1.84, 1.67-1.60 (each 1H, m, 17-CH_2CH_2), 2.01 (3H, s, 17^3-$OCOCH_3$), 1.82 (3H, d, *J* = 8 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 0.33, -1.76 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 567. Calcd. for $C_{34}H_{39}N_4O_4$: MH^+, 567.

17^2-Decarboxy-3-devinyl-17^2-dodecanoyloxymethyl-3-hydroxymethyl-pyropheophorbide-*a* (10b). Similarly to synthesis of **6a**, reduction of **9b** (99.7 mg, 141 μmol) by *t*BuNH$_2$·BH$_3$ (18.4 mg, 212 μmol) in CH_2Cl_2 (20 ml) gave **10b** (84.5 mg, 85%) as a black solid after FCC (6-15%

Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 118-120 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.48), 605 (0.09), 535 (0.10), 504 (0.11), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.54, 9.46, 8.58 (each 1H, s, 5-, 10-, 20-H), 5.93 (2H, s, 3-CH_2), 5.22, 5.10 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.51 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.29 (1H, dt, *J* = 9, 3 Hz, 17-H), 4.10 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.71 (2H, q, *J* = 8 Hz, 8-CH_2), 3.69, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.42-2.36, 2.12-2.06, 1.92-1.85, 1.68-1.61 (each 1H, m, 17-CH_2CH_2), 2.24 (3H, t, *J* = 8 Hz, 17^3-$OCOCH_2$), 1.83 (3H, d, *J* = 7 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.24-1.17 (18H, m, 17^3-$OCOC(CH_2)_9$), 0.84 (3H, t, *J* = 7 Hz, 17^3-$OCOC_{10}CH_3$), 0.36, -1.74 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 707. Calcd. for $C_{44}H_{59}N_4O_4$: MH^+, 707.

17^2-Decarboxy-3-devinyl-17^2-docosanoyloxymethyl-3-hydroxymethyl-pyropheophorbide-*a* (10c). Similarly to synthesis of **6a**, reduction of **9c** (101.0 mg, 120 μmol) by *t*$BuNH_2 \cdot BH_3$ (17.0 mg, 196 μmol) in CH_2Cl_2 (20 ml) gave **10c** (94.3 mg, 93%) as a black solid after FCC (8-15% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol): mp 130-131 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 605 (0.09), 535 (0.11), 504 (0.11), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.51, 9.44, 8.57 (each 1H, s, 5-, 10-, 20-H), 5.91 (2H, s, 3-CH_2), 5.21, 5.09 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.51 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.27 (1H, dt, *J* = 9, 2 Hz, 17-H), 4.10 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.70 (2H, q, *J* = 8 Hz, 8-CH_2), 3.68, 3.43, 3.26 (each 3H, s, 2-, 7-, 12-CH_3), 2.41-2.35, 2.11-2.04, 1.92-1.85, 1.66-1.61 (each 1H, m, 17-CH_2CH_2), 2.25 (3H, t, *J* = 7 Hz, 17^3-$OCOCH_2$), 1.82 (3H, d, *J* = 7 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.30-1.17 (38H, m, 17^3-$OCOC(CH_2)_{19}$), 0.87 (3H, t, *J* = 7 Hz, 17^3-$OCOC_{20}CH_3$), 0.07, -1.76 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 847. Calcd. for $C_{54}H_{79}N_4O_4$: MH^+, 847.

17^2-Decarboxy-3-devinyl-3-hydroxymethyl-17^2-pivaloyloxymethyl-pyropheophorbide-*a* (10d). Similarly to synthesis of **6a**, reduction of **9d** (109.0 mg, 180 μmol) by *t*$BuNH_2 \cdot BH_3$ (26.7 mg, 307 μmol) in CH_2Cl_2 (20 ml) gave **10d** (97.1 mg, 89%) as a black solid after FCC (6-10% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 238-241 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 606

(0.08), 535 (0.09), 505 (0.10), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.53, 9.45, 8.58 (each 1H, s, 5-, 10-, 20-H), 5.92 (2H, s, 3-CH_2), 5.20, 5.09 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.51 (1H, dq, *J* = 2, 7 Hz, 18-H), 4.29 (1H, dt, *J* = 9, 2 Hz, 17-H), 4.09 (2H, t, *J* = 7 Hz, 17^2-CH_2), 3.70 (2H, q, *J* = 8 Hz, 8-CH_2), 3.68, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.44-2.36, 2.13-2.06, 1.91-1.85, 1.67-1.61 (each 1H, m, 17-CH_2CH_2), 1.83 (3H, d, *J* = 7 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 1.15 (9H, s, 17^3-$OCOC(CH_3)_3$), 0.35, -1.75 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 609. Calcd. for $C_{37}H_{45}N_4O_4$: MH^+, 609.

17^2-Benzoyloxymethyl-17^2-decarboxy-3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (10e). Similarly to synthesis of **6a**, reduction of **9e** (69.0 mg, 110 μmol) by *t*$BuNH_2$·BH_3 (16.0 mg, 184 μmol) in CH_2Cl_2 (10 ml) gave **10e** (64.7 mg, 94%) as a black green solid after FCC (8-10% Et_2O/CH_2Cl_2) and recrystallization (CH_2Cl_2/hexane): mp 124-126 °C; VIS (CH_2Cl_2) λ_{max} = 662 (rel., 0.49), 606 (0.09), 535 (0.10), 505 (0.11), 410 nm (1.00); ^{1}H-NMR ($CDCl_3$) δ = 9.53, 9.46, 8.59 (each 1H, s, 5-, 10-, 20-H), 7.97 (each 1H, dd, *J* = 1, 8 Hz, 2-, 6-H of Ph), 7.52 (1H, tt, *J* = 1, 7 Hz, 4-H of Ph), 7.40 (2H, t, *J* = 8 Hz, 3-, 5-H of Ph), 5.93 (2H, s, 3-CH_2), 5.23, 5.11 (each 1H, d, *J* = 19 Hz, 13^2-H_2), 4.55 (1H, dq, *J* = 2, 8 Hz, 18-H), 4.36, 4.34 (each 1H, dt, *J* = 11, 6 Hz, 17^2-CH_2), 4.34 (1H, dt, *J* = 9, 3 Hz, 17-H), 3.71 (2H, q, *J* = 8 Hz, 8-CH_2), 3.68, 3.43, 3.27 (each 3H, s, 2-, 7-, 12-CH_3), 2.51-2.46, 2.23-2.17, 2.05-1.97, 1.77-1.73 (each 1H, m, 17-CH_2CH_2), 1.84 (3H, d, *J* = 8 Hz, 18-CH_3), 1.70 (3H, t, *J* = 8 Hz, 8^1-CH_3), 0.35, -1.75 (each 1H, s, NH × 2); MS (ESI) found: *m/z* 629. Calcd. for $C_{39}H_{41}N_4O_4$: MH^+, 629.

Zinc ethyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (1a). A methanol solution (0.3 ml) saturated with $Zn(OAc)_2$·$2H_2O$ was added to a CH_2Cl_2 solution (5 ml) of **6a** (5.3 mg, 9.3 μmol). After stirring for 2 h, the solution was washed with aq. 4% $NaHCO_3$ and H_2O, dried over Na_2SO_4 and evaporated to dryness. The residue was purified by RP-HPLC (methanol) to give **1a** [the retention (RT) time was 17.4 min] as a dark green solid: VIS (THF) λ_{max} = 647 (rel., 0.74), 600

(0.11), 566 (0.06), 521 (0.04), 424 (1.00) and 404 nm (0.55); MS (APCI) found: *m/z* 629. Calcd. for $C_{34}H_{36}N_4O_4{}^{64}Zn$: MH^+, 629.

Zinc dodecyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (1b). Similarly to synthesis of **1a**, zinc-metallation of **6b** (6.3 mg, 8.9 μmol) gave **1b** as a dark green solid after NP-HPLC [methanol-THF-hexane = 2:25:175 (v/v), RT = 18.1 min]: VIS (THF) λ_{max} = 647 (rel., 0.74), 601 (0.10), 563 (0.06), 518 (0.04), 424 (1.00) and 404 nm (0.55); MS (APCI) found: *m/z* 769. Calcd. for $C_{44}H_{56}N_4O_4{}^{64}Zn$: MH^+, 769.

Zinc docosyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (1c). Similarly to synthesis of **1a**, zinc-metallation of **6c** (5.5 mg, 6.5 μmol) gave **1c** as a dark green solid after NP-HPLC [methanol-THF-hexane = 2:25:175 (v/v), RT = 16.2 min]: VIS (THF) λ_{max} = 647 (rel., 0.72), 601 (0.11), 566 (0.06), 521 (0.04), 424 (1.00) and 404 nm (0.55); MS (APCI) found: *m/z* 909. Calcd. for $C_{54}H_{76}N_4O_4{}^{64}Zn$: MH^+, 909.

Zinc neopentyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (1d). Similarly to synthesis of **1a**, zinc-metallation of **6d** (4.7 mg, 7.7 μmol) gave **1d** as a dark green solid after RP-HPLC (methanol, RT = 19.6 min): VIS (THF) λ_{max} = 647 (rel., 0.74), 600 (0.11), 566 (0.06), 521 (0.04), 424 (1.00) and 404 nm (0.56); MS (APCI) found: *m/z* 671. Calcd. for $C_{37}H_{42}N_4O_4{}^{64}Zn$: MH^+, 671.

Zinc benzyl 3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (1e). Similarly to synthesis of **1a**, zinc-metallation of **6e** (4.5 mg, 7.2 μmol) gave **1e** as a dark green solid after RP-HPLC (methanol, RT = 18.5 min): VIS (THF) λ_{max} = 647 (rel., 0.75), 601 (0.11), 566 (0.06), 521 (0.04), 424 (1.00) and 404 nm (0.56); MS (APCI) found: *m/z* 691. Calcd. for $C_{39}H_{38}N_4O_4{}^{64}Zn$: MH^+, 691.

Zinc 17^2-acetoxymethyl-17^2-decarboxy-3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (2a). Similarly to synthesis of **1a**, zinc-metallation of **10a** (5.5 mg, 9.7 μmol) gave **2a** as a dark green

solid after RP-HPLC (methanol, RT = 18.0 min): VIS (THF) λ_{max} = 647 (rel., 0.75), 601 (0.10), 565 (0.06), 520 (0.04), 425 (1.00) and 405 nm (0.56); MS (APCI) found: *m/z* 629. Calcd. for $C_{34}H_{36}N_4O_4{}^{64}Zn$: MH^+, 629.

Zinc 17^2-decarboxy-3-devinyl-17^2-dodecanoyloxymethyl-3-hydroxymethyl-pyropheophorbide-*a* (2b). Similarly to synthesis of **1a**, zinc-metallation of **10b** (6.2 mg, 8.8 μmol) gave **2b** as a dark green solid after RP-HPLC [pyridine-acetonitrile-ethyl acetate = 1:50:50 (v/v), RT = 15.3 min]: VIS (THF) λ_{max} = 647 (rel., 0.75), 601 (0.10), 565 (0.05), 522 (0.03), 425 (1.00) and 405 nm (0.55); MS (APCI) found: *m/z* 769. Calcd. for $C_{44}H_{56}N_4O_4{}^{64}Zn$: MH^+, 769.

Zinc 17^2-decarboxy-3-devinyl-17^2-docosanoyloxymethyl-3-hydroxymethyl-pyropheophorbide-*a* (2c). Similarly to synthesis of **1a**, zinc-metallation of **10c** (5.8 mg, 6.9 μmol) gave **2c** as a dark green solid after RP-HPLC [pyridine-acetonitrile-ethyl acetate = 1:50:50 (v/v), RT = 23.2 min]: VIS (THF) λ_{max} = 647 (rel., 0.73), 601 (0.10), 565 (0.05), 521 (0.03), 425 (1.00) and 404 nm (0.55); MS (APCI) found: *m/z* 909. Calcd. for $C_{54}H_{76}N_4O_4{}^{64}Zn$: MH^+, 909.

Zinc 17^2-decarboxy-3-devinyl-3-hydroxymethyl-17^2-pivaloyloxymethyl-pyropheophorbide-*a* (2d). Similarly to synthesis of **1a**, zinc-metallation of **10d** (6.3 mg, 10.4 μmol) gave **2d** as a dark green solid after RP-HPLC (methanol, RT = 21.2 min): VIS (THF) λ_{max} = 647 (rel., 0.75), 601 (0.10), 565 (0.06), 523 (0.04), 425 (1.00) and 405 nm (0.56); MS (APCI) found: *m/z* 671. Calcd. for $C_{37}H_{42}N_4O_4{}^{64}Zn$: MH^+, 671.

Zinc 17^2-benzoyloxymethyl-17^2-decarboxy-3-devinyl-3-hydroxymethyl-pyropheophorbide-*a* (2e). Similarly to synthesis of **1a**, zinc-metallation of **10e** (5.8 mg, 9.2 μmol) gave **2e** as a dark green solid after RP-HPLC (methanol, RT = 22.6 min): VIS (THF) λ_{max} = 647 (rel., 0.74), 602 (0.10), 564 (0.06), 521 (0.04), 425 (1.00) and 405 nm (0.58); MS (APCI) found: *m/z* 691. Calcd. for $C_{39}H_{38}N_4O_4{}^{64}Zn$: MH^+, 691.