

## Synthesis of Diblock Codendrimer by Double Click Chemistry

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Efficient double click methods for the synthesis of diblock codendrimers were developed. The synthetic strategy involved the sequential click reactions between an alkyne and an azide. The short core building block, 1,4-diazidobutane, was chosen to serve as the azide functionalities for dendrimer growth *via* click reactions with the alkyne-functionalized PAMAM dendrons as hydrophilic dendron and alkyne-functionalized Fréchet-type dendrons as hydrophobic dendron. The structure of diblock codendrimers was confirmed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, IR spectroscopy, mass spectrometry, and GPC analysis.

**Key Words :** Alkyne, Azide, Click reaction, Diblock dendrimer, Triazole

### Introduction

Dendrons and dendrimers are the most intensely investigated subset of dendritic polymers.<sup>1</sup> 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.<sup>2</sup> The amphiphilic dendrimers consisting of both hydrophobic and hydrophilic regions in the same molecule appear as an important issue throughout the physical and life sciences and can be considered unimolecular micelles.<sup>1,3</sup> In addition, the diblock codendrimer composed of two different dendrons is intriguing macromolecule, which offers challenge and fascination as purely synthetic objects at the boundary of organic and polymer chemistry and as promising materials for diverse advanced applications. The diblock codendrimer could function as polymeric amphiphiles, which have the advantages of linear-linear amphiphilic block copolymers, and promise superior performance. Relatively few diblock codendrimers have been reported so far. Most of the diblock

codendrimers are the surface-modified block dendrimers.<sup>4</sup> A general strategy for the facile synthesis of diblock codendrimers from distinct component blocks is still needed. The reaction, which leads to quantitative formation of dendritic structures, is absolutely necessary for their synthesis.

In this respect, particular inspiration is found in chemistry explored by Sharpless and Tornøe.<sup>5,6</sup> This solid chemistry is the click chemistry which is the copper-catalyzed 1,3-dipolar cycloaddition reaction between alkyne and azide. 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.<sup>7</sup> Recent years have seen tremendous growth in many fields including organic chemistry and polymer chemistry. This methodology is considered as efficient, simple and greener routes to design dendrimers.<sup>8</sup> In addition, the click chemistry paved the way for a conceptually new way in the synthesis of dendritic and polymer materials<sup>9,10</sup> and provided a bridge between dendritic architectures and nanomaterials.<sup>11</sup> We were among the first to recognize that the copper-catalyzed 1,3-dipolar cycloaddition reaction bet-

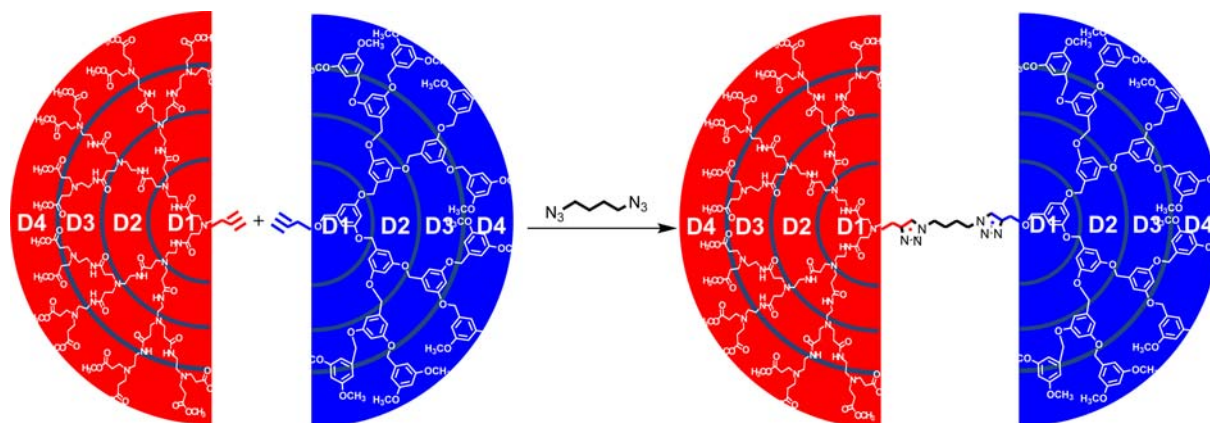


Figure 1. Synthetic strategy of diblock codendrimers.

ween alkyne and azide possess high value for convergent synthetic strategy of dendrimer. As a result, the fusion and stitching methods for the convergent synthesis of dendrimers using click chemistry between an alkyne and an azide have been developed over the years.<sup>12,13</sup> Taking advantage of this fact, herein we report the synthesis of diblock codendrimers by sequential double click reactions which involved double stitching methods of different dendrons with a short core (Figure 1).

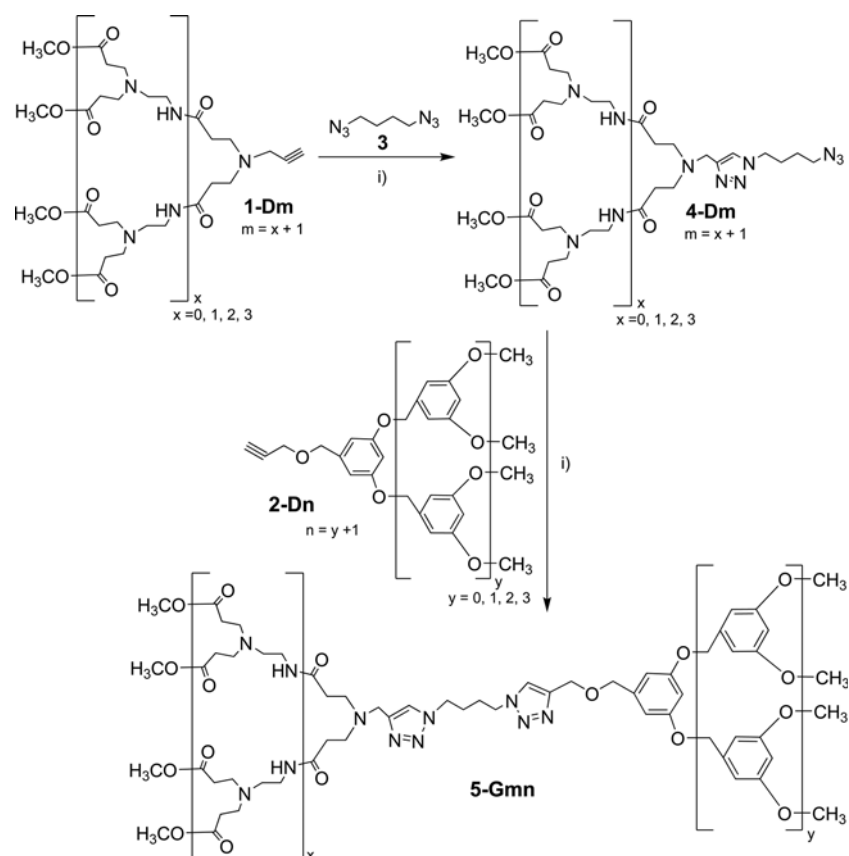
## Results and Discussion

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.<sup>14</sup> The convergent methodology installs the core in the final step, enabling the incorporation of functionalities. The ability to prepare well-defined symmetrical dendrimers is the most attractive features of the convergent synthesis. The inward growth employed by the convergent synthesis is ideally suited for the synthesis of dendritic-linear-dendritic polymers.<sup>1</sup> The building blocks of the linear-dendritic copolymers are only two, but they could be positioned in several distinct configurations due to the presence of multiple anchoring points in both of them.<sup>3</sup> The size (length and generation) and the polarity of the blocks would determine the relative hydrophobic/hydrophilic balance. The characteristic

feature of the linear-dendritic triblock copolymers is the attachment of two monodendrons to the extremities of a single linear chain. The variation of chain length and dendrimer size in this group also offers interesting macromolecular geometries. This method, however, could be limited to obtain unsymmetric systems which are included the different generation and polarity. To solve this problem, we were intrigued to investigate the sequential double click reactions for the synthesis of diblock codendrimer which are characterized by half hydrophobic and half hydrophilic dendrons.

The synthetic strategy for diblock codendrimers, linked by the triazole units, utilized double click methods using the alkyne-functionalized PAMAM dendrons **1-Dm** and alkyne-functionalized Fréchet-type dendrons **2-Dn** (Scheme 1). The bis(azide) core **3**, designed to present two azide functionalities available for dendrimer growth *via* click reactions with the alkyne-dendrons, was synthesized readily from 1,4-dibromobutane and sodium azide. The propargyl-functionalized PAMAM dendrons **1-Dm** ( $m = 1-4$ : generation of dendron) as hydrophilic dendron are synthesized by the divergent approach using propargyl amine as a propargyl focal point.<sup>13d</sup> The Fréchet-type alkyne-dendrons **2-Dn** ( $n = 1-4$ : generation of dendron) as hydrophobic dendron were prepared by the propargylation of the corresponding dendritic benzyl alcohols with propargyl bromide.<sup>12d</sup>

Considering product isolation viewpoint, we first have investigated the reaction of the alkyne-functionalized PAMAM



**Scheme 1.** Synthesis of diblock codendrimers **5-Gmn**. Reagents and conditions: i) 10 mol % of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ /20 mol % of sodium ascorbate, DMF/ $\text{H}_2\text{O}$  (4:1).

dendrons **1-Dm** and bis(azide) core **3** to provide the mono-dendritic compounds **4-Dm** with one more reactive azide focal group. Reaction of alkyne-focal dendron **1-D1** and 15 equiv of 1,4-diazidobutane **3** in the presence of 10 mol %  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  with 20 mol % sodium ascorbate in a 4:1 solvent ratio of DMF to  $\text{H}_2\text{O}$  at 50 °C gave the azide-focal dendron **4-D1** in 99% yield after 1 h. Given the success in the synthesis of first-generation dendron, therefore we expanded this reaction to get higher-generation dendrons. Reactions of alkyne-focal dendrons **1-D2**, **1-D3**, and **1-D4** and 15 equiv of 1,4-diazidobutane **3** in the presence of 10 mol %  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  with 20 mol % sodium ascorbate in a 4:1 solvent ratio of DMF to  $\text{H}_2\text{O}$  at 50 °C gave the azide-focal dendrons **4-D2**, **4-D3**, and **4-D4** in yields of 95, 92, and 90% after 1.5, 4, and 5.5 h, respectively. The disappearance of dendron **1-Dm** and generation of the mono-triazole derivative **4-Dm** were observed by TLC runs of the reaction mixture.

Structural characterization of the dendrons **4-Dm** with  $^1\text{H}$ -NMR and IR spectroscopy showed complete stitching of dendrons. The IR spectra showed the disappearance of the acetylene peak at  $3277\text{--}3298\text{ cm}^{-1}$  and the appearance of azide peak at  $2099\text{ cm}^{-1}$  in dendron **4-Dm** (Figure 2), while the  $^1\text{H}$  NMR revealed no alkyne peak around 2.19 ppm. The  $^1\text{H}$  NMR signals of the triazole proton, the methylene protons adjacent to the nitrogen of triazole, and the methylene protons adjacent to the azide in dendrons **4-Dm** were observed at 7.49, 4.36, and 3.31 ppm for **4-D1**, 7.52, 4.32, and 3.28 ppm for **4-D2**, 7.61, 4.35, and 3.30 ppm for **4-D3**, and 7.70, 4.39, and 3.33 ppm for **4-D4**, respectively. As the dendron generation increased, the peaks of the triazole proton shifted gradually to down-field which may be influenced by the dendritic microenvironment effect.<sup>15</sup> The peaks of the amide protons (NH) in the  $^1\text{H}$  NMR spectra were found at 7.07 ppm for **4-D2**, 7.02 and 7.69 ppm for **4-D3**, and 7.06, 7.65, and 7.84 ppm for **4-D4**, respectively. Their FAB or MALDI mass spectra for dendrimer exhibited very good correlation with the calculated molecular masses.

Next, we tried the second click reaction to obtain the diblock codendrimers by stitching with different dendron. The reaction of first generation azido-focal PAMAM den-

dron **4-D1** with alkyne-functionalized Fréchet-type dendron **2-D1** in the presence of 10 mol %  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  with 20 mol % sodium ascorbate in a 4:1 solvent ratio of DMF to  $\text{H}_2\text{O}$  at 50 afforded the dendrimer **5-G11** in yield of 97% after 1 h. The disappearance of two dendrons as well as generation of product could be completely monitored by TLC runs of the reaction mixture. Given the success in the synthesis of first generation dendrimer, therefore we expanded this reaction to get higher-generation dendrimers. The reaction of second generation azido-focal dendron **4-D2** with alkyne-focal dendron **2-D2** under same condition gave the dendrimer **5-G22** in yield of 94% after 4 h. The reaction of **4-D3** with **2-D3** provided the diblock codendrimer **5-G33** in 93% yield after 8 h. Finally, the diblock codendrimer **5-G44** was obtained in 90% yield from reaction of **4-D4** with **2-D4** after 12 h. For completion of the reaction, the higher generation dendron takes longer time than the lower generation dendron which could be caused by the limitation of the accessibility of acetylide due to the steric hindrance (bulkiness) of dendron. This result showed that the successive formation of triazole by click chemistry between an azide and an alkyne is found to be an efficient connector to construct the diblock codendrimers from different kinds of dendrons.

All diblock codendrimers **5-Gmn** were also confirmed by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy, IR spectroscopy, and mass spectra. From the  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ), the peaks of two triazole protons in dendrimers **5-Gmn** were found around 7.50 and 7.53 ppm for **5-G11**, 7.55 and 7.55 ppm for **5-G22**, 7.59 and 7.61 ppm for **5-G33**, and 7.65 and 7.71 ppm for **5-G44**, respectively. As the dendrimer generation increased, the peaks of the triazole protons shifted gradually to down-field which may be influenced by the dendritic microenvironment effect.<sup>15</sup> The  $^1\text{H}$  NMR revealed no alkyne peak at around 2.47 ppm and methylene peak adjacent to the azide at  $\sim 3.28$  ppm in the final dendrimer. IR data also confirmed that neither azide ( $\sim 2099\text{ cm}^{-1}$ ) nor alkyne ( $\sim 3285\text{ cm}^{-1}$ ) residues remain in the final dendrimer (Figure 2). Their FAB or MALDI mass spectra for dendrimer exhibited very good correlation with the calculated molecular masses. From the analysis of gel-permeation chromatography (Figure 3), the

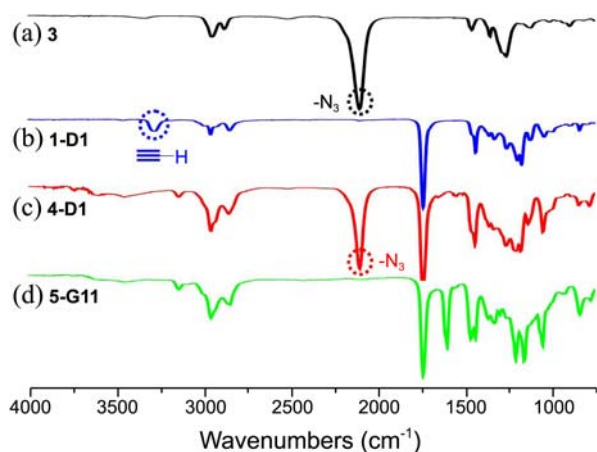


Figure 2. IR spectra for (a) **3**, (b) **1-D1**, (c) **4-D1**, and (d) **5-G11**.

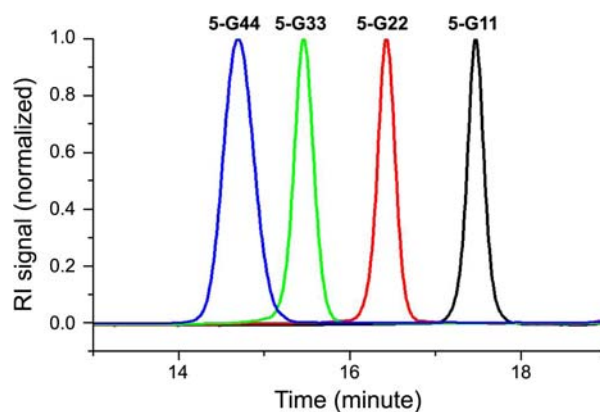


Figure 3. GPC diagrams of dendrimers **5-Gmn** obtained from THF eluent.

dendrimers showed very low polydispersity values (PDI = 1.01).

In summary, we have demonstrated for the first time that successive click reactions between a core unit and different polar dendrons (the Fréchet-type polyether and the Tomalia-type PAMAM dendrons) afford the component differentiated diblock codendrimers. The double stitching using the different generation dendrons will afford the size- and component-differentiated diblock codendrimers. Therefore double click reactions can be applied for the fast synthesis of specific dendrimers with a chromophore or different lengths (spacers) at core and may then provide an insight into designing various block dendrimers such as amphiphilic dendrimers. We are currently working toward synthesis of various functional dendrimers using this strategy for various applications.

### Experimental Section

$^1\text{H}$  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.  $^{13}\text{C}$  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  $\mu\text{m}$  silica gel. Analytical thin layer chromatography was performed on silica plates with  $\text{F}_{254}$  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 5  $\mu\text{m}$  MIXED-C, refractive index detector) in THF solution.

**General Procedure for the Preparation of Azide-focal PAMAM Dendrons 4-Dm from Alkyne-focal PAMAM Dendrons 1-Dm and 1,4-Diazidobutane 3.** A mixture of alkyne-functionalized PAMAM dendrons **1-Dm** (0.1 mmol) and 1,4-diazidobutane **3** (1.5 mmol) in DMF- $\text{H}_2\text{O}$  (4:1, 1 mL) in the presence of 10 mol %  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  with 20 mol % sodium ascorbate was stirred at 50  $^\circ\text{C}$  for ~5.5 h. The reaction mixture was poured into brine (20 mL) and the resulting solution was extracted with EtOAc (20 mL  $\times$  3). The combined organic phase was dried with sodium sulfate, concentrated, and purified by column chromatography to afford the desired product **4-Dm**.

**Compound 4-D1.**  $R_f = 0.25$  (EtOAc/hexane = 3:1); A yellowish oil; 99% yield; IR: 3136, 2951, 2851, 2099, 1736, 1439, 1261, 1204  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.58 (quin,  $J = 7.7$  Hz, 2H), 1.98 (quin,  $J = 7.6$  Hz, 2H), 2.48 (t,  $J = 7.0$  Hz, 4H), 2.79 (t,  $J = 7.0$  Hz, 4H), 3.31 (t,  $J = 6.5$  Hz, 2H), 3.63 (s, 6H), 3.78 (s, 2H), 4.36 (t,  $J = 7.0$  Hz, 2H), 7.49

(s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  25.8, 27.4, 32.4, 48.7, 48.8, 49.5, 50.6, 51.5, 122.5, 144.6, 172.6; MS (FAB):  $m/z$  368.2 [ $\text{M}^+\text{H}$ ]; HRMS (FAB): Calcd for  $\text{C}_{15}\text{H}_{25}\text{N}_7\text{O}_4$ : 367.1968. Found: 368.2049 [ $\text{M}^+\text{H}$ ].

**Compound 4-D2.**  $R_f = 0.2$  (EtOAc/MeOH = 5:1); A yellowish oil; 95% yield; IR: 3368, 2955, 2851, 2099, 1736, 1651, 1539, 1439, 1258, 1200  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.55 (quin,  $J = 7.3$  Hz, 2H), 1.95 (quin,  $J = 7.5$  Hz, 2H), 2.37 (t,  $J = 6.3$  Hz, 12H), 2.49 (t,  $J = 5.8$  Hz, 4H), 2.70 (t,  $J = 6.5$  Hz, 8H), 2.74 (t,  $J = 6.5$  Hz, 4H), 3.23 (q,  $J = 5.5$  Hz, 4H), 3.28 (t,  $J = 6.5$  Hz, 2H), 3.60 (s, 12H), 3.78 (s, 2H), 4.32 (t,  $J = 6.8$  Hz, 2H), 7.07 (t,  $J = 4.6$  Hz, 2H), 7.52 (s, 1H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  25.5, 27.1, 32.4, 33.3, 36.8, 47.5, 48.95, 48.98, 49.2, 50.3, 51.3, 52.6, 122.4, 143.9, 171.7, 172.7; MS (FAB):  $m/z$  768.2 [ $\text{M}^+\text{H}$ ]; HRMS (FAB): Calcd for  $\text{C}_{33}\text{H}_{57}\text{N}_{11}\text{O}_{10}$ : 767.4290. Found: 768.2936 [ $\text{M}^+\text{H}$ ].

**Compound 4-D3.**  $R_f = 0.2$  (EtOAc/MeOH = 1:1); A yellowish oil; 92% yield; IR: 3298, 3078, 2955, 2835, 2099, 1736, 1651, 1543, 1439, 1258, 1200  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.56 (quin,  $J = 7.4$  Hz, 2H), 1.97 (quin,  $J = 7.5$  Hz, 2H), 2.32 (t,  $J = 6.4$  Hz, 8H), 2.39 (t,  $J = 6.5$  Hz, 20H), 2.48-2.54 (m, 12H), 2.71 (t,  $J = 6.7$  Hz, 20H), 2.76 (t,  $J = 6.3$  Hz, 8H), 3.24 (q,  $J = 5.1$  Hz, 12H), 3.30 (t,  $J = 6.5$  Hz, 2H), 3.63 (s, 24H), 3.78 (s, 2H), 4.35 (t,  $J = 6.9$  Hz, 2H), 7.02 (t,  $J = 4.9$  Hz, 4H), 7.61 (s, 1H), 7.69 (t,  $J = 4.7$  Hz, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  25.7, 27.3, 32.5, 33.4, 33.7, 37.0, 37.3, 47.5, 49.1, 49.4, 49.7, 50.5, 51.4, 52.3, 52.7, 122.7, 143.9, 172.1, 172.2, 172.9; MS (FAB):  $m/z$  1568.7 [ $\text{M}^+\text{H}$ ]; HRMS (FAB): Calcd for  $\text{C}_{69}\text{H}_{121}\text{N}_{19}\text{O}_{22}$ : 1567.8934. Found: 1568.9019 [ $\text{M}^+\text{H}$ ].

**Compound 4-D4.**  $R_f = 0.2$  (MeOH only); A brownish oil; 90% yield; IR: 3286, 3078, 2955, 2847, 2099, 1736, 1651, 1555, 1439, 1261, 1200  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.60 (quin,  $J = 7.5$  Hz, 2H), 1.99 (quin,  $J = 7.3$  Hz, 2H), 2.35 (m, 24H), 2.42 (t,  $J = 6.5$  Hz, 36H), 2.52-2.57 (m, 28H), 2.74 (t,  $J = 6.5$  Hz, 36H), 2.80 (m, 24H), 3.26-3.27 (m, 28H), 3.33 (t,  $J = 6.5$  Hz, 2H), 3.66 (s, 48H), 3.82 (s, 2H), 4.39 (t,  $J = 6.8$  Hz, 2H), 7.06 (t,  $J = 4.0$  Hz, 8H), 7.65 (m, 4H), 7.70 (s, 1H), 7.84 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  25.5, 27.2, 32.4, 33.2, 33.5, 34.0, 36.9, 37.1, 47.1, 48.9, 49.2, 49.5, 49.7, 50.3, 51.3, 52.0, 52.1, 52.6, 122.8, 143.7, 171.91, 171.96, 172.04, 172.7; MS (MALDI): Calcd for  $\text{C}_{141}\text{H}_{249}\text{N}_{35}\text{O}_{46}$ : 3168.8221. Found: 3169.6533 [ $\text{M}^+\text{H}$ ].

**General Procedure for the Preparation of Diblock Codendrimers 5-Gmn from Azide-focal Dendrons 4-Dm and Alkyne-focal Dendrons 2-Dn.** A mixture of **4-Dm** (0.10 mmol) and **2-Dn** (1.05 mmol) in DMF- $\text{H}_2\text{O}$  (4:1, 1 mL) in the presence of 10 mol %  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  with 20 mol % sodium ascorbate was stirred at 50  $^\circ\text{C}$  for ~12 h. The reaction mixture was poured into brine (20 mL) and the resulting solution was extracted with EtOAc (20 mL  $\times$  3). The combined organic phase was dried with sodium sulfate, concentrated, and purified by column chromatography to afford the desired diblock codendrimers **5-Gmn**.

**Compound 5-G11.**  $R_f = 0.2$  (EtOAc/hexane = 5:1); A yellowish oil; 97% yield; IR: 3136, 2951, 2843, 1736, 1597, 1462, 1435, 1204, 1157  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$

1.91 (m, 4H), 2.50 (t,  $J = 6.9$  Hz, 4H), 2.80 (t,  $J = 6.9$  Hz, 4H), 3.62 (s, 6H), 3.75 (s, 6H), 3.79 (s, 2H), 4.35 (m, 4H), 4.51 (s, 2H), 4.63 (s, 2H), 6.35 (s, 1H), 6.48 (s, 2H), 7.50 (s, 1H), 7.53 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  27.0, 32.2, 48.6, 48.8, 49.19, 49.23, 51.5, 53.4, 55.3, 63.5, 72.4, 99.7, 105.5, 122.5, 122.9, 140.1, 144.3, 145.2, 160.8, 172.5; MS (FAB):  $m/z$  574.2 [ $\text{M}^+\text{H}$ ]; HRMS (FAB): Calcd for  $\text{C}_{27}\text{H}_{39}\text{N}_7\text{O}_7$ : 573.2911. Found: 574.2988 [ $\text{M}^+\text{H}$ ].

**Compound 5-G22.**  $R_f = 0.2$  (EtOAc/MeOH = 3:1); A yellowish oil; 94% yield; IR: 3314, 2951, 2839, 1736, 1659, 1597, 1458, 1435, 1204, 1153  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.92 (m, 4H), 2.41 (t,  $J = 6.6$  Hz, 12H), 2.52 (t,  $J = 5.9$  Hz, 4H), 2.73 (t,  $J = 6.6$  Hz, 8H), 2.77 (t,  $J = 6.7$  Hz, 4H), 3.26 (q,  $J = 5.7$  Hz, 4H), 3.64 (s, 12H), 3.77 (s, 12H), 3.79 (s, 2H), 4.35-4.37 (m, 4H), 4.52 (s, 2H), 4.63 (s, 2H), 4.95 (s, 4H), 6.39 (t,  $J = 2.2$  Hz, 2H), 6.51 (t,  $J = 2.1$  Hz, 1H), 6.55 (d,  $J = 2.2$  Hz, 4H), 6.59 (d,  $J = 2.1$  Hz, 2H), 7.10 (t,  $J = 5.0$  Hz, 2H), 7.55 (s, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  27.0, 32.6, 33.6, 37.1, 48.0, 49.2, 51.6, 52.9, 55.3, 63.6, 70.0, 72.4, 99.9, 101.4, 105.2, 106.7, 122.6, 122.7, 139.2, 140.2, 144.5, 145.2, 159.9, 160.9, 172.1, 173.0; MS (FAB):  $m/z$  1246.3 [ $\text{M}^+\text{H}$ ]; HRMS (FAB): Calcd for  $\text{C}_{61}\text{H}_{87}\text{N}_{11}\text{O}_{17}$ : 1245.6281. Found: 1246.6364 [ $\text{M}^+\text{H}$ ].

**Compound 5-G33.**  $R_f = 0.2$  (EtOAc/MeOH = 1:2); A yellowish oil; 93% yield; IR: 3298, 2951, 2839, 1736, 1651, 1597, 1458, 1435, 1204, 1153  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.92 (m, 4H), 2.35 (t,  $J = 6.1$  Hz, 8H), 2.41 (t,  $J = 6.5$  Hz, 20H), 2.51 (t,  $J = 5.7$  Hz, 8H), 2.57 (m, 4H), 2.73 (t,  $J = 6.5$  Hz, 20H), 2.79 (t,  $J = 6.1$  Hz, 8H), 3.26 (q,  $J = 5.2$  Hz, 12H), 3.65 (s, 24H), 3.77 (s, 26H), 4.36 (m, 4H), 4.53 (s, 2H), 4.64 (s, 2H), 4.96 (s, 12H), 6.39 (m, 4H), 6.51 (m, 1H), 6.55-6.56 (m, 10H), 6.59 (m, 2H), 6.66 (m, 4H), 7.04 (t,  $J = 5.0$  Hz, 4H), 7.59 (s, 1H), 7.61 (s, 1H), 7.72 (t, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  27.1, 32.6, 33.6, 33.8, 37.1, 37.4, 49.2, 49.8, 51.6, 52.5, 52.9, 55.3, 63.6, 69.9, 70.0, 72.4, 99.9, 101.4, 101.5, 105.2, 106.4, 106.7, 122.7, 122.9, 139.1, 139.3, 140.3, 144.3, 145.1, 159.9, 160.0, 160.9, 172.2, 172.3, 173.0; MS (MALDI): Calcd for  $\text{C}_{129}\text{H}_{183}\text{N}_{19}\text{O}_{37}$ : 2590.3022. Found: 2591.2699 [ $\text{M}^+\text{H}$ ].

**Compound 5-G44.**  $R_f = 0.1$  (MeOH only); A yellowish oil; 90% yield; IR: 3283, 2924, 2851, 1736, 1651, 1597, 1458, 1435, 1204, 1134  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  1.95 (m, 4H), 2.38 (m, 24H), 2.43-2.45 (m, 36H), 2.55-2.60 (m, 28H), 2.75-2.77 (m, 36H), 2.82 (m, 24H), 2.30 (m, 28H), 3.68 (s, 48H), 3.76 (s, 50H), 4.36 (m, 4H), 4.53 (s, 2H), 4.63 (s, 2H), 4.95 (s, 28H), 6.40 (m, 8H), 6.56 (m, 23H), 6.61 (m, 2H), 6.67 (m, 12H), 7.11 (m, 8H), 7.65 (s, 1H), 7.71 (m, 5H), 7.87 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  27.3, 32.6, 33.7, 34.1, 37.1, 37.4, 49.2, 49.8, 50.0, 51.0, 51.4, 51.6, 52.4, 52.6, 52.8, 55.2, 63.5, 69.85, 69.92, 72.3, 99.8, 101.5, 101.6, 105.1, 106.3, 106.8, 122.6, 122.8, 139.0, 139.1, 139.7, 143.7, 145.1, 159.9, 160.0, 160.9, 161.4, 171.9, 172.0, 172.2, 173.0; MS (MALDI): Calcd for  $\text{C}_{265}\text{H}_{375}\text{N}_{35}\text{O}_{77}$ : 5279.6504. Found: 5302.4756 [ $\text{M}^+\text{Na}$ ].

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