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Regioselective Transformation of Octaethylporphyrin into a Phytoporphyrin Analogue

Michio Kunieda,[†] Yuji Mikata,[‡] and Hitoshi Tamiaki*,[†]

Department of Bioscience and Biotechnology, Faculty of Science and Engineering, Ritsumeikan University, Kusatsu, Shiga 525-8577, and KYOUSEI Science Center, Nara Women's University, Nara 630-8506, Japan

tamiaki@se.ritsumei.ac.jp

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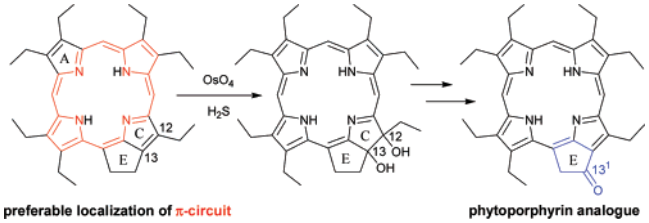

An octaethylporphyrin derivative, **1**, possessing an exo-five-membered ring fused at the 13- and 15-positions was oxidized by osmium tetroxide to give two isomeric chlorins, **3** and **5**, possessing β,β'-dihydroxy groups at the A- and C-rings, respectively. Single dehydration of 2,3-dihydroxychlorin **3** gave a mixture of 2- and 3-(1-hydroxyethyl)-porphyrins **7**, while that of 12,13-dihydroxychlorin **5** resulted in the sole formation of 13^1-hydroxyporphyrin **9**. The latter was modified smoothly to the phytoporphyrin analogue **2**, whose molecular skeleton was similar to that of naturally occurring chlorophylls possessing a 13^1-oxo group fixed on an exo-five-membered ring.

Phytoporphyrin (upper right drawing in Figure 1) is one of the well-known semisynthetic porphyrins and is structurally characterized by the presence of the 13^1-oxo group fixed on an exo-five-membered E-ring, similar to the molecular structures of naturally occurring photoactive chlorophylls (Chl's) (molecular structures of Chl's *a* and c_1, upper left drawing in Figure 1).[1] The copresence of the 13^1-oxo group[2] and E-ring in a cyclic tetrapyrrole has a significant effect on its optical properties; absorption bands of porphyrins[3] or chlorins[4] possessing a 13^1-oxo group with the E-ring (for example, octaethylporphyrin (OEP) derivative **2**, lower drawing of Figure 1) shifted to a longer wavelength region than those possessing a flexible 13-acetyl group without the E-ring, which is suitable for efficient light-harvesting. Thus, porphyrin derivatives possessing an oxo group on the E-ring have attracted attention as good models of naturally occurring Chl's.

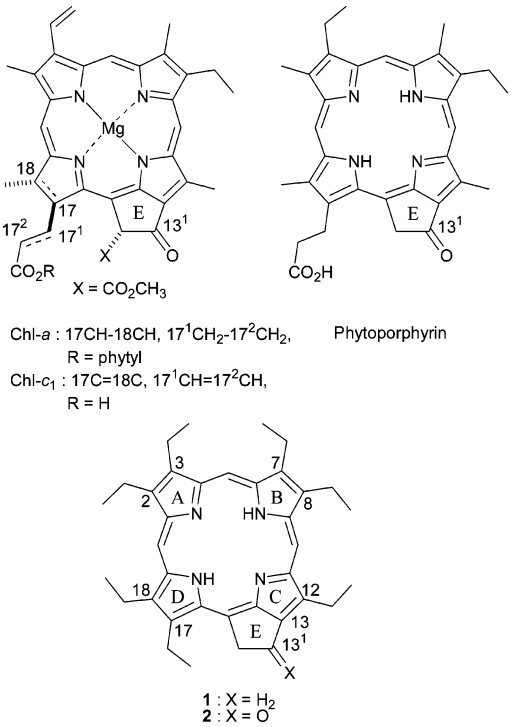

FIGURE 1. Molecular structures of naturally occurring Chl's *a* and c_1 (upper left), phytoporphyrin (upper right), and synthetic porphyrins **1** and **2** (lower).

Several synthetic strategies for introducing the 13^1-oxo group with the E-ring were reported.[4,5] In this paper we focus on a dihydroxylation of β,β'-positions in a porphyrin by osmium tetroxide as a key step for synthesizing phytoporphyrin analogues. Dihydroxylation of porphyrin derivatives by OsO_4 is a useful method to modify the β-positions on the porphyrin macrocycle.[6] Typically, the reaction occurs at the $\beta-\beta'$ bond (C2−C3, C7−C8, C12−C13, or C17−C18) of the porphyrin macrocycle, and the resulting osmate is cleaved by H_2S gas to afford the corresponding β,β'-dihydroxychlorin (*cis*-diol). Unsymmetric free-base porphyrins have basically 26 π-electrons, in which a 22(or 18)π-system including all the π-electrons (or all the α,β-carbon π-electrons) on a set of diagonal pyrroles (rings A and C or B and D) gives the compounds their

* To whom correspondence should be addressed. Fax: +81 77 561 2659.
[†] Ritsumeikan University.
[‡] Nara Women's University.

(1) (a) Scheer, H. In *Light Harvesting Antennas in Photosynthesis*; Green, B. R., Parson, W. W., Eds.; Kluwer Academic Publisher: Dordrecht, The Netherlands, 2003; pp 29−81. (b) Tamiaki, H.; Shibata, R.; Mizoguchi, T. *Photochem. Photobiol.* **2007**, *83*, 152−162.

(2) In this paper, the numbering of the positions in all the synthetic compounds is the same as that in the natural chlorophylls and does not follow the IUPAC-IUB nomenclature to avoid any confusion for readers (see also ref 3).

(3) Kunieda, M.; Nakato, E.; Tamiaki, H. *J. Photochem. Photobiol., A: Chem.* **2007**, *185*, 321−330.

(4) Laha, J. K.; Muthiah, C.; Taniguchi, M.; Lindsey, J. S. *J. Org. Chem.* **2006**, *71*, 7049−7052.

(5) (a) Fischer, H.; Laubereau, O. *Justus Liebigs Ann. Chem.* **1938**, *535*, 17−37. (b) Smith, K. M.; Lewis, W. M. *Tetrahedron, Suppl.* **1981**, 399−403.

(6) (a) Chang, C. K.; Sotiriou, C. *J. Org. Chem.* **1987**, *52*, 926−929. (b) Pandey, R. K.; Shiau, F. Y.; Sumlin, A. B.; Dougherty, T. J.; Smith, K. M. *Bioorg. Med. Chem. Lett.* **1992**, *2*, 491−496. (c) Pandey, R. K.; Isaac, M.; MacDonald, I.; Medforth, C. J.; Senge, M. O.; Dougherty, T. J.; Smith, K. M. *J. Org. Chem.* **1997**, *62*, 1463−1472. (d) Gerlach, B.; Brantley, S. E.; Smith, K. M. *J. Org. Chem.* **1998**, *63*, 2314−2320. (e) Chen, Y.; Medforth, C. J.; Smith, K. M.; Alderfer, J.; Dougherty, T. J.; Pandey, R. K. *J. Org. Chem.* **2001**, *66*, 3930−3939. (f) Tamiaki, H.; Kimura, S.; Kimura, T. *Tetrahedron* **2003**, *59*, 7423−7435.

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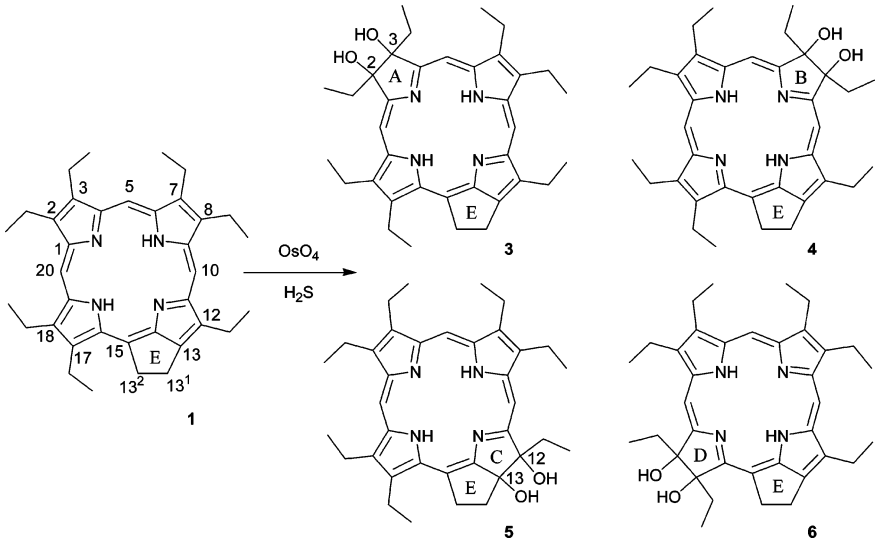
SCHEME 1. Dihydroxylation of 1 by OsO_4



aromaticity and two $\beta-\beta'$ double bonds of the other pyrrole rings are excluded from the aromatic π-system. The relatively isolated Cβ═Cβ' bonds are more reactive than those in the strongly conjugated pyrrole rings on the aromatic pathway.[7] To control the regioselectivity in OsO_4 oxidation at the β,β'-positions in a free-base porphyrin, a substituent effect at the peripheral position was reported to be useful; the pyrrole ring opposite a pyrrole ring possessing an electron-withdrawing group (acetyl and formyl groups) reacted with OsO_4.[6e] The resulting *cis*-diols were readily modified to give a variety of β-substituted porphyrins.[6a,c,d,f,8] Typically, single and double dehydration of the β,β'-dihydroxy-β-ethylchlorin afforded (1-hydroxyethyl)- and vinylporphyrins, respectively, which were further converted to acetyl and formyl compounds. Here we employed 13^2,15-cyclized OEP **1** as the substrate for the OsO_4 dihydroxylation and revealed that the unsymmetric molecular structure of **1** with the E-ring had its major π-circuit between the B- and D-rings, which induced the selective dihydroxylation: dihydroxylation of **1** occurred only at the β-positions of the A- or C-rings to afford *cis*-dihydroxychlorin **3** or **5** (Scheme 1). Moreover, we describe a new route for obtaining phytoporphyrin analogue **2** by chemical modification of regioisomer **5**.

13^2,15-Cyclized OEP **1**, prepared from OEP by three steps (see Scheme S1 in the Supporting Information), was treated with OsO_4 in CH_2Cl_2 and successively by H_2S gas to give a mixture of chlorins. The two major products were easily separated by flash silica gel column chromatography (FCC), yielding the first (1% Et_2O/CH_2Cl_2) and second (3−4% Et_2O/CH_2Cl_2) elutions. The separated products had the same molecular ion peak at 566 (*m*/*z*, FAB) corresponding to that of the dihydroxylated form of **1**, to be regioisomeric diols. Selective production of the two monoadducts from four possible β,β'-dihydroxychlorins, **3**−**6** (Scheme 1), indicated that the two $\beta-\beta'$ double bonds were more reactive than the others. Their molecular structures were determined by their ^1H and $^1H-^1H$ COSY/NOESY and $^1H-^{13}C$ heteronuclear correlation NMR spectra in $CDCl_3$; the first elution was 2,3-dihydroxy **3**, and the second was 12,13-dihydroxy **5**.[9] The isolated yields of **3** and **5** were 25% and 31%, respectively, and starting material **1** was recovered in 24% yield. Some minor pigments possessing chlorin-like absorption bands were detected during FCC separation, but their quantities were so small that the molecular structures could not be determined. Bacteriochlorin-like pigment (bisadduct) was also obtained in monitoring the reaction; the Qy band was observed at 717 nm, but it was degraded during the FCC purification. Thus, the present dihydroxylation of **1** selectively occurred at the A- and C-rings and showed that the C2═C3 and C12═C13 double bonds were more reactive in the oxidation than the C7═C8 and C17═C18 double bonds.

The E-ring in **1** affects the geometry of four pyrrole units (A−D-rings) to make an unsymmetric porphyrin π-system. Compared to highly symmetrical OEP, 13^2,15-cyclized OEP derivative **1** composed of a relatively disordered tetrapyrrolic skeleton would change the aromatic pathway in its porphyrin moiety and show a different reactivity of the $\beta-\beta'$ double bonds as in the present oxidation. A ring current study on a porphyrin[7] suggested that the 22π-circuit went on two pyrrole rings ($6\pi \times 2$) possessing an inner hydrogen atom (NH), four *meso*-carbon atoms ($\pi \times 4$), and two imide nitrogen atoms ($\pi \times 2$) and their neighboring α-carbon atoms ($2\pi \times 2$) in the other two pyrrole rings as shown in two possible tautomers, **1a** and **1b** (red in Figure 2). From molecular modeling calculation (MM+/PM3)[10] of **1a** (two inner hydrogen atoms were on the A- and C-rings) and **1b** (two inner hydrogen atoms on the B- and D-rings), the total energies of **1a** and **1b** were estimated as 14.5 and 6.8 kcal/mol, respectively, indicating that the 22π-system in **1b** would be preferable to that in **1a**. Preliminary X-ray crystallographic analysis also supported **1** to be a tautomer **1b**: the angles of Cα−N−Cα′ in the B- and D-rings (ca. 111°) were wider than those in the A- and C-rings (ca. 106°), meaning that the two inner hydrogen atoms were located on the nitrogen atoms in the B- and D-rings.[11] In tautomer **1b**, the $\beta-\beta'$ double bonds

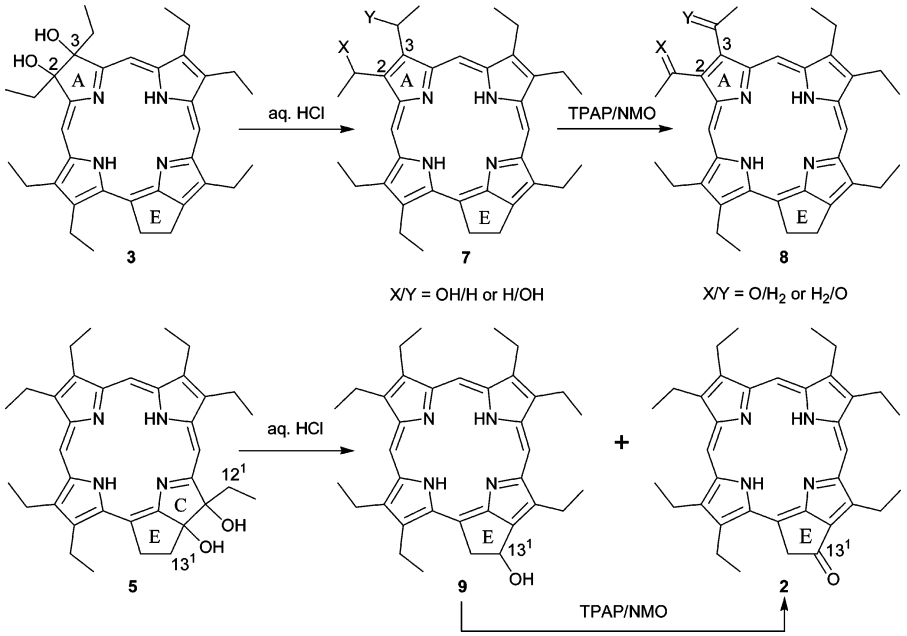
(7) (a) Juselius, J.; Sundholm, D. *Phys. Chem. Chem. Phys.* **2000**, *2*, 2145−2151. (b) Steiner, E.; Fowler, P. W. *ChemPhysChem* **2002**, *3*, 114−116.

(8) (a) Li, G.; Dobhal, M. P.; Graham, A.; Shibata, M.; Zheng, G.; Kozyrev, A.; Pandey, R. K. *J. Org. Chem.* **2003**, *68*, 3762−3772. (b) Tamiaki, H.; Omoda, M.; Saga, Y.; Morishita, H. *Tetrahedron* **2003**, *59*, 4337−4350. (c) Kunieda, M.; Mizoguchi, T.; Tamiaki, H. *Tetrahedron* **2004**, *60*, 11349−11357. (d) Kunieda, M.; Tamiaki, H. *J. Org. Chem.* **2005**, *70*, 820−828.

(9) *cis*-Dihydroxychlorins **3** and **5** had two chiral centers on C2/3 and C12/13, respectively, and were racemates.

(10) Kureishi, Y.; Tamiaki, H. *J. Porphyrins Phthalocyanines* **1998**, *2*, 159−169.

SCHEME 2. Chemical Modifications of Dihydroxychlorins 3 and 5



on the A- and C-rings were relatively excluded from the 22π-system and were more reactive, which was consistent with the present regioselective dihydroxylation. The total energies of the resulting dihydroxychlorins were also distinguished in two groups: in the energetically minimized molecular structures obtained by MM+/PM3 calculations,[10] the total energies of each dihydroxychlorin were 30.0, 44.2, 28.2, and 43.5 kcal/mol for **3**, **4**, **5**, and **6**, respectively. The regioselectivity in the oxidation products might be due to thermodynamic control.

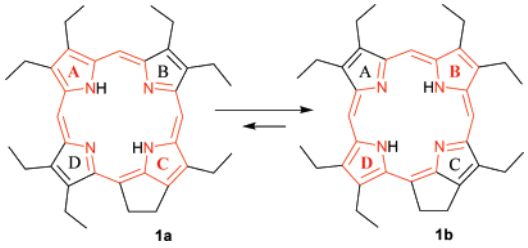


FIGURE 2. Two possible tautomers, **1a** and **1b**, conjugated by a 22π-system (red).

Electronic absorption spectra of **3** and **5** in CH_2Cl_2 were different: Soret and Qy maxima of 12,13-dihydroxy **5** were at 400 and 654 nm, respectively, which were red-shifted from those of 2,3-dihydroxy **3** (395 and 637 nm). The observed difference was clearly estimated from the absorption maxima calculated by ZINDO/S:[12] the energetically lowest electronic transitions of **5** and **3** were situated at 655 and 642 nm, respectively.

The *cis*-dihydroxy moiety in chlorins **3** and **5** can be used as a clue for modifying the β-substituent group in a porphyrin. Single dehydration of the *cis*-dihydroxy moiety in **3** by acidic treatment (Scheme 2) gave a mixture of 2- and 3-(1-hydroxyethyl)porphyrins **7** (73% yield).[13] The regioisomeric ratio of the mixture was determined as 2:1 by the integral ratio of its ^{1}H NMR spectral peaks. Oxidation of the 2- and 3-(1-hydroxyethyl) groups in regioisomerically mixed **7** was easily achieved by treatment of tetrapropylammonium perruthenate (TPAP) with NMO, affording a mixture of 2- and 3-acetylporphyrins **8** (63% yield, regioisomeric ratio of 2:1). In contrast to the slightly controlled regioselectivity in monodehydration of 2,3-diol **3**, the regioisomeric 12,13-diol **5** showed an alternative modification as follows. The same treatment of 12,13-diol **5** as in **3** → **7** afforded two porphyrins as isolatable pigments on FCC, in which the first (minor, CH_2Cl_2 only) and second (major, 2% Et_2O/CH_2Cl_2) elutions showed a molecular ion peak at 546 and 548 (*m*/*z*, FAB), respectively. From ^{1}H and ^{1}H−^{1}H NOESY NMR spectra of the second elution, the major product was assigned to be 13^1-hydroxylated **9** (75% yield)[13] as one of two possible monodehydrated compounds, the 12^1- and 13^1-hydroxyporphyrins. ^{1}H NMR and UV−vis spectra of the first elution indicated that the minor product was **2** reported previously.[3] During the acidic treatment, dehydrogenation of **9** to **2** slightly occurred (7% yield). The single dehydration of **5** would proceed via a carbocation intermediate species. The present result affording the sole formation of 13^1-hydroxyporphyrin **9** indicated that the carbocation intermediate might be produced only on the conformationally restricted 13^1-position (see Scheme S2 in the Supporting Information for the proposed mechanism of **5** → **9**). Secondary alcohol **9** was oxidized by combination of TPAP with NMO to give phytoporphyrin analogue **2** in 67% yield. Although the reported yield of **2** from OEP was lower (<0.4% by nine steps)[3] and some of the steps were inconvenient for a large-scale preparation, the present route would conveniently provide **2** because the total yield of **2** from OEP through the present **1** → **5** → **9** → **2** was 5.7%, which is about 15-fold superior to that of the previous route.

13^2,15-Cyclized OEP **1** could be modified to the phytoporphyrin analogue **2** with a similar skeleton of natural Chl molecules via a regioselective dihydroxylation of **1** to **5**. The chemical modifications from **1** to **2** were smoothly achieved without any difficult procedures. Dihydroxychlorin **3** also has

(11) Senge, M. O.; Smith, K. M. *Acta Crystallogr., C* **1997**, *C53*, 1314−1318.
(12) Kunieda, M.; Tamiaki, H. *J. Org. Chem.* **2007**, *72*, 2443−2451.
(13) Monodehydrated porphyrins **7** and **9** were racemates, 2^1(or 3^1)- and 13^1-epimeric mixtures, respectively.

potential to modify some β-substituted porphyrins possessing a vinyl, 1-hydroxyethyl, acetyl, or formyl group. In the molecular structures of naturally occurring chlorophyllous pigments, functional groups playing an important role in the molecular interactions are on the A- and C-rings so that the present dihydroxychlorins **3** and **5** and their derivatives would be good precursors of Chl models.

Experimental Section

Synthesis of 2,3-Dihydroxychlorin 3 and 12,13-Dihydroxychlorin 5. To a CH_2Cl_2 solution (40 mL) of **1** (120.0 mg, 0.23 mmol) was added a pyridine solution (2 mL) of OsO_4 (71.0 mg, 0.28 mmol), and the resulting mixture was stirred for 24 h under nitrogen. Methanol (10 mL) was added to the reaction mixture for quenching, and H_2S gas was bubbled. After filtration to remove OsS_4, the CH_2Cl_2 solution was evaporated to dryness. The residue was purified on FCC to afford **1** (CH_2Cl_2, 28.2 mg, recovered in 24% yield), **3** (1−2% Et_2O/CH_2Cl_2, 32.0 mg, 25% yield), and **5** (3−4% Et_2O/CH_2Cl_2, 39.1 mg, 31% yield) as pure forms. Spectral data for **3** and **5** were as follows.

Data for 3: $\lambda_{max}(CH_2Cl_2)$/nm 637 (relative intensity 0.16), 585 (0.02), 526 (0.02), 498 (0.06), 395 (1.00); ^{1}H NMR ($CDCl_3$) δ = 9.54 (1H, s, 10-H), 8.89 (1H, s, 5-H), 8.83 (1H, s, 20-H), 4.88 (2H, m, 13^1-CH_2), 3.93−3.81 (6H, m, 7-, 8-, 12-CH_2), 3.81−3.70 (4H, m, 13-, 18-CH_2), 3.66 (2H, m, 17-CH_2), 3.56, 3.26 (each 1H, br s, 2-, 3-OH), 2.57 (2H, q, J = 7 Hz, 2-CH_2), 2.52, 2.43 (each 1H, dq, J = 14, 7 Hz, 3-CH_2), 1.84−1.78 (6H, m, 8^1-, 12^1-CH_3), 1.76 (3H, t, J = 7 Hz, 7^1-CH_3), 1.73 (3H, t, J = 7 Hz, 18^1-CH_3), 1.59 (3H, t, J = 7 Hz, 17^1-CH_3), 1.03 (3H, t, J = 7 Hz, 2^1-CH_3), 0.85 (3H, t, J = 7 Hz, 3^1-CH_3), −1.57, −2.41 (each 1H, br s, NH × 2); ^{13}C NMR ($CDCl_3$) δ = 164.7, 161.9, 157.8, 157.5, 149.4, 139.3, 138.0, 137.6, 135.73, 135.70, 135.2, 134.4, 134.2, 129.1, 121.3, 86.3, 85.3 (C1, C2, C3, C4, C6, C7, C8, C9, C11, C12, C13, C14, C15, C16, C17, C18, C19), 99.0 (C10), 91.4 (C5), 90.8 (C20), 37.4 ($C13^2$), 28.4 ($C3^1$), 28.0 ($C2^1$), 24.2 ($C13^1$), 20.7, 20.0, 19.3, 19.2, 18.9 ($C7^1$, $C8^1$, $C12^1$, $C17^1$, $C18^1$), 18.3, 18.2, 18.0, 17.5, 15.4 ($C7^2$, $C8^2$, $C12^2$, $C17^2$, $C18^2$), 8.5 ($C3^2$), 8.3 ($C2^2$); HRMS (FAB) *m*/*z* 566.3617 (M^+), calcd for $C_{36}H_{46}N_4O_2$ 566.3621.

Data for 5: $\lambda_{max}(CH_2Cl_2)$/nm 654 (relative intensity 0.26), 601 (0.02), 526 (0.02), 502 (0.07), 400 (1.00); ^{1}H NMR ($CDCl_3$) δ = 9.56 (1H, s, 5-H), 9.38 (1H, s, 20-H), 8.79 (1H, s, 10-H), 4.48−4.40 (2H, m, 13^1-CH_2), 3.92−3.70 (8H, m, 2-, 3-, 7-, 8-CH_2), 3.62−3.51, 3.46−3.38 (3H + 1H, m, 17-, 18-CH_2), 2.89−2.81, 2.33−2.25 (each 1H, m, 13-CH_2), 2.00−1.85 (2H, m, 12-CH_2), 1.79, 1.76 (each 3H, t, J = 7 Hz, 3^1-, 7^1-CH_3) 1.73 (3H, t, J = 7 Hz, 8^1-CH_3), 1.72 (3H, t, J = 7 Hz, 2^1-CH_3), 1.67 (3H, t, J = 7 Hz, 18^1-CH_3), 1.53 (3H, t, J = 7 Hz, 17^1-CH_3), 0.65 (3H, t, J = 7 Hz, 12^1-CH_3), −2.01, −2.65 (each 1H, br s, NH × 2); ^{13}C NMR ($CDCl_3$) δ = 171.9 (C11), 166.9 (C14), 151.1, 149.7, 142.7, 139.3, 133.1 (C1, C3, C4, C6, C7), 143.3 (C2), 140.4 (C18), 138.6 (C9), 135.3 (C8), 134.1 (C16), 133.5 (C17), 131.1 (C19), 105.3 (C15), 99.3 (C20), 98.6 (C5), 93.3 (C10), 88.3 (C13), 86.9 (C12), 34.9 ($C13^2$), 31.8 ($C13^1$), 29.8 ($C12^1$), 19.7 ($C2^1$), 19.5 ($C17^1$), 19.3, 18.6, 18.5, 18.2, 17.9 ($C3^1$, $C7^1$, $C2^2$, $C3^2$, $C7^2$, $C8^2$, $C18^2$, two carbon signals which overlapped the others), 19.1 ($C8^1$), 18.8 ($C18^1$), 17.5 ($C17^2$), 8.1 ($C12^2$); HRMS (FAB) *m*/*z* 566.3632 (M^+), calcd for $C_{36}H_{46}N_4O_2$ 566.3621.

Synthesis of 2/3-(1-Hydroxyethyl)porphyrins 7. To a 1,4-dioxane solution (10 mL) of **3** (9.8 mg, 0.017 mmol) was added 10% aq HCl (3 mL), and the resulting mixture was stirred at 50 °C for 1 h under nitrogen. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was washed with water twice, dried over Na_2SO_4, and evaporated to dryness. The residue was purified by FCC to give **7** (3% Et_2O/CH_2Cl_2). The secondary alcohol **7** was purified by recrystallization from CH_2Cl_2/hexane as a red solid (6.9 mg, 73%, regioisomeric ratio 2:1): $\lambda_{max}(CH_2Cl_2)$/nm 617 (relative intensity 0.07), 564 (0.08), 537 (0.07), 502 (0.14), 403 (1.00); ^{1}H NMR (major/minor, $CDCl_3$) δ = 10.66/10.60, 10.05/10.10, 10.02 (each 1H, s, 5-, 10-, 20-H), 6.54−6.47 (1H, m, 2- or 3-CH), 5.48−5.43 (2H, m, 13^1-CH_2), 4.23−4.03 (14H, m, 2- or 3-, 7-, 8-, 12-, 13-, 17-, 18-CH_2), 2.80 (1H, br s, 2^1- or 3^1-OH), 2.35−2.31 (2H, m, 2^1- or 3^1-CH_3), 2.18, 1.97−1.90, 1.88, 1.85−1.80 (3H + 9H + 3H + 3H, m, 2^1- or 3^1-, 7^1-, 8^1-, 12^1-, 17^1-, 18^1-CH_3), −3.04, −3.80 (each 1H, br s, NH × 2); HRMS (FAB) *m*/*z* 548.3527 (M^+), calcd for $C_{36}H_{44}N_4O$ 548.3515.

Synthesis of 2/3-Acetylporphyrin 8. To a CH_2Cl_2 solution (10 mL) of regioisomeric **7** (5.6 mg, 0.010 mmol) was added NMO (9.6 mg, 0.082 mmol), and the resulting solution was stirred under nitrogen. After 5 min of stirring, TPAP (4.7 mg, 0.013 mmol) was added to the solution, and the resulting mixture was stirred for 1 h under nitrogen. The reaction mixture was passed through FCC to remove TPAP and NMO, and **8** was eluted later with CH_2Cl_2. Recrystallization from CH_2Cl_2/methanol gave **8** as a pure form (3.5 mg, 63%): $\lambda_{max}(CH_2Cl_2)$/nm 621 (relative intensity 0.05), 572 (0.08), 550 (0.08), 511 (0.11), 411 (1.00); ^{1}H NMR (major/minor, $CDCl_3$) δ = 10.73/10.66, 10.02/10.17, 9.99/9.97 (each 1H, s, 5-, 10-, 20-H), 5.45−5.39 (2H, m, 13^1-CH_2), 4.41−4.36, 4.21−4.08 (2H + 12H, m, 2- or 3-, 7-, 8-, 12-, 13-, 17-, 18-CH_2), 3.36 (3H, s, 2- or 3-$COCH_3$), 2.03−1.98, 1.97−1.90, 1.84−1.79 (6H + 9H + 3H, m, 2^1- or 3^1-, 7^1-, 8^1-, 12^1-, 17^1-, 18^1-CH_3), −2.88/−2.90, −3.71/−3.60 (each 1H, br s, NH × 2); HRMS (FAB) *m*/*z* 546.3352 (M^+), calcd for $C_{36}H_{42}N_4O$ 546.3359.

Synthesis of 13^1-Hydroxyporphyrin 9. Similar to the dehydration of **3**, a 1,4-dioxane solution (30 mL) of **5** (32.0 mg, 0.056 mmol) was treated with 6% aq HCl (4 mL). After the workup procedure, the residue was purified by FCC to give **2** (CH_2Cl_2) and **9** (2% Et_2O/CH_2Cl_2). The secondary alcohol **9** was purified by recrystallization from CH_2Cl_2/hexane as a purple solid (23.2 mg, 75%): $\lambda_{max}(CH_2Cl_2)$/nm 618 (relative intensity 0.02), 565 (0.03), 503 (0.06), 405 (1.00); ^{1}H NMR ($CDCl_3$) δ = 10.05, 10.04 (2H + 1H, s, 5-, 10-, 20-H), 6.48 (1H, m, 13-CH), 5.97−5.89, 5.26−5.18 (each 1H, m, 13^1-CH_2), 4.28−4.12, 4.09−3.98 (8H + 6H, m, 2-, 3-, 7-, 8-, 12-, 17-, 18-CH_2), 2.38 (1H, br s, 13^1-OH), 2.05 (3H, t, J = 7 Hz, 12^1-CH_3), 1.94, 1.89 (9H + 6H, t, J = 7 Hz, 2^1-, 3^1-, 7^1-, 8^1-, 18^1-CH_3), 1.81 (3H, t, J = 7 Hz, 17^1-CH_3), −2.89, −3.72 (each 1H, br s, NH × 2); HRMS (FAB) *m*/*z* 548.3501 (M^+), calcd for $C_{36}H_{44}N_4O$ 548.3515.

Synthesis of 13^1-Oxoporphyrin 2. Similar to the oxidation of **7**, a CH_2Cl_2 solution (20 mL) of **9** (20.1 mg, 0.037 mmol) was treated with NMO (50.7 mg, 0.43 mmol) and TPAP (25.4 mg, 0.072 mmol) followed by FCC (CH_2Cl_2) and recrystallization (CH_2Cl_2/methanol), affording the desired **2** in a pure form (13.5 mg, 67%): $\lambda_{max}(CH_2Cl_2)$/nm 637 (relative intensity 0.02), 586 (0.06), 563 (0.10), 521 (0.06), 418 (1.00); ^{1}H NMR ($CDCl_3$) δ = 10.09, 9.90, 9.81 (each 1H, s, 5-, 10-, 20-H), 5.83 (2H, s, 13^1-CH_2), 4.30, 4.09, 4.08, 4.00, 3.96, 3.95, 3.88 (each 2H, q, J = 7 Hz, 2-, 3-, 7-, 8-, 12-, 17-, 18-CH_2), 2.06, 1.94−1.84, 1.73 (3H + 15H + 3H, t, J = 7 Hz, 2^1-, 3^1-, 7^1-, 8^1-, 12^1-, 17^1-, 18^1-CH_3), −2.46, −3.44 (each 1H, br s, NH × 2); HRMS (FAB) *m*/*z* 546.3367 (M^+), calcd for $C_{36}H_{42}N_4O$ 546.3359. See also ref 3 for spectral data of **2**.

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Supporting Information Available: Preliminary X-ray crystal data for **1**, preparation of 13^2,15-cyclized OEP **1**, proposed reaction mechanism of **5** → **9**, 1D/2D ^{1}H and ^{13}C NMR spectra of **3** and **5**, 1D ^{1}H NMR spectra of **7** and **8**, and 1D/2D ^{1}H NMR spectra of **9** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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