Dendronized Aliphatic Polymers by a Combination of ATRP and Divergent Growth

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ABSTRACT: Dendronized, hybrid dendritic−linear polymers were synthesized by either the "graft-onto" route or by atom transfer radical polymerization (ATRP) of macromonomers. In both ways, the main chain was composed of acrylate repeating units and the dendrons were based on the aliphatic ester skeleton obtained from 2,2-bis(methylol)propionic acid (bis-MPA). ATRP of macromonomers was not a viable route for monomers with side chains larger than second-generation dendrons, which is why a combination of the two approaches was required to obtain polymers with larger side chains. The "graft-onto" route was conducted by reacting hydroxyl groups on the main chain with the acetonide-protected 2,2-bis-(hydroxymethyl)propionic anhydride. The acetonide protecting group was easily removed by treating a solution of the polymer with an acidic ion-exchange resin. Dendronized polymers with 1−3 generation dendron side groups were synthesized with a maximum molecular weight of ca. 86 kDa. The products were analyzed by ^{1}H and ^{13}C NMR, SEC, and MALDI−TOF.

Introduction

Rodlike polymers with pendant dendron side chains were first described in a patent by Tomalia in the late 1980s.[1] In the early 1990s, Hawker and Fréchet reported one of the first synthesis of such copolymers, composed of styrene and styrenic derivatives containing Fréchet-type dendrons.[2] In 1997, Percec et al. found that dendrons with flexible end groups self-assemble into hexagonal columnar or cubic thermotropic liquid-crystal phases with high conformity.[3] In 1998, Percec et al. further extended this concept by the introduction of a polymerizable group at the focal point and showed that lower degrees of polymerization resulted in a spherical shape and higher degrees of polymerization rendered a cylindrical shape.[4] Since then, the interest for hybrid dendritic−linear copolymers has increased, and the term "dendronized" polymers was coined by Schlüter et al.[5] The growing interest for dendronized polymers is fueled by their ability to adopt cylindrical, rodlike conformations while still having a very large number of end groups accessible for functionalization. A linear polymer most often forms random-coil structures in solution or bulk, but the attachment of (large) dendritic wedges imposes that the fully extended backbone is formed as a consequence of sterical hindrance.[3,4]

In general, either of two synthetic approaches is utilized to construct dendronized polymers: the "graft-onto" route (Figure 1, route A) or the macromonomer route (Figure 1, route B).[6]

The "graft-onto" approach comprises the coupling of dendrons to a polymer backbone while in the "macromonomer" route dendron-containing monomers are polymerized. The "graft-onto" approach offers some synthetic freedom in terms of the dendrons, which can be achieved by divergent or convergent growth. The purification is usually straightforward since the dendronized polymer is easily isolated by precipitation. However, steric crowding of larger dendrons may prevent full coupling of the dendrons. The "macromonomer" approach is considered a straightforward route to dendronized polymers since it offers accurate control over the dendritic side groups.[6] However, steric hindrance may become a problem. Once the dendrons become too large, the polymerizable group may be "shielded" and inhibit polymerization. The "macromonomer" approach has been explored using various chemistries such as radical polymerization,[7] ring-opening metathesis polymerization (ROMP),[8] Suzuki polycondensation,[9] and Heck coupling.[10] The "graft-onto" route was recently employed by Fréchet et al. when dendronized polymers were synthesized using commercially available poly(*p*-hydroxystyrene) as a backbone and benzylidene-2,2-bis-(oxymethyl)propionic anhydride as a building block.[11]

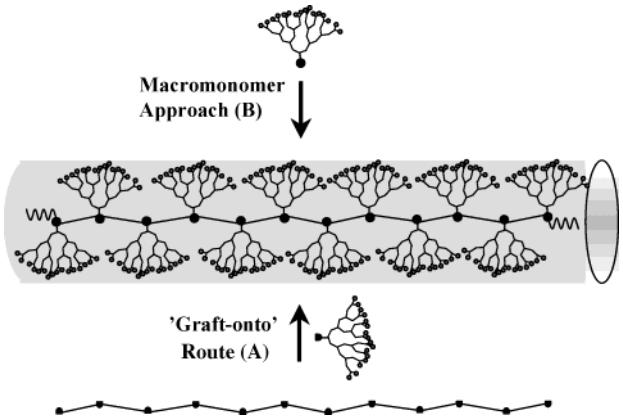

Figure 1. Schematic representation of different synthetic approaches to dendronized polymers: the "graft-onto" route (A) and the macromonomer approach (B).

The very complex architecture of dendronized polymers brings about challenging tasks for organic and polymer chemists as well as for analytical chemists. The

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analytical techniques usually employed by organic/polymer chemists are often insufficient for dendronized polymers.

The molecular architecture, including backbone chemistry, size of the dendrons, the presence of a flexible spacer, and the loading of dendritic wedges, will influence the conformation.[5] Also, the complex chemical/physical interactions between dendron/backbone, dendron/dendron, and dendron/backbone/solvent will contribute.[5] To elucidate the structure−property relationship for dendronized polymers, it is important to elaborate versatile synthetic procedures to access structurally different hybrids.

The aim of the present paper is to report our latest finding when synthesizing dendronized polymers by atom transfer radical polymerization[12−14] (ATRP). ATRP has previously proven to be a versatile technique when polymerizing macromonomers, yielding well-defined comb polymers.[15,16] We found that a combination of ATRP and divergent growth was required to assess dendronized polymers with dendrons of generation three or higher. In the "graft-onto" route, acrylate-functionalized monodendrons of the first and second generation were successfully polymerized with ATRP. In route B, the resulting first-generation dendronized polymer was used to grow polymers of the second and third generation employing the divergent approach.[11,17] This was achieved by using the acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride.[18]

Experimental Section

Materials. 1,10-Decanediol (98%), acryloyl chloride (96%), *N*,*N*,*N*′,*N*′,*N*″-pentamethyldiethylenetriamine (PMDETA) (99%), and 4-(dimethylamino)pyridine (DMAP) (99%) were purchased from Aldrich. Tris(2-(dimethylamino)ethyl)amine (Me_6-TREN) prepared according to a procedure described by Ciampolini and Nardi[19] from tris(2-aminoethyl)amine (98%, Aldrich). Acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride (**2**) was prepared according to the literature[18] from 2,2-bis(hydroxymethyl)propionic acid (bis-MPA), kindly supplied by Perstorp AB, Sweden. The DOWEX 50W-X2 ion-exchange resin, ethyl 2-bromoisobutyrate (98%), and copper(I) bromide (98%) were obtained from Acros Organics. Aluminum oxide, 90 active neutral, was purchased from Merck. Dichloromethane (CH_2Cl_2), methanol, and pyridine were HPLC grade and purchased from Lab-Scan. Ethyl acetate (EtOAc) and hexane were P.A. grade and obtained from Fischer.

Instrumentation. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 using $CDCl_3$, DMSO-d_6, and MeOD-d_4. The solvent signal was used as internal standard. All purifications were performed by medium-pressure liquid chromatography (MPLC) or by flash chromatography. MALDI−TOF experiments were conducted on a Bruker Reflex III MALDI-MS instrument, equipped with a N_2 laser, 337 nm (Bruker Daltonik GmbH, Bremen, Germany). All mass spectra were obtained in linear mode. The matrices utilized were either *trans*-3-indoleacrylic acid (t3iA) or 2,5-dihydroxybenzoic acid (DHB). Matrix solutions were prepared as 0.1 M solutions in THF. Sample preparation: the samples were dissolved in THF (2−5 mM), and 1 μL of the sample solution was added to the matrix solution (10 μL). The samples were prepared both as sample−matrix solutions and as sample−matrix−NaTFA solutions, employing a 0.1 M NaTFA solution in THF. The preparation protocol included mixing of 0.5−1.0 μL of sample with 10 μL of matrix and/or 0.5−1.0 μL of NaTFA (cationization agent). Then 0.2−0.4 μL of the mixture was spotted on the MALDI target and was left to crystallize in room temperature. Normally 100 pulses were acquired for each sample. Size exclusion chromatography (SEC) using THF (1.0 mL min^{-1}) as the mobile phase was performed at 35 °C using a Viscotek TDA model 301 equipped with a GMH_{HR}-M column with TSK-gel from Tosoh Biosep, a Viscotek VE 5200 GPC autosampler, a Viscotek VE 1121 GPC solvent pump, and a Viscotek VE 5710 GPC degasser. A universal calibration method was created using linear polystyrene standards, both broad and narrow. Corrections for the flow rate fluctuations were made by using THF as an internal standard. Viscotek Trisec 2000 version 1.0.2 software was used to process data. Molecular weights and polydispersities were also determined by SEC on a Waters 717plus autosampler and a Waters model 510 apparatus equipped with two PLgel 10 μm mixed-B columns, 300 × 7.5 mm (Polymer Labs., U.K.), using $CHCl_3$ as the mobile phase (1 mL min^{-1}) and at 30 °C. Linear polystyrene standards were used for calibration, ranging from 1700 to 706 000 g mol^{-1}.

Preparation of 1-Acrylate-10-decanol (3). 1,10-Decanediol, **1** (20.0 g, 115 mmol), triethylamine (TEA) (17.4 g, 172 mmol), and DMAP (1.40 g, 11.5 mmol) were stirred in CH_2Cl_2 (500 mL). Acryloyl chloride (10.4 g, 115 mmol) was added dropwise at −78 °C, and thereafter the reaction was allowed to reach room temperature. After stirring overnight, the precipitate was filtered off and the solvent evaporated. Hexane, 500 mL was added to the crude product, and the precipitated solids were discarded by filtration. The organic phase was concentrated in a vacuum and purified by medium-pressure liquid chromatography (MPLC) on silica gel, eluted with hexane, and gradually increasing the polarity to 20:80 (EtOAc) ethyl acetate:hexane to give **3** as a colorless oil (8.7 g, 33%). TLC (silica) EtOAc:hexane (20:80), R_f = 0.42. ^{1}H NMR ($CDCl_3$): δ 1.10−1.32 (m, 12H, $-CH_2CH_2-$), 1.40−1.60 (m, 4H, $-CH_2CH_2O-$), 2.83 (br, −OH), 3.50 (t, 2H, J = 13.4 Hz, $-OCOCHCH_2$), 4,05 (t, 2H, J = 13.3 Hz, $-CH_2OH$), 5,72 (d, 1H, $-CH_2CH-$), 5.99−6.06 (m, 1H, $-CHCH_2-$), 6.30 (d, 1H, $-CH_2CH-$). ^{13}C NMR ($CDCl_3$): δ 25.69−32.63 (alkyl chain), 62.58 ($-CH_2CH_2O-$), 64.63 ($-CH_2CH_2OCOCH=CH_2$), 128.51 ($-OCOCHC=H_2$), 130.43 ($-OCOCH=CH_2$), 166.33 ($-OCOCH=CH_2$).

Acetonide-[G#1]-$CO_2(CH_2)_{10}OCOCH=CH_2$ (4): General Esterification Procedure. 1-Acrylate-10-decanol, **3** (2.70 g, 11.8 mmol), and DMAP (281 mg, 2.30 mmol) were stirred in pyridine (ca. 5 mL ≈5 equiv/OH group) at room temperature. A solution of acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride, **2** (5.07 g, 15.4 mmol), in 15 mL of CH_2Cl_2 was added to the reaction flask. The progression of the reaction was monitored by ^{13}C NMR. Once the reaction reached completion, the excess of anhydride was quenched with 1−2 mL of water under vigorous stirring. The solution was diluted with 500 mL of CH_2Cl_2 and extracted with 10% $NaHSO_4$ (3 × 50 mL), 10% Na_2CO_3 (3 × 50 mL), and brine (1 × 50 mL). The organic phase was dried ($MgSO_4$), filtered, concentrated, and purified by medium-pressure liquid column chromatography on silica gel, eluting with hexane, and gradually increasing the polarity to 20:80 EtOAc:hexane to give **4** as a colorless oil (4.31 g, 96%). TLC (silica) EtOAc:hexane (20:80), R_f = 0.55. ^{1}H NMR ($CDCl_3$): δ 1.10 (s, 3H, $-CCH_3$), 1.18−1.42 (m, 18H, CH_2CH_2 and $-CH_3$), 1.50−1.65 (m, 4H, $-CH_2CH_2O$), 3.56 (d, 2H, J = 12.0 Hz, $-OCH_2$), 3.52 (d, 4H, J = 12.0 Hz, $-OCH_2$), 4.04−4.11 (m, 6H, $-OCOCHCH_2$ and $-CH_2C$), 5.72 (d, 1H, $-CH_2=CH$), 5.99−6.06 (m, 1H, $-CH=CH_2$), 6.30 (d, 1H, $-CH_2=CH$). ^{13}C NMR ($CDCl_3$): δ 18.75 ($-OCOC(-CH_2)_2CH_3$), 23.01 and 24.37 ($-O_2C(CH_3)_2$ acetonide group), 25.82−29.41 (alkyl chain), 41.78 ($-OCOC(-CH_2)_2CH_3$), 64.64 ($-CH_2CH_2-OCOCH=CH_2$), 64.90−66.03 ($-CH_2CH_2OCOC(-CH_2)_2CH_3$) and $-CH_2O-$), 97.99 ($-O_2C(CH_3)_2$ acetonide group), 128.70 ($-OCOCHC=H_2$), 130.41 ($-OCOCH=CH_2$), 166.25 ($-OCOCH=CH_2$), 174.25 ($-OCOC(-CH_2)_2CH_3$).

$(HO)_2$-[G#1]-$CO_2(CH_2)_{10}OCOCH=CH_2$ (5): General Procedure for the Deprotection of the Acetonide Group. Acetonide-[G#1]-$CO_2(CH_2)_{10}OCOCH=CH_2$, **4** (2.34 g, 6.10 mmol), was dissolved in 50 mL of methanol, and 2 teaspoons of DOWEX 50W-X2 resin was added. The mixture was stirred at room temperature and was monitored by TLC and NMR until the reaction reached completion. The resin was filtered off and thoroughly washed with methanol. The filtrate was concentrated in a vacuum to give **5** as a colorless oil (2.03 g, 97%). ^{1}H NMR ($CDCl_3$): δ 1.03 (s, 3H, $-CH_3$), 1.24−1.37 (m,

12H, $-CH_2CH_2$), 1.40−1.60 (m, 4H, $-CH_2CH_2O$), 3.14 (br, 2H, −OH), 3.65 (d, 2H, J = 11.2 Hz, $-CH_2C$), 3.82 (d, 2H, J = 11.4 Hz, $-CH_2C$), 4.07−4.11 (m, 4H, $-OCOCH_2CH_2$), 5.77 (d, 1H, J = 10.0 Hz, $-CH_2$=CH), 6.03−6.10 (m, 1H, $-CH$=CH_2), 6.36 (d, 1H, J = 10.0 Hz, $-CH_2$=CH). ^{13}C NMR ($CDCl_3$): δ 17.04 ($-CH_3$), 25.67−29.21 (alkyl chain), 49.08 ($-OCOC(CH_2OH)_2CH_3$),64.54($-CH_2CH_2OCOCH$=CH_2),64.94−67.34($-CH_2CH_2OCOC(CH_2OH)_2CH_3$ and $-CH_2O-$), 128.47 ($-OCOCHC$=H_2), 130.33 ($-OCOCH$=CH_2), 166.24 ($-OCOCH$=CH_2), 175.80 ($-OCOC(CH_2OH)_2CH_3$).

Acetonide-[G#2]-$CO_2(CH_2)_{10}OCOCH$=CH_2 (6). Compound **5** (1.90 g, 5.52 mmol), DMAP (263 mg, 2.15 mmol), 4.5 mL of pyridine, 10 mL of CH_2Cl_2, and acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride, **2** (4.74 g, 14.4 mmol), were reacted according to the general esterification procedure. The residue was purified by medium-pressure liquid chromatography on silica gel, eluting from hexane, and gradually increasing the polarity to 30:70 EtOAc:hexane to give **6** as colorless oil (3.02 g, 84%). TLC (silica) EtOAc:hexane (30:70), R_f = 0.37. ^{1}H NMR ($CDCl_3$): δ 1.08 (s, 6H, CH_3), 1.21−1.34 (m, 27H), 1.52−1.62 (m, 4H, $-CH_2CH_2O$), 3.54 (d, 4H, J = 12.0 Hz, $-CH_2C$), 4.02−4.09 (m, 8H, $-CH_2C$ and $-OCOCH_2CH_2$), 4.25 (s, 4H, $-CH_2C$), 5.74 (d, 1H, J = 10.4 Hz, $-CH_2$=CH), 6.00−6.10 (m, 1H, $-CH$=CH_2), 6.32 (d, 1H, J = 10.4 Hz, $-CH_2$=CH). ^{13}C NMR ($CDCl_3$): δ 17.55 ($-OCOC(-CH_2)_2CH_3$ of G#1), 18.30 ($-OCOC(-CH_2)_2CH_3$ of G#2), 22.03 and 24.74 ($-O_2C(CH_3)_2$ acetonide group), 25.63−29.18 (alkyl chain), 41.78 ($-OCOC(-CH_2)_2CH_3$ of G#2), 46.47 ($-OCOC(-CH_2)_2CH_3$ of G#1), 64.40−65.73 ($-CH_2CH_2OCOCH$=CH_2, $-CH_2CH_2OCOC(-CH_2)_2CH_3$ and $-CH_2O-$), 97.83 ($-O_2C(CH_3)_2$ acetonide group), 128.43 ($-OCOCHC$=H_2), 130.23 ($-OCOCH$=CH_2), 166.00 ($-OCOCH$=CH_2), 172.37 ($-OCOC(-CH_2)_2CH_3$ of G#1), 173.28 ($-OCOC(-CH_2)_2CH_3$ of G#2). Calcd: $[M]^+$ m/z = 656.38. Found: MALDI−TOF: $[M + Na^+]^+$ = 679.37.

Acetonide-[G#1]-Dendronized Polymer (7). Acetonide-[G#1]-$CO_2(CH_2)_{10}OCOCH$=CH_2, **4** (0.75 g, 1.95 mmol), was dissolved in ethyl acetate (0.75 g). PMDETA (6.8 mg, 39 μmol), Cu(I)Br (5.6 mg, 39 μmol), and ethyl 2-bromoisobutyrate (7.6 mg, 39 μmol) were added to the solution, and the flask was sealed with a rubber septum. The vessel was quickly evacuated and back-filled with argon three times. The flask was inserted into an oil bath thermostated at 70 °C, and the polymerization was left to proceed for 3 h. During the reaction the viscosity increased dramatically. The reaction mixture was diluted with 6 mL of THF and passed through a column of Al_2O_3 in order to remove the Cu complex. The crude product was precipitated to cold (−78 °C) hexane to give **7** (0.71 g, 95%) as a slightly yellow, sticky polymer. ^{1}H NMR ($CDCl_3$): δ 1.18 (s, 3H, $-CH_3$), 1.27−1.42 (m, 18 H, $-CH_3$ and $-CH_2CH_2-$), 1.59−1.65 (m, 4H, $-CH_2CH_2O-$), 1.87 (br, 2H, $-CH_2CH$), 2.24 (br, 1H, $-CHCH_2-$), 3.63 (d, 2H, J = 11.4 Hz, $-CH_2C-$), 3.98 (br, 2H, $-CH_2OCO-$), 4.10−4.19 (m, 4H, $-CH_2C-$ and $-CH_2OCO-$). ^{13}C NMR ($CDCl_3$): δ 18.88 ($-OCOC(-CH_2)_2CH_3$), 23.13 and 24.51 ($-O_2C(CH_3)_2$ acetonide group), 26.03−29,75 (alkyl chain and polymer chain), 41.88 ($-OCOC(-CH_2)_2CH_3$), 65.03−66.14 ($-CH_2CH_2OCO-$ and $-CH_2O-$), 98.13 ($-O_2C(CH_3)_2$ acetonide group), 174.35 $-OCOC(-CH_2)_2CH_3$ and $-OCOC(-CH_2)_2H$).

Acetonide-[G#2]-Dendronized Polymer (8). Acetonide-[G#2]-$CO_2(CH_2)_{10}OCOCH$=CH_2, **6** (0.75 g, 1.14 mmol), was dissolved in ethyl acetate (1.5 g). Me_6-TREN (5.3 mg, 22 μmol), Cu(I)Br (3.3 mg, 22 μmol), and ethyl 2-bromoisobutyrate (3.3 mg, 22 μmol) were added to the solution, and the flask was sealed with a rubber septum. The vessel was quickly evacuated and back-filled with argon three times. The flask was inserted into an oil bath thermostated at 50 °C, and the polymerization was left to proceed for 24 h. During the reaction the viscosity increased dramatically. The reaction mixture was diluted with THF (7 mL) and passed through a column of Al_2O_3 in order to remove the Cu complex. The crude product was precipitated into hexane (−78 °C) to give **8** (0.67 g, 90%) as slightly yellow, sticky polymer. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 6H, $-CH_3$), 1.27−1.40 (m, 27H, $-CH_3$ and-CH_2CH_2-), 1.61−1.63 (m, 4H, $-CH_2-CH_2O-$), 1.85 (br, 2H, $-CH_2CH-$), 2.24 (br, 1H, $-CH-CH_2$), 3.61 (d, 4H, J = 12.8 Hz, $-CH_2C$), 3.98 (br, 2H, $-CH_2CH_2-OCO$), 4.07−4.16 (m, 6H, $-CH_2C-$ and $-CH_2CH_2OCO$), 4.28−4.35 (m, 4H, $-CH_2C$). ^{13}C NMR ($CDCl_3$): δ 17.64 ($-OCOC(-CH_2)_2CH_3$ of G#1), 18.39 ($-OCOC(-CH_2)_2CH_3$ of G#2), 22.19 and 24.73 ($-O_2C(CH_3)_2$ acetonide group), 25.76−29.48 (alkyl chain and polymer chain), 41.83 ($-OCOC(-CH_2)_2CH_3$ of G#2), 41.88 ($-OCOC(-CH_2)_2CH_3$ of G#1), 64.51−65.87 ($-CH_2CH_2-OCO-$ and $-CH_2O-$), 97.95 ($-O_2C(CH_3)_2$ acetonide group), 172.36 ($-OCOC(-CH_2)_2CH_3$ of G#1), 173.39 ($-OCOC(-CH_2)_2-CH_3$ of G#2 and $-OCOC(-CH_2)_2H$).

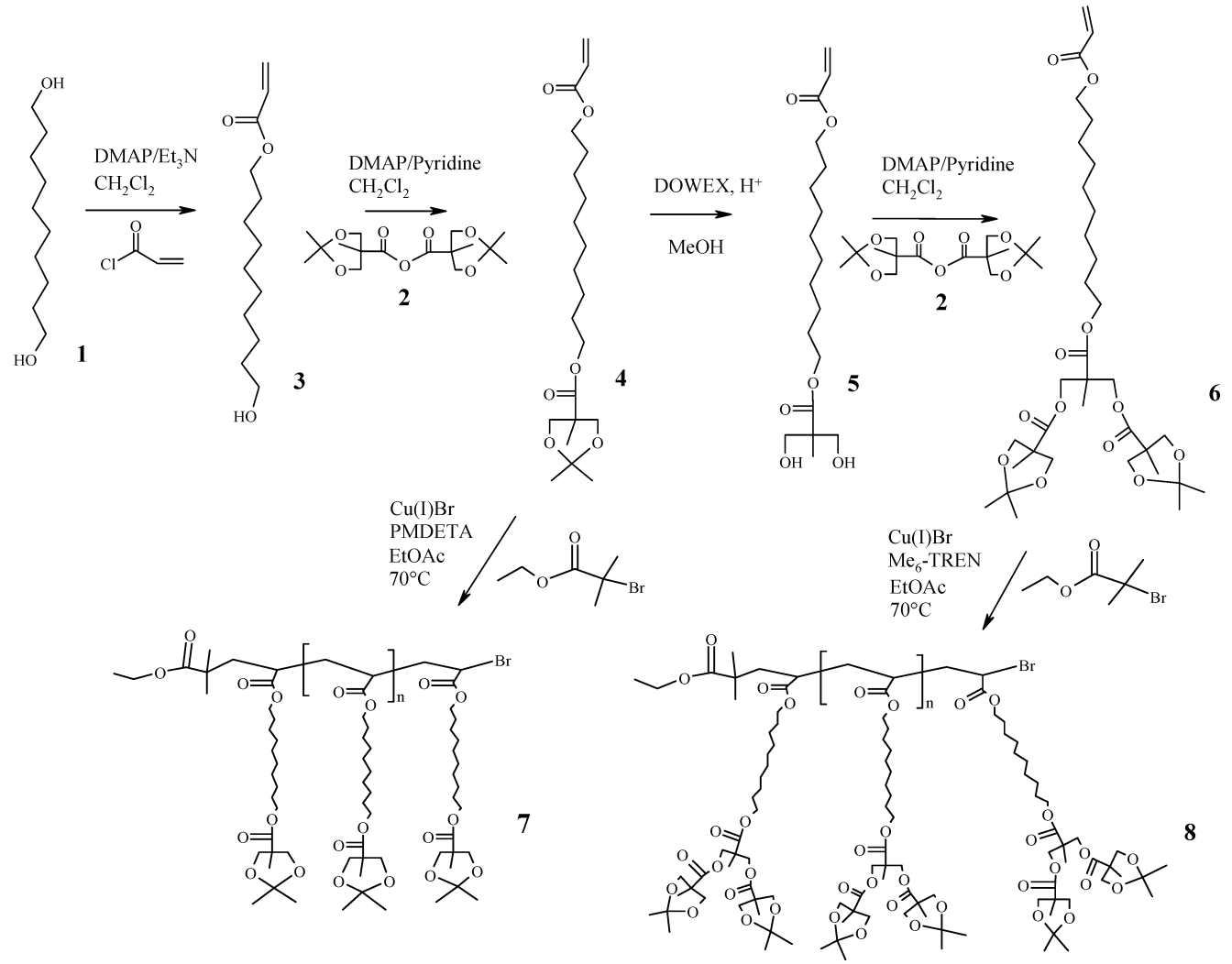
$(HO)_{100}$-$[G#1]_{50}$-Dendronized Polymer (9). Acetonide-[G#1]-polymer **7** was deprotected at 50 °C employing the general deprotection procedure. The reaction mixture was stirred at 50 °C to give **9** (0.55 g, 77%) as a white solid. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 3H, $-CH_3$), 1.36 (br, 12H, $-CH_2CH_2$), 1.60−1.70 (m, 4H, $-CH_2CH_2O$), 1.91 (br, 2 H, $-CH_2CH$), 2.13 (br, 1H, $-CH-CH_2$), 3.62−3.69 (m, 4H, $-CH_2C$), 4.08−4.10 (m, 4H, $-OCOCH_2CH_2$). ^{13}C NMR ($CDCl_3$): δ 17.56 ($-CH_3$), 27.19−30.64 (alkyl chain and polymer chain), 51.47 ($-OCOC(CH_2-OH)_2CH_3$), 65.77−65.84 ($-CH_2CH_2OCO-$ and $-CH_2O-$)), 176.69 ($-OCOC(CH_2OH)_2CH_3$ and $-OCOC(-CH_2)_2H$).

Acetonide-$[G#2]_{50}$-Dendronized Polymer (10). Dendronized polymer **9** was reacted according to the general esterification procedure. A large excess of acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride, **2**, with respect to OH group, was employed to ensure full substitution. The residue was dissolved in a small amount of CH_2Cl_2, and the product precipitated into cold hexane to give acetonide-$[G#2]_{50}$-polymer **10** (0.51 g, 54%) as colorless sticky polymer. ^{1}H NMR ($CDCl_3$): δ 1.12 (s, 6H, CH_3), 1.25−1.38 (m, 27H), 1.48−1.65 (m, 4H, $-CH_2CH_2O$), 1.84 (br, 2 H, $-CH_2CH$), 2.20 (br, 1H, $-CH-CH_2$), 3.59 (d, 4H, J = 12.4 Hz, $-CH_2C$), 3.96 (br, 2H, −OCOCH2CH2), 4.06−4.13 (m, 6H, $-CH_2C$ and $-OCOCH_2-CH_2$), 4.30 (m, 4H, $-CH_2C$), 5.74 (d, 1H, J = 10.4 Hz, $-CH_2$=CH), 6.00−6.10 (m, 1H, $-CH$=CH_2), 6.32 (d, 1H, J = 10.4 Hz, $-CH_2$=CH). ^{13}C NMR ($CDCl_3$): δ 17.74 ($-OCOC(-CH_2)_2CH_3$ of G#1), 18.47 ($-OCOC(-CH_2)_2CH_3$ of G#2), 22.18 and 24.94 ($-O_2C(CH_3)_2$ acetonide group), 25.84−29.63 (alkyl chain and polymer chain) 41.93 ($-OCOC(-CH_2)_2CH_3$ of G#2), 46.58 ($-OCOC(-CH_2)_2CH_3$ of G#1), 65.10−65.89 ($-CH_2CH_2OCO-$ and $-CH_2O-$), 97.98 ($-O_2C(CH_3)_2$ acetonide group), 172.43 ($-OCOC(-CH_2)_2CH_3$ of G#1), 172.50 ($-OCOC(-CH_2)_2CH_3$ of G#2 and $-OCOC(-CH_2)_2H$).

$(HO)_{200}$-$[G#2]_{50}$-Dendronized Polymer (11). Acetonide-[G#2]-polymer **10** was deprotected at 50 °C employing the general deprotection procedure to give compound **11** (0.28 g, 80%) as a white solid. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 6H, $-CCH_3$), 1.29−1.45 (m, 15H, $-CH_2CH_2$ and $-CH_3$), 1.60−1.75 (br, 4H, $-CH_2CH_2O$), 1.91 (br, 2 H, $-CH_2CH$), 2.33 (br, 1H, $-CH-CH_2$), 3.60−3.69 (m, 8H, $-CH_2C$), 3.95−4.20 (br, m, 4H, $-OCOCH_2CH_2$), 4.25−4.33 (m, 4H, $-CH_2C$). ^{13}C NMR ($CDCl_3$): δ 17.43 ($-CH_3$ of G#2), 18.44 ($-CH_3$ of G#1), 27.16−30.84 (alkyl chain and polymer chain), 47.73 ($-OCOC-(-CH_2)_2CH_3$ of G#1), 51.71 ($-OCOC(CH_2OH)_2CH_3$ of G#2), 65.78−66.49 ($-CH_2CH_2OCO-$ and $-CH_2O-$), 174.49 ($-OCOC-(-CH_2)_2CH_3$ of G#1), 175.84 ($-OCOC(-CH_2)_2H$), 176.09 ($-OCOC(-CH_2)_2CH_3$ of G#2).

Acetonide-$[G#3]_{50}$-Dendronized Polymer (12). Dendronized polymer **11** was reacted according to the general esterification procedure. A large excess of acetonide-protected 2,2-bis(hydroxymethyl)propionic anhydride, **2**, with respect to OH groups, was employed to ensure full substitution. The residue was dissolved in a small amount of CH_2Cl_2, and the product precipitated into cold hexane to give acetonide-$[G#2]_{50}$-polymer **12** (0.39 g, 75%) as opaque sticky polymer. ^{1}H NMR ($CDCl_3$): δ 1.07 (s, 12H, $-CH_3$), 1.19−1.38 (m, 45H, $-CH_3$ and $-CH_2CH_2$), 1.40−1.65 (br, 4H, $-CH_2CH_2O$), 3.56 (d, 8H, J = 12.0 Hz, $-CH_2C$), 3.70−4.09 (br, 12H, $-OCOCH_2CH_2$ and $-CH_2C$), 4.17−4.28 (m, 12H, $-CH_2C$). ^{13}C NMR ($CDCl_3$): δ 17.58 ($-OCOC(-CH_2)_2CH_3$ of G#1), 18.25 ($-OCOC(-CH_2)_2CH_3$ of G#2 and G#3), 21.89 and 24.83 ($-O_2C(CH_3)_2$ acetonide group), 25.15−28.61 (alkyl chain and polymer chain), 41.88 ($-OCOC(-CH_2)_2CH_3$ of G#3), 46.32 ($-OCOC(-CH_2)_2CH_3$ of G#1), 46.69 ($-OCOC(-CH_2)_2CH_3$ of G#2), 64.70−65.82 ($-CH_2CH_2-OCO-$ and $-CH_2O-$), 97.90 ($-O_2C(CH_3)_2$ acetonide group), 171.71($-OCOC(-CH_2)_2CH_3$ of G#1), 171.95 ($-OCOC(-CH_2)_2-$

Scheme 1. Divergent Synthesis of Dendrons 4, 5, and 6 Utilizing the Anhydride Building Block (DMAP = 4-(Dimethylamino)pyridine)[a]



[a] Dendronized polymers **7** and **8** were synthesized by atom transfer radical polymerization.

CH_3 of G#1), 173.31 (−O*C*OC(−CH_2)$_2$$CH_3$ of G#3 and −O*C*OC-(−CH_2)$_2$H).

(HO)$_{400}$-[G#3]$_{50}$-Dendronized Polymer (13). Acetonide-[G#2]- polymer **12** was deprotected at 50 °C employing the general deprotection procedure to give compound **13** (0.22 g, 89%) as white solid. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 12H, −CCH_3), 1.29−1.45 (m, 21H, −CH_2CH_2 and −CH_3), 1.60−1.80 (br, 4H, −CH_2CH_2O), 3.59−3.69 (dd, 16H, −CH_2C), 3.90−4.40 (m, 4H, −OCOCH_2CH_2 and −CH_2C). ^{13}C NMR ($CDCl_3$): δ 17.46 (−CH_3 of G#1), 18.32 (−CH_3 of G#2), 18.43(−CH_3 of G#3), 27.14−30.88 (alkyl chain and polymer chain), 47.81 (−OCO*C*(−CH_2)$_2$$CH_3$ of G#1), 47.84 (−OCO*C*(−CH_2)$_2$$CH_3$ of G#2), 51.71 (−OCO*C*-(CH_2OH)$_2$$CH_3$), 65.78−67.14 (−$CH_2CH_2OCO$− and −$CH_2O$−), 173.72 (−O*C*OC(−$CH_2$)$_2$$CH_3$ of G#1), 173.93 (−O*C*OC-(−CH_2)$_2$$CH_3$ of G#2), 175.83 (−O*C*OC(−CH_2)$_2$$CH_3$ of G#3 and −O*C*OC(CH_2OH)$_2$H). Poor NMR resolution was due to the complex structure of the dendronizd polymer. MALDI−TOF analysis failed.

Results and Discussion

Macromonomer Route. A controlled, or "living", polymerization technique must be utilized to polymerize the dendron-containing macromonomers in order to obtain well-defined polymers. Since our aim was to obtain dendronized polymers with ester chemistry in the side group, no ionic living polymerization technique was viable. However, the focal point of the dendrons can easily be functionalized with an acrylate or a methacrylate group. Controlled radical polymerization, e.g. ATRP, is an interesting approach since it is known to work well for (meth)acrylates, yielding well-defined polymers with low polydispersity.[20]

Macromonomer Synthesis. The macromonomers were synthesized according to Scheme 1. A flexible spacer between the dendron and the acrylate group was introduced to increase the availability of the polymerizable group.[21−23] One equivalent of 1,10-decandiol (**1**) was reacted with half an equivalent of acryloyl chloride in the presence of DMAP and TEA. The resulting product was a mixture of unreacted 1,10-decanediol and the corresponding mono- and diacrylates. The desired monoacrylated moiety **3** was isolated by medium-pressure liquid chromatography (MPLC) in 33% yield. Attempts to favor the formation of the monoacrylated product by varying reaction parameters such as solvent (THF, ethyl acetate), reagents (pyridine, TEA, DMAP, and acryloyl chloride), and temperature failed. The synthesis of the first-generation macromonomer was accomplished by reacting the acrylate-functional alcohol **3** with the acetonide-protected 2,2-bis(hydroxymethyl)-propionic anhydride (**2**) according to a procedure described previously.[18] This yielded an acrylate-functional macromonomer, acetonide-[G#1]-$CO_2(CH_2)_{10}$OCOCH=

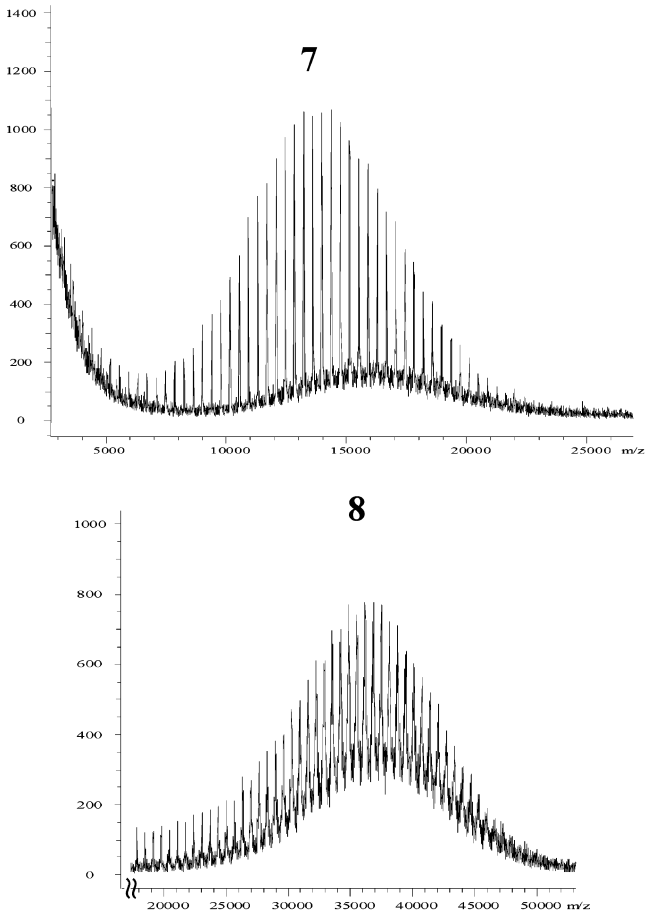


Figure 2. MALDI−TOF of acetonide-protected polymers **7** and **8** synthesized through ATRP. In both spectra, the difference in molecular weight between successive peaks corresponds to the repeating unit of the monodendron.

CH_2, **4**, having a first-generation dendron in the side chain in 96% yield. The macromonomer **4** was either polymerized by ATRP as described below or used for the synthesis of the macromonomer having a second-generation dendron in the side chain, **6**. To prepare compound **6**, the protecting acetonide group had to be removed. This was conveniently achieved by stirring **4** in methanol in the presence of an acidic ionic exchange resin, DOWEX 50W-X2. ^{13}C NMR spectroscopy is a useful technique to follow the deprotection. The quaternary carbon in the repeating unit resonates at ca. 42 ppm ($CDCl_3$) if acetonide protected and at 51 ppm (MeOD-d_4) if deprotected.[18] Once deprotected, the esterification reaction using **2** was repeated to give the targeted macromonomer **6**. The macromonomers were characterized by ^1H and ^{13}C NMR, SEC, and MALDI−TOF.

Polymerization of Macromonomers with ATRP. Macromonomers **4** and **6** were subjected to MPLC prior to polymerization to remove small amounts of impurities.[18] ATRP of **4** was performed in ethyl acetate since the macromonomer itself is quite viscous. The polymerization was conducted at 70 °C using conventional ATRP conditions.[20] The reaction mixture became very viscous after ca. 3 h whereafter it was diluted with THF and passed through a column of aluminum oxide to remove the copper. Unreacted macromonomer was removed by repeated precipitation from THF into hexane to obtain the pure polymer **7**. The polymer was analyzed by SEC, in both $CHCl_3$ and THF. The $CHCl_3$−SEC was calibrated according to conventional methods (CC) using linear polystyrene standards to give M_n = 22 100 Da and a PDI of 1.16. The same polymer was also characterized by a THF−SEC utilizing universal calibration (UC),[24] a method where the chromatograph is calibrated using polystyrene standards of both narrow and broad polydispersity. This gave a molecular weight (M_n) of 27 000 Da and a PDI of 1.65. MALDI−TOF analysis of the same polymer **7** gave a considerably lower molecular weight, ca. 13 000 Da, but also a low PDI value of 1.08 (Figure 2). However, the MALDI−TOF results were significantly affected by the choice of matrix and laser intensity.

ATRP of the larger macromonomer, **6**, was also conducted in ethyl acetate. The macromonomer has a molecular weight of 656 Da, and since the macromonomer itself was of quite high molecular weight, the concentration of reactive sites in the solution was low. Because of this, Me_6-TREN was used as a ligand since it is a highly potent ligand for ATRP of acrylates.[20] This ligand is normally used in an equivalence of 0.1 to the initiator.[20] However, in this case, where the concentration of polymerizable groups in the solution was very low, a higher concentration of Me_6-TREN and the copper salt was used (1:1) to increase the concentration of radicals in the solution and enhance the rate of the polymerization. The resulting polymer **8** was analyzed by SEC in the same way as polymer **7**. $CHCl_3$−SEC gave M_n = 20 500 Da and a PDI of 1.07, and THF−SEC gave M_n = 41 000 Da and a PDI of 1.28 (Table 1), roughly indicating that the polymerization of **6** was more controlled than that of **4**. MALDI−TOF analysis of this polymer gave a molecular weight of 33 000 Da, close to the theoretical molecular weight, and a low PDI of 1.06.

The slightly increased control in the polymerization of **6** compared to **4** might be due to the change of ligand but could also be due to the lower concentration of vinyl groups in the reaction solution.

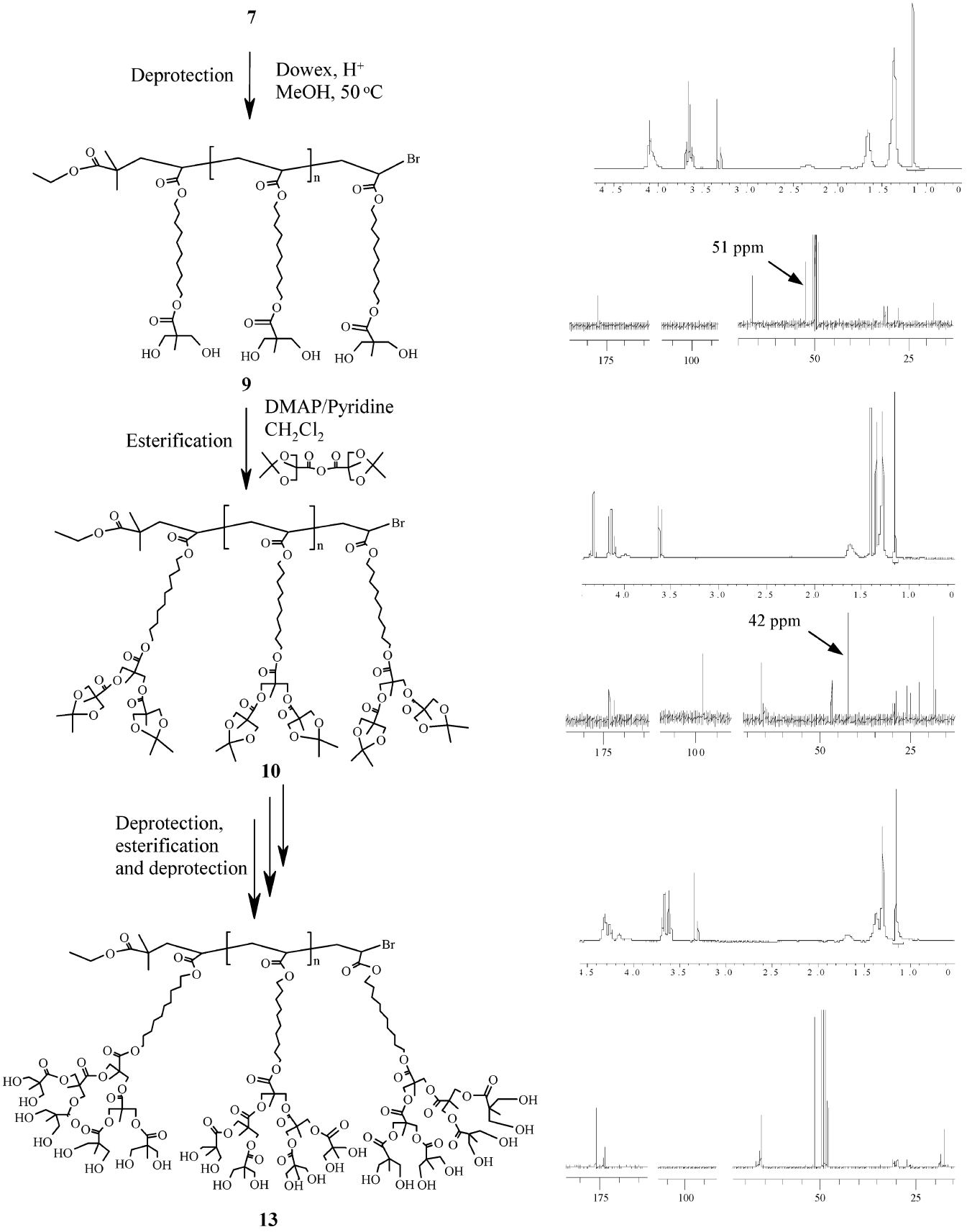
As can be seen in Table 1, there is a large difference in molecular weights and molecular weight distributions between the different analytical methods. In this context it is important to point out that SEC analysis of dendritic polymers is a difficult task. Calibration is most often pursued by linear polymer standards, obeying a different relationship between hydrodynamic volume and molecular weight than dendritic polymers do. Since the hydrodynamic volume of a dendritic polymer is anticipated to be smaller than its linear counterpart, SEC is known to underestimate the molecular weight

Table 1. Dendronized Polymers Obtained through the Macromonomer Approach[a]

		SEC					
		UC		CC		MALDI-TOF	
compound	M_{calc}, g mol^{-1}	M_n, g mol^{-1}	PDI	M_n, g mol^{-1}	PDI	M_n, g mol^{-1}	PDI
acetonide-[G#1]-polymer **(7)**	19 400	27 000	1.65	22 100	1.16	13 000	1.08
acetonide-[G#2]-polymer **(8)**	33 000	41 000	1.28	20 500	1.07	34 000	1.06

[a] M_n obtained by SEC using conventional calibration (CC) in $CHCl_3$ and universal calibration (UC) in THF.

Scheme 2. ^{1}H and ^{13}C NMR Spectra Used To Monitor the Different Steps in the Divergent Growth of the Dendronized Polymers 9, 10, and 13 (DMAP = 4-(Dimethylamino)pyridine)



of dendrimers.[25] As for dendronized molecules the situation is even more difficult. Large side groups may influence the backbone so that different conformers are obtained.

The difference in molecular weight in the SEC analyses was anticipated since different solvents, columns, and calibrations were utilized. The large deviation in polydispersity was more of a surprise; however, it can

Table 2. M_n for Different Dendronized Polymer Obtained by the "Graft-Onto" Route As Determined by SEC, Employing Universal Calibration

	SEC (UC)		
compound	M_{calc}, g mol^{-1}	M_n, g mol^{-1}	PDI
(OH)100-[G#1]50-dendronized polymer **(9)**	17 400	20 800	1.72
acetonide-[G#2]50-dendronized polymer **(10)**	33 000	54 900	1.53
(OH)200-[G#2]50-dendronized polymer **(11)**	29 000	19 200	1.99
acetonide-[G#3]50-dendronized polymer **(12)**	60 200	84 000	1.96

possibly be explained by the use of different columns and maybe also by that the solubility properties are different in the two solvents.

Lower polydispersity values were obtained by MALDI−TOF; however, this method is known to fractionate samples, thereby discriminating the higher molecular weight fraction of the sample, especially when the sample has a broad polydispersity. This will lower the PDI.

ATRP was also explored for the macromonomer of generation three. However, under similar reaction conditions no polymer was formed even though higher radical concentrations were used. This is currently being explored in more detail in our laboratory. No optimizations of the polymerizations were conducted; nevertheless, with some optimization, e.g., change of ligand, etc., it should be possible to increase the degree of control and thereby lower the PDI of the polymers.

"Graft-Onto" Route. Since it was not possible to synthesize dendronized polymers by ATRP of macromonomers having larger dendrons in the side chain, we decided to explore the "graft-onto" route. The acetonide-protected polymer **7** was deprotected to give the hydroxy-functional dendronized polymer **9** and was used as a starting material for subsequent growth of the dendritic side chains (Scheme 2).

When utilizing the "graft-onto" route complete substitution in each step is necessary. Because of steric hindrance in higher generation polymers it is important to use highly efficient chemistry during buildup. The divergent growth approach for the synthesis of bis-MPA-based dendrimers has been successful previously, by the use of either benzylidene-[17] or acetonide-protected[18] anhydride building blocks.

The hydroxy-functional polymer **9** was reacted with a 2−3-fold excess of the acetonide-protected 2,2-bis-(hydroxymethyl)propionic anhydride **(2)** to ensure complete substitution of the hydroxyl groups to give the second-generation dendronized polymer **10** having acetonide groups in the outer layer. The esterification reaction was conducted in a pyridine/CH_2Cl_2 mixture that was polar enough to efficiently dissolve the higher molecular weight polymers. The progress of the esterification reaction was monitored by ^{13}C NMR. When the esterification is complete, the peak at 51 ppm, originating from the quaternary carbons having adjacent hydroxyl-groups, is absent (Scheme 2). This in combination with the presence of the peak at 169 ppm, emanating from the carbonyl carbon of the excess anhydride, ensures complete substitution of the hydroxyl groups. After completion, the excess of anhydride was quenched and removed according to a procedure described earlier.[18]

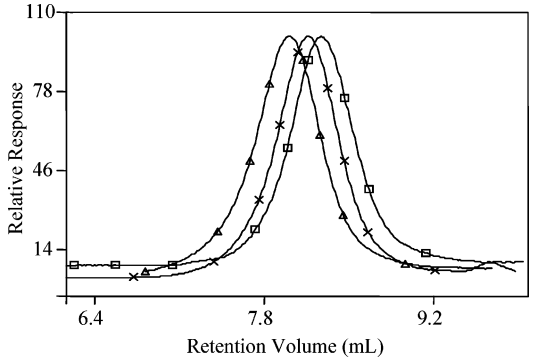


Figure 3. SEC chromatogram (□) first **7**, (×) second **10**, and (△) third **12** generation acetonide-protected dendronized polymers.

The pure polymer was obtained by repeated precipitation from CH_2Cl_2 into cold hexane. The dendronized polymers of higher generations were synthesized according to a similar procedure. However, higher generations required longer reactions time (70−80 h).

^1H and ^{13}C NMR spectroscopies were used to verify the structure and purity of the dendronized polymers (Scheme 2). The anhydride chemistry is apparently efficient since no traces of not fully reacted components are observed. As seen in Scheme 2, the NMR peaks from the structural units closest to the main chain are rather broad and poorly resolved. The outer groups, in contrast, give rise to resolved peaks facilitating quantification. This is probably attributed to the bulkiness/crowding of the molecules closer to the backbone while the outer groups are still rather mobile.

In this work, the synthesis of dendronized polymers up to the fourth generation was attempted. However, unwanted deprotection of the acetonide groups was observed during the NMR acquisition time. This is in agreement with findings already discussed by Schlüter and Rabe,[5] where they hypothesized that the exceptionally high density of functional groups promotes degradation reactions. At this time, no reliable analytical data have been acquired for the fourth-generation dendronized polymer. This is still underway in our laboratory.

The dendronized polymers of generation one, two, and three, synthesized through the "graft-onto" route, were characterized by size exclusion chromatography in THF utilizing universal calibration (Table 2).

The dendronized polymers all have rather broad molecular weight distributions. As can be seen in Table 1, the starting material **7** for the "graft-onto" route has a high distribution in THF. It is therefore expected that **9**, **10**, **11**, and **12** also will exhibit high PDI values in THF.

The retention volumes for polymers **7**, **10**, and **12** (Figure 3) increased with increasing theoretical molecular weight. MALDI−TOF analysis of the dendronized acetonide-protected polymers failed due to difficulties in the ionization step.

Conclusions

Dendronized polymers, based on bis-MPA, have been synthesized through two different approaches: the macromonomer route and the "graft-onto" route. Both synthetic strategies were employed, ATRP of an acrylate functional dendritic macromonomer, and dendritic growth using the acetonide-protected 2,2-bis(hydroxymethyl)-propionic anhydride. A flexible spacer between the

dendron and the acrylate group was introduced to ensure availability of the polymerizable group. In the macromonomer approach, first- and second-generation acetonide-protected polymers were achieved. From SEC and MALDI−TOF analyses the conclusion was drawn that dendronized polymers of controlled molecular weight and low PDI values could be obtained by ATRP. Attempts were made to polymerize macromonomer of generation three by ATRP. However, under similar reaction conditions no polymer was formed. In the divergent "graft-onto" route hydroxyl-functional dendronized polymers up to the third generation were synthesized. NMR appeared to be the most viable technique to monitor the progress of each reaction step. No characterization of the fourth-generation acetonide-protected dendronized polymer was possible due to uncontrolled deprotection. Dendronized polymers of the first, second, and third generation were analyzed with NMR, SEC, and MALDI−TOF. The SEC technique, using a universal calibration method, showed an increase of both PDI and hydrodynamic volume with generation.

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