Synthesis of Poly(benzyl ether) Dendrimers Containing Core Diversities by Click Chemistry

Jae Wook Lee,[†,‡,*] Byoung-Ki Kim,[†] Seung Choul Han,[‡] and Ji Hyeon Kim[§,*]

[†]Department of Chemistry and [‡]Department of Medical Bioscience, Dong-A University, Busan 604-714, Korea
[*]E-mail: jlee@donga.ac.kr
[§]Department of Chemical and Bio Engineering, Kyungwon University, Seongnam 461-701, Korea
[*]E-mail: jihyeon@kyungwon.ac.kr

General, fast, and efficient methods for the synthesis of Fréchet-type dendrimers having core diversities were elaborated. Two core building blocks, 4,4'-(3,5-bis(propargyloxy)benzyloxy)bisphenyl and *N,N,N',N'*-tetra(prop-2-ynyloxycarbonylethyl)-1,2-diaminoethane, were designed to serve as the alkyne functionalities for dendrimer growth via click reactions with the azide-dendrons. The synthetic strategy involved an 1,3-dipolar cycloaddition reaction between an alkyne and an azide- functionalized Fréchet-type dendrons in the presence of Cu(I) species which is known as the best example of click chemistry.

Key Words : Alkyne, Azide, Click chemistry, Fréchet-type dendrimers

Introduction

Dendrimers, which are prepared by repetition of a given set of reactions using either divergent or convergent strategies, are highly branched and regular macromolecules with well-defined structures and have served as functional objects in nanotechnology and nanoscience.[1,2] The convergent approach to dendrimer synthesis introduced by Fréchet and co-workers revolutionized the synthetic approaches to monodisperse dendrimers.[3,4] The convergent methodology installs the core in the final step, enabling the incorporation of functionalities. It provides greater structural control than the divergent approach due to its relatively low number of coupling reactions at each growth step. The ability to prepare well-defined (un)symmetrical dendrimers is the most attractive features of the convergent synthesis. The convergent approach allows for a large degree of chemical diversity such that functional groups can be incorporated at nearly central position in the dendritic architecture.

The reactions employed in the synthesis of dendrimers should be high yielding without any side reactions. Well known processes, such as the Michael reaction, Williamson ether synthesis, amidations and reductions have been used extensively in the synthesis of dendrimers.[4] Recent solid chemistry is the click chemistry which is the copper-catalyzed 1,3-dipolar cycloaddition reaction between alkyne and azide developed by Sharpless and Tornøe.[5] This reaction is characterized by mild and simple reaction conditions, reliable 1,4-regiospecific 1,2,3-triazole formations, and tolerance towards water as well as a wide range of functionalities, and is clearly a breakthrough in the synthesis of dendrimers[6,7] and dendritic and polymer materials.[8-10] In the convergent synthesis of the dendrimers, two feasible methods are the fusion of two dendrons and the stitch of multi-functional group with dendrons. We have developed the fusion and stitching methods for the synthesis of symmetric and unsymmetric dendrimers and diblock codendrimers using click chemistry between an alkyne and an azide.[7] Herein

we report the synthesis of Fréchet-type dendrimers containing core diversities by the stitching method of dendrons with tetra-core moieties (Figure 1). Because of the high yields and lack of byproducts provided by the click chemistry for stitching together dendrons and core unit, the various dendrimers having functional building block at core could be obtained easily and shown the characteristic behaviors.

Results and Discussion

The inward growth employed by the convergent synthesis is ideally suited for the attachment of diverse core moieties.[4] As a result, building dendrimers via the convergent approach allows for the synthesis of symmetric dendrimers and for specific incorporation of function into the dendrimer interior. The synthetic strategy for Fréchet-type dendrimers, linked by the triazole units, utilized a convergent method using the azido-functionalized Fréchet-type dendrons **1-Dm** and the tetra-alkynes (Figure 1). To efficiently connect the azide focal point Fréchet-type dendrons with core units, the synthetic approach selected is based on the click condition using Cu (I) species.[11] The azide focal point Fréchet-type dendrons **1-Dm** (m = 1~4: generation of dendron, Figure 1) are synthesized according to the reported procedure.[7c,12] The 4,4'-(3,5-bis(propargyloxy) benzyloxy)bisphenyl **2** and *N,N,N',N'*-tetra(prop-2-ynyloxycarbonylethyl)-1,2-diaminoethane **3**, designed to present alkyne functionalities available for dendrimer growth via click reactions with the dendrons, were synthesized readily from and the bis-alkylations of 4,4'-bisphenol with 3,5-bis(propargyloxy) benzyl chloride[7j] in the presence of a base and the Michael addition of 1,2-diaminoethane with propargyl acrylate,[7] respectively.

To test the effectiveness of the dipolar cycloaddition reactions of the tetra(alkynes) core **2** and azide-dendron **1-D1** (Scheme 1), we have screened with several conditions using various Cu(I) sources in different solvents.[5,11] We have found that the reaction conducted from the condition of 5 mol % of
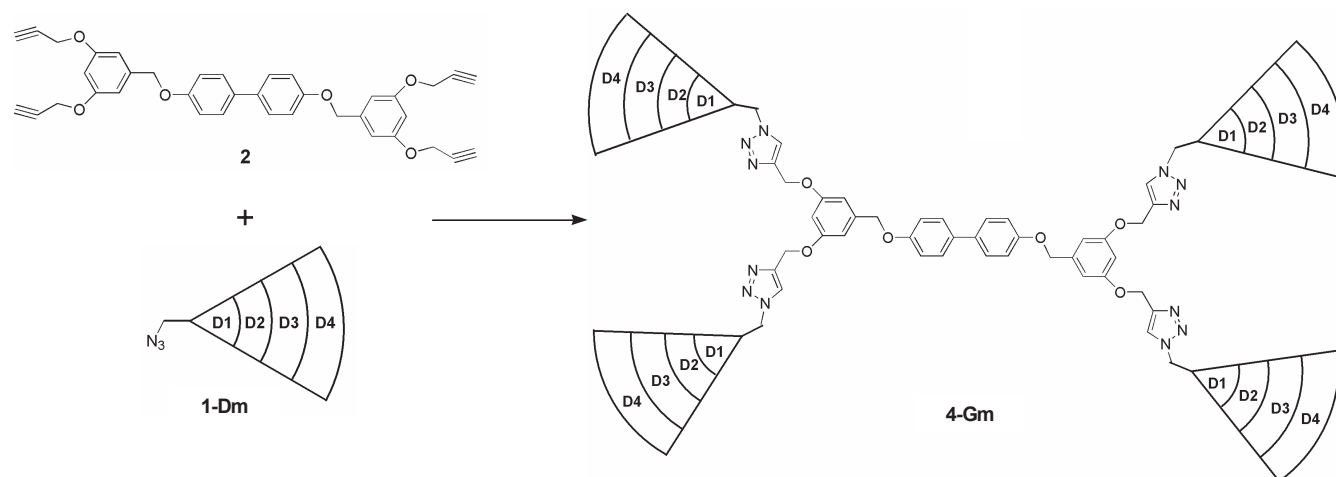
CuSO$_4$·5H$_2$O with 10 mol % of sodium ascorbate with respect to the alkyne in a 4:1 solvent ratio of DMF to H$_2$O for 4 h at 50 °C afforded the desired product **4-G1** in yield of 96%. The disappearance of tetra(alkynes) **2** as well as generation and disappearance of the mono-, di-, and tri-triazole derivatives were monitored by TLC runs of the reaction mixture. The dendrimer **4-G1** was purified by column chromatography and the structure of dendrimer was confirmed by ^{1}H and ^{13}C NMR spectroscopy, IR spectroscopy, and FAB mass spectra. Given the success in the synthesis of first generation dendrimer, we expanded this reaction to get higher generation dendrimers with 5 mol % of CuSO$_4$·5H$_2$O with 10 mol % of sodium ascorbate with respect to the alkyne in a 4:1 solvent ratio of DMF to H$_2$O. Reactions of the tetra(alkynes) **2** with 4.4 equiv of **1-D2** and

1-D3 afforded the dendrimers **4-G2** and **4-G3** in yields of 96 and 95%, respectively, after 6 and 7 h, which were separated by column chromatography. In case of **1-D4**, the triazole dendrimer **4-G4** was obtained in 97% yield after 7h. This comparative efficiency of the click methodology is emphasized by the synthesis of the dendrimers with the tailed made core units. Therefore this approach may provide new methodological insight into introduction of various functional cores and would greatly contribute to researches on the application side. We are now investigating for self-emissive dendrimer with a fluorescent or phosphorescent probe in core region.

Structural characterization of the dendrimers **4-Gm** with ^{1}H NMR, ^{13}C NMR, and IR spectroscopy showed no defects due to incomplete reaction. From the ^{1}H NMR spectra (CDCl$_3$), the
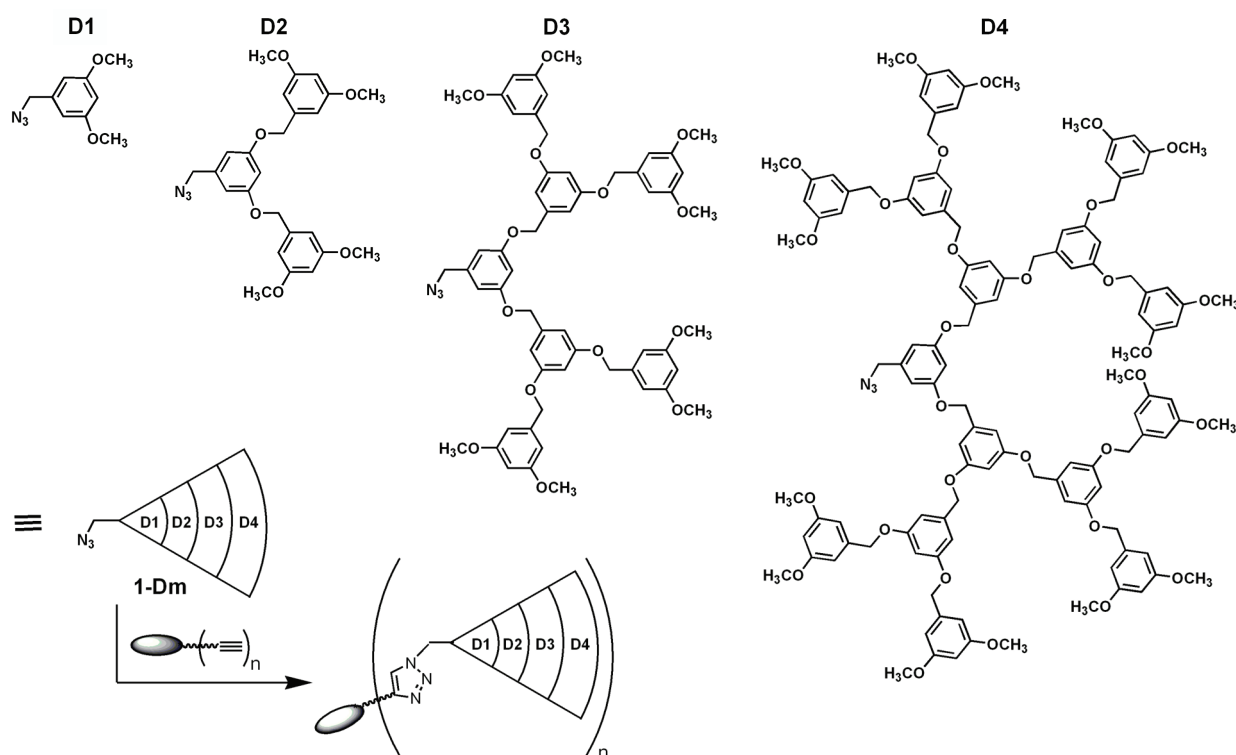
Figure 1. Structures of dendrons **1-Dm** and synthetic strategy of dendrimers.

Scheme 1. *Reagents and conditions:* 20 mol % of CuSO$_4$·5H$_2$O/40 mol % of sodium ascorbate, DMF/H$_2$O (4:1), 50°C.

peaks of the methylene protons adjacent to the nitrogen of tri-azole, the triazole proton, and the methylene protons adjacent to the carbon of triazole in dendrimers **4-Gm** were found at 5.16, 7.56, and 5.43 ppm for **4-G1**, 5.15, 7.53, and 5.41 ppm for **4-G2**, 5.11, 7.53, and 5.38 ppm for **4-G3**, and 5.06, 7.49, and 5.32 ppm for **4-G4**, respectively (Figure 2). The peaks of the methylene protons adjacent to the oxygen of bisphenyl in den-drimers **4-Gm** were found at 5.01 ppm for **4-G1**, 4.98 ppm for **4-G2**, 4.93 ppm for **4-G3**, and 4.91 ppm for **4-G4**, respectively. As the dendrimer generation increased, the peaks of all dis-cussed protons shifted gradually to down-field which may be influenced by the dendritic microenvironment effect.[13] Analysis of the dendrimers by FAB or MALDI-TOF mass spectrometry as well as by gel-permeation chromatography (GPC) provides no signs of products with defects that would arise from incomplete coupling (Figure 3). As expected, the obtained dendrimer pos-sessed a very well-defined molecular structure with very low polydispersity values (PDI = 1.01-1.02). IR data also confirmed that neither alkyne (~ 3279 cm^{-1}) nor azide (2100 cm^{-1}) residues remain in the final dendrimer (Figure 4).

Encouraged by this successful proof of concept, we decided to apply this methodology to the synthesis of Fréchet-type den-drimer containing hydrolysable amino-ester at the core. The hydrolysable dendrimer may show the characteristic potential applications such as a drug delivery system. With this in mind and as a continuation of our studies on the design and synthesis of

more applicable dendrimer, the Fréchet-type dendrimers **5-Gm** with diamino-tetraester unit were synthesized from the click re-action between the azide-dendrons **1-Dm** and *N,N,N',N'*-tetra (prop-2-ynyloxycarbonylethyl)-1,2-diaminoethane **3** (scheme 2). After screening with several conditions using various Cu(I) sources in different solvents, the selected condition is 5 mol % of CuSO₄·5H₂O with 10 mol % of sodium ascorbate with respect to the alkyne in a 4:1 solvent ratio of THF to H₂O for 5 h at 50 °C. The reactions of the tetra(alkynes) **3** and 4.4 equiv of azido-dendrons **1-D1** and **1-D2** afforded the Fréchet-type dendrimers **5-G1** and **5-G2** in yields of 94 and 96%, respectively, after 5 h, which were separated by column chromatography. The dis-appearance of tetra (alkynes) **3** as well as generation and dis-appearance of the mono, di, and tri-triazole derivatives were al-so monitored by TLC runs of the reaction mixture. Reactions of the tetra(alkynes) **3** and 4.4 equiv of azido-dendrons **1-D3** and **1-D4** gave the Fréchet-type dnedrimer **5-G3** and **5-G4** in yields of 96 and 94%, respectively, after 6 h, which also were sepa-rated by column chromatography. This approach may provide new methodological insight into introduction of various func-tional cores and would greatly contribute to researches on the application side.

Structural characterization of the dendrimers **5-Gm** with ¹H NMR, ¹³C NMR, and IR spectroscopy showed complete stitch-ing of dendrons. From the ¹H NMR spectra (CDCl₃), the peaks of the methylene protons adjacent to the nitrogen of triazole, the triazole proton, and the methylene protons adjacent to the carbon of triazole in dendrimers **5-Gm** were found at 5.14,
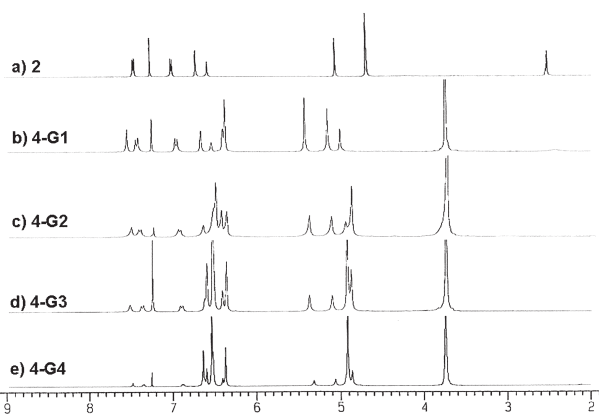

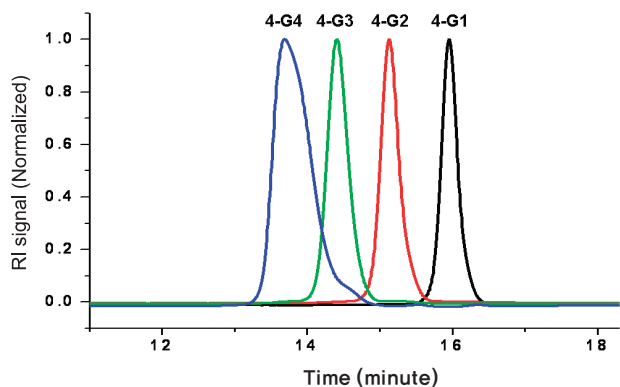**Figure 2.** ¹H-NMR spectra for (a) **2**, (b) **4-G1**, (c) **4-G2**, (d) **4-G3**, and (e) **4-G4**.

Figure 4. IR spectra for (a) **1-D2**, (b) **2**, and (c) **4-G2**.

Figure 3. GPC diagrams of dendrimers **4-Gm** obtained from THF eluent.

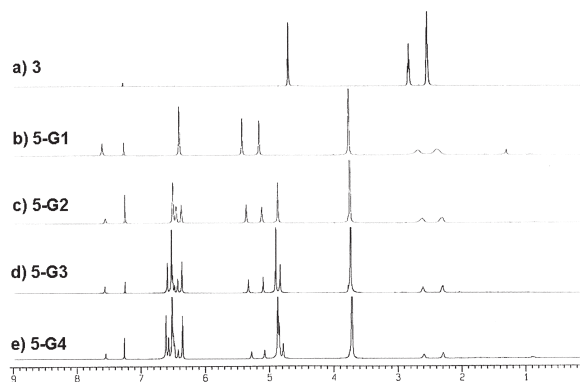**Figure 5.** ¹H-NMR spectra for (a) **3**, (b) **5-G1**, (c) **5-G2**, (d) **5-G3**, and (e) **5-G4**.
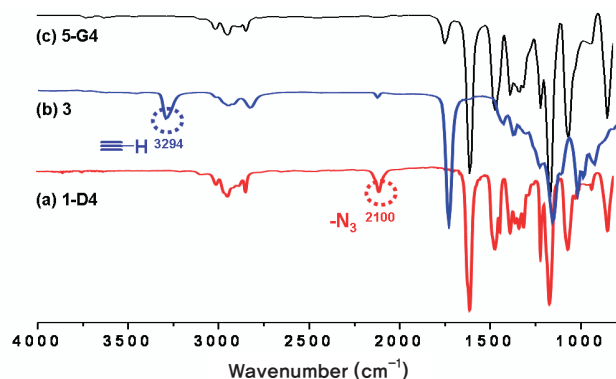
Figure 6. J. W. Lee et al.

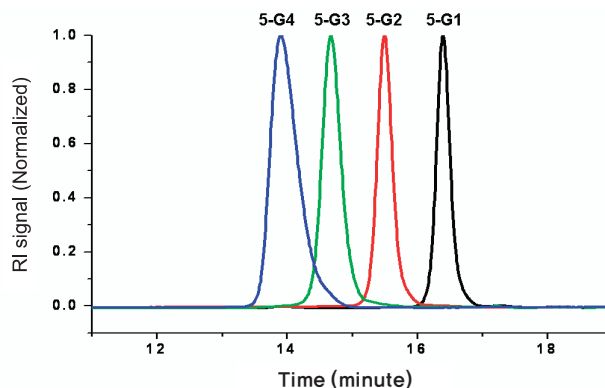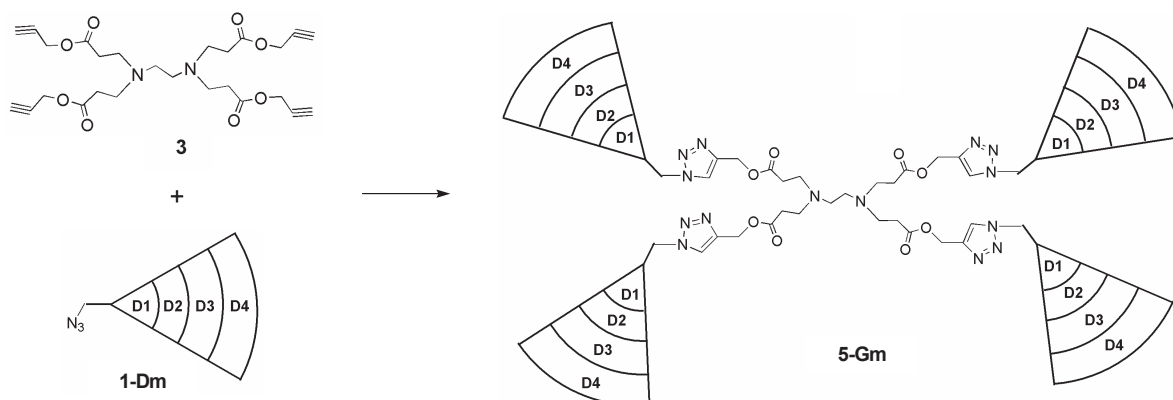**Figure 7.** J. W. Lee et al.

Scheme 2. *Reagents and conditions:* 20 mol % of CuSO$_4$·5H$_2$O/40 mol % of sodium ascorbate, THF/H$_2$O (4:1), 50°C.

7.60, and 5.41 ppm for **5-G1**, 5.13, 7.56, and 5.37 ppm for **5-G2**, 5.11, 7.57, and 5.34 ppm for **5-G3**, and 5.08, 7.55, and 5.28 ppm for **5-G4**, respectively (Figure 5).

As the dendrimer generation increased, the peaks of all methylene protons shifted gradually to down-field which may be influenced by the dendritic microenvironment effect.[13] The IR spectra shows the disappearance of the acetylene peak at ~3294 cm^{-1} and the azide peak at ~2100 cm^{-1} in the final dendrimer (Figure 6) while the ^{1}H NMR revealed no alkyne peak at around δ2.47 ppm (Figure 5). Analysis of the dendrimers by FAB or MALDI-TOF mass spectrometry as well as by gel-permeation chromatography (GPC) provides no signs of products with defects that would arise from incomplete coupling (Figure 7). As expected, the obtained dendrimer possessed a very well-defined molecular structure with very low polydispersity values (PDI = 1.01-1.02).

In summary, we have demonstrated that click reactions between the tetra(alkynes) core and the azide-functionalized Fréchet-type dendrons lead to the formation of symmetric Fréchet-type dendrimers in high yields. This method can be applied for the fast synthesis of Fréchet-type dendrimers with functional units at core and may then provide an insight into designing various dendrimers with the functional cores.

Experimental Section

^{1}H NMR spectra were recorded on a 300 or 500 MHz NMR spectrometer using the residual proton resonance of the solvent as the internal standard. Chemical shifts are reported in parts per million (ppm). When peak multiplicities are given, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; d of d, doublet of a doublet; m, multiplet; br, broad. ^{13}C NMR spectra were proton decoupled and recorded on a 75 or 125 MHz NMR spectrometer using the carbon signal of the deuterated solvent as the internal standard. FAB and MALDI mass spectra were obtained from Korea Basic Science Institute (KBSI) in Daegu or Daejeon and POSTECH. Flash chromatography was performed with 37–75 μm silica gel. Analytical thin layer chromatography was performed on silica plates with F$_{254}$ indicator and the visualization was accomplished by UV lamp or using an iodine chamber. Polydispersity (PDI) of dendrimers was determined by gel permeation chromatography (GPC) analysis relative to polystyrene calibration (Agilent 1100 series GPC, Plgel 5μm MIXED-C, refractive index detector) in THF solution.

General procedure for the preparation of dendrimers 4-Gm from azide- dendrons 1-Dm and tetra(alkynes) 2. A mixture of azido-dendrons **1-Dm** (0.22 mmol) and 4,4'-**(**3,5-bis(propargyloxy)benzyloxy)bisphenyl **2** (0.05 mmol) in DMF-H$_2$O (4:1, 1 mL) in the presence of 20 mol % CuSO$_4$·5H$_2$O with 40 mol % sodium ascorbate was stirred at 50°C for ~7 h. The reaction mixture was poured into brine (20 mL) and the resulting solution was extracted with EtOAc (20 mL x 3). The combined organic phase was dried with sodium sulfate, concentrated, and purified by column chromatography to afford the desired product.

4-G1. A yellowish oil; 96% yield; IR 3009, 2947, 2839,

1597, 1458, 1211, 1157, 1057 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ3.74 (s, 24H), 5.01 (s, 4H), 5.16 (s, 8H), 5.43 (s, 8H), 6.39 (m, 8H), 6.41 (d, J = 1.5 Hz, 4H), 6.55 (m, 2H), 6.67 (m, 4H), 6.97 (d, J = 8.5 Hz, 4H), 7.44 (d, J = 8.5 Hz, 4H), 7.56 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ54.7, 55.8, 62.5, 70.1, 100.9, 101.7, 106.5, 106.9, 115.5, 123.2, 128.1, 134.0, 136.9, 140.1, 144.7, 158.1, 160.0, 161.7; MS (FAB): *m/z* 1354.6 [M$^+$]; HRMS (FAB) Calcd for C$_{74}$H$_{74}$N$_{12}$O$_{14}$: 1354.5447. Found: 1355.5527 [M$^+$ + H]. PDI: 1.01.

4-G2. A yellowish oil; 96% yield; IR 3009, 2940, 2839, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ3.76 (s, 48H), 4.91 (s, 16H), 4.98 (s, 4H), 5.15 (s, 8H), 5.41 (s, 8H), 6.40 (m, 8H), 6.46 (m, 8H), 6.52-6.55 (m, 22H), 6.67 (m, 4H), 6.95 (d, J = 8.4 Hz, 4H), 7.42 (d, J = 8.4 Hz, 4H), 7.53 (s, 4H); ^{13}C NMR (125 MHz, CDCl$_3$) δ54.6, 55.8, 62.4, 70.1, 70.5, 100.4, 101.7, 102.7, 105.7, 107.0, 107.6, 115.5, 123.3, 128.1, 134.0, 137.0, 139.2, 140.2, 144.6, 158.1, 160.0, 160.8, 161.4; MS (MALDI): Calcd for C$_{138}$H$_{138}$N$_{12}$O$_{30}$: 2442.9642. Found: 2481.8971 [M$^+$ + K]. PDI: 1.01.

4-G3. A yellowish oil; 95% yield; IR 3009, 2940, 2839, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ3.74 (s, 96H), 4.88 (s, 16H), 4.93 (s, 36H), 5.11 (s, 8H), 5.38 (s, 8H), 6.38 (m, 16H), 6.43 (m, 8H), 6.54 (m, 46H), 6.61 (m, 16H), 6.64 (m, 4H), 6.91 (d, J = 8.2 Hz, 4H), 7.38 (d, J = 8.2 Hz, 4H), 7.53 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 54.7, 55.7, 62.3, 70.0, 70.4, 100.3, 101.6, 102.1, 102.6, 105.6, 106.7, 107.0, 107.5, 115.5, 123.5, 128.1, 133.9, 137.0, 139.3, 139.5, 140.1, 144.6, 158.1, 159.9, 160.5, 160.7, 161.4; MS (MALDI): Calcd for C$_{266}$H$_{266}$N$_{12}$O$_{62}$: 4619.8031. Found: 4643.6601 [M$^+$ + Na+H]. PDI: 1.01.

4-G4. A yellowish oil; 97% yield; IR 3009, 2940, 2839, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ3.74 (s, 192H), 4.86 (s, 16H), 4.91 (s, 100H), 5.06 (s, 8H), 5.32 (s, 8H), 6.38 (m, 32H), 6.42 (m, 8H), 6.53-6.55 (m, 94H), 6.61 (m, 16H), 6.63-6.65 (m, 36H), 6.89 (d, J = 8.4 Hz, 4H), 7.36 (d, J = 8.3 Hz, 4H), 7.49 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ54.4, 55.7, 62.3, 70.4, 100.3, 102.0, 102.5, 105.7, 106.8, 107.5, 115.4, 123.4, 128.0, 133.9, 137.3, 139.3, 139.55, 139.61, 140.1, 144.6, 158.1, 159.9, 160.5, 160.7, 161.4; MS (MALDI): Calcd for C$_{522}$H$_{522}$N$_{12}$O$_{126}$: 8973.4808. Found: 8999.7983 [M$^+$+Na+3H]. PDI: 1.02.

General procedure for the preparation of dendrimers 5-Gm from azidedendrons 1-Dm and tetra(alkynes) 3. A mixture of azidodendrons **1-Dm** (0.22 mmol) and *N,N,N',N'*-tetra (prop-2-ynyloxycarbonylethyl)-1,2-diaminoethane **3** (0.05 mmol) in THF-H$_2$O (4:1, 1 mL) in the presence of 20 mol % CuSO$_4$·5H$_2$O with 40 mol % sodium ascorbate was stirred at 50°C for ~6 h. The reaction mixture was poured into brine (20 mL) and the resulting solution was extracted with EtOAc (20 mL × 3). The combined organic phase was dried with sodium sulfate, concentrated, and purified by column chromatography to afford the desired product.

5-G1. A yellowish oil; 94% yield; IR 3009, 2955, 2839, 1736, 1597, 1466, 1204, 1157, 1057 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ2.34 (m, 12H), 2.64 (m, 8H), 3.73 (s, 24H), 5.14 (s, 8H), 5.41 (s, 8H), 6.39 (s, 12H), 7.60 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ32.5, 49.5, 51.9, 54.1, 55.3, 57.6, 100.2, 106.1, 123.8, 136.6, 143.0, 161.2, 172.0; MS (FAB): *m/z* 1272.73

[M$^+$]; HRMS (FAB) Calcd for C$_{62}$H$_{76}$N$_{14}$O$_{16}$: 1272.5564. Found: 1273.5644 [M$^+$+H]. PDI: 1.01.

5-G2. A yellowish oil; 96% yield; IR 3009, 2947, 2839, 1736, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ2.31-2.36 (m, 12H), 2.63 (t, J = 6.4 Hz, 8H), 3.76 (s, 48H), 4.89 (s, 16H), 5.13 (s, 8H), 5.37 (s, 8H), 6.38 (t, J = 1.8 Hz, 8H), 6.46 (d, J = 1.7 Hz, 8H), 6.51-6.52 (m, 20H), 7.56 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ32.6, 49.5, 51.9, 54.0, 55.3, 57.5, 70.0, 99.8, 102.0, 105.2, 107.1, 123.8, 136.7, 138.7, 143.1, 160.2, 160.9, 172.1; MS (MALDI): Calcd for C$_{126}$H$_{140}$N$_{14}$O$_{32}$: 2360.9758. Found: 2383.8952 [M$^+$+Na]. PDI: 1.01.

5-G3. A yellowish oil; 96% yield; IR 3009, 2940, 2839, 1736, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ2.30-2.32 (m, 12H), 2.62 (m, 8H), 3.75 (s, 96H), 4.85 (s, 16H), 4.92 (s, 32H), 5.11 (s, 8H), 5.34 (s, 8H), 6.38 (m, 16H), 6.45 (m, 8H), 6.50 (m, 4H), 6.52 (d, J = 1.9 Hz, 8H), 6.54 (d, J = 1.8 Hz, 32H), 6.61 (d, J = 1.6 Hz, 16H), 7.57 (s, 4H); ^{13}C NMR (75 MHz, CDCl$_3$) δ32.6, 49.6, 51.8, 53.9, 55.3, 57.5, 70.0, 99.8, 101.6, 101.9, 105.2, 106.4, 107.1, 123.9, 136.8, 138.8, 139.1, 143.1, 160.0, 160.2, 160.4, 160.9, 172.2; MS (MALDI): Calcd for C$_{254}$H$_{268}$N$_{14}$O$_{64}$: 4537.8147. Found: 4564.7682 [M$^+$+Na+3H]. PDI: 1.01.

5-G4. A yellowish oil; 94% yield; IR 3009, 2940, 2839, 1736, 1597, 1458, 1204, 1150, 1049 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ2.29 (m, 12H), 2.59 (m, 8H), 3.71 (s, 192H), 4.79 (s, 16H), 4.85 (s, 32H), 5.87 (s, 64H), 5.08 (s, 8H), 5.28 (s, 8H), 6.36 (m, 32H), 6.43 (m, 8H), 6.48-6.52 (m, 88H), 6.58 (m, 20H), 6.61(m, 32H), 7.55 (s, 4H); ^{13}C NMR (125 MHz, CDCl$_3$) δ32.6, 49.5, 52.0, 53.9, 55.2, 57.5, 69.85, 69.93, 99.8, 101.6, 101.8, 105.0, 105.2, 106.4, 107.1, 123.9, 136.9, 138.8, 139.1, 139.2, 143.1, 160.0, 160.2, 160.9, 172.1; MS (MALDI): Calcd for C$_{510}$H$_{524}$N$_{14}$O$_{128}$: 8891.4925. Found: 8894.6192[M$^+$+3H]. PDI: 1.02.

References

1. Grimsdale, A. C.; Müllen, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 5592.
2. Tomalia, D. A. *Prog. Polym. Sci.* **2005**, *30*, 294.
3. Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638.
4. Grayson, S. M.; Fréchet, J. M. J. *Chem. Rev.* **2001**, *101*, 3819.
5. (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.
6. (a) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Fréchet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem. Int. Ed.* **2004**, *43*, 3928. (b) Malkoch, M.; Schleicher, K.; Drockenmuller, E.; Hawker, C. J.; Russell, T. P.; Wu, P.; Fokin, V. V. *Macromolecules* **2005**, *38*, 3663. (c) Joralemon, M. J.; O'Reilly, R. K.; Matson, J. B.; Nugent, A. K.; Hawker, C. J.; Wooley, K. L. *Macromolecules* **2005**, *38,* 5436. (d) Rijkers, D. T. S.; van Esse, G. W.; Merkx, R.; Brouwer, A. J.; Jacobs, H. J. F.; Pieters, R. J.; Liskamp, R. M. J. *Chem. Commun.* **2005**, 4581. (e) Wu, P.; Malkoch, M.; Hunt, J. N.; Vestberg, R.; Kaltgrad, E.; Finn, M. G.; Fokin, V. V.; Sharpless, K. B.; Hawker, C. J. *Chem. Commun.* **2005**, 5775. (f) Fernandez-Megia, E.; Correa, J.; Rodríguez-Meizoso, I.; Riguera, R. *Macromolecules* **2006**, *39*, 2113.

7. (a) Lee, J. W.; Kim, B. K. *Bull. Korean Chem. Soc.* **2005**, *26*, 658. (b) Lee, J. W.; Kim, B. K.; Jin, S. H. *Bull. Korean Chem. Soc.* **2005**, *26*, 833. (c) Lee, J. W.; Kim, B. K.; Kim, J. H.; Shin, W. S.; Jin, S. H. *Bull. Korean Chem. Soc.* **2005**, *26*, 1790. (d) Lee, J. W.; Kim, B. K. *Synthesis* **2006**, 615. (e) Lee, J. W.; Kim, J. H.; Kim, B. K.; Shin, W. S.; Jin, S. H. *Tetrahedron* **2006**, *62*, 894. (f) Lee, J. W.; Kim, B. K.; Kim, H. J.; Han, S. C.; Shin, W. S.; Jin, S. H. *Macromolecules* **2006**, *39*, 2418. (g) Lee, J. W.; Kim, J. H.; Kim, B. K. *Tetrahedron Lett.* **2006**, *47*, 2683. (h) Lee, J. W.; Kim, B. K.; Kim, J. H.; Shin, W. S.; Jin, S. H. *J. Org. Chem.* **2006**, *71*, 4988. (i) Lee, J. W.; Kim, J. H.; Kim, B. K.; Kim, J. H.; Shin, W. S.; Jin, S. H. *Tetrahedron* **2006**, *62*, 9193. (j) Lee, J. W.; Kim, J. H.; Kim, B. K.; Kim, J. H.; Shin, W. S.; Jin, S. H.; Kim, M. *Bull. Korean Chem. Soc.* **2006**, *27*, 1795. (k) Lee, J. W.; Kim, J. H.; Kim, H. J.; Han, S. C.; Kim, J. H.; Shin, W. S.; Jin, S. H. *Bioconjugate Chem.* **2007**, *18*, 579. (l) Lee, J. W.; Han, S. C.; Kim, J. H.; Ko, Y. H.; Kim, K. *Bull. Korean Chem. Soc.* **2007**, *28*, 1837. (m) Lee, J. W.; Kim, H. J.; Han, S. C.; Kim, J. H.; Jin, S. H. *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 1083.

8. (a) Helms, B.; Mynar, J. L.; Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2004**, *126*, 15020. (b) Mynar, J. L.; Choi, T.-L.; Yoshida, M.; Kim, V.; Hawker, C. J.; Fréchet, J. M. J. *Chem. Commun.* **2005**, 5169.

9. (a) Hawker, C. J.; Wooley, K. L. *Science* **2005**, *309*, 1200. (b) O'Reilly, R. K.; Joralemon, M. J.; Hawker, C. J.; Wooley, K. L. *Chem. Eur. J.* **2006**, *12*, 6776. (c) Nandivada, H.; Chen, H.-Y.; Bondarenko, L.; Lahann, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 3360. (d) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249.

10. (a) Lu, G.; Lam, S.; Burgess, K. *Chem. Commun.* **2006**, 1652. (b) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238. (c) Ladmiral, V.; Mantovani, G.; Clarkson, G. J.; Cauet, S.; Irwin, J. L.; Haddleton, D. M. *J. Am. Chem. Soc.* **2006**, *128*, 4823. (d) Vogt, A. P.; Sumerlin, B. S. *Macromolecules* **2006**, *39*, 5286. (e) Karim, M. A.; Cho, Y.-R.; Park, J. S.; Kim, S. C.; Kim, H. J.; Lee, J. W.; Gal, Y.-S.; Jin, S. H. *Chem. Commun.* **2008**, 1929. (f) Fournier, D.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.* **2007**, *36*, 1369. (g) Lutz, J.-F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1018. (h) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15.

11. (a) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51.

12. Lee, J. W.; Han, S. C.; Lee, Y.-g.; Kim, J. H.; Oh, J. *Bull. Korean Chem. Soc.* **2008**, *29*, 1055.

13. (a) Mong, T. K.-K.; Niu, A.; Chow, H.-F.; Wu, C.; Li, L.; Chen, R. *Chem. Eur. J.* **2001**, *7*, 686. (b) Wong, C.-H.; Chow, H.-F.; Hui, S.-K.; Sze, K.-H. *Org. Lett.* **2006**, *8*, 1811. (c) Sun, H.; Kaifer, A. E. *Org. Lett.* **2005**, *7*, 3845.