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Preparation and Binding Affinity of New Porphyrin Host Molecule for Ubiquinone Analogues

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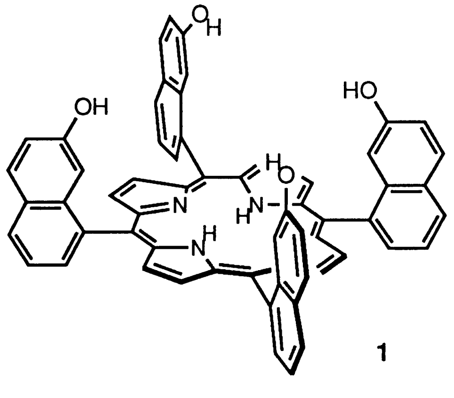
αααα-*meso*-Tetra(7-hydroxy-1-naphthyl)porphyrin (**1**) is prepared as a host molecule for ubiquinone analogue, 2,3,5,6-tetramethoxy-*p*-benzoquinone (**2**). The affinity and thermodynamic aspects in porphyrin **1** - quinone **2** pairing were determined by titrimetric measurement of electronic absorption and fluorescence spectra. The binding constant of **1** for **2** at 298 K is obtained; $K_a = 7.9 \times 10^2$ M^{-1} in toluene. The fashion of this porphyrin-quinone pairing was large different from that of previous host, αααα-*meso*-tetra(2-hydroxy-1-naphthyl)porphyrin (**3**), - quinone **2** pairing.

Intermolecular interaction between quinone and porphyrin is one of the most practical models to elucidate the mechanism of electron transfer in respiratory and/or photosynthesis systems.1) We have reported the efficient host molecule, αααα-*meso*-tetra(2-hydroxy-1-naphthyl)porphyrin (**3**), for ubiquinone analogues and discussed the structural and thermodynamic aspects in porphyrin-quinone pairing.2) Particularly, binding constant and free energy of formation of the 1:1 complex between **3** and tetramethoxy-*p*-benzoquinone (**2**) via multipoint hydrogen bonds were determined from UV-vis titration performed in toluene at 298 K; $K_a = 6.1 \times 10^5$ M^{-1} and $\Delta G° = -7.9$ kcal/mol. The distance between porphyrin ring and quinone is estimated to be ca. 3.5 Å by the CPK molecular models in **3**-**2**. We have recently prepared new host molecule, αααα-*meso*-tetra-(7-hydroxy-1-naphthyl)porphyrin (**1**) to compare with the fashion of interaction with ubiquinone analogues. This paper reports the preparation of new porphyrin **1** and binding affinity for **2**.



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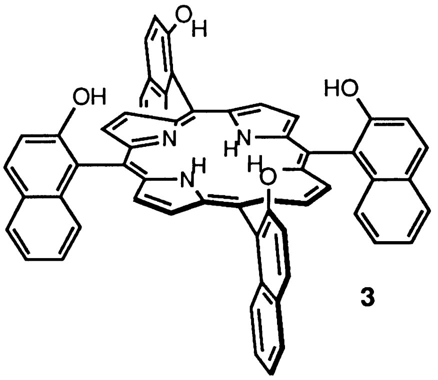

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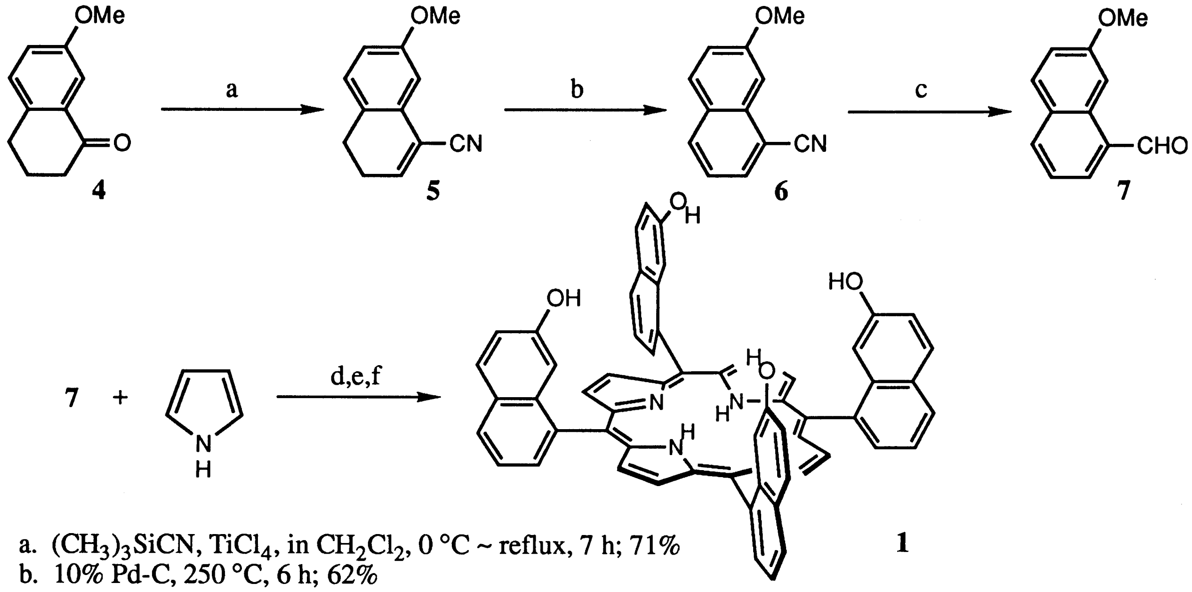
The synthetic route to porphyrin **1** is shown in Scheme 1. 7-Methoxy-1-naphthaldehyde (**7**) as a precursor of porphyrin **1** was prepared from 7-methoxy-1-tetralone (**4**) in three steps. Condensation of aldehyde **7** and pyrrole gave a mixture of atropisomers of *meso*-tetra(7-methoxy-1-naphthyl)porphyrin (**8**) in 40% yield by usual Lindsey methods.[3] Deprotection of four methyl groups of **8** with BBr_3 led to satisfactory yield of porphyrin, which was separated by silica gel column chromatography to give the α,α,α,α-atropisomer **1**. Porphyrin **1** was characterized by ^1H NMR and HRMS.[4] Atropisomerization was not detected in boiling toluene over 2 h.[5]



a. $(CH_3)_3SiCN$, $TiCl_4$, in CH_2Cl_2, 0 °C ~ reflux, 7 h; 71%
b. 10% Pd-C, 250 °C, 6 h; 62%
c. 1.0 M DIBAL, in benzene, 0 °C ~ 45 °C, 5 h; > 60%
d. $BF_3\bullet OEt_2$, EtOH, in benzene, r.t. 28 h; 40%
e. BBr_3, in CH_2Cl_2, r.t. 11 h; quant.
f. column separation by Silica Gel, eluent: benzene/AcOEt (5:1 ~ 1:1), R_f 0.4 (benzene/AcOEt = 1)

Scheme 1.

Interaction between **1** and **2** was found by ^1H NMR, electronic absorption, and fluorescence spectroscopies as observed in the previous system for binding of **3** to **2**.[2a)] ^1H NMR spectrum of **1** in the presence of **2** indicates the typical downfield shift of hydrogen-bonding OH of **1** in $C_2D_2Cl_4$ at 25 °C.[6] The binding constants (K_a) determined from the non-linear curve fitting analysis and the thermodynamic parameters ($\Delta G°$, $\Delta H°$, and $\Delta S°$) for **1**-**2** and **3**-**2** are listed in Table 1. It is of particular interest to compare the affinities of quinone for **1** and **3**, since the face-to-face separation between porphyrin and quinone in **1**-**2** and **3**-**2** are estimated as ca. 6.0 Å and 3.5 Å, respectively, by use of CPK molecular models. The affinity between **1** and **2** is large different from that of the **3**-**2** pairing, although **1** also has four convergent hydroxyl groups like **3**. Negative enthalpy and entropy changes for complexation of **1**-**2** adduct are smaller than those of **3**-**2**. Particularly, small entropy loss of **1**-**2** suggests that the flexibility of naphthyl groups of **1** remains even upon complexation compared with that of **3**. Thus, it is likely that four convergent hydroxyl groups on naphthyl 7-OH groups in **1** are more movable compared with 1-OH groups in **3** due to longer distance from the rotational axis around the C(1-position of naphthalene ring)-C(*meso* position of porphyrin ring) bonds, whereas four functional groups in **3** are efficiently preorganized to bind ubiquinone analogues *via* multi hydrogen bonds.

Table 1. Binding constant (K_a) and Thermodynamic Parameters ($\Delta G°$, $\Delta H°$, and $\Delta S°$) for Binding of **1** and **3** to **2** in toluene[a]

Complex	K_a / M^{-1}[b]	$\Delta G°_{298}$ / kcal/mol	$\Delta H°$ / kcal/mol	$\Delta S°$ / cal/mol•K
1-2[c]	(7.9 ± 0.4) x 10^2	-4.0	-8.1 ± 0.7	-14.3 ± 2.2
3-2	(6.1 ± 1.1) x 10^5	-7.9	-22.7 ± 0.3	-49.2 ± 0.9

[a] These parameters were determined from van't Hoff plot by UV-vis titration studies; temperature range for 283 - 327 K. [b] at 298 K. [c] Binding constant is also determined as K_a = (5.8 ± 0.4) x 10^2 M^{-1} from Stern-Volmer plot as shown in Fig. 1.

Efficiency of the fluorescence quenching of **1** ($[\mathbf{1}]_{initial}$ = 4.56 x 10^{-5} M) with **2** has been examined in the range of 0 to 220 equivalent in toluene at 25 °C as shown in Figure 1. Stern-Volume plot of porphyrin fluorescence emission at 652 nm displays the linear relationship (r = 0.99) in the low concentration range of quinone ([**2**] < 7.0 x 10^{-3} M). This behavior is similar to that in **3-2** pairing, although the slope of linear plot in Figure 1 is different from that in previous **3-2** pairing.[7] The binding constant is also estimated from this slope as K_a = 5.8 x 10^2 M^{-1}, which is consistent with the binding constant determined by UV-vis titration.[8] This results indicated that the static quenching occurs and the electron transfer from photoexcited porphyrin to quinone proceeds fast via the face-to-face mode.[1c,9]

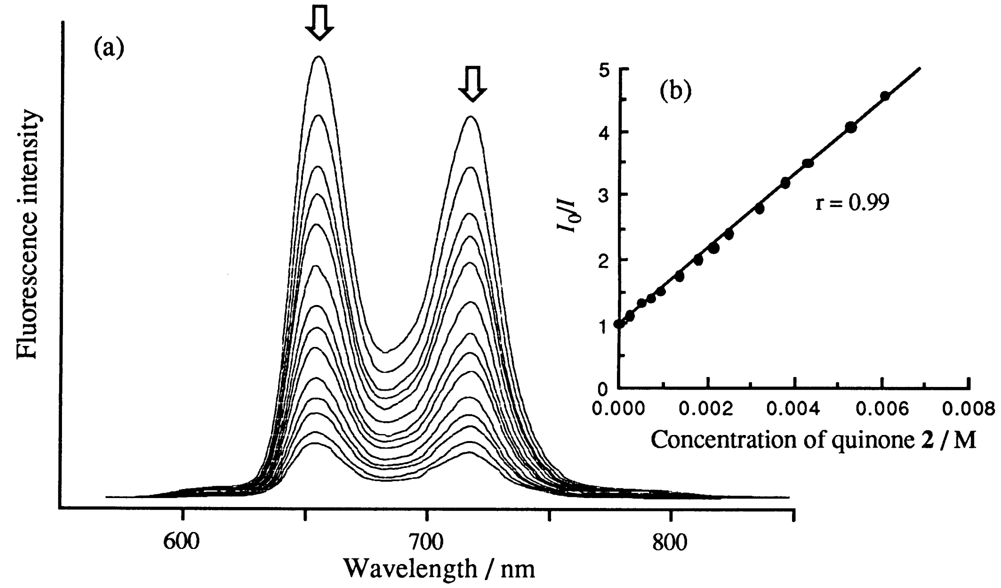


Fig. 1. (a) Fluorescence spectral changes upon addition of 220 equiv of **2** to **1** in toluene ($[\mathbf{1}]_{initial}$ = 4.56 x 10^{-5} M) at 25 °C: excitation at 510 nm. (b) Stern-Volmer plot for the fluorescence quenching of **1** with **2**: emission at 652 nm.

Further work on the structural properties of quinone-porphyrin adducts and the kinetics of electron transfer from excited porphyrin to quinone are in progress in our laboratory, and the details on these will appear in future publication.

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4) ^{1}H NMR spectrum of **1** (500 MHz, 1,1,2,2-tetrachloroethane-d$_2$) δ -2.347 (s, 2H), 4.4548 (s, 4H), 6.412 (d, J = 2.2 Hz, 4H), 7.051 (dd, J = 9.0, 2.3 Hz, 4H), 7.727 (dd, J = 8.2, 7.0 Hz, 4H), 8.010 (d, J = 9.2 Hz, 4H), 8.197 (d, J = 8.3 Hz, 4H), 8.232 (d, J = 6.7, 4H), 8.519 (s, 8H). high-resolution mass spectrum (FAB, *m*-nitrobenzyl alcohol) *m/z* 878. 2910 [M$^+$; calcd for $C_{60}H_{38}N_4O_4$: 878.2893]. UV-vis (toluene) λ_{max} 426.4 (ε 3.06 x 10^5), 515.0 (2.14 x 10^4), 548.0 (4.40 x 10^3), 589.6 (6.20 x 10^3), 646.1 (1.70 x 10^3) nm.

5) We have reported the atropisomerization of *meso*-tetra(2-hydroxy-4-nonylphenyl)porphyrin. The rate constant of rotation around one carbon-carbon bond of porphyrin-phenyl ring was determined to be k = 1.7 x 10^{-5} s^{-1} at 25 °C in CHCl$_3$,[2b,10] whereas no atropisomerization of **3** was also detected in boiling toluene over 2 h.[2a]

6) The downfield shift $\Delta\delta$, δ(**1** + **2**) - δ(**1**), is observed as follows: $\Delta\delta$ = +0.185 ppm ([**1**] = [**2**] = 1.1 mM), $\Delta\delta$ = +1.046 ppm ([**1**] = 1.1 mM, [**2**] = 21.2 mM).

7) The slopes of Stern Volmer plots in **1**-**2** and **3**-**2** pairings are calculated to be 5.8 x 10^2 and 1.4 x 10^4, respectively.

8) When both static and dynamic quenching take place, the Stern-Volmer relationship can be expressed by following equation;

$$I_0/I_{obsd} = (1 + K'[Q])(1 + k_q\tau_0[Q])$$

where $K' = (\varepsilon_{PQ}/\varepsilon_Q)K$, k_q is the quenching rate constant of dynamic process and τ_0 is the fluorescence life time in the absence of a quencher.[11] In the presence case, however, dynamic process term, $k_q\tau_0[Q]$, is negligible at the low concentration range of quinone; $K' \approx K$, $k_q \approx 10^9$ M^{-1}sec^{-1} and τ_0 = 11.9 ns.

9) Photoinduced electron transfer from porphyrin to covalently linked quinone via face-to-face mode. For example: K. N. Ganesh and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, **1980**, 1129; M. P. Irvine, R. J. Harrison, G. S. Beddard, P. Leighton, and J. K. M. Sanders, *Chem. Phys.*, **104**, 315 (1986); J. S. Lindsey and D. C. Mauzerall, *J. Am. Chem. Soc.*, **104**, 4498 (1982); J. K. Delaney, D. C. Mauzerall, and J. S. Lindsey, *ibid.*, **112**, 957 (1990); D. Mauzerall, J. Weiser, and H. Staab, *Tetrahedron*, 45, 4807 (1989); H. A. Staab, *Chem. Ber.*, **126**, 811 (1993).

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