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Phthalocyanine-centred aryl ether dendrimers with oligo(ethyleneoxy) surface groups

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Abstract—The synthesis of phthalocyanine-centred aryl ether dendrimers possessing oligo(ethyleneoxy) surface groups is described. These materials are soluble in polar protic solvents. The tendency of the non-polar phthalocyanine core to aggregate in such solvents is eliminated by placing the dendritic substituents at the axial sites, however, aggregation is not reduced by peripheral dendritic substitution.

Dendrimers are well-defined macromolecules of uniform mass which contain a core, successive layers of branched repeat units and a large number of surface groups.[1] A desirable consequence of placing a functional unit at the core of a dendrimer is steric isolation which can prevent unwanted interference of the functionality. For example, steric isolation of a porphyrin core results in enhanced fluorescence due to the absence of self-quenching mechanisms.[2,3] Phthalocyanine (Pc), a close relative of the porphyrin macrocycle, is the parent compound of one of the most studied class of functional organic materials. Pcs exhibit interesting catalytic, electronic and optical properties, in addition to being well established industrial colorants.[4] Presently, Pc derivatives substituted with hydrophilic groups are good candidates for use as photosensitisers in the photodynamic therapy (PDT) of cancer.[5] However, Pcs are notable for their strong tendency to aggregate in solution, especially in polar protic solvents (e.g. water or ethanol) due to the hydrophobic nature of the Pc ring. Self-association results in the quenching of the photochemically excited state of Pc and thus prevents both fluorescence and singlet oxygen formation—which is its primary role in PDT. Recently, we described Pc-containing poly(aryl ether) dendrimers based upon Fréchet's well established convergent route for dendrimer synthesis.[6,7] These materials possess benzyloxy terminal groups (T) and are soluble in a wide range of non-polar organic solvents. It was hoped that analogous Pc-centred dendrimers substituted with hydrophilic oligo(oxyethylene) terminal groups, T = $(OCH_2CH_2)_3OCH_3$, would be soluble in polar protic solvents and that the large dendritic substituents would prohibit aggregation of the Pc cores.

Simple modification to Fréchet's convergent synthetic route to poly(aryl ether) dendrimers[8] allows the introduction of oligo(ethyleneoxy) terminal groups. Thus, the aryl ether forming reaction between 3,5-dihydroxybenzyl alcohol and the tosylate of triethylene glycol monomethyl ether gives the first generation *dendron*, [G-1]-OH, from which the second and third oligo(ethyleneoxy) terminated dendrons, [G-2]-OH and [G-3]-OH, are assembled. The aromatic nucleophilic substitution reaction between these materials and 4-nitrophthalonitrile produces the required precursors **1**–**3** in 50–80% yield (Scheme 1). In each case, dendrimer assembly is achieved by the cyclotetramerisation of the phthalonitrile moiety of **1**–**3**, using lithium pentoxide in refluxing pentanol, to give **4**–**6** as a mixture of four inseparable isomers in 20–35% yield. Alternatively, the reaction between the anion of the appropriate [G-X]-OH dendron and dichlorophthalocyaninatosilicon produces **7**–**9**, in 10–40% yield, in which the dendritic substituents are placed in axial positions relative to the plane of the Pc ring.

All compounds **1**–**9** gave satisfactory elemental analyses and spectroscopic data consistent with their expected

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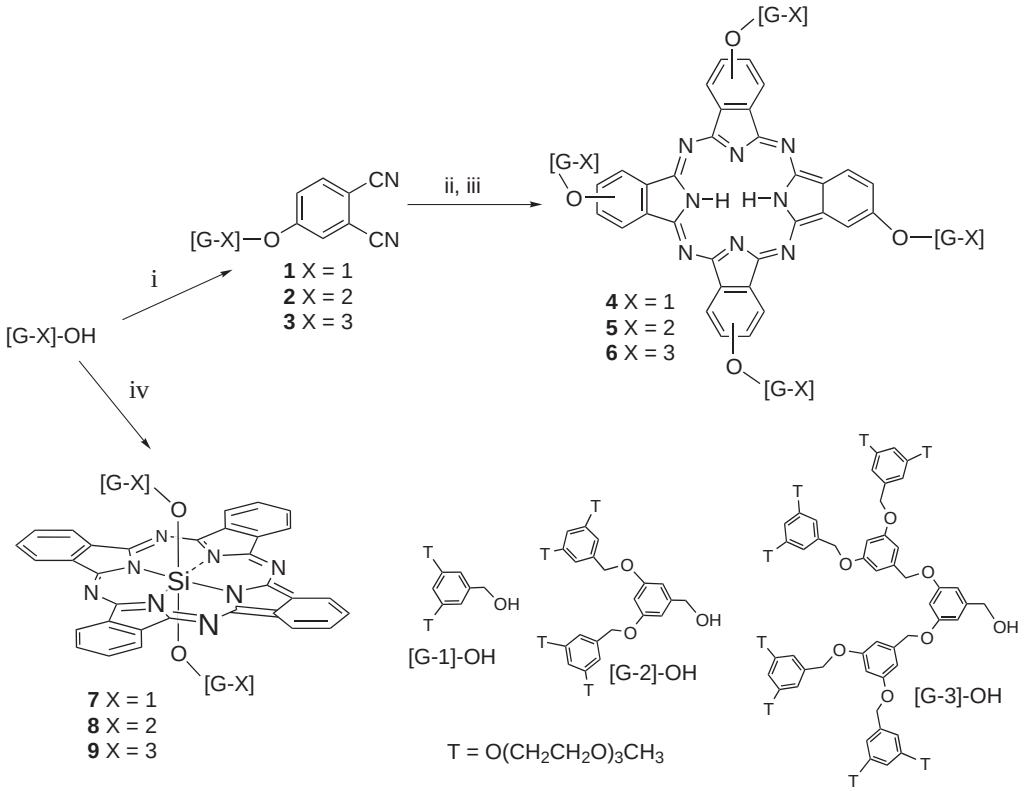

Scheme 1. *Reagents and conditions*: (i) anhydrous K_2CO_3, DMF, 50°C; (ii) $C_5H_{11}OLi$, $C_5H_{11}OH$, 135°C; (iii) acetic acid; (iv) dichlorophthalocyaninatosilicon, NaH, toluene, 80°C.

structures,[9] although the ^1H NMR spectra of **4–6** are each complicated by the presence of four regioisomers. In addition, analysis of **4–9** by gel permeation chromatography indicated that each material was pure and monodisperse ($M_w/M_n<1.01$) with an estimated mass, derived from comparison with polystyrene standards, consistent with the calculated value. For **7** it was possible to grow crystals of sufficient size and quality for a single crystal X-ray analysis by recrystallisation from a diethyl ether solution.[10] An ORTEP-type plot of the crystallographic packing of Pc **7** is given in Fig. 1 which shows a remarkable lamellar arrangement of the Pc rings with the axial [G-1] substituents acting as spacers between the 2-dimensional arrays.

As expected, the UV–vis absorption spectra of **4–9** obtained from CH_2Cl_2 solutions (1×10^{-6} mol dm^{-3}) are consistent with non-aggregated Pcs with the primary absorption band in the visible region (Q-band), centred at ~680 nm in each case (Table 1). In contrast, the large bathochromic shifts of the Q-band observed from **4–6** in EtOH solution at similar concentration indicate significant aggregation. In particular, the appearance and position of the Q-band of **4** is consistent with the formation of cofacial aggregates of significant size.[11] Examination of concentrated ethanol solutions (~20–40% by mass) using polarising optical microscopy shows that **4** behaves as a discotic amphiphile forming a distinct lyotropic liquid crystal. Its classic *schlieren* appearance indicates a columnar nematic phase. In addition, thermal analysis shows that **4** possesses a columnar mesophase at ambient temperature which is stable up to 260°C. The ability of **4** to form both thermotropic and lyotropic mesophases is similar to that of Pcs peripherally substituted with four oligo(ethyleneoxy) side-chains.[12] The position of the Q-

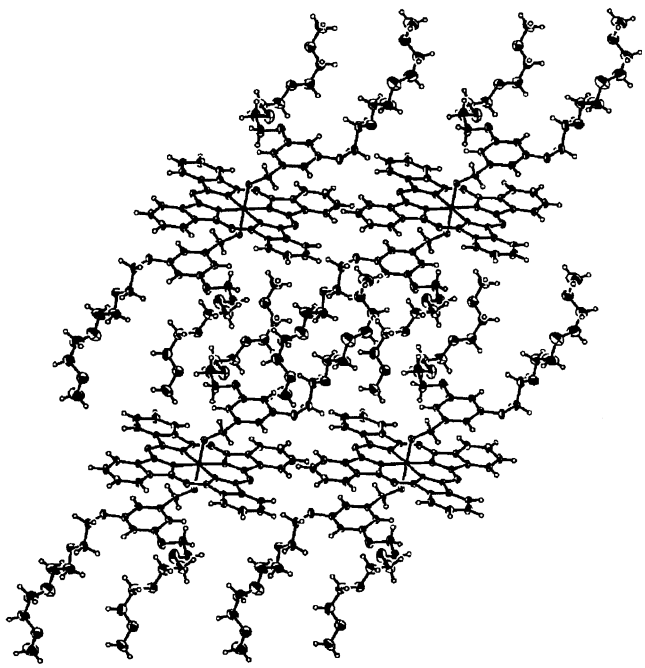

Figure 1. The crystal structure of **7** showing the sheet arrangement of the Pc units.

Table 1. The position of the primary absorption band (Q-band) of **4–9** in CH_2Cl_2 solution compared with that in EtOH solution

Pc	4	5	6	7	8	9
λ_{max} (CH_2Cl_2)	[a]705, 670	[a]705, 670	[a]705, 670	678	679	680
λ_{max} (EtOH)	610	625	635	677	679	680

All concentrations were approximately equal (1×10^{-6} mol dm^{-3}).
[a] Non-aggregated metal-free Pcs exhibit a split Q-band.

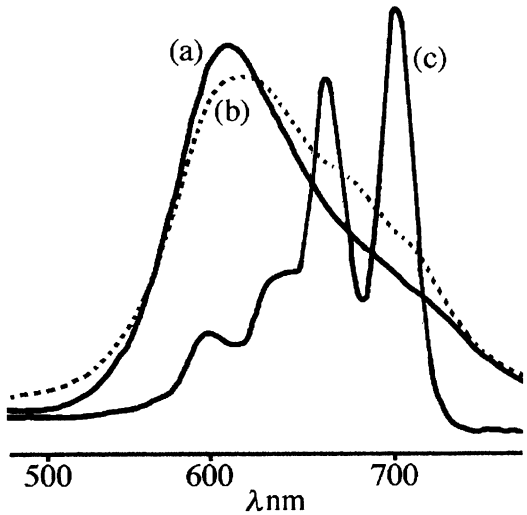

Figure 2. The Q-band absorption for (a) **4** in EtOH, (b,- - -) **6** in EtOH and (c) **6** in CH_2Cl_2.

band in the UV–vis absorption spectra of **5** and **6** shows that self-association of the Pc cores is less prevalent than in **4** for EtOH solutions of similar concentration (Table 1). Nevertheless, the appearance of the Q-band of **6** (Fig. 2) suggests that oligomeric molecular aggregates are the majority species and that only a small fraction of the Pc cores are isolated. Both **5** and **6** are isotropic liquids in the pure state and neither form a lyotropic mesophase in concentrated EtOH solution. It is apparent that peripheral substitution of Pc by four non-ionic dendritic substituents is not an efficient method of ensuring isolation in polar solvents. Similar results have been obtained by other groups using dendritic substituents bearing ionic solubilising groups, although the aggregation is reduced to some extent presumably as a result of electrostatic repulsion.[13,14] In contrast to the behaviour of **4–6**, UV–vis spectroscopy of **7–9** shows that placing the dendritic substituents in axial sites prevents aggregation in EtOH (Table 1). Preliminary fluorescence studies of EtOH solutions of **7–9** reveal that excitation at 420 nm results in strong fluorescence at 688 nm, whereas for ethanolic solutions of **4–6** no significant fluorescence was observed.

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9. Selected spectroscopic data for **4**: $\lambda(CH_2Cl_2)$/nm 705, 670, 65, 620, 422, 346; υ(KBr)/cm^{-1} 3275 (NH), 2924, 2874, 1598; δ_H ($CDCl_3$, 500 MHz, 50°C) –1.5 (2H, br s), 3.31–3.35 (24H, m), 3.49–3.53 (16H, m), 3.61–3.75 (48H, m), 3.86–3.90 (16H, m), 4.20–4.23 (16H, m), 5.45 (8H, br s), 6.57 (4H, br s), 6.92 (8H, br s), 7.66–7.73 (4H, br m), 8.64–8.72 (4H, br m), 9.06–9.10 (4H, br m); *m/z* (FAB) 2237, (M^+). For **5**: $\lambda(CH_2Cl_2)$/nm 705, 670, 65, 620, 422, 346; υ(KBr)/cm^{-1} 3275 (NH), 2924, 2874, 1598 δ_H ($CDCl_3$, 500 MHz, 50°C) –0.5 (2H, br s), 3.31–3.36 (48H, m), 3.47–3.82 (160H, br m), 4.06–4.12 (32H, m), 5.00–5.05 (16H, br m), 5.49–5.55 (8H, br m), 6.41–6.45 (8H, br m), 6.52–6.64 (20H, br m), 6.95 (8H, br s), 7.76–7.83 (4H, br m), 8.93–9.03 (4H, br m), 9.31–9.41 (4H, br m); *m/z* (MALDI) 4384, (M^+). For **6**: $\lambda(CH_2Cl_2)$/nm 705, 670, 65, 620, 422, 346; υ(KBr)/cm^{-1} 3275 (NH), 2924, 2874, 1598 δ_H ($CDCl_3$, 500 MHz, 50°C) –0.42 (2H, br s), 3.30–3.32 (96H, m), 3.44–3.80 (320H, br m), 3.96–4.07 (64H, m), 4.85–5.08 (48H, m), 5.54–5.56 (8H, br m), 6.30–6.74 (76H, br m), 6.95–6.98 (8H, br m), 7.80–7.87 (4H, br m), 8.93–9.05 (4H, br m), 9.47–9.64 (4H, br m); *m/z* (MALDI) 8678, (M^+). For **7**: $\lambda(CH_2Cl_2)$/nm 678, 650, 610, 352; υ(KBr)/cm^{-1} 2913, 2878, 1596; δ_H ($CDCl_3$, 500 MHz, 50°C) –0.78 (4H, s), 3.10 (8H, t), 3.33 (12H, s), 3.36 (4H, d), 3.40 (8H, t), 3.49 (8H, t), 3.65 (8H, t), 3.56–3.59 (16H, m), 5.51 (2H, t), 8.29 (8H, m), 9.55 (8H, m); *m/z* (FAB) 1403, (M^+). For **8**: $\lambda(CH_2Cl_2)$/nm

679, 650, 610, 352; υ(KBr)/cm^{-1} 2915, 2877, 1596; δ_H ($CDCl_3$, 500 MHz, 50°C) –0.70 (4H, s), 3.30 (24H, s), 3.48 (4H, d), 3.53 (16H, d), 3.63 (16H, t), 3.67 (16H, t), 3.72 (16H, t), 3.82 (16H, m), 3.96 (8H, s), 4.04 (16H, t), 5.64 (2H, t), 6.23 (8H, d), 6.36 (4H, t), 8.26 (8H, m), 9.55 (8H, m); m/z (FAB) 2476, (M^+). For **9**: λ(CH_2Cl_2)/nm 680, 650, 610, 352; υ(KBr)/cm^{-1} 2915, 2878, 1596; δ_H ($CDCl_3$, 500 MHz, 50°C) –0.72 (4H, s), 3.33 (48H, s), 3.48 (36H, m), 3.60–3.66 (64H, m), 3.69 (32H, t), 3.81 (32H, m), 3.98 (8H, s), 4.08 (32H, t), 4.90 (16H, s), 5.66 (2H, t), 6.30 (8H, d), 6.44 (12H, m), 6.54 (16H, d), 8.26 (8H, m), 9.55 (8H, m); m/z (MALDI) 4648, (M^++Na^+).

10. Crystal data for **7**: $C_{74}H_{86}N_8O_{18}Si$, $M=1403.62$, 0.05×0.15×0.60 mm, triclinic space group $P\bar{1}$ (no. 2), $a=13.064(4)$, $b=16.318(3)$, $c=8.208(2)$ Å, $\alpha=92.02(2)$, $\beta=96.05(2)$, $\gamma=79.55(2)°$, $U=1710.8(7)$ Å^3, $Z=1$, $D_c=1.362$ g cm^{-3}, $F(000)=744$, μ(Mo-K$_\alpha$)$=1.14$ cm^{-1}, $T=296$ K, $\lambda=0.71069$ Å, 6364 reflections measured, 6072 unique ($R_{int}=0.017$). The refinement (458 variables) was based on based on F converged with $R=0.062$, $R_w=0.055$ and GOF$=2.29$ using 4002 unique reflections ($I>3.0\sigma(I)$).
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