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Synthesis of Quinone-Bearing Peptides. Photoinduced Electron-Transfer of Peptide-Bridged Porphyrin-Quinone Molecules

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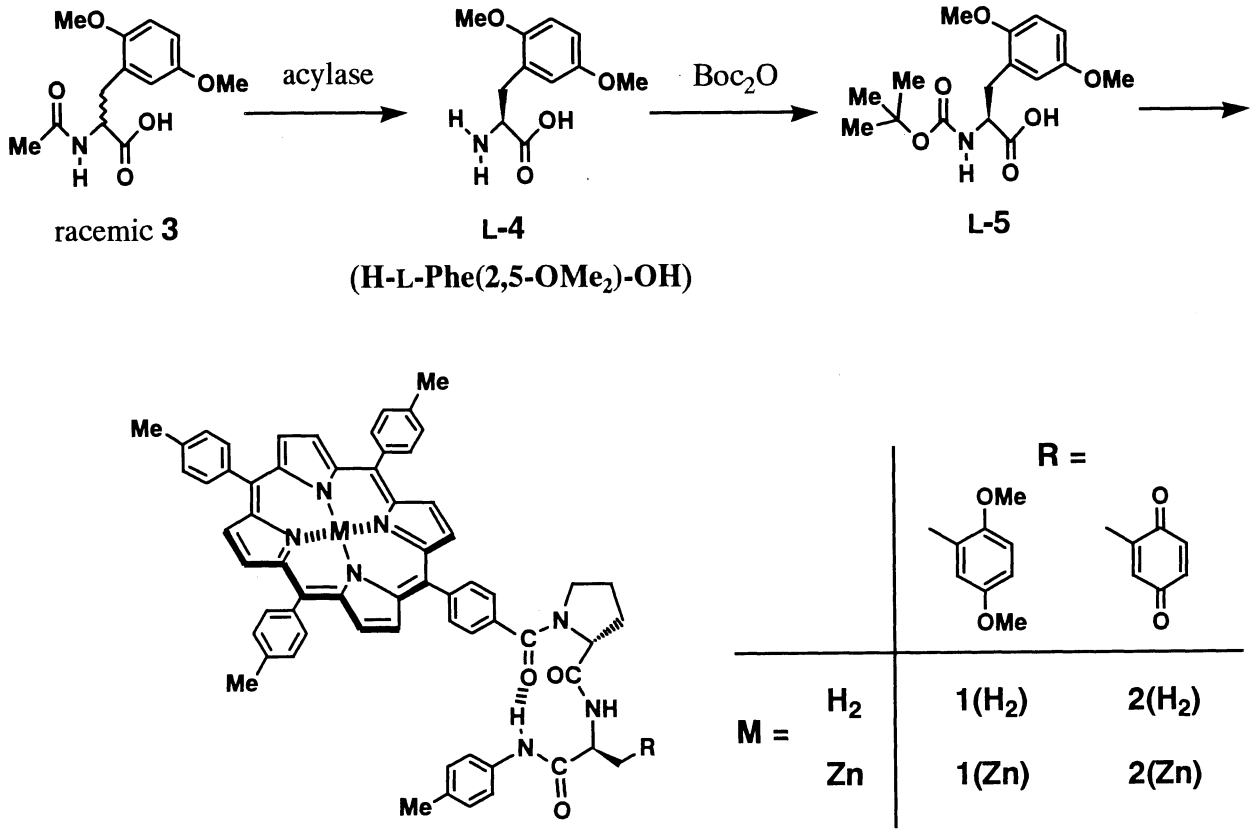
Synthetic peptide-bridged porphyrin-quinone molecules were easily available by use of a precursor for a chiral α-amino acid bearing quinone moiety on the side chain, L-(2,5-dimethoxyphenyl)alanine. Photoinduced electron transfer from porphyrin to quinone in the molecules occurred in 2-methyltetrahydrofuran.

Electron transfer from tetrapyrroles to quinones is a current topic from mechanistic elucidation on the early events of photosynthesis. Many models are available and typically, intramolecular electron transfer of synthetic porphyrin-quinone compounds has been extensively studied.[1,2] On the other hands, electron transfer in photosynthetic reaction center occurs in protein environments and some special peptide sequences are thought to affect the electron transfer rates. It is very important to investigate the electron transfer including protein environments and many theoretical works have been already done.[3] However, few models containing porphyrin, quinone and protein groups in the molecule have been synthesized, in which such a donor and an acceptor were situated on both edges of the bridged peptide.[2a] Here, we report synthesis of quinone-bearing peptides with porphyrins and photoinduced electron transfer of the molecules. Achiral quinone-bearing peptides have been recently prepared by Kotha and Kuki,[4] and synthetic *chiral* peptides containing α-amino acid component with quinone chromophore on the side chain are first, to our knowledge,[5] reported in this paper.

Hydrolysis of racemic *N*-acetyl-(2,5-dimethoxyphenyl)alanine (**3**)[6] by acylase gave enantiomerically pure (2,5-dimethoxyphenyl)alanine (**4**) as the product. HPLC analysis[7] showed the absolute configuration to be L-form as well as hydrolysis by natural acylase. The unusual α-amino acid H-L-Phe(2,5-OMe_2)-OH (**L-4**) was *N*-protected by Boc_2O to afford Boc-L-Phe(2,5-OMe_2)-OH (**L-5**: mp 120–122 °C; 84% yield for 2 steps, based



Scheme 1.

Table 1. Fluorescence Lifetimes and Electron Transfer Rate Constants[a)]

	τ_1 / ns	τ_2 / ns	k_{et} / 10^8 s^{-1}
1(H$_2$)	9.5 (100)		
2(H$_2$)	9.0 (38)	3.2 (62)	2.1
1(Zn)	1.8 (100)		
2(Zn)	1.7 (36)	0.22 (64)	40

a) Measured in 2-methyltetrahydrofuran at 22 °C with a HORIBA NAES-1100 time-resolved spectrofluorometer. Error was within ±10%. Parentheses indicate the ratio of the preexponential factors.

on **L-3**) which was easily purified by recrystallization from dichloromethane and hexane.[8] According to the previous reports (classical procedures for peptide synthesis: use of carbodiimides),[9] **L-5** was converted to porphyrin-dimethoxyphenyl **1(H2)** as shown in Scheme 1. The compound **1(H2)** was demethylated (BBr_3 in CH_2Cl_2, -78 °C) and oxidized (PbO_2 in CH_2Cl_2, 20 °C)[2b] to give porphyrin-quinone **2(H2)** under the mild conditions and corresponding zinc complexes **1(Zn)** and **2(Zn)** were prepared by standard procedures for zinc metallation[9b] of **1(H2)** and **2(H2)**, respectively.

The absorption spectra (> 400 nm, ca. 10^{-6} mol dm^{-3}) of **2(H2)** and **2(Zn)** in 2-methyltetrahydrofuran (2-MeTHF) were the same as those of **1(H2)** and **1(Zn)**, respectively, which indicated intramolecular interaction between porphyrin and quinone moieties to be negligible in the ground states. In fluorescence spectra (excitation of Soret-band, ca. 10^{-6} mol dm^{-3}, in 2-MeTHF), spectral shapes of **2(H2)** and **2(Zn)** were the same as those of **1(H2)** and **1(Zn)**, respectively, but both the intensities of **2(H2)** and **2(Zn)** reduced to be about 60% of the corresponding **1(H2)** and **1(Zn)**. This quenching might be due to intramolecular electron transfer from photoexcited porphyrin moiety to quinone moiety. The lifetimes of **1** and **2** were measured by sub-nanosecond time-correlated single photon counting technique (see Table 1). The fluorescence decay of porphyrin-dimethoxyphenyl **1** followed a single exponential curve but that of porphyrin-quinone **2** followed a biexponential curve. The minor component τ_1 of **2** was slightly smaller than the lifetime of **1** and might be due to impurities[10] in the solution and unpreferred conformers[9a] different from β-turned conformers as shown in Scheme 1. The major fast decaying component τ_2 of **2** might be related to the electron transfer process from photoexcited porphyrin moiety to quinone moiety in the β-turned conformer. Electron transfer rate constants k_{et} were estimated by the equation of $k_{et} = 1 / \tau_2(2) - 1 / \tau_1(1)$ (see Table 1). The fact that k_{et} in **2(Zn)** was 20 times larger than that in **2(H2)** must be explained by the difference of free energy gap for the electron transfer and this factor is in good agreement with reported factors (10–30) in other porphyrin-quinone molecules.[2b]

By use of a precursor for a chiral α-amino acid bearing quinone moiety on the side chain, novel unusual α-amino acid **L-4** reported here, quinone-bearing peptides were easily available. These peptides are promising for highly functionalized materials, including models for biological systems.

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7) Chiral column HPLC analyses (Chiralcel OD, Daicel Chemical Industries, 10% 2-propanol / hexane, 1.0 ml min^{-1}, 30 °C) of protected Z-Phe(2,5-OMe_2)-OMe derived from racemic **4** gave two peaks (the retention time, $15._5$ and 19 min), but Z-Phe(2,5-OMe_2)-OMe derived from the acylase-hydrolysis product **4** gave only one peak ($15._5$ min); for determination of absolute configuration for unusual α-amino acids, see T. Miyazawa, Y. Shindo, T. Yamada, and S. Kuwata, *Anal. Lett.*, **26**, 457 (1992).

8) To 400 mg of racemic **3** in 100 ml distilled water (pH ≈ 7 by addition of 0.1 mol dm^{-3} aq NaOH) were added 100 mg acylase (Tokyo Chemical Industry, *Aspergillus genus*) and 1 mg $CoCl_2$. After stirring for 3 days at 37 °C, the suspension was filtered over celite and the filtrate was acidified by 1 mol dm^{-3} aq HCl and washed with CH_2Cl_2. The aqueous solution was evaporated and the residue was washed with acetone, dried in vacuo to give crude HCl-salt of L-**4**; ^1H NMR (D_2O) δ=3.00 (1H, dd, *J*=7 and 14 Hz, β-H), 3.18 (1H, dd, *J*=6 and 14 Hz, β-H), 3.63, 3.65 (3H+3H, s, OMe), 4.21 (1H, dd, *J*=6 and 7 Hz, α-H), 6.71 (1H, d, *J*=3 Hz, 6-H), 6.80 (1H, dd, *J*=3 and 9 Hz, 4-H), and 6.85 (1H, d, *J*=9 Hz, 3-H); MS *m/z* 226 (MH^+). To ice-chilled solution (1,4-dioxane / water = 10 ml / 5 ml) of all the salt were added 1.5 ml of 1 mol dm^{-3} aq NaOH and 218 mg of Boc_2O. After 1 h stirring at room temperature, the mixture was evaporated and to the residue was acidified by 5% aq $KHSO_4$. After several extraction with EtOAc, combined extracts were dried over Na_2SO_4, evaporated and recrystallized from CH_2Cl_2 and hexane to give pure L-**5**; ^1H NMR ($CDCl_3$) δ=1.39 (9H, s, *t*-Bu), 3.10 (2H, m, β-H), 3.75, 3.79 (3H+3H, s, OMe), 4.44 (1H, m, α-H), 5.44 (1H, d, *J*=7 Hz, NH), 6.74 (1H, d, *J*=3 Hz, 6-H), 6.76 (1H, dd, *J*=3 and 9 Hz, 4-H), and 6.80 (1H, d, *J*=9 Hz, 3-H); MS *m/z* 325 (M^+). All other new compounds **1** and **2** gave the expected ^1H NMR, IR, UV-Vis, and/or MS spectra.

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10) Both quinones **2** were analytically pure from their ^1H NMR spectra, indicating that synthetic **2** should include < 5% impurities with a porphyrin moiety. Such impurities might increase slightly during the τ-measurement.

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