Synthesis of a Novel Amphiphilic Porphyrin carrying Water-soluble Polyether Side Chains of Controlled Chain Length. Formation of a Cofacial Molecular Assembly in Aqueous Media

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A novel amphiphilic porphyrin carrying poly(oxyethylene) side chains of controlled chain length was obtained by polymerization of epoxyethane initiated by an aluminium porphyrin [(5,10,15,20-tetraphenylporphyrinato)-aluminium chloride] in the presence of a porphyrin with phenolic substituents [5,10,15,20-tetrakis(4′-hydroxyphenyl)porphyrin], and was found to form cofacial aggregates spontaneously in aqueous media.

Molecular assemblies of porphyrins and metalloporphyrins have been the subject of some attention, particularly in relation to their prominent biological functions such as efficient electron transfer arising from the specifically arranged tetrapyrrole pigments in multi-chlorophyll photosynthetic centres.[1,2] Aggregations of cofacial porphyrins *via* covalent linkages[3] or electrostatic interactions between positively and negatively charged porphyrins[4] have been studied. We report here the facile synthesis of a novel amphiphilic porphyrin carrying poly(oxyethylene) (PEO) side chains of a uniform chain length, which spontaneously forms highly soluble cofacial aggregates in aqueous media.

The synthetic method employs the polymerization of epoxyethane (**6**) initiated by (TPP)AlCl† (**5**) in the presence of T(p-OH)PPH$_2$† (**3**), based on our novel concept of 'immortal' polymerization.[5] In this reaction, the four phenolic hydroxy groups of T(p-OH)PPH$_2$ also initiate the polymerization of epoxyethane, resulting in the formation of a porphyrin carrying four poly(oxyethylene) side chains of the same length, T(p-PEO)PPH$_2$ (**1**). The length (number of repeating units, n) of the PEO chains can be controlled by the molar ratio of epoxyethane to the sum of (TPP)AlCl and hydroxy groups ($n = [(\mathbf{6})]_0([(\mathbf{5})]_0 + 4\,[(\mathbf{3})]_0)^{-1}$ at 100% conversion). α-Chloro-ω-hydroxy-PEO with the same chain length (**7**) is formed simultaneously, but can be separated.

A typical example is as follows. To a 50 cm^3 glass ampoule equipped with a three-way stopcock containing T(p-OH)-PPH$_2$[6] (0.2 mmol), purged with dry nitrogen, was added a CH$_2$Cl$_2$ solution (2 cm^3) of (TPP)AlCl[5] (0.2 mmol) using a hypodermic syringe, and the mixture was evaporated to dryness under reduced pressure at room temperature. To this system was added CH$_2$Cl$_2$ (1 cm^3), and epoxyethane (10 mmol) was then introduced by distillation after several

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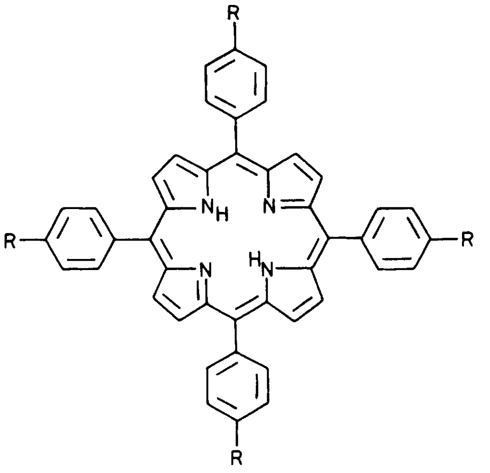
† *Abbreviations*: T(p-OH)PPH$_2$ = 5,10,15,20-tetrakis(4′-hydroxyphenyl)porphyrin; T(p-CO$_2$H)PPH$_2$ = 5,10,15,20-tetrakis(4′-carboxyphenyl)porphyrin; (TPP)AlCl = (5,10,15,20-tetraphenylporphyrinato)aluminium chloride.

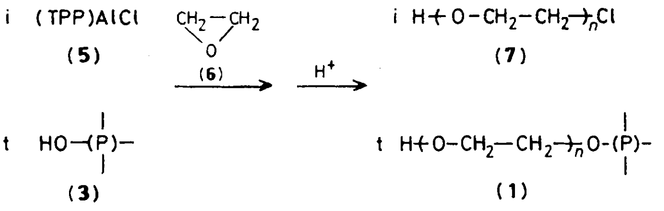


(**1**) R = $-O\!\left(CH_2-CH_2-O\right)_n H$, [T(*p*-PEO)PPH$_2$]
(**2**) R = $-CO_2\!\left(CH_2-CHMeO\right)_n H$
(**3**) R = $-OH$, [T(*p*-OH)PPH$_2$]
(**4**) R = $-CO_2H$, [T(*p*-CO$_2$H)PPH$_2$]

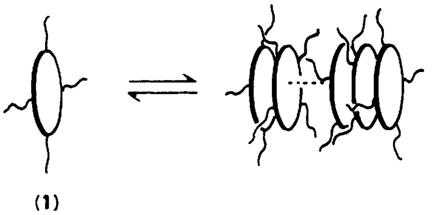
freeze–pump–thaw cycles. The tube was then sealed under reduced pressure, and the reaction mixture was stirred magnetically at 20 °C. The polymerization was completed within 160 h, as determined by the weight of the residue after the removal of the volatile fractions. Gel-permeation chromatography (g.p.c.) (tetrahydrofuran as eluant) of the residue showed two unimodal, sharp peaks A and B, when monitored by a refractometer [Figure 1(I)], while a single peak corresponding to peak A was observed when monitored by the absorbance at 425 nm. T(*p*-OH)PPH$_2$ was not detected at all. Thus, we assigned peak A in the higher molecular weight region to the polyether carrying a porphyrin moiety from T(*p*-OH)PPH$_2$, and peak B in the lower molecular weight region to the polyether carrying a chlorine terminal arising from (TPP)AlCl [(**7**), see Scheme 1]. The fraction corresponding to peak A could be easily isolated from the reaction mixture by column chromatography on silica gel followed by Sephadex resin, and gave satisfactory g.p.c. [Figure 1(II)], spectroscopic, and elemental analytical data, as required for the proposed structure of (**1**).

The uniformity of the molecular weight of (**1**) was demonstrated by the ratio of the weight- and number-average molecular weights ($\bar{M}_w/\bar{M}_n$) of 1.05, as estimated from Figure 1(II), being close to unity. In order to confirm that the four polyether side chains in a molecule of (**1**) are of the same molecular weight, the porphyrin (**2**) bearing polyether side chains *via* hydrolysable ester linkages was similarly synthesized by the 'immortal' polymerization of 1,2-epoxypropane from T(*p*-CO$_2$H)PPH$_2$† (**4**)[7] using (TPP)AlCl (**5**) as initiator ([(**6**)]$_0$: [(**4**)]$_0$: [(**5**)]$_0$ 500 : 1 : 1, 94% conversion, $\bar{M}_w/\bar{M}_n$ 1.05).

The alkaline hydrolysis of the ester linkages of (**2**) by KOH in H$_2$O–MeOH gave the potassium salt of T(*p*-CO$_2$H)PPH$_2$ (observed by i.r. spectroscopy) and a polyether which exhibited in the g.p.c. a single, sharp peak ($\bar{M}_w/\bar{M}_n$ 1.08, $\bar{M}_n$ 3400) in the lower molecular weight region. Thus, the polyether side chains in a molecule of (**2**) are uniform with respect to the molecular weight. The lengths of the polyether side chains are therefore also considered uniform in (**1**). The number of repeating oxyethylene units (*n*) was estimated by u.v.–visible‡ (9.1), ^{1}H n.m.r. (12.2), and elemental analysis (10.2). These values are close to each other, and also in excellent agreement with that calculated from $[(\mathbf{6})]_0(4[(\mathbf{3})]_0 + [(\mathbf{5})]_0)^{-1}$ (10.0). Similarly, the porphyrins (**1**) with uniform and desired numbers of repeating oxyethylene units (*n*), *e.g.* 20 and 45, were successfully obtained.



Scheme 1. i: Initiator; t = chain transfer agent.



(**1**)

Scheme 2

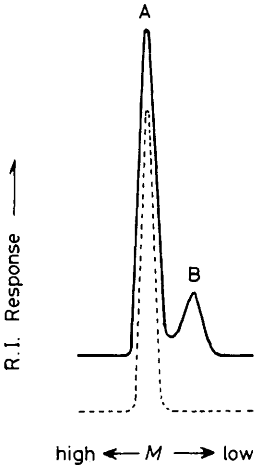


Figure 1. G.p.c. profile of the reaction mixture in the polymerization of epoxyethane (**6**; R = H) initiated by (TPP)AlCl (**5**) in the presence of T(*p*-OH)PPH$_2$ (**3**) in CH$_2$Cl$_2$ at 20 °C. I, [(**6**)]$_0$: [(**5**)]$_0$: [(**3**)]$_0$ 50 : 1 : 1, 100% conversion; II, after column chromatography.

T(*p*-PEO)PPH$_2$ (**1**), thus synthesized, was soluble in water as well as in various organic solvents other than aliphatic hydrocarbons, and the amphiphilic nature was highly dependent on the length of the water-soluble PEO side chains. Of particular interest is the spontaneous formation of the cofacial aggregates of (**1**) in aqueous media. For example, when (**1**; *n* = 10) was dissolved in water (6.1 × 10^{-8} M), the u.v.–visible spectrum of the solution at room temperature showed a single Soret band at 421 nm [Figure 2(i)]. As the concentration of (**1**) was increased, *e.g.* to 1.7 × 10^{-3} M, a shoulder blue-shifted to 407 nm appeared and became predominant, while the absorptions of the Q-band in the visible region exhibited slight red shifts. These spectral profiles are characteristic of the formation of porphyrin aggregates, in which the porphyrin disks adopt a cofacial orientation with respect to each other (see Scheme 2).[2]

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‡ Based on the absorbance at 519.6 nm calibrated with the molar absorbance of 5,10,15,20-tetrakis(4′-methoxyphenyl)porphyrin.

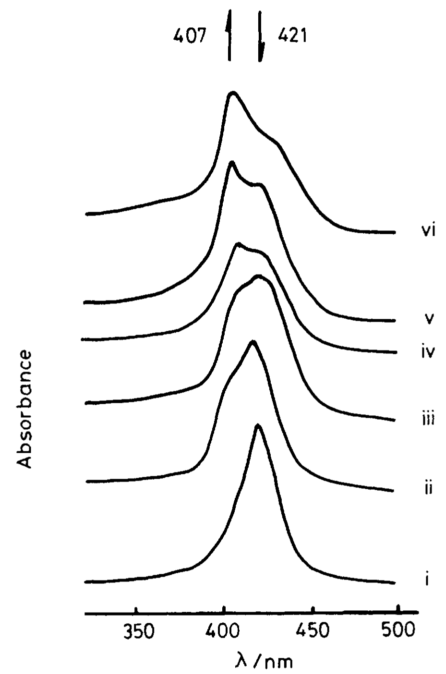

Figure 2. U.v.-visible spectra of (**1**; *n* = 10) in water at room temperature; concentration of (**1**): i, 6.1 × 10^{-8}; ii, 2.4 × 10^{-7}; iii, 9.8 × 10^{-7}; iv, 1.6 × 10^{-5}; v, 2.6 × 10^{-4}; and vi, 1.7 × 10^{-3} M.

At a certain concentration, the absorption at 407 nm due to the cofacial aggregates was less pronounced when the polyether side chains of (**1**) were longer. For example, (**1**; *n* = 45) exhibited no appreciable blue shift in the Soret region even when the concentration was increased up to 1.7 × 10^{-3} M, indicating that the longer polyether side chains placed the equilibrium shown in Scheme 2 more towards the dissociated form. On the other hand, the equilibrium was much less affected by the polyether unlinked to the porphyrin disk, as evidenced by the fact that no spectral change indicating the dissociation of the aggregates was observed upon addition of a four-fold excess of PEO diol ($n = 13.6$, $\bar{M}_n$ 600, $\bar{M}_w/\bar{M}_n$ 1.03) to an aqueous solution of (**1**; *n* = 13) at 5.0 × 10^{-5} M. We conclude that the extent of aggregation is dominated by a net balance of the hydrophilicity and hydrophobicity of the molecule of (**1**), which can be controlled by changing the length of the PEO side chains.

In sharp contrast to the cofacial aggregations of porphyrins assisted by covalent linkages[3] or electrostatic interactions,[4] the cofacial aggregation of (**1**) described herein takes place solely by the inherent aromatic interaction between the porphyrin disks, and the hydrophilic polyether side chains give the aggregates an unprecedentedly high solubility over a wide range of concentration in aqueous media.

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