Synthesis and photophysical studies on triazole bridged dendrimers with phenothiazine as surface unit

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Abstract
Synthesis and photophysical properties of some novel 1, 2, 3-triazole bridged phenothiazine dendrimers with enone and S-(-)-BINOL core is described.

Keywords: Dendrimer, phenothiazine, 1, 2, 3-triazole, click chemistry

Introduction

Dendrimers[1] are very unique type of macromolecule with hyperbranched and perfectly defined structure that have attracted much interest and an innovative area of research in supramolecular chemistry. Due to the special structure and unusual properties, dendrimers are utilized for a wide range of biomedical and material applications, such as antibacterial,[2] drug delivery,[3] light-harvesting ability,[4] nonlinear optical (NLO),[5] organic light-emitting diodes (OLEDs)[6] and so on. Moreover, dendrimers with rigid structures can possibly be regularly assembled by packing on a plate without deformation of the molecule and are expected to expand the field of nanomaterials.[7]

Click chemistry coined by Sharpless,[8] refers to a Cu(I) catalyzed Huisgen 1,3-dipolar cycloaddition of azides to alkynes, providing 1,4-disubtituted 1,2,3-triazole. The advantages of employing click chemistry are the excellent regioselectivity, tolerance of sensitive functional group, atom-economy, no protection-deprotection protocol, mild reaction conditions and excellent yields. Triazoles have interesting chemical properties, which include high aromatic stabilization and tolerance to acidic and basic as well as oxidative and reductive conditions. Moreover, 1,2,3-triazole derivatives are important materials in pharmaceuticals such as anti-HIV,[9] antiviral,[10] and antimicrobial.[11] In addition, triazole derivatives play a pivotal role in the field of supramolecular assemblies.[12] Furthermore, synthesis of dendrimers using click chemistry has received much attention during recent times due to their interesting biological applications.[13]

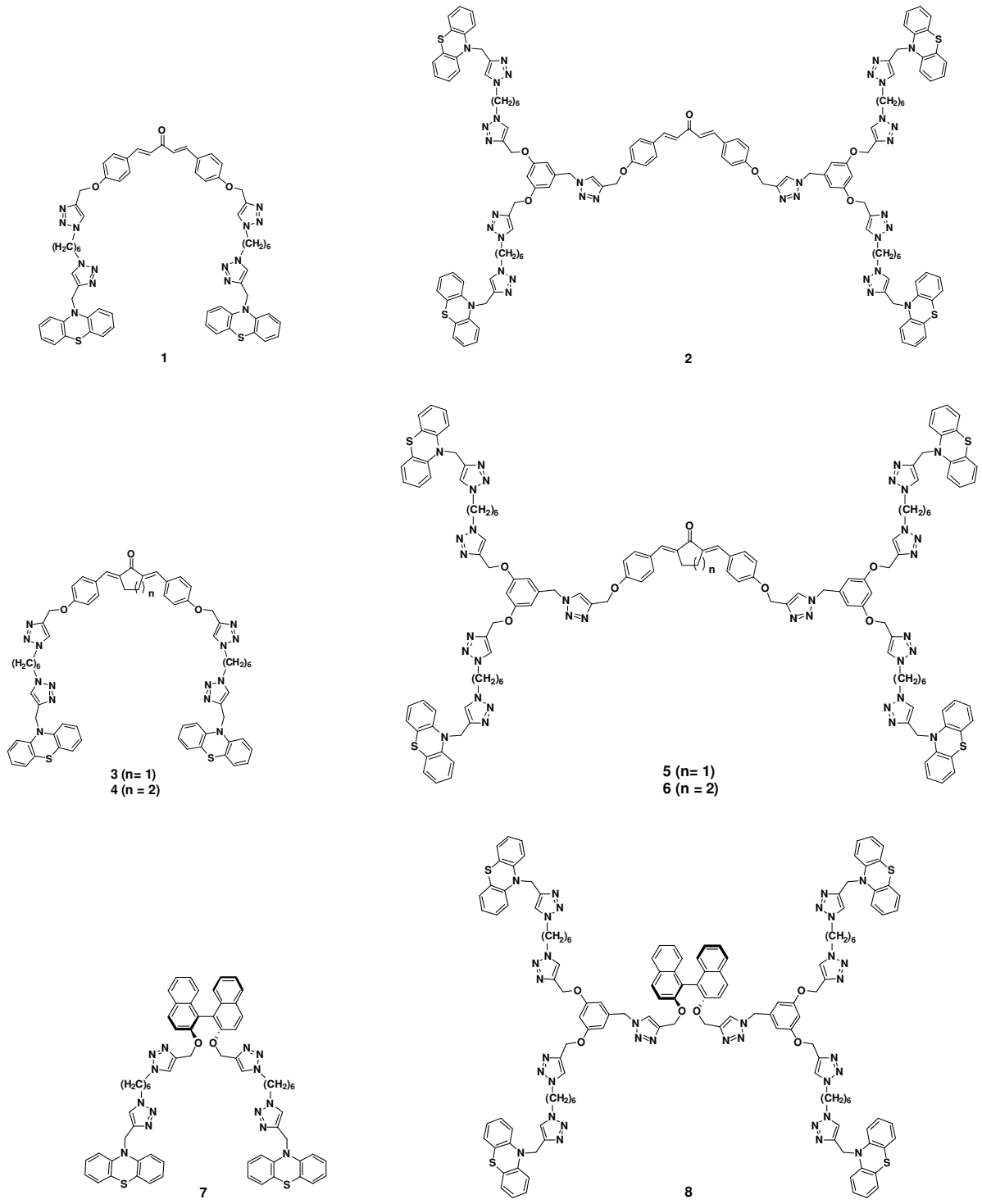


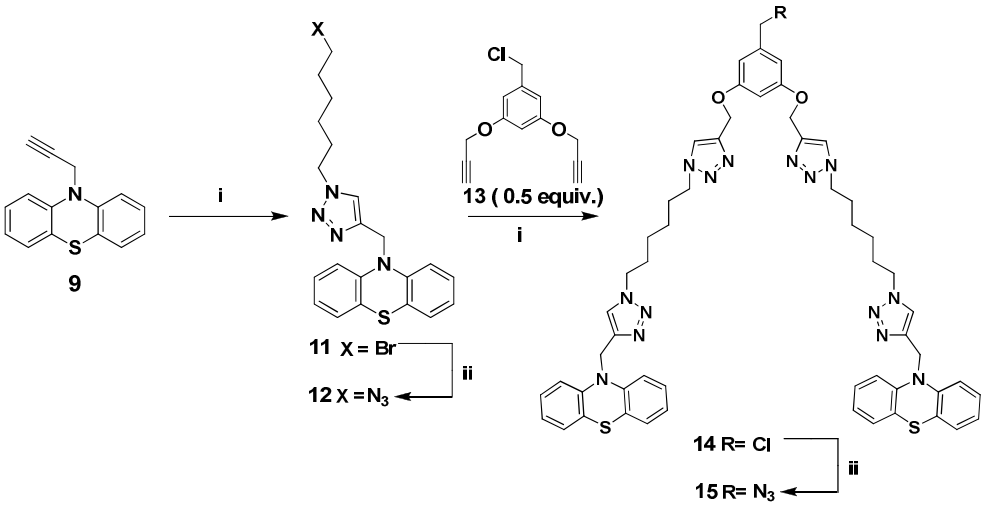
Figure 1. Molecular structure of phenothiazine dendrimers **1**-**8.**

Recently, we have reported the synthesis of dendrimer with dimethyl isophthalate,[14] pyrrolidine,[15] quinoline,[16] and pyreno-chalcone[17] as surface groups with 1,2,3-triazole as

bridging unit. Phenothiazine belongs to an important class of tricyclic nitrogen-sulphur heterocyclic compound. phenothiazine-based dendrimers exhibit remarkable optical and electrochemical properties.[18] Further, the phenothiazine heterocyclic system shows antimicrobial, anticancer, antiviral, anticonvulsant and antimalarial activity.[19] The dendrimers with S-(-)-BINOL core could exhibit chiroptical, photophysical properties,[20] and also used as enantioselective Lewis acid catalysts.[21] In connection with this, the present investigation deals with the synthesis and photophysical properties of some novel triazole bridged dendrimers **1**-**8** (Figure 1) bearing phenothiazine as surface group by convergent methodology.

Results and Discussion

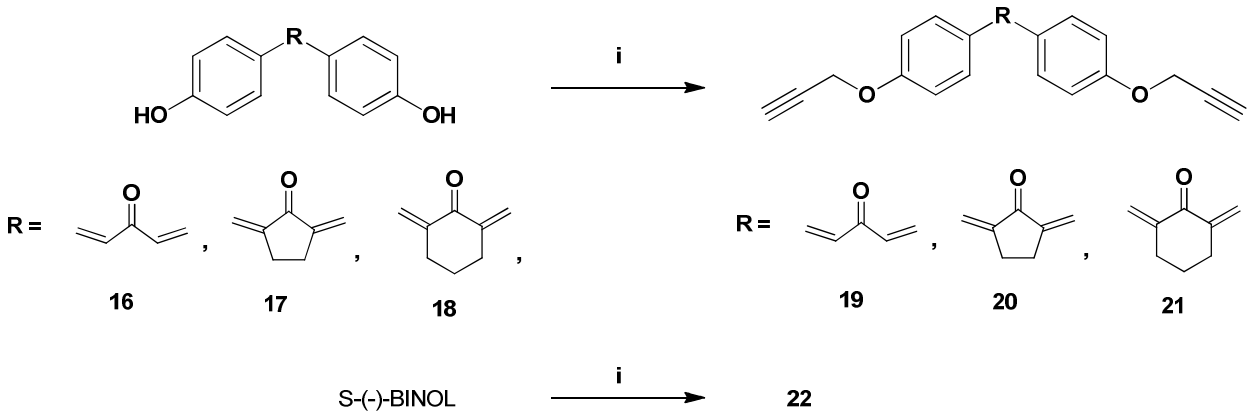
The bifunctional 1-azido-6-bromohexane **10** was synthesized by the reaction of 1,6-dibromohexane with one equivalent of NaN_3 in a mixture of acetone and water (9:1) at 60 ^oC. Further, reaction of *N*-propargyl phenothiazine[22] **9** with the azide **10** under click reaction conditions of $CuSO_4.5H_2O$ (5 mol %) and sodium ascorbate (10 mol %) in a mixture of THF and water (1:1) at room temperature for 10 h gave the bromo compound **11** in 90% yield. The bromide **11** was converted to the azide **12** in 91% yield using NaN_3. Reaction of 3,5-bis(propargyloxy)benzyl chloride[16] **13** with 2.1 equiv. of azide dendron **12** under click chemistry conditions afforded the first generation dendritic chloride (G_1-Cl) **14** in 89% yield. The dendritic chloride **14** with NaN_3 in DMF at 60 ^oC afforded the first generation dendritic azide (G_1-N_3) **15** in 87% yield (see Scheme 1).



Scheme 1. Reagents and conditions: (i) Br-$(CH_2)_6$-N_3, (**10**) (1 equiv.), $CuSO_4.5H_2O$ (5 mol %), sodium ascorbate (10 mol %), THF: H_2O (1:1, v/v), rt, 10 h, **11** (90%) and **14** (89%). (ii) NaN_3, DMF, 10 h, 60 ^oC, **12** (91%) and **15** (87%).

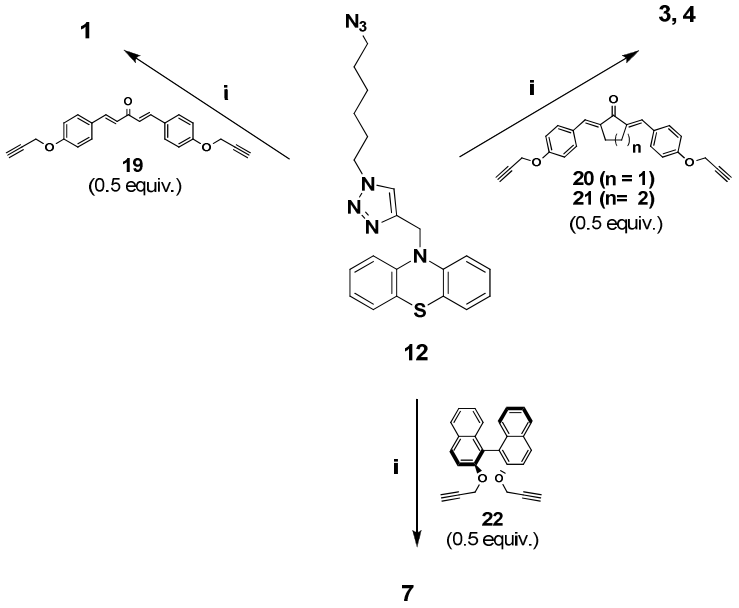
The ^{1}H NMR spectrum of compound **15** displayed the ten methylene protons adjacent to the nitrogen atom of triazole ring and azide functionality at δ 4.11-4.2, and the rest of the methylene protons of the hexyl unit appear as two set of multiplets eight proton each at δ 1.11-1.18 and 1.56-1.85 and singlets at δ 5.08 and 5.10 for *N*–CH_2- adjacent to phenothiazine and *O*-CH_2- protons respectively in addition to the other aliphatic and aromatic proton signals. The ^{13}C NMR spectrum of dendritic azide **15** showed *N*–CH_2- and *O*-CH_2- carbon signals at δ 54.5 and 61.9 in addition to the aliphatic and aromatic carbon signals. The ESI mass spectrum of **15** showed molecular ion peak *m/z* 1052 $(M+H)^+$. The molecular formula of **15** was further confirmed from analytical data.

The core units bis(propargyloxy)dienone **19**, bis(propargyloxy)pentanone **20**, bis(propargyloxy)hexanone[23] **21** and bis(propargyloxy)S-(-) BINOL **22** were obtained in 63%, 82%, 76% and 78% yields respectively by the *O*-alkylation of **16**, **17**, **18** and S-(-) BINOL with 2.1 equiv. of propargyl bromide in the presence of K_2CO_3 in DMF (Scheme 2).

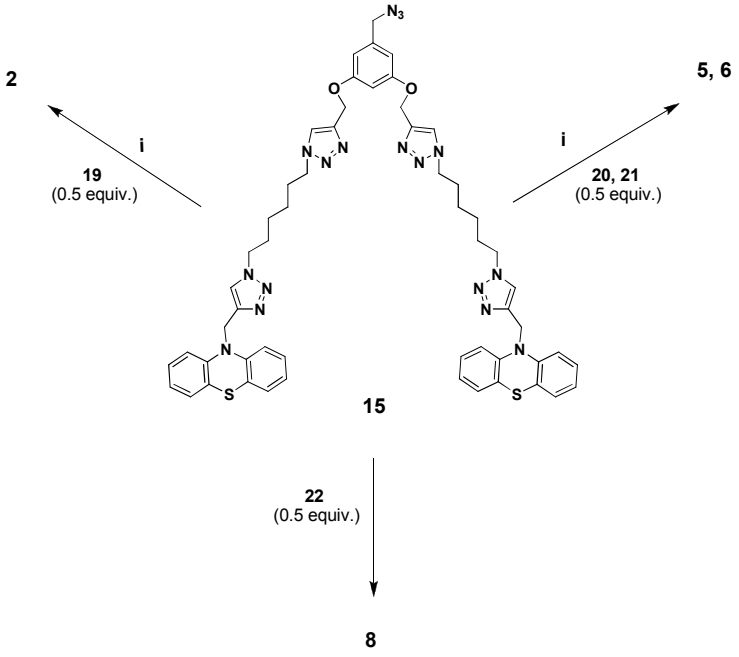


Scheme 2. Reagents and conditions: (i) Propargyl bromide (2.1 equiv.), K_2CO_3, DMF, 60 ^oC, 24 h, **19** (63%), **20** (82%), 2**1** (76%) and **22** (78%).

The synthetic pathway leading to the enone and S-(-)-BINOL based zeroth generation dendrimers with phenothiazine surface group is shown in Scheme 3. Reaction of bis-propargyloxy core unit **19-21** and **22** with phenothiazine dendritic azide **12** under click reaction conditions afforded 1, 2, 3-triazole bridged phenothiazine dendrimers **1, 3, 4** and **7** in good yields (see Scheme 3). The ^{1}H NMR spectrum of dendrimer **4** displayed singlets at δ 5.20 and 5.25 for the *N*-methylene and *O*-methylene protons, in addition to the signals for aliphatic and aromatic protons. The ^{13}C NMR spectrum of dendrimer **4** displayed *N*-methylene and *O*- methylene carbons at δ 49.8 and 61.8 respectively, the carbonyl carbon appeared at δ 189.7, in addition to the signals for aliphatic and aromatic carbons. The appearance of molecular ion peak at *m/z* 1215.6 $(M+Na)^+$ in mass spectrum of the dendrimer **4** also confirmed the structure. Similarly, the structure of the dendrimers **1**, **3** and **7** was confirmed from spectral and analytical data.



Scheme 3. Reagents and conditions: (i) $CuSO_4.5H_2O$ (5 mol %), sodium ascorbate (10 mol %), THF: H_2O (1:1, v/v), rt, 10 h, **1** (86%), **3** (84%), **4** (85%) and **7** (92%).



Scheme 4. Reagents and conditions: (i) $CuSO_4.5H_2O$ (5 mol %), sodium ascorbate (10 mol %), THF: H_2O (1:1, v/v), rt, 10 h, **2** (84%), **5** (80%), **6** (86%) and **8** (83%).

Similar technique was adopted to synthesize the first generation dendrimers. Reaction of the bis-propargyloxy core moieties **19**-**22** with 2.0 equiv. of dendritic azide (G_1-N_3) **15** in the

presence of the Cu(I)-catalyzed Huisgen click reaction conditions generated the first generation dendrimers (G_1) **2**, **5**, **6** and **8** in 84%, 80%, 86% and 83% yields, respectively (see Scheme 4). In the ^{1}H NMR spectrum, the chiral phenothiazine dendrimer **8** showed singlets at δ 5.07 for *N*-methylene and at δ 5.17 for *O*-methylene protons, in addition to the signals for aliphatic and aromatic protons. The ^{13}C NMR spectrum of dendrimer **8** displayed *N*-methylene and *O*-methylene carbons at δ 50.0, 53.7, 61.9 and 63.9 in addition to the signals for aliphatic and aromatic carbons. In the MALDI-TOF mass spectrum of **8**, the molecular ion peak appeared at *m/z* 2466 $(M)^+$ and the structure of the dendrimer **8** was further confirmed from analytical data. Similarly, the structure of the dendrimers **2**, **5** and **6** was confirmed from spectral and analytical data.

Photophysical studies

The photophysical property of phenothiazine dendrimers **1**-**8** is listed in Table 1. Figure 2a show the absorption spectra of dendrimers **1-8** in DMF.. There is a broad absorption band at 284-386 nm due to the presence of triazole and phenothiazine units. In fact this observation suggests that both the chromophores *viz* triazole and phenothiazine could be responsible for the broad absorption bands for the dendrimers **1**-**8.** Molar extinction coefficients of the absorption bands at a given concentration varies as the generation of the dendrimer increases. The absorbance in the UV spectrum is probably controlled by the number of phenothiazine and triazole units.

Table 1. Photophysical data for dendrimers **1**-**8** in DMF (1×10^{-5} mol/L)

Dendrimers	λ_{abs} max (nm)	ε x 10^{-5} M^{-1} cm^{-1}	λ_{em} max (nm)	Φ_F
1	359	1.55	445	0.0017
2	321, 358	0.96, 0.91	440, 520	0.0036
3	386	0.56	433, 462	0.0050
4	358	0.92	438	0.0032
5	385	0.65	439	0.0143
6	321, 357	0.52, 0.61	431	0.0070
7	297, 324	0.26, 0.21	433	0.0778
8	312	0.34	437	0.1148

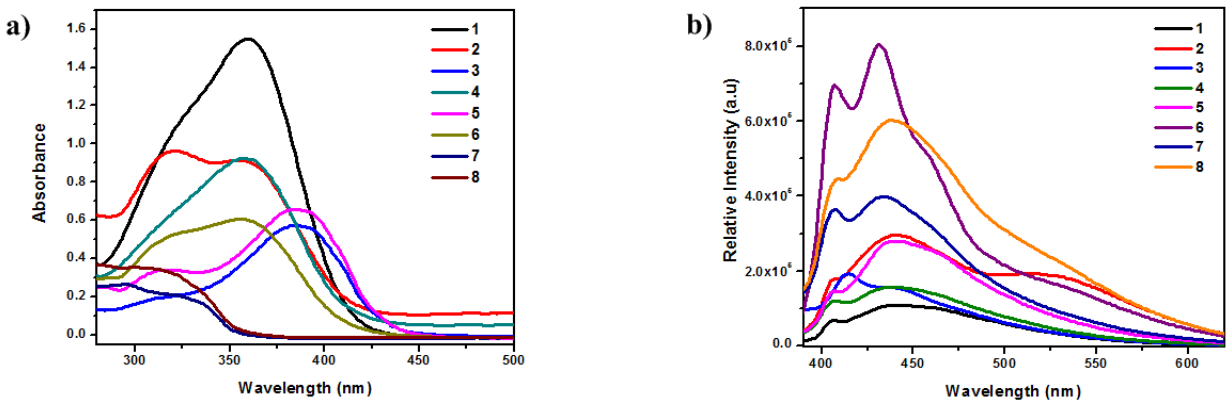


Figure 2. (a) Absorption spectra of dendrimers **1-8** in DMF (1×10^{-5} mol/L). (b) Fluorescence spectra of dendrimers **1-8** in DMF (1×10^{-5} mol/L).

Figures 2b shows the fluorescence spectra of dendrimers **1-8** in DMF and the fluorescence parameters for all the dendrimers are presented in Table 1. As shown in Figure 3, on excitation at 360 nm, the dendrimers **1-8** give emission band in range at 431-520 nm due to the triazole and phenothiazine moieties. The fluorescence intensity of the dendrimers increases as the generation increases, which are consistent with the increased number of both fluorophoric triazole and phenothiazine units, otherwise known as multivalency effect in dendrimer chemistry. The fluorescence quantum yields Φ_f of dendrimers **1-8** have been measured in DMF using quinine sulphate in 0.1N H_2SO_4 as the standard. The quantum yields of dendrimers **1-8** are listed in Table 1. Thus as the generation of the dendrimer increases, the quantum yield also increases.

Conclusions

In conclusion, we have synthesized various dendritic architectures with phenothiazine surface group and 1, 2, 3-triazole as bridging unit through click reaction by convergent approach in good yields. The dendrimers reported herein possesses biologically active enone core and phenothiazine surface group. Synthesis of other such phenothiazine dendrimers and their biological activity are under way.

Experimental Section

General. All the melting points reported were uncorrected and are determined using Toshniwal melting point apparatus by open capillary tube method. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker 300 MHz spectrometer. The chemical shifts are reported in ppm (δ) with TMS as an internal standard and coupling constant (*J*) are expressed in Hz. MALDI-TOF mass

spectra on Voyager-DE PRO mass spectrometer using a α-cyano-4-hydroxy cinnamic acid (CHCA) matrix and ESI-PerkinElmer Sciex, API 3000 mass spectrometer. The QTOF-MS spectra were recorded on Xevo G2-S QT mass spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B elemental analyzer. TLC was performed either on glass plates coated with silica gel-G (ACME) of about 0.25 mm thickness and visualized with iodine or on pre-coated plastic sheets (POLYGRAM® SIL G/U_{254}) and detected under UV light. Column chromatography was carried out with silica gel (ACME, 60-120 and 100-200 mesh).

General procedure for the synthesis of 1,2,3-triazole using click chemistry. A mixture of azide (1.0 equiv.), alkyne (0.5 equiv.), $CuSO_4.5H_2O$ (5 mol %) and NaAsc. (10 mol %) in a mixture of THF and water (1:1) was stirred for 10 h at room temperature. The residue obtained after evaporation of the solvent was washed thoroughly with water and dissolved in $CHCl_3$ (150 mL). The organic layer was washed with water (2 x 100 mL) and brine (1 × 150 mL) and dried (Na_2SO_4) and evaporated to give the crude triazole, which was purified by column chromatography (SiO_2).

Dendrimer 1 (G_0). Yield 86%, mp 78 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.20-1.25 (m, 8H), 1.77-1.86 (m, 8H), 4.24 (t, 4H, *J* = 6.9 Hz), 4.30 (t, 4H, *J* = 7.2 Hz), 5.20 (s, 4H), 5.26 (s, 4H), 6.76 (d, 4H, *J* = 8.1 Hz), 6.86-6.93 (m, 4H), 6.98-7.07 (m, 8H), 7.12 (d, 4H, *J* = 7.8 Hz), 7.26 (s, 4H), 7.55 (s, 2H), 7.58 (s, 4H), 7.69 (d, 2H, *J* = 15.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.6, 25.7, 29.8, 29.9, 44.9, 50.0, 50.1, 62.1, 115.2, 115.3, 122.3, 122.6, 122.8, 123.8, 123.9, 127.2, 127.3, 128.1, 130.1, 142.5, 143.7, 144.3, 144.9, 160.1, 188.8. ESI-MS: *m/z* = 1154 $(M+H)^+$. Anal. calcd. for $C_{65}H_{64}N_{14}O_3S_2$: C, 67.68; H, 5.59; N, 17.00%. Found: C, 67.54; H, 5.67; N, 17.10%.

Dendrimer 2 (G_1). Yield 84%, mp 100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.17-1.26 (m, 16H), 1.74-1.83 (m, 16H), 4.21 (t, 8H, *J* = 6.9 Hz), 4.24 (t, 8H, *J* = 6.9 Hz), 5.10 (s, 8H), 5.17 (s, 8H), 5.20 (s, 4H), 5.42 (s, 4H), 6.49 (d, 4H, *J* = 1.8 Hz), 6.61 (t, 2H, *J* = 2.1 Hz), 6.75 (d, 8H, *J* = 8.1 Hz), 6.84-6.90 (m, 12H), 6.95-7.04 (m, 16H), 7.08 (d, 8H, *J* = 7.5 Hz), 7.51 (s, 2H), 7.56 (s, 4H), 7.61 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.5, 25.6, 29.7, 29.8, 44.9, 49.9, 50.0, 54.0, 61.9, 102.0, 107.4, 115.2, 122.3, 122.8, 123.1, 123.7, 123.8, 127.1, 127.3, 128.1, 130.1, 136.8, 142.4, 143.4, 143.9, 144.2, 144.7, 159.8, 160.0, 188.7. QTOF-MS: *m/z* = 2445.98 (M^+). Anal. calcd. for $C_{133}H_{132}N_{34}O_7S_4$: C, 65.28; H, 5.44; N, 19.46%. Found: C, 65.42; H, 5.53; N, 19.38%.

Dendrimer 3 (G_0). Yield 84%, mp 198 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.19-1.33 (m, 8H), 1.77-1.88 (m, 8H), 3.06 (s, 4H), 4.23 (t, 4H, *J* = 6.9 Hz), 4.29 (t, 4H, *J* = 6.9 Hz), 5.19 (s, 4H), 5.26 (s, 4H), 6.76 (d, 4H, *J* = 8.1 Hz), 6.88 (t, 4H, *J* = 7.5 Hz), 7.01-7.06 (m, 8H), 7.09-7.12 (m, 4H), 7.27 (s, 2H), 7.54-7.57 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.6, 25.7, 26.5, 29.8, 29.9, 44.9, 50.0, 50.1, 62.1, 115.1, 115.3, 122.3, 122.6, 122.8, 123.9, 127.2, 127.3, 129.3, 132.5, 133.1, 135.6, 143.8, 144.3, 144.9, 159.1, 196.2. ESI-MS: *m/z* = 1179.4 $(M+H)^+$. Anal. calcd. for $C_{67}H_{66}N_{14}O_3S_2$: C, 68.23; H, 5.64; N, 16.63%. Found: C, 68.48; H, 5.53; N, 16.72%.

Dendrimer 4 (G_0). Yield 85%, mp 172-174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.20-1.25 (m, 8H), 1.78-1.86 (m, 10H), 2.91 (t, 4H, *J* = 5.1 Hz), 4.24 (t, 4H, *J* = 7.2 Hz), 4.30 (t, 4H, *J* = 7.2

Hz), 5.20 (s, 4H), 5.25 (s, 4H), 6.76 (d, 4H, *J* = 8.1 Hz), 6.89 (t, 4H, *J* = 7.5 Hz), 7.01-7.07 (m, 8H), 7.12 (d, 4H, *J* = 7.5 Hz), 7.27 (s, 2H), 7.44 (d, 4H, *J* = 8.7 Hz), 7.57 (s, 2H), 7.74 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 22.7, 25.3, 25.4, 28.2, 29.5, 29.6, 44.6, 49.7, 49.8, 61.8, 114.4, 114.9, 122.0, 122.2, 122.5, 123.6, 126.9, 127.0, 128.9, 131.9, 134.3, 136.0, 143.6, 143.9, 144.6, 158.2, 189.7. ESI-MS: *m/z* = 1193.4 $(M+H)^+$, *m/z* = 1215.6 $(M+Na)^+$. Anal. calcd. for $C_{68}H_{68}N_{14}O_3S_2$: C, 68.43; H, 5.74; N, 16.43%. Found: C, 68.64; H, 5.87; N, 16.52%.

Dendrimer 5 (G_1). Yield 80%, mp 142-144 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 1.10-1.13 (m, 16H), 1.67-1.74 (m, 16H), 3.01 (s, 4H), 4.23-4.31 (m, 16H), 5.11 (s, 16H), 5.22 (s, 4H), 5.53 (s, 4H), 6.59 (d, 4H, *J* = 1.8 Hz), 6.72 (t, 2H, *J* = 1.8 Hz), 6.86-6.92 (m, 14H), 7.05-7.10 (m, 16H), 7.14 (d, 4H, *J* = 8.7 Hz), 7.38 (s, 2H), 7.63 (d, 4H, *J* = 8.7 Hz), 7.89 (s, 4H); 8.16 (s, 4H), 8.31-8.32 (m, 4H). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 24.9, 25.1, 25.9, 29.3, 29.4, 43.9, 49.1, 49.2, 52.8, 61.2, 79.1, 101.0, 107.2, 115.2, 115.6, 122.6, 123.2, 124.3, 124.8, 126.7, 127.4, 128.4, 131.9, 132.4, 132.8, 135.6, 138.0, 142.3, 142.6, 143.3, 144.0, 159.0, 159.4, 194.9. MALDI-TOF-MS: *m/z* = 2472.2 (M^+). Anal. calcd. for $C_{135}H_{134}N_{34}O_7S_4$: C, 65.57; H, 5.46; N, 19.26%. Found: C, 65.66; H, 5.54; N, 19.18%.

Dendrimer 6 (G_1). Yield 86%, mp 104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.17-1.26 (m, 16H), 1.74-1.82 (m, 16H), 2.13-2.15 (m, 2H), 2.86 (t, 4H, *J* = 5.4 Hz), 4.19 (t, 8H, *J* = 6.9 Hz), 4.26 (t, 8H, *J* = 6.9 Hz), 5.09 (s, 8H), 5.16 (s, 8H), 5.18 (s, 4H), 5.41 (s, 4H), 6.49 (d, 4H, *J* = 1.5 Hz), 6.61 (t, 2H, *J* = 1.8 Hz), 6.74 (d, 8H, *J* = 7.8 Hz), 6.85 (t, 8H, *J* = 7.5 Hz), 6.97-7.01 (m, 10H), 7.04-7.09 (m, 10H), 7.28 (s, 4H), 7.40 (d, 4H, *J* = 8.7 Hz), 7.56 (s, 4H), 7.62 (s, 2H), 7.69 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 22.8, 25.4, 25.5, 28.3, 29.6, 29.7, 30.8, 44.8, 49.8, 49.9, 53.9, 61.8, 101.9, 107.3, 114.6, 115.2, 122.2, 122.7, 122.8, 123.0, 123.7, 127.0, 127.2, 129.1, 132.1, 134.5, 136.1, 136.8, 143.3, 143.9, 144.1, 144.6, 158.4, 159.7, 189.9. MALDI-TOF-MS: *m/z* = 2484 (M^+). Anal. calcd. for $C_{136}H_{136}N_{34}O_7S_4$: C, 65.68; H, 5.51; N, 19.15%. Found: C, 65.74; H, 5.64; N, 19.12%.

Dendrimer 7 (G_0). Yield 92%, mp 88-90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.09-1.13 (m, 8H), 1.56-1.60 (m, 4H), 1.70-1.75 (m, 4H), 3.98 (t, 4H, *J* = 6.3 Hz), 4.19 (t, 4H, *J* = 6.9 Hz), 5.07 (d, 2H, *J* = 12.6 Hz), 5.19 (s, 4H), 5.23 (s, 2H), 6.46 (s, 2H), 6.76 (d, 4H, *J* = 8.1 Hz), 6.86 (t, 4H, *J* = 7.5 Hz), 7.02 (t, 4H, *J* = 7.5 Hz), 7.09 (d, 4H, *J* = 6.9 Hz), 7.14-7.24 (m, 4H), 7.28 (s, 2H), 7.31-7.34 (m, 2H), 7.50 (d, 2H, *J* = 9.0 Hz), 7.86 (d, 2H, *J* = 8.1 Hz), 7.93 (d, 2H, *J* = 9.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.6, 29.7, 29.8, 44.9, 49.8, 50.0, 64.0, 115.3, 116.0, 120.7, 122.2, 122.4, 122.8, 123.9, 124.0, 125.4, 126.5, 127.2, 127.3, 127.9, 129.5, 129.6, 133.9, 144.3, 144.6, 144.8, 153.7. ESI-MS: *m/z* = 1174 $(M+H)^+$. Anal. calcd. for $C_{68}H_{64}N_{14}O_2S_2$: C, 69.60; H, 5.50; N, 16.71%. Found: c, 69.72; H, 5.67; N, 16.78%.

Dendrimer 8 (G_1). Yield 83%, mp 98 °C. ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.20-1.29 (m, 16H), 1.75-1.77 (m, 16H), 4.11-4.25 (m, 16H), 4.96 (d, 2H, *J* = 12.9 Hz), 5.07 (s, 12H), 5.17 (s, 10H), 6.30 (s, 4H), 6.48 (s, 2H), 6.62 (s, 2H), 6.74 (d, 8H, *J* = 8.1 Hz), 6.86 (t, 8H, *J* = 7.5 Hz), 7.02 (t, 8H, *J* = 7.5 Hz), 7.08 (d, 12H, *J* = 6.6 Hz), 7.26 (s, 6H), 7.37 (d, 2H, *J* = 9.0 Hz), 7.59 (s, 4H), 7.77 (d, 2H, *J* = 8.4 Hz), 7.83 (d, 2H, *J* = 9.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.6, 25.7, 29.8, 29.9, 44.9, 50.0, 53.7, 61.9, 63.9, 101.7, 107.3, 115.3, 116.0, 120.7, 122.4, 122.8, 123.0,

123.8, 123.9, 125.3, 126.5, 127.2, 127.3, 128.0, 129.5, 133.8, 137.0, 143.4, 144.3, 144.7, 144.9, 153.6, 159.8. MALDI-TOF-MS: *m/z* = 2466 $(M)^+$. Anal. calcd. for $C_{136}H_{132}N_{34}O_6S_4$: C, 66.21; H, 5.39; N, 19.30%. Found: C, 66.14; H, 5.53; N, 19.24%.

Bromo dendron 11. Yield 90%, mp 112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.17-1.25 (m, 2H), 1.35-1.45 (m, 2H), 1.72-1.85 (m, 4H), 3.34 (t, 2H, *J* = 6.9 Hz), 4.27 (t, 2H, *J* = 6.9 Hz), 5.21 (s, 2H), 6.77 (d, 2H, *J* = 8.1 Hz), 6.90 (t, 2H, *J* = 7.5 Hz), 7.02-7.08 (m, 2H), 7.11-7.14 (m, 2H), 7.28 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.4, 27.4, 29.9, 32.3, 33.4, 45.0, 50.2, 115.3, 122.3, 122.8, 123.9, 127.2, 127.3, 144.3, 144.8. ESI-MS: *m/z* = 444 $(M+H)^+$. Anal. calcd. for $C_{21}H_{23}BrN_4S$: C, 56.88; H, 5.23; N, 12.64%. Found: C, 56.72; H, 5.46; N, 12.48%.

Dendritic chloride 14. Yield 89%, mp 218-220 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.19-1.29 (m, 8H), 1.78-1.84 (m, 8H), 4.23 (t, 4H, *J* = 7.2 Hz), 4.28 (t, 4H, *J* = 7.2 Hz), 4.48 (s, 2H), 5.16 (s, 4H), 5.19 (s, 4H), 6.59 (t, 1H, *J* = 2.1 Hz), 6.63 (d, 2H, *J* = 2.1 Hz), 6.76 (d, 4H, *J* = 8.1 Hz), 6.85-6.90 (m, 4H), 7.01-7.12 (m, 8H), 7.28 (s, 2H), 7.56 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.6, 29.9, 41.7, 44.9, 49.4, 49.6, 50.0, 54.3, 61.8, 107.2, 115.3, 122.2, 122.6, 122.8, 123.8, 123.4, 127.1, 127.4, 143.4, 143.6, 144.2, 144.7, 159.1. ESI-MS: *m/z* = 1046.7 $(M+H)^+$. Anal. calcd. for $C_{55}H_{57}ClN_{14}O_2S_2$: C, 63.17; H, 5.49; N, 18.75%. Found: C, 63.29; H, 5.58; N, 18.69%.

General procedure for the synthesis of dendritic azide from the dendritic chloride/bromide

To the corresponding alkyl chloride/bromide (1 mmol) dissolved in dry DMF (20 ml), sodium azide (1.5 mmol) was added and stirring was continued at 60 ºC for 10 h. The reaction mixture was then allowed to cool to room temperature. It was then poured into ice-cold water (30 mL) and extracted with $CHCl_3$ (3 × 100 mL). The organic layer was washed with water (100 mL) and saturated NaCl (3 × 100 mL), dried (Na_2SO_4). Solvent was evaporated under reduced pressure to afford the crude product, which was purified by column chromatography (SiO_2).

Azido dendron 12. Yield 91%, mp 84-86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.17-1.36 (m, 4H), 1.47-1.54 (m, 2H), 1.77-1.85 (m, 2H), 3.21 (t, 2H, *J* = 6.9 Hz), 4.26 (t, 2H, *J* = 6.9 Hz), 5.21 (s, 2H), 6.76 (d, 2H, *J* = 8.1 Hz), 6.90 (t, 2H, *J* = 7.5 Hz), 7.02-7.05 (m, 2H), 7.08-7.14 (m, 2H), 7.28 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.8, 26.0, 28.6, 29.9, 45.0, 50.2, 51.2, 115.3, 122.3, 122.8, 123.9, 127.2, 127.3, 144.3, 144.8. ESI-MS: *m/z* = 406 $(M+H)^+$. Anal. calcd. for $C_{21}H_{23}N_7S$: C, 62.20; H, 5.72; N, 24.18%. Found: C, 62.04; H, 4.87; N, 24.09%.

Dendritic azide 15. Yield 87%, mp 106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.11-1.18 (m, 8H), 1.56-1.85 (m, 8H), 4.11-4.21 (m, 10H), 5.08 (s, 4H), 5.10 (s, 4H), 6.47 (d, 2H, *J* = 1.8 Hz), 6.53 (t, 1H, *J* = 2.1 Hz), 6.67 (d, 4H, *J* = 8.1 Hz), 6.79 (t, 4H, *J* = 7.2 Hz), 6.94 (t, 4H, *J* = 7.5 Hz), 7.01 (d, 4H, *J* = 7.5 Hz), 7.19 (s, 2H), 7.49 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.4, 25.6, 29.7, 29.8, 44.8, 49.8, 49.9, 54.5, 61.9, 101.6, 107.4, 115.1, 122.2, 122.6, 122.7, 123.7, 127.0, 127.2, 137.7, 143.6, 144.1, 144.6, 159.5. ESI-MS: *m/z* = 1052 $(M+H)^+$. Anal. calcd. for $C_{55}H_{57}N_{17}O_2S_2$: C, 62.78; H, 5.46; N, 22.63%. Found: C, 63.69; H, 5.52; N, 22.69%.

General procedure for synthesis of acetylenic enone core. A mixture of the corresponding phenol (1.0 equiv.), propargyl bromide (1.25 equiv.) and anhydrous potassium carbonate (3.0

equiv.) in dry DMF (15 mL) was stirred at 60 °C for 24 h. The reaction mixture was then allowed to cool to room temperature and poured into ice water. The resulting precipitate was filtered, washed thoroughly with water and dissolved in $CHCl_3$ (150 mL). The organic layer was washed with water (2 x 100 mL) and brine (1 × 150 mL), dried (Na_2SO_4) and evaporated to give the crude dendron, which was purified by column chromatography (SiO_2).

Bis(propargyloxy)dienone 19. Yield 63%, mp 83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 2.56 (t, 2H, *J* = 2.1 Hz), 4.74 (d, 4H, *J* = 2.1 Hz), 6.93 (s, 2H), 7.01 (d, 4H, *J* = 9.0 Hz), 7.58 (d, 4H, *J* = 8.7 Hz), 7.69 (d, 2H, *J* = 15.0Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 55.9, 76.0, 78.6, 114.9, 115.3, 123.9, 128.5, 130.0, 142.5, 159.4, 188.8. ESI-MS: *m/z* = 343 $(M+H)^+$. Anal. calcd. for $C_{23}H_{18}O_3$: C, 80.68; H, 5.30%. Found: C, 80.56; H, 5.38%.

Bis(propargyloxy)pentanone 20. Yield 82%, mp 172 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 2.56 (t, 2H, *J* = 2.4 Hz), 3.09 (s, 4H), 4.75 (d, 4H, *J* = 2.4 Hz), 7.05 (d, 4H, *J* = 8.7 Hz), 7.56-7.60 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 26.4, 55.8, 75.9, 78.1, 115.2, 129.6, 132.4, 133.1, 135.7, 158.4, 196.2. ESI-MS: *m/z* = 369 $(M+H)^+$. Anal. calcd. for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47%. Found: C, 81.58; H, 5.52%.

Bis(propargyloxy)hexanone 21. Yield 76%, mp 152-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.79 (m, 2H), 2.55 (t, 2H. *J* = 2.1 Hz), 2.91 (t, 4H, *J* = 5.4 Hz), 4.73 (d, 4H, *J* = 2.1 Hz), 7.51 (d, 4H, *J* = 8.7 Hz), 7.45 (d, 4H, *J* = 8.7 Hz), 7.75 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 23.0, 28.5, 55.8, 75.9, 78.2, 116.2, 128.5, 129.6, 134.7, 136.4, 157.7, 190.2. ESI-MS: *m/z* = 383 $(M+H)^+$. Anal. calcd. for $C_{26}H_{22}O_3$: C, 81.65; H, 5.80%. Found: C, 81.58; H, 5.86%.

Supplementary Material

^{1}H, ^{13}C NMR and Mass spectra for dendrimer **2** and **4** are available.

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