Structurally Diverse Dendritic Libraries: A Highly Efficient Functionalization Approach Using Click Chemistry

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ABSTRACT: The high fidelity and efficiency of Click chemistry are exploited in the synthesis of a library of chain end functionalized dendritic macromolecules. In this example, the selectivity of the Cu-catalyzed [3 + 2π] cycloaddition reaction of azides with terminal acetylenes, coupled with mild reaction conditions, permits unprecedented functional group tolerance during the derivatization of dendrimeric and hyperbranched scaffolds. The resulting dendritic libraries are structurally diverse, encompassing a variety of backbones/surface functional groups, and are prepared in almost quantitative yields under very mild conditions. The robust and simple nature of this procedure, combined with its applicability to many aspects of polymer synthesis and materials chemistry, demonstrates an evolving synergy between advanced organic chemistry and functional materials.

For dendritic macromolecules, one consequence of their symmetrical and layered structure is the large number of functional groups at the chain ends/periphery.[1,2] In repeated studies, the nature of these chain ends has been shown to strongly dictate the chemical and physical properties of dendritic macromolecules.[3] As a result, the central dendritic framework acts as a scaffold and the final properties and applications of the dendrimer are primarily determined by the numerous chain end functional groups. This novel characteristic of dendritic macromolecules, when compared to traditional linear polymers, is perhaps best represented by the PAMAM dendrimers of Tomalia,[4] or the DAB dendrimers from DSM/Meijer,[5] where a myriad of different structures have been prepared by modification of the chain end amino groups. The most dramatic illustration of this ability to tune the properties and hence applications of dendritic macromolecules emerges from the distinctly different areas of medicinal chemistry and semiconductors. For example, a novel dendritic HIV/AIDS drug from Starpharma is based on a PAMAM scaffold with sulfonic acid end groups,[6] while the same PAMAM dendritic scaffolds with oligio(ethylene glycol) end groups are used as pore generating agents in the development of dielectric thin films for advanced microelectronic devices.[7]

The importance of chain end groups in dendrimer technology is significant and widely acknowledged;[8] however, little effort has been devoted to the development of a general approach to the functionalization of dendritic macromolecules. Traditionally, the selection of functionalization chemistry is tailored to a specific dendrimer scaffold or functional moiety to be introduced and must address numerous issues to be successful.[9] For example, the highly functionalized nature of the dendritic core leads to incomplete and partially functionalized dendrimers if the chosen reactions are not quantitative. In addition, a lack of compatibility with the repeat units of the dendritic core can lead to cleavage and destruction of the dendrimer. These issues become exacerbated for higher generation dendrimers where the large numbers of chain ends and internal repeat units amplifies the effect of any side reactions or incomplete functionalization. In the functionalization of a $[G\text{-}5]_3$-[C] poly(benzyl ether) dendrimer with 96 chain ends, an average selectivity of 99% results in only a 38% yield of fully functionalized dendrimer.[10] To overcome this incomplete functionalization, a large excess of reagents can be used; however, this severely compromises the efficiency of the synthesis and in turn leads to purification problems.

For greatest versatility and efficiency, the development of a general approach to dendrimer functionalization should therefore employ a reaction that occurs with quantitative yields under mild reaction conditions and be compatible with essentially all potential surface functional groups and internal dendritic repeat units. Unfortunately, many of the current synthetic approaches to dendrimer functionalization do not satisfy all or, in some cases, any of these criteria. A versatile and highly efficient approach to the functionalization of dendrimers which proceeds with absolute fidelity, high levels of control, and functional group compatibility is therefore a grand challenge.

The key to the development of a general and efficient approach to dendrimer functionalization utilizes the concept of Click chemistry, specifically the copper(I)-catalyzed regiospecific formation of 1,2,3-triazoles from azides and terminal acetylenes. This concept and associated set of reactions have garnered a significant amount of attention due to its complete specificity, quantitative yields, and almost perfect fidelity in the presence of a wide variety of other functional groups.[15−21]

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For example, Tirrell[22] has recently demonstrated a reliable and site-specific method of labeling cell surfaces based on Cu-catalyzed [3 + 2π] cycloaddition chemistry which takes advantage of the benign reaction conditions and functional group tolerance.

This unprecedented degree of control is perfectly suited to polymeric materials. In direct contrast with small molecule chemistry, one of the greatest challenges in polymer chemistry is the ability to perform multiple functionalization reactions without cross-linking (side reactions) or incomplete functionalization occurring. The occurrence of even minor amounts of cross-linking (ca. 1−3%) can lead to gelation due to the numerous functional groups along the backbone, while the inability to separate unreacted functional groups is a significant issue. Dendrimers, due to their high functionality and monodisperse nature, are perfect test vehicles to probe the fidelity of Click chemistry as a functionalization tool in polymeric systems since cross-linking reactions or unreacted starting groups can be detected at less than 1%. In this report, a novel strategy based on Click chemistry for the functionalization of dendrimers that fulfils all of these goals is described.

Experimental Section

General Methods. Analytical TLC was performed on commercial Merck plates coated with silica gel GF254 (0.24 mm thick). Silica gel for flash chromatography was Merck Kieselgel 60 (230−400 mesh, ASTM). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) measurements were performed on a Bruker AC 400 spectrometer at room temperature. Size exclusion chromatography (SEC) was carried out at room temperature on a Waters chromatograph connected to a Waters 410 differential refractometer and six Waters Styragel columns (five HR-5 μm and one HMW-20 μm) using THF as eluant (flow rate: 1 mL/min). A Waters 410 differential refractometer and a 996 photodiode array detector were employed. The molecular weights of the polymers were calculated relative to linear polystyrene standards. Nonaqueous click reactions were performed in sealed tubes using a Smith-Creator microwave reactor (Personal Chemistry Inc.). The modulated differential scanning calorimetry (MDSC) measurements were performed with a TA Instruments DSC 2920 and a ramp rate of 4 deg/min. The thermal gravimetric analysis measurements were done with a TA Instruments Hi-Res TGA 2950, under nitrogen purge, and the ramp rate was 10 deg/min. MALDI−TOF mass spectrometry was performed on a PerSeptive Biosystems Voyager DE mass spectrometer operating in linear mode, using dithranol in combination with silver trifluoroacetate as matrix.

Materials. $Cu(PPh_3)_3Br$,[11] $CuP(OEt)_3I$,[12] traditional Frechet-type benzyl ether dendrons **32**−**34**,[13] bis-MPA dendrimers,[24] and *N*-succinimidyl 4-pentynoate (**52**)[14] were synthesized as described previously. All other reagents were obtained from Aldrich and used as received.

Nomenclature. The nomenclature used for dendritic structures described in this article is as follows: $(Acet)_n$-[G-*X*]-F for acetylene-terminated dendrons, where *n* indicates the number of chain end acetylene functionalities, *X* indicates the generation number of the dendritic framework, and *F* describes the functional group at the focal point, either COOMe for methyl ester, OH for hydroxymethyl, and Br for bromomethyl. $(Acet)_n$-$([G\text{-}X])_3$-[C] for acetylene-terminated dendrimers, where *n* indicates the number of peripheral acetylene functionalities, *X* indicates the generation number of the dendritic framework, and [C] is the tris(phenolic) core; $(Y)_n$-$([G\text{-}X])_3$-[C] for functionalized dendrimers, where *Y* describes the external functional group, either Oct for *n*-octyl, Ad for adamantyl, MeO for 2-(2-methoxyethoxy)ethyl, Hex for 6-hydrohexyl, Est for methyl 4-(azidomethyl)benzoate, PhS for methyl phenyl sulfide, Sug for 2,3-dideoxy-β-D-arabinohexopyranose, Nuc for 3′-deoxythymidine, DR for *N*-ethyl-*N*-2′-azidoethyl-4-(2″-chloro-4″-nitrophenylazo)phenylamine (Disperse Red 13), Ant for 9-(methyl)anthracene, and [G-*X*] for benzyl ether-terminated dendrons, where *X* indicates the generation number of the dendritic framework. The external functional groups Y are linked to the dendritic scaffold by a 1,4-disubstituted 1,2,3-triazole ring.

Synthesis of Acetylene-Terminated Dendrons. General Procedure for Alkylation. $(Acet)_2$-[G-1]-COOMe, 3. To a stirred solution of propargyl bromide, **1** (29.7 g, 220 mmol), and methyl 3,5-dihydroxybenzoate, **2** (16.8 g, 100 mmol), in acetone (300 mL) were added potassium carbonate (15.1 g, 109 mmol) and 18-crown-6 (0.1 g, 0.4 mmol). The reaction mixture was heated at reflux under nitrogen for 24 h, filtered, evaporated to dryness, and partitioned between water and dichloromethane. The aqueous layer was then extracted with dichloromethane (2 × 100 mL), and the combined extracts were dried and evaporated to dryness. The crude material was then crystallized in methanol to give the ester **3** as pale yellow crystals; mp 105−106 °C (20.6 g, 84.4%). ^{1}H NMR ($CDCl_3$): δ 2.55 (t, J = 2.4 Hz, C≡C**H**, 2H), 3.92 (s, C**H**$_3$O, 3H), 4.73 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 4H), 6.83 (s, *p*-Ar, 1H), 7.31 (s, *o*-Ar, 2H). ^{13}C NMR ($CDCl_3$): δ 52.76 (s, **C**H$_3$O, 1C), 56.51 (s, **C**H$_2$C≡CH, 1C), 76.38 (s, C≡**C**H, 1C), 78.34 (s, **C**≡CH, 1C), 107.91 (s, *p*-Ar, 1C), 109.27 (s, *o*-Ar, 2C), 132.54 (s, **C**COOCH$_3$, 1C), 158.90 (s, *m*-Ar, 2C), 166.86 (s, **C**OOCH$_3$, 1C). Anal. Calcd for $C_{14}H_{12}O_4$: C, 68.8; H, 4.95. Found: C, 69.0; H, 4.89.

General Procedure for Reduction. $(Acet)_2$-[G-1]-OH, 4. To a stirred solution of the ester **3** (20.6 g, 84.4 mmol) in anhydrous THF (170 mL) was added lithium aluminum hydride (3.99 g, 105 mmol) in small portions, and the reaction mixture was stirred at room temperature for 2 h. Beckstrom's reagent (20 g) was then added to quench the remaining lithium aluminum hydride. The reaction mixture was filtered under vacuum, the solid was rinsed with dichloromethane, and the filtrate was dried with $MgSO_4$. After evaporation of the solvents, the alcohol **4** was purified by recrystallization from methanol and recovered as white crystals; mp 66−67 °C (16.4 g, 90.1%). ^{1}H NMR ($CDCl_3$): δ 2.46 (t, J = 2.4 Hz, C≡C**H**, 2H), 4.45 (s, C**H**$_2$OH, 2H), 4.61 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 4H), 6.46 (s, *p*-Ar, 1H), 6.56 (s, *o*-Ar, 2H). ^{13}C NMR ($CDCl_3$): δ 56.30 (s, **C**H$_2$C≡CH, 1C), 65.50 (s, **C**H$_2$OH, 1C), 76.09 (s, C≡**C**H, 2C), 78.76 (s, **C**≡CH, 2C), 101.88 (s, *p*-Ar, 1C), 106.60 (s, *o*-Ar, 2C), 143.97 (s, **C**CH$_2$OH, 1C), 159.23 (s, *m*-Ar, 2C). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.2; H, 5.59. Found: C, 72.1; H, 5.73.

General Procedure for Bromination. $(Acet)_2$-[G-1]-Br, 5. To a stirred solution of the alcohol **4** (14.7 g, 68.0 mmol) in tetrahydrofuran (200 mL) was added carbon tetrabromide (28.2 g, 85.0 mmol) followed by the portionwise addition of triphenylphosphine (22.3 g, 85.0 mmol). The reaction was stirred at room temperature for 5 min and then quenched with 50 mL of water. Tetrahydrofuran was evaporated, and the crude product was extracted with dichloromethane (2 × 150 mL). The organic layer was dried with $MgSO_4$ and evaporated to dryness. The crude product was purified by column chromatography, eluting with a 1:1 mixture of hexane and dichloromethane. After evaporation of the solvents, the bromide **5** was recovered as a colorless solid; mp 64−65 °C (23.4 g, 94.8%). ^{1}H NMR ($CDCl_3$): δ 2.46 (t, J = 2.4 Hz, C≡C**H**, 2H), 4.33 (s, C**H**$_2$Br, 2H), 4.58 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 4H), 6.46 (s, *p*-Ar, 1H), 6.57 (s, *o*-Ar, 2H). ^{13}C NMR ($CDCl_3$): δ 33.68 (s, **C**H$_2$Br, 1C), 56.38 (s, **C**H$_2$C≡CH, 2C), 76.33 (s, C≡**C**H, 2C), 78.58 (s, **C**≡CH, 2C), 102.75 (s, *p*-Ar, 1C), 109.09 (s, *o*-Ar, 2C), 140.30 (s, **C**CH$_2$Br, 1C), 159.13 (s, *m*-Ar, 2C). Anal. Calcd for $C_{13}H_{11}BrO_2$: C, 55.9; H, 3.97. Found: C, 55.7; H, 4.04.

$(Acet)_4$-[G-2]-OH, 6. This compound was prepared from 3,5-dihydroxybenzyl alcohol (**7**) and 2.2 equiv of the bromide **5**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and diethyl ether, to give the alcohol **6** as a colorless solid; mp 64−65 °C (83.4% yield). ^{1}H NMR ($CDCl_3$): δ 2.47 (t, J = 2.4 Hz, C≡C**H**, 4H), 4.52 (s, C**H**$_2$-

OH, 2H), 4.70 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 8H), 4.96 (s, ArC**H**$_2$-OAr, 4H), 6.46−6.79 (s, *o*,*p*-Ar, 9H). ^{13}C NMR ($CDCl_3$): δ 56.17 (s, **C**H$_2$C≡CH, 4C), 63.98 (s, **C**H$_2$OH, 1C), 76.23 (s, C≡**C**H, 4C), 78.17 (s, **C**≡CH, 4C), 102.26, 102.73 (2s, *p*-Ar, 3C), 106.89, 107.87 (2s, *o*-Ar, 6C), 136.85 (s, **C**CH$_2$OAr, 2C), 137.34 (s, **C**CH$_2$OH, 1C), 159.76, 160.47 (2s, *m*-Ar, 6C). Anal. Calcd for $C_{33}H_{28}O_7$: C, 73.9; H, 5.26. Found: C, 74.2; H, 4.98.

(Acet)$_4$-[G-2]-Br, 8. This compound was prepared from the alcohol **6** according to the general procedure for bromination with carbon tetrabromide and triphenylphosphine in tetrahydrofuran. The crude product was purified by column chromatography eluting with dichloromethane to give the bromide **8** as a colorless solid; mp 68−69 °C (89.7% yield). ^{1}H NMR ($CDCl_3$): δ 2.55 (t, J = 2.4 Hz, C≡C**H**, 4H), 4.40 (s, C**H**$_2$Br, 2H), 4.67 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 8H), 4.97 (s, C**H**$_2$O, 4H), 6.48−6.75 (m, Ar, 9H). ^{13}C NMR ($CDCl_3$): δ 34.04 (s, **C**H$_2$Br, 1C), 56.27 (s, **C**H$_2$C≡CH, 4C), 70.20 (s, Ar**C**H$_2$OAr, 2C), 76.32 (s, C≡**C**H, 4C), 78.93 (s, **C**≡CH, 4C), 102.22, 102.69 (2s, *p*-Ar, 3C), 107.24, 108.67 (2s, *o*-Ar, 6C), 139.63 (s, **C**CH$_2$OAr, 2C), 140.24 (s, **C**CH$_2$Br, 1C), 159.24, 160.23 (2s, *m*-Ar, 6C). Anal. Calcd for $C_{33}H_{27}BrO_6$: C, 66.1; H, 4.54. Found: C, 66.3; H, 4.45.

(Acet)$_8$-[G-3]-OH, 9. This compound was prepared from 3,5-dihydroxybenzyl alcohol (**7**) and 2.2 equiv of the bromide **8**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and diethyl ether, to give the alcohol **9** as a colorless glass, T_g = 13 °C (90.3% yield). ^{1}H NMR ($CDCl_3$): δ 2.48 (t, J = 2.4 Hz, C≡C**H**, 8H), 4.59 (s, C**H**$_2$OH, 2H), 4.65 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 16H), 4.95,4.98 (2s, ArC**H**$_2$O, 12H), 6.43−6.77 (m, Ar, 21H). ^{13}C NMR ($CDCl_3$): δ 56.35 (s, **C**H$_2$C≡CH, 8C), 64.07 (s, **C**H$_2$OH, 1C), 70.14 (s, Ar**C**H$_2$OAr, 6C), 75.99 (s, C≡**C**H, 8C), 78.57 (s, **C**≡CH, 8C), 102.26, 102.67 (2s, *p*-Ar, 7C), 106.84, 107.22 108.57 (3s, *o*-Ar, 14C), 139.38, 139.67 (2s, **C**CH$_2$OAr, 6C), 140.45 (s, **C**CH$_2$OH, 1C), 159.34, 160.53 (2s, *m*-Ar, 14C). MALDI mass spectrum: Calcd for $C_{73}H_{60}O_{15}$: 1176.39. Found: 1176.40.

(Acet)$_8$-[G-3]-Br, 10. This compound was prepared from the alcohol **9**, according to the general procedure for bromination with carbon tetrabromide and triphenylphosphine in tetrahydrofuran. The crude product was purified by column chromatography eluting with dichloromethane to give the bromide **10** as a colorless glass, T_g = 12 °C (90.5% yield). ^{1}H NMR ($CDCl_3$): δ 2.53 (t, J = 2.4 Hz, C≡C**H**, 8H), 4.41 (s, C**H**$_2$Br, 2H), 4.66 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 16H), 4.95,4.98 (2s, ArC**H**$_2$O, 12H), 6.46−6.76 (m, Ar, 21H). ^{13}C NMR ($CDCl_3$): δ 34.09 (s, **C**H$_2$Br, 1C), 56.35 (s, **C**H$_2$C≡CH, 8C), 70.23 (s, Ar**C**H$_2$OAr, 6C), 76.29 (s, C≡**C**H, 8C), 78.76 (s, **C**≡CH, 8C), 102.16, 102.59 (2s, *p*-Ar, 7C), 106.90, 107.22, 108.61 (3s, *o*-Ar, 14C), 139.49, 139.79 (2s, **C**CH$_2$OAr, 6C), 140.25 (s, **C**CH$_2$Br, 1C), 159.24, 160.34 (2s, *m*-Ar, 14C); MALDI mass spectrum: Calcd for $C_{73}H_{59}BrO_{14}$: 1238.31 and 1240.29 (1:1). Found: 1238.29 and 1240.30 (1:1).

(Acet)$_{16}$-[G-4]-OH, 11. This compound was prepared from the alcohol **7** and 2.2 equiv of the bromide **10**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography, eluting with 9:1 mixture of dichloromethane and diethyl ether, to give **11** as a colorless glass, T_g = 17 °C (85.1% yield). ^{1}H NMR ($CDCl_3$): δ 2.52 (t, J = 2.3 Hz, C≡C**H**, 16H), 4.61 (s, C**H**$_2$OH, 2H), 4.66 (d, J = 2.3 Hz, C**H**$_2$C≡CH, 32H), 4.96 (s, ArC**H**$_2$OAr, 28H), 6.45−6.77 (m, *p*,*m*-Ar, 45H). ^{13}C NMR ($CDCl_3$): δ 56.38 (s, **C**H$_2$C≡CH, 16C), 64.47 (s, **C**H$_2$OH, 1C), 70.28 (s, Ar**C**H$_2$OAr, 14C), 76.24 (s, C≡**C**H, 16C), 78.72 (s, **C**≡CH, 16C), 102.15 (s, *p*-Ar, 15C), 106.85, 107.19 (2s, *o*-Ar, 30C), 139.72 (s, **C**CH$_2$O, 15C), 159.21, 160.33 (2s, *m*-Ar, 30C). MALDI mass spectrum: Calcd for $C_{153}H_{124}O_{31}$: 2456.8. Found: 2456.9.

(Acet)$_{16}$-[G-4]-Br, 12. This compound was prepared from the alcohol **11**, according to the general procedure for bromination with carbon tetrabromide and triphenylphosphine in tetrahydrofuran. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and hexane, to give the bromide **12** as a colorless glass, T_g = 18 °C (98.7% yield). ^{1}H NMR ($CDCl_3$): δ 2.52 (t, J = 2.3 Hz, C≡C**H**, 16H), 4.40 (s, C**H**$_2$Br, 2H), 4.66 (d, J = 2.3 Hz, C**H**$_2$C≡CH, 32H), 4.97 (s, ArC**H**$_2$OAr, 28H), 6.42−6.71 (m, *p*,*m*-Ar, 45H). ^{13}C NMR ($CDCl_3$): δ 34.18 (s, **C**H$_2$Br, 1C), 56.33 (s, **C**H$_2$C≡CH, 16C), 70.32 (s, Ar**C**H$_2$OAr, 14C), 76.37 (s, C≡**C**H, 16C), 78.84 (s, **C**≡CH, 16C), 102.55 (s, *p*-Ar, 15C), 106.90, 107.23 (2s, *o*-Ar, 30C), 139.83 (s, **C**CH$_2$O, 15C), 159.21, 160.32 (2s, *m*-Ar, 30C). MALDI mass spectrum: Calcd for $C_{153}H_{123}BrO_{30}$: 2518.7 and 2520.7 (1:1). Found: 2518.7 and 2520.7 (1:1).

Synthesis of Acetylene-Terminated Tris(phenolic) Cored Dendrimers. (Acet)$_3$-([G-0])$_3$-[C], 14. This compound was prepared from 1,1,1-tris(4-hydroxyphenyl)ethane **(13)** and 3.3 equiv of propargyl bromide (**1**), according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography eluting with a 19:1 mixture of dichloromethane and methanol, to give **14** as a colorless oil (72.2% yield). ^{1}H NMR ($CDCl_3$): δ 2.11 (s, C**H**$_3$C, 3H), 2.53 (t, J = 2.4 Hz, C≡C**H**, 3H), 4.69 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 6H), 6.83 (d, J = 6.2 Hz, *o*-Ph, 6H), 7.01 (d, J = 6.2 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 31.43 (s, **C**H$_3$C, 1C), 51.09 (s, CH$_3$**C**, 1C), 56.31 (s, **C**H$_2$C≡CH, 3C), 76.23 (s, C≡**C**H, 3C), 78.74 (s, **C**≡CH, 3C), 114.39 (s, *m*-Ph, 6C), 130.04 (s, *o*-Ph, 6C), 142.47 (s, **C**CCH$_3$, 3C), 142.28 (s, **C**OCH$_2$, 3C). Anal. Calcd for $C_{29}H_{24}O_3$: C, 82.8; H, 5.75. Found: C, 82.6; H, 5.65.

(Acet)$_6$-([G-1])$_3$-[C], 15. This compound was prepared from 1,1,1-tris(4-hydroxyphenyl)ethane (**13**) and 3.3 equiv of the bromide **5**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and hexane, to give **15** as a pale yellow oil; T_g = 10 °C (58.4% yield). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, C**H**$_3$C, 3H), 2.54 (t, J = 2.4 Hz, C≡C**H**, 6H), 4.71 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 12H), 5.01 (s, C**H**$_2$O, 6H), 6.58 (s, *p*-Ar, 3H), 6.71 (s, *o*-Ar, 6H), 6.77 (d, J = 6.4 Hz, *o*-Ph, 6H), 6.91 (d, J = 6.4 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 31.33 (s, **C**H$_3$C, 1C), 51.12 (s, CH$_3$**C**, 1C), 56.33 (s, **C**H$_2$C≡CH, 6C), 70.07 (s, Ar**C**H$_2$O, 3C), 76.14 (s, C≡**C**H, 6C), 78.68 (s, **C**≡CH, 6C), 102.06 (s, *p*-Ar, 3C), 107.22 (s, *o*-Ar, 6C), 114.41 (s, *m*-Ph, 6C), 130.02 (s, *o*-Ph, 6C), 140.17 (s, **C**CH$_2$O, 3C), 142.48 (s, **C**CCH$_3$, 3C), 157.04 (s, **C**OCH$_2$Ar, 3C), 159.23 (s, *m*-Ar, 6C). Anal. Calcd for $C_{57}H_{48}O_9$: C, 78.1; H, 5.52. Found: C, 77.9; H, 5.47.

(Acet)$_{12}$-([G-2])$_3$-[C], 16. This compound was prepared from 1,1,1-tris(4-hydroxyphenyl)ethane (**13**) and 3.3 equiv of the bromide **8**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography eluting with a 19:1 mixture of dichloromethane and diethyl ether, to give **16** as a colorless gum; T_g = 13 °C (58.9% yield). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, C**H**$_3$C, 3H), 2.52 (t, J = 2.4 Hz, C≡C**H**, 12H), 4.68 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 24H), 4.97−5.01 (2s, C**H**$_2$O, 18H), 6.35−6.81 (m, *o*,*p*-Ar, 27H), 6.86 (d, J = 8.9 Hz, o-Ph, 6H), 7.01 (d, J = 8.9 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 31.46 (s, **C**H$_3$C, 1C), 51.07 (s, CH$_3$**C**, 1C), 56.35 (s, **C**H$_2$C≡CH, 12C), 70.24 (s, Ar**C**H$_2$O, 9C), 76.27 (s, C≡**C**H, 12C), 78.73 (s, **C**≡CH, 12C), 102.18 (s, *p*-Ar, 9C), 106.94, 107.24 (2s, *o*-Ar, 18C), 114.44 (s, *m*-Ph, 6C), 130.08 (s, *o*-Ph, 6C), 139.81, 140.05 (2s, **C**CH$_2$OAr, 9C), 142.51 (s, **C**CCH$_3$, 3C), 157.14, 159.25, 160.33 (3s, **C**OCH$_2$, 21C). Anal. Calcd for $C_{117}H_{96}O_{21}$: C, 76.5; H, 5.26. Found: C, 76.7; H, 5.42.

(Acet)$_{24}$-([G-3])$_3$-[C], 17. This compound was prepared from 1,1,1-tris(4-hydroxyphenyl)ethane (**13**) and 3.3 equiv of the bromide **10**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography eluting with 49:1 mixture of dichloromethane and diethyl ether, to give **17** as a colorless gum; T_g = 17 °C (89.7% yield). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, C**H**$_3$C, 3H), 2.52 (t, J = 2.4 Hz, C≡C**H**, 24H), 4.68 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 48H), 4.97,5.01 (2s, ArC**H**$_2$O, 42H), 6.41−6.78 (m, *o*,*p*-Ar, 63H), 6.86 (d, J = 8.9 Hz, o-Ph, 6H), 7.01 (d, J = 8.9 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 31.38 (s, **C**H$_3$C, 1C), 51.14 (s, CH$_3$**C**, 1C), 56.32 (s, **C**H$_2$C≡CH, 24C), 70.16 (s, Ar**C**H$_2$O, 21C), 76.22 (s, C≡**C**H,

24C), 78.71 (s, **C**≡CH, 24C), 102.16 (s, *p*-Ar, 21C), 106.89, 107.19 (2s, *o*-Ar, 42C), 114.32 (s, *m*-Ph, 6C), 130.22 (s, *o*-Ph, 6C), 139.77, 139.95 (2s, **C**CH_2OAr, 21C), 140.02 (s, **C**CCH_3, 3C), 157.11, 159.22, 160.32 (3s, **C**OCH_2, 45C). Anal. Calcd for $C_{237}H_{192}O_{45}$: C, 75.7; H, 5.14. Found: C, 75.8; H, 5.23.

(Acet)$_{48}$-([G-4])$_3$-[C], 18. This compound was prepared from 1,1,1-tris(4-hydroxyphenyl)ethane (**13**) and 3.3 equiv of the bromide **12**, according to the general procedure for alkylation with potassium carbonate and 18-crown-6 in acetone. The crude product was purified by column chromatography eluting with a 19:1 mixture of dichloromethane and diethyl ether, to give **18** as a colorless glass; T_g = 21 °C (75.2% yield). ^{1}H NMR ($CDCl_3$): δ 2.08 (s, C**H**$_3$C, 3H), 2.51 (t, J = 2.4 Hz, C≡C**H**, 48H), 4.68 (d, J = 2.4 Hz, C**H**$_2$C≡CH, 96H), 4.77−5.04 (m, ArC**H**$_2$O, 90H), 6.42−6.77 (m, *o*,*p*-Ar, 135H), 6.84 (d, J = 8.6 Hz, *o*-Ph, 6H), 6.99 (d, J = 8.6 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 36.38 (s, **C**H_3C, 1C), 51.41 (s, CH_3**C**, 1C), 56.29 (s, **C**H_2C≡CH, 48C), 70.29 (s, Ar**C**H_2O, 45C), 76.29 (s, C≡**C**H, 48C), 78.78 (s, **C**≡CH, 48C), 102.12 (s, *p*-Ar, 45C), 106.85, 107.18 (2s, *o*-Ar, 90C), 114.46 (s, *m*-Ph, 6C), 130.05 (s, *o*-Ph, 6C), 139.79, 140.01 (2s, **C**CH_2OAr, 45C), 142.46 (s, **C**CCH_3, 3C), 157.09,159.19, 160.24 (3s, **C**OCH_2, 93C). Anal. Calcd for $C_{477}H_{384}O_{93}$: C, 75.3; H, 5.09. Found: C, 75.5; H, 4.87.

General Procedure for Preparation of Azide Derivatives by Nucleophilic Displacement. *n*-Octyl Azide, 20. A solution of *n*-octyl bromide (13.1 g, 67.8 mmol) and sodium azide (13.2 g, 203 mmol) in water (150 mL) was stirred under reflux for 16 h. The aqueous phase was extracted with dichloromethane (2 × 200 mL), dried with $MgSO_4$, and evaporated to dryness, to give **20** as a colorless oil (9.67 g, 95.7%). ^{1}H NMR ($CDCl_3$): δ 0.89 (t, J = 6.9 Hz, C**H**$_3$, 3H), 1.21−1.41 (m, CH_3(C**H**$_2$)$_5$, 10H), 1.43−1.61 (m, C**H**$_2$$CH_2N_3$, 2H), 3.26 (t, J = 7.3 Hz, C**H**$_2$$N_3$, 2H). ^{13}C NMR ($CDCl_3$): δ 14.41 (s, **C**H_3, 1C), 23.01, 27.11, 29.23, 29.51, 29.54, 32.15 (6s, CH_3(**C**H_2)$_6$, 6C), 51.85 (s, **C**H_2N_3, 1C). Anal. Calcd for $C_8H_{17}N_3$: C, 61.9; H, 11.0; N, 27.1. Found: C, 62.2; H, 10.8; N, 26.9.

1-Azido-2-(2-methoxyethoxy)ethane, 21. This compound was prepared from 1-bromo-2-(2-methoxyethoxy)ethane, according to the general procedure with sodium azide in water, to give **21** as a colorless oil (87.3% yield). ^{1}H NMR ($CDCl_3$): δ 3.29 (s, C**H**$_3$O, 3H), 3.30 (t, J = 5.2 Hz, C**H**$_2$$N_3$, 2H), 3.44−3.48 (m, CH_3OC**H**$_2$, 2H), 3.53−3.60 (m, C**H**$_2$OC**H**$_2$, 4H). ^{13}C NMR ($CDCl_3$): δ 50.89 (s, **C**H_2N_3, 1C), 59.27 (s, **C**H_3O, 1C), 70.29 (s, CH_3OCH_2**C**H_2, 1C), 70.84 (s, CH_3O**C**H_2CH_2, 1C), 72.21 (s, **C**$H_2CH_2N_3$, 1C). Anal. Calcd for $C_5H_{11}N_3O_2$: C, 39.6; H, 7.64; N, 28.9. Found: C, 39.9; H, 7.38; N, 28.9.

6-Azido-1-hexanol, 23. This compound was prepared from 6-chloro-1-hexanol according to the general procedure with sodium azide in water, to give **23** as a colorless oil (96.7% yield). ^{1}H NMR ($CDCl_3$): δ 1.29−1.68 (m, CH_2(C**H**$_2$)$_4$$CH_2$, 8H), 2.74 (s, CH_2O**H**, 1H), 3.26 (t, J = 6.9 Hz, C**H**$_2$$N_3$, 2H), 3.62 (t, J = 6.5 Hz, C**H**$_2$OH, 2H). ^{13}C NMR ($CDCl_3$): δ 25.67 (s, **C**H_2-CH_2OH, 1C), 26.85 (s, **C**$H_2CH_2CH_2$OH, 1C), 29.97 (s, **C**H_2CH_2-CH_2N_3, 1C), 34.58 (s, **C**$H_2CH_2N_3$, 1C), 51.71 (s, **C**H_2N_3, 1C), 62.91 (s, **C**H_2OH, 1C); EI Mass spectrum: Calcd for C_6-$H_{13}N_3O$: 143.1057. Found: 143.1061.

Methyl 4-(Azidomethyl)benzoate, 24. This compound was prepared from methyl 4-(bromomethyl)benzoate according to the general procedure with sodium azide in water, to give **24** as a colorless solid (96.3% yield). ^{1}H NMR ($CDCl_3$): δ 3.91 (s, C**H**$_3$O, 3H), 4.42 (s, C**H**$_2$$N_3$, 2H), 7.39 (d, J = 7.8 Hz, *m*-Ar, 2H), 8.11 (d, J = 7.8 Hz, *o*-Ar, 2H). ^{13}C NMR ($CDCl_3$): δ 52.53 (s, **C**H_2N_3, 1C), 54.59 (s, **C**H_3O, 1C), 128.29 (s, *m*-Ar, 2C), 130.40 (s, *o*-Ar and **C**$COOCH_3$, 3C), 140.43 (s, **C**CH_2N_3, 1C), 166.95 (s, **C**$OOCH_3$, 1C). Anal. Calcd for $C_9H_9N_3O_2$: C, 56.5; H, 4.74; N, 22.0. Found: C, 56.4; H, 4.92; N, 21.8.

N*-Ethyl-*N*-2′-azidoethyl-4-(2″-chloro-4″-nitrophenylazo)phenylamine, 26.** Methanesulfonyl chloride (98.0 mg, 0.860 mmol) was added dropwise to a solution of Disperse Red 13 (200 mg, 0.573 mmol) and triethylamine (87.0 mg, 0.860 mmol) in 10 mL of dichloromethane. The mixture was allowed to stir at room temperature under nitrogen for 12 h, the formed solids filtered, and the organic phase diluted with dichloromethane (100 mL) and extracted with H_2O (3 × 25 mL). After drying over $MgSO_4$ and evaporation to dryness, the crude mesylate was redissolved in DMSO (10 mL) and sodium azide (245 mg, 0.573 mmol) was added. The reaction mixture was then stirred at 50 °C for 16 h, filtered, concentrated under reduced pressure, and purified by column chromatography, eluting with a 1:9 mixture of ethyl acetate and hexane gradually increasing to 3:7 ethyl acetate and hexane. This gave the azido derivative **26** as a red solid; mp 74−75 °C (93.0% yield). ^{1}H NMR ($CDCl_3$): δ 1.26 (t, NCH_2C**H**$_3$, 3H), 3.54−3.61 (m, NC**H**$_2$$CH_3$ and NC**H**$_2$C**H**$_2$$N_3$, 6H), 6.75 (d, J = 9.20 Hz, *ArH**, 2H), 7.72 (d, J = 9.20 Hz, *Ar***H**, 1H), 7.90 (d, J = 8.80 Hz, *Ar***H**, 2H), 8.08−8.11 (m, *Ar***H**, 1H), 8.32 (d, J = 2.00 Hz, *Ar***H**, 1H). ^{13}C NMR ($CDCl_3$): δ 12.181 (s, NCH_2**C**H_3, 1C), 44.85 (s, N**C**H_2CH_3, 1C), 48.82 (s, NCH_2**C**H_2N_3, 1C), 49.46 (s, N**C**H_2-CH_2N_3, 1C), 111.42 (s, *Ar***C**, 2C), 117.87 (s, *Ar***C**, 2C), 122.47 (s, *Ar***C**, 1C), 125.87 (s, *Ar***C**, 1C), 126.83 (s, *Ar***C**, 1C), 133.94 (s, *Ar***C**, 1C), 144.37 (s, *Ar***C**, 1C), 147.05 (s, *Ar***C**, 1C), 151.20 (s, *Ar***C**, 1C), 152.81 (s, *Ar***C**, 1C). Anal. Calcd for $C_{16}H_{16}$-ClN_7O_2: C, 51.4; H, 4.31; N, 26.2. Found: C, 51.4; H, 4.52; N, 26.0.

9-(Azidomethyl)anthracene, 27. This compound was prepared from 10-(chloromethyl)anthracene according to the general procedure for azidation with sodium azide using *N*,*N*-dimethylformamide instead of water, to give **27** as a yellow solid; mp 144−145 °C (90.3% yield). ^{1}H NMR ($CDCl_3$): δ 5.40 (s, C**H**$_2$$N_3$, 2H), 7.57−7.67 (m, 2,3,6,7-*Ar***H**, 4H), 8.01 (d, J = 7.92 Hz, 1,8-Ar, 2H), 8.35 (d,, J = 7.92 Hz, 4,5-Ar, 2H), 8.56 (s, 10-Ar, 1H). ^{13}C NMR ($CDCl_3$): δ 46.35 (s, **C**H_2N_3, 1C), 123.51 (s, 5-Ar, 1C), 125.20 (s, 2-*Ar***C**, 1C), 125.77 (s, 3-Ar, 1C), 126.84 (s, 4-Ar, 1C), 128.92 (s, 7-Ar, 1C), 129.29 (s, 6-Ar, 1C), 130.70 (s, Ar, 2C), 131.37 (s, Ar, 2C). Anal. Calcd for $C_{15}H_{11}N_3$: C, 77.23; H, 4.75; N, 18.01. Found: C, 77.43; H, 4.81; N, 17.67.

[G-1]-N$_3$, 29. This compound was prepared from [G-1]-Br **32**, according to the general procedure with sodium azide using dimethyl sulfoxide instead of water, to give **29** as a white solid; mp 110−112 °C (98.2% yield). ^{1}H NMR ($CDCl_3$): δ 4.12 (s, C**H**$_2$$N_3$, 2H), 5.07 (s, C**H**$_2$O, 4H), 6.57 (s, *o*-Ar, 2H), 6. 60 (s, *p*-Ar, 1H), 7.29−7.51 (m, Ph, 10H). ^{13}C NMR ($CDCl_3$): δ 55.27 (s, **C**H_2N_3, 1C), 70.39 (s, **C**H_2O, 2C), 101.92 (s, *p*-Ar, 1C), 106.72 (s, *o*-Ar, 2C), 127.92 (s, *o*-Ph, 4C), 128.35 (s, *p*-Ph, 2C), 129.73 (s, *m*-Ph, 4C), 137.19, 139.59 (2s, **C**CH_2O, 3C), 160.57 (s, **C**OCH_2, 2C). Anal. Calcd for $C_{21}H_{19}N_3O_2$: C, 73.0; H, 5.54; N, 12.2. Found: C, 72.9; H, 5.71; N, 12.0.

[G-2]-N$_3$, 30. This compound was prepared from [G-2]-Br **33**, according to the general procedure with sodium azide in dimethyl sulfoxide, to give **30** as a white solid; mp 84−85 °C (97.9% yield). ^{1}H NMR ($CDCl_3$): δ 4.27 (s, C**H**$_2$$N_3$, 2H), 4.99 (s, C**H**$_2$O, 4H), 5.05 (s, PhC**H**$_2$O, 8H), 6.43−6.79 (m, *o*,*p*-Ar, 9H), 7−31−7.49 (m, Ph, 20H). ^{13}C NMR ($CDCl_3$): δ 55.22 (s, **C**H_2N_3, 1C), 70.41 (s, **C**H_2O, 6C), 102.12 (s, *p*-Ar, 3C), 106.78 (s, *o*-Ar, 6C), 127.98 (s, *o*-Ph, 8C), 128.42 (s, *p*-Ph, 4C), 129.99 (s, *m*-Ph, 8C), 137.13, 139.54 (2s, **C**CH_2O, 6C), 160.52 (s, **C**OCH_2, 6C). Anal. Calcd for $C_{49}H_{43}N_3O_6$: C, 76.4; H, 5.63; N, 5.46. Found: C, 76.2; H, 5.48; N, 5.71.

[G-3]-N$_3$, 31. This compound was prepared from [G-3]-Br **34**, according to the general procedure with sodium azide in dimethyl sulfoxide, to give **31** as a colorless glass; T_g = 41 °C (96.1% yield). ^{1}H NMR ($CDCl_3$): δ 4.25 (s, C**H**$_2$$N_3$, 2H), 4.98 (s, C**H**$_2$O, 12H), 5.04 (s, PhC**H**$_2$O, 16H), 6.27−6.83 (m, *o*,*p*-Ar, 31H), 7.16−7.47 (m, Ph, 40H). ^{13}C NMR ($CDCl_3$): δ 55.19 (s, **C**H_2N_3, 1C), 70.47 (s, **C**H_2O, 14C), 102.04 (s, *p*-Ar, 7C), 106.83 (s, *o*-Ar, 14C), 128.02 (s, *o*-Ph, 16C), 128.46 (s, *p*-Ph, 8C), 129.03 (s, *m*-Ph, 16C), 137.22, 139.66 (2s, **C**CH_2O, 16C), 160.60 (s, **C**OCH_2, 16C). Anal. Calcd for $C_{105}H_{91}N_3O_{14}$: C, 77.9; H, 5.67; N, 2.60. Found: C, 78.1; H, 5.49; N, 2.44.

Functionalization of Acetylene-Terminated Tris(phenolic) Cored Dendrimers Using Click Chemistry. General Procedure for the Click Reaction Catalyzed by CuP(OEt)$_3$I. (MeO)$_3$-[G-0]$_3$-[C], 35. A solution of the acetylene terminated dendrimer **14** (1.35 g, 4.33 mmol), azide **21** (2.35 g, 16.2 mmol), *N*,*N*-diisopropylethylamine (0.58 g, 4.50 mmol), and Cu(OEt)$_3$I (0.11 g, 0.30 mmol) in tetrahydrofuran (20 mL) was either submitted to microwave irradiation at a nominal temperature of 140 °C for 20 min or stirred at room

temperature for ca. 48 h. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and methanol, to give **35** as a pale yellow gum; T_g = 13 °C (72.2% yield). ^{1}H NMR ($CDCl_3$): δ 2.11 (s, C**H**$_3$C, 3H), 3.36 (s, C**H**$_3$O, 9H), 3.43−3.62 (m, $CH_3OCH_2CH_2$, 4H), 3.89 (t, J = 5.2 Hz, C**H**$_2$CH$_2$N, 6H), 4.57 (t, J = 5.2 Hz, CH_2CH_2N, 6H), 5.19 (s, OC**H**$_2$C=CH, 6H), 6.89 (d, J = 6.8 Hz, *o*-Ph, 6H),7.01 (d, J = 6.8 Hz, *m*-Ph, 6H). ^{13}C NMR ($CDCl_3$): δ 31.12 (s, **C**H$_3$C, 1C), 50.69 (s, CH$_2$**C**H$_2$N, 3C), 51.03 (s, CH$_3$**C**, 1C), 59.44 (s, **C**H$_3$O, 3C), 62.43 (s, O**C**H$_2$C=CH, 3C), 69.85 (s, CH_3OCH_2**C**H$_2$, 3C), 70.93 (s, CH_3O**C**H$_2$CH$_2$, 3C), 72.11 (s, **C**H$_2$-CH$_2$N, 3C), 114.31 (s, *m*-Ph, 6C), 124.35 (s, CH=**C**N, 3C), 130.04 (s, *o*-Ph, 6C), 142.56 (s, **C**H=CN, 3C), 144.50 (s, **C**CCH$_3$, 3C), 156.78 (s, **C**OCH$_2$C=CH, 3C). MALDI mass spectrum: Calcd for $C_{44}H_{57}N_9O_9$: 855.99. Found: 855.97.

General Procedure for the Click Reaction Catalyzed by Cu(PPh$_3$)$_3$Br. (Oct)$_6$-[G-1]$_3$-[C], 36. A solution of the acetylene-terminated dendrimer **15** (1.11 g, 1.23 mmol), *n*-octyl azide **20** (1.43 g, 7.45 mmol), *N*,*N*-diisopropylethylamine (0.48 g, 3.7 mmol), and Cu(PPh$_3$)$_3$Br (0.11 g, 0.25 mmol) in tetrahydrofuran (20 mL). The reaction mixture was then placed in a sealed vial and was then either subjected to microwave irradiation at a nominal temperature of 140 °C for 20 min or stirred at room temperature for ca. 48 h. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **36** as a colorless oil; T_g = 7 °C (92.7% yield). ^{1}H NMR ($CDCl_3$): δ 0.89 (t, J = 6.9 Hz, C**H**$_3$(CH$_2$)$_5$, 18H), 1.16−1.42 (m, CH$_3$(C**H**$_2$)$_5$, 60H), 1.84−2.01 (m, C**H**$_2$CH$_2$N, 12H), 2.13 (s, C**H**$_3$C, 3H), 4.37 (t, J = 7.3 Hz, C**H**$_2$N, 12H), 4.99 (s, ArC**H**$_2$OPh, 6H), 5.21 (s, OC**H**$_2$C=CH, 12H), 6.63 (s, *p*-Ar, 3H), 6.72 (s, *o*-Ar, 6H), 6.86,7.01 (2d, J = 8.9 Hz, Ph, 12H), 7.63 (s, C**H**=CN, 6H). ^{13}C NMR ($CDCl_3$): δ 14.47 (s, **C**H$_3$(CH$_2$)$_6$, 1C), 22.98, 26.89, 29.34, 29.42, 30.67, 32.09 (6s, CH$_3$(**C**H$_2$)$_6$, 6C), 31.54 (s, **C**H$_3$C, 1C), 50.88 (s, **C**H$_2$N, 6C), 51.07 (s, CH$_3$**C**, 1C), 62.58 (s, O**C**H$_2$C=CH, 6C), 70.15 (s, Ar**C**H$_2$OPh, 3C), 101.68 (s, *p*-Ar, 3C), 106.97 (s, *o*-Ar, 6C), 114.36 (s, *m*-Ph, 6C), 122.35 (s, CH=**C**N, 6C), 130.06 (s, *o*-Ph, 6C), 132.44 (s, **C**CH$_2$OPh, 3C), 140.20 (s, **C**H=CN, 6C), 142.48 (s, **C**CCH$_3$, 3C), 157.09 (s, *p*-Ph, 3C), 160.01 (s, **C**OCH$_2$C=CH, 6C). MALDI mass spectrum: Calcd for $C_{105}H_{150}N_{18}O_9$: 1807.18. Found: 1807.19.

(Ad)$_6$-[G-1]$_3$-[C], 37. This compound was prepared from the acetylene-terminated dendrimer **15** and 1-azidoadamantane **19**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 1:1 mixture of dichloromethane and hexane, to give **37** as a white solid; T_g = 121 °C (95.6% yield). ^{1}H NMR ($CDCl_3$): δ 1.77 (s, CHC**H**$_2$-CH, 36H), 1.89 (s, C**H**$_3$C, 3H), 2.27 (s, (C**H**$_2$)$_3$CN and (CH$_2$)$_3$C**H**, 54H), 4.99 (s, ArC**H**$_2$OPh, 6H), 5.20 (s, CH=CC**H**$_2$O, 12H), 6.65 (s, *p*-Ar, 3H), 6.72 (s, *o*-Ar, 6H), 6.87,7.01 (2d, J = 8.9 Hz, Ph, 12H), 7.96 (s, C**H**=CN, 6H). ^{13}C NMR ($CDCl_3$): δ 26.00 (s, **C**H$_3$C, 1C), 29.82,36.27,43.37 (3s, (CH$_2$)$_3$**C**H, CH**C**H$_2$CH, (**C**H$_2$)$_3$-CN, 54C), 50.98 (s, CH$_3$**C**, 1C), 60.09 (s, (CH$_2$)$_3$**C**N, 6C), 62.75 (s, O**C**H$_2$C=CH, 6C), 70.17 (s, Ar**C**H$_2$OPh, 3C), 101.61 (s, *p*-Ar, 3C), 106.91 (s, *o*-Ar, 6C), 114.49 (s, *m*-Ph, 6C), 119.67 (s, CH=**C**N, 6C), 130.04 (s, *o*-Ph, 6C), 140.14 (s, **C**CCH$_3$, 3C), 142.47 (s, **C**CH$_2$OPh, 3C), 143.28 (s, **C**H=CN, 6C), 157.17 (s, *p*-Ph, 3C), 160.32 (s, **C**OCH$_2$C=CH, 6C). Anal. Calcd for $C_{117}H_{138}N_{18}O_9$: C, 72.4; H, 7.17; N, 13.0. Found: C, 72.2; H, 6.98; N, 13.3.

(Hex)$_6$-[G-1]$_3$-[C], 38. This compound was prepared from the acetylene-terminated dendrimer **15** and the azide **23**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography eluting with a 2:1 mixture of dichloromethane and hexane, to give **38** as a orange viscous oil; T_g = 9 °C (92.6% yield). ^{1}H NMR (DMSO-d_6): δ 2.04 (s, C**H**$_3$C, 3H), 3.04−3.62 (m, **H**OC**H**$_2$(C**H**$_2$)$_4$CH$_2$, 78H), 4.54 (t, C**H**$_2$N, 12H), 5.01 (bs, ArC**H**$_2$O, 6H), 5.15 (bs, OC**H**$_2$C=CH, 12H), 6.65 (bs, o,*p*-Ar, 9H), 6.82−6.97 (m, *o*,*m*-Ph, 12H), 8.45 (s, C**H**=C, 6H). ^{13}C NMR (DMSO-d_6): δ 31.09 (s, **C**H$_3$C, 1C), 49.78 (s, **C**H$_2$N, 6C), 50.56 (s, CH$_3$**C**, 1C), 58.37,69.03,71.43 (3s, HO**C**H$_2$(**C**H$_2$)$_4$CH$_2$N, 30C), 61.54 (s, O**C**H$_2$C=CH, 6C), 69.32 (s, Ar**C**H$_2$OPh, 3C), 101.05 (s, *p*-Ar, 3C), 106.90 (s, *o*-Ar, 6C), 114.33 (s, *m*-Ph, 6C), 125.30 (s, CH=**C**N, 6C), 129.60 (s, *o*-Ph, 6C), 140.01 (s, **C**CCH$_3$, 3C), 141.92 (s, **C**CH$_2$OPh, 3C), 142.82 (s, **C**H=CN, 6C), 156.61 (s, *p*-Ph, 3C), 159.62 (s, **C**OCH$_2$C=CH, 6C). Anal. Calcd for $C_{95}H_{126}N_{18}O_{15}$: C, 65.8; H, 7.02; N, 13.9. Found: C, 65.9; H, 6.94; N, 13.7.

(Ad)$_{12}$-[G-2]$_3$-[C], 39. This compound was prepared from the acetylene-terminated dendrimer **16** and 1-azidoadamantane **19**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **39** as a pale yellow powder; T_g = 119 °C (86.6% yield). ^{1}H NMR ($CDCl_3$): δ 1.77 (s, CHC**H**$_2$CH, 144H), 2.09 (s, C**H**$_3$C, 3H), 2.24 (s, (C**H**$_2$)$_3$-CN and (CH$_2$)$_3$C**H**, 216H), 4.95,5.14 (2s, ArC**H**$_2$OAr, 42H), 5.31 (s, OC**H**$_2$C=CH, 24H), 6.49−6.72 (m, *o*,*p*-Ar, 27H), 6.85,6.98 (2d, J = 8.9 Hz, *o*,*m*-Ph, 12H), 7.71 (s, C**H**=CN, 12H). ^{13}C NMR ($CDCl_3$): δ 25.89 (s, **C**H$_3$C, 1C), 29.74,36.14,43.18 (3s, (CH$_2$)$_3$**C**H, CH**C**H$_2$CH, (**C**H$_2$)$_3$CN, 108C), 50.83 (s, CH$_3$**C**, 1C), 60.19 (s, (CH$_2$)$_3$**C**N, 12C), 62.75 (s, O**C**H$_2$C=CH, 12C), 68.20,70.28,72.25 (3s, Ar**C**H$_2$O, 21C), 101.50 (s, *p*-Ar, 9C), 107.04 (s, *o*-Ar, 18C), 114.64 (s, *m*-Ph, 6C), 119.66 (s, CH=**C**N, 12C), 130.10 (s, *o*-Ph, 6C), 139.83 (s, **C**CCH$_3$, **C**CH$_2$OPh, 6C), 142.51 (s, **C**CH$_2$OAr, 6C), 143.20 (s, **C**H=CN, 12C), 157.30 (s, *p*-Ph, 3C), 160.32 (s, **C**OCH$_2$C=CH, 12C), 160.50 (s, **C**OCH$_2$ArOCH$_2$C=CH, 6C); MALDI mass spectrum: Calcd for $C_{237}H_{276}N_{36}O_{21}$: 3962.163. Found: 3962.182.

(DR)$_{12}$-[G-2]$_3$-[C], 40. This compound was prepared from the acetylene-terminated dendrimer **16** and the azide **26**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 7:3 mixture of hexane and ethyl acetate, to give **40** as a red viscous oil; T_g = 119 °C (89.0% yield). ^{1}H NMR ($CDCl_3$): δ 0.98 (s, C**H**$_3$CH$_2$N, 36H), 1.89 (s, C**H**$_3$C, 3H), 3.07 (s, CH$_3$C**H**$_2$N, 24H), 3.80 (s, NC**H**$_2$CH$_2$N=N, 24H), 4.48 (s, NCH$_2$C**H**$_2$N=N, 24H), 4.78 (s, Ar−C**H**$_2$O−Ar, 18H), 5.05 (s, CH=C−C**H**$_2$O, 24H), 6.49−6.86 (m, dendrimer *o*,*p*-Ar, Ph, 39H), 7.37−8.23 (m, C**H**=C, dye *o*,*p*-Ar, 72H). ^{13}C NMR ($CDCl_3$): δ 12.48 (s, NCH$_2$**C**H$_3$, 12C), 26.00 (s, **C**H$_3$C, 1C), 45.85 (s, N**C**H$_2$CH$_3$, 12C), 47.46 (s, N**C**H$_2$CH$_2$N$_3$, 12C), 49.12 (s, CH$_3$**C**, 1C), 50.98 (s, NCH$_2$**C**H$_2$N=N, 12C), 62.75 (s, CH=C**C**H$_2$O, 6C), 68.14 (s, Ar**C**H$_2$OPh, 3C), 110.82, 111.85, 118.31, 123.12, 126.33, 127.22, 128.87, 130.27, 132.40, 134.30, 144.56, 145.76, 146.98, 148.45, 152.02, 161.12 (16s, *m*,*o*-Ph, **C**H=**C**N, **C**CCH$_3$, **C**OCH$_2$, dendrimer *o*,*p*-Ar, dye Ar, 168C). MALDI mass spectrum: Calcd for $C_{309}H_{288}Cl_{12}N_{84}O_{45}$: 6313.909. Found: 6313.925.

General Procedure for the Click Reaction Catalyzed by CuSO$_4$ in Water. (Nuc)$_{12}$-[G-2]$_3$-[C], 41. A solution of the acetylene-terminated dendrimer **16** (18 mg, 10 μmol), 3′-azido-3′-deoxythymidine **28** (32 mg, 0.12 mmol), sodium ascorbate (2 mg, 12 μmol), and $CuSO_4$ (1 mg, 6 μmol) in a 1:1 mixture of water and tetrahydrofuran (2 mL) was stirred at room temperature for ca. 48 h. After evaporation of the solvents, the crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **41** as a white powder; T_g = 17 °C (94.0% yield). ^{1}H NMR (DMSO-d_6): δ 2.12 (s, C**H**$_3$C, 3H), 2.47−2.74 (m, OCHC**H**$_2$-CHN, 24H), 3.41−3.67 (m, CHC**H**$_2$OH and COCH=C**H**N, 36H), 4.31 (s, COC**H**=CHN, 12H), 4.64−5.43 (m, OCHCH$_2$C**H**N, OC**H**CH$_2$OH, ArC**H**$_2$O and OC**H**$_2$C=CH, 66H), 6.21 6.97 (m, *o*,*p*-Ar, *o*,*m*-Ph and OC**H**CH$_2$CHN, 51H), 7.72 (s, N**H**, 12H), 8.36 (s, C**H**=CN, 12H), 9.28 (s, O**H**, 12H). ^{13}C NMR (DMSO-d_6): δ 12.60 (s, OCH**C**H$_2$CHN, 12C), 25.47 (s, **C**H$_3$C, 1C), 36.87 (s, CH$_3$**C**, 1C), 37.53 (s, **C**H$_2$OH, 12C), 59.74,61.2 (2s, O**C**H$_2$C=CH and CO**C**H=CHN, 24C), 83.72,84.25,84.78 (3s, Ar**C**H$_2$O, ArO**C**H$_2$C=CH and **C**HCH$_2$OH, 33C), 101.27 (s, *p*-Ar, 9C), 103.24 (s, *o*-Ar, 18C), 107.04 (s, O**C**HCH$_2$CHN, 12C), 110.00 (s, OCHCH$_2$**C**HN, 12C), 114.16 (s, *m*-Ph, 6C), 124.96 (s, CH=**C**N, 12C), 129.19 (s, *o*-Ph, 6C), 136.43 (s, **C**CCH$_3$, **C**CH$_2$OPh, 6C), 136.55 (s, **C**ONHCON, 6C), 139.45 (s, **C**CH$_2$OAr, 6C), 143.53 (s, **C**H=CN, 12C), 150.79 (s, CONH**C**ON, 24C), 159.61,

159.78, 164.07 (3s, **C**OCH$_2$, 21C). MALDI mass spectrum: Calcd for $C_{225}H_{228}N_{60}O_{69}$: 4873.618. Found: 4873.621.

(Sug)$_{12}$-[G-2]$_3$-[C], 42. This compound was prepared from the acetylene-terminated dendrimer **16** and the azide **25**, according to the general procedure for click reaction with sodium ascorbate and $CuSO_4$ in water/tetrahydrofuran. After evaporation of the solvents, the crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **42** as a colorless powder; T_g = 63 °C (93% yield). ^{1}H NMR (DMSO-d_6): δ 1.95 (s, C**H**$_3$C, 3H), 4.78−5.19 (m, Ar−C**H**$_2$O−Ar, 90H), 5.90 (s, SC**H**$_2$, 48H), 6.42−7.44 (m, *o*,*p*-Ar and Ph core, 195H), 8.13 (s, C**H**=C, 24H). ^{13}C NMR (DMSO-d_6): δ 26.00 (s, **C**H$_3$C, 1C), 29.82 (s, (CH$_2$)$_3$**C**H, 18C), 29.82 (s, (CH$_2$)$_3$**C**H, 18C), 36.27 (s, CH**C**H$_2$CH, 18C), 43.37 (s, (**C**H$_2$)$_3$CN, 18C), 50.98 (s, CH$_3$**C**, 1C), 60.09 (s, (CH$_2$)$_3$**C**N, 6C), 62.75 (s, CH=C**C**H$_2$O, 6C), 70.17 (s, Ar**C**H$_2$OPh, 3C), 114.31 (s, *m*-Ph, 6C), 124.35 (s, C=**C**NCH$_2$, 3C), 130.04 (s, *o*-Ph, 6C), 142.56 (s, **C**=CNCH$_2$, 3C), 144.50 (s, **C**CCH$_3$, 3C), 156.78 (s, **C**OCH$_2$, 3C); MALDI mass spectrum: Calcd for $C_{201}H_{252}N_{36}O_{57}$: 4081.793. Found: 4081.801.

(Ad)$_{24}$-[G-3]$_3$-[C], 43. This compound was prepared from the acetylene-terminated dendrimer **17** and 1-azidoadamantane **19**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **43** as a colorless powder; T_g = 108 °C (96.1% yield). ^{1}H NMR (CDCl$_3$): δ 1.61 (s, CHC**H**$_2$CH, 288H), 2.05 (s, C**H**$_3$C, 3H), 2.09 (s, (C**H**$_2$)$_3$-CN and (CH$_2$)$_3$C**H**, 432H), 4.95,4.98 (2s, ArC**H**$_2$O, 42H), 5.31 (s, OC**H**$_2$C=CH, 48H), 6.49−7.01 (m, *o*,*p*-Ar, *o*,*m*-Ph, 75H), 7.72 (s, C**H**=CN, 24H). ^{13}C NMR (CDCl$_3$): δ 26.00 (s, **C**H$_3$C, 1C), 29.81,36.25,43.32 (3s, (CH$_2$)$_3$**C**H, CH**C**H$_2$CH, (**C**H$_2$)$_3$CN, 216C), 53.23 (s, CH$_3$**C**, 1C), 60.07 (s, (CH$_2$)$_3$**C**N, 24C), 62.67,68.11,-70.12 (3s, Ar**C**H$_2$O, 45C), 102.30 (s, *p*-Ar, 21C), 107.04 (s, *o*-Ar, 42C), 114.37 (s, *m*-Ph, 6C), 119.83 (s, CH=**C**N, 24C), 127.41 (s, *o*-Ph, 6C), 139.54 (s, **C**CCH$_3$, **C**CH$_2$O, 24C), 143.29 (s, **C**H=CN, 24C), 157.30, 160.16, 160.32 (3s, *p*-Ph, **C**OCH$_2$C=CH, **C**OCH$_2$, 45C); MALDI mass spectrum: Calcd for $C_{437}H_{552}N_{72}O_{45}$: 7528.312. Found: 7528.317.

(Est)$_{24}$-[G-3]$_3$-[C], 44. This compound was prepared from the acetylene-terminated dendrimer **17** and the azide **24**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was precipitated in diethyl ether, to give **44** as a white powder; T_g = 72 °C (93.6% yield). ^{1}H NMR (CDCl$_3$): δ 2.01 (s, C**H**$_3$C, 3H), 3.84 (s, COOC**H**$_3$, 72H), 4.83,5.04 (2s, ArC**H**$_2$O, OC**H**$_2$C=CH, 90H), 5.49 (s, PhC**H**$_2$N, 48H), 6.53−6.92 (m, *o*,*p*-Ar and Ph core, 75H), 7.22,7.93 (2d, J = 8.1 Hz, *o*,*m*-PhCH$_2$N, 96H), 8.24 (s, C**H**=C, 24H). ^{13}C NMR (CDCl$_3$): δ 30.06 (s, **C**H$_3$C, 1C), 51.31 (s, CH$_3$**C**, 1C), 52.64 (s, **C**H$_3$O, 24C), 53.94 (s, **C**H$_2$N, 24C), 62.24 (s, O**C**H$_2$C=CH, 24C), 70.00 (s, Ar**C**H$_2$O, 21C), 101.66 (s, *p*-Ar, 21C), 106.86 (s, *o*-Ar, 42C), 114.45 (s, *m*-Ph, 6C), 123.75 (s, CH=**C**N, 24C), 128.21 (s, *m*-ArCOOMe, 48C), 129.87 (s, *o*-Ph, 6C), 128.21 (s, *o*-ArCOOMe, 48C), 139.83 (s, **C**CH$_2$O, 21C), 142.27 (s, **C**CCH$_3$, 3C), 144.65 (s, **C**H=CN, 24C), 156.98 (s, *p*-Ph, 3C), 159.84, 160.22, 166.74 (3s, **C**OCH$_2$C=CH, **C**OCH$_2$, 45C). MALDI mass spectrum: Calcd for $C_{453}H_{408}N_{72}O_{93}$: 8342.941. Found: 8342.938.

(PhS)$_{24}$-[G-3]$_3$-[C], 45. This compound was prepared from the acetylene-terminated dendrimer **17** and azidomethylphenyl sulfide **22**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was precipitated in diethyl ether, to give **45** as a colorless powder; T_g = 63 °C (92.9% yield). ^{1}H NMR (DMSO-d_6): δ 1.95 (s, C**H**$_3$C, 3H), 4.78−5.19 (m, ArC**H**$_2$O, OC**H**$_2$C=CH, 90H), 5.90 (s, SC**H**$_2$, 48H), 6.42−7.44 (m, *o*,*p*-Ar, Ph core and *o*,*m*,*p*-PhS, 195H), 8.14 (s, C**H**=C, 24H). ^{13}C NMR (DMSO-d_6): δ 30.17 (s, **C**H$_3$C, 1C), 51.23 (s, CH$_3$**C**, 1C), 52.08 (s, S**C**H$_2$N, 24C), 61.34 (s, O**C**H$_2$C=CH, 24C), 69.49 (s, Ar**C**H$_2$O, 21C), 101.13 (s, *p*-Ar, 21C), 107.01 (s, *o*-Ar, 42C), 114.24 (s, *m*-Ph, 6C), 124.66 (s, CH=**C**N, 24C), 128.01 (s, *p*-PhS, 24C), 128.97 (s, *o*-Ph, 6C), 129.51 (s, *m*-PhS, 48C), 130.81 (s, *o*-PhS, 48C), 132.78 (s, **C**SCH$_2$, 24C), 139.83 (s, **C**CH$_2$O, 21C), 141.97 (s, **C**CCH$_3$, 3C), 143.25 (s, **C**H=CN, 24C), 156.98 (s, *p*-Ph, 3C), 158.81, 159.32, 159.74 (3s, **C**OCH$_2$C=CH, **C**OCH$_2$, 45C); MALDI mass spectrum: Calcd for $C_{405}H_{360}N_{72}O_{45}S_{24}$: 7718.139. Found: 7718.147.

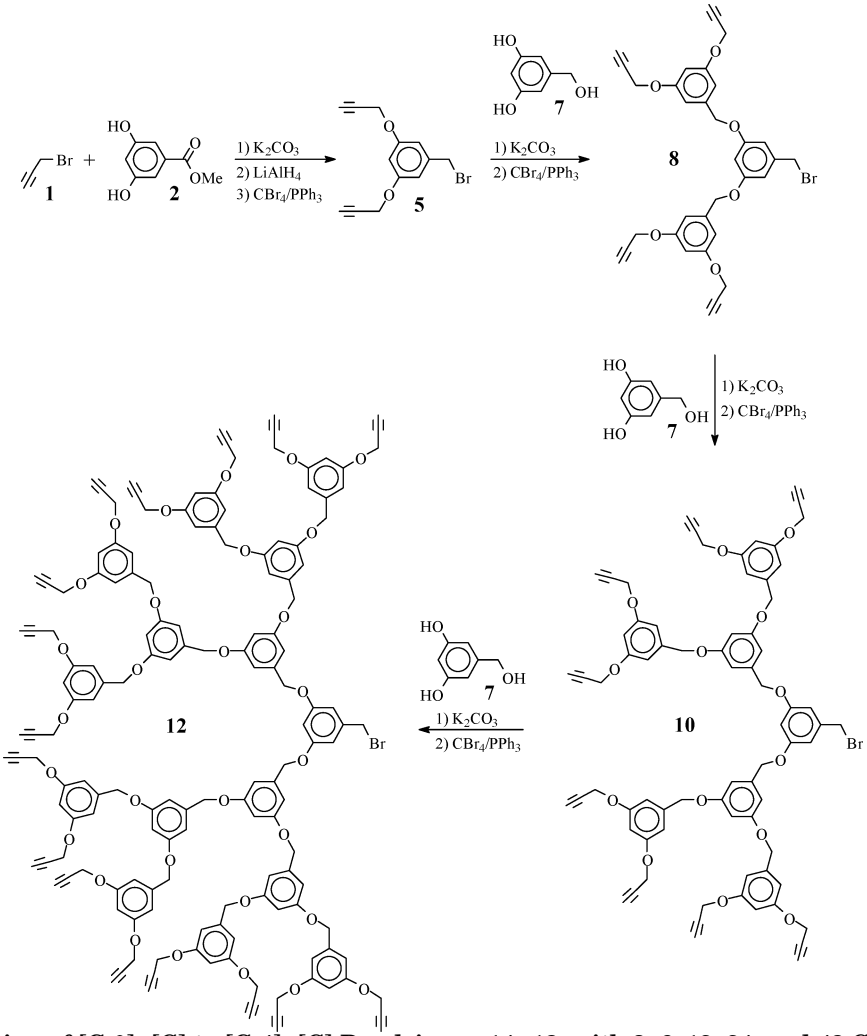
[G-1]$_{24}$-[G-3]$_3$-[C], 46. This compound was prepared from the acetylene-terminated dendrimer **17** and [G-1]-N$_3$ **29**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and methanol, to give **46** as a pale yellow glass; T_g = 74 °C (81.8% yield). ^{1}H NMR (CDCl$_3$): δ 1.98 (s, C**H**$_3$C, 3H), 4.67−5.16 (m, ArC**H**$_2$O, OC**H**$_2$C=CH, 186H), 5.29 (s, C**H**$_2$N, 48H), 6.29−6.67 (s, *o*,*p*-Ar, 115H), 6.73−6.97 (m, *o*,*m*-Ph, 12H), 7.17−7.38 (m, *o*,*m*,*p*-PhCH$_2$O, 240H), 7.45 (s, C**H**=C, 24H). ^{13}C NMR (CDCl$_3$): δ 26.02 (s, **C**H$_3$C, 1C), 54.12 (s, CH$_3$**C**, 1C), 66.27 (s, **C**H$_2$N, 24C), 70.45 (bs, O**C**H$_2$C=CH, Ar**C**H$_2$O, 45C), 102.15 (s, *m*-Ph, 6C), 102.47 (s, *p*-Ar, 21C), 106.72 (s, *o*-Ar, 42C), 107.53 (s, CH=**C**N, 24C), 127.93, 128.46, 128.97 (3s, *o*,*m*,*p*-Ph, 144C), 128.86 (s, *o*-Ph, 6C), 136.80 (s, **C**H=CN, 24C), 137.12 (s, **C**CH$_2$O, 21C), 140.71 (s, **C**CCH$_3$, 3C), 159.24, 160.70, 161.14 (3s, **C**OCH$_2$C=CH, **C**OCH$_2$, 45C).

(Ad)$_{48}$-[G-4]$_3$-[C], 47. This compound was prepared from the acetylene-terminated dendrimer **18** and 1-azidoadamantane **19**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and methanol, to give **47** as a white solid; T_g = 97 °C (96.8% yield). ^{1}H NMR (CDCl$_3$): δ 1.72 (s, CHC**H**$_2$CH, 576H), 2.10 (s, C**H**$_3$C, 3H), 2.17 (s, (C**H**$_2$)$_3$CN and (CH$_2$)$_3$C**H**, 864H), 4.86 (bs, ArC**H**$_2$O, 90H), 5.07 (s, OC**H**$_2$C=CH, 96H), 6.37−6.99 (m, *o*,*p*-Ar, *o*,*m*-Ph, 147H), 7.69 (s, C**H**=CN, 48H). ^{13}C NMR (CDCl$_3$): δ 26.97 (s, **C**H$_3$C, 1C), 29.79,36.22,43.27 (3s, (CH$_2$)$_3$**C**H, CH**C**H$_2$CH, (**C**H$_2$)$_3$CN, 432C), 51.39 (s, CH$_3$**C**, 1C), 60.07 (s, (CH$_2$)$_3$**C**N, 48C), 62.56 (s, Ar**C**H$_2$O, 93C), 99.98 (s, *p*-Ar, 45C), 106.79 (s, *o*-Ar, 90C), 114.43 (s, *m*-Ph, 6C), 119.97 (s, CH=**C**N, 48C), 128.14 (s, *o*-Ph, 6C), 139.27 (s, **C**CCH$_3$, **C**CH$_2$O, 48C), 143.02 (s, **C**H=CN, 48C), 160.13 (bs, *p*-Ph, **C**OCH$_2$C=CH, **C**OCH$_2$, 93C).

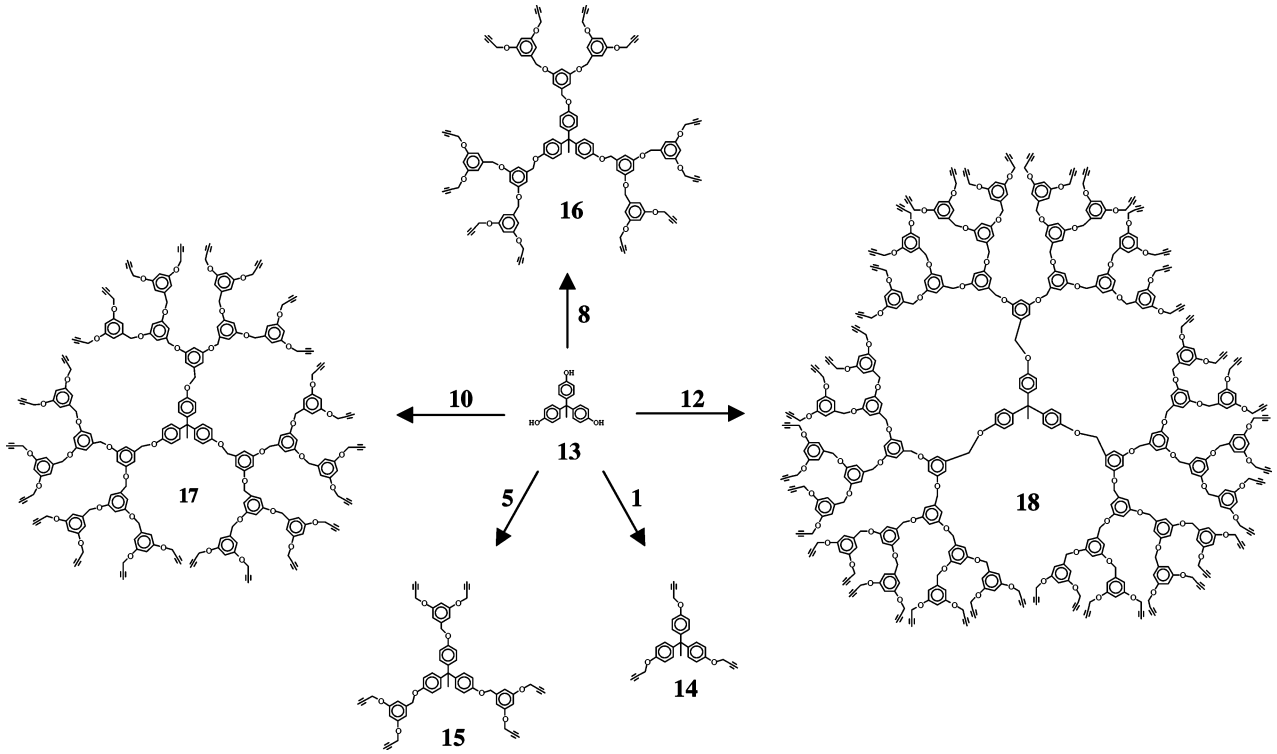
(Hex)$_{48}$-[G-4]$_3$-[C], 48. This compound was prepared from the acetylene-terminated dendrimer **18** and the azide **23**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was precipitated in diethyl ether, to give **48** as a pale yellow glass; T_g = 41 °C (94% yield). ^{1}H NMR (DMSO-d_6): δ 1.04−1.77 (m, CH$_2$-(C**H**$_2$)$_4$CH$_2$, 384H), 1.92 (s, C**H**$_3$C, 3H), 3.33 (s, CH$_2$O**H**, 48H), 4.17−4.33 (m, C**H**$_2$N, C**H**$_2$OH, 192H), 4.95 (bs, ArC**H**$_2$O, 90H), 5.06 (bs, OC**H**$_2$C=CHN, 96H), 6.46−6.99 (m, *o*,*p*-Ar, *o*-Ph, *m*-Ph, 147H), 8.13 (s, C=C**H**, 48H). ^{13}C NMR (DMSO-d_6): δ 25.23,26.09,30.10,32.58 (4s, HOCH$_2$(**C**H$_2$)$_4$CH$_2$N, 192C), 49.73 (s, CH$_2$N, 48C), 60.93 (s, Ar**C**H$_2$O, 93C), 61.55 (s, **C**H$_2$OH, 48C), 69.45 (s, *p*-Ar, 45C), 101.08 (s, *p*-Ar, 45C), 106.90 (s, *o*-Ar, 90C), 114.10 (s, *m*-Ph, 6C), 124.67 (s, CH=**C**N, 48C), 129.72 (s, *o*-Ph, 6C), 139.70 (s, **C**CCH$_3$, **C**CH$_2$O, 48C), 142.82 (s, **C**H=CN, 48C), 159.83, 159.59 (2s, *p*-Ph, **C**OCH$_2$C=CH, **C**OCH$_2$, 93C).

[G-2]$_{48}$-[G-4]$_3$-[C], 49. This compound was prepared from the acetylene-terminated dendrimer **18** and [G-2]-N$_3$ **30**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 19:1 mixture of dichloromethane and methanol, to give **49** as a pale yellow glass; T_g = 70 °C (95.1% yield). ^{1}H NMR (DMSO-d_6): δ 2.09 (s, C**H**$_3$C, 3H), 4.77 (bs, ArC**H**$_2$O, 90H), 4.85 (bs, OC**H**$_2$C=CHN, 96H), 5.29 (bs, PhC**H**$_2$O, 96H), 6.25−6.79 (m, *o*,*p*-Ar, *o*-Ph, *m*-Ph, 147H), 6.98−7.29 (m, *o*,*m*,*p*-PhCH$_2$, 480H), 8.03 (s, C=C**H**, 48H). ^{13}C NMR (CDCl$_3$): δ 54.19 (s, CH$_2$N, 48C), 62.13 (s, O**C**H$_2$C=CH, 48C), 70.32 (s, Ar**C**H$_2$O, 333C), 101.94, 102.35 (2bs, *p*-Ar, 45C), 106.72, 107.44 (2bs, *o*-Ar, 90C), 123.63 (s, CH=**C**N, 48C), 127.94, 128.35, 128.93 (3s, *o*,*m*,*p*-Ph, 960C), 137.13, 137.39, 139.36, 139.17 (4s, **C**CH$_2$O, 333C), 144.38 (s,

Scheme 1. Synthetic Route for the Preparation of Acetylene-Terminated Dendrons $(Acet)_2$-[G-1]-Br 5, $(Acet)_4$-[G-2]-Br 8, $(Acet)_8$-[G-3]-Br 10, and $(Acet)_{16}$-[G-4]-Br 12



Scheme 2. Preparation of $[G\text{-}0]_3$-[C] to $[G\text{-}4]_3$-[C] Dendrimers 14−18, with 3, 6, 12, 24, and 48 Chain End Acetylene Groups



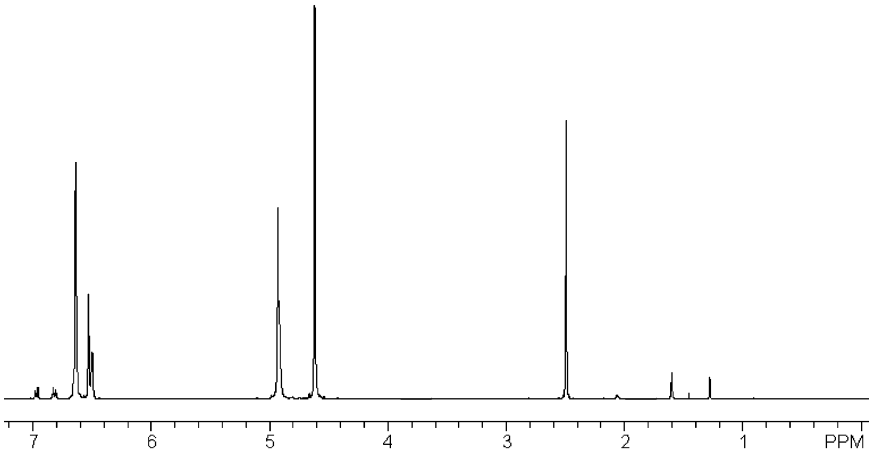
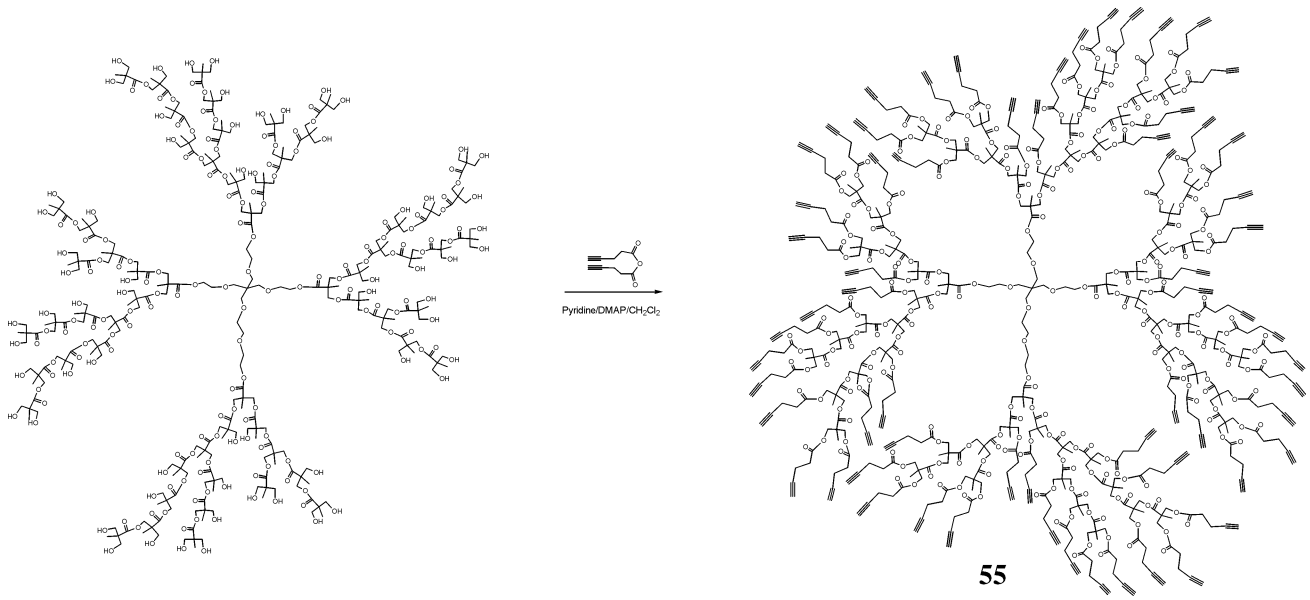


Figure 1. ^{1}H NMR spectrum for the 48-acetylene-substituted dendrimer $(Acet)_{48}$-($[G\text{-}4]$)$_3$-[C], **18**.

Scheme 3. Preparation of Acetylene-Terminated, Hyperbranched Polyester, 55, Based on Commercially Available Boltorn Resin



CH=CN, 48C), 159.87, 160.46, 160.57 (3s, **C**OCH$_2$C=CH, **C**OCH$_2$, 333C).

[G-3]$_{48}$-[G-4]$_3$-[C], 50. This compound was prepared from the acetylene-terminated dendrimer **18** and [G-3]-N_3 **31**, according to the general procedure for click reaction with *N*,*N*-diisopropylethylamine and Cu(PPh$_3$)$_3$Br in tetrahydrofuran under microwave irradiation. The crude product was purified by column chromatography, eluting with a 9:1 mixture of dichloromethane and methanol, to give **50** as a colorless foam; T_g = 64 °C (75.7% yield). ^{1}H NMR ($CDCl_3$): δ 4.37−5.22 (bm, ArC**H**$_2$O, OC**H**$_2$C=CHN, PhC**H**$_2$O, 1530H), 5.85−7.19 (bm, *o*,*p*-Ar, *o*,*m*,*p*-PhCH$_2$, C**H**=CN, 3255H). ^{13}C NMR ($CDCl_3$): δ 70.32 (s, O**C**H$_2$C=CH, Ar**C**H$_2$O, 765C), 70.95 (s, CH$_2$N, 48C), 101.87 (bs, *p*-Ar, 93C), 106.75 (bs, *o*-Ar, 186C), 125.03 (bs, CH=**C**N, 48C), 127.93 128.34 128.92 (3s, *o*,*m*,*p*-Ph, 1920C), 137.12 (bs, **C**CH$_2$O, 765C), 139.57 (bs, **C**H=CN, 48C), 160.45 (bs, **C**O-CH$_2$C=CH, **C**OCH$_2$, 861C).

General Procedure for Chemical Modification of Amino-Terminated Polyamine and Polyamide Dendrimers. (MeO)$_8$-[G-1]-PAMAM, 52. A solution of *N*-succinimidyl 4-pentynoate, **51** (0.68 g, 3.5 mmol),[14] in 10 mL of dry tetrahydrofuran was added dropwise to a solution of [G-1]-PAMAM (2.5 g, 20% in MeOH, 2.8 mmol of amine functionality) in 10 mL of dry tetrahydrofuran. After heating to reflux during 2 h, the mixture was cooled, and a solution of the azide **21** (0.97 g, 7.0 mmol), *N*,*N*-diisopropylethylamine (1.36 g, 10.5 mmol), and Cu(PPh$_3$)$_3$Br (0.7 g, 0.7 mmol) in 10 mL of dry tetrahydrofuran was added; stirring continued at room temperature for 48 h. The reaction mixture was then concentrated, filtered, and precipitated sequentially in ethyl acetate and in diethyl ether to give **52** as a slightly orange viscous oil (850 mg, 81.5%). ^{1}H NMR ($CDCl_3$): δ 2.04−3.41 (m, NC**H**$_2$C**H**$_2$N, NC**H**$_2$C**H**$_2$CO, COC**H**$_2$C**H**$_2$C=C and C**H**$_3$O, 186H), 3.52 (bs, CH$_3$OC**H**$_2$CH$_2$, 16H), 3.61 (bs, CH$_3$OCH$_2$C**H**$_2$, 16H), 3.86 (bs, C**H**$_2$CH$_2$N, 16H), 4.52 (bs, OCH$_2$C**H**$_2$N, 16H), 7.14−8.35 (2bs, CON**H** and C=C**H**, 28H). ^{13}C NMR ($CDCl_3$): δ 18.84,23.27,-31.87,36.32,38.07, 51.35 (6s, N**C**H$_2$**C**H$_2$N N**C**H$_2$**C**H$_2$CO, CO**C**H$_2$-**C**H$_2$C=C, 66C), 59.42 (s, **C**H$_3$O, 8C), 69.47 (s, CH$_2$**C**H$_2$N, 8C), 70.84 (s, CH$_3$O**C**H$_2$, 8C), 72.13 (s, CH$_3$OCH$_2$**C**H$_2$O**C**H$_2$, 16C), 96.82 (s, C=**C**H, 8C), 103.72 (s, **C**=CH, 8C), 173.33 (bs, **C**ONH, 20C).

(MeO)$_{32}$-[G-4]-DSM, 53. This compound was prepared from [G-4]-DAB-Am-32 and *N*-succinimidyl 4-pentynoate **51** (1.25 equiv)[14] in tetrahydrofuran and subsequent functionalization by Click chemistry with the azide **21** (2 equiv), *N*,*N*-diisopropylethylamine (3 equiv), and Cu(PPh$_3$)$_3$Br (0.2 equiv) in tetrahydrofuran at room temperature for 48 h. The crude product was purified by successive precipitation in ethyl acetate and in diethyl ether to give **53** as a slightly yellow viscous oil (77.5%). ^{1}H NMR ($CDCl_3$): δ 2.04−3.41 (m, NC**H**$_2$C**H**$_2$N, NC**H**$_2$C**H**$_2$CO, COC**H**$_2$C**H**$_2$C=C and C**H**$_3$O, 186H), 3.52 (bs, CH$_3$OC**H**$_2$CH$_2$, 16H), 3.61 (bs, CH$_3$OCH$_2$C**H**$_2$, 16H), 3.86 (bs, C**H**$_2$CH$_2$N, 16H), 4.52 (bs, OCH$_2$C**H**$_2$N, 16H), 7.14−8.35 (2bs, CON**H** and C=C**H**N, 28H). ^{13}C NMR ($CDCl_3$): δ 18.84 (s, **C**H$_3$C, 1C), 23.27 (s, **C**H$_3$C, 1C), 31.87 (s, **C**H$_3$C, 1C), 36.32 (s, **C**H$_3$C, 1C), 38.07 (s, CH$_3$**C**, 1C), 51.35 (s, **C**H$_2$C=

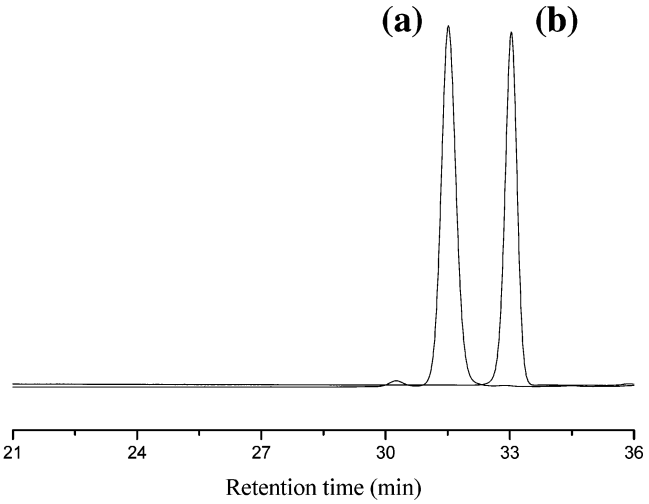


Figure 2. GPC traces for (a) the adamantane functionalized dendrimer, **37**, and (b) the hexaacetylene substituted starting material, **15**, obtained after forcing conditions.

CH, 12C), 59.42 (s, **C**H_3O, 8C), 69.47 (s, CH_3O**C**H_2, 8C), 70.84 (s, CH_3OCH_2**C**H_2, 8C), 72.13 (s, **C**H_2**C**H_2N, 8C), 70.84 (s, CH_2**C**H_2N, 8C), 72.11 (s, **C**≡CNCH_2, 8C), 124.35 (s, C≡**C**-NCH_2, 8C), 173.33 (bs, **C**ONH, 20C).

General Procedures for the Synthesis of Acetylene-Terminated Dendritic and Hyperbranched Polyesters (Boltorn). Anhydride-Activated Pentyonic Acid Acetylene, 54. To a stirred solution of 4-pentynoic acid (2.00 g, 20.4 mmol) in dichloromethane (20 mL) was added 1,3-dicyclohexylcarbodiimide (2.10 g, 1.02 mmol). The reaction mixture was stirred at room temperature for 16 h, filtered, and evaporated to dryness. The byproducts were then isolated through precipitation in 20 mL of hexane and filtration. After evaporation of the solvent, the anhydride **54** was recovered as a colorless oil (1.72 g, 95.0%). ^{1}H NMR ($CDCl_3$): δ 1.97 (t, J = 5.3 Hz, C≡C**H**, 2H), 2.41−2.46 (m, C**H**$_2$C≡CH, 4H), 2.62 (t, J = 14 Hz, **C**H_2COO, 4H). ^{13}C NMR ($CDCl_3$): δ 13.36 (s, **C**H_2C≡CH, 2C), 33.89 (s, **C**H_2COO, 2C), 69.44 (s, C≡**C**H, 2C), 81.30 (s, **C**≡CH, 2C), 166.95 (s, CH_2**C**OO, 2C).

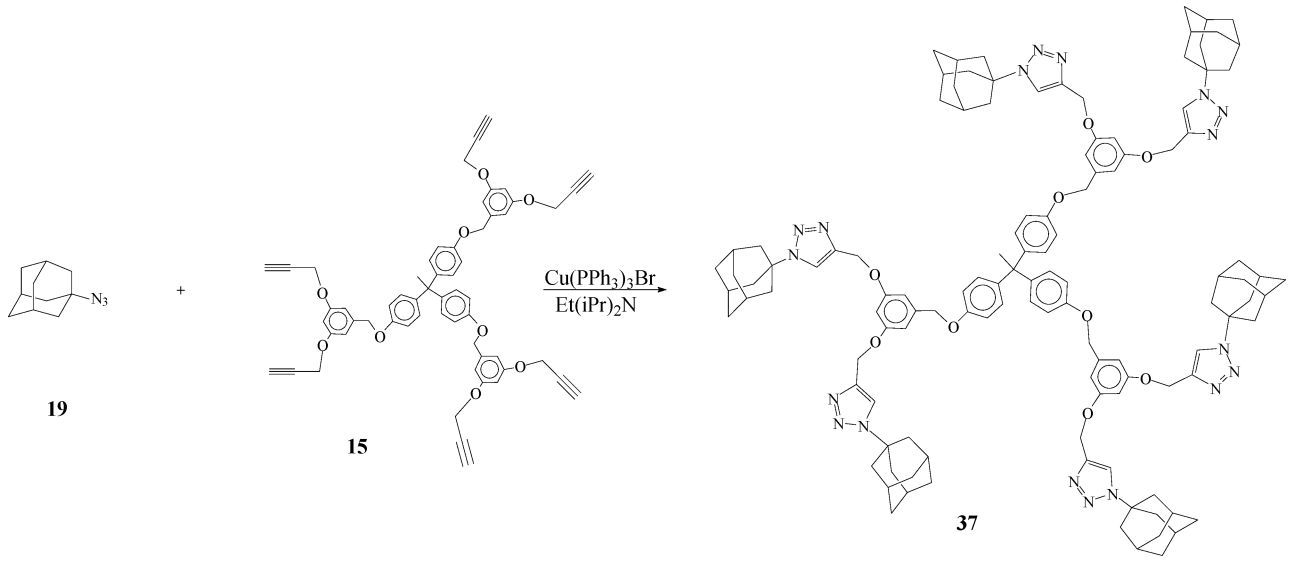
Acetylene-Terminated Boltorn-H40. (Acet)$_{64}$-[G-4]$_4$, 55. A solution of Boltorn H40 (0.370 g, 50.6 μmol), 4-(dimethylamino)pyridine (98.8 mg, 0.809 mmol), and pyridine (1.28, 16.2 mmol) in 10 mL of dichloromethane was added to the anhydride **54** (0.939 g, 5.27 mmol). The reaction was stirred for 16 h, and then all excess anhydride was converted to the acid analogue by quenching with water. The mixture was then diluted with 200 mL of dichloromethane and extracted with Na_2CO_3 (2 × 25 mL, 10% w/v) and $NaHSO_4$ (2 × 25 mL, 10% w/v). The organic phase was dried, filtered, and concentrated. To the oily residual was added a small amount of diethyl ether and the solids (byproduct) were filtered. Finally, the acetylene-functionalized polyester **55** was collected as a colorless viscous oil (0.465 g, 73.8%) after precipitation from ether into hexane. ^{1}H NMR ($CDCl_3$): δ 1.21 (bs, CC**H**$_3$, 180H), 1.96 (bs, C≡C**H**, 64H), 2.43−2.52 (m, CC**H**$_2$C**H**$_2$C≡CH, 256H), 3.18−3.33 (m,OC**H**$_2$C**H**$_2$O, 20H), 4.06−4.13 (m, CC**H**$_2$O, 240H). ^{13}C NMR ($CDCl_3$): δ 14.14 (s, **C**H_2C≡CH, 64C), 17.39 (s, C**C**H_3, 4C), 17.43 (s, C**C**H_3, 8C), 17.56 (s, C**C**H_3, 16C), 17.66 (s, C**C**H_3, 32C), 32.99 (s, **C**H_2COO, 64C), 46.24 (s, **C**CH_3, 16C), 46.37 (s, **C**CH_3, 32C), 46.45 (s, **C**CH_3, 4C), 46.24 (s, **C**CH_3, 8C), 64.97 (s, C**C**H_2O, 16C), 65.19 (s, C**C**H_2O, 32C), 65.32 (s, C**C**H_2O, 8C), 65.45 (s, C**C**H_2O, 64C), 65.55 (s, OCH_2**C**H_2OOC, 4C), 69.22 (s, C≡**C**H,64C), 69.28 (s, O**C**H_2**C**H_2O, 10C), 80.20 (s, **C**≡CH, 64C), 170.92 (s, CH_2**C**COO, 32C), 170.99 (s, CH_2**C**COO, 64C), 171.54 (s, CH_2**C**COO, 16C), 171.78 (s, CH_2**C**COO, 8C), 171.83 (s, CH_2**C**COO, 4C).

Table 1. Yields and Glass Transition Temperatures for the Library of Chain End Functionalized Dendrimers Prepared from the Azido Derivatives, 19−31, and Dendritic Cores Using Click Chemistry

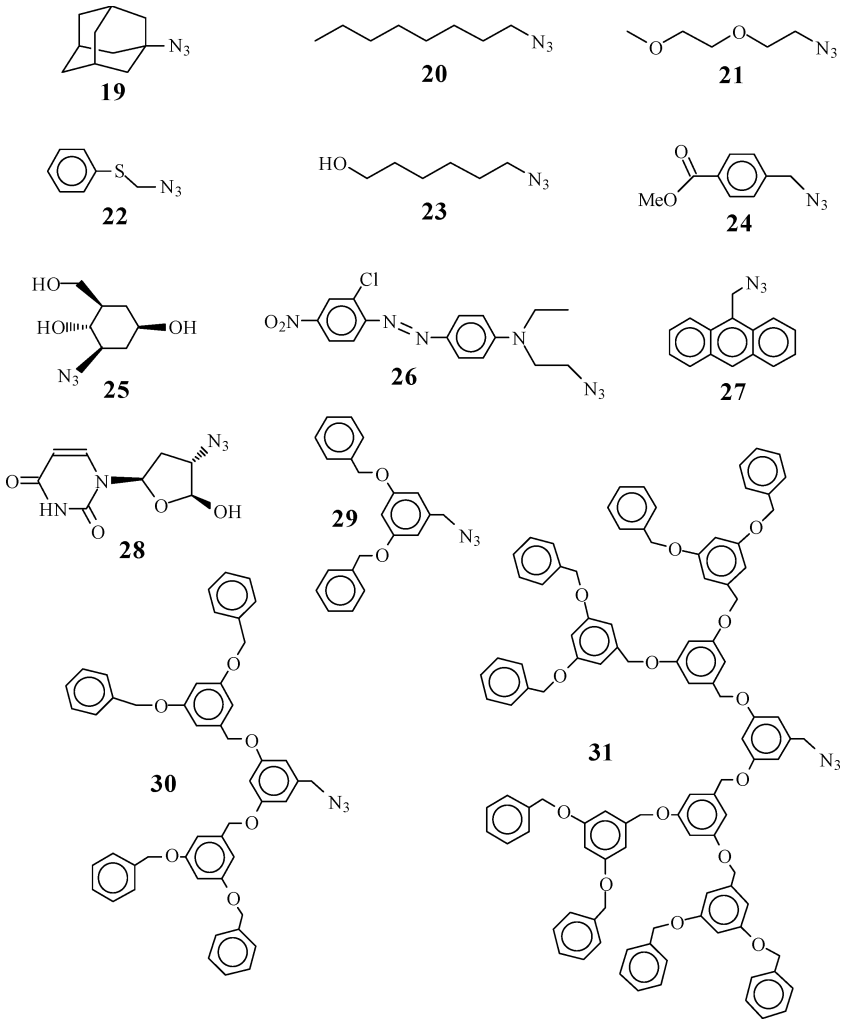
azide derivative	dendritic core	purified yield (%)	T_g (°C)
19	G-1	96	121
19	G-2	87	119
19	G-3	96	108
19	G-4	97	97
20	G-1	93	9
20	G-4	94	−5
21	G-3	88	21
21[a]	G-1 PAMAM	82	−23
21[a]	G-4 DSM	78	−14
22	G-3	93	63
23	G-1	90	9
23	G-4	94	41
24	G-3	94	72
25[a]	G-2	93	63
26	G-3	82	119
26	G-4	91	108
27	hyperbranched	75	89
27	G-2	86	114
28[a]	G-2	94	17
29	G-3	82	74
30	G-4	95	70
31	G-4	76	64

[a] Reactions were performed under aqueous conditions.

Scheme 4. Functionalization of the Hexasubstituted Dendrimer, 15, with 1-Azidoadamantane, 19, by Nonaqueous Click Chemistry



Scheme 5. Structure of Monofunctional Azides 19−31, Used in the Synthesis of Chain End Functionalized Dendrimers Based on Click Chemistry



Functionalization of Acetylene-Terminated Hyperbranched Polyester, Boltorn H40, Using $Cu(PPh_3)_3Br$-Catalyzed Click Chemistry. $(Ant)_{64}$-[G-4]$_4$, 56. A solution of the acetylene-terminated hyperbranched polyester **55** (100 mg, 8.04 μmol), azide **27** (240 mg, 1.03 mmol), *N*,*N*-diisopropylethylamine (133 mg, 1.03 mmol), and $Cu(PPh_3)_3Br$ (48.9 mg, 51.5 μmol) in tetrahydrofuran (5 mL) was sealed in a vial and submitted to microwave irradiation at 100 °C for 10 min. The crude product was concentrated and precipitated three times in diethyl ether to give **56** as a pale yellow solid (165 mg, 75.0% yield). ^{1}H NMR (DMSO-d_6): δ 0.78−1.10 (bm, CC**H**$_3$, 180H), 2.25−2.70 (bm, CC**H**$_2$C**H**$_2$C═CH, 256H), 3.08−3.42 (bs,OC**H**$_2$C**H**$_2$O, 20H), 3.80−4,17 (m, CC**H**$_2$O, 240H), 6.40 (bs, *Ar*C**H**$_2$, 128H), 7.43 (bs, 2,3,6,7-*Ar***H** and CH$_2$C═C**H**N, 320H), 7.96 (bs, 1,8-*Ar***H**, 128H), 8.55 (bs, 4,5-*Ar***H** and 10-*Ar***H**, 192H).

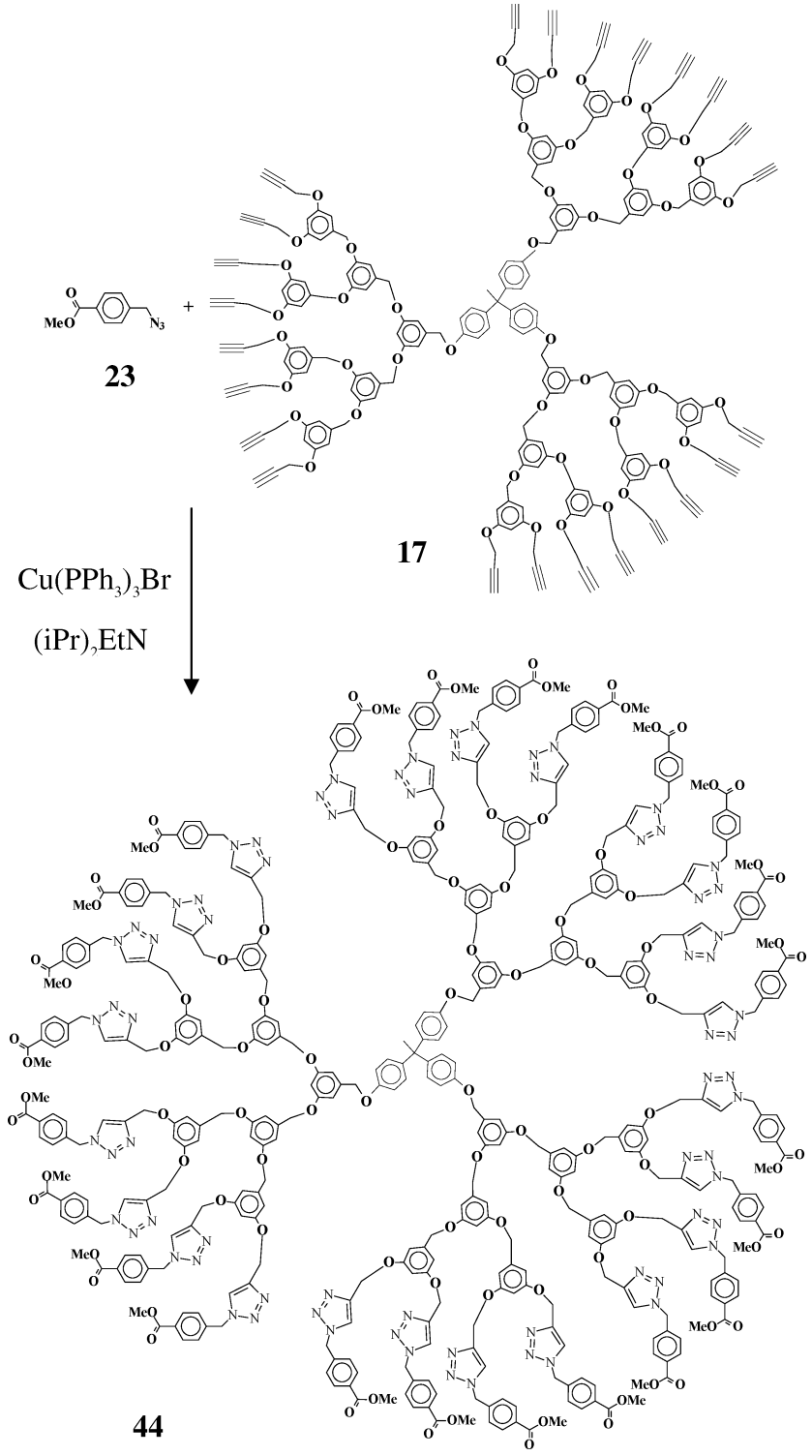
Acetylene-Terminated Bis-MPA Dendrimer. $(Acet)_{12}$-[G-2]$_3$-[C], 57. The dodecahydroxy-terminated dendrimer (1.20 g, 0.885 mmol) was dissolved in pyridine (4.15 mL) followed by the addition of CH_2Cl_2 (4 mL), DMAP (197 mg, 1.59 mmol), and 4-pentynoic anhydride (2.27 g, 12.7 mmol). The reaction mixture was stirred at room temperature overnight, and the crude reaction mixture was diluted in CH_2Cl_2 (150 mL) and washed with 10% $NaHSO_4$ (3 × 80 mL), saturated $NaHCO_3$ (2 × 50 mL), and brine (50 mL). The organic phase was dried over $MgSO_4$, filtered, concentrated, and purified by liquid column chromatography on silica gel, eluting with hexane and gradually increasing the polarity to 45:55 EtOAc:hexane to give **57** as a colorless viscous oil. ^{1}H NMR (CD_3Cl, 400 MHz): δ = 7.12 (d, J = 8.8 Hz, 6H), 6.98 (d, J = 8.8 Hz, 6H), 4.40 (s, 12H), 4.27 (t, J = 12.4 Hz, 24H), 2.53 (m, 24H), 2.45 (m, 24H), 2.17 (s, 3H), 1.97 (t, J = 2.4 Hz, 12H), 1.41 (s, 9H), 1.27 (s, 18H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.0, 171.1, 148.5, 146.4, 129.8, 120.7, 82.3, 69.3, 65.6, 65.3, 47.0, 46.4, 33.1, 17.9, 17.7, 14.2 ppm. MALDI mass spectrum: Calcd for $C_{125}H_{138}O_{42}$: 2311.866. Found: 2311.870.

Ethyl Acetate-Terminated Bis-MPA Dendrimer. $(EtO_2CCH_2)_{12}$-[G-2]$_3$-[C], 58. The acetylene-terminated dendrimer, **57** (350 mg, 0.15 mmol), and $EtOCOCH_2N_3$ (245 mg, 1.90 mmol) were mixed in THF/water (2:1, 6 mL), followed by addition of $CuSO_4 \cdot 5H_2O$ (22.6 mg, 0.09 mmol) and sodium ascorbate (79.2 mg, 0.4 mmol). The solution was stirred at room temperature overnight, and after evaporation of the solvent, the crude reaction mixture was purified by column chromatography on silica gel, initially eluting with hexane and EtOAc (2:8) and gradually increasing the polarity to 9:1 EtOAc:MeOH to give the desired triazole dendrimer, **58**, as colorless viscous oil, 530 mg (91%). ^{1}H NMR (CD_3Cl, 400 MHz): δ = 7.50 (s, 12H), 7.06 (d, J = 8.8 Hz, 6H), 6.95 (d, J = 8.8 Hz, 6H), 5.10 (s, 24H), 4.34 (s, 12H), 4.21 (q, J = 7.2 Hz, 24H), 4.14 (m, 24H), 2.98 (t, J = 7.2 Hz, 24H), 2.70 (t, J = 7.2 Hz, 24H), 2.11 (s, 3H), 1.36 (s, 9H), 1.26 (t, J = 7.2 Hz, 36H), 1.17 (s, 18H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.0, 170.9, 166.5, 148.5, 146.3, 129.7, 122.8, 120.7, 65.4, 65.1, 62.2, 50.7, 46.9, 46.4, 33.1, 20.8, 17.7, 14.0 ppm. MALDI mass spectrum: Calcd for $C_{173}H_{222}N_{36}O_{66}$: 3861.518. Found: 3861.519.

Results and Discussion

In designing dendrimers for functionalization by Click chemistry, either acetylene- or azide-terminated den-

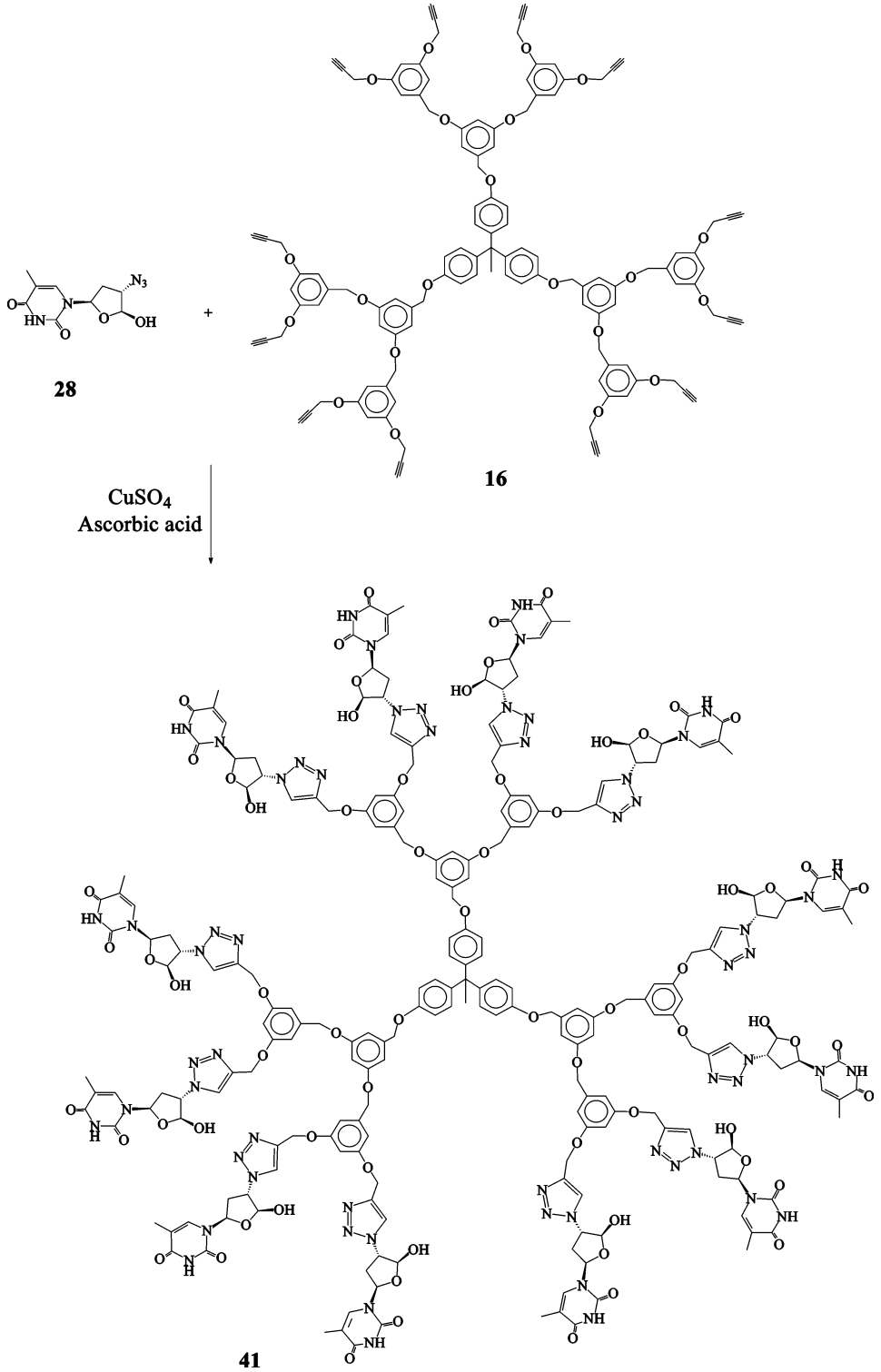
Scheme 6. Functionalization of the Third-Generation Dendrimer, 17, with Methyl 4-(Azidomethyl)benzoate, 23, by Nonaqueous Click Chemistry



dritic macromolecules can be envisaged. The ready availability of propargyl derivatives and the compatibility of acetylenic groups with a variety of chemical transformations led to the selection of acetylene-terminated dendrimers as the 3-dimensional scaffold for Click functionalization. Initially, the well-known 3,5-dioxybenzyl ether dendrimers[23] were selected as cores and prepared using a traditional convergent growth approach[13] with the respective dendrons from generation 1 to 4 being obtained in excellent yields (Scheme 1). Coupling of these acetylene-terminated dendrons to a central trifunctional core, **13**, then gave the desired dendrimers **14**−**18**, with 3, 6, 12, 24, and 48 chain end acetylene groups, respectively (Scheme 2).

Characterization of the acetylene-terminated dendrimers by standard techniques showed that the structures were monodisperse with physical properties similar to the extensively studied, benzyl ether-terminated, Fréchet-type dendrimers.[23] For example, the solubility was extremely high in common organic solvents such as tetrahydrofuran, dichloromethane, toluene, etc., and the glass transition temperature for the higher molec-

Scheme 7. Preparation of Dendrimer, 41, Functionalized with 3′-Azido-3′-deoxythymidine Groups Using Aqueous Click Chemistry



ular weight derivatives was ca. 20 °C, which is similar to the T_g value of 42 °C reported for similar molecular weight, Fréchet-type dendrimers.[8b] The unique resonances for the terminal propargyl units were readily observed in the ^{1}H NMR spectra of **14**−**18** with the acetylene proton appearing as a triplet at ca. 2.50 ppm and the propargyl-CH_2 as a sharp doublet at ca. 4.60 ppm. These unique resonances can be seen for the fourth-generation dendrimer $(Acet)_{48}$-([G-4])$_3$-[C], **18**, which also shows the classical resonances for the internal 3,5-dioxybenzyl ether repeat units (4.90 and 6.4−6.7 ppm) and the trifunctional core (2.05 and 6.80−7.00 ppm) (Figure 1).

The facile preparation of chain end functionalized poly(benzyl ether) dendrimers demonstrates that introduction of terminal acetylene groups into a dendritic structure is readily accomplished. This point was further demonstrated by the chain end modification of divergent PAMAM/DAB dendrimers, bis-MPA dendrimers, and hyperbranched polyesters with terminal acetylene groups. The terminal acetylenes were introduced by amidation or esterification of the chain end amino

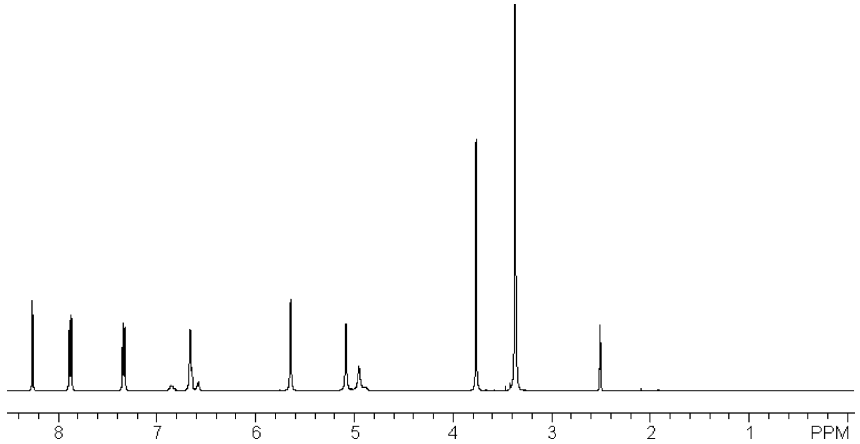
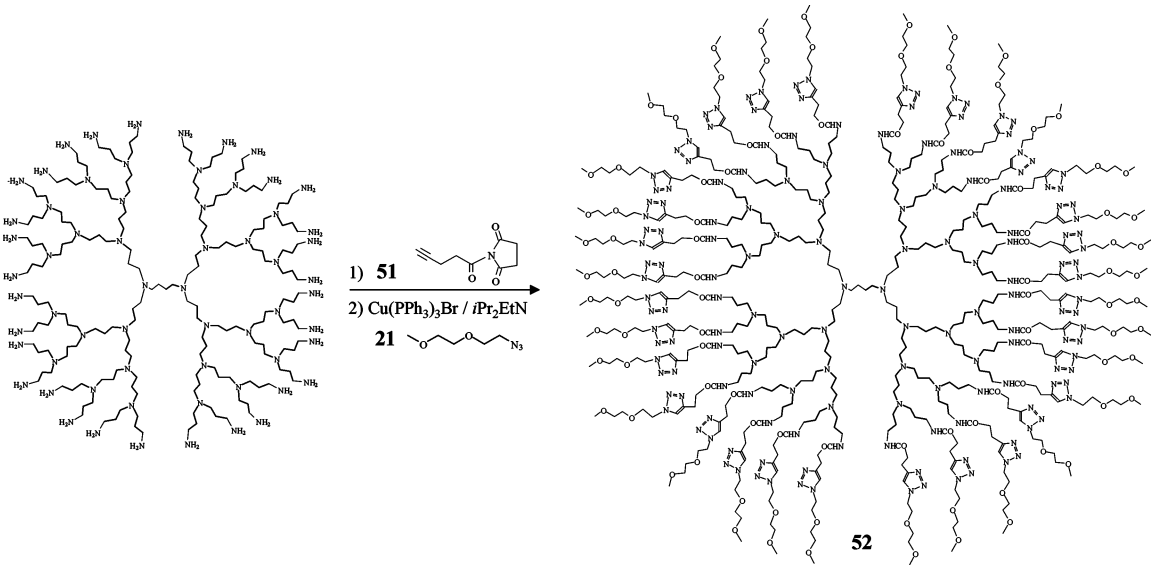


Figure 3. ^{1}H NMR spectrum for the 24-methyl benzoate-functionalized dendrimer $(Est)_{24}$-$([G\text{-}3])_3$-[C], **44**.

Scheme 8. Functionalization of the Fourth-Generation DAB Polyamine Dendrimer with 1-Azido-2-(2-methoxyethoxy)ethane, 21, by a Nonaqueous Click Chemistry Cascade Reaction



or hydroxyl groups, and the availability of a wide variety of acetylenic precursors was instrumental in the facile preparation of these derivatives. As shown in Scheme 3, reaction of the commercially available, hyperbranched polyester[24] based on 2,2-bis(hydroxymethyl)propionic acid (bis-MPA) (Boltorn) with pent-4-ynoyl anhydride affords the desired acetylene terminated derivative, **55**, in quantitative yield.

Having demonstrated the synthesis of different dendritic cores with terminal acetylene chain ends, functionalization of the chain ends with 1,4-substituted triazole rings by Click chemistry was examined. While azido derivatives are arguably an overlooked functional group in the literature, many examples are either commercially available or easily synthesized by nucleophilic displacement of alkyl halides with sodium azide. Consequently, the power of Click chemistry as a derivitization tool is significantly enhanced by the ready availability of both starting acetylene functionalized dendritic macromolecules and functionalized azido groups.

Initially, the functionalization of the hexaacetylene-terminated polyether dendrimer, **15**, with a simple azido-derivative, 1-azidoadamantane **19**, was examined. Under standard conditions, $CuSO_4$/sodium ascorbate in aqueous solution, no reaction was observed due to the insolubility of the starting materials in the reaction mixture. As we have demonstrated previously,[25] this incompatibility with aqueous reaction conditions can be overcome by employing an organosoluble catalyst, $Cu(PPh_3)_3Br$ or $(EtO_3)PCuI$. Reaction of the hexafunctionalized dendrimer, **15**, with 9.0 equiv of **19** in the presence of $(EtO)_3PCuI$ under microwave irradiation for 10 min[26] was found to give the desired hexa(adamantyl) derivative, **37**, in 72% yield after purification (Scheme 3). This result was significantly improved when the CuI catalyst was replaced with $Cu(PPh_3)_3Br$. In this case only a stoichiometric amount (6.0 equiv) of azide was required to drive the reaction to completion and afford a 95+% yield of **37** after purification. The extremely high efficiency of the Click chemistry is evidenced by comparison of the GPC traces for the crude reaction product with the starting acetylene-terminated dendrimer (Figure 2).

A clean transition to a higher molecular weight product, **37**, is observed with no detectable amount of starting dendrimer, **15**, though under these forcing conditions a small amount (<2%) of higher molecular weight product was observed at longer reaction times. This is presumably due to Cu-catalyzed coupling of terminal acetylene groups, and it was found that decreasing the reaction time, using a slight excess of azide (1.02 equiv per chain end) while working under more dilute conditions, eliminated this minor side

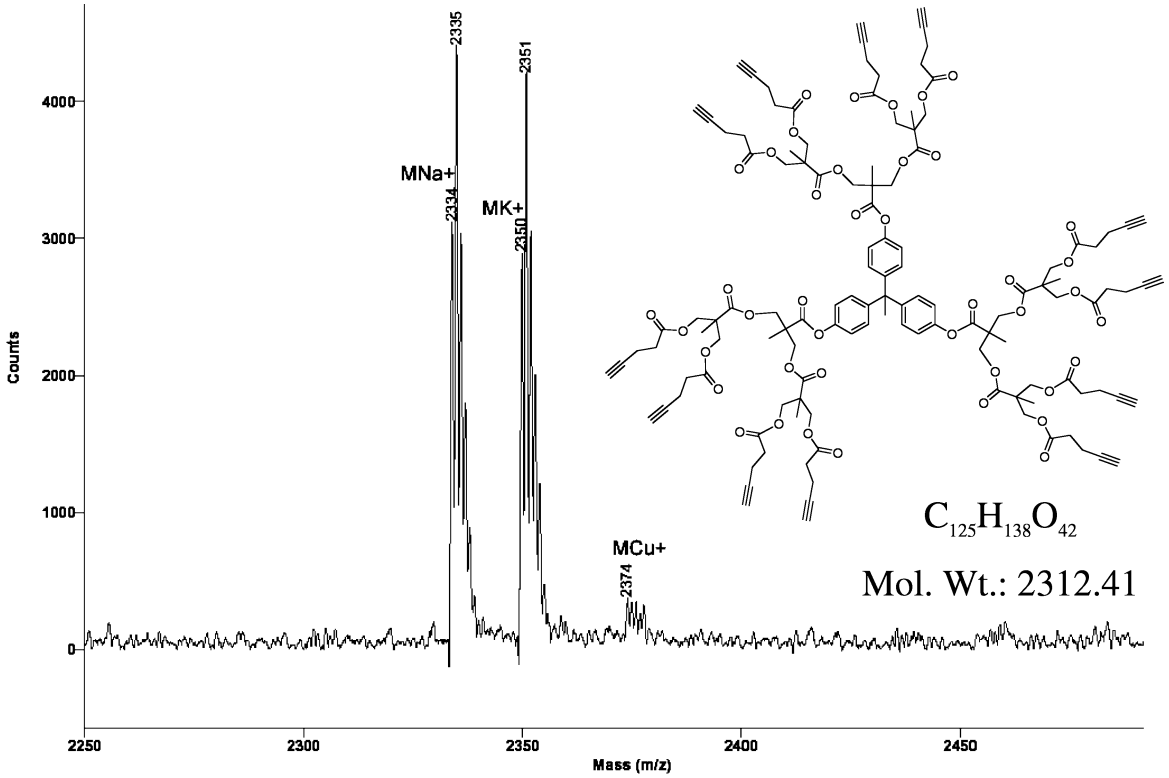


Figure 4. MALDI mass spectrum for the dodeca-acetylene polyester $(Acet)_{12}$-($[G\text{-}2]_3$-[C], **57**.

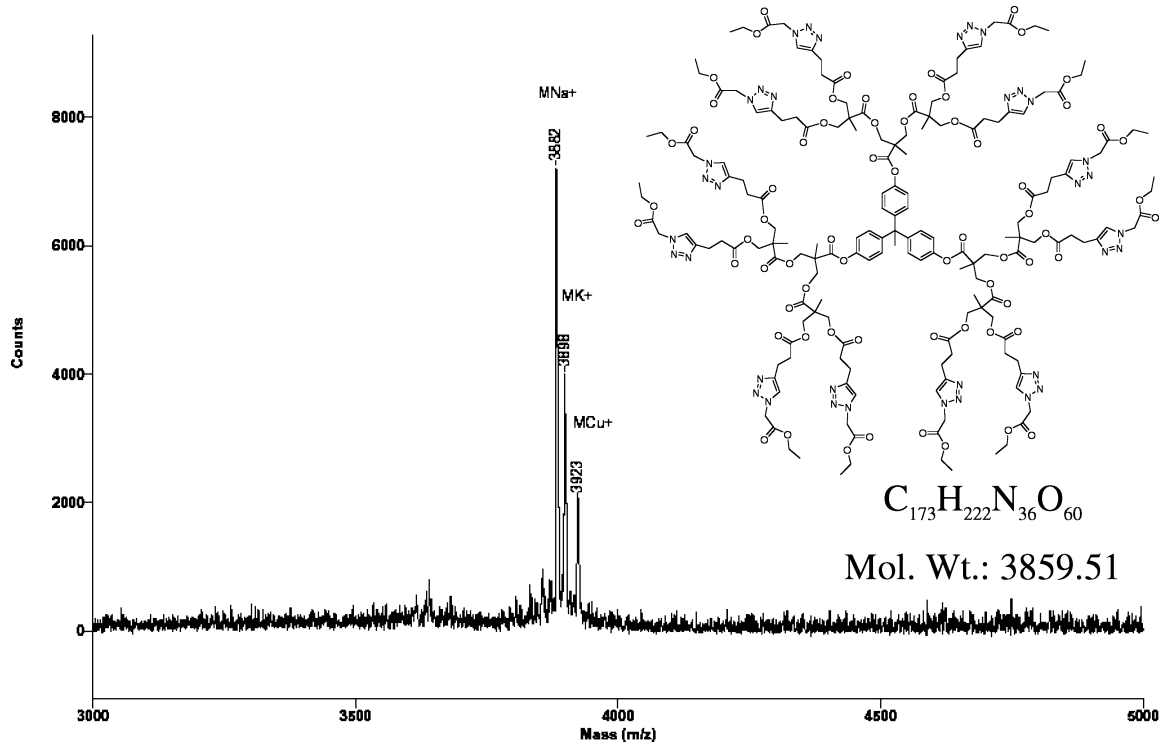


Figure 5. MALDI mass spectrum for the crude reaction product showing almost quantitative formation of the decaester, $(Est)_{12}$-($[G\text{-}2]_3$-[C], **58**.

reaction. ^{1}H NMR spectroscopy of the crude dendrimer **37** obtained under these reaction conditions showed no resonances for unreacted terminal acetylenic groups, while MALDI−TOF mass spectral analysis showed a single molecular ion for the fully hexafunctionalized derivative, **37**.

These promising initial results with a small dendrimer and a simple cycloaliphatic azide prompted a significant extension of this work to larger generation dendrimers and highly functionalized azides. In choosing the azido group, a wide selection of different structures incorporating reactive functional groups such as the nucleoside, **28**, or the unprotected sugar, **25**, dye molecules such as the Disperse Red azo derivative, **26**, and even large dendrons, **29**−**31**, were examined in order to show the functional group compatibility of Click

chemistry (Scheme 5). Similarly, a variety of different dendritic structures from generation 2−4 polyether dendrimers, **16**−**18**, to hyperbranched and dendritic polyesters, **55**, and polyamino-based DSM dendrimers, **51**, were studied in order to demonstrate both tolerance to different dendritic cores and the ability to achieve complete functionalization at high generations.

As shown in Table 1, the purified yields obtained for the preparation of chain end functionalized dendrimers from a variety of different azido derivatives **19**−**31**, and dendritic cores using Click chemistry were generally over 85−90%. Slightly lower yields were obtained in a small number of cases; however, these represent difficulties in the isolation and purification steps rather than incomplete reactions. This high efficiency of Click chemistry is perhaps best exemplified by the functionalization of the third-generation dendrimer, **17**, which contains 24 terminal acetylene groups with methyl 4-(azidomethyl)benzoate, **23**. Microwave irradiation of a 1:25 mixture of **17** and **23** for 10 min was found to give, after purification by simple precipitation, a 94% yield of the fully functionalized dendrimer, **44** (Scheme 6). Characterization of **44** by a combination of spectroscopic and chromatographic techniques demonstrated the efficiency of the functionalization chemistry. The ^{1}H NMR spectrum of **44** showed no detectable resonances for unreacted acetylene groups and unique resonances for the triazole rings (8.24 ppm), methyl benzoate groups (3.35 ppm), and dendritic core could be identified (Figure 3). The high efficiency of this functionalization reaction is even more significant when it is compared with traditional dendrimer chemistry which employs large excesses of reagents to push the reactions to completion and requires extensive purification.

Other noteworthy examples which demonstrate the compatibility of Click chemistry with highly functionalized groups were the reaction of the dodecaacetylene polyether dendritic core, **16**, with 3′-azido-3′-deoxythymidine, **28**, to give the nucleoside-terminated dendrimer, **41**, in 94% isolated yield (Scheme 7). Significantly, no protection of the nucleoside, **28**, was required, and the reaction proceeded at room temperature in aqueous solution. Similarly, the polyether dendrimer core can be replaced by a fourth-generation DAB polyamine core and in a further demonstration of the compatibility of Click chemistry, multiple reactions performed in the same reaction mixture. To illustrate this feature, a sequential series of reactions, initial acylation with the active ester of pent-4ynoic acid, **51**, followed by Click functionalization with the azido derivative of methoxy(diethylene glycol), **21**, were conducted to give the functionalized DAB dendrimer, **53**, in an overall isolated yield of 78% (Scheme 8).

In developing the Cu-catalyzed cycloaddition reaction of azides with terminal acetylenes as a new and highly efficient polymer functionalization tool, significant attention was devoted to the precise characterization of these structures, especially in terms of the fidelity of chain end functionalization. The monodisperse nature of the dendritic starting materials permitted MALDI mass spectrometry to be used for detecting very low levels of incomplete functionalization of the chain end. A typical MALDI spectrum for an acetylene-terminated starting material is shown in Figure 4 for the dodecafunctionalized bis-MPA dendritic polyester, **57**, and shows a single set of molecular ions at 2312 (2335 Na^+, 2351 K^+, and 2374 Cu^+). After Click functionalization with ethyl 2-azidoacetate under standard conditions the crude reaction mixture reveals that the peaks for the starting material are cleanly transformed to a single set of molecular ions at 3859 (3882 Na^+, 3898 K^+, and 3923 Cu^+) (Figure 5). This corresponds to the decaester, **58**, and complete reaction at all of the chain ends. Incomplete reaction would be characterized by peaks at intervals of 127 amu less that the observed fully substituted product, and these are not observed, which again confirms the high fidelity of the Cu-catalyzed cycloaddition reaction of terminal acetylenes with azides. Similar results were observed for all of the dendrimers employed in this study.

Conclusion

In conclusion, we have demonstrated the unique opportunities afforded polymer synthesis through the use of advanced organic transformations and concepts such as Click chemistry. A library of functionalized dendritic macromolecules was prepared in extremely high yields using no protecting group strategies and with only minimal purification steps. This unprecedented ability to routinely prepare functionalized dendrimers represents a significant advance compared to traditional approaches and is further evidence of the synthetic utility of Click chemistry in both biological systems and materials chemistry.[28]

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