

Monodispersed Dendritic Polyesters with Removable Chain Ends: a Versatile Approach to Globular Macromolecules with Chemically Reversible Polarities

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A versatile approach to dendritic macromolecules with aromatic polyester inner structure and a readily modified hydrophobic/hydrophilic 'surface' is described. The polyester fragments are prepared by a convergent growth process involving 3,5-bis(benzyloxy)benzoic acid as the 'surface' or chain-ending moiety and trichloroethyl 3,5-dihydroxybenzoate as the monomer unit. The key esterification step is accomplished in high yield using dicyclohexylcarbodiimide and 4-dimethylaminopyridinium toluene-*p*-sulfonate as condensing agents. The coupling step is followed by activation of the new focal point by removal of the trichloroethyl ester group with zinc-acetic acid. Repetition of this two-step process leads to large dendritic fragments that may be coupled to a polyfunctional core to complete the dendritic macromolecule. The chemistry chosen for this synthesis allows for subsequent selective removal of the numerous benzyl ether chain ends by hydrogenolysis to afford a dendritic macromolecule with phenolic chain ends. Further modification of the chain ends is readily accomplished in processes that effectively transform the initially hydrophobic dendritic molecule into one that is both hydrophilic and water-soluble. These transformations of the 'surface' functionalities are also accompanied by drastic changes in glass transition behaviour.

The need for advanced materials with improved and new properties for a variety of technological applications has created a demand for both new forms of matter and for polymers that have highly controlled molecular architectures.¹ A class of polymers that fulfils both of these criteria are dendritic macromolecules which have attracted a considerable amount of attention due to their three-dimensional structure. This novel family of macromolecules is characterized by its high degree of branching which originates from a central point, a branch point at each monomer unit, and a large number of chain ends or 'surface' functional groups, resulting in a unique, controlled macromolecular architecture. Their three-dimensional structure, which becomes progressively globular as the molecular weight increases, makes these materials a new form of matter, the closest analogues being globular proteins.

The established approach^{2,3} to dendritic macromolecules has traditionally involved a divergent process in which growth is started from a polyfunctional core and continued outwards in a stepwise manner that affords larger and larger macromolecules as the process is continued. We have pioneered a convergent growth approach first described for the synthesis of dendritic polyether macromolecules,^{4,5} while others have reported dendritic polyphenylenes also prepared by a convergent growth process.⁶ The fundamental attribute of the convergent approach is that it begins at what will be the periphery of the molecule, proceeding inwards. It is this feature more than any other that allows for unparalleled control over molecular architecture.^{4,7} Additional characteristics of the convergent process include the presence of a single, unique functional group at the focal point of each dendritic fragment; and the limited number of reactive sites that are involved in each growth step—two in all convergent syntheses reported to date. Our interest in the convergent growth process stems from our initial prediction that the unique properties of these novel dendritic macromolecules would not only be a consequence of their compact and hyperbranched structures but also of their 'surface' or chain-end functionalization. However, the importance of the monomer units used to construct the

macromolecules may also play a significant role in determining the ultimate bulk properties.

While other studies involving the extension of the convergent growth approach to polyesters, the preparation of novel dendritic block copolymers,⁸ hybrid linear-dendritic copolymers,⁹ and other uncommon structures with unsymmetrical 'surface' functionalization are in progress, this report will address several significant issues. The novel monodispersed polyesters described in this study have been designed to allow an easy comparison of bulk properties with the previously described polyethers since the two families of polymers share identical benzyl ether 'surface' functionalities. In the case of the polyesters, these hydrophobic 'surface' functional groups can be removed readily by hydrogenolysis to expose a reactive layer of phenolic groups. These phenol-terminated polyesters are valuable 'perfect' models useful for comparisons of properties with the previously reported¹⁰ less regular and polydispersed hyperbranched polyesters obtained by a rapid one-step procedure. Modification of these terminal phenolic groups drastically alter the physical properties of these dendritic polyesters. While this work was in progress, a preliminary report outlining another approach to aryl ester dendrimers with fixed 'surface' functionalities has appeared.¹¹

Results and Discussion

We have recently reported⁸ the synthesis of dendritic polyester macromolecules based on 3,5-dihydroxybenzoic acid **1** by the convergent growth approach. However, the choice of benzyloxy chain ends did not allow any chemical modification of the 'surface' functional groups. To study the effect of the chain ends on the physical properties a protecting group for the reactive phenolic chain ends was required. Its selection was influenced by the reactivity of the phenyl ester bonds and by the sequence of deprotection steps, the acid being deprotected prior to the phenolic groups. Taking these factors into consideration, the terminal phenolic groups were protected as benzyl ethers since deprotection by catalytic hydrogenolysis is performed

under specific and mild conditions. For polyesters based on **1** it has been demonstrated⁸ that the trichloroethyl ester group, introduced by Woodward,¹² could be removed in high yield by reaction with zinc in tetrahydrofuran (THF)–glacial acetic acid, the benzyl ether 'surface' groups are expected to be unreactive under these conditions. Therefore, the monomer unit was trichloroethyl 3,5-dihydroxybenzoate **2** and the other starting material was chosen to be 3,5-bis(benzyloxy)benzoic acid **3**, which incorporates the 'surface' functional groups. This was also prepared from **1** by reaction with 3 equiv. of benzyl bromide **4** and sodium hydroxide followed by saponification of the resultant ester group with potassium hydroxide.

Employing the esterification chemistry¹³ that we have previously described,⁸ dicyclohexylcarbodiimide (DCC) was added to a mixture of the acid fragment **3**, diphenol **2**, and 4-dimethylaminopyridinium toluene-*p*-sulfonate (DPTS) in dichloromethane gave the desired second generation ester **5** in 82% yield after chromatographic purification. Removal of the trichloroethyl ester under standard conditions, zinc in glacial acetic acid, gave only starting material due to the insolubility of **5**. Repetition of the reaction in THF–glacial acetic acid (1:1) gave the desired acid **6** in 89% yield after purification. Reaction of 2.05 equiv. of **6** with the monomer **1** yields the third generation trichloroethyl ester **7** in 80% yield after purification by flash chromatography. Activation of the focal point group by deprotection with zinc in THF–HOAc gave the third generation acid **8** in 86% yield after purification (Scheme 1). Reaction of **8** with the monomer unit **1**, as above, gave the fourth generation trichloroethyl ester **9** in 77% yield, which was deprotected with zinc in HOAc–THF to give the acid **10** in 85% yield (Scheme 2). An interesting feature of the synthetic blueprint is that both the coupling reaction with DCC/DPTS and the deprotection of the focal point with Zn/HOAc are rapid processes requiring 15 min or less, which greatly accelerates the pace of this multi-step synthesis when compared to previously described methods.

Coupling of the dendritic fragments was carried out as shown in Scheme 3. The polyfunctional core molecule employed was 1,1,1-tris(4'-hydroxyphenyl)ethane **11** which allowed the same DCC/DPTS chemistry to be used for ester formation. In a typical reaction, coupling of 3.30 equiv. of the acid **10** with 1 equiv. of the core **11** in the presence of DCC and DPTS in dichloromethane gave the dendritic macromolecule **12** (nominal molecular formula C₆₇₇H₄₇₉O₁₃₈; nominal molecular weight 10 746) in 79% yield after purification by flash chromatography.

As was mentioned earlier, an interesting aspect of the structure of the dendritic polyester **12** is that it has the same benzyl ether 'surface' groups as the dendritic polyethers prepared previously.^{4,5} Since the internal monomer units are, at least to a certain extent, shielded by the 'surface' groups, similar properties may be expected for both **12** and the polyethers. Indeed, the solubility of both macromolecules are very similar while differing markedly from those of a corresponding dendritic polyester with ester 'surface' groups which have generally lower solubilities.⁸

Removal of the benzyl ether phenolic protecting groups by catalytic hydrogenolysis affords a phenolic-terminated dendritic polyester macromolecule. Comparison of **12** with **13** allows the effect of the 'surface' groups on the properties of dendritic macromolecules to be investigated. The hydrogenolysis of the 'surface' benzyl ether groups was performed under standard conditions by stirring a solution of **12** in tetrahydrofuran containing 10% Pd/C under an atmosphere of hydrogen for 24 h. Purification of the crude product by flash chromatography gave the dendritic polyester **13** with 48 phenolic groups at its periphery in 82% yield (Scheme 4).

A comparison of the properties of **12** and **13** revealed

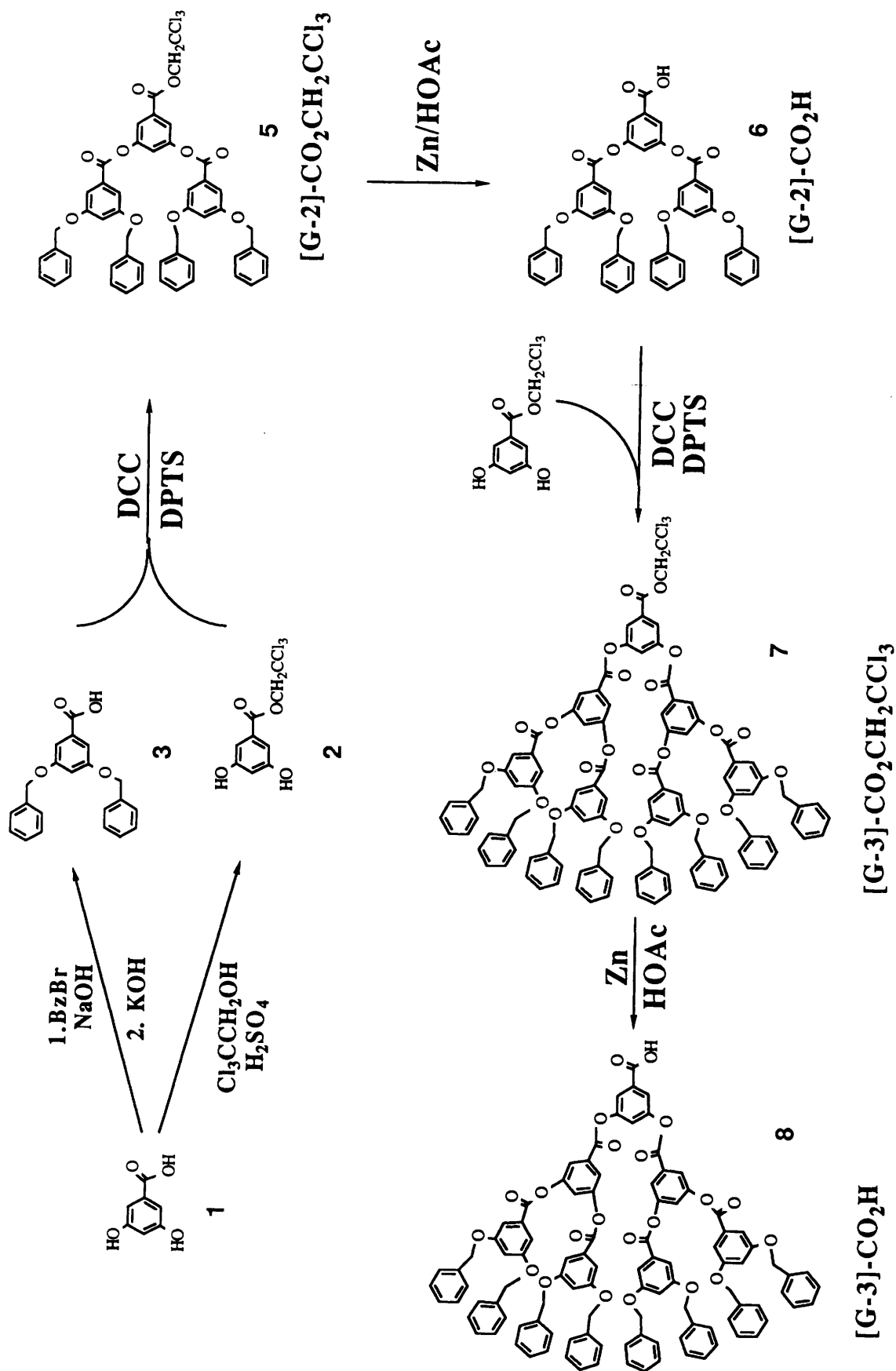
significant differences. The solubility properties of the two polyesters were drastically different. As expected, the benzyl ether terminated polyester **12** was extremely soluble in common organic solvents such as dichloromethane and tetrahydrofuran. In contrast, the phenolic terminated polyester **13**, preferred more polar solvents such as methanol and dimethyl sulfoxide in which it was highly soluble. The effect of the 'surface' functional groups on the glass transition temperature was also drastic as illustrated in Fig. 1. For the benzyl ether-terminated polyester **12** a T_g of 346 K is observed, the corresponding phenolic polyester **13** has a T_g of 474 K, while the dendritic polyether of similar molecular weight shows a T_g of 316 K. These observations demonstrate the large effect that the 'surface' functional groups have on the properties of dendritic macromolecules.

Similarly, phenolic-terminated polyesters containing 6 **14**, 12 **15**, or 24 **16** phenolic 'surface' groups were prepared from the corresponding dendritic fragments **3**, **6** and **8** respectively, by initial attachment to the core **11** followed by catalytic hydrogenolysis of the benzyl ether groups.

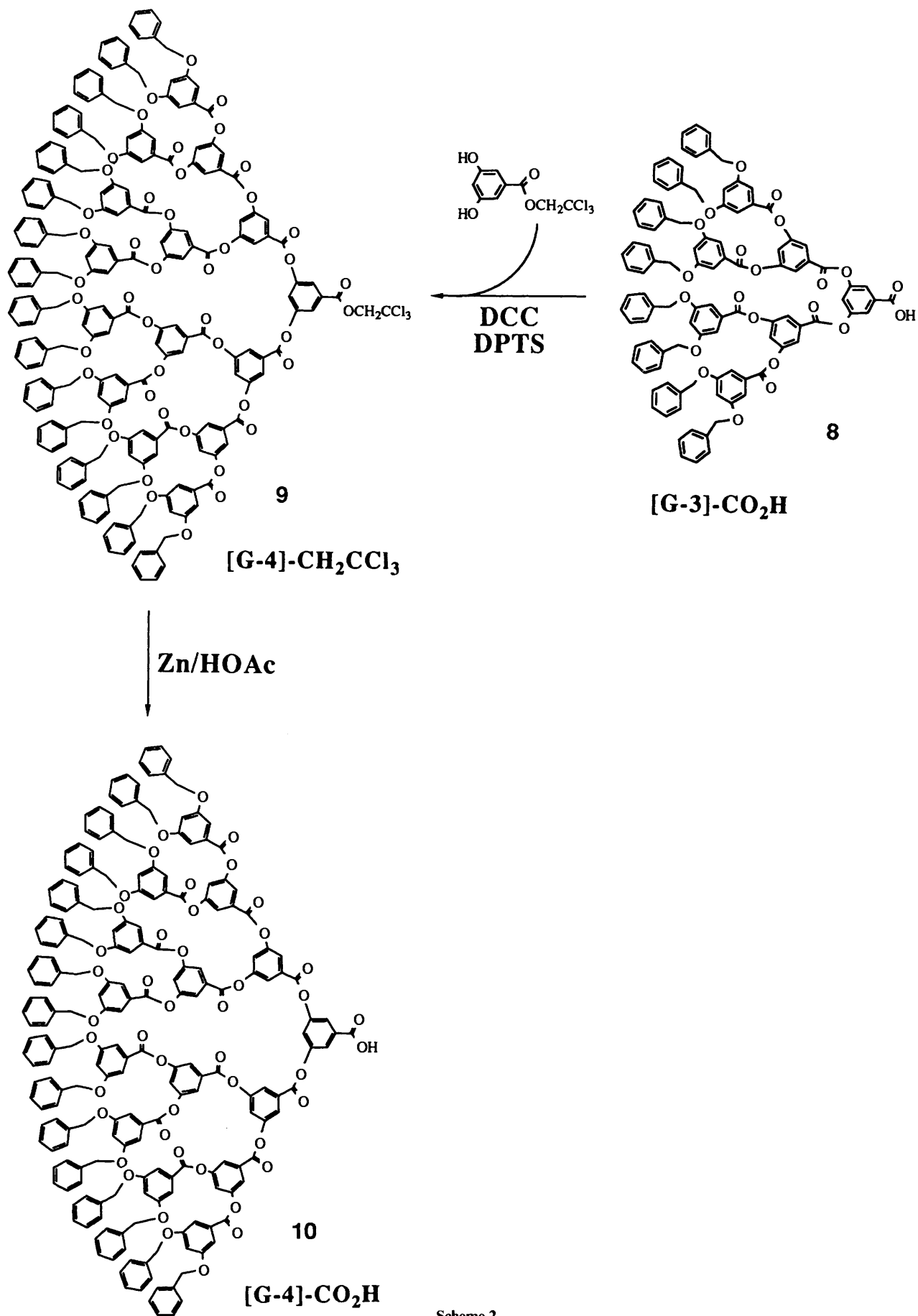
The dramatic effect of the 'surface' functional groups is further supported by the transformation of the dendritic polyesters into globular macromolecules that are water-soluble due to their ionic surfaces. This was achieved by a two-step esterification/hydrogenolysis procedure (Scheme 5). The phenolic terminated polyester **13** was treated with an excess (5.0 equiv. per phenol group) of the mono benzyl ester of adipic acid **17** in the presence of DCC and DMAP. After purification, the polyester **18** was obtained in 68% yield, **18** was shown by ¹H NMR spectroscopy to have approximately 43 of the 48 phenolic groups esterified (ca. 90% reaction of terminal groups). Incomplete functionalization of the terminal groups is a fundamental problem directly related to the large number of terminal groups to be modified. Depending on the type of reaction that is used, this may be overcome through the use of a larger excess of reagent or through a modification of the reaction conditions. Problems of this type have also been encountered in the preparation of dendritic macromolecules by the divergent or 'starburst' approach.¹⁴

Removal of the benzyl esters was performed using similar conditions to those described above for the removal of the benzyl ethers of **12**. Complete removal of the benzyl groups was shown by ¹H NMR spectroscopy and after purification by precipitation, the acid-terminated polyester **19** was obtained in 88% yield. Titration of **19** with sodium hydroxide confirmed its degree of functionalization and gave the salt **20** which was soluble in aqueous solution, similar in structure to the unimolecular micelles recently reported by Newkome.¹⁵ Addition of an excess of sodium hydroxide caused hydrolysis of the interior ester bonds. A similar set of reactions was performed on dendrimer **14** with six phenolic 'surface' groups, to give the corresponding acid derivative **21** with six terminal carboxy groups.

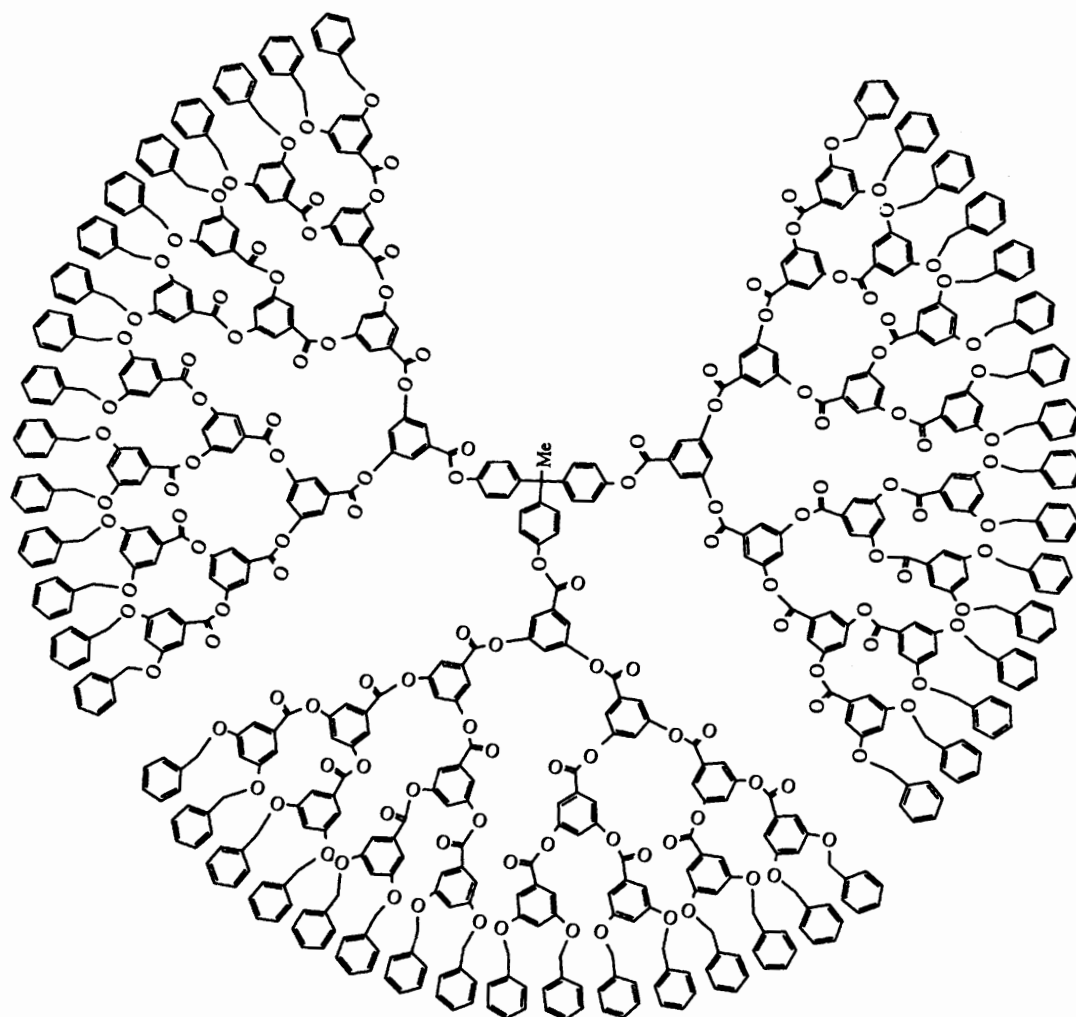
Once again, modification of the chain ends in the reaction sequence **13** → **18** → **19** results in very significant changes in glass transition temperature. The phenolic terminated polyester **13** has a glass transition temperature of 474 K, which drops to 368 K upon esterification with **17** to give the ester-terminated polyester **18**. Removal of the benzylic ester chain ends of **18** is accompanied by yet another increase in the glass transition temperature from 368 K to 491 K. Since complete functionalization of the chain ends was not achieved for **18** and **19**, the observed glass transition temperatures may be higher than for the fully functionalized derivatives due to the presence of unchanged phenolic groups. However, these findings further reinforce the suggestion^{5,7} that the 'surface' functional groups have a profound effect on the properties of dendritic macromolecules and full functionalization is not required for significant changes.



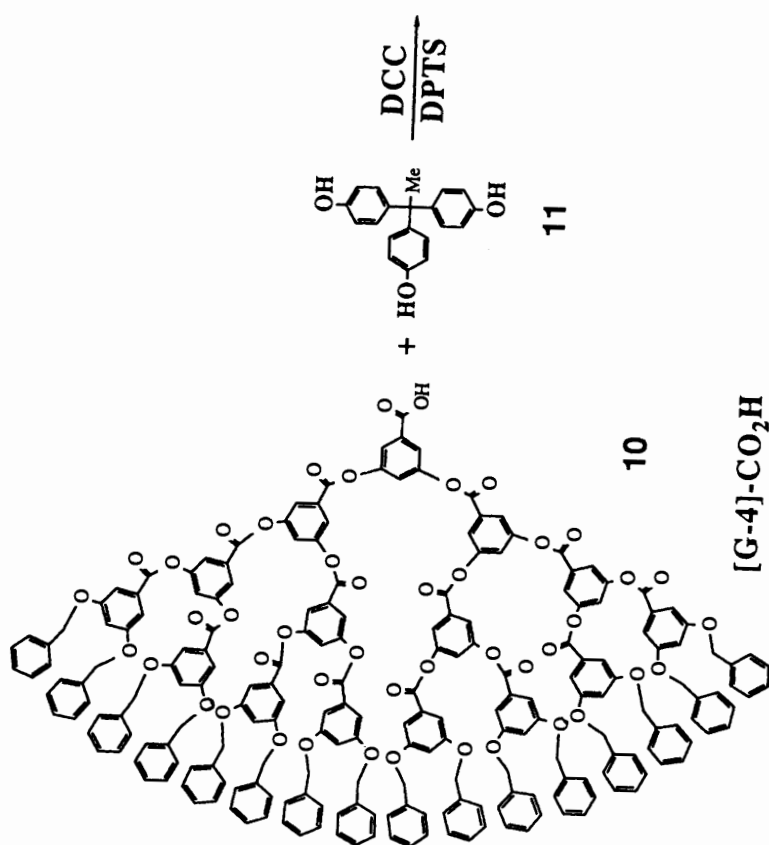
Scheme 1



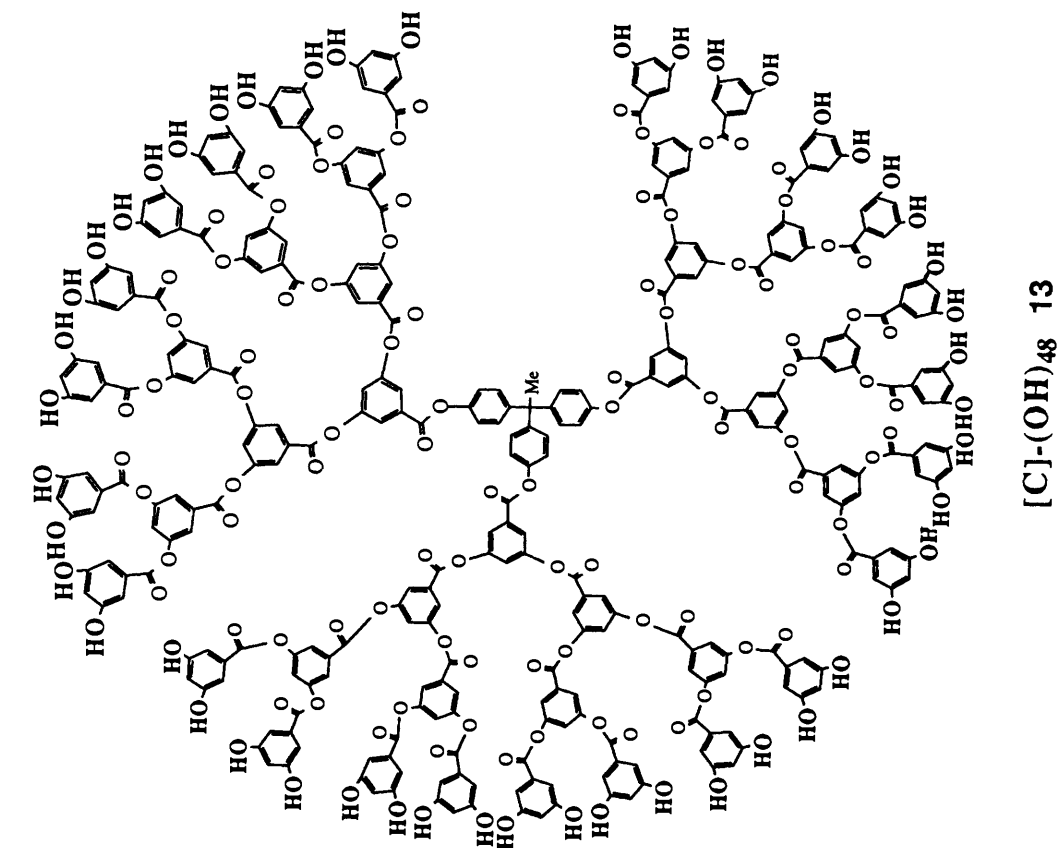
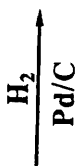
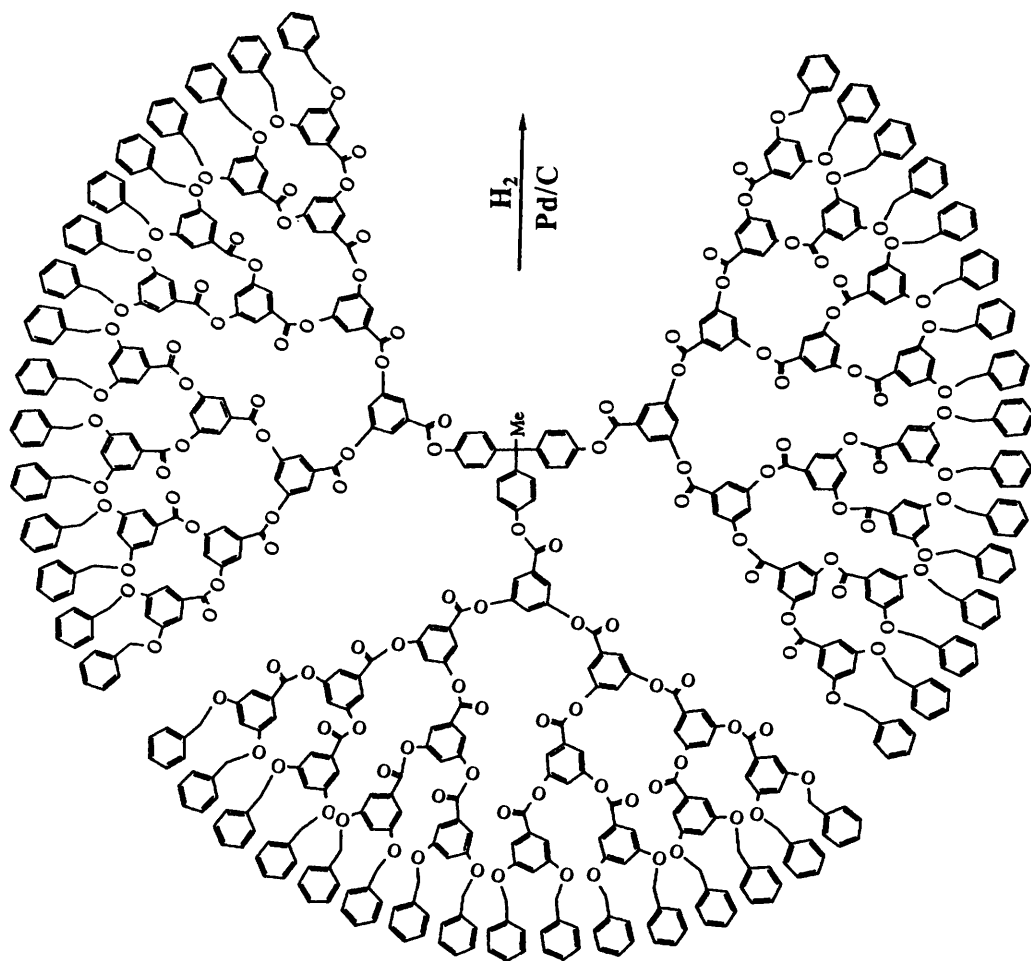
Scheme 2



[G-4]₃-[C] 12



Scheme 3

[C]-(OH)₄₈ 13[G-4]₃-[C] 12

Scheme 4

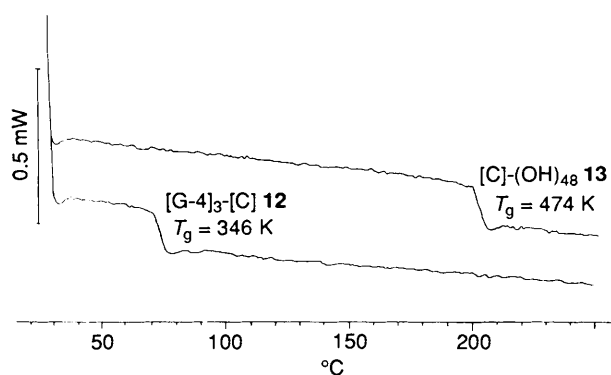


Fig. 1 Comparison of DSC traces for phenolic-terminated polyester, $[C]-(OH)_{48}$ 13, and benzyl ether-terminated polyester, $[G-4]_3-[C]$ 12

Characterization.—As with other convergent growth syntheses, 1H and ^{13}C NMR spectroscopy proved invaluable in the characterization of the final dendritic macromolecules and the intermediate dendritic fragments. The dendritic fragments could be readily identified and distinguished by the appearance and disappearance of the trichloroethyl group at the focal point. Resonances in the ^{13}C spectra were found at *ca.* 74.6 and 94.8 ppm, while the methylene protons were observed at 4.99–5.02 ppm. Integration of the resonance due to the methylene protons and comparison to other resonances in the spectrum allowed confirmation of generation number. The large difference in R_f values for the dendritic fragments having acid and ester groups at the focal point simplified their purification by flash chromatography and aided in their identification. As with the dendritic polyether macromolecules, coupling to the polyfunctional core could be readily detected since discrete resonances were observed in both the 1H and ^{13}C spectra for the core group.

Formation of the phenolic-terminated polyesters, 13–16 was readily followed by the disappearance of the resonances for the benzyl groups in the 1H NMR spectra. Fig. 2 shows the 1H NMR spectrum of 16 which has 24 phenolic groups at the periphery. The absence of a resonance at *ca.* 5.00 ppm for the CH_2 protons of the benzyl group demonstrates clearly that there are no residual benzyl groups at the chain-ends of the dendritic polyester. The presence of three doublets due to the 2-H and 6-H at 7.20, 8.08 and 8.18 ppm in the ratio 24:12:6 fully correlate with the expected structure since there are three generations, or layers, of non-equivalent monomer units in the ratio 12:6:3. Associated with the doublets are three sets of triplets for 4-H of the monomer units, and again, these correlate with the expected structure. The coupling constant for these resonances is 3 Hz. Functionalization of the phenolic-terminated polyesters with 17 and subsequent debenzoylation was readily followed by 1H NMR spectroscopy. On esterification with 17, resonances were observed at 1.65–1.90, 2.40–2.50 and 2.55–2.65 ppm for the alkyl CH_2 groups and at 5.02–5.03 ppm for the benzylic CH_2 group, areas of the spectrum not obscured by resonances for the dendritic polyester macromolecule. Integration data for these groups were used to determine the percent functionalization of the terminal groups. Removal of the benzyl groups was monitored in a manner analogous to that described above. Information from the ^{13}C NMR, IR, mass spectrometry and microanalysis provided complementary results and added further support for the proposed structures and the absence of impurities.

The purity of the dendritic polyesters were also confirmed by size exclusion chromatography (SEC). Fig. 3 shows a series of chromatograms for the various generation phenolic-terminated polyesters compared to the commercial triphenolic core molecule 11. The width of the peaks increase only slightly

on going from 11 (M , 306), to 13 (M , 6 527) and the difference in retention volumes between generations allow lower molecular weight impurities to be readily detected. The polydispersity of all the products and intermediates, as measured by SEC was less than 1.02.

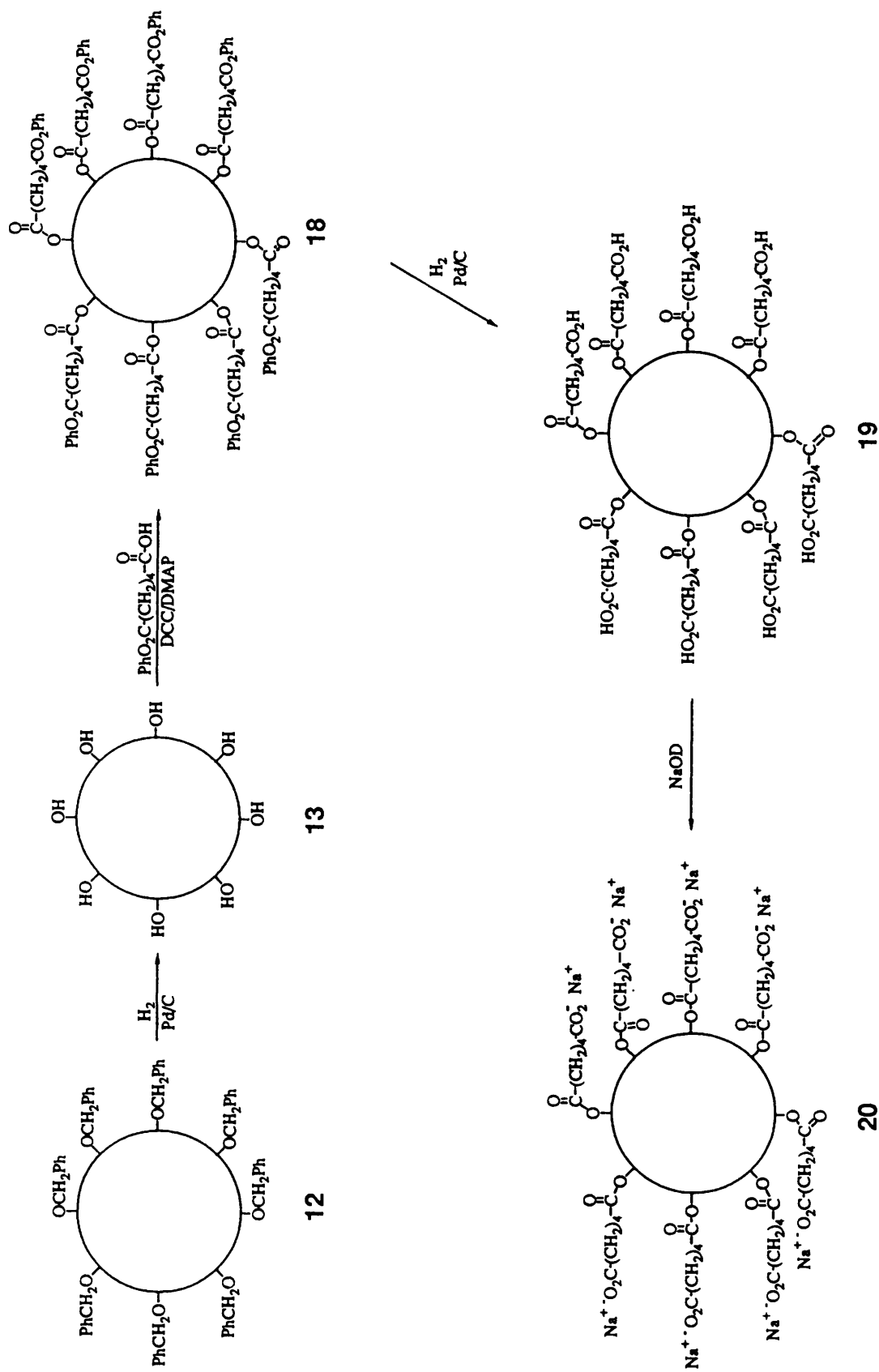
Conclusion.—The use of 3,5-bis(benzyloxy)benzoic acid as a 'surface' block has extended the convergent growth approach to the synthesis of dendritic polyester macromolecules with modifiable chain ends. The synthetic strategy employed has demonstrated the validity of a protection-deprotection approach for the modification of the chain ends of the globular macromolecules. This is particularly important for the modification of solubility and surface properties. The sequence we have demonstrated is particularly versatile since it provides access to synthetic globular molecules with highly reactive phenolic or carboxylic acid chain ends, as well as to the macromolecular mimics of micelles already demonstrated by Newkome¹⁵ using a different approach. The phenol-terminated dendritic macromolecules are also extremely useful as models for the less perfect but more readily accessible high molecular weight polyesters prepared by the one-step polycondensation approach.¹⁰

Experimental

General Directions.—Melting points and glass transition temperatures were determined on a Mettler DSC 30 thermal analysis unit. IR spectra were recorded on a Nicolet IR/44 spectrophotometer as thin films on a NaCl disks. 1H NMR spectra were recorded on solutions in $CDCl_3$, $[^2H_6]$ -acetone, or $[^2H_6]$ -DMSO on a Bruker WM 200 (200 MHz) spectrometer using the solvent proton signal as standard. ^{13}C NMR spectra were recorded at 50 MHz on a Bruker WM 200 spectrometer using $CDCl_3$, $[^2H_6]$ -acetone, or $[^2H_6]$ -DMSO as the solvent and the solvent carbon signal as internal standard. Mass spectra were obtained on a Kratos MS890 using either EI or FAB ionization; the latter were run with 3-nitrobenzyl alcohol as the matrix. Analytical TLC was performed on commercial plates coated with silica gel GF₂₅₄ (0.25 mm thick). Silica for flash chromatography was Merck Kieselgel 60 (230–400 mesh). Size exclusion chromatography was carried out on a IBM LC/9560 chromatograph connected to a Milton Roy refractoMonitor IV refractive index detector; data analysis was performed using GPC-PRO software, version 3.12 (Viscotek Corp.). Three 5 μ m PL gel columns (300 \times 7.7 mm) connected in series in order of increasing pore size (500 A, 1000 A, and mixed bed C) were used with THF as solvent. The following abbreviations are used: Ar refers to aromatic rings derived from monomer 1, Ph refers to aromatic rings derived from benzyl bromide, and Ar' refers to aromatic rings derived from the core molecule 11.

General Procedure for the Synthesis of Trichloroethyl Esters.—To a solution of the acid (10.0 mmol) in dry dichloromethane (10 cm^3) was added the diphenolic monomer unit⁸ 2 (4.8 mmol) followed by 4-dimethylaminopyridinium toluene-4-sulfonate (DPTS) (11.0 mmol) and the mixture stirred at room temperature under nitrogen for 15 min. Dicyclohexylcarbodiimide (DCC) (11.0 mmol) was then added and stirring continued at room temperature until the reaction was complete (*ca.* 15 min.); during this time a heavy precipitate of dicyclohexylurea appeared. The reaction mixture was filtered and evaporated to dryness under reduced pressure. The crude product was purified as outlined in the following text.

General Procedure for the Synthesis of Dendritic Acids.—To the trichloroethyl ester (10.0 mmol) dissolved in tetrahydrofuran (30 cm^3) was added glacial acetic acid (30 cm^3) and the



Scheme 5

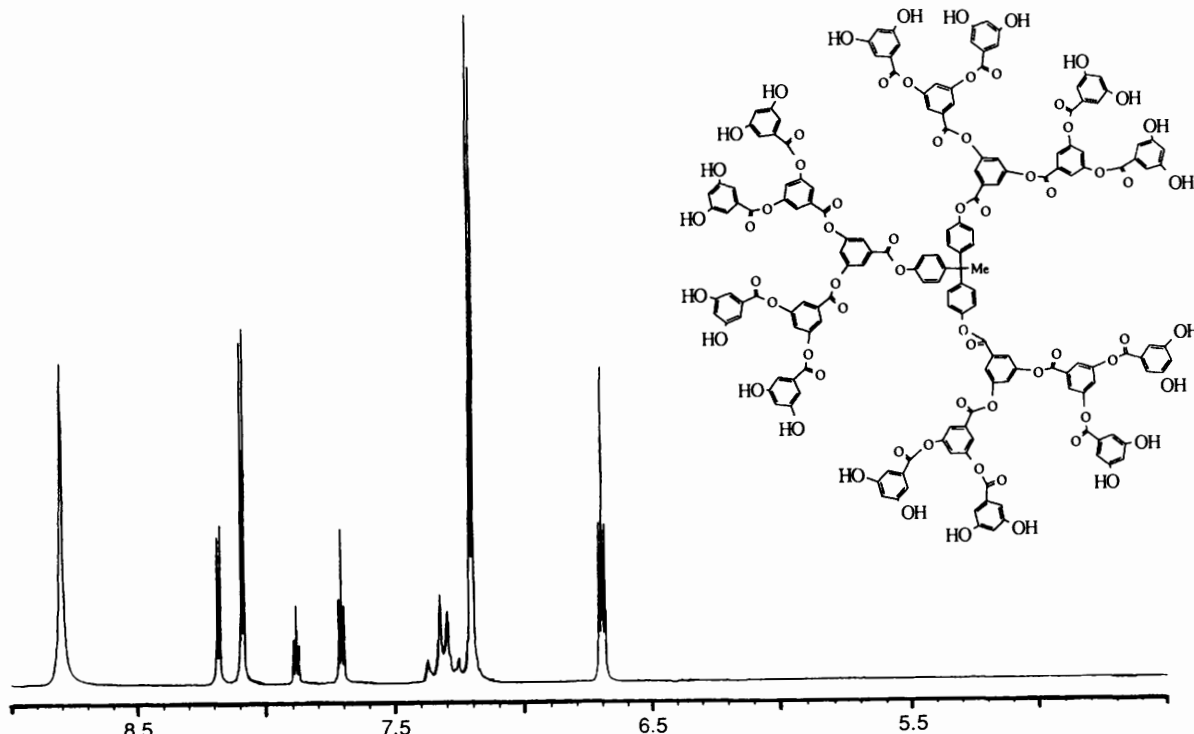


Fig. 2 ^1H NMR spectrum (4.50–9.00 ppm) of phenolic-terminated polyester, $[\text{C}]-(\text{OH})_{24}$, 16

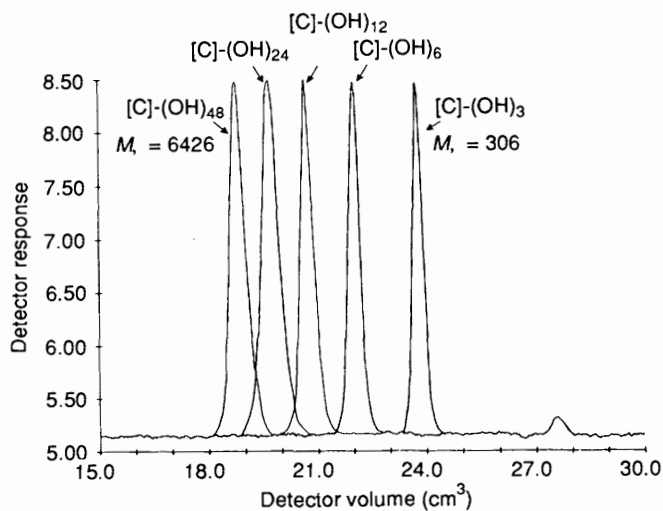


Fig. 3 Comparison of SEC traces for phenolic-terminated polyesters from $[\text{C}]-(\text{OH})_3$, 11 to $[\text{C}]-(\text{OH})_{48}$, 13

mixture stirred at room temperature under nitrogen. Zinc dust (30.0 mmol) was added and the reaction mixture stirred vigorously at room temperature for 15 min. The reaction mixture was filtered and the filtrate poured into water (300 cm³) and extracted with diethyl ether (4 × 50 cm³); the combined extracts washed with water (2 × 50 cm³), dried, and evaporated to dryness under reduced pressure. The crude product was purified by flash chromatography (dry loading recommended) as outlined in the following text.

[G-2]-CO₂CH₂CCl₃ 5. This compound was prepared from 3,5-bis(benzyloxy)benzoic acid 3 and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:2) gradually increasing to CH₂Cl₂ to give 5 as a colourless glass: yield 82%; $\nu_{\text{max}}/\text{cm}^{-1}$ 3100–2900, 1730, 1600, 1450, 1290, 1190 and 1030; $\delta_{\text{H}}(\text{CDCl}_3)$ 5.02 (s, 2 H, OCH₂CCl₃), 5.13 (s, 8 H, OCH₂Ph), 6.93 (t, 2 H, J 3, ArH), 7.35–7.51 (m, 25 H, 20 × PhH and 5 × ArH), and 7.94 (d, 2 H, J 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 70.32,

74.62, 94.82, 108.21, 109.00, 120.84, 121.73, 127.52, 128.14, 128.61, 130.50, 130.85, 136.20, 151.37, 159.90, 163.21 and 164.14; m/z (FAB), 916/918/920/922 (ca. 27:27:9:1) (Found: C, 66.5; H, 4.3, Cl, 11.9. Calc. for C₅₁H₃₉Cl₃O₁₀: C, 66.71; H, 4.28; Cl, 11.58%).

[G-2]-CO₂H 6. This compound was prepared from **[G-2]-CO₂CH₂CCl₃ 5** and purified by flash chromatography eluting with CH₂Cl₂ gradually increasing to diethyl ether to give 6 as a colourless glass: yield 89%, $\nu_{\text{max}}/\text{cm}^{-1}$ 3400–2500, 1710, 1600 and 1190; $\delta_{\text{H}}([\text{C}_6\text{H}_6]\text{-DMSO})$ 5.13 (s, 8 H, OCH₂Ph), 7.06 (t, 2 H, J 3, ArH), 7.33–7.49 (m, 24 H, 20 × PhH and 4 × ArH), 7.65 (t, 1 H, J 3, ArH) and 7.80 (d, 2 H, J 3, ArH); $\delta_{\text{C}}([\text{C}_6\text{H}_6]\text{-DMSO})$ 69.70, 107.82, 108.68, 120.47, 127.74, 127.96, 128.46, 130.47, 133.91, 136.57, 150.99, 159.63, 163.88 and 165.72; m/z (FAB) (Found: C, 75.1; H, 4.6. Calc. for C₄₉H₃₈O₁₀: C, 74.80; H, 4.87%).

[G-3]-CO₂CH₂CCl₃ 7. This compound was prepared from **[G-2]-CO₂H 6** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:1) gradually increasing to CH₂Cl₂ to give 7 as a colourless glass: yield 80%, $\nu_{\text{max}}/\text{cm}^{-1}$ 3100–2870, 1720, 1595, 1440 and 1050; $\delta_{\text{H}}(\text{CDCl}_3)$ 4.99 (s, 2 H, OCH₂CCl₃), 5.10 (s, 16 H, OCH₂Ph), 6.89 (t, 4 H, J 3, ArH), 7.35–7.46 (m, 51 H, 40 × PhH and 11 × ArH), 7.94 (d, 2 H, J 3 Hz, ArH) and 8.00 (d, 4 H, J 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 70.34, 74.68, 94.60, 108.29, 108.99, 121.02, 121.14, 127.57, 127.53, 128.14, 128.61, 130.47, 130.87, 131.08, 136.21, 151.47, 159.92, 162.82, 163.08 and 164.18 (Found: C, 70.7; H, 4.55; Cl, 5.6. Calc. for C₁₀₇H₇₉Cl₃O₂₂: C, 70.49; H, 4.37; Cl, 5.83%).

[G-3]-CO₂H 8. This compound was prepared from **[G-3]-CO₂CH₂CCl₃ 7** and purified by flash chromatography eluting with CH₂Cl₂ gradually increasing to diethyl ether to give 8 as a colourless glass: yield 86%, $\nu_{\text{max}}/\text{cm}^{-1}$ 3400–2550, 1705, 1595 and 1190; $\delta_{\text{H}}([\text{C}_6\text{H}_6]\text{-DMSO})$ 5.15 (s, 16 H, OCH₂Ph), 6.58 (s, 1 H, CO₂H), 7.04 (t, 4 H, J 3, ArH), 7.26–7.46 (m, 48 H, 40 × PhH and 8 × ArH), 7.70 (t, 1 H, J 3, ArH), 7.77 (t, 2 H, J 3, ArH), 7.88 (d, 2 H, J 3, ArH) and 8.03 (d, 4 H, J 3, ArH); $\delta_{\text{C}}([\text{C}_6\text{H}_6]\text{-DMSO})$ 69.72, 107.85, 108.75, 115.69, 120.58, 121.16, 127.80, 128.25, 128.48, 130.38, 133.57, 136.55, 149.79, 150.82,

151.21, 159.63, 162.79, 163.87 and 165.43; m/z (FAB) 1690 (Found: C, 74.3; H, 4.6. Calc. for $C_{105}H_{78}O_{22}$: C, 74.55; H, 4.65%).

[G-4]-CO₂CH₂CCl₃ **9**. This compound was prepared from [G-3]-CO₂H **8** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:1) gradually increasing to CH₂Cl₂ to give **9** as a colourless glass: yield 77%; $\nu_{\max}/\text{cm}^{-1}$ 3100-2900, 1715, 1600, 1445 and 1040; $\delta_{\text{H}}(\text{CDCl}_3)$ 5.02 (s, 2 H, OCH₂CCl₃), 5.12 (s, 32 H, OCH₂Ph), 6.93 (t, 8 H, *J* 3, ArH), 7.30-7.54 (m, 103 H, 80 × PhH and 23 × ArH), 7.97 (d, 2 H, *J* 3, ArH), 8.05 (d, 8 H, *J* 3, ArH) and 8.08 (d, 4 H, *J* 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 70.30, 74.63, 94.59, 108.26, 108.96, 121.02, 121.11, 127.51, 128.12, 128.14, 128.59, 130.45, 130.82, 131.07, 136.19, 151.08, 151.21, 151.45, 159.89, 162.68, 162.81, 162.94 and 164.13 (Found: C, 72.7; H, 4.6; Cl, 3.1. Calc. for $C_{219}H_{159}Cl_3O_{46}$: C, 72.40; H, 4.41; Cl, 2.93%).

[G-4]-CO₂H **10**. This compound was prepared from [G-4]-CO₂CH₂CCl₃ **9** and purified by flash chromatography eluting with CH₂Cl₂ gradually increasing to diethyl ether to give **10** as a colourless glass: yield 85%; $\nu_{\max}/\text{cm}^{-1}$ 3400-2600, 1710, 1600 and 1175; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}\text{-DMSO})$ 5.12 (s 32 H, OCH₂2Ph), 7.04 (t, 8 H, *J* 3, ArH), 7.22-7.49 (m, 96 H, 80 × PhH and 16 × ArH), 7.68 (t, 1 H, *J* 3, ArH), 7.79 (m, 6 H, ArH), 7.87 (d, 2 H, *J* 3, ArH) and 8.04 (d, 12 H, *J* 3, ArH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]}\text{-DMSO})$ 69.79, 107.92, 108.71, 115.19, 115.34, 120.55, 121.09, 127.82, 128.25, 128.43, 130.28, 130.35, 133.53, 136.39, 149.71, 149.96, 150.43, 151.25, 159.48, 162.71, 163.03, 163.88 and 165.25 (Found: C, 74.7; H, 4.6. Calc. for $C_{217}H_{158}O_{46}$: C, 74.43; H, 4.55%).

General Procedure for the Synthesis of Dendritic Triacylated Core Molecules.—To a solution of the acid (10.0 mmol) in dry dichloromethane (30 cm³) was added the triphenolic core unit **11** (3.0 mmol) followed by DPTS (11.0 mmol) and the mixture stirred at room temperature under nitrogen for 15 min. Dicyclohexylcarbodiimide (DCC) (11.0 mmol) was then added and stirring continued at room temperature until the reaction was complete (ca. 15 min); during this time dicyclohexylurea was precipitated. The reaction mixture was filtered and the filtrate evaporated to dryness under reduced pressure. The crude product was purified as outlined in the following text.

[G-1]₃-[C] **17**. This compound was prepared from 3,5-bis(benzyloxy)benzoic acid **3** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:2) gradually increasing to CH₂Cl₂ to give **17** as a colourless glass: yield 81%; $\nu_{\max}/\text{cm}^{-1}$ 1720, 1595, 1300 and 1190; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.05 (br s, 3 H, CH₃), 5.02 (s, 12 H, OCH₂Ph), 6.83 (t, 3 H, *J* 3, ArH) and 7.07-7.45 (m, 48 H, 30 × PhH, 6 × ArH, and 12 × Ar'H); $\delta_{\text{C}}(\text{CDCl}_3)$ 30.68, 51.49, 70.39, 107.59, 108.72, 120.92, 127.36, 127.67, 128.20, 129.56, 131.18, 136.27, 146.01, 148.99, 159.57 and 164.54; m/z (FAB) 1254 (Found: C, 79.5; H, 5.5. Calc. for $C_{83}H_{66}O_{12}$: C, 79.41; H, 5.30%).

[G-2]₃-[C] **18**. This compound was prepared from [G-2]-CO₂H **6** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:2) gradually increasing to CH₂Cl₂ to give **18** as a colourless glass: yield 83%; $\nu_{\max}/\text{cm}^{-1}$ 1715, 1600, 1295, 1190 and 1040; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.15 (br s, 3 H, CH₃), 5.02 (s, 24 H, OCH₂Ph), 6.83 (t, 6 H, *J* 3, ArH), 7.10 and 7.14 (ABq, 12 H, *J* 9, Ar'H), 7.22-7.42 (m, 75 H, 60 × PhH and 15 × ArH) and 7.93 (d, 6 H, *J* 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 30.81, 51.67, 70.29, 108.21, 108.94, 120.94, 127.49, 128.10, 128.57, 129.78, 130.52, 131.74, 136.19, 146.30, 148.87, 151.33, 159.89, 163.38 and 164.18 (Found: C, 76.4; H, 5.0. Calc. for $C_{167}H_{126}O_{30}$: C, 76.77; H, 4.86%).

[G-3]₃-[C] **19**. This compound was prepared from [G-3]-CO₂H **8** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:2) gradually increasing to CH₂Cl₂ to give **19** as a colourless glass: yield 74%; $\nu_{\max}/\text{cm}^{-1}$ 1710, 1600, 1190 and 1050; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.17 (br s, 3 H, CH₃), 5.06 (s, 48 H, OCH₂Ph), 6.84 (t, 12 H, *J* 2, ArH), 7.14 (m, 12 H, Ar'H), 7.27-7.50 (m,

153 H, 120 × PhH and 33 × ArH), 7.97 (d, 12 H, *J* 2, ArH) and 7.99 (d, 6 H, *J* 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 30.50, 51.43, 70.16, 108.32, 108.86, 109.02, 120.87, 127.65, 128.02, 128.48, 129.67, 130.61, 131.65, 136.15, 146.31, 148.74, 151.21, 151.38, 159.76, 159.92, 163.28, 163.42 and 164.03 (Found: C, 75.3; H, 4.7. Calc. for $C_{335}H_{246}O_{66}$: C, 75.53; H, 4.65%).

[G-4]₃-[C] **12**. This compound was prepared from [G-4]-CO₂H **10** and purified by flash chromatography eluting with CH₂Cl₂-hexane (1:2) gradually increasing to CH₂Cl₂ to give **12** as a colourless glass: yield 79%; $\nu_{\max}/\text{cm}^{-1}$ 1720, 1590, 1195 and 1040; $\delta_{\text{H}}(\text{CDCl}_3)$ 2.13 (br s, 3 H, CH₃), 5.04 (s, 96 H, OCH₂Ph), 6.83 (t, 24 H, *J* 2, ArH), 7.12 (m, 12 H, Ar'H), 7.23-7.53 (m, 309 H, 240 × PhH and 69 × ArH), 7.93 (m, 30 H, ArH) and 7.97 (d, 12 H, *J* 3, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 30.54, 51.53, 70.21, 108.38, 108.79, 109.05, 120.57, 127.68, 127.96, 128.39, 129.45, 130.56, 131.63, 136.09, 146.37, 148.67, 151.23, 151.35, 159.72, 159.89, 163.23, 163.28 and 163.99 (Found: C, 75.23; H, 4.7. Calc. for $C_{677}H_{486}O_{138}$: C, 75.14; H, 4.46%).

General Procedure for the Synthesis of Dendritic Phenolic-terminated Polyesters.—To a solution of the benzyl ether protected polyester (1.00 mmol) in dry tetrahydrofuran (10 cm³) was added 10% Pd/C (100 mg) followed by potassium carbonate (1.00 mmol) and the mixture stirred vigorously at room temperature under hydrogen for 24 h. The reaction mixture was then filtered and the filtrate evaporated to dryness under reduced pressure. The crude product was purified as outlined in the following text.

[C]-[OH]₆ **14**. This compound was prepared from [G-1]₃-[C] **17** and purified by flash chromatography eluting with diethyl ether gradually increasing to methanol-diethyl ether (1:10) to give **14** as a colourless glass: yield 90%; $\nu_{\max}/\text{cm}^{-1}$ 3500-3100, 1715, 1600 and 1195; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 2.25 (br s, 3 H, CH₃), 6.69 (t, 3 H, *J* 3, ArH), 7.19 (d, 6 H, *J* 3, ArH), 7.24 (m, 12 H, Ar'H) and 8.84 (br s, 6 H, OH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 30.66, 52.03, 108.33, 108.74, 116.19, 121.70, 130.00, 146.78, 149.85, 159.16 and 165.11; m/z (FAB) (Found: C, 69.1; H, 4.4. Calc. for $C_{41}H_{30}O_{12}$: C, 68.90; H, 4.23%).

[C]-[OH]₁₂ **15**. This compound was prepared from [G-2]₃-[C] **18** and purified by flash chromatography eluting with diethyl ether gradually increasing to methanol-diethyl ether (1:10) to give **15** as a colourless glass: yield 85%; $\nu_{\max}/\text{cm}^{-1}$ 3500-3100, 1715, 1595 and 1190; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 2.28 (br s, 3 H, CH₃), 6.70 (t, 6 H, *J* 3, ArH), 7.21 (d, 12 H, *J* 3, ArH), 7.28 and 7.34 (ABq, 12 H, *J* 9, Ar'H), 7.67 (t, 3 H, *J* 3, ArH), 8.04 (d, 6 H, *J* 3, ArH) and 8.87 (br s, 12 H, OH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 30.66, 52.17, 108.65, 108.93, 121.39, 121.77, 121.92, 130.13, 131.26, 132.25, 147.11, 149.78, 152.34, 159.29, 163.76 and 164.76 (Found: C, 65.2; H, 3.2. Calc. for $C_{83}H_{54}O_{30}$: C, 65.10; H, 3.55%).

[C]-[OH]₂₄ **16**. This compound was prepared from [G-3]-[C] **19** and purified by flash chromatography eluting with diethyl ether gradually increasing to methanol-diethyl ether (1:10) to give **16** as a colourless glass: yield 74%; $\nu_{\max}/\text{cm}^{-1}$ 3450-3100, 1710, 1600 and 1190; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 2.28 (br s, 3 H, CH₃), 6.70 (t, 12 H, *J* 3, ArH), 7.20 (d, 24 H, *J* 3, ArH), 7.27 and 7.34 (ABq, 12 H, *J* 9, Ar'H), 7.70 (t, 6 H, *J* 3, ArH), 7.88 (t, 3 H, *J* 3, ArH), 8.08 (d, 12 H, *J* 3, ArH), 8.17 (d, 6 H, *J* 3, ArH) and 8.80 (br s, 24 H, OH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 30.52, 52.19, 108.65, 108.95, 121.63, 121.80, 122.39, 130.16, 131.29, 131.74, 132.45, 147.15, 149.80, 152.13, 152.38, 159.30, 163.50, 163.67 and 164.75 (Found: C, 63.1; H, 3.3. Calc. for $C_{167}H_{102}O_{66}$: C, 63.38; H, 3.25%).

[C]-[OH]₄₈ **13**. This compound was prepared from [G-4]₃-[C] **12** and purified by flash chromatography eluting with diethyl ether gradually increasing to methanol-diethyl ether (1:5) to give **13** as a colourless glass: yield 82%; $\nu_{\max}/\text{cm}^{-1}$ 3500-3100, 1710, 1595 and 1190; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]}\text{-acetone})$ 2.24 (br s,

3 H, CH₃), 6.72 (t, 24 H, J 3, ArH), 7.19 (d, 48 H, J 3, ArH), 7.28 and 7.34 (ABq, 12 H, J 9, Ar'H), 7.72 (m, 18 H, J 3, ArH), 7.86 (t, 3 H, J 3, ArH), 8.08 (m, 36 H, J 3, ArH), 8.17 (d, 6 H, J 3, ArH) and 8.75 (br s, 48 H, OH); $\delta_{\text{H}}([^2\text{H}_6]\text{-acetone})$ 30.59, 51.99, 108.68, 108.90, 121.68, 121.80, 122.42, 130.15, 131.12, 131.54, 131.78, 132.49, 147.16, 149.80, 152.10, 152.33, 152.51, 159.32, 163.57, 163.66, 163.72 and 164.77 (Found: C, 62.0; H, 3.3. Calc. for C₃₃₅H₁₉₈O₁₃₈: C, 61.65; H, 3.06%).

General Procedure for Esterification of Phenolic Dendrimers.—To a solution of the polyester (1.00 mmol) in dry tetrahydrofuran (10 cm³) was added the monoacid **17** (5.00 equiv. per phenolic group) and 4-dimethylaminopyridine (5.25 equiv. per phenolic group). The reaction mixture was stirred at room temperature under nitrogen while a tetrahydrofuran solution of dicyclohexylcarbodiimide (5.25 equiv. per phenolic group) was added dropwise. After addition was complete stirring was continued for 24 h. The reaction mixture was then filtered and the filtrate evaporated to dryness. The crude product was purified as outlined in the following text.

[C]-(OCO[CH₂]₄CO₂CH₂Ph)₆ **22**. This compound was prepared from [C]-(OH)₆ **14** and purified by flash chromatography eluting with CH₂Cl₂ increasing to diethyl ether-CH₂Cl₂ (1:3) to give **22** as a colourless glass: yield 76%; $\nu_{\text{max}}/\text{cm}^{-1}$ 3050, 1720, 1715, 1600 and 1195; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.70–1.85 (m, 24 H, CH₂CH₂), 2.26 (br s, 3 H, CH₃), 2.42 (m, 12 H, CH₂CO), 2.59 (m, 12 H, CH₂CO), 5.03 (s, 12 H, CH₂Ph), 7.05–7.19 (complex m, 15 H, 3 × ArH and 12 × Ar'H), 7.30–7.35 (m, 30 H, PhH) and 7.84 (d, 6 H, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 24.12, 24.30, 30.87, 33.62, 33.81, 50.80, 66.26, 120.74, 120.95, 128.21, 128.53, 129.78, 131.60, 135.88, 146.32, 148.88, 151.04, 163.43, 171.09 and 173.10 (Found: C, 70.3; H, 5.7. Calc. for C₁₁₉H₁₁₄O₃₀: C, 70.6; H, 5.68%).

(HO)₅-[C]-(OCO[CH₂]₄CO₂CH₂Ph)_{4.3} **18**. This compound was prepared from [C]-(OH)_{4.8} **13** and purified by precipitation from dichloromethane into diethyl ether followed by flash chromatography eluting with CH₂Cl₂ gradually increasing to methanol-CH₂Cl₂ (1:20) to give **18** as a colourless glass: yield 68%; $\nu_{\text{max}}/\text{cm}^{-1}$ 1720, 1710, 1595 and 1190; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.65–1.90 (m, 172 H, CH₂CH₂), 2.30 (br s, 3 H, CH₃), 2.40–2.50 (m, 86 H, CH₂CO), 2.55–2.65 (m, 86 H, CH₂CO), 5.02 (br s, 86 H, CH₂Ph), 7.05–7.50 (complex m, 277 H, ArH, Ar'H and PhH) and 7.85–8.05 (m, 90 H, ArH); $\delta_{\text{C}}(\text{CDCl}_3)$ 24.15, 24.46, 30.80, 33.54, 33.96, 50.42, 66.75, 120.61, 120.82, 121.14, 128.19, 128.92, 129.30, 129.65, 129.78, 130.43, 131.60, 132.32, 135.57, 146.18, 146.94, 147.20, 148.47, 151.32, 152.07, 163.52, 163.72, 164.35, 171.02 and 173.44 (Found: C, 68.1; H, 5.2. Calc. for C₈₉₄H₈₀₀O₂₆₇: C, 67.9; H, 5.10%).

General Procedure for the Synthesis of Dendritic Acid-terminated Polyesters.—To a solution of the benzyl ester-terminated polyester (1.00 mmol) in dry tetrahydrofuran (10 cm³) was added 10% Pd/C (100 mg) and the mixture stirred vigorously at room temperature under hydrogen for 24 h. The reaction mixture was filtered and evaporated to dryness under reduced pressure. The crude product was purified as outlined in the following text.

[C]-(OCO[CH₂]₄CO₂H)₆ **21**. This compound was prepared from [C]-(OCO[CH₂]₄CO₂CH₂Ph)₆ **22** and purified by precipitation into diethyl ether give **21** as a colourless glass: yield 76%; $\nu_{\text{max}}/\text{cm}^{-1}$ 3500–2600, 1720, 1715, 1600 and 1195; $\delta_{\text{H}}([^2\text{H}_4]\text{-MeOH})$ 1.65–1.85 (m, 24 H, CH₂CH₂), 2.30 (br s, 3 H, CH₃), 2.39 (t, 12 H, J 7, CH₂CO), 2.68 (t, 12 H, J 7, CH₂CO), 7.19 and 7.24 (ABq, 12 H, J 8, Ar'H), 7.34 (t, 3 H, J 2, ArH) and 7.86 (d, 6 H, J 2, ArH); $\delta_{\text{C}}([^2\text{H}_4]\text{-MeOH})$ 24.78, 25.13, 30.98, 33.39, 33.76, 50.71, 120.67, 121.02, 129.61, 131.38,

146.41, 148.72, 150.96, 163.48, 166.28 and 171.14 (Found: C, 62.6; H, 5.4. Calc. for C₇₇H₇₈O₃₀: C, 62.3; H, 5.30%).

(HO)₅-[C]-(OCO[CH₂]₄CO₂H)_{4.3} **19**. This compound was prepared from (HO)₅-[C]-OCO[CH₂]₄CO₂CH₂Ph **18** and purified by precipitation from dichloromethane into diethyl ether to give **19** as a colourless glass: yield 68%; $\nu_{\text{max}}/\text{cm}^{-1}$ 3600–2700, 1720, 1710, 1595 and 1190; $\delta_{\text{H}}([^2\text{H}_4]\text{-MeOH})$ 1.60–1.90 (m, 172 H, CH₂CH₂), 2.30 (br s, 3 H, CH₃), 2.40–2.45 (m, 86 H, CH₂CO), 2.60–2.70 (m, 86 H, CH₂CO), 7.12–7.41 (complex m, 62 H, ArH and Ar'H) and 7.84–8.03 (m, 85 H, ArH); $\delta_{\text{C}}([^2\text{H}_4]\text{-MeOH})$ 24.26, 24.64, 30.51, 33.59, 34.11, 50.35, 120.63, 120.88, 121.09, 129.54, 129.81, 130.33, 131.51, 132.37, 146.22, 146.87, 147.17, 148.53, 151.29, 152.00, 163.59, 163.82, 164.27, 166.41 and 171.16 (Found: C, 59.5; H, 4.86. Calc. for C₅₉₃H₅₄₂O₂₆₇: C, 59.6; H, 4.57%).

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