Water-soluble Porphyrin Easily Derived from Tetraphenylporphyrin: Alkyloxo(methoxo)porphyrinatoantimony Bromides

Jin Matsumoto,* Tsutomu Shiragami, and Masahide Yasuda
Department of Applied Chemistry, Faculty of Engineering, University of Miyazaki,
Gakuen-Kibanadai, Miyazaki 889-2192

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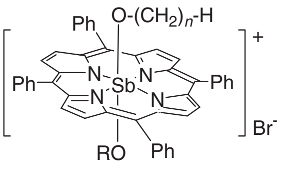
In order to develop water-soluble porphyrins, alkyloxo(methoxo)porphyrinatoantimony bromides (alkyl = decyl, dodecyl, and octadecyl) were prepared. These complexes have more than 200 mg/100 g of solubility in aqueous solution. From the analysis of absorption spectra and surface tension, it was elucidated that the porphyrin complexes are present as aggregates in aqueous solution.

There has been a great amount of interest in water-soluble chromophores utilized as fluorescent probes which are selectively incorporated into specific microorganisms sites in connection with photodynamic therapy.[1] Porphyrins and metalloporphyrins are typical fluorescent chromophores with a variety of functions. However, porphyrins are, in general, poorly soluble even in organic solvents, because of the formation of aggregates through π–π stacking (J- and H-aggregations) between porphyrin rings.[2] So far, the synthesis of water-soluble porphyrins has been achieved through the introduction of ionic groups such as pyridinium,[3] sulfonate,[4] and phosphonium[5] in porphyrin rings. Tetraphenylporphyrin (TPP) is a typical and commercially available porphyrin and can easily be converted into tetraphenylporphyrinatoantimony(V) complexes (SbTPP). SbTPP is relatively soluble in relatively polar solvents such as CH_2Cl_2, MeCN, and MeOH due to its cationic character. However, solubility is still low in water. Here, we report on the synthesis of water-soluble SbTPP through introduction of long alkyl chains as an axial ligand (Scheme 1).

According to a previously reported method,[6] the preparations of alkyloxo(hydroxo)tetraphenylporphyrinatoantimony bromides **1** and alkyloxo(methoxo)tetraphenylporphyrinatoantimony bromides **2** were started from the partial solvolysis of Br ligand on dibromotetraphenylporphyrinatoantimony bromide with H_2O and MeOH, respectively. This was followed by ligand exchange of Br with alcohols in the presence of pyridine.[7] **1** or **2** (5 mg) was suspended in pure water (1 cm^3) and was left to stand for 3 days. The supernatant solution was moved to another vessel and was diluted with MeOH to measure the absorption spectra of the solution. Solubility was defined as the saturated concentration (C_s) which was calculated using absorbance and molar absorptivity ($\mathcal{E}$) with a Soret band. The values of C_s are summarized in Table 1.



1a; R = H, $n = 0$ **2a**; R = Me, $n = 1$
1b; R = H, $n = 1$ **2b**; R = Me, $n = 6$
1c; R = H, $n = 6$ **2c**; R = Me, $n = 10$
1d; R = H, $n = 10$ **2d**; R = Me, $n = 12$
1e; R = H, $n = 18$ **2e**; R = Me, $n = 18$

Scheme 1.

Table 1. The solubilities of **1a**–**1e** and **2a**–**2e** in water

	n[a]	MW[b]	Solubility (C_s)[c]	$\mathcal{E}/10^5$[d]
1a	0	848	6.9 (0.08)	5.62
1b	1	862	8.6 (0.10)	5.01
1c	6	932	7.1 (0.08)	5.37
1d	10	988	98.6 (1.00)	5.13
1e	18	1100	1.2 (0.01)	4.90
2a	1	876	11.3 (0.13)	5.01
2b	6	946	103 (1.09)	3.98
2c	10	1002	210 (2.10)	4.61
2d	12	1030	228 (2.21)	3.74
2e	18	1114	213 (1.92)	5.12

[a]Number of methylene units on an axial ligand. [b]Molecular weight. [c]Saturated concentration in mg/100 g of water. The values in parenthesis are the saturated concentration in mM. [d]Molar absorptivity of Soret band in $M^{-1}\cdot cm^{-1}$ ($M = mol\cdot dm^{-3}$).

Di(hydroxo)tetraphenylporphyrinatoantimony bromide (**1a**) dissolve well in organic solvents with the exception of nonpolar solvents (e.g. hexane and toluene). However, the C_s of **1a** in water is low: C_s (**1a**) $= 0.08$ mM, even though **1a** is cationic and contained hydrophilic hydroxy groups. Moreover, the C_s's of **1b**–**1e** are lower than 0.1 mM with the exception of **1d**. The presence of axial HO ligand lowers the C_s, probably because of an interaction between the porphyrin rings through axial HO ligands. On the other hand, the C_s's of **2b**–**2e** are more than 10 times larger when compared with **1a**, as shown in Figure 1.

Usually, the aggregation of porphyrins results in a shift of the maximum absorption wavelength and/or broadening of the

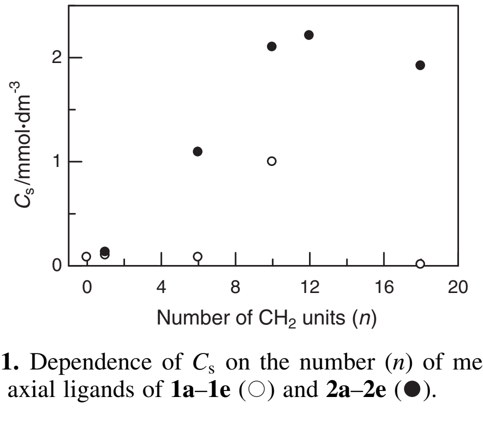


Figure 1. Dependence of C_s on the number (n) of methylene units on axial ligands of **1a**–**1e** (○) and **2a**–**2e** (●).

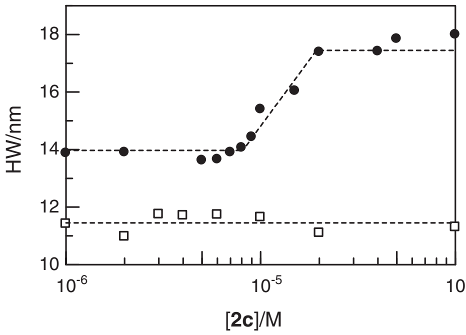


Figure 2. Dependence of HW on [**2c**] in water (●) and in MeOH (□).

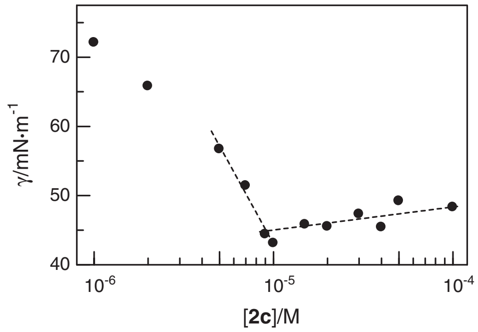


Figure 3. Plots of surface tension (γ) against [**2c**] in aqueous solution.

band.[3,8] In the case of **2b**–**2e**, the broadening takes place but the maximum absorption wavelength does not shift. Figure 2 shows an example of the dependence of the peak-width at the half height (HW) of the Soret band on the concentration of **2c** ([**2c**]).[9] The HW of **2c** in water remains constant at 14 nm when [**2c**] $< 8 \times 10^{-6}$ M. With an increase of [**2c**] up to 2.0×10^{-5} M, HW increases from 14 to 17.4 nm. HW remains constant at 17.4 nm when [**2c**] $> 2.0 \times 10^{-5}$ M. On the other hand, the HW of **2c** in MeOH remains constant at 11.7 nm irrespective of the increase of [**2c**], suggesting that **2c** does not aggregate in MeOH. Therefore, it is suggested that **2c** behaves as aggregates in aqueous solution.

The surface tensions (γ) were measured for **2c** in aqueous solution (Figure 3).[10] Upon the increase of [**2c**], γ decreases until [**2c**] reaches 1×10^{-5} M and remains constant when [**2c**] $> 1 \times 10^{-5}$ M. It is well known that the breakdown point corresponds to the critical micelle concentration of various surfactants.[11] Therefore, the results of HW and γ shows that **2c** affords aggregates of a uniform size and shape in aqueous solution at concentrations above 1×10^{-5} M.

High C_s's are achieved in **2b**–**2e** with axial long alkyloxo ligands, but C_s's of **2a** and **1** are extremely lower than that of **2b**–**2e**. Therefore, the presence of axial long alkyloxo ligands as well as the absence of an axial HO ligand are requisite for higher C_s in water. **2b**–**2e** prefer the micelle-like structure through the hydrophobic interaction of long alkyl chains and an edge-to-edge interaction of porphyrin rings (Figure 4A). This is supported by ^{1}H NMR spectra of **2c** (1 mM) in D_2O.[9] The alkyloxo ligand is strongly affected by the neighboring porphyrins, resulting in the higher field shifts of methylene protons compared with those in CD_3OD. Conversely, **1** forms a face-to-face dimer structure rather than a micelle-like structure, presumably due to the formation of hydrogen bonds formed between the HO ligands or OH–π interactions between the HO ligands and the porphyrin rings (Figure 4B). In the case of **1d**, hydrophobic van der Waals interaction predominantly stabilizes the aggregates, resulting in high C_s.

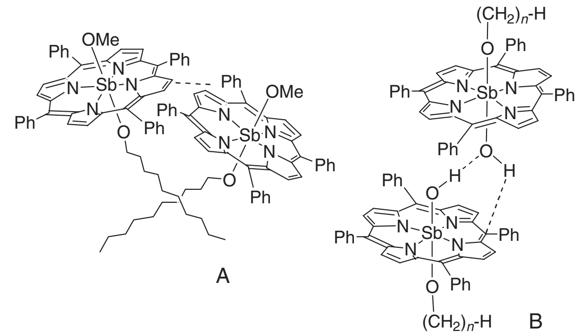


Figure 4. (A) Edge-to-edge aggregation and (B) face-to-face dimer.

In conclusion, the water-soluble porphyrin complexes **2b**–**2e**[12] have been conveniently synthesized from TPP. Moreover, C_s was controlled by the number of methylene units (n) from 6 to 12 in the alkyl chain.

References and Notes

1 R. P. Haugland, in *Handbook of Fluorescent Probes and Research Products*, 9th ed., ed. by J. Gregory, Molecular Probes, Eugene, OR, **2002**.

2 a) P. Hambright, in *The Porphyrin Handbook*, ed. by K. M. Kadish, K. M. Smith, R. Guilard, Academic Press, New York, **2000**, Vol. 3, Chap. 18, pp. 129–210. b) S. Okada, H. Segawa, *J. Am. Chem. Soc.* **2003**, *125*, 2792.

3 K. Kano, M. Takei, S. Hashimoto, *J. Phys. Chem.* **1990**, *94*, 2181.

4 X. Zhang, K. Sasaki, Y. Kuroda, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 536.

5 R.-H. Jin, S. Aoki, K. Shima, *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 3945.

6 T. Shiragami, J. Matsumoto, H. Inoue, M. Yasuda, *J. Photochem. Photobiol., C* **2005**, *6*, 227.

7 A typical example was the preparation of **2c** that was performed by the reaction of bromo(methoxo)tetraphenylporphyrinatoantimony bromide (40 mg) with decanol (50 cm^3) in MeCN–pyridine (40:1, 41 cm^3) at 65 °C. After evaporation, **2c** was isolated by column chromatography on SiO_2. Yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$): δ −2.57 (t, $J = 6.1$ Hz, 2H), −2.19 (s, 3H), −2.00–−1.93 (m, 2H), −1.63 (quint, $J = 7.6$ Hz, 2H), −0.34 (quint, $J = 7.6$ Hz, 2H), 0.33 (quint, $J = 7.6$ Hz, 2H), 0.68 (quint, $J = 7.6$ Hz, 2H), 0.81 (t, $J = 7.3$ Hz, 3H), 0.89–0.96 (m, 2H), 1.00–1.07 (m, 2H), 1.16 (sextet, $J = 7.3$ Hz, 2H), 7.92–8.02 (m, 12H), 8.29 (d, $J = 6.8$ Hz, 4H), 8.36 (d, $J = 6.8$ Hz, 4H), 9.56 (s, 8H); ^{13}C NMR: δ 14.03, 22.54, 23.17, 27.67, 28.25, 28.82, 29.02, 29.03, 31.68, 45.86, 58.02, 122.96, 127.95, 128.11, 130.03, 133.87, 134.73, 134.83, 138.12, 146.01; UV–vis (MeOH) λ_{max}/nm ($\varepsilon/10^4$ M^{-1}·cm^{-1}) 419 (46.1), 551 (1.89), 590 (1.09).

8 K. Kano, K. Fukuda, H. Wakami, R. Nishiyabu, R. F. Pasternack, *J. Am. Chem. Soc.* **2000**, *122*, 7494.

9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/.

10 The surface tensions were measured on a Kyowa Kaimen Kagaku CBVP-Z at 25 °C.

11 M. J. Rosen, *Surfactants and Interfacial Phenomena*, 2nd ed., Wiley, New York, **1989**.

12 **2b**–**2e** are also soluble in organic solvents (CH_2Cl_2, MeOH, and MeCN).