Synthesis of Trichlorodimethoxybenzene-Linked Porphyrin-Pyridine Conjugate

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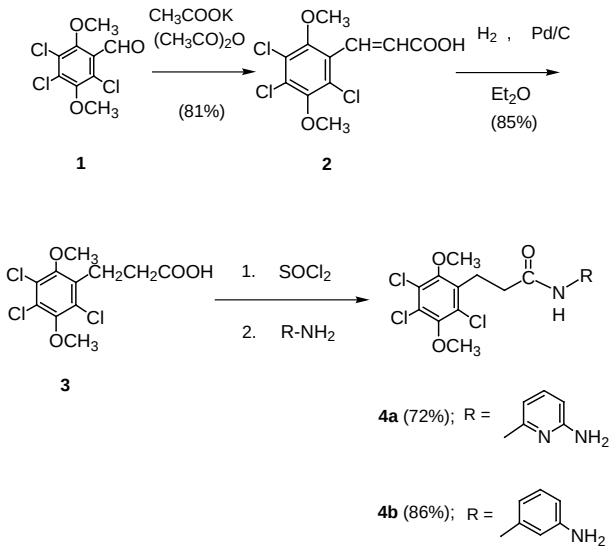
Abstract: The synthesis of a trichlorodimethoxybenzene substituted Zn(II) metalloporphyrin-pyridine conjugate **12** is reported. The structures of the porphyrins were established by MS, ^{1}H NMR and elemental analysis. Protonation of the pyridine moiety leads to a strong reduction of fluorescence intensity of **12**.

Key words: porphyrin, pyridine, electron transfer, conjugation, supramolecular chemistry

Porphyrins are remarkable coordinating ligands since they form metallocomplexes with almost all of the metals of the periodic table.[1] The considerable progress achieved in porphyrin chemistry can be attributed to the extensive studies carried out on the syntheses of variously substituted porphyrin derivatives.[2] We are interested in designing a series of donor-bridge-acceptor systems to give information on how the nature of the spacer between the donor and the acceptor influences the electron transfer process.[3] In this paper, we report the synthesis of a porphyrin donor-bridge-acceptor system. The donor and the acceptor are zinc porphyrin and trichlorodimethoxybenzene,[4] respectively.

In Scheme 1, the synthetic route to the functionalized trichlorodimethoxybenzene **4** is shown. The starting compound **1** was prepared in five steps from 2,5-dihydroxytoluene according to the reported methods.[5] Perkin reaction of **1** and acetic anhydride with potassium acetate gave the cinnamic acid **2** in 81% yield. Reduction of **2** in the presence of palladium-on-charcoal afforded the propionic acid **3** in 85% yield. Chlorination of **3** with $SOCl_2$ followed by treatment with 2,6-diaminopyridine and 1,3-phenylenediamine in Et_2O gave **4a** and **4b** in 72% and 86% yields, respectively.

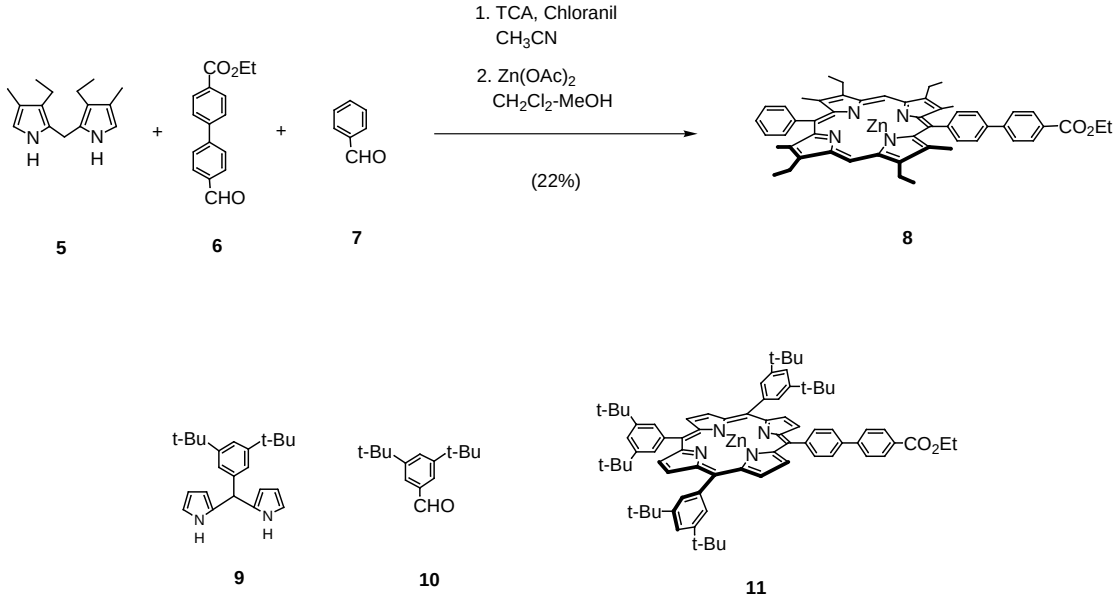


Scheme 1

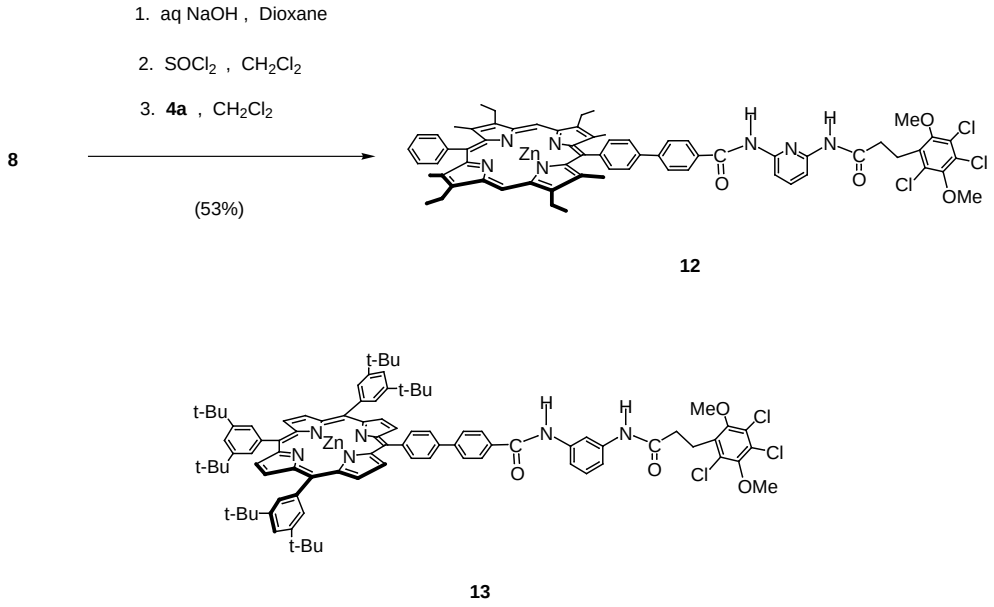
In Scheme 2, the syntheses of **8** and **11** are shown. Previously published procedures were used for the syntheses of 3,3′-dimethyl-4,4′-diethyldipyrromethane (**5**)[3b] and ethyl 4′-formyl-4-biphenylcarboxylate (**6**).[6] The porphyrin **8** was prepared in 22% yield from the cross-condensation of **5**, **6**, and benzaldehyde (**7**). The porphyrin **8**, however, showed low solubility in the organic solvent, which made the purification by silica gel column chromatography difficult and caused a low yield. Therefore, *meso*-(3,5-di-*tert*-butylphenyl)-2,2′-dipyrromethane (**9**)[7] and 3,5-di-*tert*-butylbenzaldehyde (**10**) were employed to provide enhanced solubility to the porphyrin. The porphyrin **11** was synthesized from **6**, **9**, and **10** in a 28% yield in the similar manner. The syntheses of **12** and **13** are shown in Scheme 3. Hydrolysis of **8** with NaOH in H_2O/dioxane followed by treatment with $SOCl_2$ and **4a** in CH_2Cl_2 afforded the target compound **12** in 53% yield. Compound **12** was verified by spectroscopic analyses including ^{1}H NMR and MALDI-TOF mass spectra. The porphyrin **13** was prepared from **4b** and **8** in 76% yield.

The absorption spectra of the zinc complex **12** exhibited Soret band (S_2) at 407 nm and Q bands (S_1) at 535 nm and 571 nm in CH_2Cl_2, while the absorption spectra of the zinc complex **13** showed Soret band at 423 nm and Q bands at 550 nm and 588 nm in CH_2Cl_2, respectively. The fluorescence emission bands of **12** exhibited at 576 nm and 627 nm in CH_2Cl_2, and those of **13** showed at 600 nm and 648 nm in CH_2Cl_2. The absorption and fluorescence spectra of **12** and **13** are almost identical with the corresponding reference compounds **8** and **11**, respectively, suggesting that the attachment of the trichlorodimethoxybenzene to the porphyrin moiety does not perturb its electronic property.

Bubbling of HCl through a CH_2Cl_2 solution of **12** followed by treatment with $Zn(OAc)_2$ led to a decrease in the electronic absorption at 290 nm and the formation of a new maximum at 320 nm, reflecting the protonation of the pyridine ring, and that the fluorescence intensity of **12** was strongly reduced. Moreover, changes in the absorption



Scheme 2



Scheme 3

spectrum and the fluorescence spectrum of **13** were not observed upon bubbling HCl into a CH_2Cl_2 solution of **13**. Interestingly, the C=O stretching vibration (1690 cm^{-1}) in **12** was shifted to a lower wavenumber region by about 30 cm^{-1}, indicating the formation of two intramolecular hydrogen bonds to the carbonyl oxygens (Figure). Although the detailed quenching mechanism of **12** is not clear, one might assume that the resulting conformation (**12B**) caused a static quenching process. The present paper outlines the synthesis of trichlorodimethoxybenzene substituted Zn(II) metalloporphyrin-pyridine conjugate **12** and that the pyridine moiety might play an important role in the fluorescence quenching process.

Mps were determined with an electrothermal melting point apparatus in a sealed capillary and are uncorrected. UV-visible spectra were obtained with a Shimadzu UV-3101PC spectrometer. Steady-state fluorescence spectra were taken on a Shimadzu RF-5301PC spectrofluorimeter. ^1H NMR spectra were measured on a Varian XL-300 spectrometer, and the chemical shifts (δ) are reported in ppm, referenced to TMS as an internal standard. FAB and MALDI-TOF mass spectra were recorded on JEOL-DX303 and PerSeptive Biosystems JMS-ELITE, respectively. All chemicals were reagent

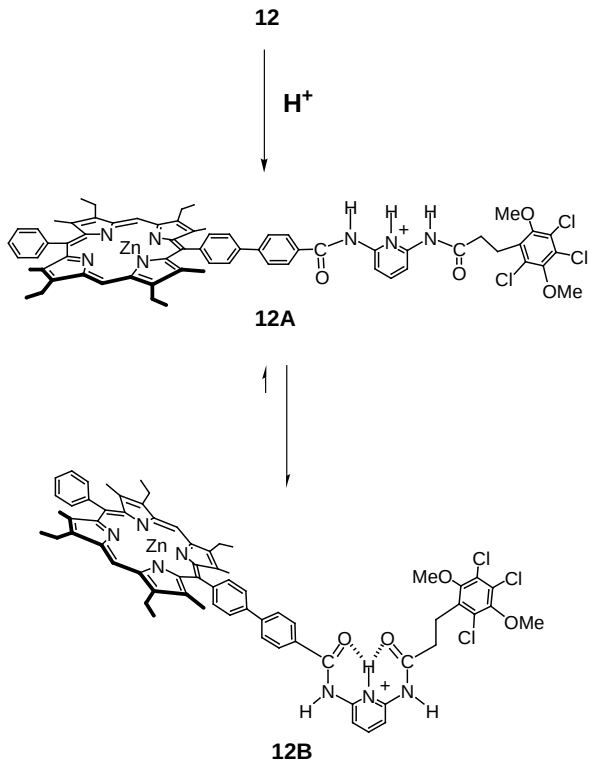


Figure Effect of protonation on hydrogen bonding orientation

grade and used without further purification. THF was freshly distilled from Na/benzophenone ketyl, while CH_2Cl_2 was distilled over CaH_2. All reactions were carried out in a N_2 atm.

2,4,5-Trichloro-3,6-dimethoxycinnamic Acid (2)
After a mixture of **1** (2.01 g, 7.46 mmol), potassium acetate (0.69 g, 6.98 mmol) and acetic anhydride (12.85 g, 125.9 mmol) was stirred at 130 °C for 3 h, it was diluted with H_2O. Na_2CO_3 was added to the aqueous suspension. After filtration, concd HCl was added to the filtrate. The precipitate was filtered off and washed with H_2O to give 1.88 g (81%) of **2** as white needles, mp: 214−216 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.80, 3.90 (s, each 3H, OC*H*$_3$), 6.90 (d, 1H, *J* = 16.2 Hz, Ar-C*H* = CH), 7.95 (d, 1H, *J* = 16.2 Hz, Ar-CH = C*H*), 12.84 (br s, 1H, COO*H*).

MS (FAB): *m/z* = 311 (M^+).

Anal. Calcd for $C_{11}H_9Cl_3O_4$: C, 42.38; H, 2.89. Found: C, 42.30; H, 2.73.

3-[2,4,5-Trichloro-3,6-dimethoxybenzene]propionic Acid (3)
A mixture of **2** (0.90 g, 2.89 mmol), palladium-on-charcoal (0.3 g), and Et_2O (60 mL) was stirred vigorously for 3 h under H_2 pressure, then filtered through Celite. The filtrate was evaporated to afford 0.77 g (85%) of **3** as colorless needles, mp: 149−151 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (t, 2H, *J* = 8.4 Hz, Ar-C*H*$_2$CH$_2$), 3.14 (t, 2H, *J* = 8.4 Hz, Ar-CH$_2$C*H*$_2$), 3.86, 3.88 (s, each 3H, OC*H*$_3$).

MS (FAB): *m/z* = 313 (M^+).

Anal. Calcd for $C_{11}H_{11}Cl_3O_4$•0.3H_2O: C, 41.34; H, 3.68. Found: C, 41.39; H, 3.19.

3-[2,4,5-Trichloro-3,6-dimethoxybenzene]-*N*-(6-amino-2-pyridyl)propanamide (4a)
After a mixture of **3** (1.0 g, 3.20 mmol) and thionyl chloride (0.60 g, 5.04 mmol) was stirred at 70 °C for 0.5 h, the excess thionyl chloride was distilled in vacuo to afford the acid chloride as a yellow oil (verified by IR spectra). The yellow residue was dissolved in Et_2O (100 mL) and 2,6-diaminopyridine (0.70 g, 6.41 mmol) was added. After stirring for 3 h, the mixture was washed with dilute HCl and H_2O, and dried (Na_2SO_4). Purification by column chromatography on silica gel (CH_2Cl_2-hexane) gave 0.93g (72%) of **4a** as colorless flakes, mp: 60−62 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59 (t, 2H, *J* = 7.8 Hz, Ar-C*H*$_2$CH$_2$), 3.21 (t, 2H, *J* = 7.8 Hz, Ar-CH$_2$C*H*$_2$), 3.87, 3.88 (s, each 3H, OCH$_3$), 4.29 (br s, 2H, NH_2), 6.26 (d, 1H, *J* = 8 Hz, pyridine-*H*), 7.47 (t, 1H, *J* = 8 Hz, pyridine-*H*), 7.54 (br s, 2H, pyridine-*H* and N*H*CO).

MS (FAB): *m/z* = 404 (M^+).

Anal. Calcd for $C_{16}H_{16}Cl_3N_3O_3$: C, 47.49; H, 3.98; N, 10.38. Found: C, 47.50; H, 3.69; N, 10.00.

3-[2,4,5-Trichloro-3,6-dimethoxybenzene]-*N*-(6-aminobenzene)propionamide (4b)
Compound **4b** was prepared from **3** and 1,3-phenylenediamine in the similar manner as for **4a**.

Colorless needles, mp: 188−189 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.58 (t, 2H, *J* = 8.1 Hz, Ar-C*H*$_2$CH$_2$), 3.21 (t, 2H, *J* = 8.1 Hz, Ar-CH$_2$C*H*$_2$), 3.69 (br s, 2H, NH_2), 3.87 (s, 6H, OCH$_3$), 6.41-6.44 (m, 1H, Ar*H*), 6.64-6.67 (m, 1H, Ar*H*), 7.07 (t, 1H, *J* = 8.4 Hz, Ar*H*), 7.17 (br s, 1H, N*H*CO) 7.19 (br s, 1H, Ar*H*).

MS (FAB): *m/z* = 403 (M^+).

Anal. Calcd for $C_{17}H_{17}Cl_3N_2O_3$: C, 50.58; H, 4.24; N, 6.94. Found: C, 50.58; H, 4.16; N, 6.79.

Zn(II) Complex of 5-Phenyl-15-(4-(4'-ethoxycarbonylbiphenyl))-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin (8)
To a stirred mixture of 3,3′-dimethyl-4,4′-diethyldipyrromethane (**5**) (238 mg, 1 mmol), ethyl 4′-formyl-4-biphenylcarboxylate (**6**) (127 mg, 0.50 mmol), and benzaldehyde (**7**, 53 mg, 0.50 mmol) in MeCN (10 mL) was added trichloroacetic acid (56 mg, 0.34 mmol). The mixture was stirred overnight at r.t. in the dark. *p*-Chloranil (400 mg, 1.63 mmol) dissolved in THF (20 mL) was added, and the stirring was continued for 5 h, then the solution was poured into H_2O and extracted with CH_2Cl_2. To the organic extracts, sat. $Zn(OAc)_2$/MeOH solution (5 mL) was added and the solution was refluxed for 2 h. The mixture was washed with H_2O, dried (Na_2SO_4), and evaporated in vacuo to leave a residue, which was purified by silica gel column chromatography (CH_2Cl_2-hexane) to afford 92 mg (22%) of **8** as purple prisms, mp: > 300 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3H, *J* = 6.9 Hz, CO$_2$CH$_2$C*H*$_3$), 1.76 (m, 12H, pyrrole-CH$_2$C*H*$_3$), 2.44, 2.54 (s, each 6H, pyrrole-C*H*$_3$), 3.77 (q, 2H, *J* = 6.9 Hz, CO$_2$C*H*$_2$CH$_3$), 3.98 (m, 8H, pyrrole-C*H*$_2$CH$_3$), 6.89−8.25 (m, 13H, Ar*H*), 10.14 (s, 2H, meso-*H*).

MS (FAB): *m/z* = 841 (M^+).

Anal. Calcd for $C_{53}H_{52}N_4O_2Zn$•0.5H_2O: C, 74.77; H, 6.27; N, 6.58. Found: C, 74.53; H, 6.12; N, 6.43.

Compound 11
Compound **11** was prepared from **6**, **9**, and **10** in the similar manner as for **8**.

Purple powder, mp: > 300 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 3H, *J* = 7.3 Hz, $CO_2CH_2CH_3$), 1.53 (m, 54H, t-*Bu*), 4.45 (q, 2H, *J* = 7.3 Hz, $CO_2CH_2CH_3$), 7.80 (t, 3H, *J* = 2 Hz, Ar*H*), 8.02 (m, 4H, biphenyl-*H*), 8.10 (m, 6H, Ar*H*), 8.25 (d, 2H, *J* = 8.1 Hz, biphenyl-*H*), 8.35 (d, 2H, *J* = 8.1 Hz, biphenyl-*H*), 9.02 (m, 8H, pyrrole-*H*).

MS (FAB): *m/z* = 1162 (M^+).

Anal. Calcd for $C_{77}H_{84}N_4O_2Zn•H_2O$: C, 78.32; H, 7.34; N, 4.74. Found: C, 78.06; H, 7.57; N, 4.30.

Compound 12

After a mixture of **8** (200 mg, 0.24 mmol), NaOH (40 mg, 1.0 mmol), and dioxane (20 mL) was refluxed for 2 h, the solution was poured into H_2O containing concd HCl, extracted with $CHCl_3$, and neutralized with aqueous $NaHCO_3$. To the organic extracts, sat. $Zn(OAc)_2$/MeOH solution (5 mL) was added and the solution was refluxed for 1 h. The mixture was washed with H_2O and evaporated in vacuo to afford the porphyrin carboxylic acid (verified by IR spectra). After a mixture of the porphyrin carboxylic acid and thionyl chloride (0.5 g, 4.2 mmol) was stirred at 80 °C for 0.5 h, the excess thionyl chloride was distilled in vacuo. The residue dissolved in CH_2Cl_2 (10 mL) was added to a solution of the propionamide **4a** (100 mg, 0.25 mmol) in CH_2Cl_2 (30 mL). The solution was stirred for 3 h, and evaporated in vacuo to leave the residue, which was worked up as described for the preparation of **8** to afford 153 mg (53%) of **12** as purple prisms, mp: > 300 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (m, 12H, pyrrole-CH_2CH_3), 2.45, 2.55 (s, each 6H, pyrrole-CH_3), 2.66 (t, 2H, *J* = 7.2 Hz, Ar-CH_2CH_2), 2.95 (t, 2H, *J* = 7.5 Hz, Ar-CH_2CH_2), 3.76, 3.79 (s, each 3H, OCH_3), 4.03 (m, 8H, pyrrole-CH_2CH_3), 6.51 (d, 1H, *J* = 6.2 Hz, pyridine-*H*), 6.69−8.32 (m, 15H, pyridine-*H* and Ar*H*), 10.09, 10.17 (s, each 1H, meso-*H*).

MS (MALDI-TOF): 1073.13 (M−2OCH_3−Zn).

Anal. Calcd for $C_{67}H_{62}Cl_3N_7O_4Zn•H_2O$: C, 66.02; H, 5.29; N, 8.04. Found: C, 65.84; H, 4.99; N, 7.98.

Compound 13

Compound **13** was prepared from **4b** and **8** in the similar manner as for **12**.

Purple powder, mp: 229−231 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53 (s, 54H, t-*Bu*), 2.65 (t, 2H, *J* = 8.4 Hz, Ar-CH_2CH_2), 3.25 (t, 2H, *J* = 8.4 Hz, Ar-CH_2CH_2), 3.91 (s, 6H, OCH_3), 7.00−7.30 (m, 4H, Ar*H*), 7.53 (br s, 2H, N*H*), 7.80 (d, 3H, *J* = 1.8 Hz, Ar*H*), 8.05 (d, 4H, *J* = 8 Hz, biphenyl-*H*), 8.10 (m, 6H, Ar*H*), 8.37 (d, 4H, *J* = 8 Hz, biphenyl-*H*), 9.02, 9.03 (s, each 4H, pyrrole-*H*).

MS (FAB): *m/z* 1520 (M^+).

Anal. Calcd for $C_{92}H_{95}Cl_3N_6O_4Zn•0.5CHCl_3$: C, 70.31; H, 6.09; N, 5.32. Found: C, 70.09; H, 6.13; N, 5.09.

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