Double-Stage Convergent Approach for the Synthesis of Functionalized Dendritic Aliphatic Polyesters Based on 2,2-Bis(hydroxymethyl)propionic Acid

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ABSTRACT: The fourth generation tridendron dendrimer based on 2,2-bis(hydroxymethyl)propionic acid (bis-MPA) with 48 hydroxyl groups was synthesized in high yields using *N*,*N*′-dicyclohexylcarbodiimide (DCC) for the coupling steps. A double-stage convergent approach reduced the number of synthetic and liquid chromatographic steps required in the synthesis and purification of the final dendrimers. The hydroxyl functional dendrimer was subjected to a variety of surface modifications by reaction with different acid chlorides. The acetonide, hydroxy, acetate, *n*-octanoate, *n*-palmitoate, and benzoate end-functionalized dendrimers showed large differences in thermal and solution behavior depending on the nature of their end groups. The glass transition temperature varied from −4 °C for the acetate-terminated dendrimer to +57 °C for the hydroxyl-functionalized dendrimer. Dendrimers terminated with long alkyl chains were highly soluble in hexane and dichloromethane and poorly soluble in water and methanol whereas the hydroxy-terminated dendrimer showed the opposite solution behavior. All surface modified dendrimers were amorphous according to differential scanning calorimetry (DSC) except for the *n*-palmitoate-terminated dendrimer that showed a distinct melting transition at +28 °C in its DSC trace due to the crystallization of the long alkyl chains.

Introduction

Following the early work of Tomalia et al.[1] and Newkome et al.[2] well-defined highly branched structures represented by dendrimers have gained much attention. Many of the unique properties observed for dendritic macromolecules, such as viscosity[3] or thermal behavior,[4] differ significantly from those of linear polymers. A variety of applications, including, for example, molecular encapsulation,[5a,b] catalysis,[6] and polymerization initiators,[7a,b] have been shown for these highly branched globular macromolecules.

One of the intriguing properties of the dendritic architecture is the large number of end groups that may be modified to afford dendrimers with tailored chemical and physical properties. In linear polymers, the influence of end groups on physical properties such as solubility and thermal behavior is negligible at infinite molecular weight. However in dendritic polymers, the situation is quite different. The fraction of end groups approaches a final and constant high value at infinite molecular weight, and therefore, the nature of the end groups is expected to strongly influence both the solution and the thermal properties of a dendrimer.

The two different synthetic strategies employed to construct regular dendritic frameworks have involved either a divergent or a convergent growth approach. In the divergent approach the dendrimer is grown radially outward by the addition of monomers that afford regular branching around a core molecule whereas in the convergent approach growth is started from the chain ends proceeding toward a focal point to afford a monodendron that may then be coupled to the core molecule. Many successful examples have been shown in the multistep synthesis of dendrimers by both the divergent[1,2a,8] and the convergent growth.[9]

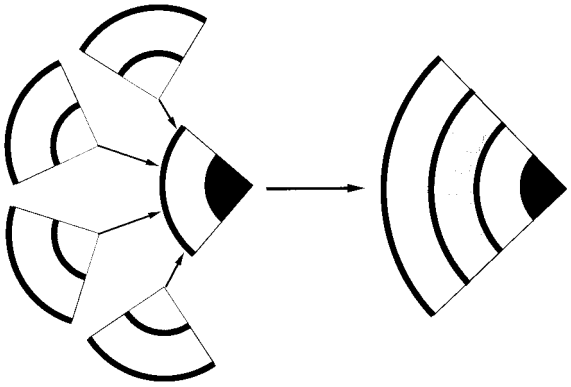

Figure 1. Schematic representation of a *double-stage convergent* synthesis of the fourth generation monodendron.

Considering the large number of steps involved in the synthesis and purification of higher generation dendrimers, it is desirable to reduce the number of synthetic steps to simplify their preparation and to improve the overall yield of the final dendrimer. This may be achieved in a double stage convergent growth approach where the focal points of the monodendrons are coupled in a divergent manner to the periphery of a monodendron or a dendrimer prepared by convergent or divergent growth (Figure 1).[10]

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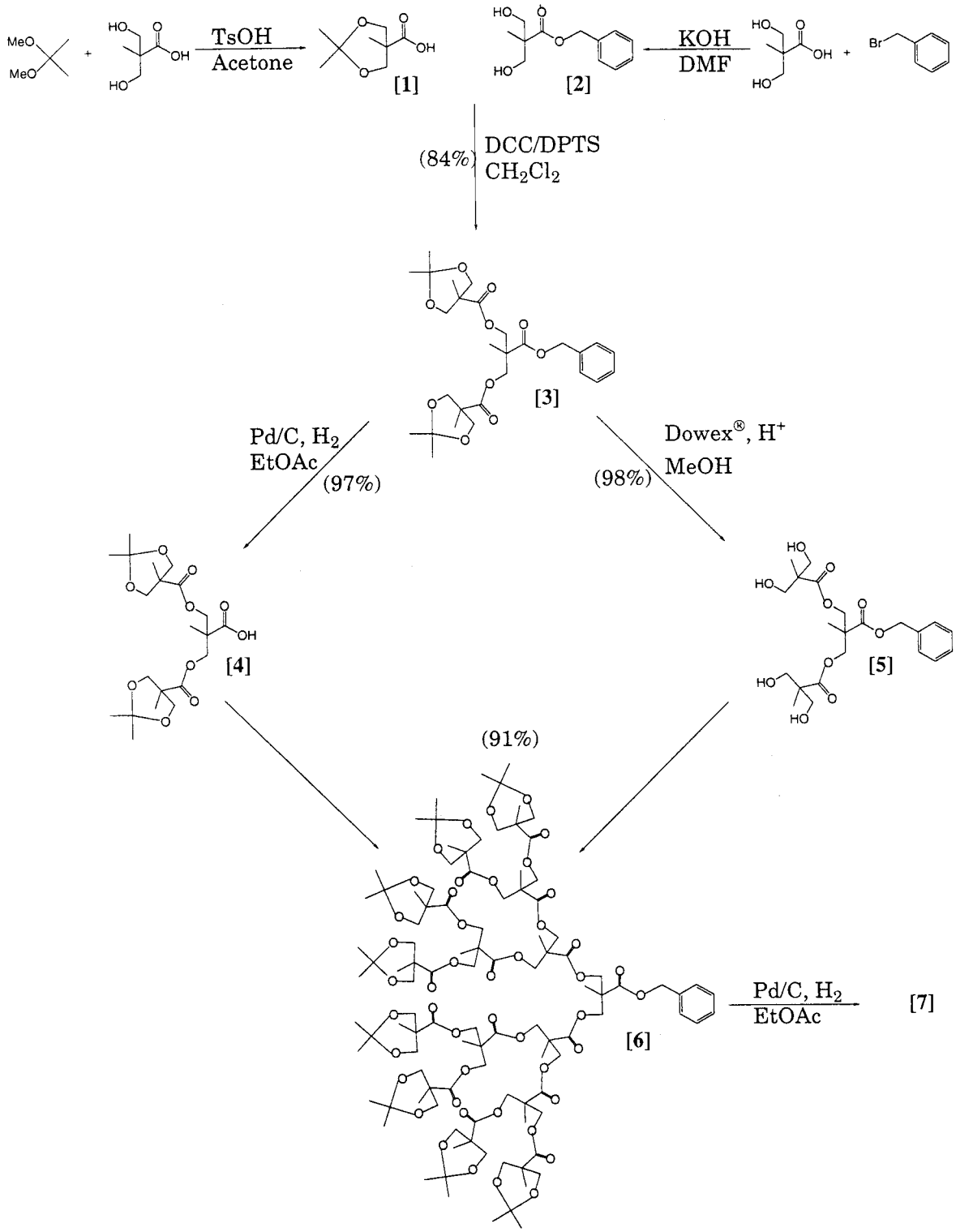
Scheme 1. Double-Stage Convergent Approach for the Synthesis of the Fourth Generation Monodendron Based on Bis-MPA



Synthesizing the fourth generation monodendron in a strict convergent approach requires *seven* synthetic steps and *three* purifications by column chromatography. A hypothetic divergent approach in the synthesis of the fourth generation monodendron would require the same number of synthetic and purification steps. By combination of the convergent and the divergent approach in a double-stage convergent approach, the fourth generation monodendron could be synthesized in *six* steps only involving *two* purifications by column chromatography. While this reduction of the total number of steps is of some significance, the combination of convergent and divergent growth allows us to enhance the versatility of the synthesis as will be shown in the discussion below.

Here we present a double-stage convergent synthesis of the fourth generation acetonide-protected monodendron based on bis-MPA as the repeat unit. The fourth generation dendron containing 16 acetonide protected hydroxyl groups may readily be coupled to a triphenolic core and deprotected to afford a tridendron dendrimer containing 48 hydroxyl groups. Reaction of the periph-

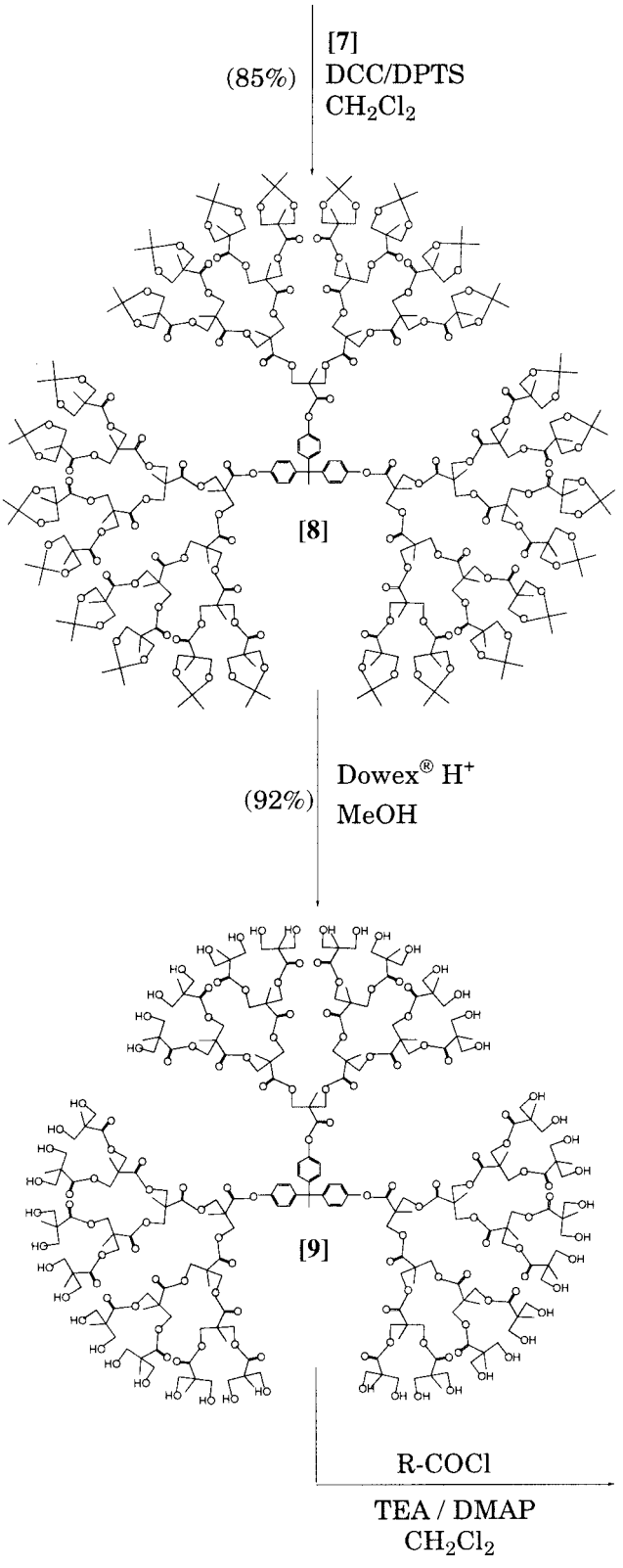
eral hydroxyl groups with different acid chlorides results in fully substituted surface-modified dendrimers with very different solution and solid-state properties.

Results and Discussion

Synthesis. In earlier work, acetate-terminated polyester dendrons based on 2,2-bis(hydroxymethyl)propionic acid (bis-MPA) ranging from generation one to four were synthesized according to a strictly convergent growth approach.[11] Attempts to selectively deprotect the acetate groups in order to obtain the corresponding hydroxyl functional dendrimers for further chemical surface modification were not successful due to the lack of selectivity in the hydrolysis of the acetate−ester groups, a process that also affected the dendritic polyester backbone. In addition a lower yield was obtained in the final coupling step of the fourth generation dendrons to the core molecule when compared to the coupling steps used to prepare lower generation dendrons. Therefore a better synthetic route was sought to allow the high yield preparation of the fourth generation hydroxyl functional dendrimer. This was achieved by a double-stage convergent growth, allowing the fourth generation hydroxyl functional tridendron dendrimer to be synthesized in nine steps involving only three purifications by column chromatography. The reduced number of steps in the new synthetic route also affords a significantly improved yield of product when compared to a strict convergent growth approach. In addition the modified synthetic route allows the selection of different protective groups for bis-MPA, allowing the selective and high yield deprotection of the fourth generation protected tridendron dendrimer at the end of the synthesis.

Therefore, the 1,3 diol moiety of bis-MPA (Scheme 1) was protected to afford acetonide group **1** by reaction of bis-MPA with 2,2-dimethoxypropane and a catalytic amount of *p*-toluenesulfonic acid (TsOH) in dry acetone. The acid group in bis-MPA was protected by a benzyl ester group. The benzyl ester of bis-MPA **2** was prepared first by forming the potassium salt of bis-MPA and then, in a second step, by reacting the salt with benzyl bromide. All esterifications were performed in dichloromethane by *N*,*N*′-dicyclohexylcarbodiimide (DCC) coupling using the catalyst 4-(dimethylamino)pyridinium *p*-toluenesulfonate (DPTS) developed by Moore and Stupp.[12] Other catalysts investigated resulted in low yields and the formation of significant amounts of *N*-acylurea, which also previously has been observed.[9d] In the general procedure for the preparation of esterdendrons, the acetonide-protected monomer **1**, the benzyl-protected monomer unit **2**, and DPTS were mixed in CH_2Cl_2 under argon atmosphere; DCC was then added as a neat reagent. After the mixture was stirred at room temperature for 20 h and purification by column chromatography on silica gel was performed, the second generation dendron **3** in was obtained in 84% yield. The benzyl ester group was selectively removed in very high yields by catalytic hydrogenolysis without affecting the ester bonds of the polyester backbone. Hydrogenolysis was performed at atmospheric pressure using 10 wt % of Pd/C (10%) as catalyst. The benzyl ester derivative was dissolved in ethyl acetate; the flask was then evacuated from air and filled with H_2. Deprotection was complete in all cases after the reaction was stirred at minimum 1000 rpm for a few hours. Removal of the benzyl ester group of **3** by catalytic hydrogenolysis gave

Scheme 2. Formation and Deprotection of the Acetonide Protected Fourth Generation Tridendron Dendrimer



the corresponding acid **4** in 97% yield. The acetonide groups can be easily deprotected under mild conditions by stirring the acetonide derivatives in methanol in the presence of an acidic Dowex 50W-X2 resin. During the trans-etherification of the acetonide groups with metha-

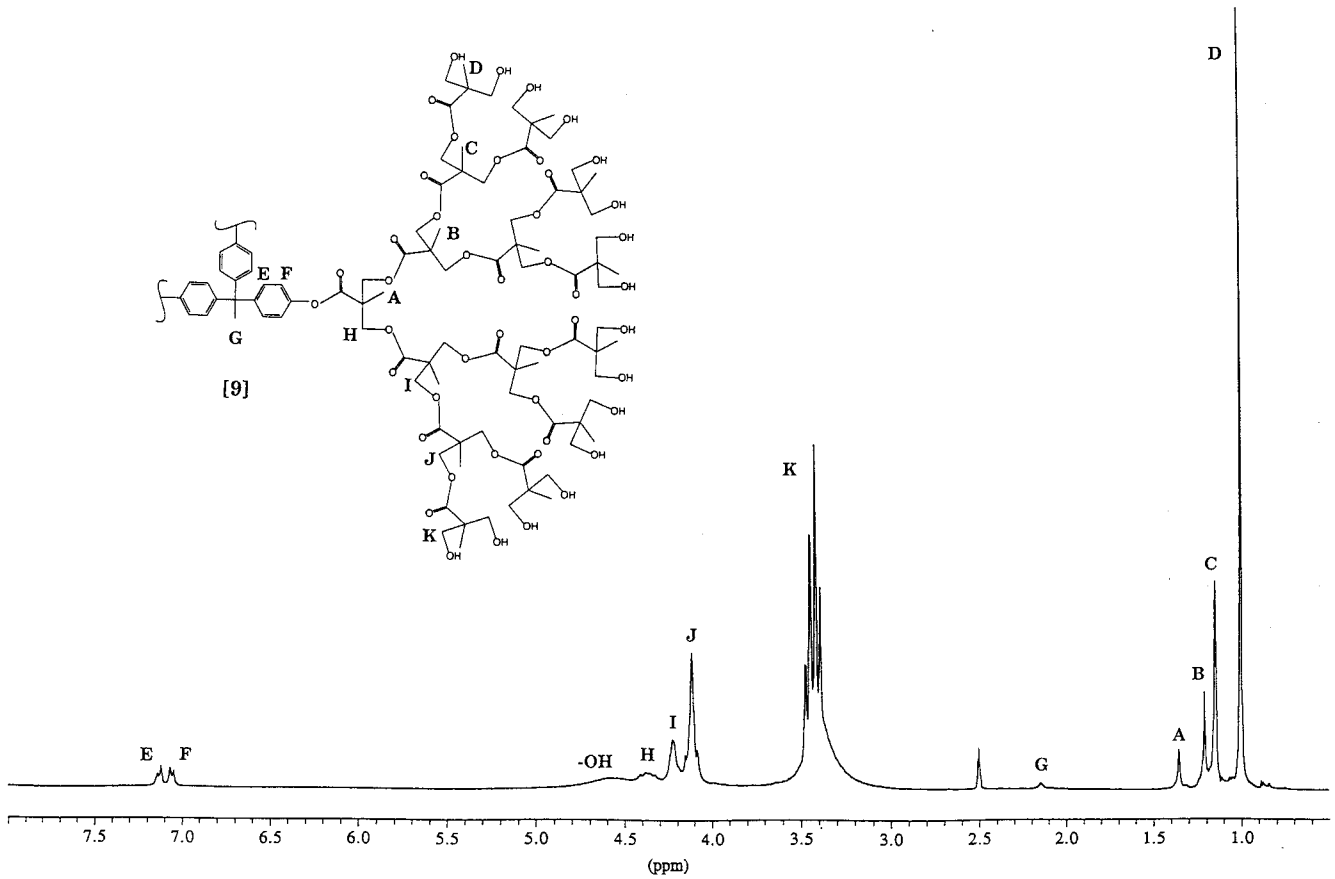


Figure 2. ^{1}H NMR spectrum in DMSO-d_6 of hydroxy functional dendritic polyester **9**.

nol, 2,2-dimethoxypropane (bp 80 °C) is formed which is easily evaporated with the rest of the solution. The deprotection reaction is easily monitored by either thin-layer chromatography (TLC) or ^{1}H NMR spectroscopy, and the product is isolated quantitatively after removal of the ion-exchange resin by filtration; deprotection of the acetonide protective group in **3** gave **5** in 98% yield. The fourth generation dendron **6** was formed in 91% yield by a double-stage coupling of compound **4** and **5** according to the general procedure for the preparation of esters. After deprotection of **6** by hydrogenolysis, the fourth generation dendron **7** was obtained in 97% yield. Compound **7** was then coupled with the core molecule 1,1,1-tris(hydroxyphenyl)ethane to give the fourth generation tridendron dendrimer **8** in 85% yield (Scheme 2). After removal of the 24 isopropylidene protective groups of **8**, the hydroxyl functional dendrimer **9** was obtained in 92% yield.

Surface Modifications. The hydroxyl functional dendrimer **9** was subjected to a variety of chain-end modifications by reaction of its hydroxyl groups with various acid chlorides (benzoyl, octanoyl, and palmitoyl chloride) in the presence of triethylamine (TEA) and 4-(dimethylamino)pyridine (DMAP) in CH_2Cl_2 to give high yields of dendrimers **10**, **11**, and **12** respectively. Surprisingly, only the fully substituted dendrimers were obtained, and no evidence for unsubstituted hydroxymethyl groups could be seen in the ^{1}H NMR or ^{13}C NMR spectra of the products. Size exclusion chromatography and elemental analyses also suggest that monodisperse structures only were obtained. A similar observation relating to the preference for the total rather than the partial modification of the chain ends of a dendrimer was made by Wooley et al.[10a] in an etherfication reaction and later by Meijer et al.[13] Attempts to perform the same chain-end functionalization by coupling of the corresponding acids and the hydroxyl functional dendrimer **9** using DCC/DPTS did not lead to the formation of the desired fully modified dendrimers. One possible explanation for this phenomenon might invoke hydrogen bonding between TEA and the hydroxyl groups of dendrimer **9**. While the hydroxyl functional dendrimer **9** has a very low solubility in CH_2Cl_2, addition of an excess of TEA helps break up aggregates of the strongly hydrogen-bonded dendrimers to afford a clear solution. As a result, reaction of the hydroxyl groups with the added acid chloride is facilitated greatly.

Table 1. SEC- and DSC Data of Surface Modified Dendritic Polyesters 8−13

surface-modified dendritic polyester	M_w (calcd)	M_w (SEC)	M_n (SEC)	T_g (°C)	T_m (°C)
acetonide (**8**)	6493	4400	4250	+24	
hydroxyl (**9**)	5532			+57	
benzoate (**10**)	10529	5740	5640	+19	
octanoate (**11**)	11589	8040	7930		
palmitoate (**12**)	16975	11200	10750		+28
acetate (**13**)	7549	4660	4440	−4	

Characterization of Dendrimers with End Groups. General Characterization. The techniques used for the characterization of dendrimers **8**−**12** were ^{1}H NMR, ^{13}C NMR, size exclusion chromatography (SEC), differential scanning calorimetry (DSC), and elemental analyses. Examination of the ^{1}H NMR spectra reveals features specially attributed to the different generations. The unique methyl resonances at 1.00, 1.15, 1.21, and 1.36 ppm shift downfield for the successive generational layers in dendrimer **9** (D, C, B, and A). All result in singlets but of significantly

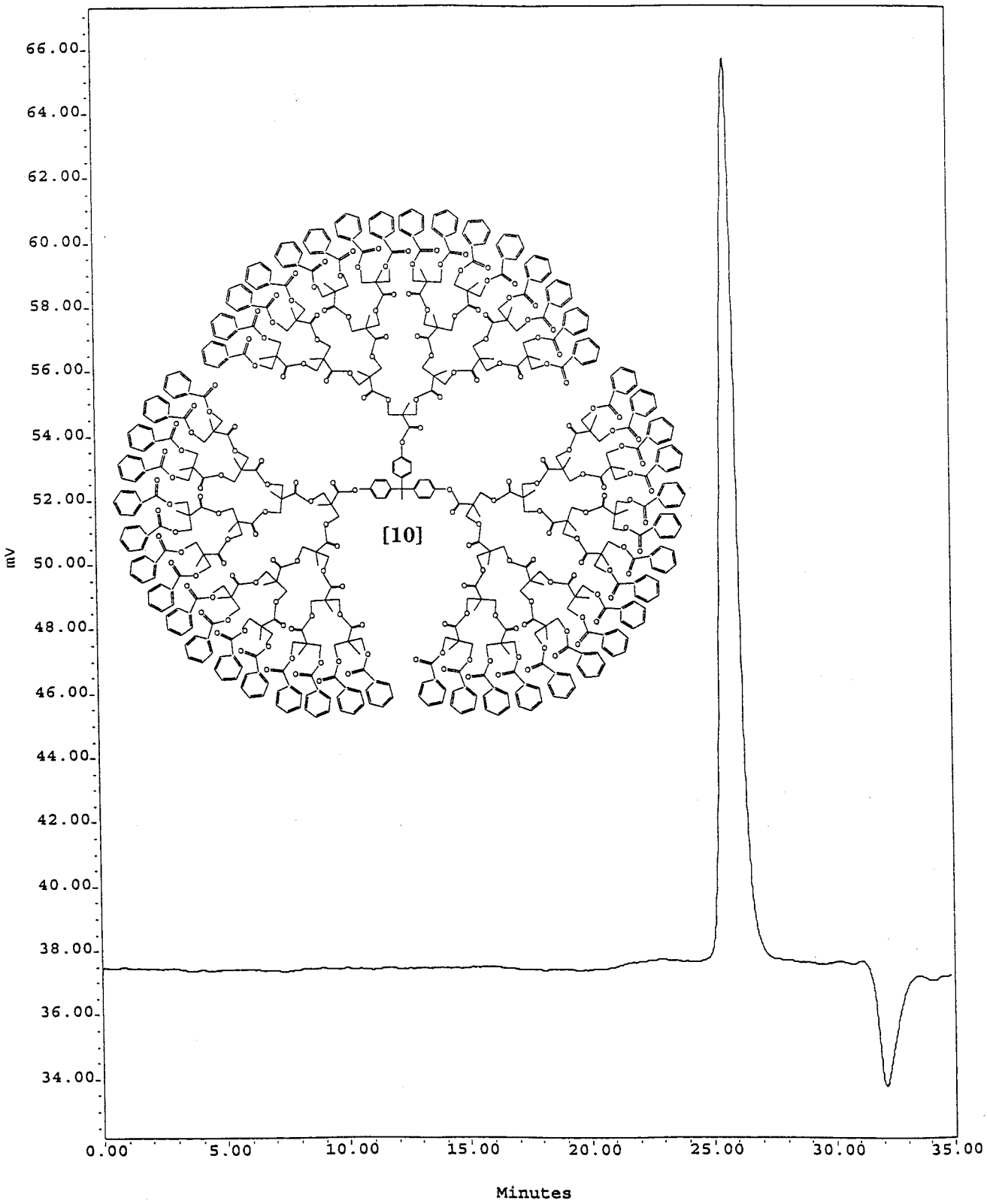


Figure 3. SEC trace of benzoate-terminated dendritic polyesters **10**.

different chemical shifts, reflecting the generation number as shown in Figure 2. The methylene resonances (H, I, J, and K) are also well separated, reflecting the different generations. In addition ^{1}H NMR spectrometry proved invaluable for the monitoring of coupling of dendrons to the core molecule since thin-layer chromatography was ineffective due to the low UV-activity of the aliphatic fragments. The symmetry of the two doublets emanating from the core molecule at 7.05−7.14 ppm (E and F) suggests a fully substituted core molecule. In contrast resonances between 6.6 and 6.8 ppm would indicate a partly substituted core molecule. As expected,[14a,b] the molecular weights determined by SEC were not in agreement with the theoretical molecular weights as seen in Table 1. This is obviously related to the globular shape adopted by these very compact

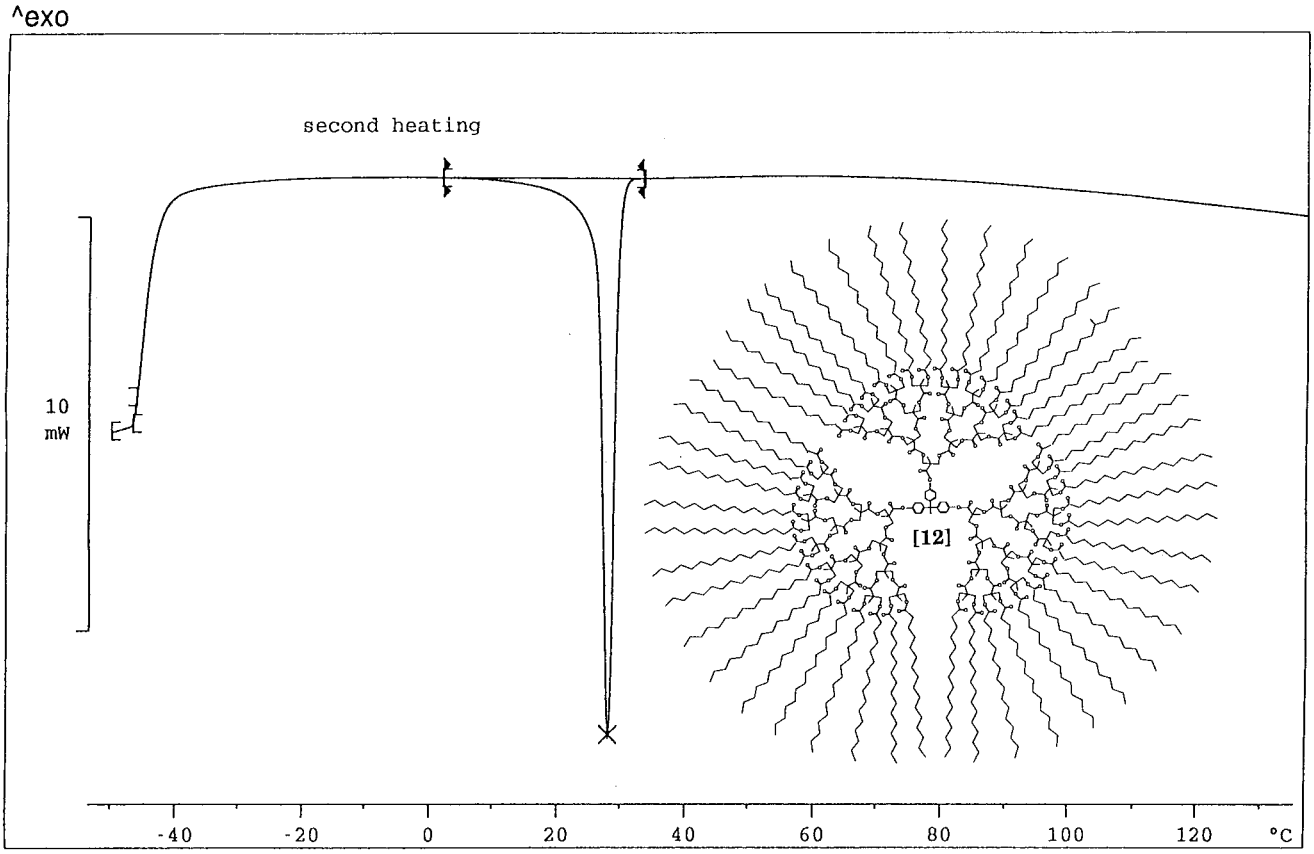


Figure 4. DSC trace of palmitoate-terminated dendritic polyester **12**.

dendrimers. However SEC analysis showed polydispersity values (M_w/M_n) below that of the linear polystyrene standards, indicating the high purity of dendrimers **8** and **10**−**12** (Figure 3). Due to interactions between the hydroxyl-functionalized dendrimer **9** and the SEC column packing material, significant peak broadening was observed and no direct SEC data could be obtained.

Characterization of Physical Properties. As expected, the nature of the end groups strongly influences the thermal and solution behavior of the various surface modified dendrimers. The acetate- and octanoate-terminated dendrimers **13** and **11** were obtained as viscous oils whereas the palmitoate-terminated dendrimer **12** was obtained as a wax. The acetonide-, hydroxyl-, and benzoate-functional dendrimers **8**, **9**, and **10** were all obtained as colorless glasses.

The acetonide-, benzoate- and acetate-terminated dendrimers **8**, **10**, and **13** were completely soluble in most organic solvents but not in water or hexane. As expected, the long alkyl chain-terminated dendrimers **11** and **12** were completely soluble in hexane and CH_2Cl_2, but insoluble in methanol and water. In contrast the hydroxyl-functionalized dendrimer **9** was soluble in water and methanol in all proportions but insoluble in both CH_2Cl_2 and hexane.

Previous experimental[4a] and theoretical studies[15] suggest that the glass transition temperature (T_g) of dendritic polymers depends mainly on the internal monomer units and the polarity and number of end groups. The thermal transition temperatures of the six differently end-capped fourth generation tridendron dendrimers are presented in Table 1. The variations in T_g correlate well with the expected behavior and an increase in the end group polarity from acetate to benzoate to hydroxyl results in an increase in T_g from −4 to +19 to +57 °C. The relatively high T_g of +24 °C measured for the less polar acetonide-terminated dendrimer **8** is likely a reflection of the restricted chain end mobility when compared to the other surface-modified dendrimers. Suprisingly the octanoate-terminated dendrimer **11** showed no thermal transition between −100 and +280 °C. In contrast to the otherwise amorphous dendrimers the palmitoate terminated dendrimer **12** showed no glass transition but a distinct melting transition at + 28 °C due to the crystallization of its linear hydrocarbon chains (Figure 4).

In a previous study, the fourth generation hyperbranched polymer based on bis-MPA was subjected to a similar modification with linear alkyl chain ends.[16] The thermal properties of the resulting palmitoate-modified hyperbranched polymer were in good agreement with findings in this study.

Conclusions

The double stage-convergent growth of dendrimers consisting of esterified bis-MPA units leads to a novel fourth generation dendritic polyester containing 48 acetonide-protected chain ends. The double stage approach used in the preparation of this polymer allows for the first time the preparation of a stable alcohol-terminated aliphatic polyester dendrimer that is highly soluble in polar solvents. Several functionalization reactions show that this versatile hydroxyl-terminated dendrimer can be readily modified. Dendritic polyesters with different glass transition temperatures, crystallinities, and solubilities could readily be designed using the hydroxyl functional dendrimer as a precursor.

Experimental Section

General Procedures. Bis-MPA was obtained from Perstorp Polyols AB, Sweden. All other chemicals were purchased from Aldrich and used without any further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400, at 400 and 100 MHz respectively, using $CDCl_3$ and DMSO-d_6 as solvent. The solvent signals were used as internal standards for both ^{1}H NMR and ^{13}C NMR recordings. All purifications were performed by medium-pressure liquid chromatography as described by Baeckström et al.[17] Size-exclusion chromatography (SEC) with double detection was performed at 45 °C on a chromatography line consisting of an M510 pump, a U6K universal injector, three 7-μm ultra-Styragel columns with pore sizes 100 and 500 Å and a linear column, a differential refractive index (DRI) detector M410, and a photodiode array (PDA) detector M991 (Waters). THF was used as eluent at a nominal flow of 1 mL/min. The molecular weights were computed using a calibration curve constructed by PSt standards with a narrow molecular weight distribution. Corrections for the flow rate fluctuation were made by using toluene as an internal standard. The thermal characteristics of the materials obtained were investigated on a differential scanning calorimetry (DSC) module from Seiko Instruments, Inc. The analysis conditions were as follows: heating/cooling rate, 10 °C /min; purging gas, nitrogen at 50 mL/min; sample containers, crimped aluminum pans. The calculations were carried out on an SSC 5200H thermal analysis station (Seiko Instruments) using Seiko thermal analysis software, Version 3.

Isopropylidene-2,2-bis(methoxy)propionic Acid (1). Bis-MPA, 10.00 g (74.55 mmol), and 13.8 mL (111.83 mmol) of 2,2-dimethoxypropane and 0.71 g (3.73 mmol) of *p*-toluenesulfonic acid monohydrate were dissolved in 50 mL of acetone. The reaction mixture was stirred for 2 h at room temperature. After the catalyst was neutralized by adding approximatively 1 mL of a NH_3/EtOH (50:50) solution, the solvent was evaporated at room temperature. The residue was then dissolved in (250 mL) CH_2Cl_2 and extracted with two portions of (20 mL) water. The organic phase was dried with $MgSO_4$ and evaporated to give **1** as white crystals: 12.0 g (92%). ^{1}H NMR ($CDCl_3$): δ 1.20 (s, 3H, $-CH_3$), 1.39 (s, 3H, $-CH_3$), 1.42 (s, 3H, $-CH_3$), 3.65 (d, 2H, $-CH_2O$), 4.18 (d, 2H, $-CH_2O$). ^{13}C NMR ($CDCl_3$): δ 18.48, 22.17, 25.03, 41.78, 65.84, 98.37, 180.40. Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 54.97; H, 8.17.

Benzyl-2,2-bis(methylol)propionate (2). Bis-MPA, 9.00 g (67.11 mmol), and 4.30 g (76.79 mmol) of KOH were dissolved in 50 mL of DMF. The potassium salt was allowed to form at 100 °C for 1 h, 13.80 g (80.71 mmol) of benzyl bromide was then added. After 15 h of stirring at 100 °C, the DMF was evaporated off. The residue was dissolved in 200 mL of CH_2Cl_2 and extracted with two portions (50 mL) of water. The crude product was recrystallized from hexane/CH_2Cl_2. **2** was obtained as white crystals: 10.0 g (67%). ^{1}H NMR ($CDCl_3$): δ 1.09 (s, 3H, $-CH_3$), 3.73 (d, 2H, $-CH_2OH$), 3.92 (d, 2H, $-CH_2OH$), 5.19 (s, 2H, $-CH_2Ar$), 7.36 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.16, 49.35, 66.64, 67.49, 127.84, 128.28, 128.63, 175.69. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.00; H, 7.17.

[G#2]-$CO_2CH_2C_6H_5$ (3) and a General Esterification Procedure. Isopropylidene-2,2-bis(methoxy)propionic acid (**1**), 3.26 g (18.70 mmol), and 2.00 g (8.92 mmol) of benzyl-2,2-bis(methylol)propionate (**2**) and 1.05 g (3.57 mmol) of DPTS were mixed in 30 mL of CH_2Cl_2. After the reaction flask was flushed with argon, 4.60 g (22.30 mmol) of DCC was added. Stirring at room temperature was continued for 15 h under argon atmosphere. Once the reaction was complete the DCC−urea was filtered off in a glass filter and washed with a small volume of CH_2Cl_2. The crude product was purified by liquid chromatography on silica gel, eluting with hexane gradually increasing to 40:60 ethyl acetate/hexane to give **3** as a colorless viscous oil: 4.00 g (84%). ^{1}H NMR ($CDCl_3$): δ 1.08 (s, 6H, $-CH_3$), 1.29 (s, 3H, $-CH_3$), 1.33 (s, 6H, $-CH_3$), 1.39 (s, 6H, $-CH_3$), 3.56 (d, 4H, $-CH_2O$), 4.09 (d, 4H, $-CH_2O$), 4.33 (s, 4H, $-CH_2C$), 5.14 (s, 2H, $-CH_2Ar$), 7.29−7.34 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.74, 18.49, 22.28, 25.00, 42.04, 46.85, 65.37, 65.95, 65.97, 66.99, 98.12, 128.25, 128.45, 128.65, 135.51, 172.43, 173.56. Anal. Calcd for $C_{28}H_{40}O_{10}$: C, 62.67; H, 7.51. Found: C, 62.48; H, 7.55.

[G#2]-COOH (4) and a General Procedure for Removal of the Benzyl Ester Group. Pd/C (10%) 0.36 g, was added to a solution of 3.60 g (6.71 mmol) of [G#2]-$CO_2CH_2C_6H_5$ (**3**) in 30 mL of ethyl acetate. The apparatus for catalytic hydrogenolysis was evacuated from air and filled with H_2. Approximatively 170 mL of H_2 were consumed. The catalyst was filtered off in a glass filter and carefully washed with ethyl acetate. The filtrate was evaporated to give **4** as white crystals: 2.90 g, (97%). ^{1}H NMR ($CDCl_3$): δ 1.11 (s, 6H, $-CH_3$), 1.27 (s, 3H, $-CH_3$), 1.31 (s, 6H, $-CH_3$), 1.37 (s, 6H, $-CH_3$), 3.58 (d, 4H, $-CH_2O$), 4.12 (d, 4H, $-CH_2O$), 4.29 (s, 4H, $-CH_2C$). ^{13}C NMR ($CDCl_3$): δ 17.67, 18.47, 22.25, 24.92, 42.04, 46.51, 65.09, 65.89, 65.92, 98.26, 173.51, 177.27. Anal. Calcd for $C_{21}H_{34}O_{10}$: C, 56.49; H, 7.68. Found: C, 56.60; H, 7.70.

$(OH)_4$-[G#2]-$CO_2CH_2C_6H_5$ (5) and a General Procedure for Removal of the Acetonide Protective Group. [G#2]-$CO_2CH_2C_6H_5$ (**3**), 4.00 g (7.45 mmol), was dissolved in 50 mL of methanol. One teaspoon of a Dowex, H^+ resin was added, and the reaction mixture was stirred for 3 h at room temperature. When the rection was complete the Dowex, H^+ resin was filtered off in a glass filter and carefully washed with methanol. The methanol was evaporated to give **5** as white crystals: 3.35 g, (98%). ^{1}H NMR ($CDCl_3$): δ 0.97 (s, 6H, $-CH_3$), 1.32 (s, 3H, $-CH_3$), 3.63−3.81 (m, 8H, $-CH_2OH$), 4.29 (d, 2H, $-CH_2C$), 4.45 (d, 2H, $-CH_2C$), 5.18 (s, 2H, $-CH_2-Ar$), 7.35 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.67, 18.47, 42.04, 46.51, 65.09, 65.89, 65.92, 173.51, 177.27. Anal. Calcd for $C_{22}H_{32}O_{10}$: C, 57.89; H, 7.07. Found: C, 57.82; H, 7.00.

[G#4]-$CO_2CH_2C_6H_5$ (6). [G#2]-COOH (**4**), 1174 mg (2.63 mmol), and 200 mg (0.44 mmol) of $(OH)_4$-[G#2]-$CO_2CH_2C_6H_5$ (**5**), 516 mg (1.75 mmol) of DPTS, and 588 mg (2.85 mmol) of DCC were allowed to react according to the general esterification procedure in 10 mL of dry CH_2Cl_2 for 48 h. The crude product was purified by liquid chromatography on silica gel, eluting with hexane gradually increasing to 80:20 ethyl acetate/hexane to give **6** as a colorless viscous oil: 870 mg (91%). ^{1}H NMR ($CDCl_3$): δ 1.09 (s, 24H, $-CH_3$), 1.14 (s, 6H, $-CH_3$), 1.22 (s, 12H, $-CH_3$), 1.26 (s, 3H, $-CH_3$), 1.30 (s, 24H, $-CH_3$), 1.37 (s, 24H, $-CH_3$), 3.57 (d, 16H, $-CH_2O$), 4.10 (d, 16H, $-CH_2O$), 4.15−4.20 (m, 16H, $-CH_2C$), 4.23−4.26 (m, 12H, $-CH_2C$), 5.12 (s, 2H, $-CH_2Ar$), 7.26−7.32 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.41, 17.50, 17.68, 18.50, 22.02, 25.25, 33.97, 42.03, 46.65, 46.74, 46.81, 64.82, 65.49, 65.92, 66.40, 67.19, 98.09, 128.11, 128.39, 128.53, 128.71, 135.43, 171.40, 171.81, 173.48. Anal. Calcd for $C_{106}H_{160}O_{46}$: C, 58.66; H, 7.43. Found: C, 58.29; H, 7.43.

[G#4]-COOH (7). [G#4]-$CO_2CH_2C_6H_5$ (**6**), 4.14 g (1.80 mmol), was dissolved in 60 mL of ethyl acetate and 0.41 g of Pd/C (10%) was added. **6** was deprotected according to the general procedure for the removal of the benzyl ester group to give **7** as a colorless viscous oil: 3.87 g, (97%). ^{1}H NMR ($CDCl_3$): δ 1.10 (s, 24H, $-CH_3$), 1.24 (s, 18H, $-CH_3$), 1.28 (s, 3H, $-CH_3$), 1.31 (s, 24H, $-CH_3$), 1.38 (s, 24H, $-CH_3$), 3.59 (d, 16H, $-CH_2O$), 4.12 (d, 16H, $-CH_2O$), 4.20−4.31 (m, 28H, $-CH_2C$). ^{13}C NMR ($CDCl_3$): δ 17.47, 17.56, 17.68, 18.49, 21.86, 25.39, 42.10, 46.06, 46.70, 46.88, 64.97, 65.71, 65.94, 65.97, 66.79, 76.79, 77.10, 77.42, 98.20, 171.49, 171.81, 173.06, 173.62. Anal. Calcd for $C_{99}H_{154}O_{46}$: C, 57.16; H, 7.46. Found: C, 56.35; H, 7.48.

[G#4]-Acetonide Tridendron Dendrimer (8). [G#4]-COOH (**7**), 7.22 g (3.19 mmol), and 272 mg (0.89 mmol) of 1,1,1-tris(hydroxyphenyl)ethane, 783 mg (2.66 mmol) of DPTS, and 732 mg (3.55 mmol) of DCC were allowed to react according to the general esterification procedure in 10 mL of dry CH_2Cl_2 for 24 h. The crude product was purified by liquid chromatography on silica gel, eluting with hexane gradually increasing to 100% ethyl acetate to give **8** as a colorless viscous oil: 5.30 g (85%). ^{1}H NMR ($CDCl_3$): δ 1.10 (s, 72H, $-CH_3$), 1.24 (s, 36H, $-CH_3$), 1.26 (s, 18H, $-CH_3$), 1.30 (s, 72H, $-CH_3$),

1.37 (s, 72H, $-CH_3$), 1.40 (s, 9H, $-CH_3$), 2.14 (s, 3H, $-CH_3$), 3.58 (d, 48H, $-CH_2C$), 4.11 (d, 48H, $-CH_2C$), 4.21−4.28 (m, 72H, $-CH_2C$), 4.31−4.39 (m, 12H, $-CH_2C$), 6.96 (d, 6H, ArH), 7.09 (d, 6H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.62, 17.73, 18.50, 22.02, 25.99, 42.04, 46.74, 46.83, 47.03, 64.79, 65.38, 65.92, 65.97, 98.09, 120.78, 129.85, 146.44, 148.58, 170.69, 171.48, 171.86, 173.48. Anal. Calcd for $C_{317}H_{474}O_{138}$: C, 58.64; H, 7.36. Found: C, 58.55; H, 7.29.

[G#4]-OH Tridendron Dendrimer (9). [G#4]-tridendron dendrimer (**8**), 4.50 g (0.64 mmol), was dissolved in 100 mL of methanol. Using the general procedure for removal of the acetonide protective group, **9** was obtained as a white glass after 48 h of reaction: 3.60 g (92%). ^1H NMR (DMSO-d_6): δ 1.00 (s, 72H, $-CH_3$), 1.15 (s, 36H, $-CH_3$), 1.21 (s, 18H, $-CH_3$), 1.36 (s, 9H, $-CH_3$), 2.15 (s, 3H, $-CH_3$), 3.43 (q, 96H, $-CH_2$-OH), 4.08−4.15 (m, 48H, $-CH_2C$), 4.22−4.21 (m, 24H, $-CH_2C$), 4.57 (br.s, 48H, −OH), 4.38 (m, 12H, $-CH_2C$), 7.06 (d, 6H, ArH), 7.13 (d, 6H, ArH). ^{13}C NMR (DMSO-d_6): δ 16.61, 16.85, 17.06, 46.17, 46.46, 50.15, 63.59, 63.77, 64.26, 65.15, 120.89, 129.35, 146.14, 148.18, 170.67, 171. 37, 171.77, 173.97. Anal. Calcd for $C_{245}H_{378}O_{138}$: C, 53.20; H, 6.89. Found: C, 52.96; H, 7.01.

[G#4]-Benzoate (10) and a General Procedure for Surface Modification. Benzoyl chloride 1040 mg (7.41 mmol), diluted in a small amount of dry CH_2Cl_2, was added dropwise to a solution of 750 mg (0.124 mmol) of [G#4]-OH tridendron dendrimer (**9**), 15 mg (0.124 mmol) of DMAP, and 875 mg (8.65 mmol) of TEA in 10 mL of dry CH_2Cl_2 at 0 °C under argon atmosphere. After the mixture was stirred at 0 °C for 1 h, the temperature was raised to 25 °C and the reaction was allowed to reach completion overnight. The CH_2Cl_2 was evaporated and the yellow crude product was purified by liquid chromatography on silica gel eluting with hexane, gradually increasing to 20:80 hexane/ethyl acetate to give **10** as a colorless glass: 1120 mg (82%). ^1H NMR ($CDCl_3$): δ 1.11 (s, 63H, $-CH_3$), 1.29 (s, 48H, $-CH_3$), 1.94 (s, 3H, $-CH_3$), 4.01−4.33 (m, 84H, $-CH_2C$), 4.44−4.51 (k, 96H, $-CH_2C$), 6.89 (d, 6H, ArH), 6.98 (d, 6H, ArH), 7.30 (t, 96H, ArH), 7.44 (t, 48H, ArH), 7.93 (d, 96H, ArH). ^{13}C NMR ($CDCl_3$): δ 17.48, 17.91, 46.53, 46.63, 46.80, 46.95, 65.29, 65.84, 120.80, 128.50, 129.63, 133.26, 146.36, 148.57, 165.82, 170.67, 171.37, 171.97. Anal. Calcd for $C_{581}H_{570}O_{186}$: C, 66.28; H, 5.46. Found: C, 66.11; H, 5.35.

[G#4]-Octanoate (11). [G#4]-OH tridendron dendrimer (**9**), 750 mg (0.124 mmol), and 1210 mg (7.41 mmol) of octanoyl chloride, 15 mg (0.124 mmol) of DMAP, and 875 mg (8.65 mmol) of TEA were reacted according to the general surface modification procedure overnight in 10 mL of dry CH_2Cl_2 to give a slightly yellow crude product that was purified by liquid chromatography on silica gel eluting with hexane gradually increasing to 60:40 hexane/ethyl acetate to give **11** as a colorless oil: 1100 mg (73%). ^1H NMR ($CDCl_3$): δ 0.83 (t, 144H, $-CH_3$), 1.19 (s, 72H, $-CH_3$), 1.22−1.28 (m, 1206H, $-CH_3$, $-CH_2-$), 1.42 (s, 9H, $-CH_3$), 1.55 (t, 96H, $-CH_2CH_2$-COO−), 2.15 (s, 3H, $-CH_3$), 2.26 (t, 144H, $-CH_2CH_2COO-$), 4.12−4.33 (m, 168H, $-CH_2C$), 4.40 (s, 12H, $-CH_2C$), 6.96 (d, 6H, ArH), 7.09 (d, 6H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.10, 17.59, 17.82, 22.62, 24.87, 28.99, 29.09, 31.70, 34.00, 46.33, 46.63, 47.03, 64.80, 65.24, 120.75, 129.80, 146.40, 148.66, 170.57, 171.49, 172.03, 173.10. Anal. Calcd for $C_{629}H_{1050}O_{186}$: C, 65.19; H, 9.13. Found: C, 65.22; H, 9.12.

[G#4]-Palmitoate (12). [G#4]-OH tridendron dendrimer (**9**), 350 mg (5.76×10^{-5}mol), and 950 mg (3.46 mmol) of palmitoyl chloride, 35 mg (0.29 mmol) of DMAP, and 408 mg (4.03 mmol) of TEA were reacted according to the general surface modification procedure overnight in 6 mL of dry CH_2Cl_2 to give a slightly yellow crude product that was purified by liquid chromatography on silica gel, eluting with hexane gradually increasing to 60:40 hexane/ethyl acetate to give **12** as a colorless oil: 610 mg, (61%). ^1H NMR ($CDCl_3$): δ 0.86 (t, 144H, $-CH_3$), 1.19 (s, 72H, $-CH_3$), 1.22−1.28 (m, 1206H, $-CH_3$, $-CH_2-$), 1.44 (s, 9H, $-CH_3$), 1.56 (t, 96H, $-CH_2CH_2$-COO−), 2.26 (t, 144H, $-CH_2CH_2COO-$), 4.12−4.42 (m, 180H, $-CH_2C$), 6.96 (d, 6H, ArH), 7.09 (d, 6H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.14, 17.59, 17.85, 22.72, 24.92, 29.24, 29.42, 29.62, 29.79, 31.97, 34.00, 46.33, 46.64, 47.00, 64.74, 65.23, 120.74, 129.82, 146.38, 148.66, 170.58, 171.42, 171.50, 172.00, 173.01. Anal. Calcd for $C_{1013}H_{1818}O_{186}$: C, 71.68; H, 10.87. Found: C, 71.60; H, 10.79.

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