Synthesis of Bipyridylene-Bridged Bisporphyrin by Nickel-Mediated Coupling Reaction: ON-OFF Control of Cofacial Porphyrin Unit by Reversible Complexation

Yasufumi Tomohiro, Akiharu Satake, and Yoshiaki Kobuke*
Graduate School of Material Science, Nara Institute of Science and Technology, and CREST, Japan
Science and Technology Corporation (JST), 8916-5 Takayama, Ikoma, Nara, 630-0101, Japan

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Novel bipyridylene-bridged bisporphyrin 1a, in which two porphyrin units were attached directly to symmetrical 4,4′-positions of the 2,2′-bipyridyl group, was synthesized by a nickel(0)-mediated homocoupling reaction of 5,10,15-tris(n-heptyl)-20-(2-bromo-4′-pyridyl)porphyrinatonic (3a) in 58% yield. Spatial geometries of two porphyrins in 1a were regulated by reversible complexation of the bipyridyl part with PdCl2. Thus, the addition of 2.2 equiv of palladium chloride to 1a converted the freely rotating conformation to the cofacial porphyrin 2a. The subsequent addition of 4,4′-dimethyl-2,2′-bipyrindine 9 regenerated the initial bisporphyrin 1a.

Introduction

Cofacial bisporphyrins are interesting molecular tools in various research fields, especially, supramolecular chemistry and materials science. Placement of two porphyrin units in a proximity can be expected to produce characteristic functions such as efficient energy transfer, cooperative molecular recognition, and multielectron activation of small molecules. Since their properties depend much on their mutual geometries and distances, various units to link two porphyrins have been proposed. If external signals or ligands control the relative positions of two porphyrins, these properties can now be controlled on demand. Such a bisporphyrin is applicable as a molecular switch and of use in molecular devices and molecular machines. Here, a molecular unit attached to porphyrin was designed to control the relative orientation of two porphyrins. For this purpose, two porphyrin units were connected directly to symmetrical 4,4′-positions of the bipyridyl group to afford 1. Since bipyridyl groups are known as strong ligands toward various transition metal ions, the relative position of two porphyrins can be controlled by the addition/elimination equilibrium of metal ions even in dilute concentrations less than the μM scale. Normally, two porphyrins can rotate freely upon the bond connecting two pyridines. Complexation at the bipyridyl part switches the orientation of two porphyrin units to the same side with a dihedral angle of 60° (Scheme 1). In this paper, we report a facile synthesis of 1a by nickel-mediated coupling reaction of bromopyridinylporphyrin 3a. Complexation of 1a with palladium chloride and subsequent removal of the palladium unit with 4,4′-dimethyl-2,2′-bipyridine were also described.

Results and Discussion

In our search for a simple and efficient strategy for the synthesis of bisporphyrin 1, the first attempt (Scheme 2), consisting of a one-step introduction of two porphyrin units by condensation of 4,4′-diformyl-2,2′-bipyrindine and octanal with the alkyl dipyrromethane 4a, was unsuccessful, as the desired bisporphyrin was identifiable only as a trace component by a MALDI-TOF mass spectrometry and TLC analysis. A homocoupling reaction of bromopyridinylporphyrin 3a was next examined (Scheme 3). Nickel(0)-mediated coupling reaction of aryl halide normally proceeds under mild conditions, and many successful preparative examples of biaryl compounds


The use of a large excess of Ni(cod)$_2$ (ca. 25 equiv) in the presence of 2,2'-bipyridyl (1.3 equiv) and cyclooctadene (ca. 30 equiv) with use of 6.6 x 10$^{-4}$ M 3a in dry DMF. The starting material 3a was completely consumed within 24 h, yielding the desired bisporphyrin 1a as the major product and the debrominated mono-porphyrin 6a as the byproduct. A detailed reaction mechanism is not clear, but the result suggests the following pathway. Under dilute conditions with use of excess amounts of Ni(cod)$_2$, bromide 3a must be smoothly converted into pyridylnickelbromide complex. Then, they react intermolecularly to give bispyridylnickel compound. Finally, the coupling product 1a is produced by reductive elimination of bispyridylnickel compound. Quick consumption of bromide 3a seems to be important to prevent production of 6a and 7a and proceed with the coupling reaction. After gel permeation chromatography, pure 1a was isolated in 58% yield. The presence of axial coordination with two molecules of pyridine (from eluent) was consistent with NMR data.

The proton NMR spectrum of 1a (20 μM in CDCl$_3$) was shown in Figure 1A. Although bipyridyl signals partly overlapped on β-protons of the porphyrin ring protons, H$_3$, H$_6$, and H$_8$ could be assigned as peaks at 9.6, 8.2, and 9.1 ppm, respectively, by $^1$H COSY and TOCSY spectra. Protons of the axial pyridines (PyH$_3$, PyH$_4$, and PyH$_6$) were significantly shielded by the porphyrin and appeared at 3.5, 5.8, and 6.6 ppm, respectively. The shift behavior of pyridine is consistent with previous observations.

The effect of the environment surrounding the porphyrin moieties on the complexation behavior of 1a was monitored by NMR spectroscopy as shown in Figure 1. Solutions of 1a in CDCl$_3$ were prepared in NMR sample tubes at two concentrations: (A) 20 μM and (B) 1.6 μM. The spectra were different. In the more dilute solution (B), signals of axial pyridine, especially PyH$_2$, became unclear by peak broadening based on fast exchange between free and coordinated pyridines. Upon addition of 1.1 equiv of PdCl$_2$(CH$_3$CN)$_2$ to sample B, new signals appeared at 9.9, 9.5, 8.8, 8.5, 7.8, 7.3, 4.8, and 2.4 ppm (indicated as arrows in Figure 1C), and signals of 1a (9.6, 9.0, 8.1, 5.0, and 2.5 ppm) gradually diminished (Figure 1C). After the addition of 2.2 equiv of PdCl$_2$(CH$_3$CN)$_2$, palladium complex 2a was completely formed along with PdCl$_2$(pyridine)$_2$ complex 8 (Figure 1D). Three signals (at...
8.8 (d, 2H), 7.8 (t, 1H), and 7.3 (t, 2H)) were assigned to 8 by comparison with the authentic sample prepared independently.14

To assign signals of 2a in Figure 1D, a TOCSY NMR spectrum was obtained (Figure 2). Three protons (at 9.9, 8.8 (overlapped with $\beta$ proton), and 8.4 ppm) were correlated to one another by $3^J$ and long-range coupling in $^1$H–$^1$H COSY (spectrum is not shown) and TOCSY spectra. They were assigned as H$_6$, H$_3$, and H$_5$ on the bipyridyl moiety. The large downfield shift of H$_6$ (+0.9 ppm) reflects the development of $\delta^+$ charge upon complexation with PdCl$_2$. On the other hand, H$_3$ and $\beta$-protons moved to upper fields upon complexation in varying degrees. The most sensitive shielding effect of the porphyrin ring current appeared at the H$_3$ proton (−0.6 ppm). Another change in the $^1$H NMR spectrum was observed at the alkyl chain parts. According to the symmetry, there are two sets of meso-heptyl groups in porphyrin 1a, namely, the four R groups adjacent to, and the two R' groups opposite to, the bipyridyl groups, respectively. Before complexation, however, they were not distinguishable from one another in the $^1$H NMR spectrum because of free and rapid rotation around the bond connecting two pyridyl units. Thus, the protons H$_a$'s in both R and R' appear as a single peak near δ 4.8; the H$_b$'s appear as a single peak near δ 2.4. When palladium complex 2a is formed, each of the single peaks splits into a doublet. Peak separation between the H$_a$'s, as well as between the H$_b$'s, in the two sets of heptyl groups is now

\[ \text{Scheme 3} \]

\[ \text{Figure 1.} \quad \text{1H NMR titration of 1a with PdCl}_2 \text{(600 MHz, (CDCl)}_2)\text{. (A) 1a (20 \mu M). (B) 1a (1.6 \mu M). (C) B + 1.1 equiv PdCl}_2\text{(CH}_3\text{CN)}_2\text{. (D) B + 2.2 equiv PdCl}_2\text{(CH}_3\text{CN)}_2 = 2a + 8. (C) Coordinated pyridine, (O) PdCl}_2\text{(pyridine), 8.} \]

\[ \text{Figure 2.} \quad \text{A TOCSY spectrum of 2a (the same sample of Figure 1D); spin lock time, 0.1 s.} \]

(14) $^1$H NMR of PdCl$_2$(pyridine); complex 8 in (CDCl)$_2$: δ 8.80 (H$_2$, 2H), 7.82 (H$_4$, 1H), 7.37 (H$_3$, 2H). $^1$H NMR of free pyridine in (CDCl)$_2$: δ 8.58 (H$_2$, 2H), 7.68 (H$_4$, 1H), 7.29 (H$_3$, 2H).
bipyridylene-bridged bisporphyrin 1a and uncomplexed bisporphyrin addition of 5.8 ppm (open circles in Figure 3B). Upon further ligation of pyridines, increased. Finally, the addition of 6.8 equiv of nated almost all of the signals of bisporphyrin 1a (indicated as arrows), 9–PdCl2 complex (10).
detectable because of differences in distances from the facing porphyrin plane. These results show that the addition of 2.2 equiv of Pd(II) completely converts the compound from a freely rotating conformation to an open-mouth one even at such an extremely dilute solution as 1.6 μM.15

Next, to break the cofacial conformation of bisporphyrin 2a, 4,4’-dimethyl-2,2’-bipyridine 9 was added to the mixture. The reaction course was monitored by 1H NMR spectrometry (Figure 3). When 1.3 equiv of 9 was added, signals of 8 at 8.8, 7.8, and 7.4 ppm (filled circles in Figure 3A) disappeared completely with concomitant appearance of signals of coordinating pyridines at 6.5 and 5.8 ppm (open circles in Figure 3B). Upon further addition of 9, signals of palladium complex 2a decreased, and uncomplexed bisporphyrin 1a (indicated as arrows) increased. Finally, the addition of 6.8 equiv of 9 eliminated almost all of the signals of 2a, and signals of bisporphyrin 1a (arrows), 9–PdCl2 complex (10) (filled squares), and free 9 (open squares) were observed (Figure 3D). Signals of pyridine coordinated to zincporphyrin then reappeared at 6.7 and 6.1 ppm (Figure 1B). These results are summarized in Figure 4, where reversible complexation of the bipyridyl part with PdCl2 controls the orientation of two porphyrins along with the axial ligation of pyridines.

Conclusion

We have established a facile synthetic method of bipyridylene-bridged bisporphyrin 1a by a nickel-mediated homocoupling reaction. The homocoupling reaction conditions are mild and expected to be applicable to the synthesis of other bipyridyl- and biarylborphyrins having functional groups after further suitable optimization for each porphyrin. The addition of 2.2 equiv of palladium chloride to 1a converted the freely rotating conformation to the cofacial bisporphyrin 2a. The subsequent addition of 4,4’-dimethyl-2,2’-bipyridine 9 regenerated the initial conformation of bisporphyrin 1a. In this manner, spatial geometries of two porphyrins were easily regulated by reversible complexation of the bipyridyl part. Cofacial porphyrin with a unit capable of reversible on–off complexation may be utilized as a molecular switch in supramolecular chemistry.

Experimental Section

General Methods. NMR spectra were obtained from a JEOL EX-270 and ECP-600 instruments. 1H NMR chemical shifts are reported in parts per million (ppm) from tetramethylsilane (0 ppm) in CDCl3 and (CDCl3). UV–vis spectra were obtained from a Shimadzu UV-3100PC instrument. MALDI-TOF mass spectra were measured with a Perseptive Biosystems Voyager DE-STRApparatus. Dithranol purchased from SIGMA was used as a matrix in MALDI-TOF mass spectrometric measurements. Chromatographies were performed by using Merck silica gel 60 (0.063–0.200 mm). Thin layer chromatographies were performed on commercial Merck silica gel 60F254 plates.

1H NMR titration of 2a with 4,4’-dimethyl-2,2’-bipyridine 9 (600 MHz, (CDCl3)2). (A) 2a (1.6 μM, the same spectrum as Figure 1D). (B) A + 9 (1.3 equiv). (C) A + 9 (2.7 equiv). (D) A + 9 (6.8 equiv) = 1a + 10. (O) Coordinated axial pyridine. (O) PdCl2(pyridine)2 8, (O) 9, (O) 9–PdCl2 complex (10).
Figure 4. Reversible conversion between 1a and 2a.

(H), 112.3 (C), 39.1 (CH2, b), broad, 28.8 (CH2, f, f’), 14.2 (CH3, g, g’) (signals of α carbons of pyroles were missing because of broadening); MALDI-TOF mass (dithranol) m/z 760.6 (M + H) +. Text. C60H12Br6Ni, 759.39; UV-vis (λmax nm (abs. in CHCl3)) 419.5 (0.114), 520.5 (0.005), 557.0 (0.003), 593.0 (0.001), 655.0 (0.002).

5,10,15-Tris(n-heptyl)-20(2-bromo-4-pyridyl)porphyrinatozinc (3a). Saturated zinc acetone solution in MeOH (20 mL) was added to a solution of 5a (480 mg, 0.630 mmol) in CHCl3 (50 mL) while the mixture was stirred. After stirring for 1 h at room temperature, the mixture was washed with water (100 mL × 3), dried over Na2SO4 and evaporated under reduced pressure to give purple solid 3a (458 mg, 0.556 mmol, 88%); mp 136–141 °C; 1H NMR (600 MHz, CDCl3) δ 9.18 (d, 1H, J = 4.4 Hz), 8.79 (d, 1H, J = 4.4 Hz), 8.74 (d, 1H, J = 4.4 Hz), 8.64 (d, 1H, J = 4.4 Hz), 8.59 (d, 1H, J = 4.4 Hz), 8.34 (s, 1H), 7.96 (d, 1H, J = 4.4 Hz), 4.40–4.32 (m, 4H), 4.14–4.06 (m, 2H), 2.35–2.26 (m, 4H), 2.18–2.08 (m, 2H), 1.79–1.71 (m, 4H), 1.71–1.64 (m, 2H), 1.40–1.20 (m, 18H), 0.98–0.85 (m, 8H); 13C NMR (150 MHz, CDCl3) δ 154.6 (C), 148.7 (C), 148.6 (C), 147.6 (C), 147.6 (C), 147.6 (C), 147.6 (C), 147.6 (C), 147.6 (C), 133.6 (PyCH), 130.0 (jCH), 128.9 (jCH), 128.7 (PyCH), 128.0 (jCH), 127.6 (jCH), 120.3 (C), 119.8 (C), 112.5 (C), 39.0 (CH2), 38.8 (CH2), 35.1 (CH2), 35.0 (CH2), 32.2 (CH2), 32.1 (CH2), 30.8 (CH2), 30.7 (CH2), 29.5 (CH2), 29.4 (CH2), 23.0 (CH2), 14.4 (CH3); MALDI-TOF mass (dithranol) m/z 822.7 (M + H) +, calcld for C60H12Br6N22Zn213; UV–vis (λmax nm (abs. in CHCl3)) 423.5 (0.273), 556.5 (0.014), 598.5 (0.006). Anal. Calcld for C60H12Br6N22Zn2H2O·C, 65.59; H, 6.94; N, 8.31. Found: C, 66.17; H, 6.84; N, 7.60.

Bipyridylbisporphyrin (1a). Dry DMF (50 mL) and cyclooctadiene (69 mL, 0.105 mmol) was added to bromopyridylborphyrin 3a (25 mg, 0.033 mmol) and 2,2′-bipyridine (6.5 mg, 0.042 mmol) in a Schlenk flask (100 mL) under an argon atmosphere. After the mixture was stirred for 5 min, Ni(cod)2 (220 mg, 0.8 mmol) was added and the mixture was stirred for 24 h at room temperature. DMF was evaporated under reduced pressure, and the residue was dissolved into CHCl3 (50 mL). The chloroform solution was washed with 5% ethylendiaminetetraacetic acid solution adjusted to pH 12 (30 mL × 5) to remove excess nickel species. The organic layer was dried over Na2SO4 and evaporated in vacuo. The crude mixture of bisporphyrin 1a and monoporphyrin 7a was separated roughly first by using Bio-Beads S-X1 (Bio-Rad Laboratories 200–400 mesh, poly styrene, exclusion limit 14 000, eluent: toluene). Further purification was performed by use of recycle HPLC (J s an Analytical Industry, LC-908) attached to a GPC column (Tosoh TSK-GEL G2500HHR, exclusion limit 20 000) with pyridine as an eluent to give pure 1a (15.7 mg, 58%) as a purple solid. 1a: mp 45–60 °C; 1H NMR (20 μM in CDCl3, 600 MHz, 25 °C) δ 9.65–9.58 (β2 β4, m, 8H), 9.59–9.50 (H3, m, 2H), 9.58–9.55 (β3, m, 4H), 9.01–8.98 (H1, m, 4H), 9.01–8.98 (H4, m, 4H), 8.98–8.86 (H5, m, 2H), 8.20–8.16 (H6, m, 2H), 6.58 (PyH4, br, 2H), 5.84 (PyH3, br, 4H), 5.10–4.98 (Hg, m, 3H), 3.65 (PyH2, br, 4H), 2.62–2.48 (Hs, m, 12H), 1.85–1.75 (Ht, m, 12H), 1.65–1.48 (Hs, m, 12H), 1.45–1.30 (Ht, m, 24H, 0.99–0.80 (Hg, m, 18H); 13C NMR (20 μM in CDCl3, 150 MHz, 25 °C) δ 154.68, 153.52, 150.06, 149.30, 148.42, 147.49, 144.60 (PyC), 135.87 (PyC4), 131.16, 130.08, 129.42, 129.35, 129.11, 127.47, 122.54 (PyC5), 121.03, 120.26, 115.14, 39.45 (Py), 39.40 (Cb), 36.15 (Ca), 36.02 (Ca), 32.22 (Cl, Fr), 30.84 (Cc, Cc), 29.66 (Cd, Cd), 22.99 (Ce, Ce), 14.49 (Cg, Cg); UV–vis (λmax nm (abs. in CHCl3)) 300.5 (0.014), 428.0 (0.157), 557.5 (0.094), 599.0 (0.004); MALDI-TOF mass m/z 1484.8 (1a–2pyridine + H) +, calcld 1484.8 (1a–2pyridine + H) +.

Palladium Complex (2a). A solution of PdCl2(CH2CN)2 in acetonitrile (6.17 × 10−2 M, 50 μL, 3.16 μmol) was added to a solution of bisporphyrin 1a (4.7 mg, 3.16 μmol) in CHCl3 (20 mL). After the mixture was stirred for 1 h at room temperature, the solvent was removed under reduced pressure. The residual solid was washed with methanol (10 mL × 3) and dried under reduced pressure to give purple solids 2a (4.0 mg, 76%). 2a: 1H NMR ((CDCl3)2, 600 MHz, 25 °C) δ 9.93–9.91 (Hs, m, 2H), 9.56–9.44 (β2 β4 β3 β4, m, 12H), 8.88–8.81 (H1, m, 4H), 8.88–8.81 (H4, m, 4H), 8.50–8.46 (H5, m, 2H), 4.90–4.85 (H6, m, 4H), 4.85–4.78 (H7, m, 8H), 2.50–2.41 (H8, m, 4H), 2.41–2.35 (H9, m, 8H), 1.65–1.15 (H10, H11, H12, H13, H14, H15, H16, m, 36H), 0.92–0.84 (H17, m, 4H), 0.88–0.75 (H18, m, 12H); UV–vis (λmax nm (abs. in CHCl3)) 312.0 (0.013), 422.0 (0.092), 562.5 (0.009), 616.5 (0.002); MALDI-TOF mass m/z found 1661.9 (M + H) +, calcld 1660.61 (C60H12Br6Ni2Na2P2D2Zn2Na).