Supplementary Material (ESI) for Chemical Communications

Multivalent, Bifunctional Dendrimers prepared by Click Chemistry

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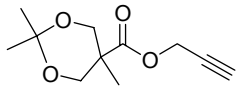
General Methods. Analytical TLC was performed on commercial Merck Plates coated with silica gel GF254 (0.24 mm thick). Silica for flash chromatography was Merck Kieselgel 60 (230-400 mesh, ASTM). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) measurements were performed on a Bruker AC 400, 500 or 600 spectrometer at room temperature. Coupling constants (*J*) are reported in Hertz, and chemical shifts are reported in parts per million (δ) relative to $CHCl_3$ (7.26 for ^{1}H and 77.2 for ^{13}C) or MeOD (3.31 for ^{1}H and 49.1 for ^{13}C as internal reference. Size exclusion chromatography (SEC) was carried out at room temperature on a Waters chromatograph connected to a Waters 410 differential refractometer and six Waters Styragel® columns (five HR-5 μm and one HMW-20 μm) using THF as eluant (flow rate: 1 mL/min). A Waters 410

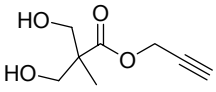
differential refractometer and a 996 photodiode array detector were employed. The molecular weights of the polymers were calculated relative to linear polystyrene standards. Non-aqueous copper(I)-catalyzed cycloaddition were performed in sealed tubes using a SmithCreator microwave reactor (Personal Chemistry Inc.). The modulated differential scanning calorimetry (MDSC) measurements were performed with a TA Instruments DSC 2920 and a ramp rate of 4 degrees per minute. The thermal gravimetric analysis measurements were done with a TA Instruments Hi-Res TGA 2950, under nitrogen purge, and the ramp rate was 10 degrees per minute. MALDI-TOF mass spectrometry was performed on a PerSeptive Biosystems Voyager DE mass spectrometer operating in linear mode, using dithranol in combination with silver trifluoroacetate as matrix.

Nomenclature. The nomenclature used for dendritic structures described in this chapter is as follows: $(P)_n$-[G-X]-FG for dendrons, where P describes the external functional group, either OH for hydroxyl, An for acetonide, Bzl for benzylidene, Acet for acetylene; n indicates the number of chain end functionalities; X indicates the generation number of the dendritic framework and FG describes the functional group at the focal point; either Acet for acetylene, or Az for azide. $(P)_n$-[G-X]-[G-X]-$(P)_n$ for triazole linked amphiphilic dendrimers, P describes the external functional group, Cm stands for 7-Diethylaminocoumarin, Mann stands for 1-(2-[1,2,3]-triazolethoxy)-*α-D*-mannopyranodise.



15

General Procedure for the Dendritic Generation Growth Through Anhydride Coupling Reaction, $(An)_1$-[G-1]-Acet, 15 Propargyl alcohol (10.0 g, 178 mmol) and DMAP (3.26 g, 26.7 mmol) were dissolved in pyridine (41.8 g, 535 mmol) in a 250 mL round bottom flask, followed by the addition of 100 mL CH_2Cl_2 . The anhydride of isopropylidene-2,2-bis(methoxy)propionic acid (bis-MPA) **1** (76.4 g, 231 mmol) was added slowly. The solution was stirred at room temperature overnight and monitored with ^{13}C NMR until the reaction reached completion (determined by the presence of the excess anhydride at~169 ppm). The reaction was quenched with 5 mL of water under vigorous stirring, followed by dilution with 500 ml of CH_2Cl_2 and the solution was washed with 10% of $NaHSO_4$ (3×200 mL), and 10% of Na_2CO_3 (3×200 mL) and brine (100 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography on silica, eluting with hexane (100 mL) and gradually increasing the polarity to EtOAc:hexane (10:90, 700 mL), followed by EtOAc:hexane (15:85) to give **15** as a colorless oil. Yield: 35.9 g (95 %). ^1H NMR ($CDCl_3$) δ: 1.08 (s, CH_3CCOO, 3H), 1.25 (s, CCH_3, 3H), 1.29 (s, CCH_3, 3H), 2.43 (t, C≡CH, 1H), 3.20 (d, CCH_2OCCH_3, 2H), 4.06 (d, CCH_2OCCH_3, 2H), 4.61 (d, $CH_2C{\equiv}CH$, 2H). 13C NMR (CDCl3): δ 18.67, 22.92, 24.83, 42.11, 52.59, 65.87, 75.00, 77.83, 98.32, 173.60. ESI MS: 213 (MH^+).



2

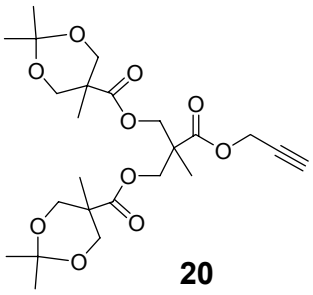
General Deprotection Procedure of the Acetonide group using DOWEX 50W-X2-200 resin, $(HO)_2$-[G-1]-Acet, 2. 15 g DOWEX 50W-X2-200 resin were added to a solution of **6.1** (10.0 g, 47.1 mmol) in 300 mL of methanol in a 500 mL round bottom flask. The mixture was stirred at 40 °C and the deprotection was followed with ^{13}C NMR until complete disappearance of peaks unique for the acetonide group was achieved, (i.e. the quaternary carbon at ~ 98 ppm). The resin was filtered off and the filtrate was concentrated and dried under high vacuum to give **$(HO)_2$-[G-1]-Acet, 2,** as a colorless oil. Yield: 7.87 g (97 %). ^1H NMR ($CDCl_3$) δ: 1.06 (s, C**H**$_3$CCOO, 3H), 2.50 (t, C≡C**H**, 1H), 3.54 (s (br), CCH$_2$O**H**, 2H), 3.63 (d, CC**H**$_2$OH, 2H), 3.78 (d, CC**H**$_2$OH, 2H), 4.67 (s, C**H**$_2$C≡CH, 2H); ^{13}C NMR (CDCl3) δ: 18.86, 49.36, 52.24, 65.87**,** 75.21, 77.35, 174.77. ESI MS: 173 (MH^+).

General Procedure for the Azide/Alkyne Cycloaddition Catalyzed by $Cu(PPh_3)_3Br$ (method B). To a 50 mL THF solution of $(An)_2$-[G2]-Acet, **16**, (5.00 g, 10.3 mmol) and $(HO)_4$-[G2]-N_3, **17,** (4.83 g, 9.83 mmol) were added *N*,*N*-diisopropylethylamine (0.66 g, 5.2 mmol) and $Cu(PPh_3)_3Br$ (19.0 mg, 206 μmol). The reaction mixture was then allowed stir at room temperature for 12 h. LC-MS indicated the complete consumption of the azide. The solvent was evaporated and the crude product was purified by column chromatography eluting with ethylacetate and gradually increasing the polarity to MeOH:EtOAc (20:80) to give **18** as a colorless solid. Yield: 8.95 g (91 %).

General Procedure for the Azide/Alkyne cycloaddition Catalyzed by $CuSO_4 \cdot 5H_2O$ and Sodium Ascorbate (method A). To a 20 mL THF:H_2O (3:1) solution of $(An)_2$-[G2]-

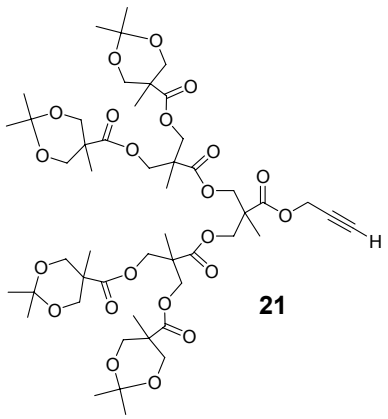
Acet, **16**, (5.00 g, 10. 3 mmol) and $(HO)_4$-[G2]-N_3 **17** (4.83 g, 9.83 mmol) were added sodium ascorbate (306 mg, 1.55 mmol) and $CuSO_4 \cdot 5H_2O$ (129 mg, 515 μmol). The reaction mixture was then allowed to stir for 12 h at ambient temperature. The solvents were evaporated and the crude product was purified by column chromatography eluting with ethylacetate and gradually increasing the polarity to 20:80 MeOH:EtOAc to give to give **18** as a colorless solid. Yield: 9.33 g (95 %).

General Procedure for the Acetylene Modification of the Periphery Via the Acetylene Anhydride Coupling Reaction, $(An)_2$-[G-2]-[G-2]-$(OH)_4$, 19. To a 20 mL CH_2Cl_2 solution of $(An)_2$-[G-2]-[G-2]-$(OH)_4$, **18** (5.00 g, 5.12 mmol), pyridine (8.10 g, 102 mmol), and DMAP (375 mg, 3.07 mmol) the anhydride of pent-4-ynoic acid (4.74 g, 26.6 mmol) was added. The solution was stirred at RT over night and monitored with ^{13}C NMR until the reaction reached completion (determined by the presence of the excess anhydride~167 ppm). The excess anhydride was quenched with 2 ml of water under vigorous stirring, followed of dilution with 300 ml of CH_2Cl_2 and the solution was extracted with 10 % of $NaHSO_4$ (3 × 500 ml), and 10 % of Na_2CO_3 (3×500 ml). The organic phase was dried ($MgSO_4$), filtered, concentrated and purified by liquid column chromatography on silica gel, eluting with hexane and gradually increasing the polarity to EtOAc:hexane (80:20) to give $(Acet)_4$-[G-2]-[G-2]-$(An)_2$, **19**, as colorless oil. Yield: 6.04 g (91%).



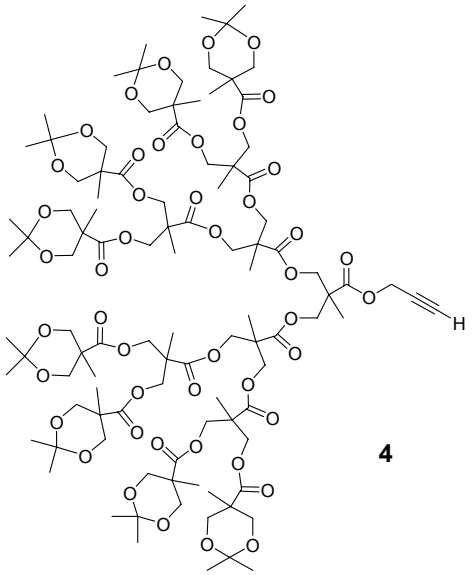
20

$(An)_2$-[G-2]-Acet, 20. Isolated as white solid. Yield: 25.6g (91%). ^{1}H-NMR ($CDCl_3$, 400MHz): δ = 4.72 (d, 2H), 4.33(s, 4H), 4.16 (d, 4H), 3.62 (d, 4H), 2.47 (t, 1H), 1.42 (s, 6H); 1.36 (s, 6H); 1.32 (s, 3H) 1.16 (s, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 173.5, 171.8, 101.4, 77.2, 75.3, 66.0, 65.3, 52.7, 46.8, 42.0, 25.0, 22.2, 18.5, 17.6 ppm. ESI MS: 486 (MH^+).



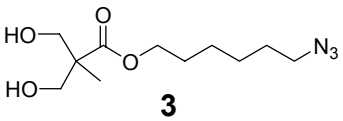
21

$(An)_4$-[G-3]-Acet, 21. Isolated as white solid. Yield: 20g (81%). ^{1}H-NMR ($CDCl_3$, 400MHz): δ = 4.73 (d, J =2.4 Hz, 2H), 4.31 (m, 8H), 4.28 (s, 2H), 4.24 (s, 2H), 4.16 (s, 4H), 4.13(s, 4H), 3.63(s, 4H), 3.60 (s, 4H), 2.54 (t, 1H), 1.41 (s, 12H); 1.35 (s, 12H); 1.30 (s, 3H), 1.28 (s, 6H), 1.14 (s, 12H) ppm; ^{13}C-NMR ($CDCl_3$, 150 MHz): δ = 173.5, 171.8, 171.4, 98.1, 77.1, 75.7, 66.0, 65.9, 64.9, 52.8, 46.9, 46.6, 42.0, 25.3, 21.9, 18.5, 17.6, 17.5. MALDI MS Calcd for $C_{50}H_{76}O_{22}$: 1028.48. Found: 1028.52 (MH^+).



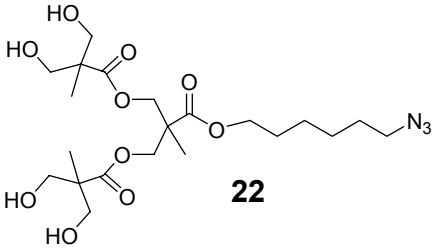
4

$(An)_8$-[G-4]-Acet, 4. Isolated as colorless gel. Yield: 25g (92%).^{1}H-NMR ($CDCl_3$, 400MHz): δ = 4.72 (d, 2H), 4.27 (m, 28H), 4.14 (d, 16H), 3.61(d, 16H), 2.57 (t, 1H), 1.40 (s, 24H); 1.34 (s, 24H); 1.31 (s, 3H), 1.27 (s, 12H), 1.26 (s, 6H), 1.14 (s, 24H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ =173.5, 171.8, 171.4, 171.2, 98.1, 77.2, 75.8, 66.4, 65.9(4), 65.5, 64.8, 52.8, 46.8, 46.7, 42.0, 25.2, 22.0, 18.4, 17.7, 17.5 ppm. MALDI MS Calcd for $C_{102}H_{156}O_{46}$: 2116.99. Found: 2117.04. T_g = 5 °C.



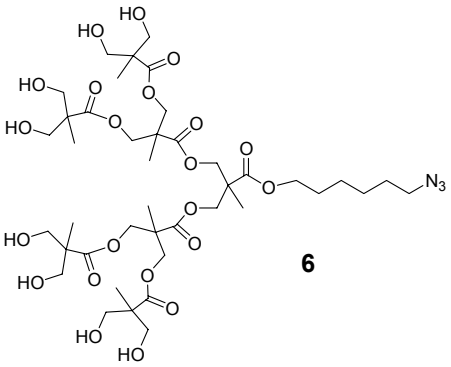
3

$(OH)_2$-[G-1]-Az, 3. Isolated as white solid. Yield 16.5g (83%). ^{1}H-NMR (CD_3OD, 400MHz): δ = 4.08 (t, 2H), 3.66 (d, 2H), 3.59 (d, 2H), 3.28 (t, 2H), 1.61 (m, 4H), 1.40 (m, 4H), 1.12 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 176.8, 65.9, 65.6, 52.4, 51.6, 29.8, 29.6, 27.5, 26.6, 17.4 ppm. ESI MS: 260 (MH^+).



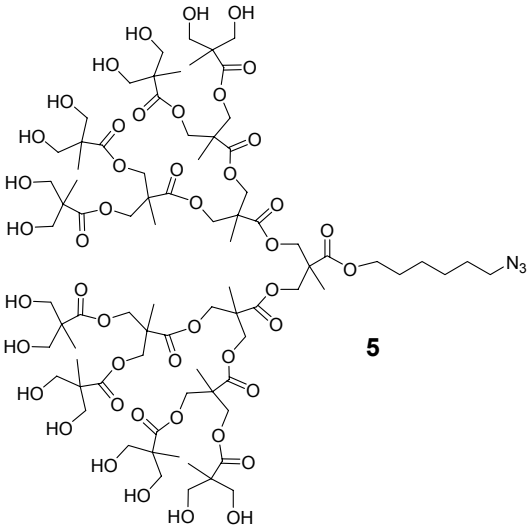
22

$(OH)_4$-[G-2]-Az, 22. Isolated as white solid. Yield: 15.0 g (92%). ^{1}H-NMR (CD_3OD, 400MHz): δ = 4.27 (d, 2H), 4.23 (d, 2H), 4.12 (t, 2H), 3.58 (m, 8H), 3.28 (m, 2H), 1.66 (m, 2H), 1.58 (m, 2H), 1.42 (m, 4H), 1.26 (s, 3H), 1.11 (s, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 175.9, 174.6, 66.5, 66.4, 65.8, 52.4, 51.8, 47.9, 29.9, 29.6, 27.5, 26.7, 18.3, 17.3 ppm. ESI MS: 493 (MH^+).



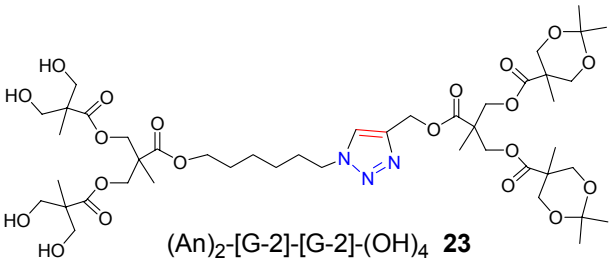
6

$(OH)_8$-[G-3]-Az, 6. Isolated as white solid. 15.2g (91%). ^{1}H-NMR (CD_3OD, 400MHz): δ 4.64 (t, 8H), 4.14 (m, 14H), 3.44 (m, 16H), 3.31 (t, 2H), 1.59 (m, 2H), 1.53 (m, 2H), 1.33 (m, 4H), 1.19 (s, 3H), 1.16 (s, 6H), 1.01 (s, 12H) ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 174.0, 172.0, 171.8, 65.8, 64.7, 64.5, 63.6, 50.5, 50.2, 46.3, 46.1, 28.0, 27.8, 25.6, 24.8, 17.1, 16.9, 16.6 ppm. ESI MS: 957 (MH^+).



5

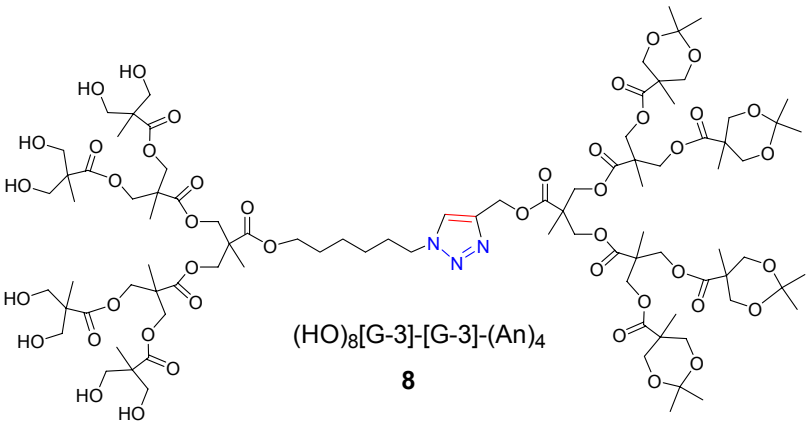
$(OH)_{16}$-[G-4]-Az, 5. Isolated as white solid. Yield: 16g (93%).^{1}H-NMR (CD_3OD, 400MHz): δ 4.27 (m, 28H), 4.15 (t, 2H), 3.66 (d, 6H), 3.63 (d, 10H), 3.58 (d, 16H), 3.32 (s, 16H), 3.28 (t, 2H), 1.69 (m, 2H), 1.60 (m, 2H), 1.43 (m, 4H), 1.31 (s, 3H), 1.28 (m, 18H), 1.13 (s, 24H)ppm; ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 175.0, 174.0, 173.8, 173.3, 67.6, 67.1, 66.7, 66.2, 66.0, 52.4, 51.9, 49.9, 48.1, 48.0, 29.9, 29.6, 27.5, 26.7, 18.3, 18.2(3),18.1(8), 17.4ppm. MALDI MS Calcd for $C_{81}H_{133}N_3O_{46}$: 1883.82. Found: 1883.90. T_g = 57 °C.



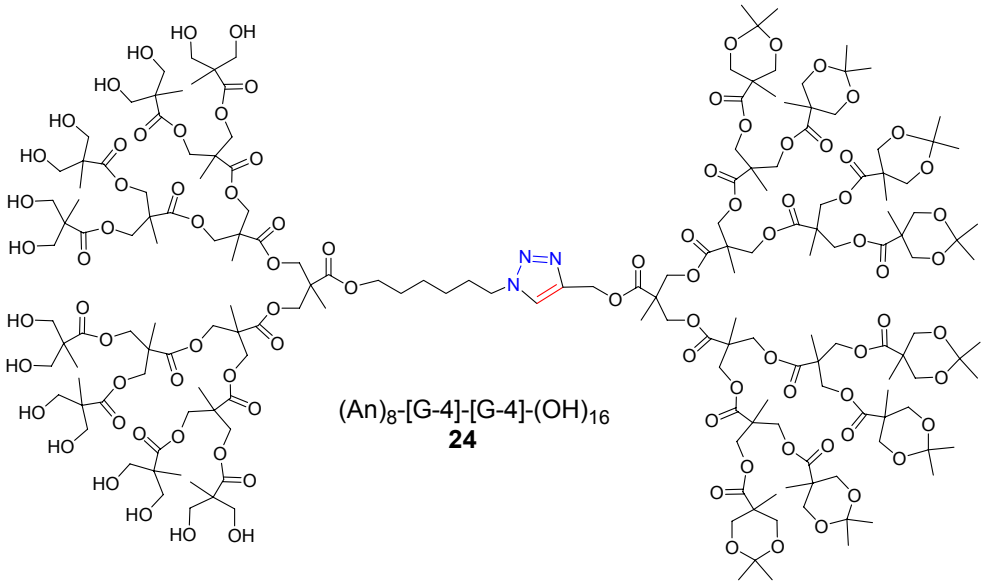
$(An)_2$-[G-2]-[G-2]-$(OH)_4$ **23**

$(An)_2$-[G-2]-[G-2]-$(OH)_4$, 23. Isolated as white solid. Yield: 9.93 g (95%). ^{1}H-NMR (CD_3OD, 400MHz): δ = 8.04 (s. 1H), 5.26 (s, 2H), 4.40 (t, 2H), 4.31 (s, 4H), 4.28 (d, 2H), 4.24 (d, 2H), 4.12 (t, 2H), 4.05 (d, 2H), 3.67-3.62 (m, 8H), 3.58 (2H, J=10.8Hz, 2H), 1.92 (m, 2H), 1.66 (m, 2H), 1.43 (m, 2H), 1.40 (s, 6H), 1.35 (m, 2H), 1.27 (m, 12H), 1.13

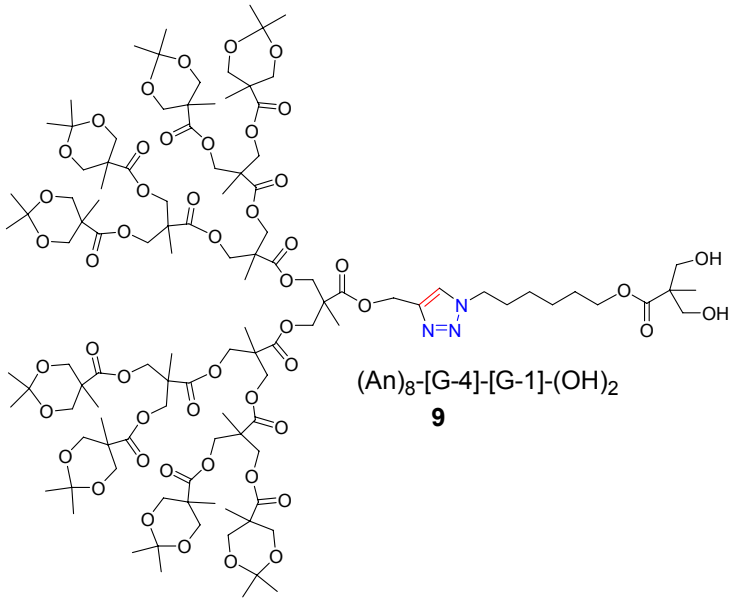
(s, 6H), 1. 03 (s, 6H). ^{13}C-NMR (CD_3OD, 150 MHz): δ = 175.9, 175.0, 174.5, 173.9, 143.6, 126.2, 99.4, 67.0, 66.9, 66.4, 66.3, 65.8, 59.0, 51.8, 51.3, 48.0, 47.8, 43.3, 31.1, 29.4, 27.1, 26.5, 23.9, 21.6, 18.5, 18.3, 18.1, 17.3. ESI MS: 977 (MH^+).



$(An)_4$-[G-3]-[G-3]-$(OH)_8$, 8. Isolated as white solid. Yield: 4.0 g (92%). ^{1}H-NMR ($CDCl_3$, 400MHz): δ 7.76 (s. 1H), 5.25 (s, 2H), 4.40-4.34 (m, 6H), 4.30-4.20 (m, 20H), 4.15-4.13 (m, 10H), 3.81 (d, 8H), 3.71 (d, 8H), 3.62 (d, 8H), 1.93 (m, 2H), 1.66 (m, 2H), 1.41 (m, 16H), 1.33 (s, 12H), 1.27-1.23 (m, 18H), 1.13(s, 12H), 1.07(s, 12H). ^{13}C-NMR (CD_3OD, 125 MHz): δ 176.0, 175.3, 174.1, 173.9, 173.7, 173.5,143.5, 126.4, 99.5, 67.4, 67.2, 67.1(5), 67.1, 66.7, 66.6, 66.3, 65.9, 61.7, 59.2, 51.9, 51.5, 48.2, 48.1, 43.5, 31.3, 29.6, 27.2, 26.9, 26.6, 21.7, 18.8, 18.4, 18.3, 18.2, 17.5, 17.4(8) ppm. MALDI MS Calcd for $C_{91}H_{145}N_3O_{44}$: 1983.92. Found: 1983.94.



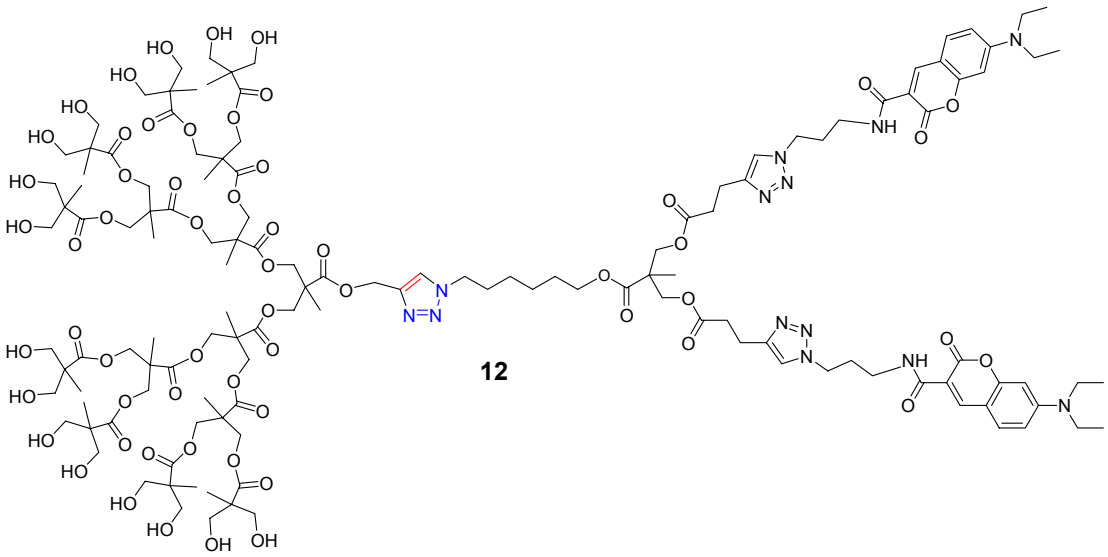
$(An)_8$-[G-4]-[G-4]-$(OH)_{16}$, 24. Isolated as white solid. Yield: 5.2g (91%). ^{1}H-NMR (CD_3OD, 400MHz): δ = 8.08 (s. 1H), 5.29 (s, 2H), 4.45(t, 2H), 4.38-4.24 (m, 56H), 4.14 (m, 18H), 3.70-3.66 (m, 32H), 3.60 (d, 16H), 1.97 (m, 2H), 1.70 (m, 2H), 1.41 (m, 28H), 1.30 (m, 60H), 1.27(s, 6H), 1.15 (s, 24H), 1.11 (s, 24H). ^{13}C-NMR (CD_3OD, 150 MHz): δ = 176.0, 175.4, 175.3, 174.0, 173.9, 173.6, 173.4, 173.3, 143.5, 126.4, 99.5, 67.6, 67.5, 67.2, 67.1, 66.8, 66.3, 66.0, 59.4, 51.9, 51.8(6), 48.3, 48.2, 48.1, 48.0, 43.5, 43.4, 31.4, 29.7, 27.4, 26.8, 26.6, 21.9, 18.9, 18.5, 18.4, 18.3(6), 18.3, 17.5. MALDI MS Calcd for $C_{183}H_{289}N_3O_{92}$: 4000.8. Found: 4000.82.



$(An)_8$-[G-4]-[G-1]-$(OH)_2$

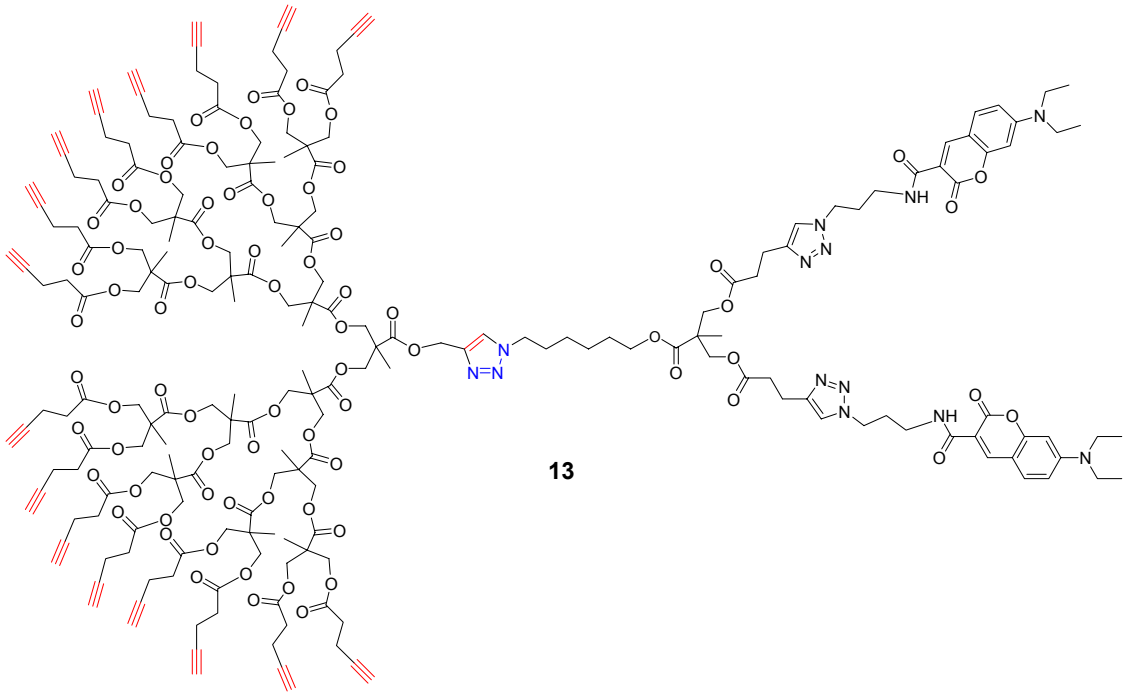
9

$(An)_8$-[G-4]-[G-1]-$(OH)_2$, 9. Isolated as colorless oil. Yield: 3.2 g (92 %). ^{1}H-NMR ($CDCl_3$, 400MHz): δ 7.74 (s, 1H), 5.24 (s, 1H), 4.37 (t, 2H), 4.34-4.26 (m, 18H), 4.22-4.12 (m, 28H), 3.87 (d, 2H), 3.71 (d, 2H), 3.61 (d, 16H), 1.93 (m, 2H), 1.67 (m, 2H), 1.46-1.40 (m, 28H), 1.34 (s, 24H), 1.27-1.26 (m, 15H), 1.21 (s, 6H), 1.13 (s, 24H), 1.05 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 175.9, 173.5, 171.9, 171.8, 171.4, 98.1, 68.3, 66.3, 65.9(5), 65.8(9), 65.5, 64.8, 64.6, 56.8, 50.1, 49.1, 46.8, 46.6, 42.0, 30.1, 28.3, 25.2, 22.0, 18.5, 17.7, 17.4, 17.2 ppm. MALDI MS Calcd for $C_{113}H_{177}N_3O_{50}$: 2376.14. Found: 2376.09.



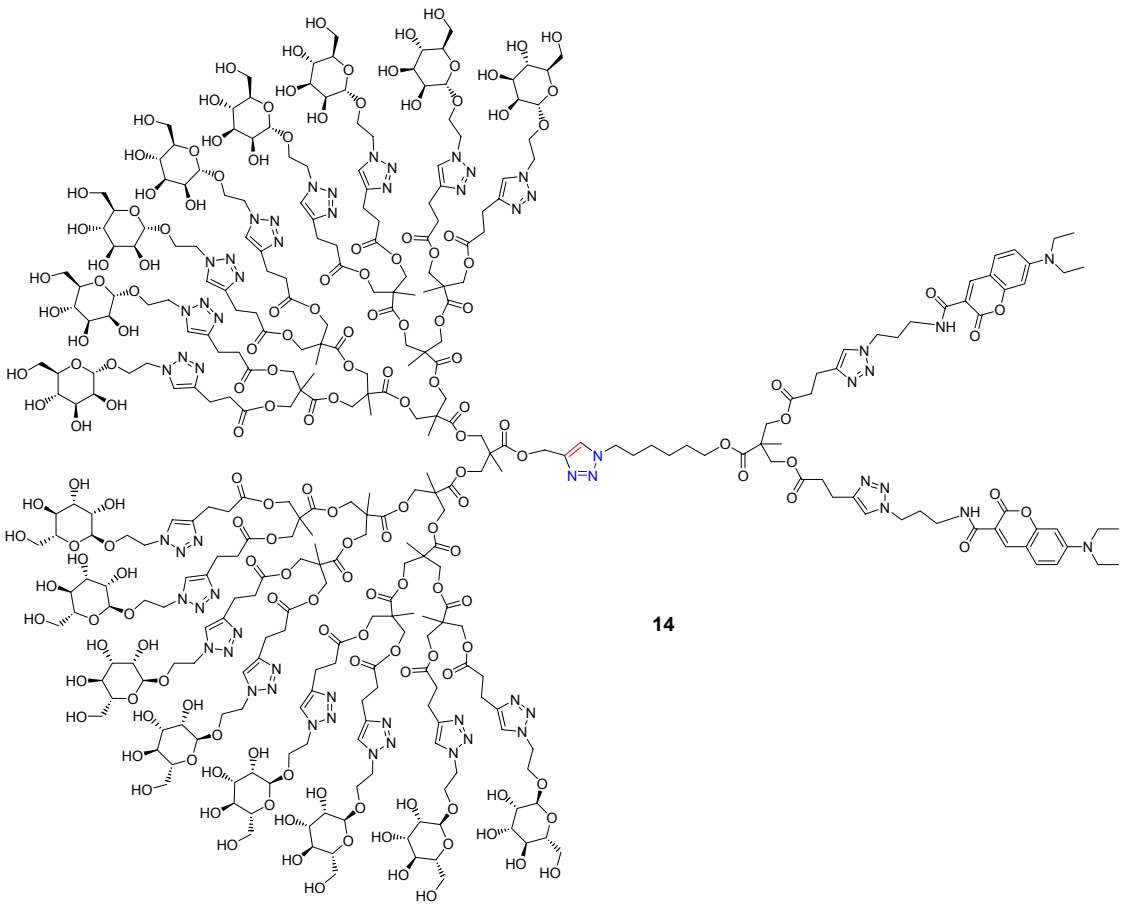
12

12. Isolated as a yellow solid. Yield; 0.89 g (91%). ^{1}H-NMR (MeOD, 500MHz): δ 9.04 (t, J=6.0 Hz, 2H), 8.52 (s, 2H), 8.09 (s, 1H), 7.83 (s, 2H), 7.47 (d, 2H), 6.76 (d, 2H), 6.49(s, 2H), 5.28 (s, 2H), 4.49 (t, 4H), 4.42 (t, 2H), 4.34-4.25 (m, 28H), 4.18 (m, 4H), 4.07 (t, 2H), 3.69 (d, 16H), 3.61 (d, 16H), 3.51-3.44 (m, 12H), 2.98 (t, 4H), 2.73 (t, 4H), 2.22 (m, 4H), 1.91 (m, 2H), 1.60 (m, 2H), 1.42-1.30 (m, 18H), 1.26-1.18 (m, 46H). ^{13}C-NMR (MeOD, 125 MHz): δ 175.9, 174.2, 173.8, 173.6, 173.4, 173.2, 165.4, 163.8, 159.0, 154.5, 149.2, 147.4, 143.4, 132.7, 126.3, 123.8, 111.6, 110.1, 109.4, 97.3, 79.5, 67.0, 66.6, 66.1, 66.0, 65.8, 61.5, 51.8, 51.4, 48.0, 47.9, 47.6, 46.0, 37.9, 37.8, 37.7, 34.2, 31.2, 29.4, 27.1, 26.4, 21.8, 18.4, 18.2, 18.1(2), 18.1, 17.4, 12.9. PDI: 1.01.



13

13. Isolated as yellow oil. Yield: 0.81 g (90%). ^{1}H-NMR ($CDCl_3$, 400MHz): δ 8.91 (t, 2H), 8.66 (s, 2H), 7.74 (s, 1H), 7.55 (s, 2H), 7.41 (d, 2H), 6.63 (dd, 2H), 6.47(d, J=2.4 Hz, 2H), 5.22 (s, 2H), 4.42-4.34 (m, 6H), 4.29-4.15 (m, 64H), 4.05 (t, 2H), 3.46-3.41 (m, 12H), 3.00 (t, 4H), 2.73 (t, 4H), 2.54 (m, 32H), 2.44 (m, 32H), 2.19 (m, 4H), 1.98 (t, 16H), 1.91 (m, 2H), 1.60 (m, 2H), 1.36 (m, 4H), 1.26-1.18 (m, 60H). ^{13}C-NMR ($CDCl_3$, 150 MHz): δ 172.6, 172.0, 171.9, 171.8(6), 171.4, 171.3, 171.1, 163.6, 162.7, 157.6, 152.6, 148.1, 145.7, 141.7, 131.2, 128.1, 124.0, 122.0, 110.0, 109.8, 108.3, 96.5, 82.3, 69.3, 66.3, 65.6, 65.3, 65.2, 64.9, 58.5, 53.4, 50.2, 47.9, 46.6, 46.5(7), 46.3, 46.2, 45.1, 36.4, 33.4, 33.1, 30.5, 30.2, 28.3, 26.1, 25.5, 25.2, 20.7, 17.8, 17.5, 17.4, 17.3, 14.2, 12.4. MALDI MS Calcd for $C_{213}H_{259}N_{13}O_{74}$: 4182.69. Found: 4182.71. PDI: 1.02.



14

3.21. Isolated as yellow solid. Yield: 80 mg (90%). ^{1}H-NMR (DMSO-*d*6, 600MHz): δ 8.69 (t, 2H), 8.61 (s, 2H), 8.09 (s, 1H), 7.88 (s, 2H), 7.81, (s, 16H), 7.64 (d, 2H), 6.77 (d, 2H), 6.59 (s, 2H), 5.15 (s, 2H), 4.70 (t, 32H), 4.60 (s, 16H), 4.54-4.29 (m, 72H), 4.18-4.10 (br, 64H), 3.91 (m, 16H), 3.75 (m, 16H), 3.60 (m, 16H), 3.54 (s, 16H), 3.46- 3.29 (m, 68H), 3.13 (m, 16H), 2.84 (m, 32H), 2.65 (m, 32H), 2.03 (m, 4H), 1.76 (m, 2H), 1.50 (m, 2H), 1.16-1.10 (m, 64H). MALDI MS Calcd for $C_{341}H_{499}N_{61}O_{170}$: 8168.23. Found: 8168.24.

Hemagglutination Assay.

Rabbit erythrocytes (10%) resuspended in PBS pH 7.4 was purchased from Lampire, Inc. Buffer (35 µL) containing Ca^{2+} and Mn^{2+} (0.1 M each) was added to all wells except

those of the first column of a standard 96-well polycarbonate microtiter plate. Samples (35 μL) at the highest concentrations were then added to the first and second columns of every lane. The mixtures in column 2 were then taken through serial 2-fold dilutions by mixing and transferring 35 μL into the next column, with the last 35 μL being discarded. ConA (35 μL, 0.0125 mg/mL) was then added to all wells and mixed well. As a control to display the gelation of conA and rabbit erythrocytes in the absence of an inhibitor, one lane contained only conA (35 μL, 0.00625 mg/mL) + buffer (35 μL) in every well. As a control to show the settling properties of the rabbit erythrocytes, one lane contained only 70 μL buffer. The mixed solutions were incubated at room temperature for one hour. After this time, 6 μL of 10% rabbit erythrocytes was added to every well and mixed well. The plate was monitored every few hours, with final settling of the erythrocytes occurring after one day. The polyvalent effect is defined as the ratio of minimum concentration of mannose required to inhibit agglutination vs. the corresponding concentration of mannose provided by the material of interest. Since the experiment involves serial two-fold dilutions, the experimental error is usually assumed to be 50%, although repeated experiments were highly reproducible.