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Synthesis of Fréchet type dendritic benzyl propargyl ether and Fréchet type triazole dendrimer

Jae Wook Lee,[a,*] Jung Hwan Kim,[a] Byung-Ku Kim,[a] Won Suk Shin[b] and Sung-Ho Jin[b]

[a]*Department of Chemistry, Dong-A University, Hadan-2-dong, Busan 604-714, South Korea*
[b]*Department of Chemistry Education and Center for Plastic Information System, Pusan National University, Busan 609-735, South Korea*

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Abstract—Fréchet type dendritic benzyl propargyl ethers were synthesized by the reaction of propargyl bromide with the corresponding Fréchet type dendritic benzyl alcohol. A propargyl focal point functionalized dendrons were applied for the construction of symmetric and unsymmetric dendrimers containing 1,2,3-triazole rings as connectors via click chemistry with a tripodal azide core or a azide focal point functionalized Fréchet type dendrons.

1. Introduction

Terminal alkynes are versatile intermediates in synthetic organic and material chemistry due to their characteristic reactions such as metathesis reaction, metal-catalyzed coupling reactions including sonogashira coupling reaction and oxidative homocoupling, and so on. Another important viewpoint in synthetic chemistry is 1,3-dipolar cycloaddition reaction with organoazides to provide heterocyclic five membered rings. Since the 1,3-dipolar cycloaddition of alkynes with azides was investigated by Huisgen et al.[1] it has been attracted much attention because of the synthetic importance of the aromatic and nonaromatic five-membered [1,2,3]-triazole heterocycles.[2] The traditional method for producing the triazole by cycloaddition requires elevated temperature, typically in refluxing conditions and also provides a mixture of 1,4-disubstituted and 1,5-disubstituted triazoles.

Recently, Tornøe and Sharpless independently reported a copper(I)-catalyzed Huisgen [2+3] dipolar cycloaddition reaction between an terminal alkyne and an organic azide in which the 1,4-regioisomer is exclusively formed and which also allows the rapid synthesis of compound libraries.[3] The reaction is highly chemoselective affording only the desired 1,2,3-triazole even in the presence of a large variety of other functional groups. In addition, the reaction is high yielding and can be carried out in water. The Cu(I)-catalyzed Huisgen's 1,3-dipolar cycloaddition reaction between alkynes and azides is one of the prototype reactions in click chemistry.[4] This click chemistry is a modular approach that uses the most practical and reliable chemical transformations and has found in many applications in organic chemistry,[5] drug discovery,[6] bioconjugations,[7] material science,[8] and synthesis of polymer[9] and dendrimer.[10]

Because dendrimers contain three distinct structural parts that are the core, end-groups, and branched units connecting core and periphery, there are three strategies for triazole dendrimers. Therefore, three types of triazole dendrimer having triazole unit(s) at core(s), every branching points, and peripheries, have been synthesized convergently and/or divergently. The convergent method for dendrimer containing triazole unit(s) at core can be facilitated by fewer coupling reaction(s) between a dendron-azide and a dendron-alkyne, between a dendron-azide and multi-alkynes, or between a dendron-alkyne and multi-azides and by convenient purifications. A relatively few applications using the alkynyl-dendron in dendrimer synthesis have been reported. 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. Due to our interest in developing new functional dendrimers, we became involved in exploring efficient cycloaddition reaction that provides an easy access to dendrimers. Here we present the synthesis of propargyl-functionalized Fréchet-type

Keywords: Alkyne; Azide; Cycloaddition; Dendrimer; 1,2,3-Triazoles.
* Corresponding author. Tel.: +82 51 200 7251; fax: +82 51 200 7259; e-mail: jlee@donga.ac.kr

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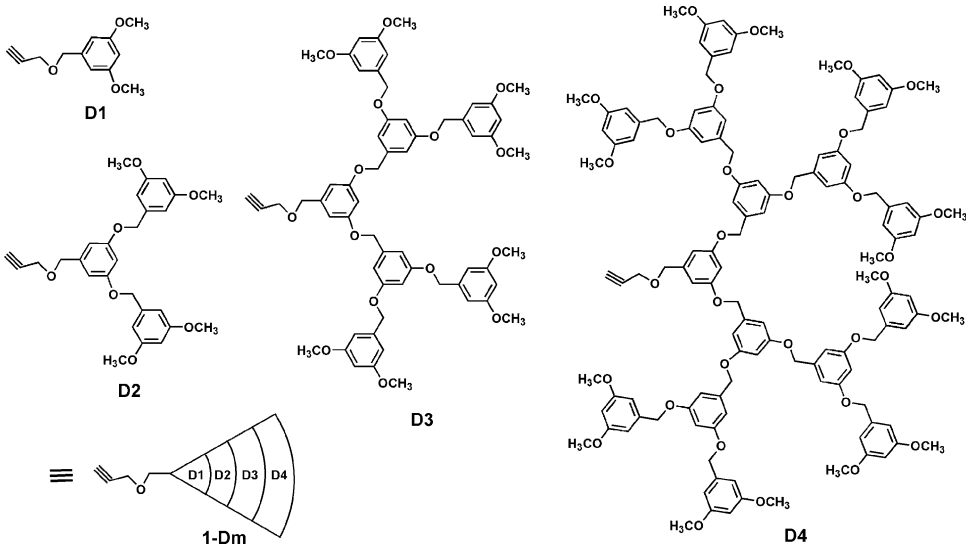


Figure 1. Structures of acetylenic-dendrons **1-Dm** (m=1–4: generation of dendron).

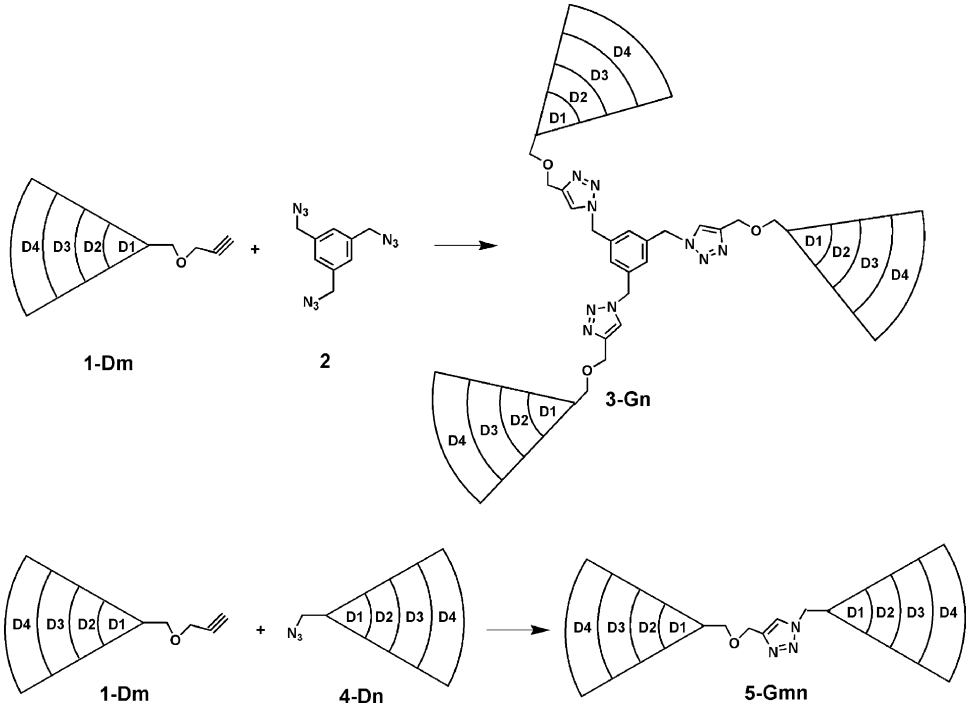
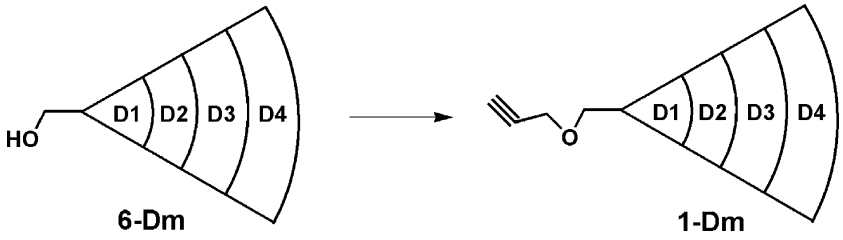


Figure 2. Synthetic strategies of triazole dendrimers via the Cu(I)-catalyzed 1,3-dipolar cycloaddition reactions. Conditions: 5 mol% $CuSO_4 \cdot 5H_2O$/10 mol% sodium ascorbate with respect to alkyne, DMF/H_2O (4:1), 50–60 °C.

dendrons **1-Dm** (Fig. 1) and their application to the convergent synthesis of dendrimers using click chemistry with a tripodal azide core or an azide focal point functionalized Fréchet type dendrons (Fig. 2). The fundamental study reported herein details the growth of dendrimers convergently with triazole linkages between the core and dendrons.

2. Results and discussion

The poly(benzyl ether) dendrons, now frequently referred to as Fréchet-type dendrons, have been utilized by a number of groups because they are relatively readily accessed and exhibit the chemical stability associated with ether linkages and good solubility in organic solvents.[11] Due to these reasons we selected the Fréchet-type dendrons in the design and synthesis of the propargyl focal point functionalized dendrons. The terminal acetylenic Fréchet-type dendrons **1-Dm** (m=1–4: generation of dendron) were synthesized by the propargylation of the corresponding dendritic benzyl alcohols with propargyl bromide (Scheme 1). The Fréchet-type benzyl alcohols **6-Dm** (m=1–4: generation of dendron) were prepared according to the reported procedure.[12] For the synthesis of the propargyl focal point functionalized Fréchet-type dendrons **1-Dm**, we have reacted the corresponding dendritic benzyl alcohols **6-Dm** with propargyl bromide in the presence of NaH in THF.



Scheme 1. Synthesis of acetylenic-dendrons **1-Dm**. Conditions: NaH, THF, propargyl bromide, rt, ~10 h.

The reaction of propargyl bromide with first generation dendritic benzyl alcohol **6-D1** in THF in the presence of NaH provided the first generation dendritic benzyl propargyl ether **1-D1** in 97% yield. Next, we conducted the reaction for the preparation of higher generation dendrons. The reactions of propargyl bromide with **6-D2**, **6-D3**, and **6-D4** in the same condition gave the dendritic benzyl propargyl ether **1-D2**, **1-D3**, and **1-D4** in yields of 92, 93, and 88%, respectively. All dendrons were confirmed by ^{1}H and ^{13}C NMR spectroscopy, IR spectroscopy, and their FAB mass spectra.

For the construction of the triazole dendrimer **3-Gn** via the 1,3-dipolar cycloaddition reactions between acetylene-dendrons **1-Dm** and the tripodal azide **2**, we simply utilized the click chemistry condition, which is well-documented. The active Cu(I) species, generated in situ by reacting $CuSO_4 \cdot 5H_2O$ with sodium ascorbate as the reducing agent, provide the 1,4-disubstituted 1,2,3-triazole in excellent yield.[3a] We carried out the reactions in a 4:1 solvent ratio of DMF to H_2O using 5 mol% $CuSO_4 \cdot 5H_2O$ with 10 mol% sodium ascorbate with respect to alkyne at 50–60 °C. The reaction progress could be checked by TLC. The generation and disappearance of the intermediates, which are mono- and/or di-triazole derivatives, were monitored by TLC runs of the reaction mixture. The reaction of 1,3,5-tris(azidomethyl)benzene **2** with **1-D1** in 0.1 M solution provided the triazole dendrimer **3-G1** having just 1,4-disubstituted 1,2,3-triazole units in yield of 89% after 18 h. Given the success in using cycloaddition reaction in the synthesis of first generation dendrimer, we expanded this reaction to get higher generation dendrimers. Reaction of 1,3,5-tris(azidomethyl)benzene **2** with **1-D2** and **1-D3** afforded the triazole dendrimers **3-G2** and **3-G3** in yields of 88 and 80%, respectively, after 26 h. In case of **1-D4**, the triazole dendrimer **3-G4** was obtained in 80% yield after 28 h. For completion of the reaction between the dendritic acetylene and the tripodal core, the higher generation dendron takes longer time than the lower generation dendron. This observation led us to imagine that the reaction between the dendritic acetylene and the tripodal azide core was kinetically controlled by the accessibility of acetylide due to the steric hindrance (bulkiness) of dendron and spatial congestion of tripodal core region. Therefore, the results showed that the formation of triazole between tripodal azide and propargyl-dendrons can be regarded as a new connector to construct various dendrimers and functional materials.

All dendrimers **3-Gn** were confirmed by ^{1}H and ^{13}C NMR spectroscopy. From their ^{1}H NMR spectra ($CDCl_3$), the peaks of the benzene protons of core and the triazole protons in dendrimers **3-Gn** were found at 7.11 and 7.49 ppm for **3-G1**, 7.11 and 7.49 ppm for **3-G2**, 7.04 and 7.39 ppm for **3-G3**, and 6.96 and 7.34 ppm for **3-G4**, respectively. The peaks of the benzylic protons adjacent to the nitrogen of triazole in dendrimers **3-Gn** were found at 5.43 ppm for **3-G1**, 5.42 ppm for **3-G2**, 5.32 ppm for **3-G3**, and 5.22 ppm for **3-G4**, respectively. As the dendrimer generation increased, the peaks of the benzene protons of core, the triazole protons, and the benzylic protons adjacent to the nitrogen of triazole showed up-field shift. In third and fourth generation dendrimers it is observed that the benzene protons of core, the triazole protons, and the benzylic protons adjacent to the nitrogen of triazole are influenced by the larger dendritic effect changing their microenvironment.[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 (Fig. 3). As expected, the obtained dendrimer possessed a very well-defined molecular structure with very low polydispersity values (PDI=1.01–1.04). IR data also confirmed that neither alkyne (~3285 cm^{-1}) nor azide (2098 cm^{-1}) residues remain in the final dendrimer.

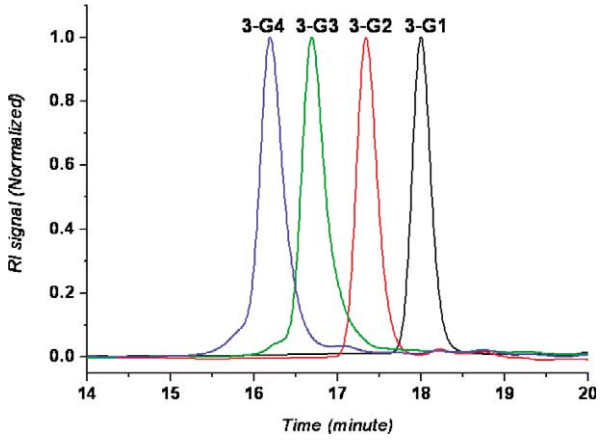


Figure 3. GPC diagrams of dendrimers **3-Gn** obtained from THF eluent.

To probe the viability of our approach, we next investigated the synthesis of triazole dendrimer **5-Gmn** from the coupling reactions between acetylenic-dendron **1-Dm** and azido-dendron **4-Dn** (entries 1–4 in Table 1). The same reaction condition as the previous trimerization was utilized in the hetero-dimerization reaction between an azide and an alkyne. The reaction of **1-D1** with **4-D1** in a 4:1 solvent ratio of DMF to H_2O using 5 mol% $CuSO_4 \cdot 5H_2O$ with 10 mol% sodium ascorbate at 50–60 °C provided the just 1,4-disubstituted 1,2,3-triazole product **5-G11** in 90% yield. Given the success in using cycloaddition reaction in the synthesis of first generation dendrimer, we expanded this

reaction to get higher generation dendrimers (entries 2–4 in Table 1). Reactions of **1-D2** with **4-D2**, **1-D3** with **4-D3**, and **1-D4** with **4-D4** in a same conditions provided 1,4-disubstituted 1,2,3-triazole symmetrical dendrimers **5-G22**, **5-G33**, and **5-G44** in yields of 89, 94, and 95%, respectively. For completion of the reaction between two dendrons, the higher generation dendrons take slightly longer time than the lower generation dendrons which can be imagined by the simple steric hindrance of dendrons. Whereas the trimerization reaction between dendrons and core to provide **3-Gn** is more sluggish than the coupling reaction between two dendrons because there are some limitation in the accessibility of acetylide due to the additional spatial congestion of core region. All symmetric dendrimers were also confirmed by ^{1}H and ^{13}C NMR spectroscopy and FAB and MALDI mass spectra. From their ^{1}H NMR spectra ($CDCl_3$), the peaks of the benzylic protons adjacent to the nitrogen of triazole and the triazole proton in dendrimers **5-Gmn** were found at 5.42 and 7.48 ppm for **5-G11**, 5.42 and 7.44 ppm for **5-G22**, 5.39 and 7.44 ppm for **5-G33**, and 5.34 and 7.42 ppm for **5-G44**, respectively. As the dendrimer generation increased, the peaks of the benzylic protons adjacent to the nitrogen of triazole and the triazole proton showed slightly up-field shift. Analysis of the higher dendrimers by gel-permeation chromatography (GPC) shows very low polydispersity values, PDI = 1.02 and 1.04 for **5-G33** and **5-G44**, respectively (Fig. 4).

Table 1. Synthesis of triazole dendrimers **5-Gmn** from azido-dendrons **1-Dm** and acetylenic-dendrons **4-Dn**

Entry	1-Dm	4-Dn	Rxn time (h)	Product	Yield (%)[a]
1	**1-D1**	**4-D1**	5	**5-G11**	90
2	**1-D2**	**4-D2**	6	**5-G22**	89
3	**1-D3**	**4-D3**	7	**5-G33**	94
4	**1-D4**	**4-D4**	8	**5-G44**	95
5	**1-D1**	**4-D2**	6	**5-G12**	84
6	**1-D1**	**4-D3**	6	**5-G13**	90
7	**1-D1**	**4-D4**	7	**5-G14**	85
8	**1-D2**	**4-D1**	6	**5-G21**	85
9	**1-D2**	**4-D4**	7	**5-G24**	92
10	**1-D3**	**4-D1**	7	**5-G31**	92
11	**1-D4**	**4-D2**	7	**5-G42**	88

[a] Isolated yields.

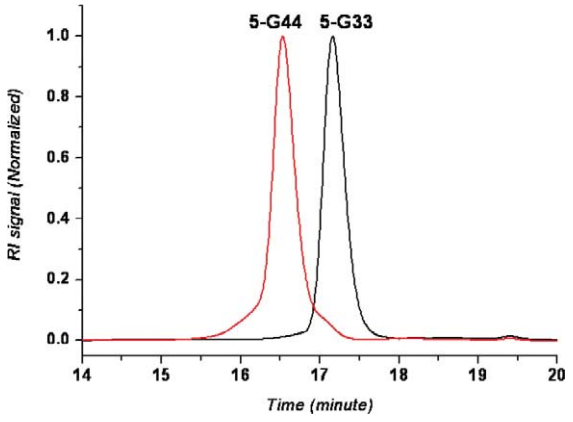


Figure 4. GPC diagrams of dendrimers **5-Gmn** obtained from THF eluent.

Next, we turned our attention toward the formation of unsymmetrical 1,2,3-triazole dendrimers. We have investigated two synthetic strategies. The first one is based on the reactions of lower generations acetylenic-dendrons **1-D1** or **1-D2** with **4-Dn** (entries 5–9 in Table 1). The second strategy involves the reactions using higher generations acetylenic dendrons **1-D3** and **1-D4** (entries 10–11 in Table 1). The reactions of **1-D1** with **4-D2**, **4-D3**, and **4-D4** provided 1,4-disubstituted 1,2,3-triazole unsymmetrical dendrimers **5-G12**, **5-G13**, and **5-G14** in yields of 84, 90, and 85%, respectively. The reactions of **1-D2** with **4-D1** and **4-D4** provided 1,4-disubstituted 1,2,3-triazole unsymmetrical dendrimers **5-G21** and **5-G24** in yields of 85 and 92%, respectively. The reactions of **1-D3** with **4-D1** and of **1-D4** with **4-D2** provided 1,4-disubstituted 1,2,3-triazole unsymmetrical dendrimers **5-G31** and **5-G42** in yields of 92 and 88%, respectively. Therefore, the results showed that the formation of triazole between azide-dendrons and propargyl-dendrons are found to be an efficient connector to construct various unsymmetric dendrimers and may be applied for the synthesis of functional materials. We are currently investigated the synthesis of various unsymmetric functional dendrimers using the different kinds of dendrons. All unsymmetric dendrimers were confirmed by ^{1}H and ^{13}C NMR spectroscopy and FAB mass spectra.

3. Conclusion

We have demonstrated that the propargyl-functionalized Fréchet-type dendrons are synthesized by the propargylation of the corresponding Fréchet type dendritic benzyl alcohol and that the trimerization reactions between tripodal azide and acetylene-dendrons and the coupling reactions between azido dendrons and acetylenic dendrons lead to the formation of symmetric triazole dendrimers in high yields. Furthermore, such reactions between dendrons of different size afford unsymmetrical triazole dendrimers. This reaction may then provide an insight into designing various (un)symmetrical dendrimers such as amphiphilic dendrimers. We are currently working towards various functional dendrimers using this strategy for various applications.

4. Experimental

^{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. EI, FAB, and MALDI mass spectra were obtained from Korea Basic Science Institute 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 5 μm MIXED-C, refractive

index detector) in THF solution. All chemicals were obtained from commercial sources and used as received, unless otherwise mentioned. THF was distilled over Na/Ph_2CO ketyl. Dendritic benzyl alcohols **6-Dm** and azides **4-Dn**[12] and 1,3,5-tris(azidomethyl)benzene[14] used here were prepared according to previously reported procedure.

4.1. Synthesis of dendritic benzyl propargyl ether (1-Dm)

General procedure. Dendritic benzyl alcohol **6-Dm** (1 mmol) was added to a THF (10 mL) solution of sodium hydride (1.2 mmol). After stirred under nitrogen for 30 min, propargyl bromide (1.2 mmol) was added and the mixture was stirred for ~10 h. The reaction mixture was poured slowly into cold 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 (EtOAc/Hex system) to afford the desired product **1-Dn**.

4.1.1. Compound 1-D1. A colorless oil; 97% yield; IR 3286, 2942, 2840, 2115, 1599, 1463, 1205, 1155, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.47 (t, J= 2.4 Hz, 1H), 3.79 (s, 6H), 4.18 (d, J=2.4 Hz, 2H), 4.56 (s, 2H), 6.40 (d, J=2.1 Hz, 1H), 6.52 (d, J=2.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 139.6, 105.7, 100.0, 79.6, 74.6, 71.5, 57.0, 55.3; MS (EI): m/z 206 [M^+], 166, 152, 137; HRMS (EI) Calcd for $C_{12}H_{14}O_3$: 206.0943. Found: 206.0943.

4.1.2. Compound 1-D2. A colorless oil; 92% yield; IR 3285, 2939, 2838, 2116, 1598, 1459, 1204, 1154, 1054 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.46 (t, J= 2.4 Hz, 1H), 3.80 (s, 12H), 4.16 (d, J=2.4 Hz, 2H), 4.55 (s, 2H), 4.98 (s, 4H), 6.41 (d, J=2.1 Hz, 2H), 6.55 (d, J= 2.1 Hz, 1H), 6.57(m, 4H), 6.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 160.0, 139.7, 139.2, 106.9, 105.2, 101.7, 100.0, 79.6, 74.7, 71.4, 70.0, 57.1, 55.4; MS (EI): m/z 478 [M^+], 438, 301, 151; HRMS (EI) Calcd for $C_{28}H_{30}O_7$: 478.1992. Found: 478.1992.

4.1.3. Compound 1-D3. A colorless gum; 93% yield; IR 3284, 2938, 2838, 2117, 1598, 1458, 1203, 1153, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.46 (t, J= 2.4 Hz, 1H), 3.79 (s, 24H), 4.16 (d, J=2.4 Hz, 2H), 4.55 (s, 2H), 4.97 (s, 12H), 6.41 (m, 4H), 6.53–6.60 (m, 13H), 6.67 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 160.1, 160.0, 139.7, 139.2, 139.1, 106.9, 106.4, 105.2, 101.6, 100.0, 79.6, 74.7, 71.4, 70.04, 70.0, 57.1, 55.3; MS (FAB): m/z 1021.5 [M^+], 966.7, 572.9 410.2, 340.2; HRMS (FAB) Calcd for $C_{60}H_{62}O_{15}$: 1022.4089. Found: 1023.4167 [M^++H].

4.1.4. Compound 1-D4. A colorless gum; 88% yield; IR 3285, 2942, 2840, 2116, 1599, 1458, 1206, 1153, 1069, 1054 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.44 (t, J= 2.4 Hz, 1H), 3.77 (s, 48H), 4.14 (d, J=2.3 Hz, 2H), 4.53 (s, 2H), 4.95 (s, 28H), 6.39 (m, 8H), 6.55–6.60 (m, 26H), 6.66 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.0, 160.1, 160.0, 139.7, 139.2, 139.1, 107.0, 106.4, 105.2, 101.6, 100.0, 79.6, 74.7, 71.4, 70.03, 70.0, 75.1, 55.3; MS (FAB): m/z 2110.9 [M^+], 1960.9, 1687.9; HRMS (FAB): Calcd for $C_{124}H_{126}O_{31}$: 2110.8283. Found: 2111.8361 [M^++H].

4.2. Synthesis of 1,2,3-triazole dendrimers 3-Gn by reaction between 1,3,5-tris(azidomethyl)benzene 2 and acetylene-dendrons 1-Dm

General procedure: A solution of 1,3,5-tris(azidomethyl)-benzene **2** (0.01 mmol) and acetylene-dendrons **1-Dm** (0.03 mmol) in DMF–H_2O (4:1, 1 mL) in the presence of 15 mol% $CuSO_4\cdot5H_2O$ with 30 mol% sodium ascorbate was stirred at 50–60 °C for 18–28 h. The reaction was monitored by TLC regarding on the disappearance of **1-Dm** and the generation and disappearance of mono- and/or di-triazole derivatives. 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 (EtOAc/Hex system) to afford the desired product.

4.2.1. Compound 3-G1. A yellowish gum; 89% yield; IR 2923, 2854, 1597, 1465, 1203, 1154, 1067, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 18H), 4.51 (s, 6H), 4.62 (s, 6H), 5.43 (s, 6H), 6.36 (m, 3H), 6.48 (m, 6H), 7.11 (s, 3H), 7.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 146.2, 140.5, 137.3, 128.0, 123.2, 106.1, 100.1, 73.0, 64.0, 55.7, 53.7; MS (FAB): m/z 862.3 [M^+], 694.2, 647.4, 544.2; HRMS (FAB) Calcd for $C_{45}H_{51}N_9O_9$: 861.3810. Found: 862.3888 [M^++H]. PDI: 1.01.

4.2.2. Compound 3-G2. A yellowish gum; 88% yield; IR 2926, 2854, 1596, 1461, 1203, 1156, 1054 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 36H), 4.50 (s, 6H), 4.61 (s, 6H), 4.94 (s, 12H), 5.42 (s, 6H), 6.39 (m, 6H), 6.52 (m, 3H), 6.55 (m, 12H), 6.57 (m, 6H), 7.11 (s, 3H), 7.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 160.4, 146.2, 140.6, 139.6, 137.3, 128.0, 123.1, 107.2, 105.7, 101.9, 100.3, 72.9, 70.4, 64.0, 55.8, 53.6; MS (FAB): m/z 1678.9 [M^+], 663.5, 647.5; HRMS (FAM) Calcd for $C_{93}H_{99}N_9O_{21}$: 1677.6956. Found: 1678.7034 [M^++H]. PDI: 1.01.

4.2.3. Compound 3-G3. A yellowish gum; 80% yield; IR 2923, 2854, 1596, 1461, 1203, 1153, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 72H), 4.48 (s, 6H), 4.59 (s, 6H), 4.92 (s, 36H), 5.32 (s, 6H), 6.38 (m, 12H), 6.49–6.64 (m, 39H), 6.64 (m, 12H), 7.04 (s, 3H), 7.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 160.47, 160.37, 146.1, 140.6, 139.7, 139.5, 137.3, 131.2, 128.0, 123.1, 107.1, 106.8, 105.7, 105.4, 102.0, 101.9, 100.4, 72.9, 70.5, 70.3, 64.0, 55.8, 53.6; MS (MALDI): Calcd for $C_{189}H_{195}N_9O_{45}$: 3310.3247. Found: 3333.2024 [M^+ + Na]. PDI: 1.03.

4.2.4. Compound 3-G4. A yellowish solid; mp 78–80 °C; 80% yield; IR 2933, 2839, 1599, 1462, 1203, 1157, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 144H), 4.44 (s, 6H), 4.54 (s, 6H), 4.89 (s, 84H), 5.22 (s, 6H), 6.36 (m, 24H), 6.52 (m, 73H), 6.62 (m, 38H), 6.96 (s, 3H), 7.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 160.45, 160.37, 146.2, 146.0, 140.7, 139.7, 139.63, 139.56, 137.2, 132.6, 129.0, 128.9, 127.9, 123.2, 107.1, 106.8, 105.7, 105.4, 102.0, 101.9, 101.8, 100.3, 72.8, 70.4, 70.3, 69.9, 64.0, 55.7, 55.3, 55.1, 53.5; MS (MALDI): Calcd

for $C_{381}H_{387}N_9O_{93}$: 6580.15. Found: 6603.42 [M^+ + Na]. PDI: 1.04.

4.3. Synthesis of 1,2,3-triazole dendrimers 5-Gmn by reaction between propargyl-dendrons 1-Dm and azido-dendrons 4-Dn

General procedure: A mixture of propargyl-dendrons **1-Dm** (0.10 mmol) and azido-dendrons **4-Dn** (0.10 mmol) in DMF–H_2O (4:1, 1 mL) in the presence of 5 mol% $CuSO_4 \cdot 5H_2O$ with 10 mol% sodium ascorbate was stirred at 50 °C for ~8 h. The reaction was monitored by TLC regarding on the disappearance of **4-Dn**. 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 (EtOAc/Hex system) to afford the desired product.

4.3.1. Compound 5-G11. A colorless oil; 90% yield; IR 2939, 2839, 1599, 1462, 1203, 1157, 1066, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.75 (s, 6H), 3.78 (s, 6H), 4.52 (s, 2H), 4.65 (s, 2H), 5.42 (s, 2H), 6.37 (m, 1H), 6.40 (m, 3H), 6.49 (m, 2H), 7.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.4, 161.0, 145.6, 140.2, 136.7, 122.5, 106.2, 105.6, 100.5, 99.9, 72.6, 63.8, 55.5, 55.4, 54.3; MS (EI): *m/z*=399 [M^+], 233, 151; HRMS (EI): *m/z* Calcd for $C_{21}H_{25}N_3O_5$: 399.1794. Found: 399.1796.

4.3.2. Compound 5-G22. A yellowish gum; 89% yield; IR 2939, 2839, 1596, 1458, 1206, 1153, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 24H), 4.52 (s, 2H), 4.64 (s, 2H), 4.92 (s, 4H), 4.95 (s, 4H), 5.42 (s, 2H), 6.40 (m, 4H), 6.49–6.60 (m, 14H), 7.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 160.96, 160.3, 159.97, 145.5, 139.2, 138.8, 136.7, 122.5, 107.2, 106.8, 105.2, 102.1, 101.5, 100.0, 99.9, 72.6, 70.1, 70.0, 63.7, 55.4, 54.1; MS (FAB): *m/z*=944.4 [M^+]; HRMS (FAB): *m/z* Calcd for $C_{53}H_{57}N_3O_{13}$: 943.3891. Found: 944.3970 [M^+ + H].

4.3.3. Compound 5-G33. A yellowish gum; 94% yield; IR 2939, 2840, 1597, 1456, 1203, 1154, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.77 (s, 48H), 4.51 (s, 2H), 4.63 (s, 2H), 4.89 (s, 4H), 4.94 (s, 20H), 5.39 (s, 2H), 6.40 (m, 6H), 6.45 (m, 2H), 6.55 (m, 24H), 6.62 (m, 4H), 6.65 (m, 6H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.1, 160.4, 160.2, 160.1, 160.0, 145.6, 140.4, 139.6, 139.4, 139.23, 139.2, 139.0, 136.9, 122.7, 107.2, 106.8, 106.5, 105.3, 102.2, 101.8, 101.7, 100.03, 100.0, 72.4, 70.1, 70.0, 63.7, 55.4, 54.1; MS (MALDI): Calcd for $C_{117}H_{121}N_3O_{29}$: 2031.8086. Found: 2054.7959 [M^+ + Na]. PDI: 1.02.

4.3.4. Compound 5-G44. A yellowish solid; mp 76–78 °C; 95% yield; IR 2936, 2836, 1596, 1456, 1206, 1153, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.75 (s, 96H), 4.49 (s, 2H), 4.61 (s, 2H), 4.86 (s, 6H), 4.92 (s, 50H), 5.34 (s, 2H), 6.38 (m, 16H), 6.42 (m, 2H), 6.55 (m, 54H), 6.60 (m, 4H), 6.65 (m, 14H), 7.42 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.7, 161.4, 161.1, 160.7, 160.5, 160.4, 160.2, 145.9, 140.8, 139.8, 139.7, 139.63, 139.59, 139.3, 137.4, 123.1, 108.1, 107.5, 107.1, 106.8, 105.9, 105.7, 105.4, 102.4, 102.1, 101.9, 100.4, 72.7, 70.444, 70.37, 64.0, 55.7, 54.4; MS (MALDI): Calcd for $C_{245}H_{249}N_3O_{61}$: 4211.58. Found: 4234.70 [M^+ +Na]. PDI: 1.04.

4.3.5. Compound 5-G12. A yellowish gum; 84% yield; ^1H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 6H), 3.79 (s, 12H), 4.53 (s, 2H), 4.65 (s, 2H), 4.93 (s, 4H), 5.42 (s, 2H), 6.37 (m, 1H), 6.41 (m, 2H), 6.49 (m, 4H), 6.54 (m, 4H), 6.57 (m, 1H), 7.45 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.4, 161.3, 160.8, 146.0, 140.6, 139.2, 137.1, 122.9, 107.7, 106.0, 105.6, 102.6, 100.4, 100.3, 73.0, 70.5, 64.1, 55.8, 55.7, 54.6; MS (FAB): *m/z*=672.3 [M^+ +H]; HRMS (FAB): *m/z* Calcd for $C_{37}H_{41}N_3O_9$: 671.2843. Found: 672.2921 [M^+ +H].

4.3.6. Compound 5-G13. A yellowish gum; 90% yield; ^1H NMR (300 MHz, $CDCl_3$): δ 3.75 (s, 6H), 3.78 (s, 24H), 4.52 (s, 2H), 4.64 (s, 2H), 4.92 (s, 4H), 4.97 (s, 8H), 5.41 (s, 2H), 6.36 (m, 1H), 6.41 (m, 4H), 6.46–6.49 (m, 4H), 6.57 (m, 11H), 6.54 (m, 4H), 7.46 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.7, 161.4, 161.3, 160.7, 160.5, 160.49, 160.4, 146.0, 140.7, 139.7, 139.6, 139.5, 139.3, 137.1, 122.9, 107.7, 107.2, 106.83, 106.8, 106.5, 106.0, 105.7, 102.1, 102.0, 101.9, 100.8, 100.38, 100.35, 100.27, 72.9, 72.8, 70.5, 70.4, 64.1, 55.8, 55.7, 54.6; MS (FAB): *m/z*=1216.4 [M^+ +H], 663.5; HRMS (FAB): *m/z* Calcd for $C_{69}H_{73}N_3O_{17}$: 1215.4940. Found: 1216.5018 [M^+ +H].

4.3.7. Compound 5-G14. A yellowish gum; 85% yield; ^1H NMR (300 MHz, $CDCl_3$): δ 3.72 (s, 6H), 3.77 (s, 48H), 4.50 (s, 2H), 4.63 (s, 2H), 4.91 (s, 4H), 4.96 (s, 24H), 5.38 (s, 2H), 6.35 (m, 1H), 6.40 (m, 8H), 6.48 (m, 3H), 6.56 (m, 22H), 6.63 (m, 4H), 6.67 (m, 10H), 7.45 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 160.9, 160.3, 160.1, 145.6, 140.2, 139.2, 139.1, 138.7, 136.8, 122.6, 107.3, 106.4, 105.6, 105.2, 102.0, 101.7, 101.6, 99.9, 99.8, 99.6, 72.5, 70.04, 70.0, 63.6, 55.33, 55.27, 54.1; MS (FAB): *m/z*= 1216.4 [M^+ +H], 663.5; MS (FAB): Calcd for $C_{133}H_{137}N_3O_{33}$: 2305.5. Found: 2305.9 [M^+].

4.3.8. Compound 5-G21. A yellowish gum; 85% yield; ^1H NMR (300 MHz, $CDCl_3$): δ 3.73 (s, 6H), 3.78 (s, 12H), 4.51 (s, 2H), 4.63 (s, 2H), 4.95 (s, 4H), 5.41 (s, 2H), 6.40 (m, 5H), 6.53–6.59 (m, 7H), 7.47 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.3, 161.0, 160.7, 160.0, 145.5, 140.3, 139.2, 139.1, 136.7, 136.5, 122.5, 106.7, 106.1, 105.9, 105.2, 105.0, 101.5, 100.4, 99.9, 72.4, 70.0, 63.7, 55.4, 55.3, 54.2; MS (FAB): *m/z*=672.3 [M^+ +H]; HRMS (FAB): *m/z* Calcd for $C_{37}H_{41}N_3O_9$: 671.2843. Found: 672.2921 [M^+ +H].

4.3.9. Compound 5-G24. A yellowish gum; 92% yield; ^1H NMR (300 MHz, $CDCl_3$): δ 3.75 (s, 12H), 3.78 (s, 48H), 4.49 (s, 2H), 4.62 (s, 2H), 4.91 (s, 8H), 4.95 (s, 24H), 5.39 (s, 2H), 6.40 (m, 10H), 6.47 (m, 2H), 6.56 (m, 30H), 6.62 (m, 4H), 6.66 (m, 8H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.4, 161.36, 160.7, 160.5, 160.4, 146.0, 140.7, 139.7, 139.6, 139.55, 139.3, 137.3, 123.0, 107.6, 107.1, 106.8, 106.1, 105.7, 102.5, 102.0, 101.9, 100.3, 72.8, 70.5, 70.4, 64.0, 55.7, 54.5; MS (FAB): Calcd for $C_{149}H_{153}N_3O_{37}$: 2577.8. Found: 2577.4 [M^+].

4.3.10. Compound 5-G31. A yellowish gum; 92% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 3.73 (s, 6H), 3.78 (s, 24H), 4.52 (s, 2H), 4.64 (s, 2H), 4.96 (s, 4H), 4.98 (s, 8H), 5.40 (s, 2H),

6.39–6.41 (m, 7H), 6.52 (m, 1H), 6.57 (m, 13H), 6.67 (m, 3H), 7.46 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.7, 161.4, 160.5, 160.4, 145.9, 140.7, 139.7, 139.6, 137.1, 122.9, 107.2, 106.8, 106.6, 105.7, 102.0, 101.9, 100.9, 100.4, 72.9, 70.5, 70.4, 64.1, 55.8, 54.6; MS (FAB): m/z= 1216.4 [M^++H], 753.5, 647.5; HRMS (FAB): m/z Calcd for $C_{69}H_{73}N_3O_{17}$: 1215.4940. Found: 1216.5018 [M^++H].

4.3.11. Compound 5-G42. A yellowish gum; 88% yield; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.75 (s, 12H), 3.77 (s, 48H), 4.52 (s, 2H), 4.63 (s, 2H), 4.87 (s, 8H), 4.95 (s, 24H), 5.36 (s, 2H), 6.40 (m, 10H), 6.45 (m, 2H), 6.51 (m, 4H), 6.56 (m, 24H), 6.60 (m, 2H), 6.66 (m, 12H), 7.43 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.1, 160.6, 160.4, 160.1, 160.0, 145.6, 140.4, 139.4, 139.3, 139.2, 138.9, 136.9, 122.6, 107.6, 107.2, 106.8, 106.5, 105.3, 102.2, 102.0, 101.7, 100.0, 72.5, 70.1, 69.8, 63.7, 55.4, 54.1; MS (FAB): Calcd for $C_{149}H_{153}N_3O_{37}$: 2577.8. Found: 2577.4 [M^+].

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