Supplementary Data

Experimental

General

UV-Vis absorption and CD spectra were measured with a Hitachi U-3500 spectrophotometer and a Jasco J-720W spectropolarimeter, respectively. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded on a JEOL ECA-600 (600, 151, 564, and 243 MHz) spectrometer; tetramethylsilane (0.00 ppm) was used as an internal reference for ^{1}H and ^{13}C, and hexafluorobenzene (−164.90 ppm) and 85wt% deuterium phosphate in deuterium oxide (0.00 ppm) were used as external references for ^{19}F and ^{31}P, respectively. High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF II spectrometer with electrospray ionization (ESI) in acetonitrile; ESI-L Low Concentration Tuning Mix (Agilent Technologies) was used as an internal reference. Flash column chromatography (FCC) was performed with silica gel (Wakogel C300). RP-HPLC was performed on a packed octadecylated column (Cosmosil 5C_{18}AR-II, Nacalai Tesque) with a Shimadzu LC-10ADvp pump, SPD-M10Avp photodiode-array detector, and SCL-10Avp system controller.

Methyl 13^{1}-deoxopyropheophorbide-*a* (**3**) was prepared according to reported procedures [s1]. All the reagents and solvents for preparation were obtained from commercial suppliers and used as received. For optical spectroscopy, dichloromethane was purchased from Nacalai Tesque as reagents prepared specially for HPLC.

Synthesis of methyl 13^1-deoxo-22-methyl-pyropheophorbide-*a* hexafluorophosphate (H_2-1)

To a dry dichloromethane solution (10 mL) of methyl 13^1-deoxopyropheophorbide-*a* (**3**, 50.8 mg, 95.0 μmol) was added methyl fluorosulfonate (1 mL, 13 mmol) and stirred at room temperature under nitrogen for 2 days. After evaporation, the residue was purified with FCC to recover the starting material (**3**, 10.1 mg, 18.9 μmol, 20% recovery) as the first fraction (CH_2Cl_2 : Et_2O = 100 : 5 as eluent) and give the *N*-methylated product as the second fraction (CH_2Cl_2 : MeOH = 100 : 5). The product was dissolved in a small amount of dichloromethane and washed with an aqueous 2% sodium hexafluorophosphate solution (three times). The organic phase was diluted with an excess amount of hexane and the resulting precipitates were filtered and dried in vacuo to afford **H_2-1** (44.5 mg, 64.1 μmol) in 67% isolated yield and 84% conversion yield based on consumed **3**. The product was a 9:11 diastereomeric mixture from its ^{1}H NMR spectrum (Fig. S1). The following ^{1}H NMR data exhibit minor/major peaks. **H_2-1**: blue black solid; Vis (CH_2Cl_2) λ_{max} = 629 (relative intensity, 0.11), 565 (0.06), 429 (0.93), 408 nm (1.00); ^{1}H NMR ($CDCl_3$) δ = 10.10/10.06 (1H, s, 10-H), 9.96/9.91 (1H, s, 5-H), 9.28/9.26 (1H, s, 20-H), 8.17/8.16 (1H, dd, *J* = 17, 11 Hz, 3^1-H), 6.40/6.38 (1H, d, *J* =11 Hz, 3^2-H *cis* to 3-C–H), 6.38 (1H, d, *J* = 17 Hz, 3^2-H *trans* to 3-C–H), 5.09–5.01/4.96–4.90 (2H, m, 13^1-CH_2), 4.86/4.73 (1H, q, *J* = 8 Hz, 18-H), 4.56/4.62 (1H, br-d, *J* = 10 Hz, 17-H), 4.13–4.01/4.29–4.23 (2H, m, 13-CH_2), 3.76 (2H, q, *J* = 8 Hz, 8-CH_2), 3.69 (3H, s, 17^2-$COOCH_3$), 3.60/3.59 (3H, s, 12-CH_3), 3.59/3.56 (3H, s, 2-CH_3), 3.22/3.19 (3H, s, 7-CH_3), 2.88–2.80, 2.72–2.67, 2.44–2.39, 2.24–2.18/2.97–2.91, 2.88–2.80, 2.54–2.49, 2.36–2.30 (each 1H, m, 17-CH_2CH_2), 1.75/2.06 (3H, d, *J* = 8 Hz, 18-CH_3), 1.47/1.45 (3H, t, *J* = 8 Hz, 8^1-CH_3), –4.13/–4.23 (3H, s, 22-

CH_3), −4.31, −4.49/−4.14, −4.38 (each 1H, s, NH×2); ^{19}F NMR ($CDCl_3$) δ = −70.78 (d, *J* = 710 Hz, PF_6^-); ^{31}P NMR ($CDCl_3$) δ = −144.66 (sep, *J* = 712 Hz, PF_6^-); HRMS (ESI) found: *m/z* = 549.3220 and 144.9649, calcd for $C_{35}H_{41}N_4O_2$: $[M-PF_6]^+$, 549.3224 and PF_6^-, 144.9647.

The epimeric mixture of **H_2-1** was separated by RP-HPLC (Cosmosil 5C_{18}-AR-II, 10 mmϕ × 250 mm) with methanol : water : trifluoroacetic acid = 75 : 25 : 0.1 (1.0 mL/min), and the first and second fractions were treated with an aqueous 2% sodium hexafluorophosphate solution (vide supra) to give **H_2-1a** and **H_2-1b**, respectively. **H_2-1a** [from the first fraction, (22*R*)-epimer]: blue black solid; Vis (CH_2Cl_2) λ_{max} = 629 (relative intensity, 0.11), 565 (0.06), 429 (0.93), 408 nm (1.00); ^{1}H NMR ($CDCl_3$) δ = 10.13 (1H, s, 10-H), 9.98 (1H, s, 5-H), 9.30 (1H, s, 20-H), 8.18 (1H, dd, *J* = 17, 11 Hz, 3^1-H), 6.43 (1H, d, *J* = 11 Hz, 3^2-H *cis* to 3-C–H), 6.41 (1H, d, *J* = 17 Hz, 3^2-H *trans* to 3-C–H), 5.09, 4.94 (each 1H, dd, *J* = 16, 6 Hz, 13^1-CH_2), 4.88 (1H, q, *J* = 8 Hz, 18-H), 4.57 (1H, br-d, *J* = 10 Hz, 17-H), 4.25, 4.15 (each 1H, dd, *J* = 16, 6 Hz, 13-CH_2), 3.80 (2H, q, *J* = 8 Hz, 8-CH_2), 3.71 (3H, s, 17^2-$COOCH_3$), 3.62 (3H, s, 12-CH_3), 3.61 (3H, s, 2-CH_3), 3.25 (3H, s, 7-CH_3), 2.97–2.92, 2.87–2.82, 2.57–2.52, 2.35–2.30 (each 1H, m, 17-CH_2CH_2), 1.75 (3H, d, *J* = 8 Hz, 18-CH_3), 1.45 (3H, t, *J* = 8 Hz, 8^1-CH_3), −4.04 (3H, s, 22-CH_3), −4.55, −4.74 (each 1H, s, NH×2); ^{13}C NMR ($CDCl_3$) δ = 173.49, 172.56, 170.57, 149.18, 148.81, 148.56, 141.90, 138.53, 137.97, 132.67, 131.08, 130.52, 129.07, 128.01, 125.62, 116.97, 100.21, 100.00, 99.27, 98.95, 98.20, 97.53, 96.48, 52.30, 51.32, 32.31, 31.37, 19.93, 16.18, 15.34, 12.50, 12.20, 11.78, 11.64, 11.36; HRMS (ESI) found: *m/z* = 549.3222 and 144.9648, calcd for $C_{35}H_{41}N_4O_2$: $[M-PF_6]^+$, 549.3224 and PF_6^-, 144.9647. **H_2-1b** [from the second fraction, (22*S*)-epimer]: blue black solid; UV-Vis (CH_2Cl_2) λ_{max} = 629 (relative intensity, 0.11), 565 (0.06), 429 (0.93), 408 nm

(1.00); ^{1}H NMR ($CDCl_3$) δ = 10.03 (1H, s, 10-H), 9.89 (1H, s, 5-H), 9.21 (1H, s, 20-H), 8.11 (1H, dd, *J* = 17, 11 Hz, 3^1-H), 6.35 (1H, dd, *J* = 11 Hz, 3^2-H *cis* to 3-C–H), 6.34 (1H, d, *J* = 17 Hz, 3^2-H *trans* to 3-C–H), 4.98–4.80 (2H, m, 13^1-CH_2), 4.68 (1H, q, *J* = 7 Hz, 18-H), 4.58 (1H, br-d, *J* = 13 Hz, 17-H), 4.22–4.00 (2H, m, 13-CH_2), 3.79 (2H, q, *J* = 7 Hz, 8-CH_2), 3.61 (3H, s, 17^2-$COOCH_3$), 3.53 (3H, s, 12-CH_3), 3.52 (3H, s, 2-CH_3), 3.16 (3H, s, 7-CH_3), 3.07–3.03, 2.80–2.74, 2.66–2.61, 2.35–2.30 (each 1H, m, 17-CH_2CH_2), 1.98 (3H, d, *J* = 7 Hz, 18-CH_3), 1.39 (3H, t, *J* = 7 Hz, 8^1-CH_3), −4.20 (3H, s, 22-CH_3), −4.43, −4.77 (each 1H, s, NH×2); ^{13}C NMR ($CDCl_3$) δ = 173.71, 172.79, 170.76, 149.58, 149.07, 148.86, 148.76, 142.08, 138.88, 138.15, 132.81, 130.78, 129.23, 128.19, 117.37, 116.42, 100.43, 99.83, 99.51, 99.37, 98.78, 97.94, 96.67, 52.48, 51.50, 36.83, 32.70, 25.23, 20.11, 12.84, 12.68, 12.42, 11.96, 11.84, 11.57; HRMS (ESI) found: *m/z* = 549.3221 and 144.9648, calcd for $C_{35}H_{41}N_4O_2$: $[M-PF_6]^+$, 549.3224 and PF_6^-, 144.9647.

Synthesis of zinc methyl 13^1-deoxo-22-methyl-pyropheophorbide-*a* hexafluorophosphate (Zn-1)

RP-HPLC separated free base **H_2-1a** or **H_2-1b** (ca. 1 mg) was dissolved in dichloromethane (3 mL), to which was added a methanol solution (1 mL) saturated with zinc acetate dihydrate. The mixture was stirred at room temperature in the dark for 1 h. The reaction mixture was diluted with dichloromethane, washed with an aqueous solution saturated with sodium hydrogen carbonate, water, and an aqueous 2% sodium hexafluorophosphate solution (twice), and dried over sodium sulfate. After filtration, the solvent was evaporated to give the corresponding zinc complex, **Zn-1a** or **Zn-1b** as green solid. **Zn-1a**: Vis (CH_2Cl_2) λ_{max} 630 (relative intensity, 0.11), 437 (0.81), 416 nm

(1.00; HRMS (ESI) found: *m/z* 611.2359 and 144.9651, calcd for $C_{35}H_{39}N_4O_2Zn$: $[M-PF_6]^+$, 611.2356 and PF_6^-, 144.9647. **Zn-1b**: Vis (CH_2Cl_2) λ_{max} = 630 (relative intensity, 0.11), 437 (0.81), 416 nm (1.00); HRMS (ESI) found: *m/z* = 611.2356 and 144.9652, calcd for $C_{35}H_{39}N_4O_2Zn$: $[M-PF_6]^+$, 611.2356 and PF_6^-, 144.9647.

Synthesis of zinc methyl 13^1-deoxo-22-methyl-pyroprotopheophorbide-*a* hexafluorophosphate (Zn-2)

Zinc chlorin **Zn-1a** or **Zn-1b** (ca. 1 mg) was dissolved in dry acetone (3 mL), to which was added DDQ (2 mg). The mixture was stirred at room temperature under nitrogen in the dark for 10 min. The reaction mixture was diluted with dichloromethane, washed with an aqueous 1% potassium hydrogen sulfate solution, water, and an aqueous 2% sodium hexafluorophosphate solution (twice), and dried over sodium sulfate. After filtration, the solvent was evaporated and the residue was purified with FCC (CH_2Cl_2 : MeOH = 100 : 1) to give the corresponding zinc porphyrin, **Zn-2a** or **Zn-2b** as purple solid. **Zn-2a**: Vis (CH_2Cl_2) λ_{max} = 585 (relative intensity, 0.07), 547 (0.06), 440 (0.63), 424 nm (1.00); HRMS (ESI) found: *m/z* = 609.2200 and 144.9646, calcd for $C_{35}H_{37}N_4O_2Zn$: $[M-PF_6]^+$, 609.2202 and PF_6^-, 144.9647. **Zn-2b**: Vis (CH_2Cl_2) λ_{max} = 585 (relative intensity, 0.07), 547 (0.06), 440 (0.63), 424 nm (1.00); HRMS (ESI) found: *m/z* = 609.2194 and 144.9651, calcd for $C_{35}H_{37}N_4O_2Zn$: $[M-PF_6]^+$, 609.2202 and PF_6^-, 144.9647.

Synthesis of methyl 13^1-deoxo-22-methyl-pyroprotopheophorbide-*a* hexafluorophosphate (H_2-2)

Zinc porphyrin **Zn-2a** or **Zn-2b** (ca. 1 mg) was dissolved in dichloromethane (1 mL), to which was added TFA (1 mL). The mixture was stirred at room temperature in the dark for 3 min. The reaction mixture was diluted with dichloromethane, washed with an aqueous solution saturated with sodium hydrogen carbonate, water, and an aqueous 2% sodium hexafluorophosphate solution (twice), and dried over sodium sulfate. After filtration, the solvent was evaporated to give the corresponding free base porphyrin, **H_2-2a** or **H_2-2b** as purple solid. **H_2-2a** [(22*R*)-enantiomer]: Vis (CH_2Cl_2) λ_{max} = 575 (relative intensity, 0.09), 548 (0.08), 407 nm (1.00); HRMS (ESI) found: *m/z* = 547.3067 and 144.9650, calcd for $C_{35}H_{39}N_4O_2$: $[M-PF_6]^+$, 547.3068 and PF_6^-, 144.9647. **H_2-2b** [(22*S*)-enantiomer]: Vis (CH_2Cl_2) λ_{max} = 575 (relative intensity, 0.09), 548 (0.08), 407 nm (1.00); HRMS (ESI) found: *m/z* = 547.3064 and 144.9651, calcd for $C_{35}H_{39}N_4O_2$: $[M-PF_6]^+$, 547.3068 and PF_6^-, 144.9647. **H_2-2**: ^{1}H NMR ($CDCl_3$) δ = 10.45 (1H, s, 10-H), 10.42 (1H, s, 5-H), 10.38 (1H, s, 20-H), 8.31 (1H, dd, *J* = 18, 13 Hz, 3^1-H), 6.51 (1H, dd, *J* = 13 Hz, 3^2-H *cis* to 3-C–H), 6.50 (1H, d, *J* = 18 Hz, 3^2-H *trans* to 3-C–H), 5.58 (2H, br-s, 13^1-CH_2), 4.31 (2H, q, *J* = 8 Hz, 8-CH_2), 4.28 (2H, t, *J* = 8 Hz, 17-CH_2), 3.96 (2H, br-s, 13-CH_2), 3.83 (3H, s, 12-CH_3), 3.83 (3H, s, 17^2-$COOCH_3$), 3.77 (3H, s, 7-CH_3), 3.61 (3H, s, 18-CH_3), 3.39 (3H, s, 2-CH_3), 3.15 (2H, t, *J* = 8 Hz, 17-CH_2), 1.56 (3H, t, *J* = 8 Hz, 8^1-CH_3), −4.84 (3H, s, 22-CH_3) [The two inner NH signals were invisible.]; ^{13}C NMR ($CDCl_3$) δ = 153.43, 152.93, 152.43, 146.53, 144.89, 141.98, 138.76, 136.33, 134.03, 129.85, 129.13, 128.09, 126.44, 126.35, 102.83, 101.80, 100.04, 99.08, 98.97, 98.03. 52.66, 51.69, 39.08, 32.46, 22.87, 13.12, 12.96, 12.75, 12.29, 12.26, 12.10, 11.89, 11.45, 1.57, 0.79.

Synthesis of methyl 13^1-deoxo-pyroprotopheophorbide-*a* (4)

Chlorin **3** (ca. 1 mg) was dissolved in dry acetone (3 mL), to which was dropwise added a dry acetone solution (1 mL) of DDQ (2 mg). The mixture was stirred at room temperature under nitrogen in the dark for 10 min. The reaction mixture was diluted with dichloromethane, washed with an aqueous 1% potassium hydrogen sulfate solution and water (twice), and dried over sodium sulfate. After filtration, the resulting filtrate was directly purified with FCC (CH_2Cl_2) to give the corresponding porphyrin **4** as purple solid: VIS (CH_2Cl_2) λ_{max} = 620 (relative intensity, 0.02), 568 (0.03), 542 (0.03), 505 (0.07), 404 nm (1.00): see its spectral data also in ref [s2].

References

[s1] H. Tamiaki, S. Yagai, T. Miyatake, *Bioorg. Med. Chem.*, **6**, 2171–2178 (1998).

[s2] L. Ma, D. Dolphin, *Can. J. Chem.*, **75**, 262–275 (1997).

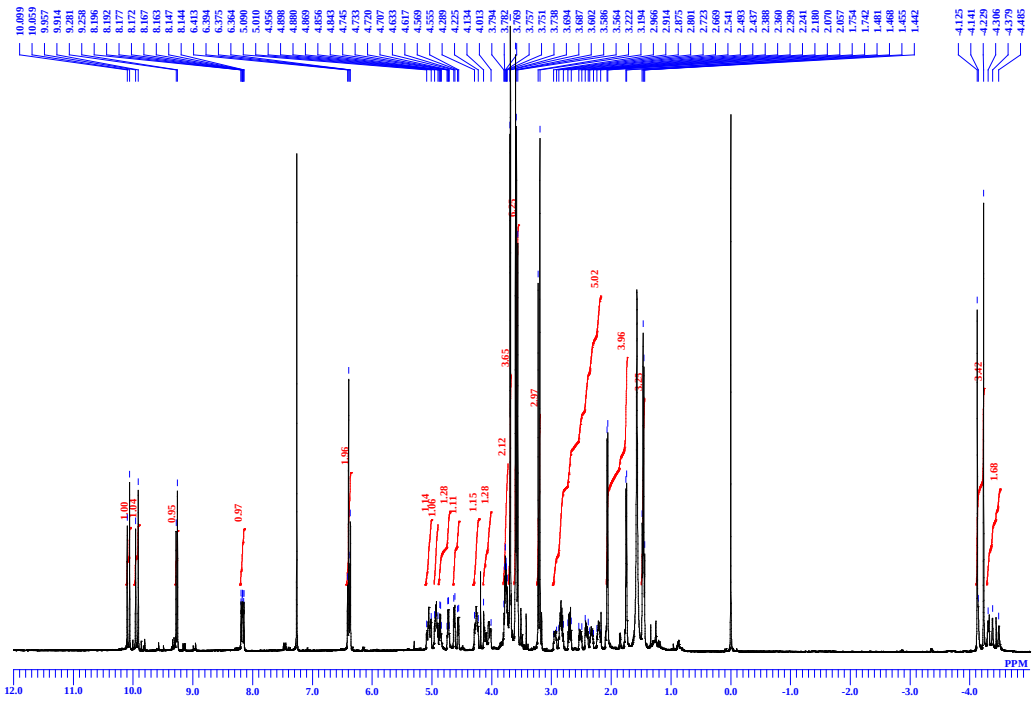

Fig. S1 ^{1}H NMR spectrum of **H_2-1** in $CDCl_3$.

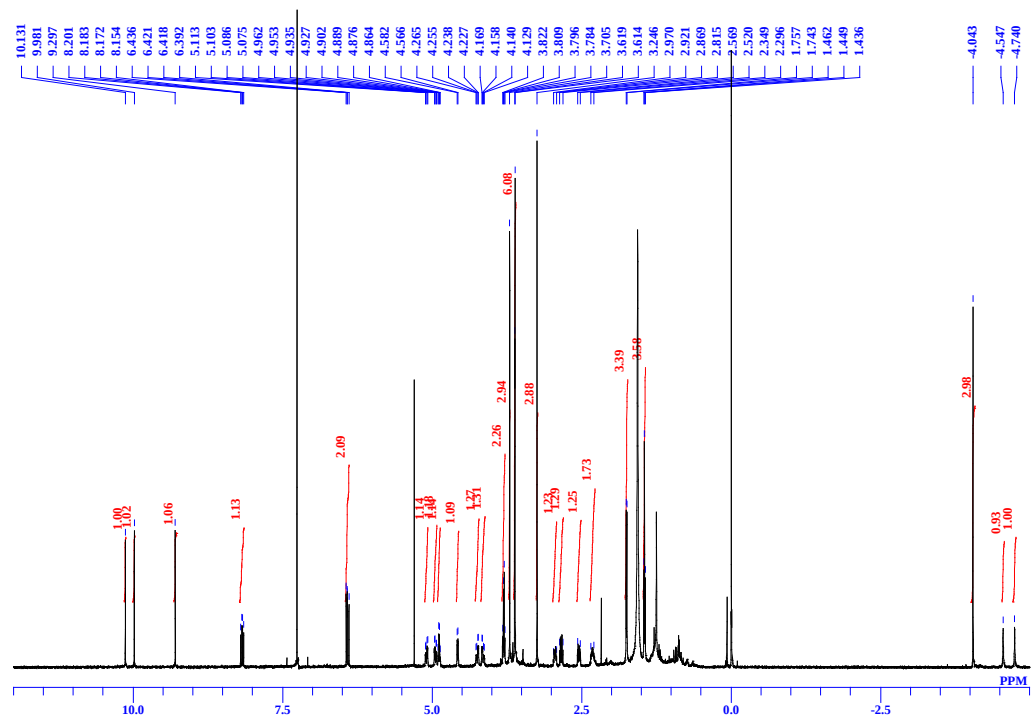

Fig. S2 ^{1}H NMR spectrum of **H_2-1a** in $CDCl_3$.

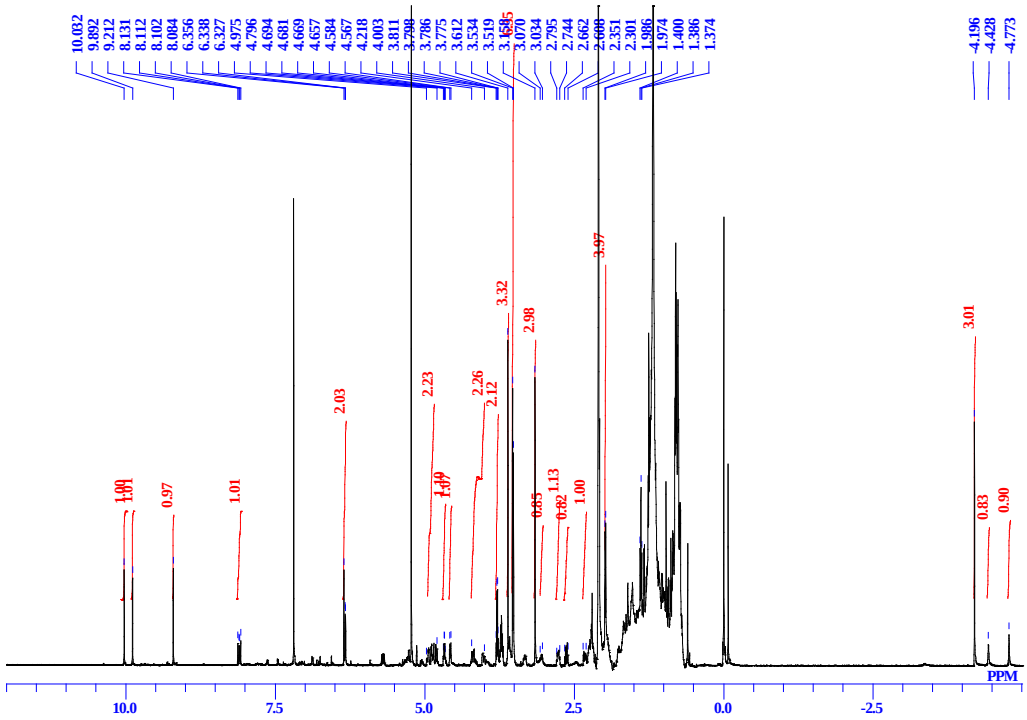

Fig. S3 ^{1}H NMR spectrum of **H_2-1b** in $CDCl_3$.

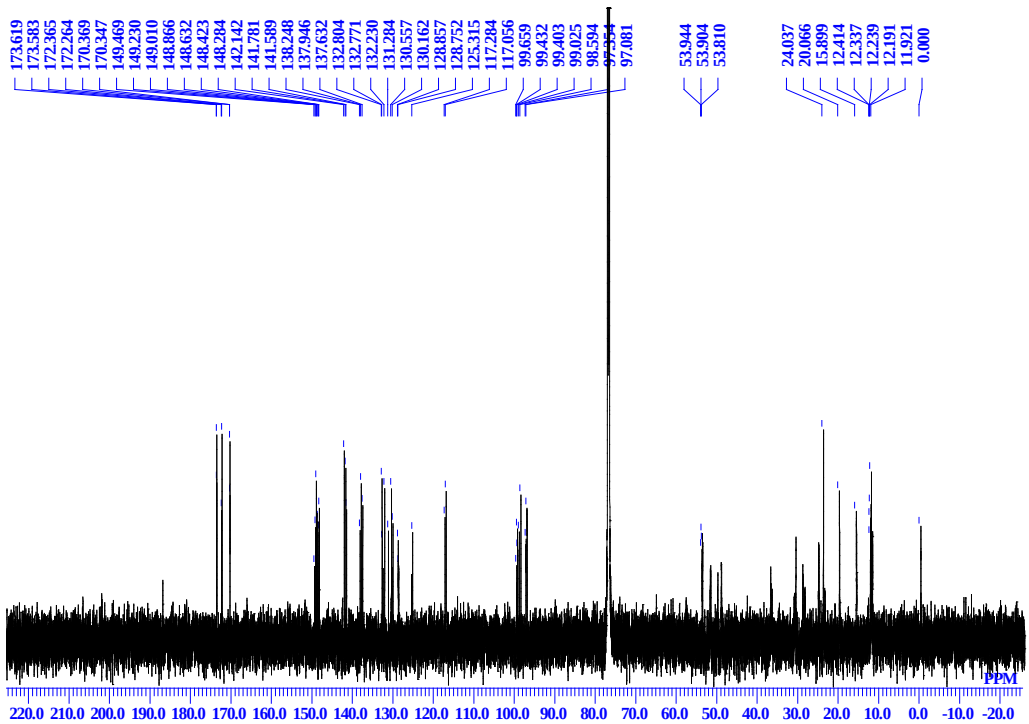

Fig. S4 ^{13}C NMR spectrum of **H_2-1** in $CDCl_3$.

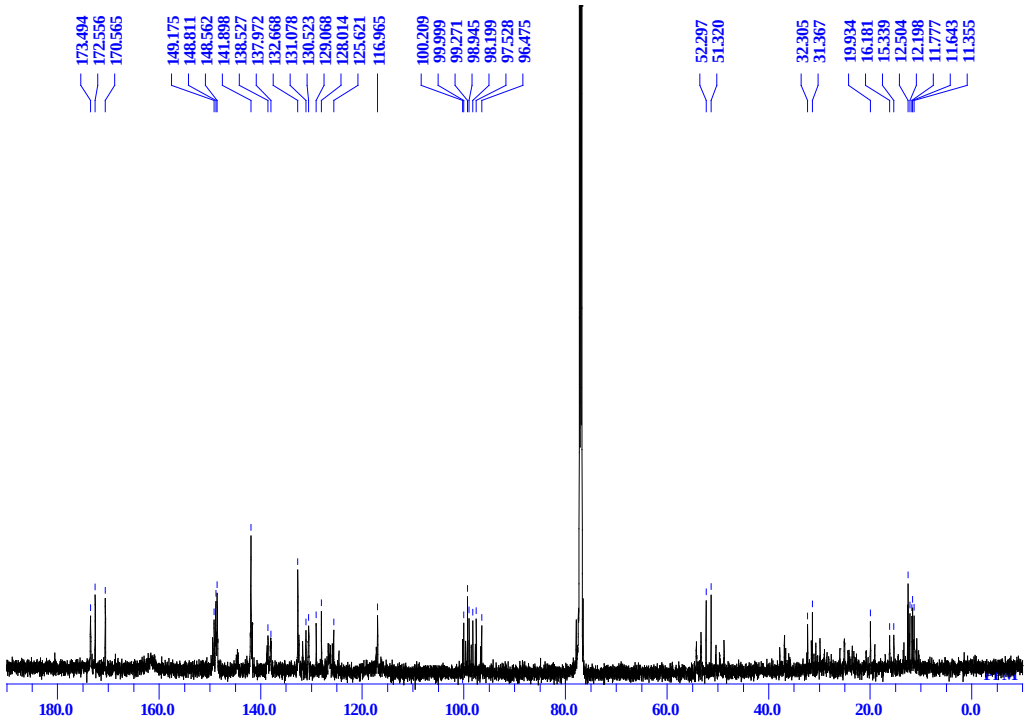

Fig. S5 ^{13}C NMR spectrum of **H_2-1a** in $CDCl_3$.

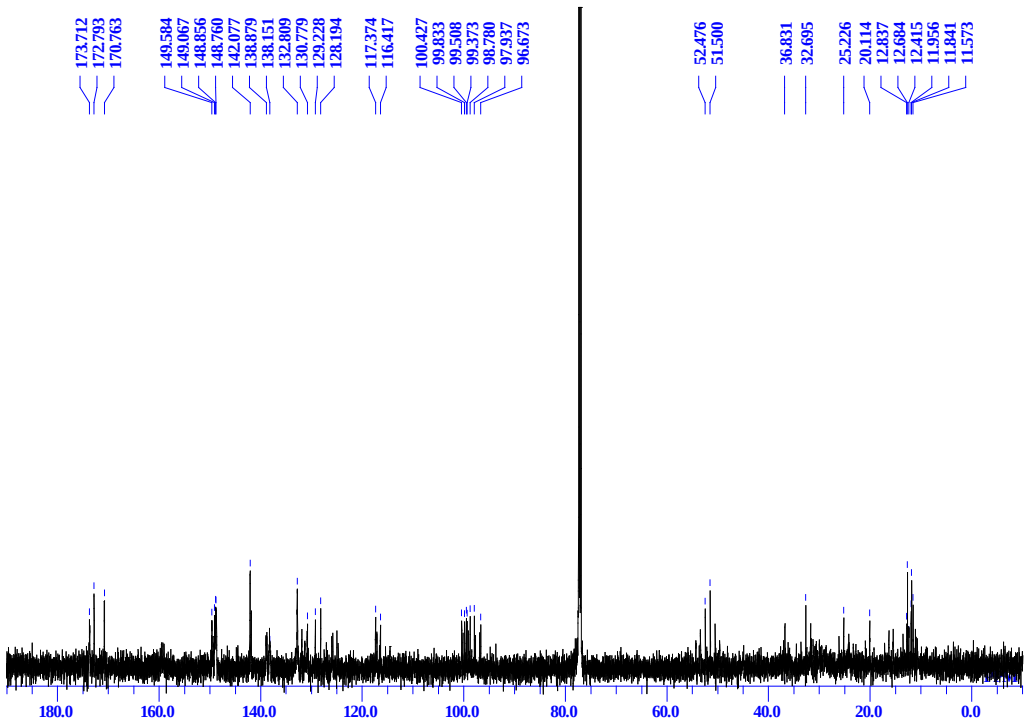

Fig. S6 ^{13}C NMR spectrum of **H_2-1b** in $CDCl_3$.

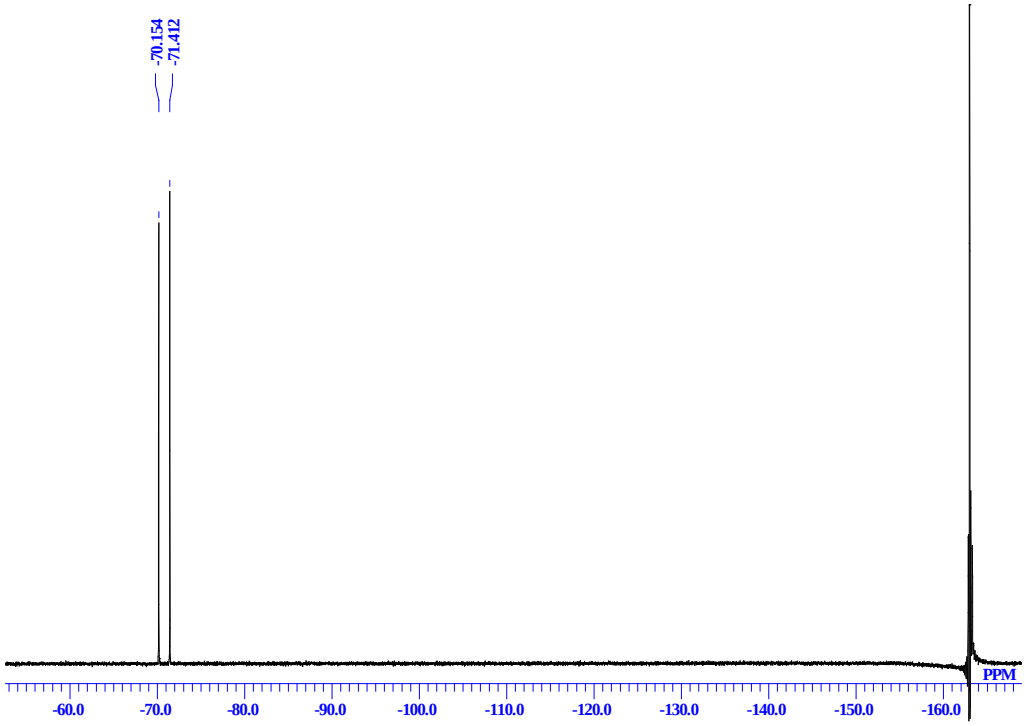

Fig. S7 ^{19}F NMR spectrum of **H_2-1** in $CDCl_3$.

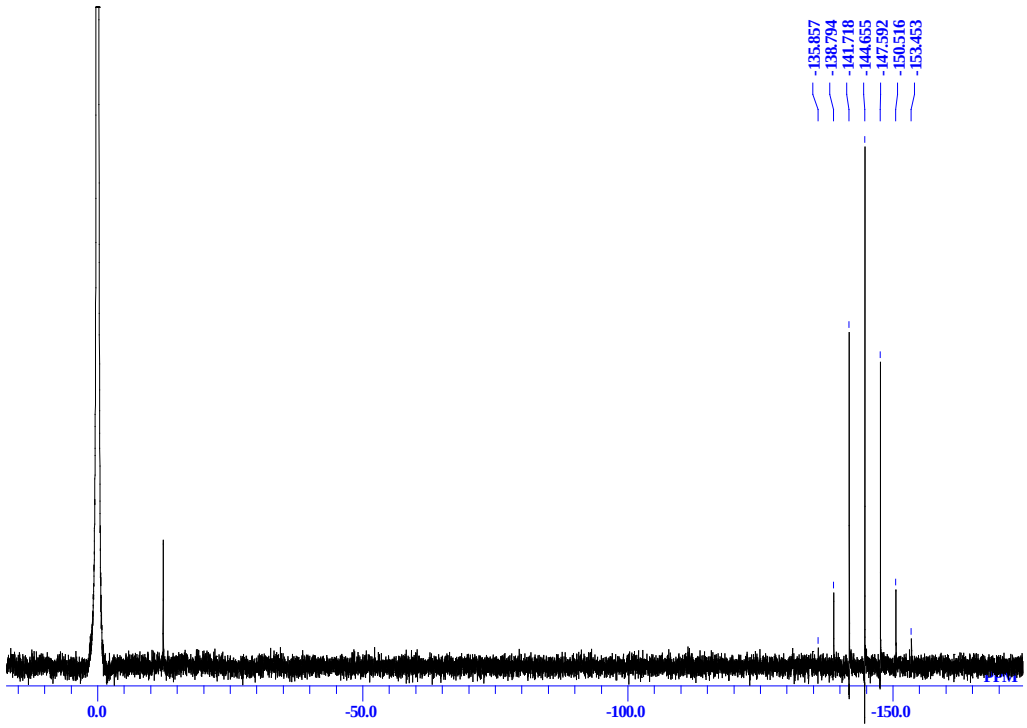

Fig. S8 ^{31}P NMR spectrum of **H_2-1** in $CDCl_3$.

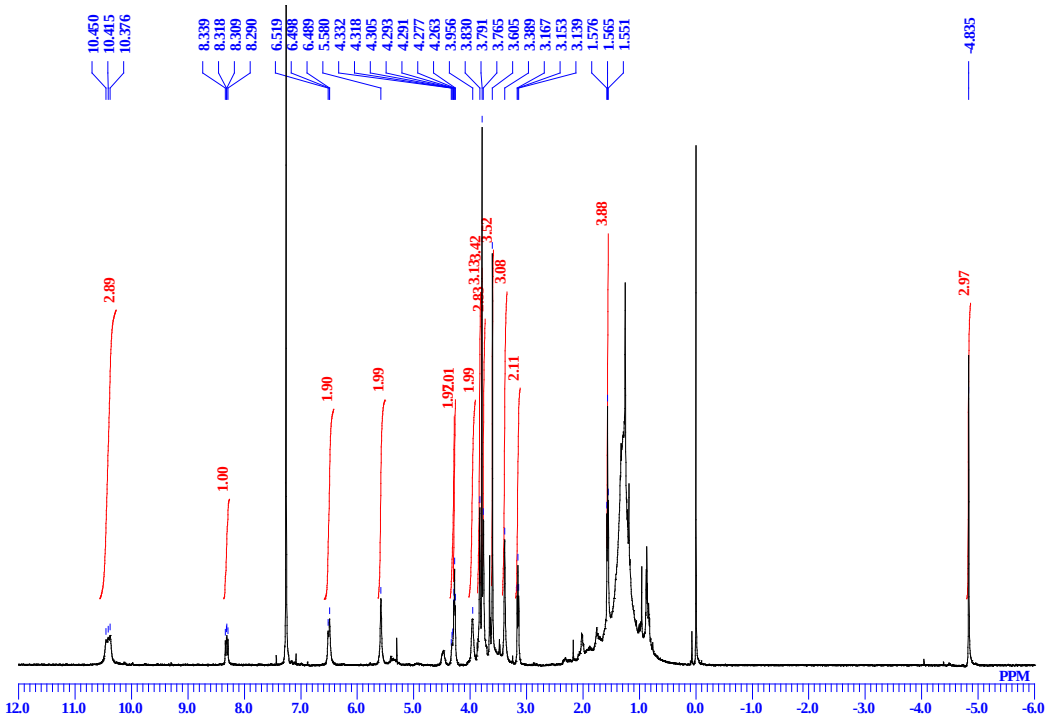

Fig. S9 ^{1}H NMR spectrum of **H_2-2** in $CDCl_3$.

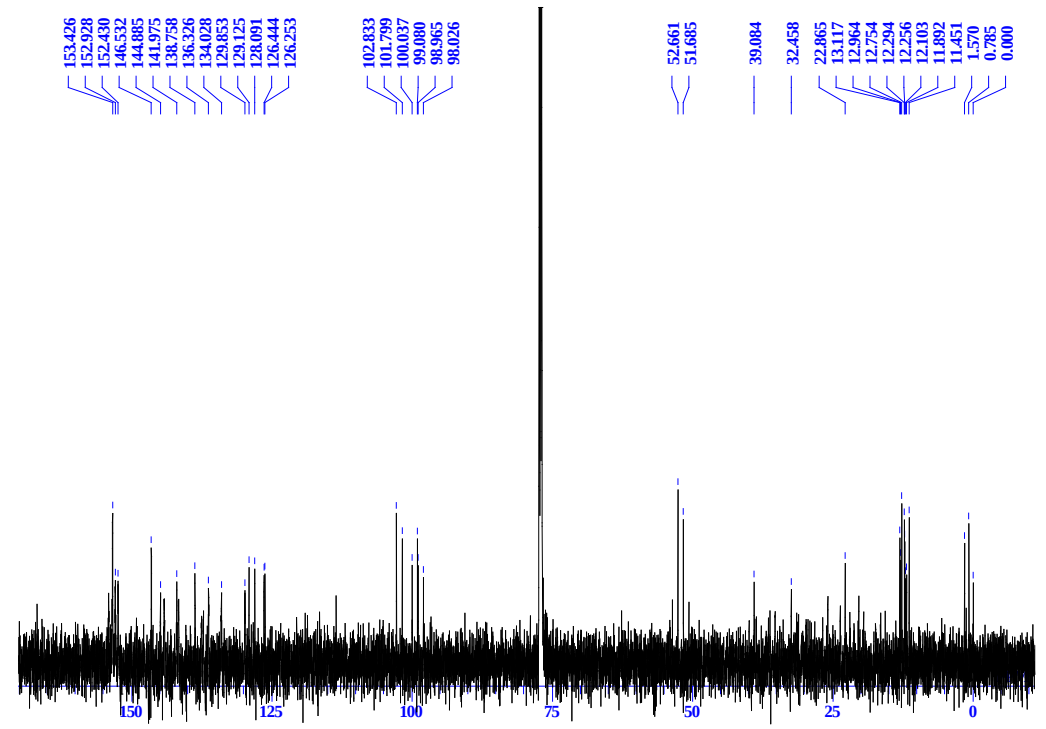

Fig. S10 ^{13}C NMR spectrum of **H_2-2** in $CDCl_3$.

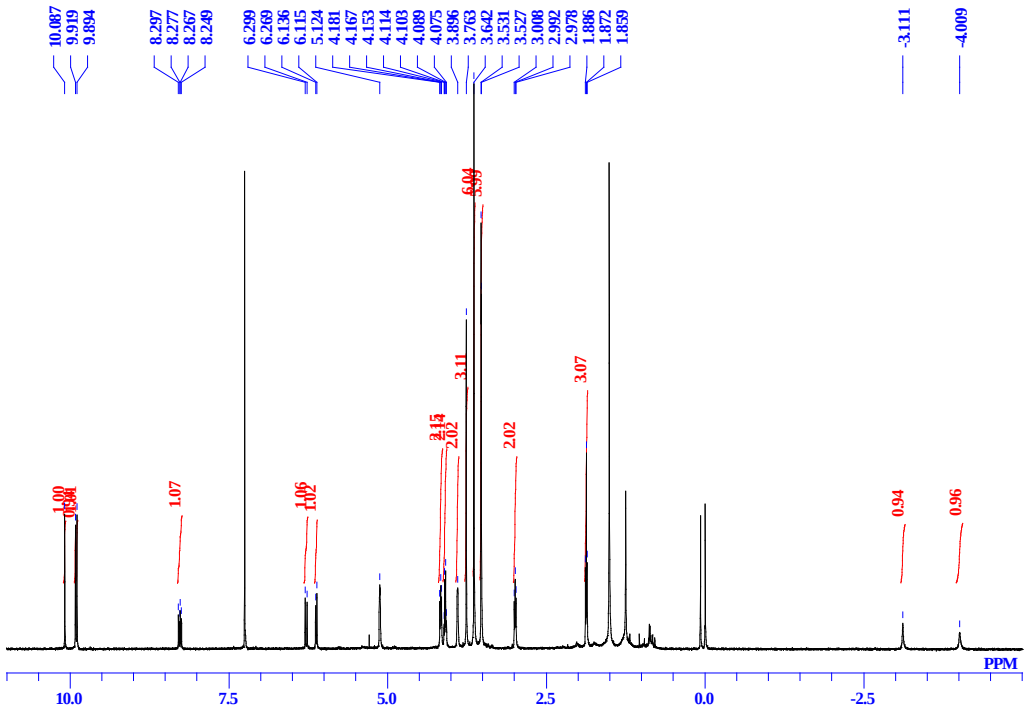

Fig. S11 ^{1}H NMR spectrum of **4** in $CDCl_3$.

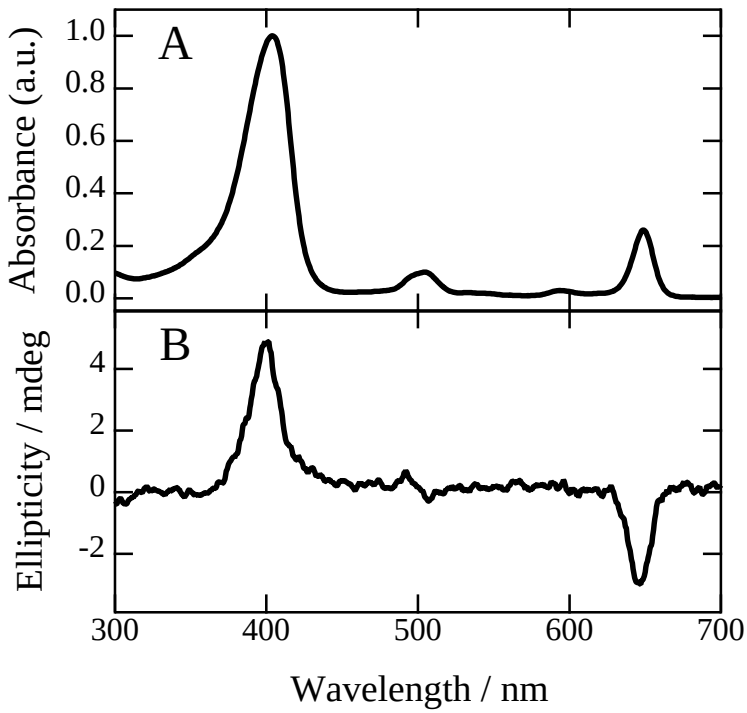

Fig. S12 UV-Vis absorption (A) and CD spectra (B) of **3** in CH_2Cl_2.

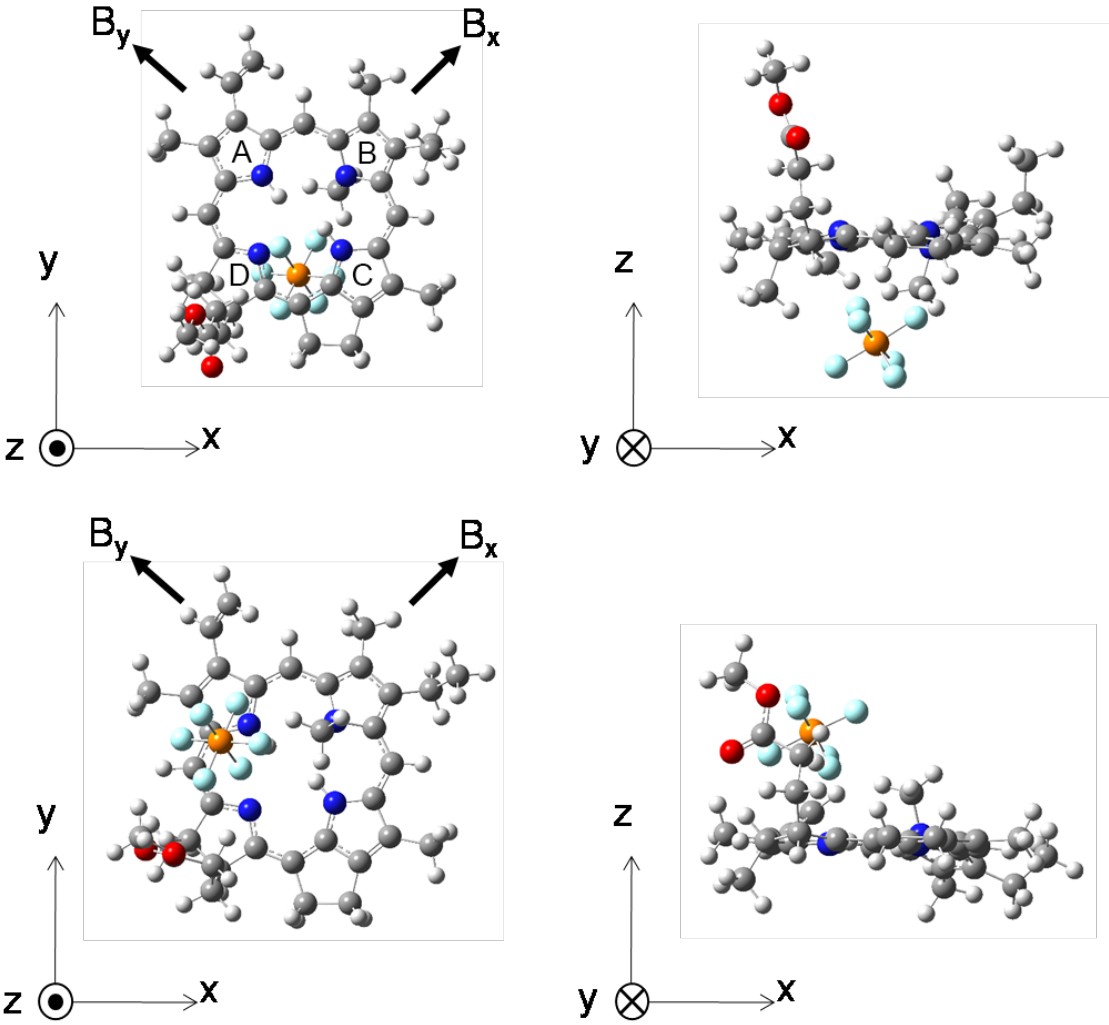

Fig. S13 Optimized structures of (22*R*)-**H$_2$-1** (upper) and (22*S*)-**H$_2$-1** epimers (lower) using DFT calculation [B3LYP/6-31G(D)].

The center positions of A-, B-, C-, and D-rings (see the upper left drawing of Fig. S13) were first estimated on the basis of their composite four carbon and one nitrogen atom positions. The transition dipole moment vectors in By and Bx bands were approximately estimated by the calculated vector from the C- to A-ring centers, and D- to B-ring centers, respectively. The exciton centers in By and Bx bands were also estimated by the middle point between the A- and C-ring centers, and the B- and D-ring

centers, respectively. The deviations of exciton center in the By and Bx axes for (22*R*)-**H_2-1** and (22*S*)-**H_2-1** were estimated to be 0.14 Å and 0.18 Å, respectively. The distance vector was estimated by the positions of the two exciton centers. Based on these parameters, their CD signs at Soret region using exciton coupling theory were proposed (Fig. S14).

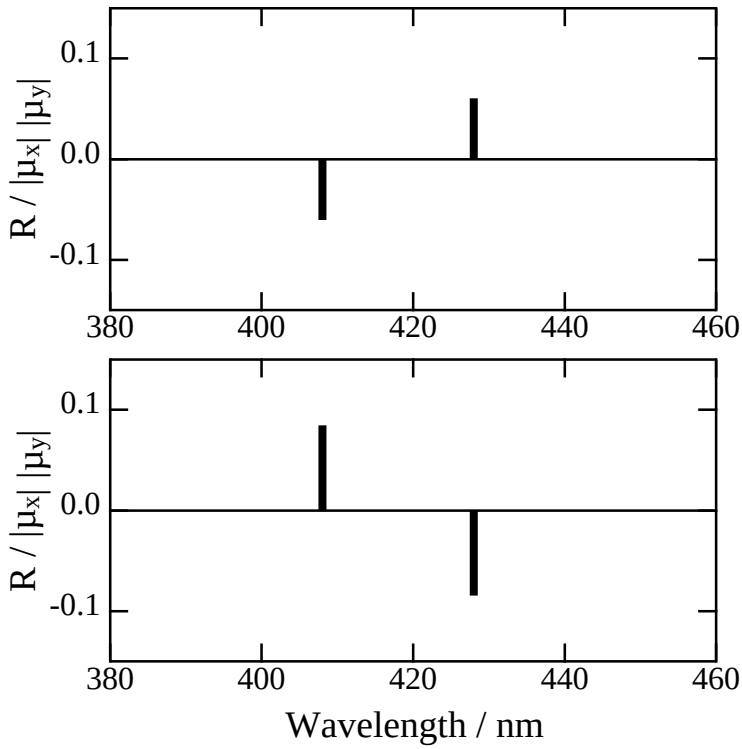

Fig. S14 Proposed CD spectra of (22*R*)-**H_2-1** (upper) and (22*S*)-**H_2-1** epimers (lower) at the Soret region.

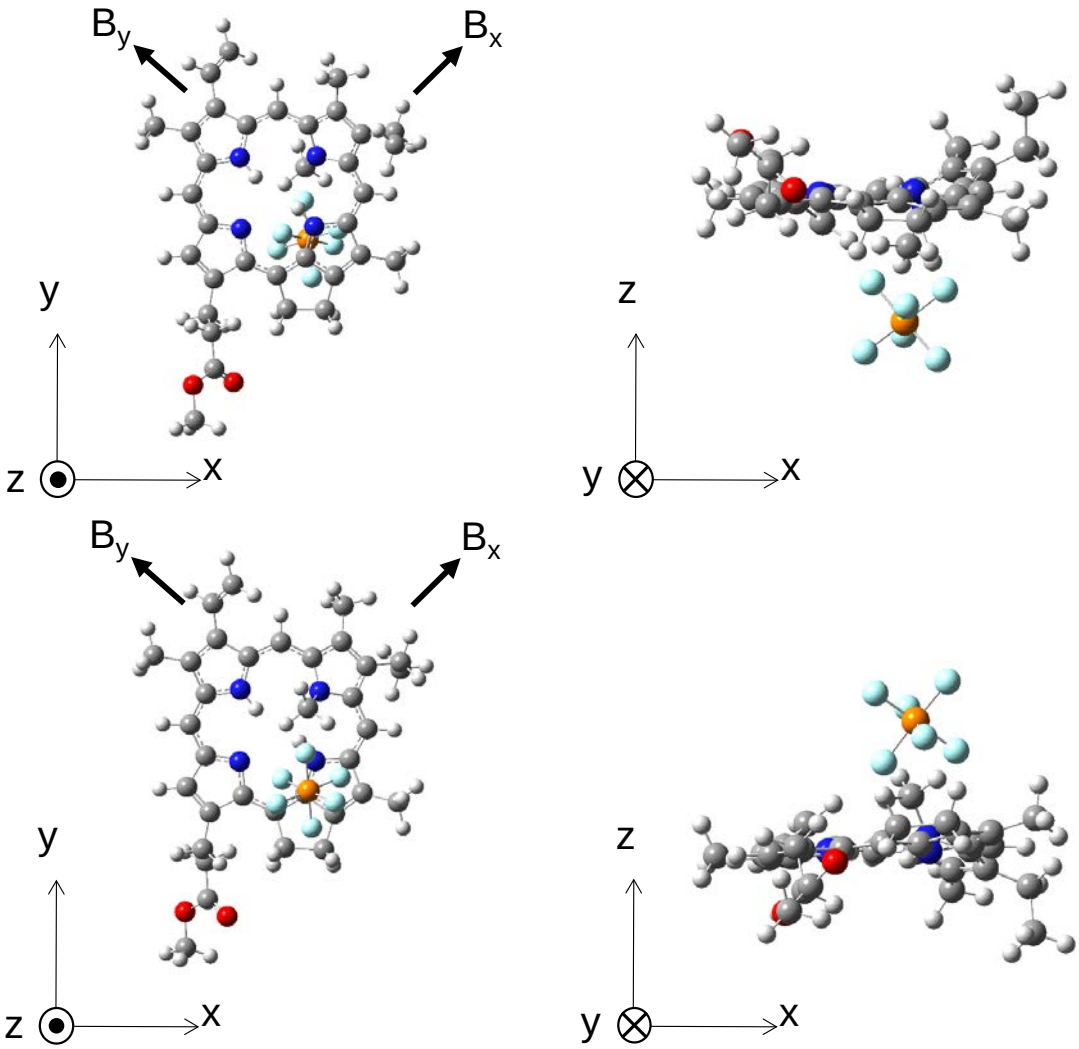

Fig. S15 Optimized structures of (22*R*)-**H$_2$-2** (upper) and (22*S*)-**H$_2$-2** epimers (lower) using DFT calculation [B3LYP/6-31G(D)].

The calculation method was the same as that of (22*R*)-**H$_2$-1** (upper) and (22*S*)-**H$_2$-1** epimers (vide supra). Both the deviations of exciton centers in the By and Bx axes for (22*R*)-**H$_2$-2** and (22*S*)-**H$_2$-2** were estimated to be 0.26 Å (see Fig. S15). Similar to the aforementioned exciton coupling theory, their CD signs were shown in Fig. S16.

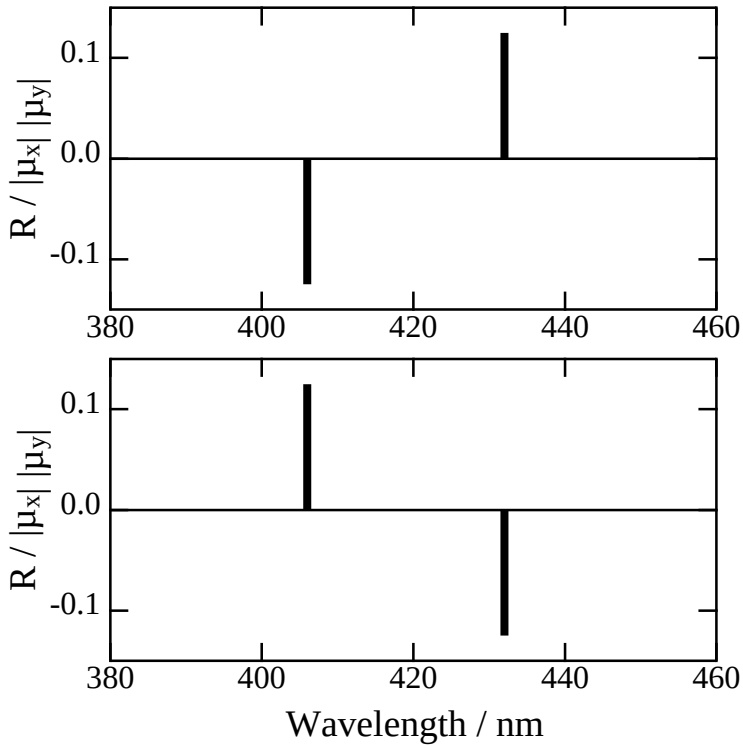

Fig. S16 Proposed CD spectra of (22*R*)-**H$_2$-2** (upper) and (22*S*)-**H$_2$-2** epimers (lower) at the Soret region.

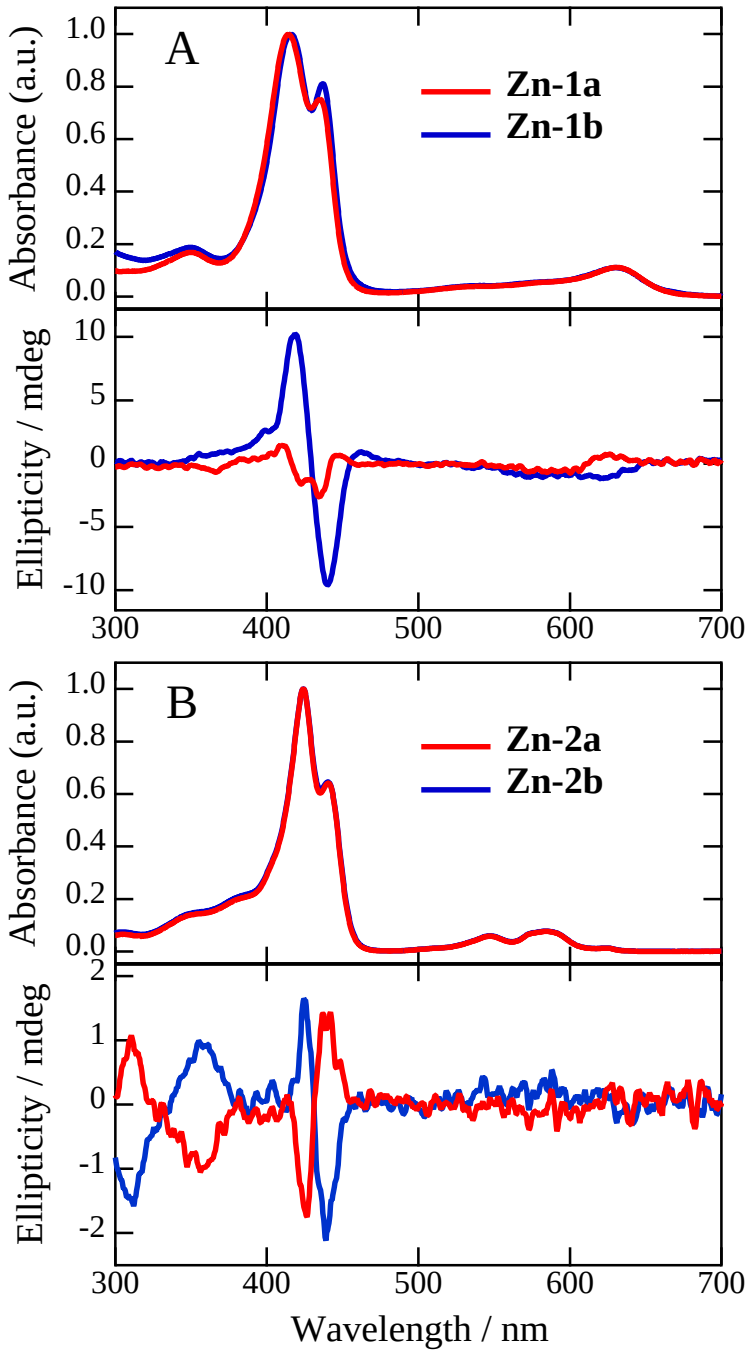

Fig. S17 UV-Vis (upper) and CD spectra (lower) of (N22*R*)-**Zn-1a**/**2a** (red) and (N22*S*)-**Zn-1b**/**2b** (blue) in CH_2Cl_2 (A/B).

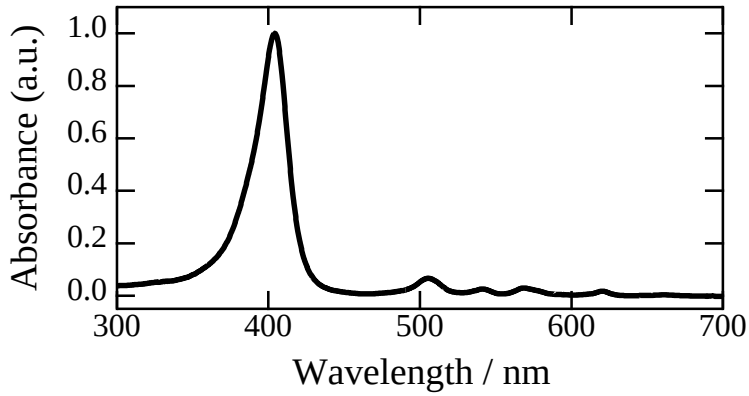

Fig. S18 UV-Vis spectrum of **4** in CH_2Cl_2.

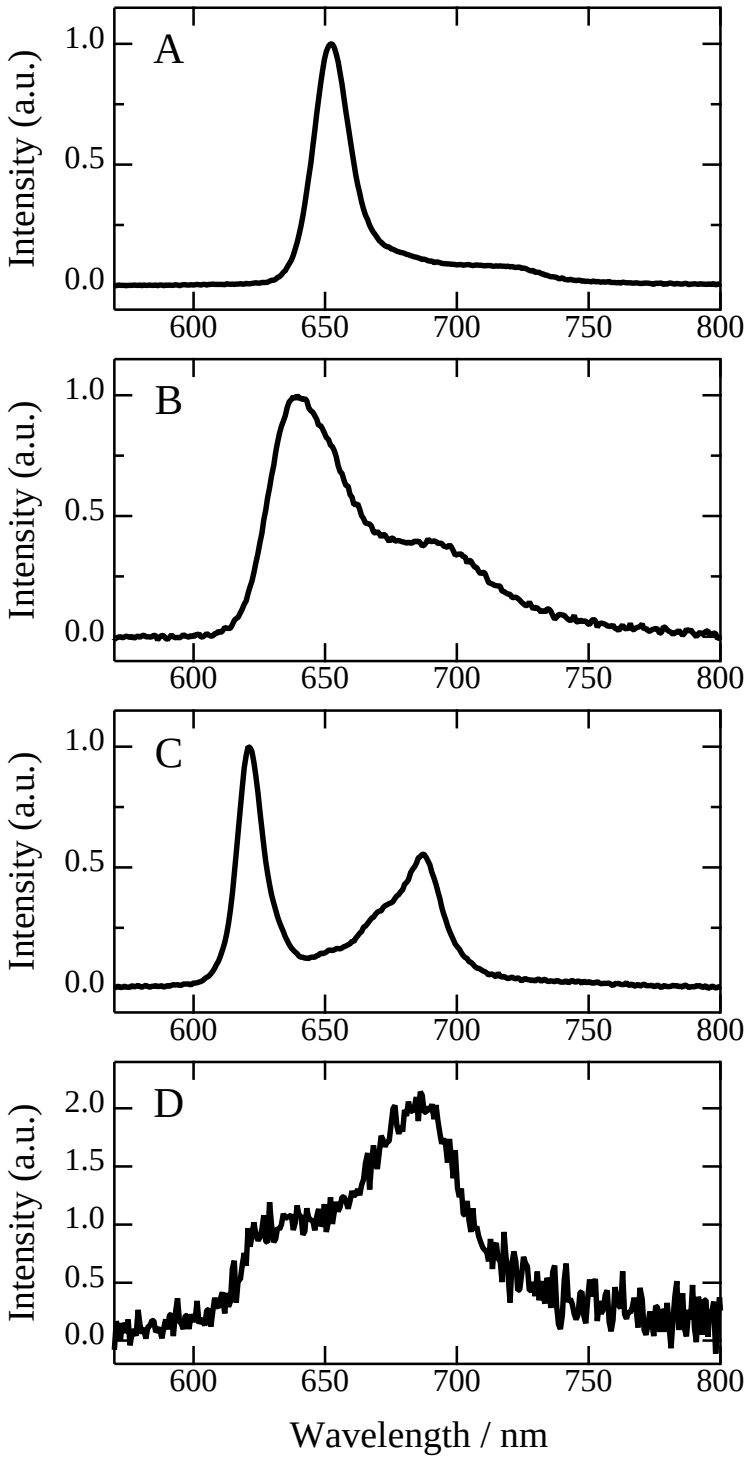

Fig. S19 Fluorescence emission spectra of **3** (A), **H_2-1** (B), **4** (C), and **H_2-2** (D) in aerated CH_2Cl_2 at rt: excited at main Soret maxima.