

A Facile Route to Triazole Dendrimers via Click Chemistry Linking Tripodal Acetylene and Dendrons

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Dendrimers are highly branched macromolecules, which are prepared by repetition of a given set of reactions using either divergent or convergent strategies.¹ Generally, the reactions employed are high yielding without any side reactions. Well known processes, such as the Michael reaction, Williamson ether synthesis, amidations and reductions have been used extensively.² Recent investigation of the click chemistry, the Cu(I)-catalyzed Huisgen [2 + 3] dipolar cycloaddition reaction between an organic azide and an alkyne, has attracted attention which has found many applications in organic chemistry,³ supramolecular chemistry,⁴ drug discovery,⁵ bioconjugations,⁶ and materials science.⁷ The reaction is characterized by very high yields, mild and simple reaction conditions, oxygen and water tolerance, and ease of product isolation. It is highly chemoselective affording only the desired 1,2,3-triazole even in the presence of a large variety of other functional groups.⁸ There are few reports to synthesize the triazole-mediated dendritic materials using click chemistry.⁹ Due to our interest in developing new dendrimers,¹⁰ we became involved in exploring efficient click reaction. Herein we present the convergent synthesis of triazole dendrimers by the trimerization reaction of Fréchet-type azido-dendrons via click chemistry using trispropargyl amine as a tripodal core.

Experimental Section

General procedure for the preparation of 1,2,3-triazole dendrimers 3-Gn by reaction between tripropargylamine 1 and azido-dendrons 2-Dn. A mixture of tripropargylamine **1** (0.05 mmol) and azido-dendrons **2-Dn** (0.15 mmol) in DMF-H₂O (4 : 1) in the presence of 5 mol % CuSO₄·5H₂O with 10 mol % sodium ascorbate was stirred at 50-60 °C. The reaction was monitored by TLC regarding on the disappearance of **2-Dn** and the generation and disappearance of mono- and/or di-triazole derivatives. The mixture was cooled to room temperature and then normal workup was carried out. The desired product was isolated by column chromatography.

3-G1: 93% yield; ¹H NMR (300 MHz, CDCl₃) δ 3.71 (s, 6H), 3.75 (s, 18H), 5.42 (s, 6H), 6.39 (br, 9H), 7.67 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 161.2, 144.2, 136.9, 123.7, 105.8, 100.3, 55.3, 54.0, 47.1; MS (FAB): *m/z* 710.8 [M⁺]; HRMS (FAB) calcd for C₃₆H₄₂N₁₀O₆: 710.3289. found: 710.3282.

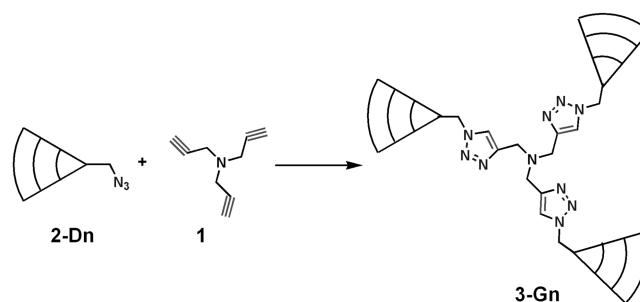
3-G2: 88% yield; ¹H NMR (500 MHz, CDCl₃) δ 3.72 (s, 6H), 3.75 (s, 36H), 4.90 (s, 12H), 5.37 (s, 6H), 6.38 (m, 6H), 6.47 (m, 6H), 6.53 (m, 15H), 7.66 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 161.1, 161.09, 161.07, 161.02, 160.97, 160.96, 160.4, 144.4, 138.9, 137.0, 123.8, 107.1, 105.2, 102.1, 100.0, 70.1, 55.48, 55.46, 55.45, 55.43, 55.37, 55.32, 55.3, 55.29, 55.27, 54.1, 47.3; MS (FAB): *m/z* 1527.5 [M⁺]; HRMS (FAB) calcd for C₈₄H₉₀N₁₀O₁₈: 1526.6435. found: 1526.6338.

3-G3: 42% yield; ¹H NMR (500 MHz, CDCl₃) δ 3.70 (s, 6H), 3.75 (s, 72H), 4.86 (s, 12H), 4.92 (s, 24H), 5.34 (s, 6H), 6.38 (m, 12H), 6.42 (m, 6H), 6.50-6.55 (m, 33H), 6.61 (m, 12H), 7.63 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 161.0, 160.3, 160.1, 144.4, 139.1, 138.9, 137.0, 123.8, 107.0, 106.4, 105.3, 105.0, 102.1, 101.7, 99.9, 70.0, 55.3, 54.0, 47.3; MS (FAB): *m/z* 3161.7 [M⁺]; HRMS (FAB) calcd for C₁₈₀H₁₈₆N₁₀O₄₂: 3159.2726. found: 3159.2754.

Results and Discussion

The synthetic strategy for triazole dendrimers **3-Gn** utilized a convergent method using the tripodal acetylenes **1** and the Fréchet-type azido-dendrons **2-Dn** (Scheme 1). The Fréchet-type azido-dendrons **2-Dn** (n = 1, 2, and 3: generation of dendron, Figure 1) were prepared according to the reported procedure.¹¹

To probe the effectiveness for the construction of the triazole dendrimer **3-Gn** via the 1,3-dipolar cycloaddition reactions of the tripodal acetylene **1** and azido-dendrons **2-Dn**, we simply utilized the click chemistry condition, which is well-documented. The active Cu(I) species, generated in situ by reacting 5 mol % CuSO₄·5H₂O with 10 mol %



Scheme 1. Synthetic strategies of triazole dendrimers by trimerization.

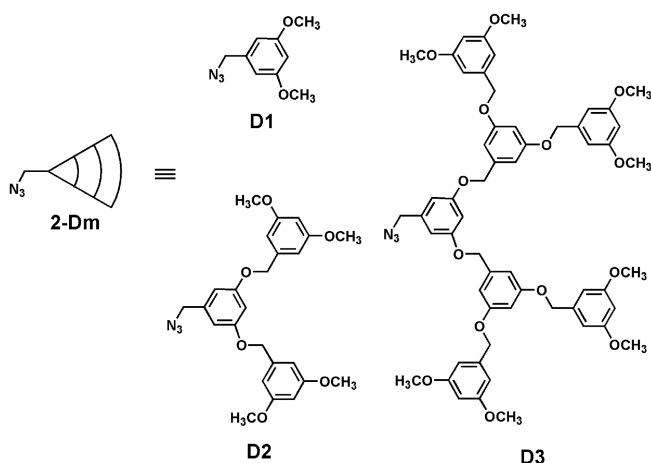


Figure 1. Structures of azido-dendrons.

sodium ascorbate as the reducing agent, provide the 1,4-disubstituted 1,2,3-triazole in excellent yield.¹²

We carried out the reactions in a 4 : 1 solvent ratio of DMF to H₂O using 5 mol % CuSO₄·5H₂O with 10 mol % sodium ascorbate at 50–60 °C. The reaction could be checked by IR spectroscopy by following the disappearance of the N₃ stretching band at around 2100 cm⁻¹. 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 tripropargylamine **1** with **2-D1** in 0.09 M solution provided the triazole dendrimer **3-G1** having just 1,4-disubstituted 1,2,3-triazole units in yield of 93% after 12 h. For the second generation dendrimer, the reaction of trispropargyl amine **1** with **2-D2** in 0.06 M solution provided the triazole dendrimer **3-G2** in 81% yield after 12 h, which went up to 88% in 24 h. The reaction of trispropargyl amine **1** with **2-D3** in 0.02 M solution afforded the triazole dendrimer **3-G3** in 40–42% after 24 h. It was also found that the reaction in 0.1 M solution provided the desired product in around 42% yield. We do not understand the reasons to get at low yield even though we do not observe any side product(s). We just suspect not to recover completely from silica-gel column chromatography. However we could not rule out the steric hindrance and/or spatial congestion of nitrogen core and dendron. We plan to investigate this further by changing the tripodal core component. Therefore, the results showed that the formation of triazole between tripodal acetylene and azido-dendrons can be regarded as a new connector to construct various dendrimers and functional materials.

All compounds were confirmed by ¹H and ¹³C NMR spectroscopy and FAB mass spectra. From their ¹H NMR spectra (CDCl₃), the peaks of the methylene protons adjacent to the nitrogen core and the triazole protons in dendrimers **3-Gn** were found at 3.71 and 7.67 ppm for **3-G1**, 3.72 and 7.66 ppm for **3-G2**, and 3.70 and 7.63 ppm for **3-G3** (Figure 2), respectively. There are no characteristic differences according to the dendrimer generations.

In summary, we have demonstrated that the trimerization reactions between tripodal acetylene and azido-dendrons

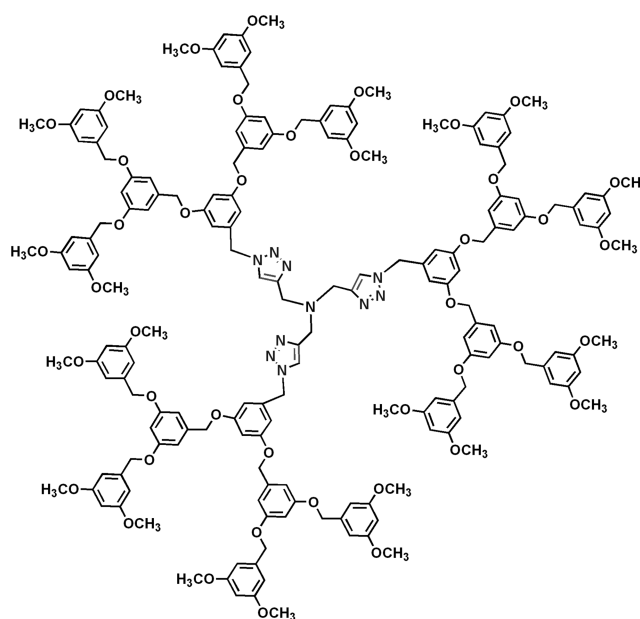


Figure 2. Structure of the third generation of triazole dendrimer **3-G3**.

lead to the formation of 1,4-disubstituted triazole dendrimers. This unique reaction may then provide an insight into designing various symmetrical dendrimers. We are currently working towards various functional dendrimers using this strategy for various applications, such as the templated synthesis of nanomaterials.

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