

An Approach for the Rapid Synthesis of Moderately Sized Dendritic Macromolecules

Lance J. Twyman, Anthony E. Beezer and John C. Mitchell*
The Chemical Laboratory, The University of Kent, Canterbury, Kent CT2 7NH, UK

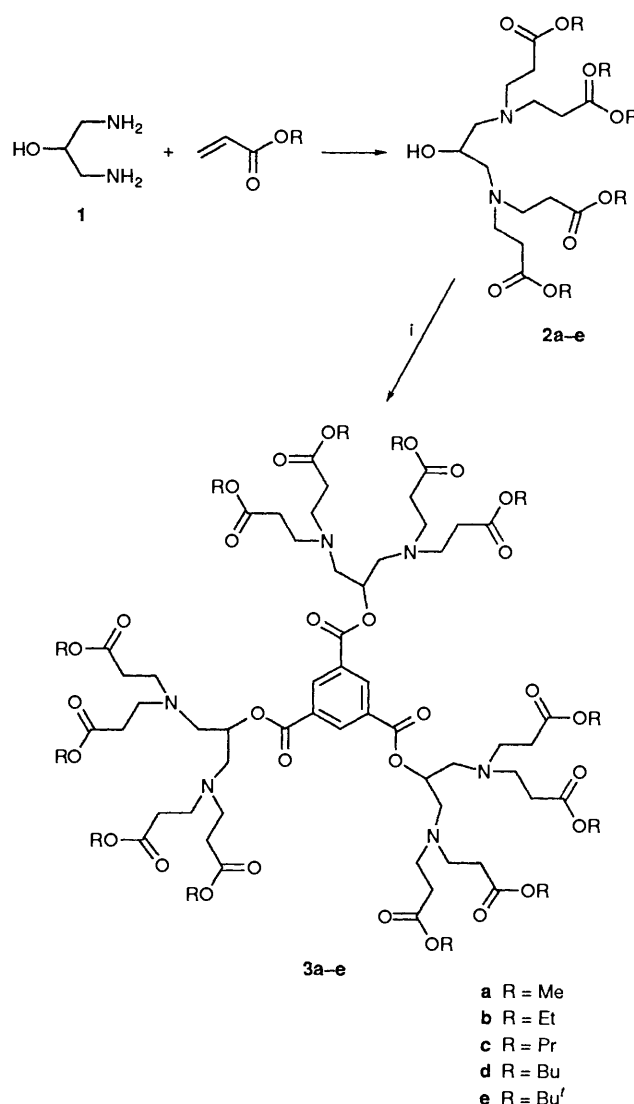
A general method for the synthesis of a dendrimeric series with homologous terminal groups is described. FABMS measurements confirm the molecular mass of the reported dendrimers. The result of size exclusion chromatographic (SEC) analysis correlates well with the relative molecular mass (RMM) of the early members of the series. However, deviations in measurements of molecular mass by SEC and FABMS begin to appear for larger members of the series, suggesting a more spherical conformation when the terminal group exceeds propyl.

The development of new macromolecules possessing highly ordered molecular architecture is currently receiving much attention. Early work on dendrimers was carried out in the mid eighties primarily by Newkome *et al.*¹ and Tomalia *et al.*,² and an excellent review on both the synthesis and theoretical implications of this early work has now appeared.³ Since that time the subject has grown dramatically and many different types of dendrimers have now appeared, these include phosphorus,⁴ silicon,⁵ organometallic⁶ and even nucleic acid based dendrimers.⁷ Early attempts at dendrimer synthesis revolved around, what is now known as the divergent approach. The principle of this method involves growth from a central core, where branching is encouraged *via* a series of repetitive steps. This method is characterised by reactions occurring at an ever increasing number of sites, with the dendrimer in effect being built up from the inside out. However, these characteristics soon led to problems with both purification and monodispersity.

More recently Frechet and Hawker have established a new synthetic technique that has been termed the convergent approach.⁸ Using this method the synthesis is started at what will ultimately become the outside of the dendrimer. The essential principle of this approach first involves the synthesis of small wedges or dendrons, these can then be brought together at a central core giving the final dendrimer. This method is characterised by reactions occurring at only one site, the focus of the dendron. Unfortunately, many of the recently reported dendrimers are based on either aromatic repeat units, which are biologically unacceptable, or require lengthy and difficult synthetic steps, that command both skill and patience. The work within our research group is targeted towards the study of both the synthesis, and the potential applications of these macromolecules, of particular interest are possible pharmacological applications. As such, we can now report a rapid and general method for the synthesis of a variety of moderately sized dendrimers *via* a convergent growth strategy.

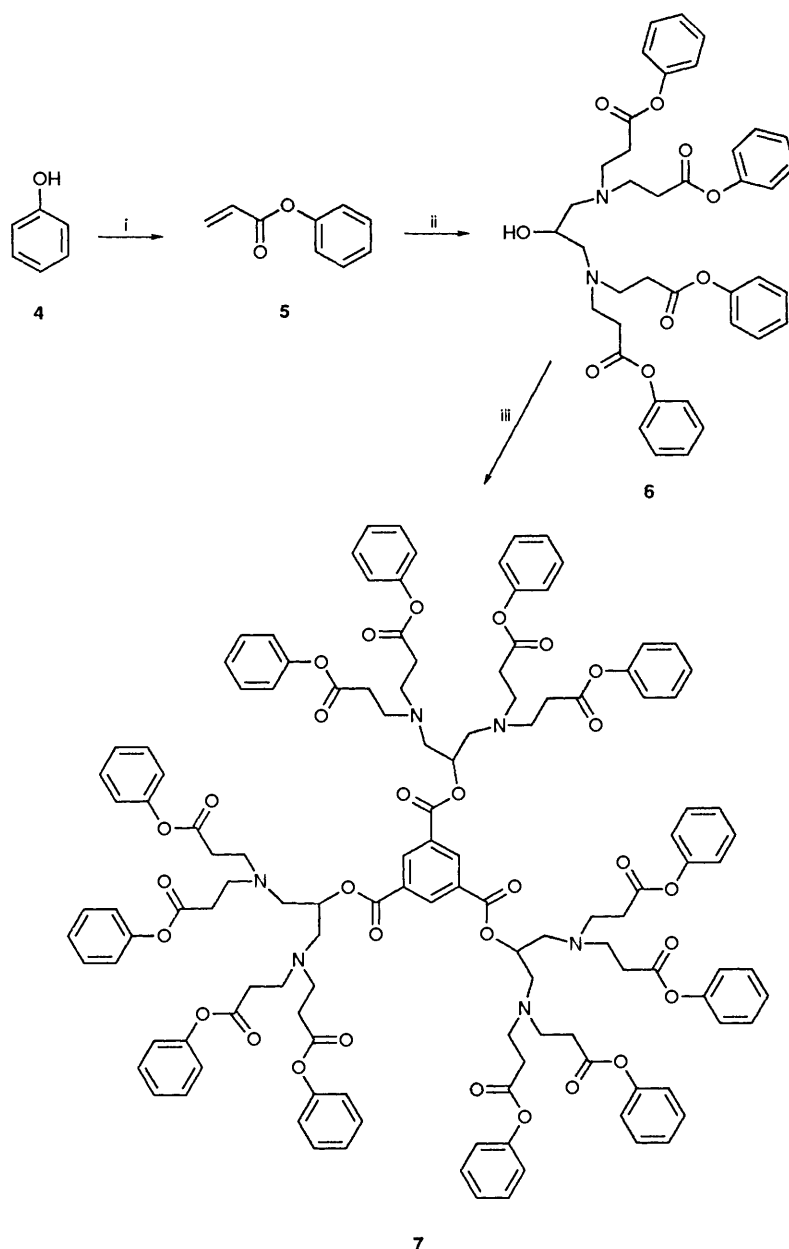
Results and Discussion

1,3-Diaminopropan-2-ol **1** was chosen as the pivotal molecule for our synthetic scheme. This molecule possesses two amine groups, giving the possibility of branching in up to four directions. The remaining alcoholic functionality is kept free, and will enable the resulting dendrons to be bound to a central core. This simple strategy first involved exhaustive Michael addition of a suitable α,β unsaturated carbonyl to the diamine **1**. The resulting dendrons can then be combined with the central core, benzene-1,3,5-tricarbonyl trichloride (Scheme 1). Following this strategy, 1,3-diaminopropan-2-ol was treated with



Scheme 1 Reagents: i, benzene-1,3,5-tricarbonyl trichloride, NEt_3 , THF

methyl acrylate in methanol, to give the desired dendron **2a** in 98% yield. The corresponding dendrimer was then prepared by combining three equivalents of the wedged dendron **2a** with the triacid chloride core in tetrahydrofuran (THF) giving the final dendrimer **3a** in 33% yield (Scheme 1).



Scheme 2 Reagents: i, acryloyl chloride, Et₂O, NEt₃; ii, 1,3-diaminopropan-2-ol, MeCN; iii, benzene-1,3,5-tricarbonyl trichloride, NEt₃, THF

Following this success, the formation of the ethyl terminated dendrimer, using the same procedure, was attempted. Ethyl acrylate was treated with 1,3-diaminopropan-2-ol in methanol, however the major product was found to be the methyl terminated dendron **2a**, and only a small amount of the expected ethyl terminated dendron **2b** could be isolated. Presumably 1,3-diaminopropan-2-ol is sufficiently basic to form a small amount of the methoxide anion in methanol. The methoxide anion is then free to attack either the ethyl terminated dendrons as they are formed, or the ethyl acrylate itself (this attack could also occur from the unionised alcohol, but such reactions are uncommon). This problem was initially overcome by substituting methanol for the corresponding alcohol, *i.e.* for the propyl terminated dendrimer propanol was used. Using this technique, ethyl **2b**, propyl **2c** and butyl **2d** dendrons were readily synthesised in 96–98% yield. The corresponding dendrimers were subsequently constructed after reaction with the central core, benzene-1,3,5-tricarbonyl tri-

chloride, to give the final products **3b**, **3c** and **3d** in 21–33% yield (Scheme 1).

This method is only suitable for alcohols with a relatively low boiling point. In order for this to be a general procedure an alternative method was required. A suitable modification might involve the use of an aprotic solvent, this would prevent the formation of the problematic alkoxide anion. In an effort to test this proposal 1,3-diaminopropan-2-ol was treated with *tert*-butyl acrylate in acetonitrile. This indeed afforded the desired dendron **2e** in 73% yield. The *tert*-butyl terminated dendrimer **3e** was then prepared, as previously described, in 27% yield (Scheme 1). To complete this dendrimeric series the synthesis of a phenyl terminated dendrimer was attempted. Before this dendron could be produced, the corresponding α , β unsaturated carbonyl, phenyl acrylate, had first to be synthesised. Phenyl acrylate **5** was prepared in excellent yield by treatment of phenol **4** with acryloyl chloride in diethyl ether. The resulting phenyl acrylate **5** was converted to the

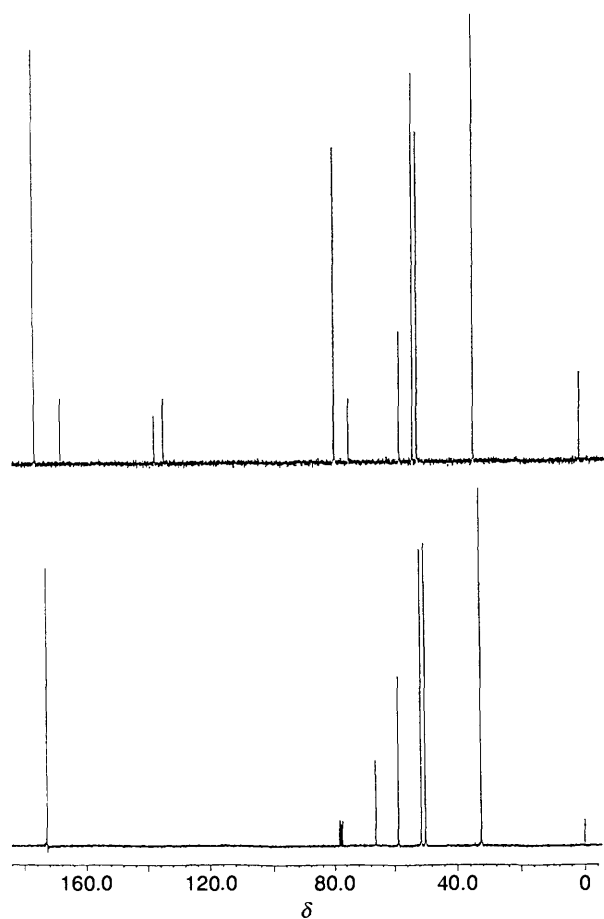


Fig. 1 Top spectrum: ^{13}C NMR of methyl terminated dendrimer **3a**. Bottom spectrum: ^{13}C NMR of methyl terminated dendron **2a**.

phenyl terminated dendron **6** by treatment with 1,3-diaminopropan-2-ol in acetonitrile, giving the desired product in 79% yield, Scheme 2.

Finally, the phenol terminated dendrimer **7** was prepared in 48% yield (crude), using the same triacid chloride central core. Unfortunately, the product proved unstable and some terminal phenyl ester cleavage was observed (either after purification or upon storage). This was confirmed by the presence of a new peak at δ 11.52 observed in the ^1H NMR spectrum, characteristic of carboxylic acid protons. The ratio of this resonance to the remaining terminal peaks was 3:45, suggesting that one phenyl group was lost from each dendron arm. This loss was further confirmed by IR spectroscopy (see Experimental section). In an initial bid to increase the extent of branching, and provide a more pharmacologically acceptable molecule, an attempt was made to use ethylenediaminetetraacetic acid (EDTA) as the central core. The methyl terminated dendron **2a** was therefore reacted with EDTA, in dichloromethane, using 1,3-dicyclohexylcarbodiimide (DCC) as the coupling reagent. Unfortunately none of the desired product could be isolated.

Characterisation.—As with most other reported dendrimers, the high symmetry of these molecules makes structural verification by NMR spectroscopy very simple (see, for example, the ^{13}C NMR spectra of the methyl terminated dendron and dendrimer, Fig. 1). All of these dendrimers have been fully characterised by ^1H and ^{13}C NMR, IR and mass spectrometry and size exclusion chromatography (SEC). In the ^1H NMR spectrum of the wedged dendrons a quintet is observed at approximately δ 4, corresponding to the proton on

Table 1

R Group	RMM	MS (FAB)	M_w (SEC)	M_w/M_n (SEC)
Me	1460	1460 (M^+)	1389.3	1.05
Et	1628	1629 ($\text{M}^+ + \text{H}$)	1418.9	1.06
Pr	1795	1795 (M^+)	1754.3	1.05
Bu	1965	1966 ($\text{M}^+ + \text{H}$)	1711.1	1.07
Bu'	1965	1966 ($\text{M}^+ + \text{H}$)	1668.8	1.10

the tertiary carbon bearing the reactive hydroxy group. When the wedged dendrons are finally brought together onto the central aromatic core the same quintet is shifted further upfield, to around δ 5. The protons of the central aromatic core resonate as a new singlet, found between δ 8.8 and 9.0. On closer inspection, when $\text{R} = \text{Bu}$, Bu' and Ph , this singlet is split into two peaks. This splitting is observed more acutely for the phenol terminated dendrimer, when two peaks are clearly seen at δ 8.94 and 8.86, integration of these two signals shows a ratio of 2:1 respectively. The three aromatic protons are no longer equivalent, it is thought that this is due to an increased steric interaction of the dendrimeric arms, and consequently two distinct aromatic proton environments may be possible. To test this proposal the Bu terminated dendrimer, where the splitting was smallest (2.20 Hz), was heated to 50 $^\circ\text{C}$ (CDCl_3). High field NMR studies showed that the two peaks did indeed collapse into the expected singlet.

It is accepted that dendrimers can achieve a spherical configuration⁹ as both molecular weight and size reach a critical limit. This critical point is often noted as a dramatic deviation in the expected molecular weight when using SEC columns calibrated with *linear, non-spherical* calibrants.¹⁰ The results of the SEC analysis for our dendrimeric series are displayed in Table 1. The molecular weight average (M_w) as calculated from this data correlates well with the relative molecular mass (RMM) for the early members of the dendrimeric series. However, it can be seen that later members of the series deviate from this trend, suggesting, perhaps, a change in solution molecular conformation. This may reflect a more spherical conformation when the terminal group volume exceeds that of propyl. Although SEC fails to give a reasonable RMM for higher molecular weight members of this series, it can provide a means of determining polydispersity (M_w/M_n), and therefore provide an indication of purity (Table 1). Also present in Table 1 are the fast atom bombardment (FAB) mass spectrometry results. These correlate precisely with the expected relative molecular masses for the dendrimers, giving further evidence of structure.

More recently a new technique has been introduced to probe changes in solution conformation related to dendrimer size. The technique involves the use of a solvatochromic central core, where sudden changes in the UV absorbance spectrum can be observed when plotted against generation number. The change in the UV absorbance spectra occurs as a result of the dendrimer adopting a more spherical configuration.⁹ To investigate this effect in our systems we have analysed the chemical shifts of the aromatic protons of the various dendrimers. A sudden increase occurs in the resonance positions of the aromatic proton when the terminal group exceeds propyl. This suggests that when R is larger than propyl the dendrimers adopt a more spherical conformation, resulting in an increase in the position of the aromatic resonances as well as the appearance of additional resonances in the ^{13}C NMR of the butyl and *tert*-butyl terminated dendrimers.

This is further confirmed by UV measurements, where again, a striking break in absorbance is observed when R is larger than propyl (see Experimental section).

Conclusions.—The field of dendrimeric synthesis is now almost a decade old, however, little attention has been paid to the chemical and physical properties of these molecules. This is due to the difficulty in conveniently synthesising a variety of relatively large dendrimers. We have demonstrated a suitable procedure for the rapid synthesis of dendrimeric macromolecules, with molecular weights approaching 2000, employing only two synthetic steps. Moreover, for the dendrimeric species bearing a butyl, *tert*-butyl or phenyl substituent, spectral and chemical evidence suggest a spherical conformation. Work is proceeding in our laboratories to extend the branching of these dendrimers, and therefore to construct the second and third generation dendrimers. Although our use of EDTA as a central core failed, investigations are continuing with the use of other, larger tetra acid cores, as well as other coupling techniques.

Experimental

IR spectra were recorded on a Perkin-Elmer 983 IR spectrophotometer as thin films on KBr disks. ^1H NMR spectra were recorded as solutions in CDCl_3 on a JEOL FMX270 FT (270.05 MHz) spectrometer, with tetramethylsilane as internal reference. ^{13}C NMR spectra were recorded at 67.8 MHz on a JEOL FMX270 FT spectrometer, with tetramethylsilane as internal reference. J values are given in Hz. Mass spectra were obtained on a VG Autospec mass spectrometer with FAB ionisation in a matrix of 3-nitrobenzyl alcohol. Analytical TLC was performed on commercial Merck plates with silica gel GF₂₅₄ (0.25 mm thick). Silica for flash chromatography was Merck Kiesel gel 60 (230–400 mesh).

SEC was carried out on a Polymer Laboratories PLgel mixed E column, with tetrahydrofuran (THF) as solvent, connected to a Knauer refractive index detector and a Pye Unicam PU 410 computing integrator. The column was calibrated using narrow dispersity linear polystyrene standards.

General Procedure for Dendron Formation using an Alcoholic Solvent. Preparation of **2a**, **b**, **c** and **d**.—The corresponding acrylate (13 mmol) was added dropwise *via* a syringe, under a nitrogen atmosphere, to a stirred solution of 1,3-diaminopropan-2-ol (3 mmol) in the corresponding alcoholic solvent (20 cm^3) at 0 °C. The resulting solution was allowed to warm to room temperature and was stirred for a further 12 h. The solvent and excess reagents were removed under reduced pressure. The crude product was purified as outlined below.

Methyl terminated dendron 2a. This was prepared using methyl acrylate in methanol, and was purified by flash chromatography with ethyl acetate–hexane (9:1) as eluent to give the compound **2a** as a clear oil, yield 99% (Found: C, 52.5; H, 8.0; N, 6.5. $\text{C}_{19}\text{H}_{33}\text{N}_2\text{O}_9$ requires C, 52.6; H, 7.7; N, 6.5%); ν/cm^{-1} 3470, 1744 and 1178; δ_{H} 2.46 (12 H, t, CH_2N), 2.81 (8 H, m, CH_2CO), 3.66 (12 H, s, OCH_3) and 3.75 [1 H, quintet, $\text{HOCH}(\text{CH}_2)_2$]; δ_{C} 32.51, 50.04, 51.42, 58.77, 66.40 and 172.84.

Ethyl terminated dendron 3b. This was prepared using ethyl acrylate in ethanol, and was purified by flash chromatography with ethyl acetate–hexane (9:1) as eluent to give the compound **2b** as a clear oil, yield 98% (Found: C, 57.5; H, 8.2; N, 5.0. $\text{C}_{23}\text{H}_{41}\text{N}_2\text{O}_9$ requires C, 57.5; H, 8.2; N, 5.2%); ν/cm^{-1} 3478, 1744 and 1260; δ_{H} 1.23 (12 H, t, CH_2CH_3), 2.41 (12 H, t, CH_2N), 2.77 (8 H, m, CH_2CO), 3.77 (8 H, q, CH_2CH_3) and 4.08 [1 H, quintet, $\text{HOCH}(\text{CH}_2)_2$].

Propyl terminated dendron 2c. This was prepared using propyl acrylate in propanol, and was purified by flash chromatography with ethyl acetate–hexane (8:1) as eluent to give the compound **2c** as a clear oil, yield 98% (Found: C, 59.2; H, 9.2; N, 5.4. $\text{C}_{27}\text{H}_{49}\text{N}_2\text{O}_9$ requires C, 59.4; H, 9.1; N 5.1%); ν/cm^{-1} 3456, 1728 and 1182; δ_{H} 1.1 (12 H, t, CH_2CH_3), 1.4 (8 H,

m, CH_2CH_3), 2.4 (12 H, t, CH_2N), 2.77 (8 H, m, CH_2CO), 3.77 (8 H, t, $\text{CH}_2\text{CH}_2\text{CH}_3$) and 4.08 [1 H, quintet, $\text{HOCH}(\text{CH}_2)_2$].

Butyl terminated dendron 2d. This was prepared using butyl acrylate in butanol, and was purified by flash chromatography with ethyl acetate–hexane (5:1) as eluent to give the compound **2d** as a clear oil, yield 97% (Found: C, 61.6; H, 10.0; N, 4.8. $\text{C}_{31}\text{H}_{57}\text{N}_2\text{O}_9$ requires C, 61.9; H, 9.7; N, 4.7%); ν/cm^{-1} 3474, 1728 and 1184; δ_{H} 0.93 (12 H, t, CH_2CH_3), 1.49 (16 H, m, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.45 (12 H, t, CH_2N), 2.81 (8 H, m, CH_2CO), 3.75 [1 H, quintet, $\text{HOCH}(\text{CH}_2)_2$] and (8 H, t, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$).

General Procedure for Dendron Formation using Acetonitrile as Solvent. Preparation of **2e** and **6**.—A round bottomed flask was charged with 1,3-diaminopropan-2-ol (3 mmol) and acetonitrile and the resulting solution stirred at 40 °C under a nitrogen atmosphere. When all the diamino alcohol had dissolved, heating was stopped and the corresponding acrylate was added dropwise *via* syringe. The resulting solution was stirred overnight, the reaction was then deemed to be complete (TLC). The solvent was removed under reduced pressure. The crude product was then extracted into dichloromethane and washed with water. The organic layer was dried (MgSO_4) and the product was purified as outlined below.

tert-Butyl terminated dendron 2e. This was prepared using *tert*-butyl acrylate in acetonitrile, and was purified by flash chromatography with ethyl acetate–hexane (8:1) as eluent to give the compound **2e** as a clear oil, yield 73% (Found: C, 61.7; H, 9.9; N, 4.9. $\text{C}_{31}\text{H}_{57}\text{N}_2\text{O}_9$ requires C, 61.9; H, 9.8; N, 4.7%); ν/cm^{-1} 3470, 1728 and 1154; δ_{H} 1.45 (36 H, s, CH_3), 2.53 (12 H, t, CH_2N), 2.92 (8 H, m, CH_2CO) and 3.76 [1 H, quintet, $\text{HOCH}(\text{CH}_2)_2$].

Phenyl acrylate 5. An oven dried round bottomed flask equipped with a stirring bar was charged with a solution of phenol (5 g, 53 mmol) and triethylamine (5.9 g, 58 mmol) in diethyl ether (20 cm^3). Acryloyl chloride (4.8 g, 53 mmol) was added dropwise *via* syringe under a nitrogen atmosphere at –5 °C. The reaction mixture was quenched after 15 min with saturated aqueous NaHCO_3 (30 cm^3) and transferred to a separating funnel. The diethyl ether layer was washed with saturated aqueous NaHCO_3 (3 \times 30 cm^3) and water (3 \times 30 cm^3) before being dried (MgSO_4) and then concentrated under reduced pressure. The crude product was purified by vacuum distillation giving the compound **6** as a clear liquid, yield 91%, b.p. 98 °C/24 mmHg (Found: C, 73.3; H, 5.5. $\text{C}_9\text{H}_8\text{O}_2$ requires C, 73.0; H, 5.4%); ν/cm^{-1} 3070, 1742, 750 and 688; δ_{H} 5.86 (1 H, dd, J_{gem} 2.5, J_{cis} 10.5), 6.29 (1 H, dd, J_{cis} 10.5, J_{trans} 17.5) and 6.49 (1 H, dd, J_{trans} 17.5, J_{gem} 2.5).

Phenyl terminated dendron 6. This was prepared using phenyl acrylate **5** in acetonitrile to give the compound **6** as a clear thick oil, yield 79%. This compound was used directly in the next stage without any further purification. ν/cm^{-1} 3342, 1750, 1196, 756 and 690; δ_{H} 2.25–3.22 (23 H, m, CH and CH_2) and 7.11 (20 H, m, Ar).

General Procedure for the Condensation of Dendrons with the Core Molecule. Preparation of **3a–e** and **7**.—Benzene-1,3,5-tricarbonyl trichloride (3 mmol) was dissolved in THF (10 cm^3). This solution was added dropwise to a stirred solution of wedged dendron **2a–e** and **6** (10 mmol) and triethylamine (10 mmol) in THF (10 cm^3) under nitrogen. Reaction was complete after 2 h. The solvent was removed under reduced pressure and the resulting slurry taken up in CH_2Cl_2 (20 cm^3) and washed with saturated aqueous NaHCO_3 (3 \times 20 cm^3) and water (3 \times 20 cm^3). The organic layer was dried (MgSO_4) and then concentrated under reduced pressure. The crude products were purified as outlined below.

Methyl terminated dendrimer 3a. This was prepared using the

methyl terminated dendron **2a**, and was purified by flash chromatography using ethyl acetate–hexane (9:1) as eluent to give the compound **2d** as a pale-honey coloured oil, yield 33% (Found: C, 54.6; H, 7.1; N, 5.8. $C_{66}H_{102}N_6O_{30}$ requires C, 54.3; H, 7.0; N, 5.8%); ν/cm^{-1} 1798, 1242, 742 and 664; δ_H 2.47 (24 H, t, NCH_2CH_2), 2.73 (12 H, m, CH_2N), 2.87 (24 H, t, NCH_2CH_2), 3.62 (36 H, s, OCH_3), 5.29 [3 H, quintet, $OCH(CH_2)_2$] and 8.83 (3 H, s, Ar). δ_C 32.51, 49.99, 51.47, 55.85, 72.40, 131.49, 134.44, 164.33 and 172.67; m/z (FAB) 1460 (M^+); λ_{max}/nm 292.3.

Ethyl terminated dendrimer 3b. This was prepared using the ethyl terminated dendron **2b**, and was purified by flash chromatography with ethyl acetate–hexane (8:1) as eluent to give the compound **3b** as a honey coloured oil, yield 31% (Found: C, 58.0; H, 8.0; N, 5.55. $C_{78}H_{126}N_6O_{30}$ requires C, 57.8; H, 7.8; N, 5.2%); ν/cm^{-1} 1728, 1242, 742 and 722; δ_H 1.99 (36 H, t, OCH_2CH_3), 2.43 (24 H, t, NCH_2CH_2), 2.79 (36 H, m, CH_2N and NCH_2CH_2), 4.02 (24 H, q, OCH_2CH_3), 5.21 [3 H, quintet, $OCH(CH_2)_2$] and 8.82 (3 H, s, Ar); δ_C 14.21, 32.59, 49.90, 55.75, 60.34, 72.26, 131.48, 134.51, 164.33 and 172.26; m/z (FAB) 1629 ($M^+ + H$), 1651 (M^+Na); λ_{max}/nm 292.9.

Propyl terminated dendrimer 3c. This was prepared using the propyl terminated dendron **2c**, and was purified by flash chromatography with ethyl acetate–hexane (6:1) as eluent to give the compound **3c** as a honey coloured oil, yield 27%; ν/cm^{-1} 1724, 1236, 740 and 682; δ_H 0.92 (36 H, t, $CH_2CH_2CH_2$), 1.61 (24 H, sextet, $CH_2CH_2CH_3$), 2.46 (24 H, t, NCH_2CH_2), 2.74 (12 H, m, CH_2N), 2.86 (24 H, m, $NCH_2CH_2CO_2$), 3.99 (24 H, t, CO_2CH_2), 5.28 [3 H, quintet, $OCH(CH_2)_2$] and 8.81 (3 H, s, Ar); δ_C 21.99, 32.64, 49.94, 50.07, 55.78, 65.97, 72.28, 131.57, 134.47, 164.35 and 172.34 [m/z (FAB) Found: M^+ , 1795.040 $C_{90}H_{150}N_6O_{30}$ requires, M , 1795.039]; λ_{max}/nm 291.5.

Butyl terminated dendrimer 3d. This was prepared using the butyl terminated dendron **2d**, and was purified by flash chromatography with ethyl acetate–hexane (2:1) as eluent to give the compound **3d** as a clear oil, yield 30% (Found: C, 62.5; H, 9.1; N, 4.0. $C_{102}H_{174}N_6O_{30}$ requires C, 62.4; H, 8.9; N, 4.3%); ν/cm^{-1} 1730, 1242 and 742; δ_H 0.92 (36 H, t, $CH_2CH_2CH_2CH_3$), 1.46 (48 H, m, $CH_2CH_2CH_2CH_3$), 2.46 (24 H, t, NCH_2), 2.79 (12 H, m, CH_2N), 4.03 (24 H, t, CO_2CH_2), 5.30 [3 H, quintet, $OCH(CH_2)_2$], 8.22 (1 H, s, Ar) and 8.30 (2 H, s, Ar); δ_C 13.74, 19.15, 30.70, 32.65, 49.93, 55.71, 64.23, 72.34, 131.57, 134.44, 134.53, 164.38 and 172.35; m/z (FAB) 1966 ($M^+ + H$) and 1988 (M^+Na); λ_{max}/nm 292.6.

tert-Butyl terminated dendrimer 3e. This was prepared using the *tert*-butyl terminated dendron **2e**, and was purified by flash chromatography with ethyl acetate–hexane (4:1) as eluent to give the compound **3e** as a clear oil, yield 27% (Found: C, 62.1; H, 8.85; N, 4.3. $C_{102}H_{174}N_6O_{30}$ requires C, 62.4; H, 8.9; N,

4.3%); ν/cm^{-1} 1728, 1244, 1156 and 742; δ_H 1.42 (108 H, s, Bu'), 2.38 (24 H, t, NCH_2), 2.74 (12 H, m, CH_2N), 2.82 (24 H, t, CH_2CO_2), 5.32 [3 H, quintet, $OCH(CH_2)_2$], 8.81 (1 H, s, Ar) and 8.82 (2 H, s, Ar); δ_C 28.04, 33.71, 49.98, 55.73, 80.07, 131.61, 134.49, 134.56, 164.23 and 171.57; m/z (FAB) 1966 ($M^+ + H$) 1988 (M^+Na); λ_{max}/nm 293.0.

Phenyl terminated dendrimer 7. This was prepared using the phenyl terminated dendron **6**, and gave the compound **7** as a honey coloured oil, yield 48% (crude). R_f 0.41 (ethyl acetate–hexane, 2:1); ν/cm^{-1} 1728, 1230, 1196 and 690; δ_H 2.99 (60 H, m, all CH_2), 5.58 [3 H, quintet, $OCH(CH_2)_2$], 7.38 (60 H, m, Ar *out*), 8.86 (1 H, s, Ar *in*) and 8.94 (2 H, s, Ar *in*);* m/z (FAB) no parent ion observed. On standing the IR spectrum additionally showed ν/cm^{-1} 3075, 1752 and 1690s.

* Ar *in* refers to the protons on the core phenyl group; Ar *out* refers to the protons on the terminal phenyl groups.

Acknowledgements

This research was supported by a quota award (to L. J. T.) from the SERC. We are grateful to S. Webb and N. Halliday for setting up and helping to run the SEC Equipment. We thank the SERC mass spectroscopy service, University College Swansea, for FABMS measurements.

References

- 1 G. R. Newkome, Z. Yao, G. R. Baker, V. K. Gupta, P. S. Russo and M. J. Saunders, *J. Am. Chem. Soc.*, 1986, **108**, 849.
- 2 D. A. Tomalia, H. Baker, M. Hall, G. Kallos, S. Martin, J. Roeck, J. Ryder and P. Smith; *Polym. J.*, 1985, **17**, 117.
- 3 D. A. Tomalia, A. M. Naylor and W. A. Goddard III, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 138.
- 4 K. Rengan and R. Engal, *J. Chem. Soc., Perkin Trans. 1*, 1991, 987.
- 5 A. van der Mode, *J. Chem. Soc., Chem. Commun.*, 1992, 1400.
- 6 G. R. Newkome, F. Cardullo, E. C. Constable, C. N. Moorfield and A. M. W. Cargill Thompson, *J. Chem. Soc., Chem. Commun.*, 1993, 925.
- 7 R. H. E. Hudson and M. J. Damba, *J. Am. Chem. Soc.*, 1993, **115**, 2119.
- 8 C. J. Hawker and J. M. J. Frechet, *J. Am. Chem. Soc.*, 1990, **112**, 7638.
- 9 C. J. Hawker, K. L. Wooley and J. M. J. Frechet, *J. Am. Chem. Soc.*, 1993, **115**, 4375.
- 10 (a) C. J. Hawker and J. M. J. Frechet, *Macromolecules*, 1990, **23**, 4726; (b) K. L. Wooley, C. J. Hawker and J. M. J. Frechet, *J. Am. Chem. Soc.*, 1991, **113**, 4252.

Paper 3/05468C

Received 13th September 1993

Accepted 21st October 1993