A new route to water soluble porphyrins: phosphonium and ammonium type cationic porphyrins and self-assembly

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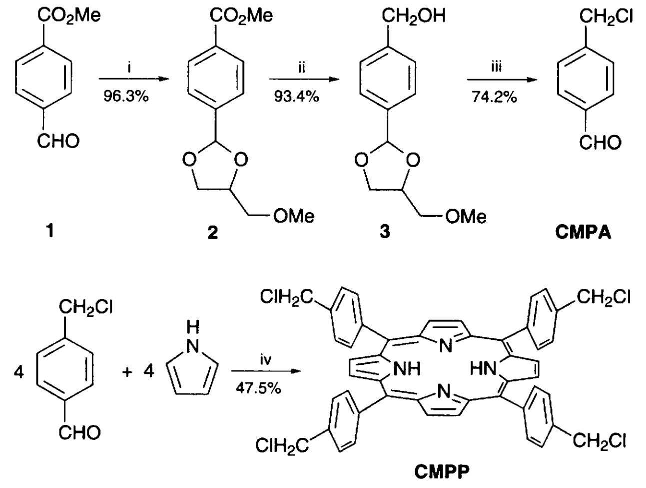
From a precursor porphyrin, tetrakis(*p*-chloromethylphenyl)porphyrin, the novel phosphoniumyl and ammoniumyl cationic porphyrins are synthesized, and the unusual spontaneous assembly for the two cationic porphyrins is discussed.

Water-soluble porphyrins, including cationic, anionic and sugar-substituted types, have attracted a great deal of attention in the areas of photo-synthetic models, supramolecular architecture, intercalation with DNA and phototherapy.[1] Cationic porphyrins are usually derived from tetra(pyridyl)porphyrin or tetra(aminophenyl)porphyrin.[2] In this approach the peripheral atoms, such as nitrogen, already attached to the porphyrin precursor are transformed into cationic centres. A limitation of this method is that the nature of the cationic centre cannot be changed, but is fixed by the precursor porphyrin. It is known that the chemical and physical properties of water soluble porphyrins are influenced by the peripheral structure,[3] but a systematic investigation of the effect of peripheral structure on the functionality of the porphyrins is required. This paper reports a new methodology for the synthesis of water soluble cationic porphyrins containing phosphonium and ammonium residues derived from one precursor, tetrakis(*p*-chloromethylphenyl)porphyrin (**CMPP**) and its unusual aggregation properties.

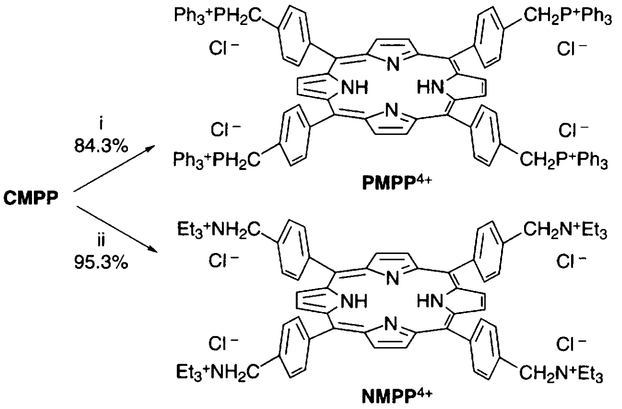
The strategy to **CMPP** is shown in Scheme 1. Using methyl *p*-formylbenzoate as a starting material, *p*-chloromethylbenzaldehyde (**CMBA**)[†] was prepared *via* protection of the aldehyde as an acetal, reduction of the ester to a hydroxy group, substitution of the OH with chloride and deprotection of the acetal to give the aldehyde. The porphyrin **CMPP**[‡] was afforded in high yield (47.5%, purified by crystallization from CH_2Cl_2–MeOH and column chromatograph, eluent $CHCl_3$) from the Lindsey condensation of **CMBA** with pyrrole. The porphyrin **CMPP** was soluble in organic solvents such as DMF, Me_2SO, $CHCl_3$ and acetone. In the proton NMR spectrum the protons of the chloromethyl groups resonated as a single sharp peak at δ 5.0.



Scheme 1 *Reagents and conditions*: i, glycidyl methyl ether (excess), tetrabutylammonium bromide (cat), 80 °C, 3 d; ii, (*a*) $LiAlH_4$ in THF, 70 °C; 16 h, (*b*) NH_4Cl (aq); iii, (*a*) PPh_3, CCl_4, reflux, 3 h; (*b*) EtOH, 2 M HCl, room temp., 1 h; iv, (*a*) BF_3–Et_2O, $CHCl_3$, room temp. 1 h; (*b*) chroranil, NEt_3, $CHCl_3$, reflux, 1 h

In order to obtain the water-soluble cationic porphyrins, the reactions of **CMPP** with triphenylphosphine and triethylamine were examined using DMF as solvent (see Scheme 2). After the reaction had been carried out with excess phosphine or amine (more than 40 equiv.) for 40 h at 80 °C, the peak at δ 5.0 due to the chloromethyl groups on **CMPP** entirely disappeared, to give a doublet at δ 5.5–5.7 due to $-CH_2P^+$ or a singlet at δ 4.9 due to $-CH_2N^+Et$. With the above method, porphyrin **PMPP**$^{4+}$[§] and **NMPP**$^{4+}$[¶] were prepared conveniently.

We found that the cationic porphyrin **PMPP**$^{4+}$ is of particular interest. In the ^1H NMR spectrum, the spectral pattern was dependant upon the solvent: in $(CD_3)_2SO$, the protons for **PMPP**$^{4+}$ resonate in a resolved manner without aggregation, the β-protons appearing at δ 8.76 as a sharp singlet. But in D_2O, the β-protons on the pyrrole ring are shifted upfield to overlap with



Scheme 2 *Reagents and conditions*: i, PPh_3, DMF, 80 °C, 48 h; ii, NEt_3, DMF, 80 °C, 48 h

Table 1 Absorbance at the Soret band for cationic porphyrins in water and methanol

	PMPP^{4+}				**NMPP**$^{4+}$	
Porphyrin concentration/ 10^{-5} M	H_2O		MeOH		H_2O	MeOH
	Abs	$W_{1/2}$/nm	Abs	$W_{1/2}$/nm	Abs	
0.01	—	—	0.026	12.5	—	0.003
0.05	0.071	16.3	0.151	12.6	0.086	0.113
0.1	0.143	21.3	0.401	12.6	0.216	0.282
0.2	0.337	24.5	0.789	12.6	0.594	0.663
0.5	1.087	27.0	1.922	15.0	1.716	1.735
0.7	1.460	28.8	2.254	16.3	2.217	2.091
1	1.830	29.5	2.381	18.8	2.351	2.357
5	—	—	2.610	57.5	2.569	2.600
10	—	—	2.703	—	2.671	2.657

Table 2 Effect of the concentration of NaCl on the Soret band of cationic porphyrins[a]

NaCl concentration/ M	Abs. (wavelength/nm)				
		NMPP^{4+}		**NMPP^{4+}**	$W_{1/2}$/nm
0.0	—	1.116 (415.8)	—	1.612 (412.7)	12.50
0.1	—	0.838 (427.5)	—	1.462 (412.8)	12.50
0.3	0.329 (407.4)	0.553 (426.9)	0.589 (441.1)	1.375 (412.8)	12.58
0.5	0.364 (407.9)	0.598 (426.9)	0.606 (440.7)	1.221 (413.1)	17.58
0.7	0.359 (407.3)	0.593 (425.9)	0.577 (440.3)	1.141 (414.0)	20.03
1.0	0.334 (407.4)	0.530 (425.9)	0.492 (440.3)	1.066 (415.2)	22.50
2.0	—	0.526 (425.9)	0.459 (439.1)	0.974 (421.1)	25.13

[a] The concentration of the porphyrins was held at 5 × 10^{-6} M.

the signals of the phenyl groups, which resonate over the range δ 6–8 as a very complex pattern. When CD_3OD was used as solvent, a single very broad peak due to the β-protons appeared at δ 8.6–8.9. This indicates that the cationic porphyrin **PMPP^{4+}** aggregates *via* π-stacking, both in water and methanol. Unusual π-stacking behaviour was also observed in the UV–VIS spectrum. In water, the Soret band (λ_{max} 416 nm) of **PMPP^{4+}** has a fat shape with a shoulder at short wavelength, even at low concentration (5 × 10^{-7} M). Therefore, we investigated further, paying particular attention to the change of the half-width ($W_{1/2}$) of the Soret band. As the porphyrin concentration was adjusted from 5 × 10^{-7} to 1 × 10^{-5} M, the half-width increased from 16.3 to 29.5 nm (see Table 1). On the other hand, in methanol, the half-width of the Soret band of **PMPP^{4+}** did not change from 12.6 nm below 2 × 10^{-6} M concentration. As the concentration increased beyond 5 × 10^{-6} M, however, it became larger. Under the same concentration conditions, however, the half-width of the Soret band was noticeably smaller in methanol than in water. In the higher concentration case (above 1 × 10^{-5} M), the significant changes are that the top of the Soret band became very broad towards short wavelength. This result led us to consider that there might be a coalescence of new absorption bands due to new species formation. Nevertheless, the porphyrin **PMPP^{4+}** obviously existed in the aggregated form, due to the strong π-stacking effect in water and in methanol, as no change in shape and wavelength for the Q bands was observed. Addition of NaCl (up to 2 M) to the solution of **PMPP^{4+}** (5 × 10^{-6} M) did not cause major changes in the shape and wavelength of the Q bands. But, surprisingly, the Soret band at 416 nm (abs. = 1.116) in the absence of NaCl was completely altered, with three clear bands at 407, 427 and 441 nm upon addition of 0.3 M NaCl (see Table 2). The ratio of absorption of the bands at 441 and 427 nm (A_{441}/A_{427}) decreased with increasing concentration of NaCl (from 1.065 under [NaCl] = 0.3 M to 0.873 under [NaCl] = 2.0 M) and the band at 407 nm overlapped the band at 427 nm. This result means that the spontaneous assembly of **PMPP^{4+}** occurs in response to the electrolyte concentration. These unusual phenomenon, such as the new band at λ_{max} 441 nm, which arise from the polymeric porphyrin assembly have not been reported for previous water soluble phorphyrin systems.[2c] A very similar result was also found upon addition of anthraquinone-2,6-disulfonic acid disodium salt (**AQDS^{2-}**) to the aqueous **PMPP^{4+}** solution (5 × 10^{-6} M), for which a new band at 441 nm appeared accompanied by bands at 409 and 429 nm when the concentration of **AQDS^{2-}** is over 1 × 10^{-5} M. Increasing the concentration of **AQDS^{2-}** further to 1 × 10^{-4} M resulted in the disappearance of the band at 441 nm, and one extra band with λ_{max} 429 nm was formed.

For **PMPP^{4+}**, the peripheral triphenylphosphonium residues are linked to the phenyl rings by methylene units, so the cation cannot be delocalized by the phenyl rings. This is also the case for the cationic porphyrin **NMPP^{4+}**. However, **NMPP^{4+}** did not show the same behaviour as the phosphonium-type porphyrin **PMPP^{4+}**. In the case of **NMPP^{4+}**, it was found that the patterns and the absorbancies at the Soret band in water and methanol were entirely in agreement (see Table 1). As the concentration was increased beyond 5 × 10^{-6} M, the Soret band became very broad with a blue-shift. On the other hand, the effect of NaCl addition on the Soret band of the ammonium porphyrin is entirely different from the case of the phosphonium porphyrin. First, no new bands appeared in the presence of NaCl. Upon addition of NaCl (0 to 2.0 M), the intensity of the Soret band of **NMPP^{4+}** (5 × 10^{-6} M) decreased (from 1.612 to 0.974) while the half-width of the Soret band increased (from 12.50 to 25.13 nm). Addition of **AQDS^{2-}** to aqueous **NMPP^{4+}** did not lead to a major change of the Soret band pattern or half-width. Consequently, it must be concluded that the two cationic porphyrins bearing phosphonium and ammonium salts differ in their aggregation behaviour due to differences in the peripheral structure of the porphyrins, *i.e.* the π-stacking interactions of **PMPP^{4+}** are stronger than those of **NMPP^{4+}**. More importantly, the assembly of the phosphonium porphyrin **PMPP^{4+}** could be controlled precisely by adjusting the concentration of additive salts.

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Footnotes

† *Selected data* for **CMBA**: a white solid, mp 71–73 °C; ^{1}H NMR (250 MHz, $CDCl_3$, Me_4Si) δ 4.6 (s, 2 H, CH_2), 7.4–7.6 (d, 2 H, H-aromatic), 7.8–8.0 (d, 2 H, H-aromatic), 10 (s, 1 H, CHO). (Found, 154.0233. Calc. for C_8H_7ClO, 154.0184.

‡ *Selected data* for **CMPP**: ^{1}H NMR (250 MHz, $CDCl_3$, Me_4Si) δ −2.8 (s, 2 H, NH), 5.0 (s, 8 H, CH_2Cl), 7.7–7.9 (d, 8 H, H-Ph), 8.1–8.3 (d, 8 H, H-Ph), 8.8 (s, 8 H, β-H); UV–VIS (in $CHCl_3$) λ_{max}/nm 419, 515, 551, 591, and 646; *m*/*z* 808 (M^+).

§ *Selected data* for **PMPP^{4+}**: ^{1}H NMR [250 MHz, $(CD_3)_2SO$, Me_4Si] δ −3.1 (s, 2 H, NH), 5.6–5.7 (d, 8 H, CH_2P), 7.3–8.0 (m, 76 H, H-Ph), 8.76 (s, 8 H, β-H); UV–VIS (in MeOH) λ_{max}/nm 414.8, 519.2, 555.6, 585.2 and 642.8; 1855 (M^{4+} + 4 Cl^-), 1819 (M^{4+} + 3 Cl^-).

¶ *Selected data* for **NMPP^{4+}**: ^{1}H NMR [250 MHz, $(CD_3)_2SO$, Me_4Si] δ −2.9 (s, 2 H, NH), 1.4–1.6 (t, 34 H, CH_3), 3.5 (s, 24 H, CH_2C), 4.9 (s, 8 H, CH_2N), 7.9–8.1 (d, 8 H, H-Ph), 8.1–8.4 (d, 8 H, H-Ph), 8.9 (s, 8 H, β-H); UV–VIS (in MeOH) λ_{max}/nm 413.4, 512.4, 545.6, 589.9 and 643.1; *m*/*z* 1175 (M^{4+} + 3Cl^-), 1070 (M^{4+} −3 H^+).

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