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Factors Influencing Self-Aggregation Tendencies of Cationic Porphyrins in Aqueous Solution

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Abstract: The self-aggregation of cationic porphyrins in aqueous solution has been studied by means of absorption, ^{1}H NMR, and resonance light scattering spectroscopy. The aim of the present study is clarification of the factors which most influence porphyrin self-aggregation in water. Cationic 5,10,15,20-tetrasubstituted porphyrins [PorSub$_4$: PC3Py (Sub = $-(CH_2)_3$-Py$^+$Cl$^-$), PC5Py (Sub = $-(CH_2)_5$-Py$^+$Cl$^-$), PC7Py (Sub = $-(CH_2)_7$-Py$^+$Cl$^-$), TPPOC2Py (Sub = p-C$_6$H$_4$-O(CH$_2$)$_2$-Py$^+$Br$^-$), and TPPOC3Py (Sub = p-C$_6$H$_4$-O(CH$_2$)$_3$-Py$^+$Br$^-$), where Py$^+$ = N-alkylpyridinium] were used. PC3Py forms a dimer in aqueous solution with or without an added inorganic salt. In the presence of KNO$_3$, dimer formation of PC3Py is dominated by a large and negative enthalpy change. The entropy change for aggregation increases with increasing concentrations of added KNO$_3$, while enthalpy changes are almost constant. The thermodynamic parameters suggest that dimer formation of PC3Py is the result of a large enthalpic gain due to extended van der Waals interactions, in cooperation with enhanced hydrophobic interactions. Electrostatic repulsion suppresses further association. However, other cationic porphyrins studied show evidence of higher self-aggregate formation. X-ray crystallographic studies of PC5Cl (Sub = $-(CH_2)_5$-Cl), a precursor of PC5Py, show the formation of a slipped face-to-face dimer as the basic unit for forming a crystal lattice, while that of TPP (Sub = $-C_6H_5$) indicates the absence of face-to-face stacking interaction in the crystals. Judging from these results, it is assumed that the slipped face-to-face dimer is the unit of the higher self-aggregates of PC5Py or PC7Py in water with or without KNO$_3$. Elongated alkyl chains of PC5Py and PC7Py may be responsible by enhancing hydrophobic interaction of the porphyrins studied. TPPOC2Py alone forms a *J*-aggregate, characterized by a sharp and red-shifted Soret band and a strongly enhanced resonance light scattering signal. Higher self-aggregates having face-to-face arrangement are formed with TPPOC3Py; these provide no enhanced RLS feature. The present study reveals the dependence of aggregate formation of water-soluble porphyrins on the peripheral meso-substituents.

Introduction

Water-soluble porphyrins have been shown to form a variety of molecular complexes in aqueous solution through noncovalent interactions.[1] It is well-known that anionic porphyrins such as TPPS$_3$, TPPS$_4$, and TCPP (Figure 1) dimerize in neutral aqueous media in the absence and the presence of inorganic salts.[2] In addition, TPPS$_3$ and TPPS$_4$ have been shown to form extended *J*-aggregates under acidic conditions[2,3] or in the presence of cationic polymers such as protonated polypeptides.[4] On the other hand, a tetracationic porphyrin, TMPyP, exists as the monomer

in water even in the presence of concentrated inorganic salts.[2a,5] It had been proposed that the positive charges at the periphery of TMPyP are delocalized over the porphyrin ring resulting in electrostatic repulsive forces, thereby preventing dimer formation.[6] By way of contrast, other tetracationic porphyrins such as TAPP and TOPP aggregate spontaneously in aqueous solution in both the absence and the presence of NaCl.[7] Moreover, two dicationic porphyrin derivatives having *N*-methylpyridinium moieties at their peripheral positions (5,10-DiMPyP and 5,15-DiMPyP) are known to form self-aggregates.[7,8] The latter porphyrin, in particular, readily forms large aggregate as-

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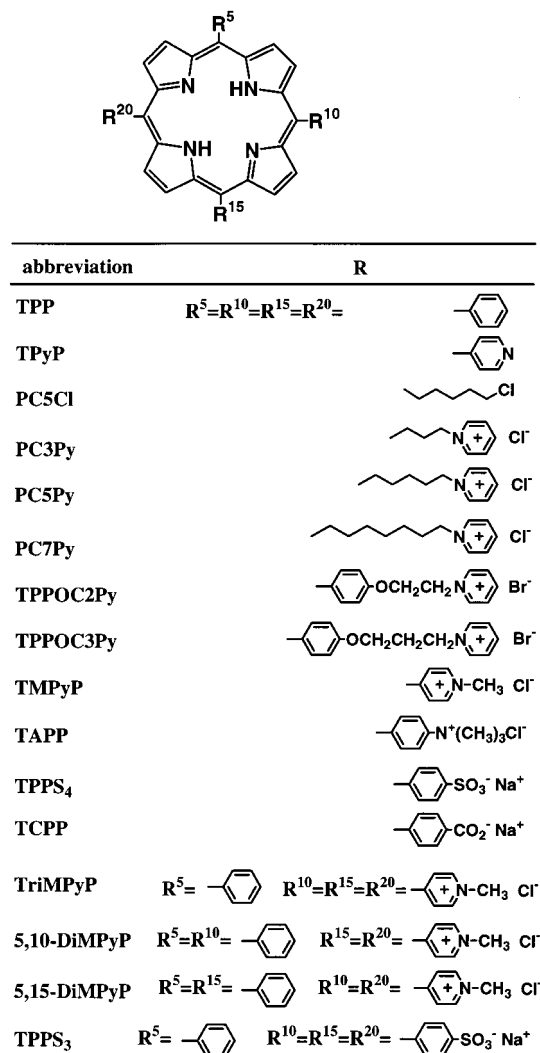(7) Kano, K.; Takei, M.; Hashimoto, S. *J. Phys. Chem.* **1990,** *94,* 2181−2187.

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Figure 1. Porphyrin structures and abbreviations.

Table 1. The pK_a Values of Water-Soluble Porphyrins at 25 °C

porphyrin	pK_a	ref
TPPS$_3$	~4.8	2a
TPPS$_4$	4.8	16
TMPyP	0.62, 1.51	2a
TMPyP	1.4	13b
TriMPyP	1.9	6
5,10-DiMPyP	2.9	6
5,15-DiMPyP	2.8	6
TAPP	3.0	6
PC3Py	~2.5	this work
PC5Py	3.6	this work
PC7Py	4.0	this work
TPPOC2Py	4.8	this work
TPPOC3Py	4.7	this work

interactions are generally regarded as due to attractive $\pi-\pi$ interactions. However, recent reports by Sanders and co-workers[10,11] have suggested that $\pi-\pi$ interactions are always repulsive, unlike $\sigma-\pi$ interactions which are attractive.[11] Theoretical calculations support the importance of $\sigma-\pi$ interactions for molecular associations of π-conjugated systems.[12] The present study is intended, in part, to address this crucial subject in molecular complex chemistry.

Results and Discussion

pK_a Values of the Porphyrins. Values of pK_a can be used as a measure to evaluate effects of peripheral groups at meso positions on electron density on a porphyrin ring. The pK_a values of PCnPy and TPPOCnPy were measured via absorption spectroscopy. As an example, the absorbance of the Soret band of PC3Py (5×10^{-6} M) at 412 nm decreases with decreasing pH, with the concomitant appearance of a new band at 417 nm. An isosbestic point is observed at 414 nm in the Soret band region. We were unable to distinguish the two acid−base equilibria of the porphyrin, i.e., the formation of the monoacid and diacid forms, and therefore we determined the apparent overall pK_a values for the two-proton equilibrium. The results are summarized in Table 1 together with the reported pK_a values of several other representative water-soluble porphyrins.[2,7,13] The largest pK_a values were determined to be ca. 4.8 for TPPS$_3$, TPPS$_4$, TPPOC2Py, and TPPOC3Py. The PC3Py derivative, which has a spacer of a trimethylene chain between the porphyrin ring and the pyridinium moiety, exhibits a smaller pK_a value (~2.5). Significantly strong inductive effects through σ-bonds seem to reduce the basicity of this porphyrin. Elongation of the alkyl chain spacer increases the basicity of the porphyrin (see the pK_a values of PC5Py and PC7Py).

Self-Aggregation of PCnPy. Deviations from the Beer−Lambert law have been previously ascribed to self-aggregation of water-soluble porphyrins in water.[2a] Such deviation of the absorbances at 521 nm occurred at [PC3Py or PC7Py] $> 2 \times 10^{-4}$ mol dm^{-3} and at [PC5Py] $> 5 \times 10^{-4}$ mol dm^{-3} at pH 9.5 (NaOH) without added electrolyte. Figure 2 shows the

semblies. Therefore, although, as previously suggested,[6] delocalization of positive charges onto the porphyrin ring might affect self-aggregation of certain cationic porphyrins, the effects of the cationic peripheral groups should be investigated more extensively.

The present study deals with the self-aggregation of two classes of pyridyl porphyrins, PCnPy and TPPOCnPy, in aqueous media (Figure 1). The pyridinium moieties of these cationic porphyrins are separated from the porphyrin ring by methylene chain spacers, preventing the delocalization of positive charges onto the ring system by direct coupling. The positive charges of these cationic porphyrins can impact the charge distribution of the porphyrin ring through inductive effects only. Therefore, these substances permit a study of the self-aggregation of homologous cationic water-soluble porphyrins without having to consider electrostatic repulsion between the polarized porphyrin ring systems. The aim of the present study is to provide a clarification of the factors involved in the self-aggregation in aqueous solution of the 22-π conjugated system. Since the porphyrin ring is highly polarizable (calculated α is 39.8 Å^3 for the nonsubstituted porphyrin molecule),[9] strong van der Waals interactions are expected between rings. Such

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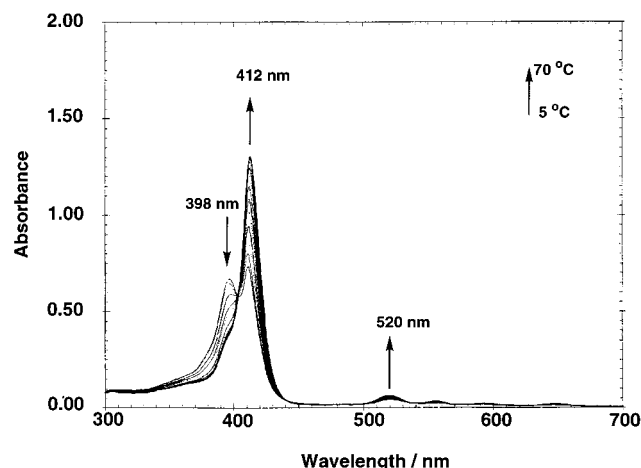
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Figure 2. Absorption spectral changes of PC3Py (5×10^{-4} mol dm^{-3}) in 5×10^{-3} mol dm^{-3} carbonate buffer at pH 9.5 as a function of temperature. The measurements were carried out every 5 °C from 5 to 70 °C. A quartz cell with a 0.1-mm optical length was used.

absorption spectra of 5×10^{-4} mol dm^{-3} PC3Py in water at pH 9.5 (5×10^{-3} mol dm^{-3} carbonate buffer) at various temperatures. Under these conditions, PC3Py forms a self-aggregate at room temperature. The absorption maximum at 398 nm at low temperature shifts to longer wavelength ($\lambda_{max} = 412$ nm) upon increasing the temperature, with an isosbestic point observed at 404 nm in the Soret band region. It is known that the Soret bands of face-to-face dimers as well as higher *H*-type aggregates and of higher edge-to-edge aggregates (*J*-type) appear at shorter and longer wavelengths, respectively, compared to the Soret bands of corresponding porphyrin monomers.[2a,7,8a,14] The *J*-aggregate generally displays an intense and narrow absorption band.[2a,8a,14] On the other hand, the higher self-aggregates without *J*-type arrangement exhibit a broad band near the wavelength region of the Soret band of the corresponding monomer.[7] The change in the UV−vis spectrum of PC3Py indicates the dissociation of the face-to-face dimer of this porphyrin to the monomer upon raising the temperature. Addition of KNO$_3$ to a solution of PC3Py (5×10^{-6} mol dm^{-3}) promotes the formation of the dimer at the expense of the monomer, as expected from Debye−Hückel considerations (Figure 3). Under the conditions used, PC3Py exists as the monomer in the absence of added electrolyte.

Figure 4 shows the ^{1}H NMR spectra of PC3Py in D$_2$O at pD 9.5 (Na$_2$CO$_3$) as a function of the porphyrin concentration. At [PC3Py] = 5×10^{-4} mol dm^{-3}, all proton signals except those for 2-Py are broad because of the monomer−dimer equilibrium. Increasing the concentration of the porphyrin causes the upfield shifts of the β-pyrrol protons and the methylene protons at the 1-, 2-, and 3-positions. On the contrary, the signals due to the ring protons of the pyridinium moieties shift to lower magnetic fields with increase of porphyrin concentration. The changes in the chemical shifts are explained by the formation of a partially sideslipped face-to-face dimer. The temperature-dependent ^{1}H NMR spectral change also supports the dimer formation at low temperature (see Supporting Information).

Absorption spectral changes were measured with 5×10^{-4} mol dm^{-3} PC5Py in carbonate buffer (5×10^{-3} mol dm^{-3}, pH 9.5) without inorganic salt as a function of temperature. As the temperature is raised from 5 to 70 °C, the intensity of the Soret
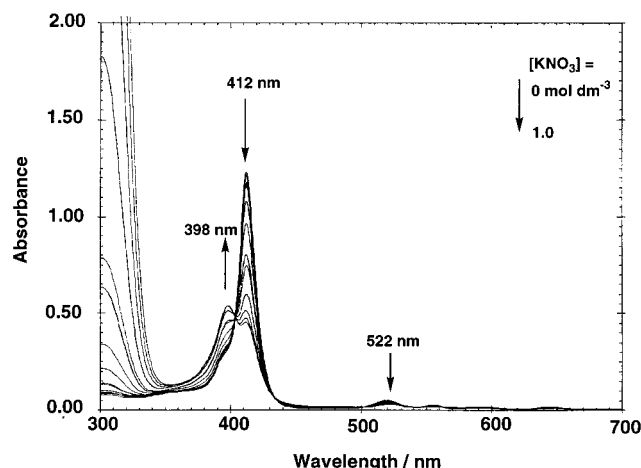
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Figure 3. Absorption spectral changes of PC3Py (5×10^{-6} mol dm^{-3}) in 5×10^{-3} mol dm^{-3} carbonate buffer at pH 9.5 upon addition of KNO$_3$ at 25 °C. The concentrations ($\times 10^{-2}$ mol dm^{-3}) of KNO$_3$ are 0.1, 0.25, 0.50, 0.75, 1.0, 2.5, 5.0, 7.5, 10, 25, 50, 75, and 100. A quartz cell with a 10-mm optical length was used.
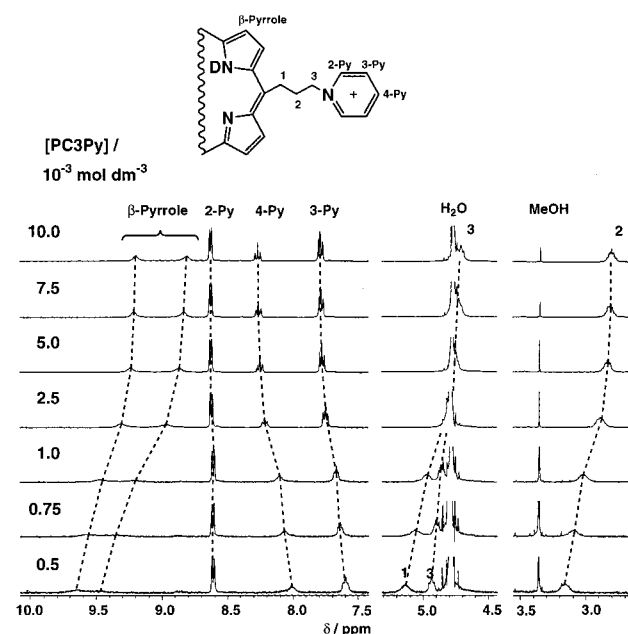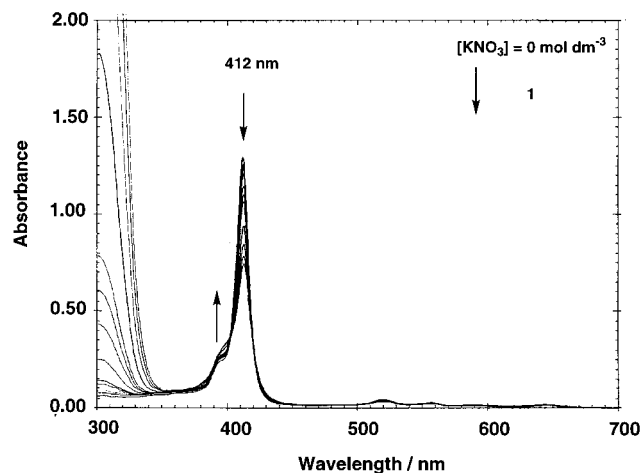

Figure 4. ^{1}H NMR spectral changes of PC3Py in D$_2$O at pD 9.5 and 25 °C as a function of the porphyrin concentration.

band at 412 nm is slightly increased while the shoulder band at ca. 395 nm is decreased (Supporting Information). Since most of the PC5Py molecules exist as the monomer at this concentration, the temperature-dependent spectral changes are not remarkable. The porphyrin concentration of 5×10^{-4} mol dm^{-3} is at the limit that can be considered by absorption measurements using a quartz cell having a 0.1 mm optical length. The addition of KNO$_3$ to an aqueous solution of PC5Py (5×10^{-6} mol dm^{-3}) in carbonate buffer causes a reduction in the intensity of the Soret band at 412 nm and a slight increase in the intensity of the shoulder band at ca. 395 nm (Figure 5). However, it is not straightforward to conclude that PC5Py forms a dimer similar to the one observed for PC3Py, because no clear band appears at wavelengths shorter than λ_{max} of the Soret band of the monomer. To determine the structure of the self-aggregate of PC5Py, the ^{1}H NMR spectra were measured as a function of the porphyrin concentration (Figure 6). At [PC5Py] = 5×10^{-4} mol dm^{-3}, two broad signals of the β-pyrrole protons were observed at 9.63 and 9.76 ppm. The two signals due to pyrrole

Figure 5. Absorption spectral changes of PC5Py (5×10^{-6} mol dm^{-3}) in 5×10^{-3} mol dm^{-3} carbonate buffer at pH 9.5 upon addition of KNO$_3$ at 25 °C. The concentrations ($\times 10^{-2}$ mol dm^{-3}) of KNO$_3$ are 0.1, 0.25, 0.50, 0.75, 1.0, 2.5, 5.0, 7.5, 10, 25, 50, 75, and 100. A quartz cell with a 10-mm optical length was used.
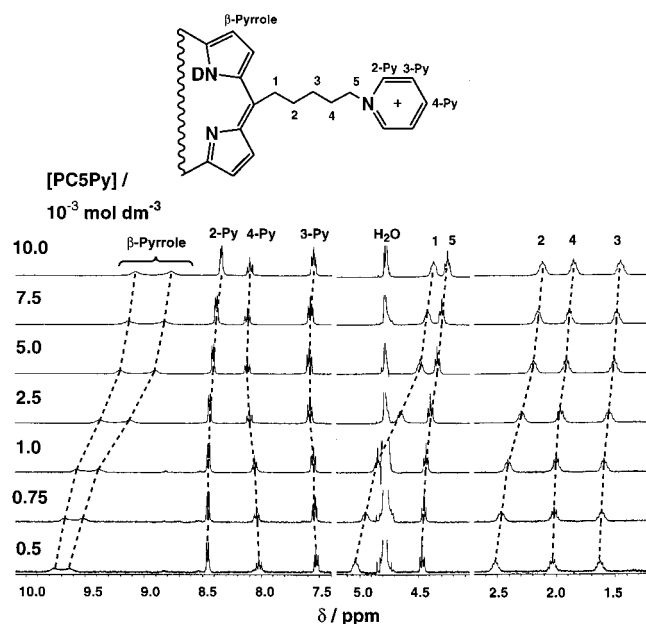

Figure 6. ^{1}H NMR spectral changes of PC5Py in D$_2$O at pD 9.5 and 25 °C as a function of the porphyrin concentration.

are ascribed to a slow N−D tautomerism of this porphyrin.[6] These signals markedly shift to higher magnetic fields with increasing porphyrin concentration. Another striking shift was measured for the methylene protons at the α-position of the porphyrin ring. The upfield shifts of the methylene protons at the linkages and the downfield shifts of the 3-Py and 4-Py protons clearly indicate the formation of face-to-face stacked self-aggregate. The signals of the 3-Py and 4-Py protons shift once to lower magnetic fields and then to higher magnetic fields with increasing porphyrin concentration. These results suggest more than one aggregation step for PC5Py. The slipped face-to-face dimer is quite likely the unit involved in the formation of higher aggregates of PC5Py (vide infra). The dissociation rate of the self-aggregate seems to be faster than the exchange rates of the nuclear spins (the NMR time scale) because all signals remain sharp at all porphyrin concentrations.

Only slight increases in the intensity of the absorption band at 413 nm were observed with a solution of 5×10^{-4} mol dm^{-3} PC7Py in carbonate buffer (5×10^{-3} mol dm^{-3}, pH 9.5) without
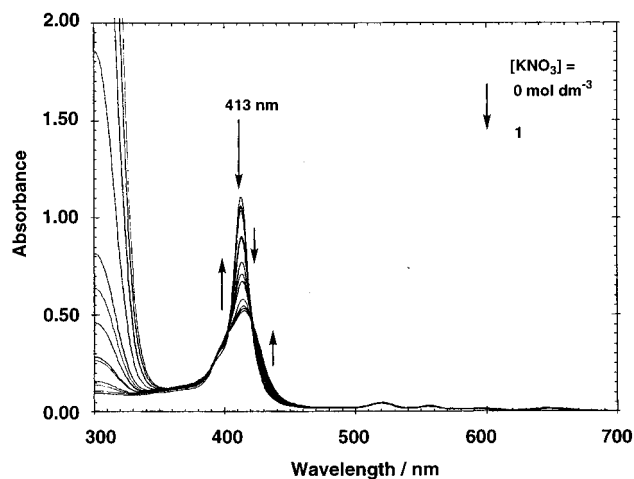

Figure 7. Absorption spectral changes of PC7Py (5×10^{-6} mol dm^{-3}) in 5×10^{-3} mol dm^{-3} carbonate buffer at pH 9.5 upon addition of KNO$_3$ at 25 °C. The concentration ($\times 10^{-2}$ mol dm^{-3}) of KNO$_3$ are 0.1, 0.25, 0.50, 0.75, 1.0, 2.5, 5.0, 7.5, 10, 25, 50, 75, and 100. A quartz cell with a 10-mm optical length was used.

inorganic salt when the temperature was elevated from 5 to 70 °C. The effects of added KNO$_3$ on the absorption spectrum of PC7Py (5×10^{-6} mol dm^{-3}) in carbonate buffer are shown in Figure 7. Higher aggregates are suggested to be formed in concentrated KNO$_3$ solution, because no distinct absorption band due to the dimer was observed, while the absorbance of the Soret band of the PC7Py monomer monotonically decreases upon addition of KNO$_3$. The aggregates formed in 1.0 mol dm^{-3} aqueous KNO$_3$ solution did not dissociate into monomers when the temperature was raised from 5 to 70 °C. All proton signals of PC7Py were broad in the concentration range of $(0.5-10) \times 10^{-3}$ mol dm^{-3} (Supporting Information). The characteristic of this porphyrin in the ^{1}H NMR spectra is that all proton signals involving those of the pyridinium ring protons shift to higher magnetic fields upon increasing the porphyrin concentration. It is assumed, therefore, that the regularity in the orientation of the PC7Py molecules in the self-aggregates is poorer than that of the PC5Py molecules.

Self-Aggregation of TPPOCnPy. In the cases of TPPOC2Py and TPPOC3Py, the deviation of the absorbances at 589 nm from the Beer−Lambert linear relationship occurred above 1×10^{-4} mol dm^{-3} in water at pH 7.0. These cationic porphyrins appear to exist as self-aggregates at [TPPOCnPy] > 1×10^{-4} mol dm^{-3}. To verify the formation of the self-aggregate of TPPOC2Py, the ^{1}H NMR spectra were measured as a function of the porphyrin concentration. The results are exhibited in Figure 8. At 2×10^{-5} mol dm^{-3}, sharp NMR signals were observed, indicating that TPPOC2Py exists as the monomer at this concentration. Above 1×10^{-4} mol dm^{-3}, each signal becomes broadened due to self-aggregation in D$_2$O. Interestingly, however, each proton signal shifts slightly with increasing porphyrin concentration. If the slipped face-to-face porphyrin dimer is the unit of the self-aggregates, each signal would be expected to be affected by the ring current effects due to the porphyrin ring in a manner similar to that observed for the PCnPy porphyrins. Figure 9 shows the ^{1}H NMR spectral change of TPPOC2Py (5×10^{-4} mol dm^{-3}) as a function of temperature. At 25 °C, all proton signals are broad, indicating the formation of a self-aggregate whose dissociation rate is comparable to the NMR time scale. The spectrum at 75 °C is similar to that of the TPPOC2Py monomer. With a decrease in the temperature from 75 °C, each proton signal shifts once to higher magnetic field and shifts again to lower magnetic field,
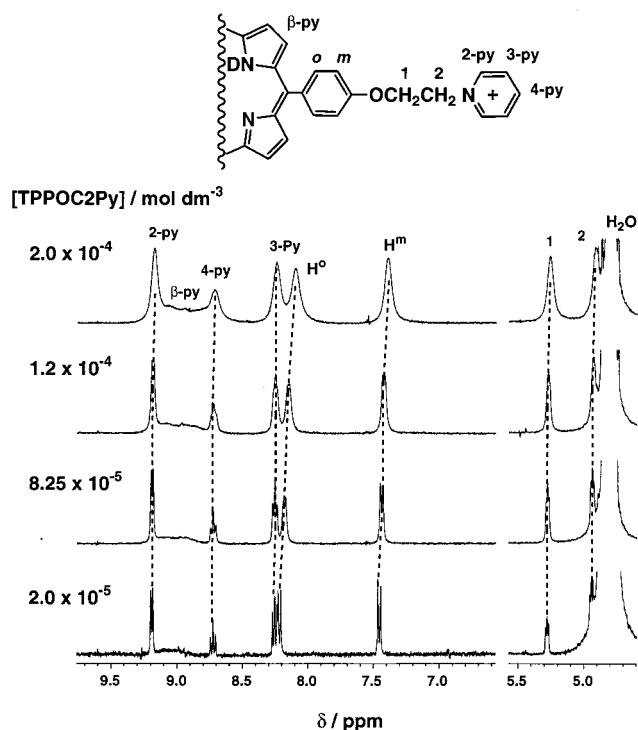
[TPPOC2Py] / mol dm⁻³

Figure 8. ¹H NMR spectral changes of TPPOC2Py in D₂O containing 2% (v/v) DMSO at pD 7.0 and 25 °C as a function of the porphyrin concentration.
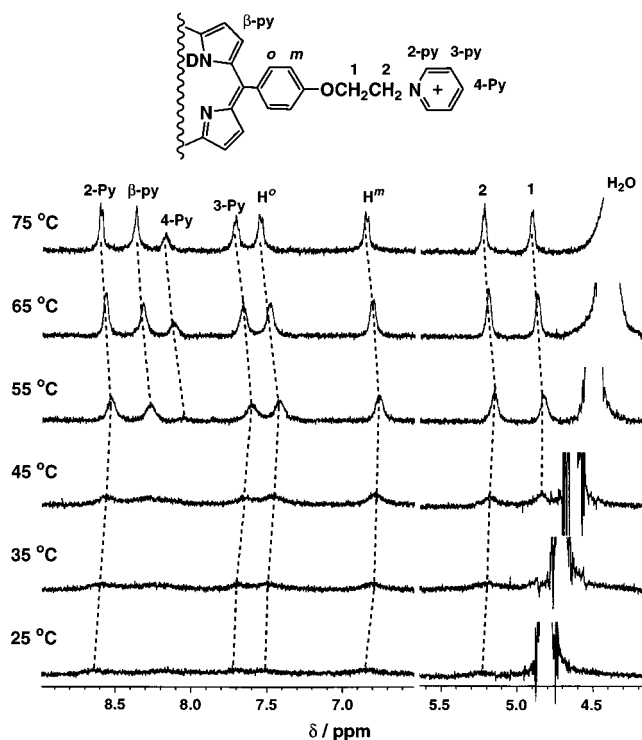

Figure 9. ¹H NMR spectral changes of TPPOC2Py (5×10^{-4} mol dm⁻³) in D₂O containing 2% (v/v) DMSO at pD 7.0 as a function of temperature.

indicating more than one self-aggregation step. The shifts of all proton signals, however, are relatively small. Such NMR spectral behavior of TPPOC2Py cannot be explained by self-aggregation involving the unit of the slipped face-to-face dimer.

The TPPOC2Py porphyrin shows a new, sharp absorption band ($\lambda_{max} = 449$ nm) at a wavelength considerably longer than that of the Soret band of the monomer ($\lambda_{max} = 417$ nm) when
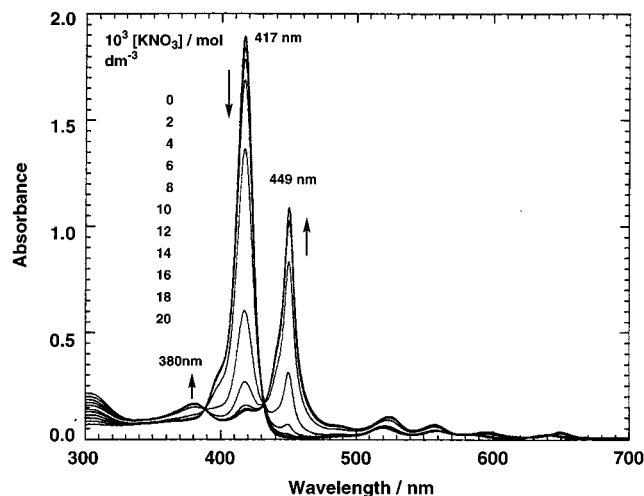

Figure 10. Absorption spectral changes of TPPOC2Py (5×10^{-6} mol dm⁻³) in water at pH 7.0 upon addition of KNO₃ at 25 °C. A quartz cell with a 10-mm optical length was used.

the self-aggregation is promoted by the addition of KNO₃ (Figure 10). Such a sharp band suggests the formation of a *J*-aggregate.[15] Porphyrin *J*-bands in UV−vis absorption spectra were first reported for TPPS₃ and TPPS₄ in acidic solutions.[2a,16] *J*-aggregates of the sulfonated porphyrins form through Coulomb interactions between the dicationic porphyrin center and the anionic groups at the periphery.[3,14] The free base forms of the cationic porphyrins 5,15-DiMPyP[8a] and the phosphonium derivatives of tetraphenylporphyrin[17] have been shown to form the *J*-aggregates in water containing NaCl, although for the latter porphyrin, the intensities of the *J*-bands are much weaker than that of the diacid sulfonated porphyrins.[17] The UV−vis spectrum of the Langmuir−Blodgett film of 5-(4-*N*-octadecylpyridyl)-10,15,20-tris(*p*-tolyl)porphyrin on a CaF₂ plate also suggests the formation of the *J*-aggregate.[18]

To confirm the formation of the *J*-aggregate of TPPOC2Py in aqueous solution in the presence of KNO₃, we applied a resonance light scattering (RLS) method developed by Paster-nack and co-workers.[3b,8a,19] Ordinary light scattering is per-formed at wavelengths removed from absorption bands. In the RLS measurement, however, light scattering is measured at the wavelengths corresponding to the absorption band of the aggregated chromophore. In this method, the sensitivity is enhanced by several orders of magnitude when strong electronic coupling exists between the chromophores in the aggregate.[19] This method has been applied for studying the *J*-aggregates of 5,15-DiMPyP,[8a] the diacid form of TPPS₄,[3,4a,14b] and chlorophyll *a* in aqueous formaldehyde.[19b]

The RLS spectrum of the aggregated TPPOC2Py is shown in Figure 11. A very strong RLS peak was observed near 450 nm which corresponds to λ_{max} of the putative *J*-band. Addition of methanol causes the reduction in the intensity of the scattering peak, which disappeared in 40% (v/v) methanol−water. Light scattering depends on the polarizability of the aggregate. If the

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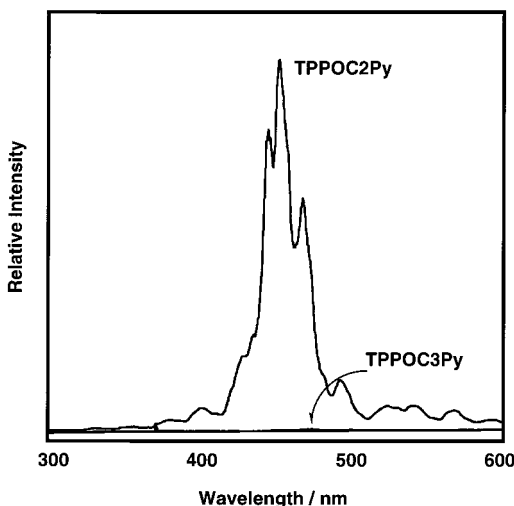
Figure 11. RLS spectra of TPPOC2Py and TPPOC3Py (5×10^{-6} mol dm^{-3}) in water at pH 7.0 in the presence of 2×10^{-2} mol dm^{-3} KNO$_3$ at 25 °C. The band-pass was 2 nm and the scan speed was 60 nm min^{-1}.
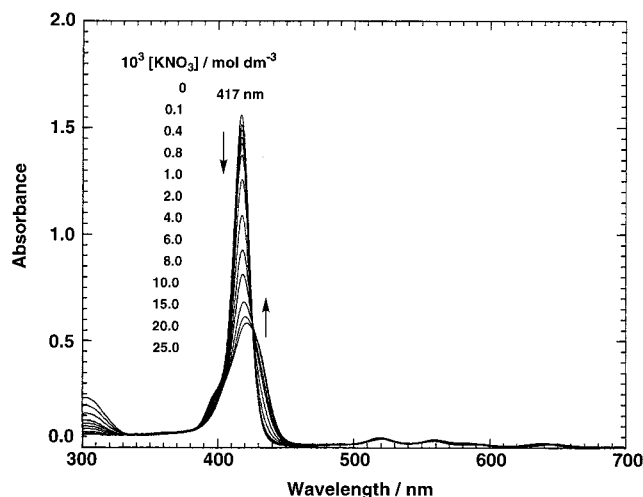

Figure 12. Absorption spectral changes of TPPOC3Py (5×10^{-6} mol dm^{-3}) in water at pH 7.0 upon addition of KNO$_3$ at 25 °C. A quartz cell with a 10-mm optical length was used.

porphyrin molecules interact with one another to yield an electronically coupled array, the polarizability of such an aggregate is much larger than that of the monomer, resulting in strong light scattering. The intense RLS signal for TPPOC2Py suggests that this cationic porphyrin forms a *J*-aggregate having a large aggregation number,[19b] and the edge of a porphyrin ring overlaps with the edge of the neighboring porphyrin ring to give the edge-to-edge assembly. Such an edge-to-edge packing arrangement has also been measured for the TPyP diacid in the crystal by means of X-ray crystallography.[20] No RLS signals were measured with the solutions of other porphyrins used in this study.

　　Figure 12 shows the absorption spectral change of TPPOC3Py (5×10^{-6} mol dm^{-3}) in water at pH 7.0 upon addition of KNO$_3$. Addition of salt leads to a reduction in the intensity of the Soret band to yield a broad, characterless band. Such spectral behavior suggests the formation of the higher self-aggregates but perhaps of a modest size. The marked broadening accompanied by the upfield shifts in the ^{1}H NMR spectrum of TPPOC3Py with

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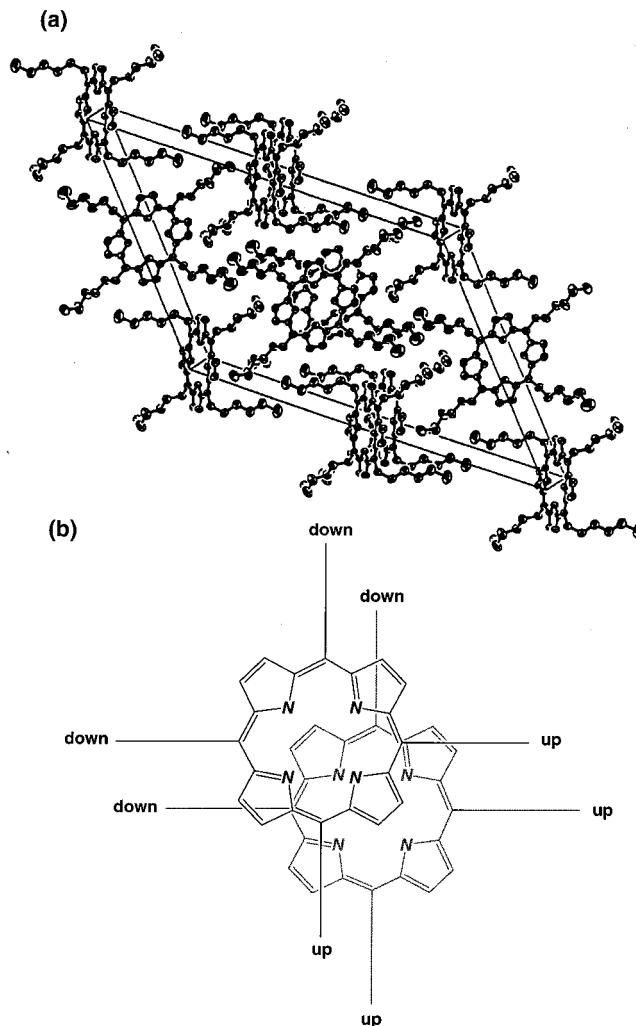

Figure 13. ORTEP view of the PC5Cl crystal lattice (a) and the structure of the PC5Cl dimer unit determined by the X-ray analysis (b). The hydrogen atoms are omitted for clarity.

increasing porphyrin concentration supports the formation of higher aggregates having a slipped face-to-face arrangement (Supporting Information). An RLS experiment with this porphyrin did not reveal an enhanced signal, in contrast to TPPOC2Py. In summary TPPOC2Py forms a *J*-aggregate while TPPOC3Py, under similar conditions, produces a slipped face-to-face higher aggregate of more modest size. The reason for such a difference between these two cationic porphyrins in self-aggregation behavior has not been clear.
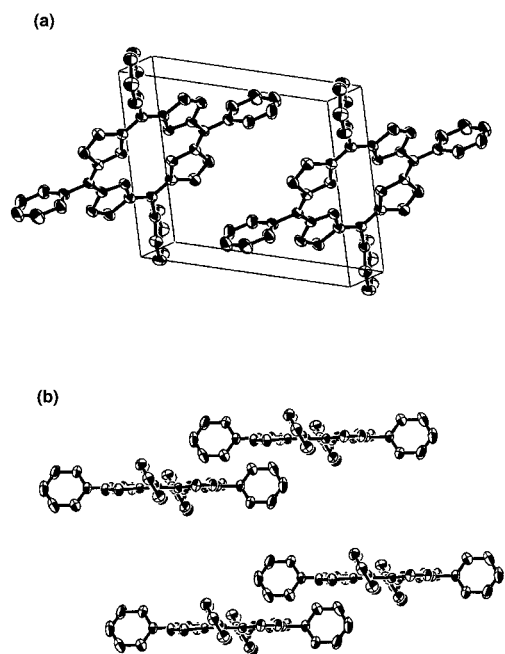
　　X-ray Crystallography of Lipophilic Porphyrins. We were unsuccessful in our attempts to grow single crystals of the water-soluble cationic porphyrins used here. However, we carried out an X-ray crystallographic analysis of PC5Cl, a precursor of PC5Py, and TPP to study the effects of alkyl and aryl groups on the crystal structures of the porphyrins. The ORTEP view of a PC5Cl crystal lattice is shown in Figure 13a. The crystal system is monoclinic. In the crystal of PC5Cl, two porphyrin molecules are close to each other. The average distance between the porphyrin planes is 0.36 nm, which is in good agreement with the distance calculated by Hunter and Sanders, who assumed that the $\pi-\pi$ interactions are always repulsive and the $\sigma-\pi$ interactions are attractive.[11] About one-fourth of a porphyrin ring overlaps another in the dimer unit (Figure 13b). Such a structure of the dimer is in complete agreement with calculations.[11] Figure 13b suggests the $\sigma-\pi$ interaction as the attractive force for dimerization of PC5Cl. The $\pi-\pi$ overlapping

Table 2.   Stability Constants for PC3Py Dimer in H_2O Containing KNO_3 as a Function of Temperature[a]

	K/dm³ mol⁻¹			
T/K	[KNO_3] = 0 mol dm⁻³	[KNO_3] = 0.01 mol dm⁻³	[KNO_3] = 0.1 mol dm⁻³	[KNO_3] = 1.0 mol dm⁻³
283	212 ± 53	(213 ± 28) × 10²	(59 ± 97) × 10⁴	(483 ± 194) × 10⁴
293	35 ± 29	(97 ± 17) × 10²	(25 ± 28) × 10⁴	(202 ± 52) × 10⁴
303		(37 ± 4.8) × 10²	(10 ± 7.7) × 10⁴	(88 ± 16) × 10⁴
313		(16 ± 2.4) × 10²	(5.1 ± 2.8) × 10⁴	(41 ± 4.7) × 10⁴
323		(8.2 ± 1.6) × 10²	(2.5 ± 1.1) × 10⁴	(19 ± 2.5) × 10⁴
333		(4.5 ± 1.2) × 10²	(1.4 ± 0.4) × 10⁴	(9.5 ± 2.2) × 10⁴
343		(2.2 ± 0.9) × 10²	(0.65 ± 0.22) × 10⁴	(5.2 ± 2.3) × 10⁴

[a] The K values in water without and with 0.01 and 0.1 mol dm⁻³ KNO_3 were determined by following the changes in absorbances of PC3Py (1×10^{-4} to 1×10^{-3} mol dm⁻³) at 521 nm. In the presence of 1.0 mol dm⁻³ KNO_3, the absorbance changes of PC3Py (2.5×10^{-6} to 2.0×10^{-5} mol dm⁻³) were followed at 412 nm.

(a)

(b)

Figure 14. ORTEP view of the TPP crystal lattice. The hydrogen atoms are omitted for clarity.

Table 3. Enthalpy (ΔH) and Entropy Changes (ΔS) for Dimerization of PC3Py in H_2O in the Presence of KNO_3

[KNO_3]/mol dm⁻³	ΔH/kJ mol⁻¹	ΔS/J mol⁻¹K⁻¹	$T\Delta S$/kJ mol⁻¹ [a]
0.01	−62 ± 1	−135 ± 3	−40 ± 0.9
0.1	−60 ± 1	−105 ± 2	−31 ± 0.6
1.0	−61 ± 1	−89 ± 1	−27 ± 0.3

[a] The $T\Delta S$ values are calculated for 25 °C.

aryl groups at the meso positions. It has been known that intermolecular interactions between apolar molecules in water are significantly stronger than those in organic solvents. One of the contributors to this relatively strong interaction in water is the classical hydrophobic interaction which is entropically favorable.[23] Another putative contributor is extremely strong van der Waals interactions which result from the strong cohesive-interaction of water.[24−26] Conclusions concerning the driving forces for self-aggregation arising from the present study are discussed in the following section.

Factors Important for Self-Aggregation of Cationic Porphyrins. The association constants (K) for the dimerization of PC3Py in water in the presence of 0.01, 0.1, and 1.0 mol dm⁻³ KNO_3 were determined from data on the deviation from the Beer−Lambert law using the method of Pasternack and co-workers.[2a] The values, shown in Table 2, increase with increasing concentration of KNO_3. The K values were determined also as a function of temperature, providing thermodynamic parameters for the dimerization of PC3Py. These values are shown in Table 3. The dimerization is dominated by the enthalpy term (ΔH). Very large and negative enthalpy changes suggest attractive van der Waals interactions as the main driving force for the association. The ΔH values are almost constant (ca. −61 kJ mol⁻¹) in aqueous media containing differing concentrations of KNO_3. In contrast, the ΔS values increase markedly with increasing KNO_3 concentration. The small K value in water in the absence of added salt can be ascribed to the large, unfavorable entropy term.

Few studies have been done on the thermodynamics of porphyrin dimerization. It had been previously reported that

seems to be minimized presumably to prevent electrostatic repulsion. Monte Carlo simulation also demonstrates that the π−π stacking is a repulsive interaction.[12] The porphyrin ring is completely flat and the dihedral angles between the porphyrin ring and the alkyl chains at the 5-, 10-, 15-, and 20-positions are 100.4°, 87.4°, −100.4°, and −87.1°, respectively. The slipped dimer requires the up-up-down-down conformation of the alkyl chains to prevent their collision with the porphyrin ring. Although the result of the X-ray analysis of PC5Cl cannot be correlated directly with the structure of the PC5Py aggregate(s) in water, the slipped face-to-face dimer similar to that shown in Figure 13 is, at least, one of the candidates of the dimer unit of the PC5Py self-aggregates.

The ORTEP view of the TPP crystal lattice is shown in Figure 14. As shown previously,[20] the crystal system is triclinic and no stacking interaction was observed for this porphyrin having aryl groups at the meso positions. The average distance between the porphyrin planes is 0.65 nm, which is much longer than that for PC5Cl (0.36 nm). The dihedral angles of the phenyl groups to the porphyrin plane are 116.3 and 119.2°. Steric effects due to the aryl groups at the meso positions may suppress the stacking interaction between the TPP porphyrin rings. The absence of stacking interaction has also been found for metal complexes of the porphyrins having aryl groups at the meso positions.[22] In aqueous solution, however, both TPPOC2Py and TPPOC3Py form self-aggregates, though these porphyrins have

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Cationic Porphyrins in Aqueous Solution

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deuteroporphyrin IX dimerizes in water ($K = 2.3 \times 10^6$ dm^3 mol^{-1}) and the ΔH and ΔS values for this dimerization are -46.0 kJ mol^{-1} and -32.2 J mol^{-1} K^{-1}, respectively.[24] In the case of the dimerization of iron(III)uroporphyrin, -48.4 kJ mol^{-1} and -115 J mol^{-1} K^{-1} were determined as ΔH and ΔS values, respectively.[27] It can be concluded from this and previously studied systems that porphyrin dimerization in aqueous medium is in general enthalpy driven. It is well-known that self-assembly of water-soluble porphyrins is inhibited by the addition of miscible organic solvents. Indeed, no aggregation was detected for the cationic porphyrins used here in pure organic solvents such as methanol and DMSO. Clearly, water plays an important role for forming such molecular complexes.

Diederich and co-workers[26] have concluded that both the strong cohesive interactions and low polarizability of water are the origin of the enthalpy-dominated complexation of apolar solutes in water. Margalit and Rotenberg[25] have explained the self-association of deuteroporphyrin IX in water by the strong cohesive interaction of water. An apolar solute molecule interacts weakly with surrounding water molecules through van der Waals interactions because of a low polarizability of water. A cavity needs to be created to accommodate an apolar solute molecule in water. Considerable enthalpic work against the large surface tension of water is required to produce these cavities. Under such circumstances, the apolar solute molecules tend to aggregate to reduce the number of such cavities which need be formed. Such an aggregation process is expected to be exothermic. This analysis seems equally applicable to the present system; the strong cohesive interaction of water promotes the self-aggregation of the amphiphilic water-soluble porphyrin and the van der Waals interactions control the orientation of the porphyrin aggregate. Both types of intermolecular interactions can be used to explain the large and negative enthalpy change. In neat water, however, the significant entropic loss suppresses the self-aggregation of the porphyrins. KNO$_3$ enhances the self-aggregation of the water-soluble porphyrins due to its influence on ΔS as a consequence of its orientation of water molecules ("salting out" effect[28]). The inorganic salt thus serves to enhance the hydrophobic interaction between the porphyrin molecules.

The porphyrin dimer is the only aggregate observed under these conditions in the case of PC3Py. Presumably, trimer formation is inhibited by electrostatic repulsive force between 12 positive charges of the porphyrin trimer. When the intermolecular attractive force overcomes the electrostatic repulsive force, higher self-aggregates are formed. Such is the case for the remaining PCnPy derivatives. The more basic TPPOCnPy porphyrins form aggregates more readily than do the PCnPy derivatives. Of the porphyrins considered here, TPPOC2Py appears unique in its ability to form an extended *J*-aggregate as evidenced by the new wavelength absorption feature and, more compellingly, by the enhanced RLS signal it produces. Quite surprisingly, adding one additional methylene group to the alkyl chain has a dramatic impact on aggregation properties. It is clear that the tendency for porphyrins to self-assemble is a complicated mixture of electronic and structural effects.

Experimental Section

Preparation of Porphyrins. PCnPys were prepared using the method developed by Izumi et al., who showed that montmorillonite K10 is an effective catalyst for preparing *meso*-alkyl-substituted

Table 4. Crystallographic Data of PC5Cl and TPP

	PC5Cl	TPP
formula	C$_{40}$H$_{50}$N$_4$Cl$_4$	C$_{44}$H$_{30}$N$_4$
formula weight	728.67	614.75
crystal color, habit	purple, prismatic	dark purple, prismatic
crystal system	monoclinic	triclinic
space group	$C2/c$	$P\bar{1}$
lattice constants		
a (Å)	37.314(4)	10.464(1)
b (Å)	5.008(5)	12.395(1)
c (Å)	25.474(5)	6.4330(6)
α (Å)		99.332(8)
β (deg)	127.184(7)	101.209(9)
g (deg)		95.744(8)
V (Å^3)	3792(3)	800.1(2)
temperature (°C)	20.0	20.0
density (g cm^{-3})	1.276	1.276
radiation (λ) (Å)	Mo Kα 0.71069	Mo Kα 0.71069
μ (cm^{-1})	3.46	0.75
R, $R_w{}^a$	0.055, 0.051	0.044, 0.044

^{a} $R = \sum||F_o| - |F_c||/\sum|F_o|$. $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w(F_o)^2]^{1/2}$, where $w = 1/\sigma^2(F_o)$.

porphyrins from aldehydes and pyrrole.[29] The alkyl aldehydes having chlorine at the ends of the alkyl chains were synthesized from corresponding alcohols by literature methods.[30] An equimolar mixture of chloroalkanal and pyrrole (10 mmol) in dichloromethane (1 dm^3) in the presence of dried montmorillonite K10 (10 g) was stirred for 1 h at room temperature. The reaction mixture was further stirred under reflux conditions for 1 h after addition of chloranil (7.5 mmol). The solvent was evaporated in vacuo and the residue was purified by silica gel column chromatography with chloroform. The yields of PC3Cl, PC5Cl, and PC7Cl were 13, 39, and 34%, respectively. The structures of the PCnCl were confirmed by means of FAB-MS and ^{1}H NMR spectroscopy. PCnCl (1 mmol) was placed in dry pyridine (0.3 dm^3) and heated under reflux conditions for 48 h. The solvent was evaporated. The residue was dissolved in methanol and the solid PCnPy was precipitated upon addition of ethyl acetate. The yields of PC3Py, PC5Py, and PC7Py were 96, 84, and 93%, respectively. The structures of PCnPys were confirmed by means of ^{1}H NMR spectroscopy. The synthesis of TPPOC3Py has been reported.[31] The same method was applied to prepare TPPOC2Py. TPP was prepared according to Adler's method.[32]

Spectroscopy. Absorption spectra were recorded on a Shimadzu UV-2100 spectrophotometer. RLS spectra were measured by a Hitachi 650-60 spectrofluorometer (band-pass: 2.0 nm). ^{1}H NMR spectra were taken using a JEOL JNM-A400 spectrometer (400 MHz). FAB-mass spectra were recorded on a JEOL JMS-700 spectrometer.

X-ray Crystallography. Single crystals of PC5Cl and TPP were obtained at the interfaces of chloroform and methanol. The measurements were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo Kα radiation and a 12 kW rotating anode generator at 20 °C. The cell constants and the orientation matrices for data collection were obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections. The angle ranges were $27.04 < 2\theta < 29.45°$ and $20.58 < 2\theta < 23.01°$ for PC5Cl and TPP, respectively. Total numbers of reflections were 4950 and 3887 for PC3Cl and TPP, respectively. The intensities of three representative reflections were measured after every 150 reflections. The structures were solved by direct methods (SHELX86)[33] and expanded using

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Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The fine cycle of full-matrix least-squares refinement was based on 1590 observed reflections and 218 variable parameters for PC5Cl and 2109 observed reflections and 218 variable parameters for TPP, and converged with unweighted (R) and weighted agreement factors (R_w), R and R_w being 0.055 and 0.051, respectively, for PC5Cl and 0.044 and 0.044, respectively, for TPP. The neutral atom scattering factors were taken from Cromer and Waber.[34] All calculations were performed using the teXan[35] crystallographic software package of Molecular Structure Corporation. The crystallographic data of PC5Cl and TPP are summarized in Table 4. Further details of the crystal data and structure solutions and refinements are listed in the Supporting Information.

Methods. PCnPys were so hygroscopic that these materials were dried in vacuo at 100 °C for 1 h prior to use. In most cases, the absorption spectra of PCnPys were measured in 5×10^{-3} mol dm^{-3} carbonate buffer at pH 9.5. In the case of TPPOCnPy, the stock solutions were prepared using DMSO. Therefore, the samples for

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(35) Single-crystal structure analysis software, version 1.6, Molecular Structure Corp.: The Woodlands, TX 77381, 1993.

absorption and RLS spectra contained 2% (v/v) DMSO. The pH value of the samples of TPPOCnPy was adjusted to 7.0 by using minimum amounts of Na$_2$CO$_3$. The pD values for the samples of NMR spectra of PCnPy and TPPOCnPy were adjusted by Na$_2$CO$_3$. 3-Trimethylsilyl-[2,2,3,3,-^{2}H$_4$]propionate (TSP, Aldrich) was used as an external standard for determining the chemical shifts in D$_2$O (CEA, 99.8%).

Supporting Information Available: ^{1}H NMR spectral changes of PC3Py as a function of temperature and ^{1}H NMR spectral changes of PC7Py and TPPOC3Py as a function of porphyrin concentration (PDF) and X-ray crystallographic files (CIF) format for PC5Cl and TPP. This material is available free of charge via the Internet at http://pubs.acs.org.

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