ELECTRONIC SUPPORTING INFORMATION

A fast track strategy toward highly functionalized dendrimers with different structural layers: "Onion peel approach"

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Contents

1. Materials and methods:

All reactions in organic medium were performed in standard oven dried glassware under an inert atmosphere of nitrogen using freshly distilled solvents. CH_2Cl_2 and DMF were distilled from CaH_2 and ninhydrin respectively, and kept over molecular sieves. Solvents and reagents were deoxygenated when necessary by purging with nitrogen. All reagents were used as supplied without prior purification unless otherwise stated, and obtained from Sigma-Aldrich Chemical Co. Ltd. Reactions were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F254 precoated plates (E. Merck) and compounds were visualized by 254 nm light, a mixture of iodine/silica gel and/or mixture of ceric ammonium molybdate solution (100 ml H_2SO_4, 900 ml H_2O, 25g $(NH_4)_6Mo_7O_{24}H_2O$, 10g $Ce(SO_4)_2$) and subsequent development by gentle warming with a heat-gun. Purifications were performed by flash column chromatography using silica gel from Silicycle (60 Å, 40-63 µm) with the indicated eluent.

^1H NMR and ^{13}C $\{^1H\}$ NMR spectra were recorded at 300 or 600 MHz and 75 or 150 MHz, respectively, on a Bruker spectrometer (300 MHz) and Varian spectrometer (600 MHz). All NMR spectra were measured at 25°C in indicated deuterated solvents. Proton and carbon chemical shifts (δ) are reported in ppm and coupling constants (J) are reported in Hertz (Hz). The resonance multiplicity in the ^1H NMR spectra are described as "s" (singlet), "d" (doublet), "t" (triplet), "quint" (quintuplet) and "m" (multiplet) and broad resonances are indicated by "br". Residual protic solvent of $CDCl_3$ (^1H, δ 7.27 ppm; ^{13}C, δ 77.0 ppm (central resonance of the triplet)), D_2O (^1H, δ4.79 ppm and 30.9 ppm for CH_3 of Acetone for ^{13}C spectra, MeOD (^1H, δ3.31 ppm and ^{13}C, δ 49.0 ppm. 2D Homonuclear correlation ^1H-^1H COSY experiments were used to confirm NMR peak assignments. Gel Permeation Chromatography (GPC) was performed using Chloroform and THF as the eluent, at 40°C with a 1 ml/min flow rate on a Viscotek VE 2001 GPCmax (SEC System) with Wyatt DSP/Dawn EOS and refractive index RI/LS system as detectors. 2 PLGel mixed B LS (10 µm, 300×7.5 mm) and LS-MALLS detection with performances verified with polystyrene 100 kDa and 2000 kDa were used to determine the number-average molecular weight (*Mn*) and polydispersity index (*Mw/Mn*). Calculations were performed with Zimm Plot (model). Fourier transform infrared (FTIR) spectra were obtained with Thermo-scientific, Nicolet model 6700 equipped with ATR. The absorptions are given in wave numbers (cm^{-1}). Accurate mass measurements (HRMS) were performed on a LC-MSD-TOF instrument from Agilent Technologies in positive electrospray mode. Either protonated molecular ions $[M+nH]^{n+}$ or adducts $[M+nX]^{n+}$ (X = Na, K, NH_4) were used for empirical formula confirmation. MALDI-TOF experiments were performed on an Autoflex III from Brucker Smarteam in linear positive mode (Mass Spectrometry Laboratory (McGill University)) to afford adducts $[M+nX]^{n+}$ (X = Na, K or Li). DLS experiments were carried out at ambient temperature using a Zeta sizer nano S-90 from Malvern instruments equipped with 4mW He-Ne Laser 633 nm and avalanche photodiode positioned at 90° to the beam. The Non-Negatively constrained Least Squares (NNLS) algorithm was used to generate raw intensity *vs* particle size data for a single measurement. A Gaussian curve was fitted to estimate the average particle size and coefficient of variation, defined as the ratio of standard deviation to mean particle size. Polydispersity is calculated from a cumulants analysis of the dynamic light scattering intensity

autocorrelation function and is a measure of the deviation of the correlation function from the initial slope.

NMR diffusion experiments: NMR diffusion measurements were performed at 25^{o}C on a Bruker Avance III HD (Bruker BioSpin Ltd., Milton, ON, Canada) operating at a frequency of 599.95 MHz for ^{1}H using a 5 mm broadband z-gradient temperature-regulated probe. The measurement of the diffusion rate (D) allows calculating the solvodynamic diameter of a molecule.[1] The application of the Stokes-Einstein equation gives an estimate of the diameter of the molecule.

Stokes–Einstein equation: $D = K_B T / 6\pi\eta r_s$
D: Diffusion rate ($m^2 \cdot s^{-1}$); K_B: Boltzmann's constant (k_B = 1.38 × 10^{-23} $m^2 \cdot kg \cdot s^{-2} \cdot K^{-1}$); T: Temperature (K) (T = 298.15 K); η: solvent viscosity in Pa s; r_s: Solvodynamic radius of the species.

2. Synthetic protocols and characterization:

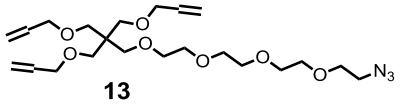
A. General procedure for the microwave-assisted copper catalyzed reactions:

An acetylene terminated dendrimer (1eq) and azide terminated building block (1.5 eq per acetylene) were suspended in a 3:1 mixture of tetrahydrofuran (THF) and water (5ml/mmol) in a 5 ml glass vial equipped with a small magnetic stirring bar. To this was added the copper sulphate (0.5 eq /acetylene) and sodium ascorbate (0.5 eq /acetylene), and the vial was tightly sealed with an aluminum/Teflon® crimp top. The mixture was then irradiated for 5h at 50^{o}C using an irradiation power of 100 W. After completion of the reaction, the vial was cooled to 25^{o}C by gas jet cooling before it was opened. The solvent was then removed and dichloromethane (DCM) was added to reaction mixture. Organic layer was washed a few times with saturated solution of ethylenediaminetetraacetic acid (EDTA) till the green color of copper disappeared followed by washing with brine. The organic layer was dried using anhydrous sodium sulphate, filtered and finally solvent was evaporated. The crude mixture was purified using silica gel column chromatography to provide pure desired compounds in good yields.

B. General procedure for the microwave-assisted thiol-ene reactions:

An alkene terminated dendrimer (1eq) and 1- thioglycerol (5 eq per alkene) were suspended in methanol (0.5ml) in a 5 ml glass vial equipped with a small magnetic stirring bar. To this was added AIBN (10 mol% /acetylene) and the vial was tightly sealed with an aluminum/Teflon® crimp top. The mixture was then irradiated for 6h at 90^{o}C using an irradiation power of 100 W. After completion of the reaction, the vial was cooled to 25^{o}C by gas jet cooling before it was opened. Solvent was removed and diethyl ether was added to the reaction mixture. The precipitates formed were washed few times with diethyl ether to remove excess of 1-thioglycerol and disulfide. Crude product was then completely dissolved in minimum volume of methanol, diluted with 4 ml water and loaded in the dialysis bag of 1000 cut-off. Dialysis was performed for 12 h changing water every 3h interval.

Note: For dialysis, all dendrimers were first dissolved completely in minimum volume of methanol and added to dialysis bag which already contained milli-Q water because none of dendrimers was soluble in water.



13

Synthesis of compound 13: To a stirred solution of 3-(allyloxy)-2,2-bis((allyloxy)methyl)propan-1-ol **11** (1000 mg, 3.9 mmol) in dry DMF, added powdered NaH (60% in oil, 280 mg, 11.7 mmol) in portions at 0^oC under N_2 environment. The reaction mixture was stirred for 10-15 minutes followed by the slow addition of 2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate **12** (1600 mg, 4.29 mmol) dissolved in minimum volume of DMF. The reaction mixture was allowed to come to room temperature. Upon completion, reaction was quenched at 0^oC with saturated NH_4Cl solution followed by the addition of DCM (100 ml) The organic layer was washed few times with cold water to get rid of DMF. It was dried with anhydrous sodium sulphate, filtered and concentrated in *vacuo*. The purification by column chromatography was performed and the desired product **13** was isolated using 25% EtOAc in hexanes as colourless oil in 80% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (ddt, J = 17.2, 10.5, 5.3 Hz, 3H), 5.36 – 5.03 (m, 6H), 3.95 (dt, J = 5.3, 1.5 Hz, 6H), 3.74 – 3.55 (m, 14H), 3.47 (d, J = 8.4 Hz, 8H), 3.43 – 3.36 (m, 2H).

^{13}C {^{1}H} NMR (75 MHz, CDCl3) δ 135.2, 115.97, 72.1, 70.97, 70.7, 70.6, 70.5, 70.2, 69.9, 69.2, 50.60, 45.36.

HRMS (ESI$^+$) *m/z* calc. For $C_{22}H_{39}N_3O_7$, 457.5610; Found, 458.2848 $[M + H]^+$, 475.3112 $[M + NH_4]^+$.

I.R (cm^{-1}) : 2866, 2102, 1478, 1349, 1288, 1091, 992, 923.

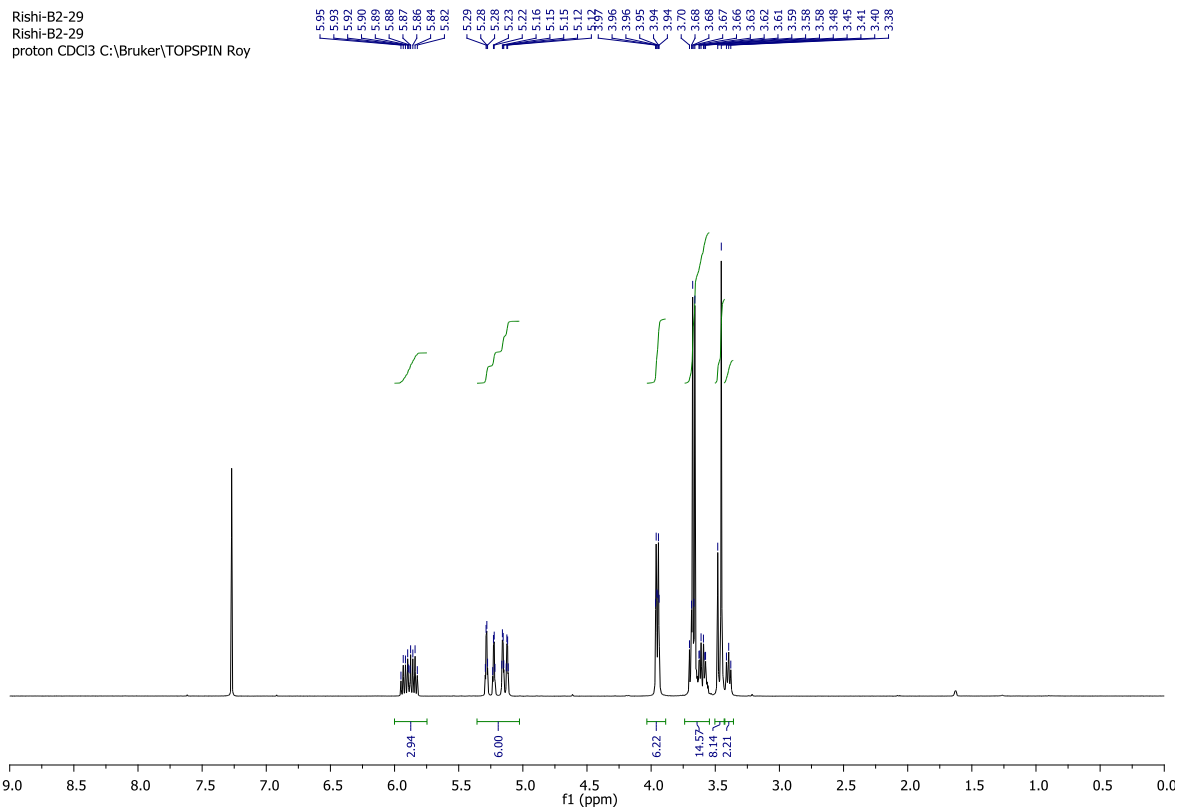


Figure S1. ^{1}H NMR spectrum of compound **13** ($CDCl_3$, 300 MHz).

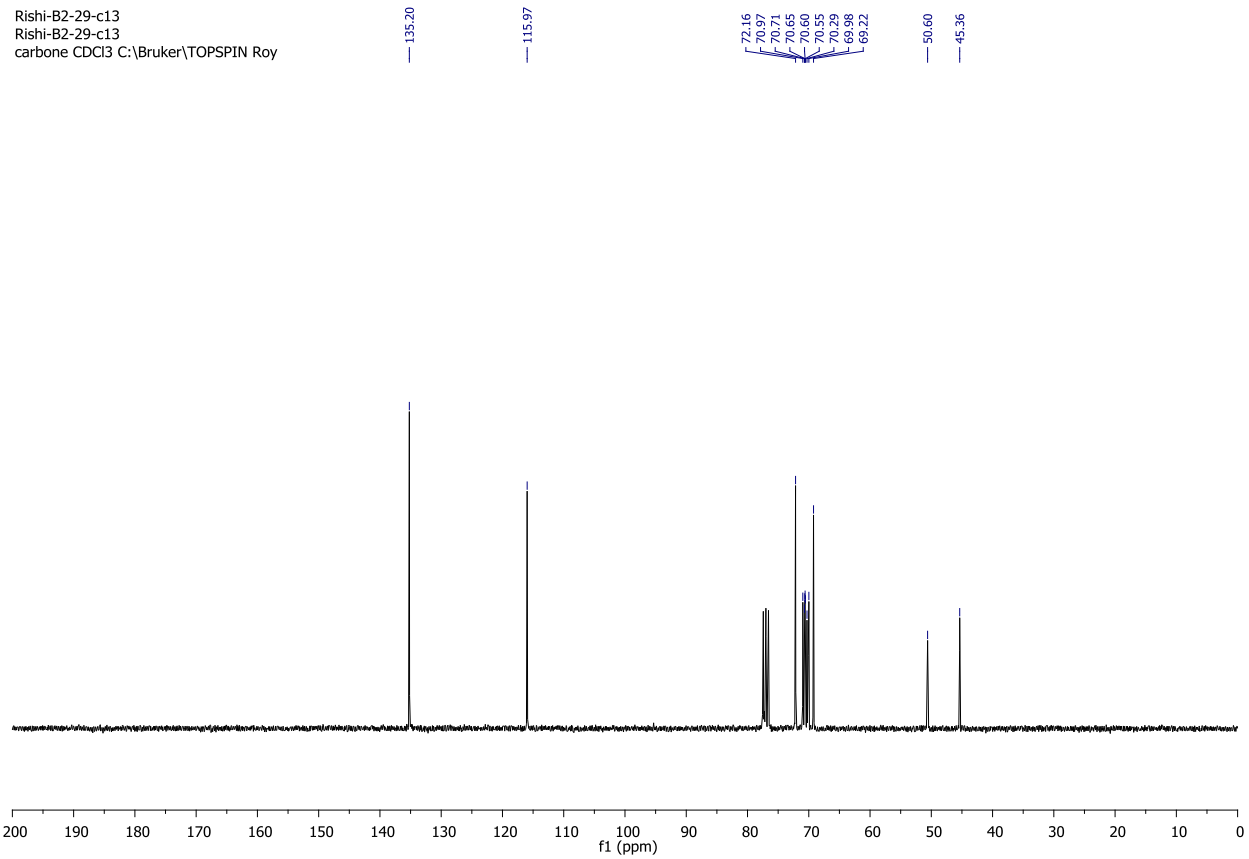


Figure S2. $^{13}C\{^{1}H\}$ NMR of compound **13** ($CDCl_3$, 75 MHz).

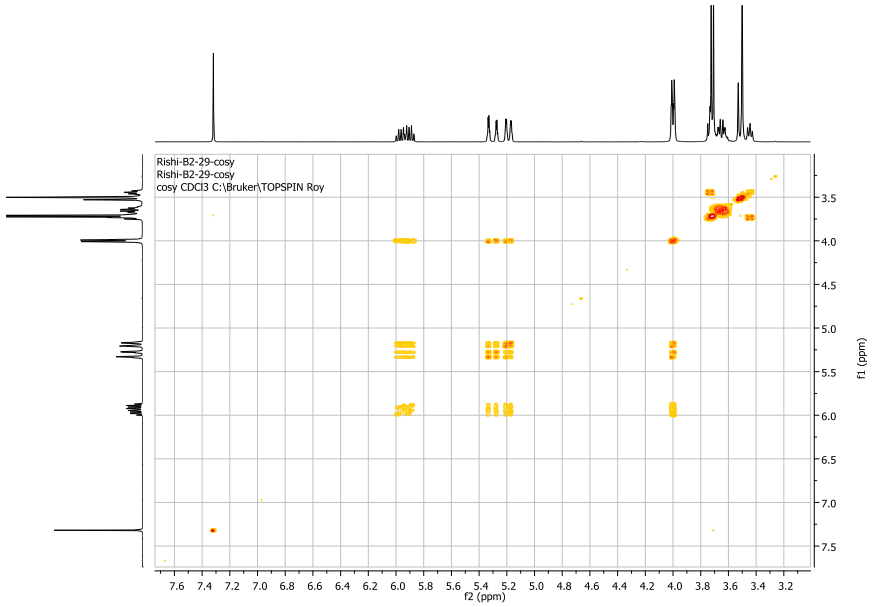


Figure S3. COSY spectrum of compound **13.**

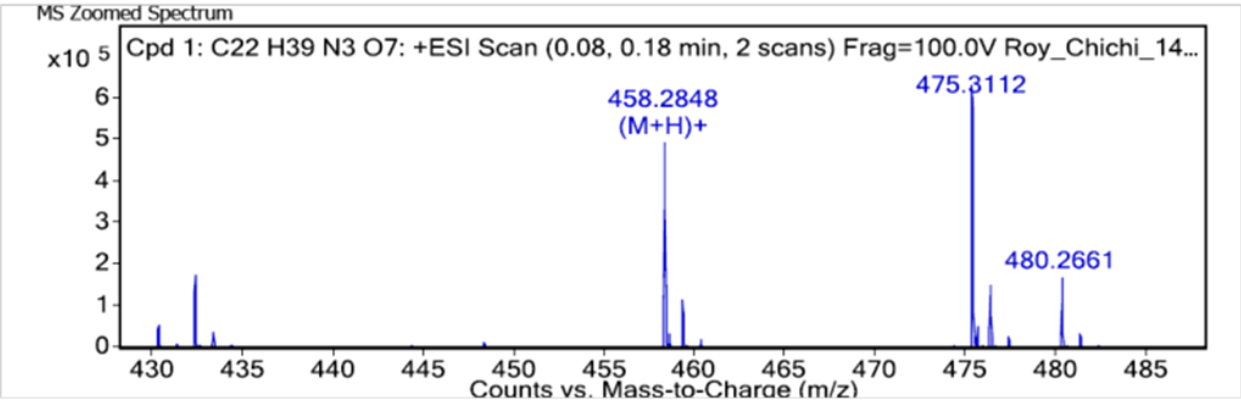


Figure S4. HRMS (ESI^+) spectrum of compound **13**.

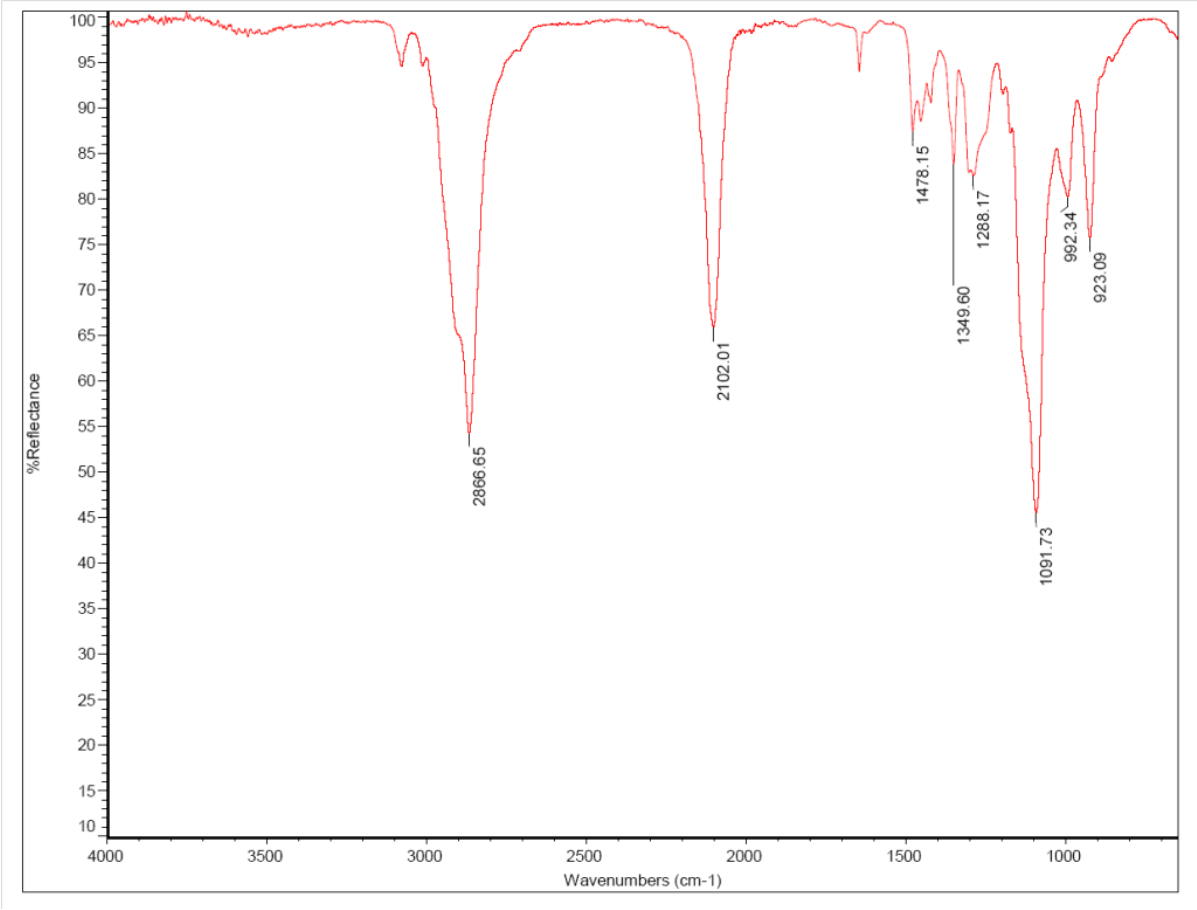
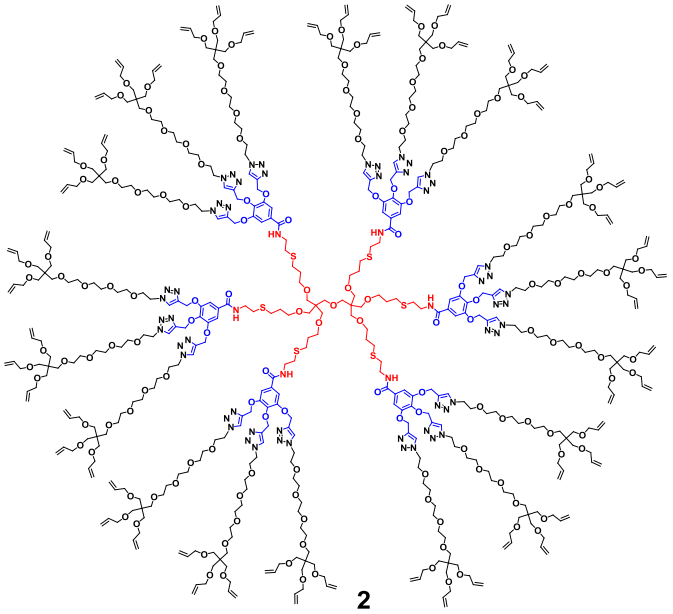


Figure S5. IR spectrum of compound **13**.



2

Synthesis of compound 2: A mixture of propargyl terminated dendrimer **1** (30 mg, 0.0117 mmol, 1eq), compound **13** (144 mg, 0.315 mmol, 27 eq.), $CuSO_4.5H_2O$ (26 mg, 0.1053 mmol, 9 eq.) and sodium ascorbate (21 mg, 0.1053 mmol, 9 eq.) was reacted together following the procedure A and was purified by column chromatography (4% MeOH in DCM as eluent) to yield compound **2** as a colourless oil in 78% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s, 12H), 7.84 (s, 6H), 7.25 (s, 12H), 5.93 – 5.80 (m, 54H), 5.26 – 5.07 (m, 152H), 4.51 (dt, J = 34.4, 5.2 Hz, 38H), 3.93 (d, J = 5.3 Hz, 112H), 3.86 (dt, J = 25.9, 5.3 Hz, 38H), 3.63 – 3.53 (m, 226H), 3.46 (s, 40H), 3.43 (s, 112H), 3.37 (s, 12H), 2.77 (br s, 12H), 2.65 (t, J = 6.8 Hz, 12H), 1.85 (d, J = 6.0 Hz, 12H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 166.7, 152.0, 144.0, 143.2, 140.0, 135.2, 134.7, 130.0, 124.7, 124.5, 116.5, 116.0, 107.1, 72.3, 72.1, 72.0, 70.9, 70.5, 70.4, 70.3, 70.1, 69.7, 69.3, 69.2, 66.2, 62.9, 50.1, 49.9, 45.6, 45.3, 39.6, 31.3, 29.7, 28.5.

(MALDI-TOF) m/z: calculated for $C_{532}H_{850}N_{60}O_{157}S_6$: 10791.1392, found: 10814.3920 [M+Na]$^+$

I.R (cm^{-1}) 3705, 3680, 2981, 2937, 2922, 2865, 2844, 1454, 1426, 1346, 1098, 1054, 1033, 1012.

GPC ($CHCl_3$) M*n*= 10770 g/mol. M*w*/*Mn*= 1.08

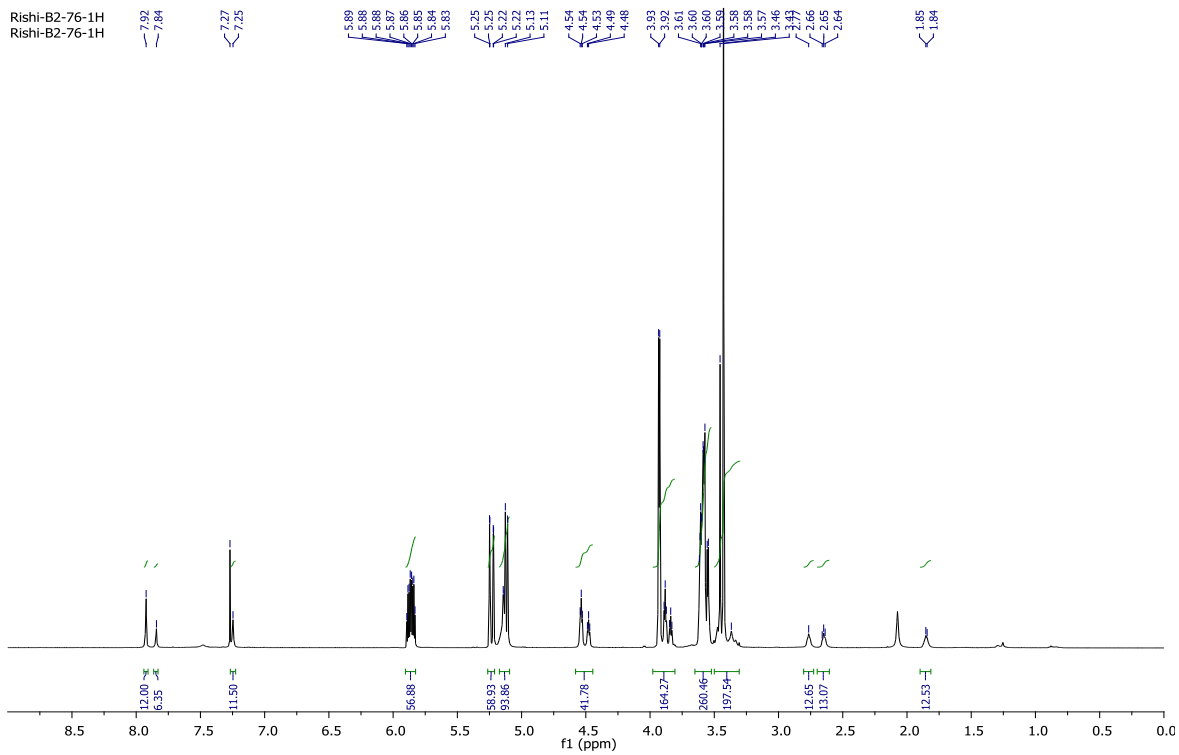


Figure S6. ^{1}H NMR spectrum of compound **2** ($CDCl_3$, 600 MHz).

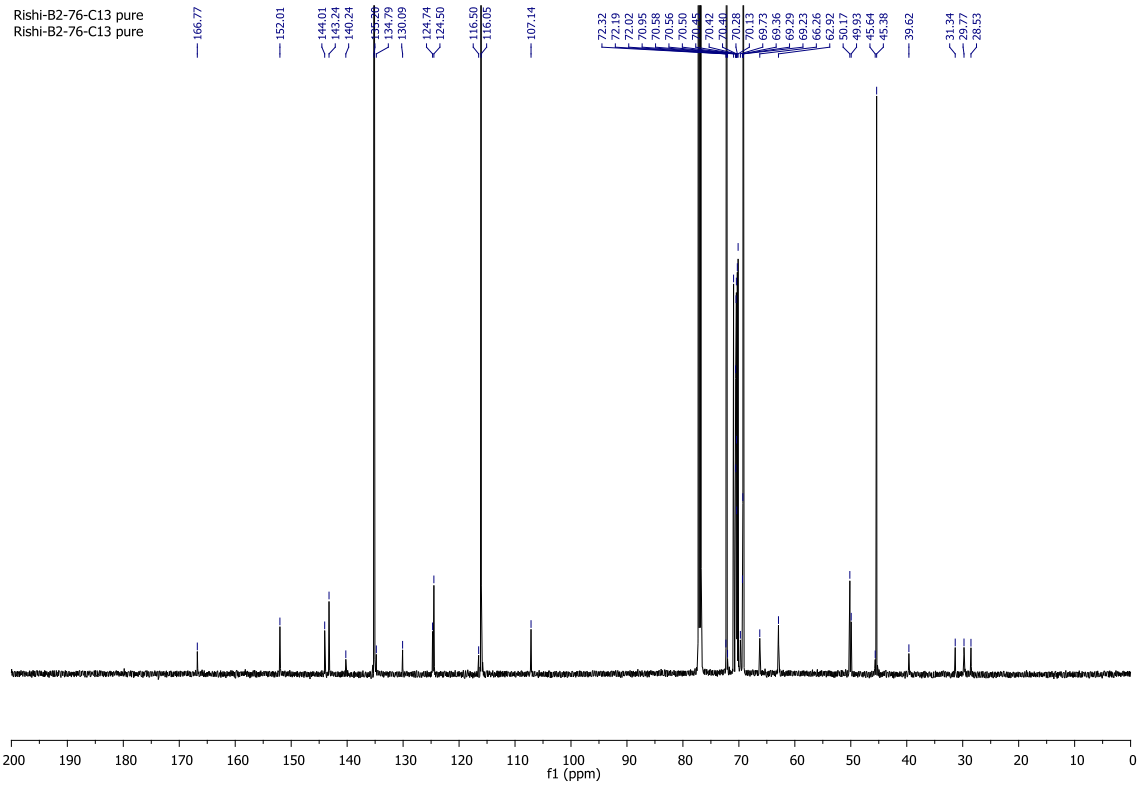


Figure S7. ^{13}C {^{1}H} NMR of compound **2** ($CDCl_3$, 75 MHz)

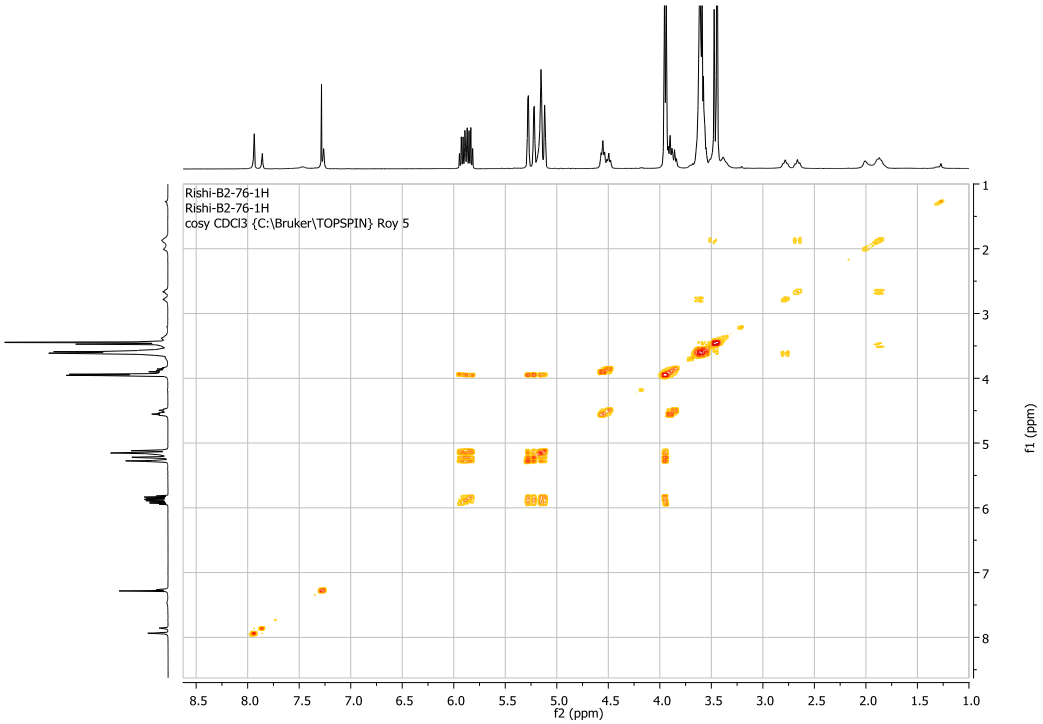


Figure S8. COSY spectrum of compound **2**

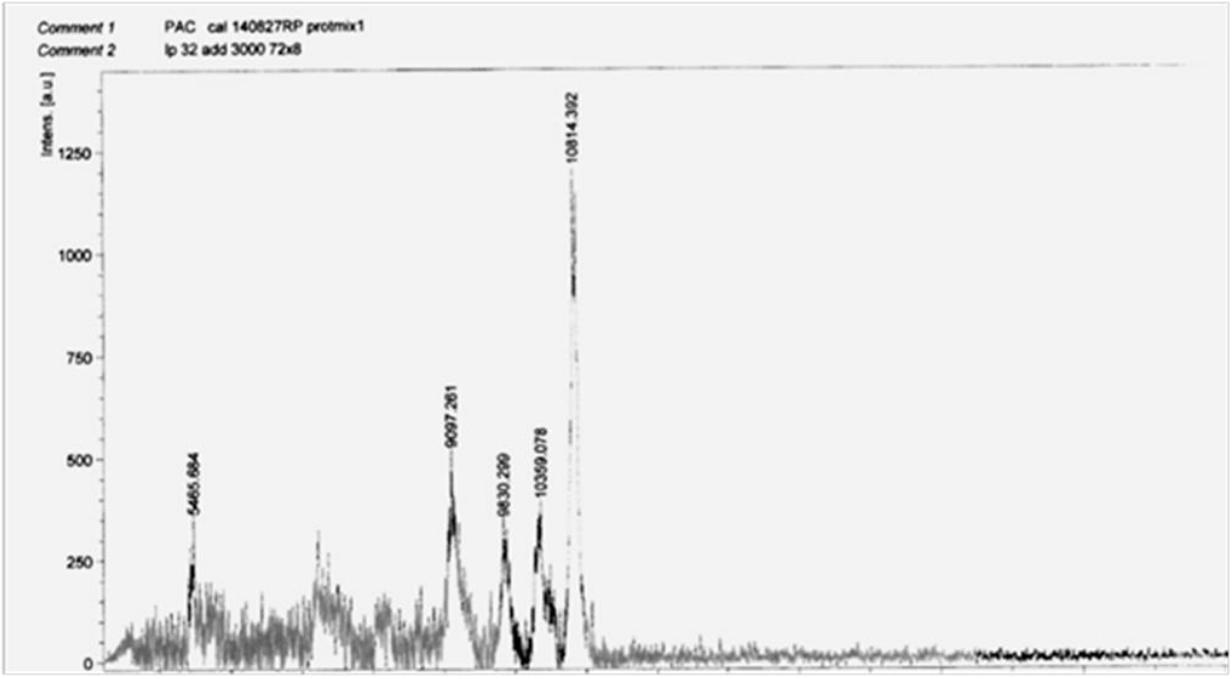
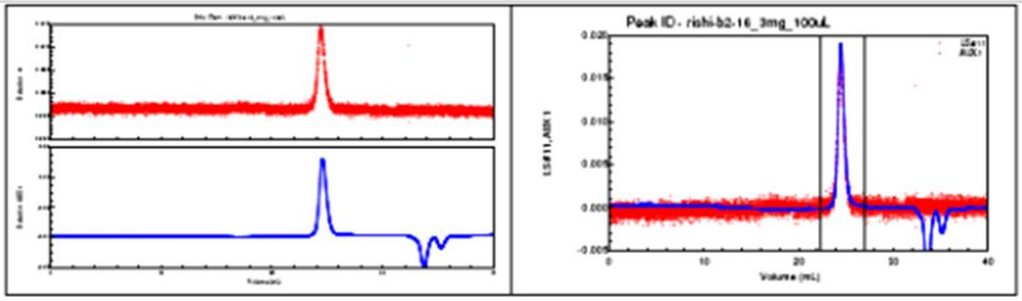


Figure S9. MALDI-TOF spectrum of compound **2**



COLLECTION INFORMATION

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Solvent name	:	water
Solvent RI	:	1.330
Calibration constants		
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» AUX1	:	3.5650e-04
AUX2	:	1.0000e-04
Flow rate	:	1.000 mL/min
Collection interval	:	0.250 sec
Number of slices	:	9600
Volume (mL)	:	22.325 - 26.887
Slices (used)	:	1096 (795)
A2 (mol mL/g^2)	:	0.000e+00
Fit degree	:	1
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dn/dc (mL/g)	:	0.074
Polydispersity(Mw/Mn)	:	1.084±0.163 (15%)
Polydispersity(Mz/Mn)	:	1.482±0.681 (46%)

Molar Mass Moments (g/mol)

Mn	:	1.077e+04 (8%)
Mw	:	1.168e+04 (12%)
Mz	:	1.597e+04 (45%)

Figure S10. GPC traces of compound **2**

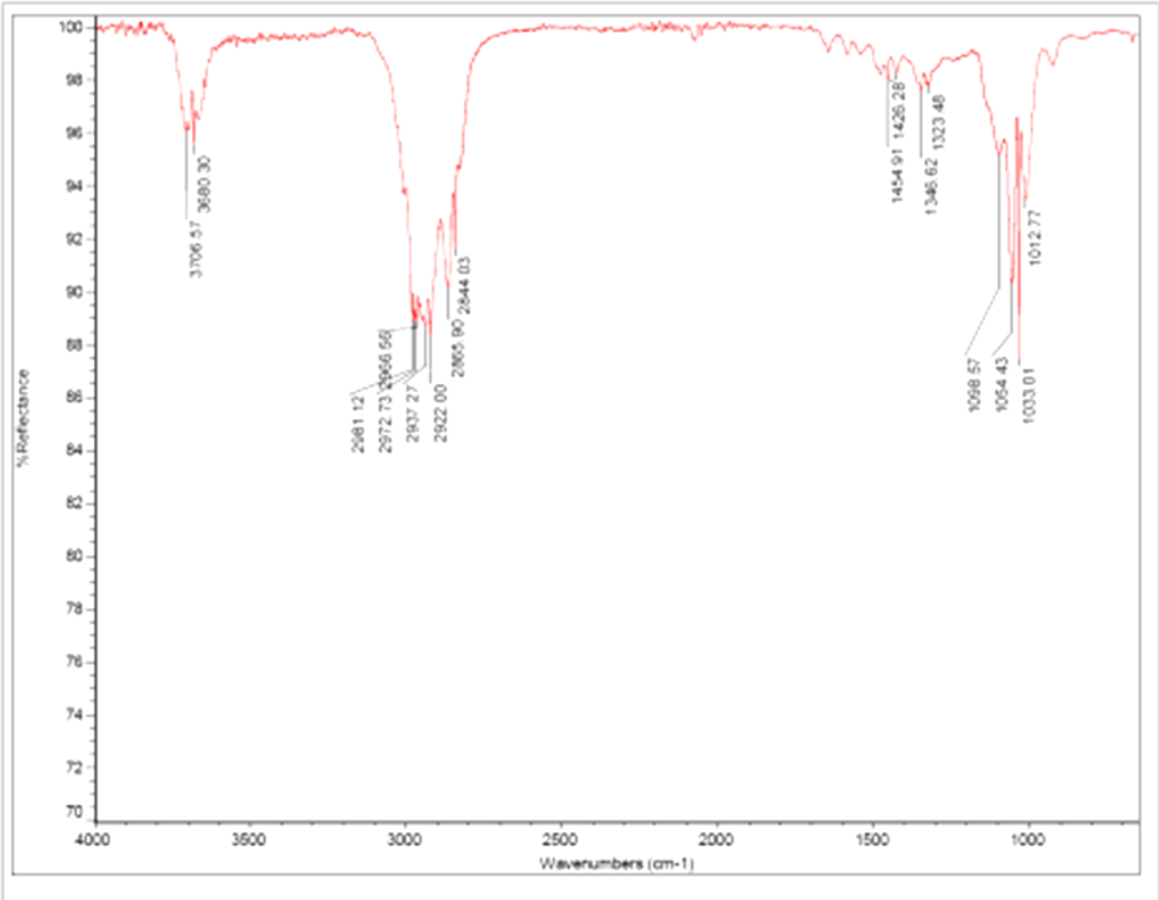
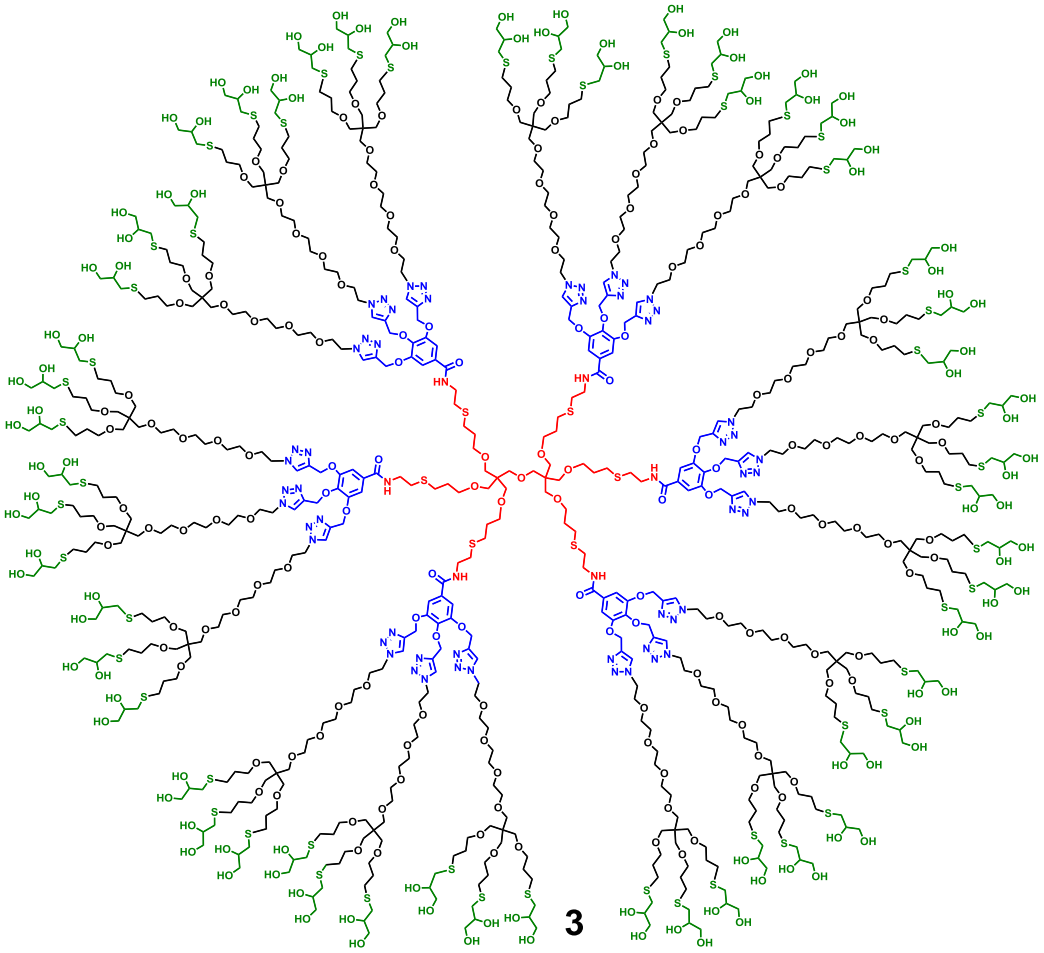


Figure S11. IR spectrum of compound **2**.



3

Synthesis of compound 3: Alkene terminated dendrimer **2** (65 mg, 0.006 mmol, 1eq), 1-thioglycerol (0.139 ml, 1.62 mmol, 270 eq.), and AIBN (5.3 mg, 0.0324 mmol, 5.4 eq.) were reacted together following the procedure B and was purified by dialysis to yield compound **3** as a colourless oil in 85% yield.

^{1}H NMR (300 MHz, MeOD) δ 8.52 (br s, 6H), 8.17 (s, 12H), 7.92 (s, 6H), 7.34 (s, 12H), 5.16 (d, *J* = 26.5 Hz, 46H), 4.57 (d, *J* = 28.4 Hz, 38H), 3.95 – 3.33 (m, 798H), 2.79 – 2.47 (m, 244H), 1.93 – 1.72 (m, 120H).

^{13}C{^{1}H} NMR (151 MHz, MeOD) δ 168.7, 153.5, 145.2, 144.4, 141.4, 131.2, 129.4, 126.6, 126.5, 108.4, 77.6, 73.2, 73.1, 72.8, 72.2, 71.6, 71.5, 71.4, 71.1, 71.0, 70.9, 70.5, 70.3, 66.9, 66.0, 63.8, 51.5, 51.4, 49.8, 46.8, 46.7, 41.2, 36.4, 35.2, 35.1, 32.1, 31.0, 30.7, 30.4, 29.6, 19.1.

HRMS (ESI^{+}) *m/z* calc. For $C_{694}H_{1282}N_{60}O_{265}S_{60,}$ 16631.7479; Found: 16631.7480.

I.R (cm^{-1}) 3349, 2920, 2870, 1643, 1425, 1227, 1094, 1032.

Differential light scattering Hydrodynamic diameter: 5.70 nm

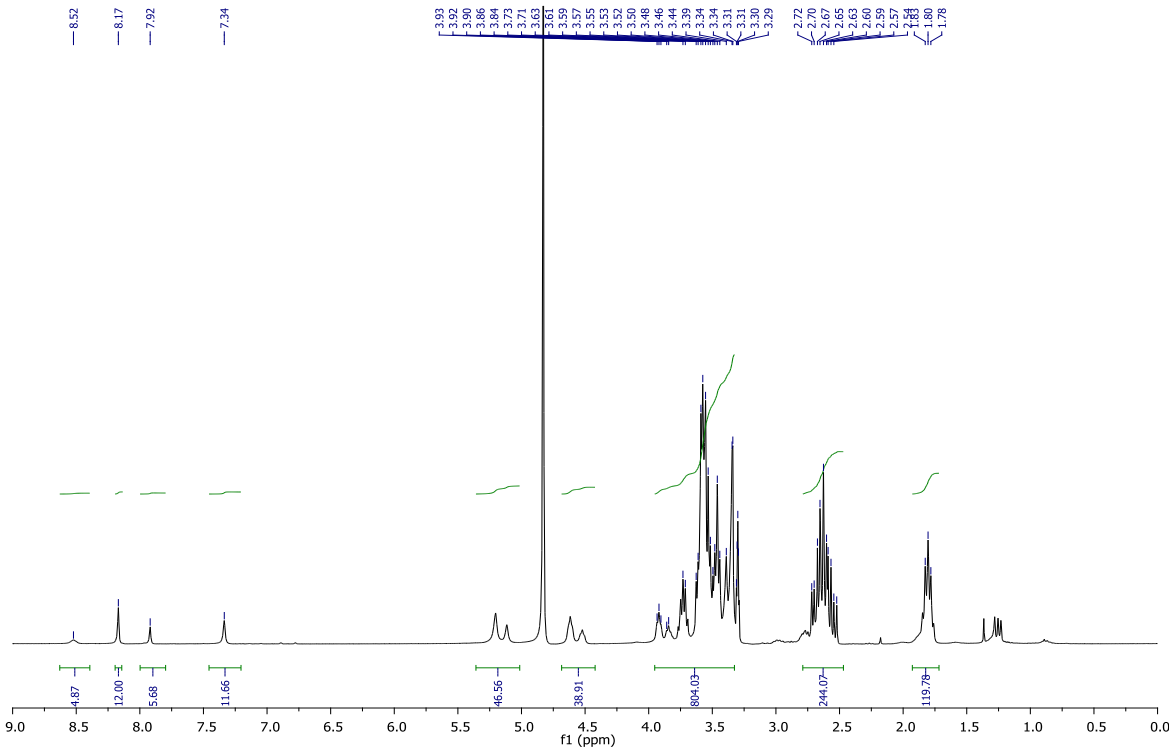


Figure S12. ^{1}H NMR spectrum of compound **3** (CD_3OD, 300 MHz)

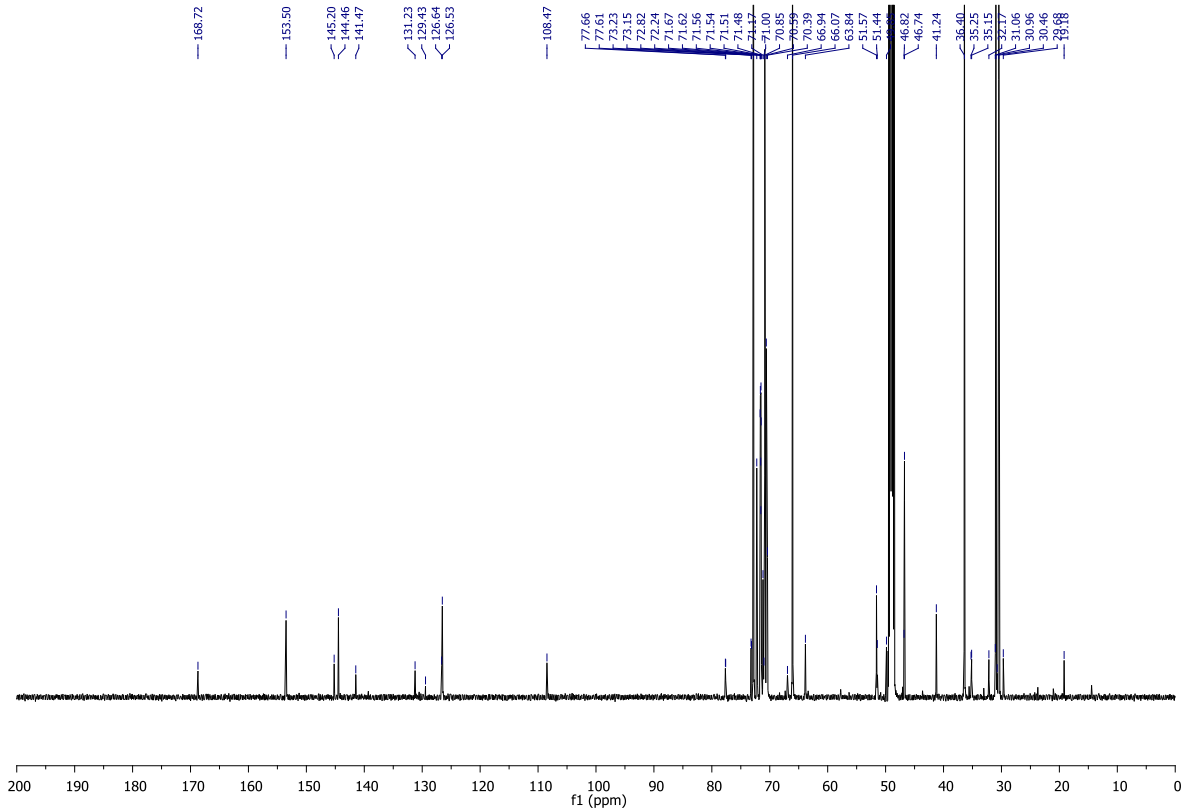


Figure S13. ^{13}C {^{1}H} NMR of compound **3** (CD_3OD, 151 MHz)

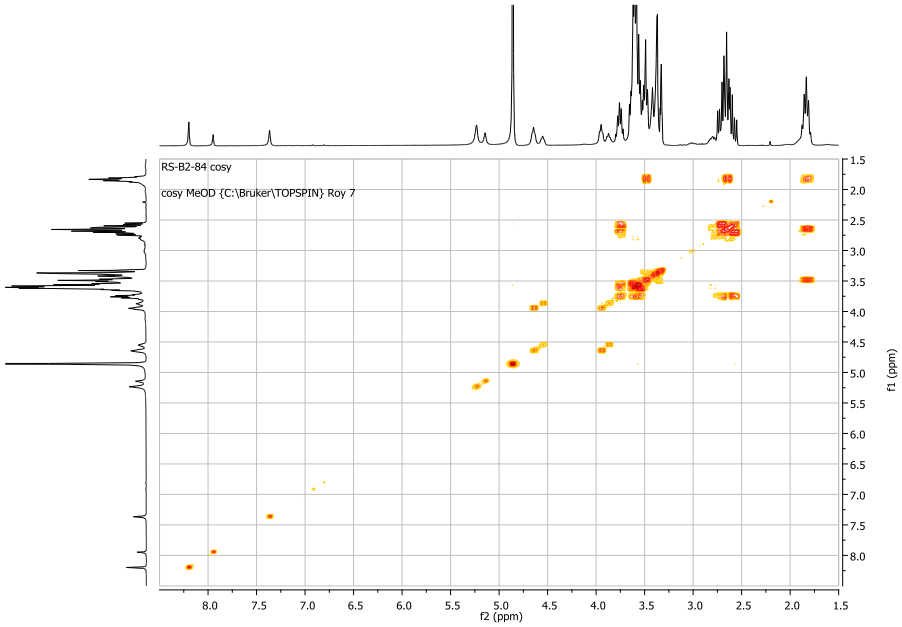


Figure S14. COSY spectrum of compound **3**

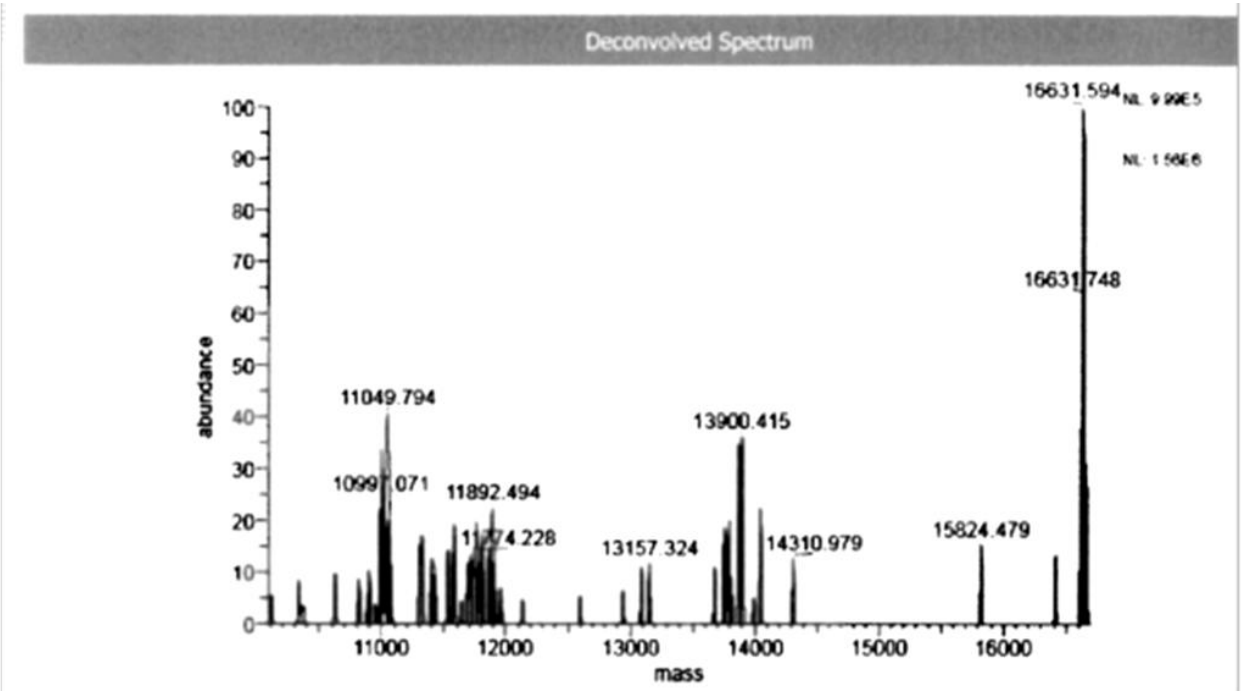


Figure S15. HRMS (ESI^+) spectrum of compound **3.**

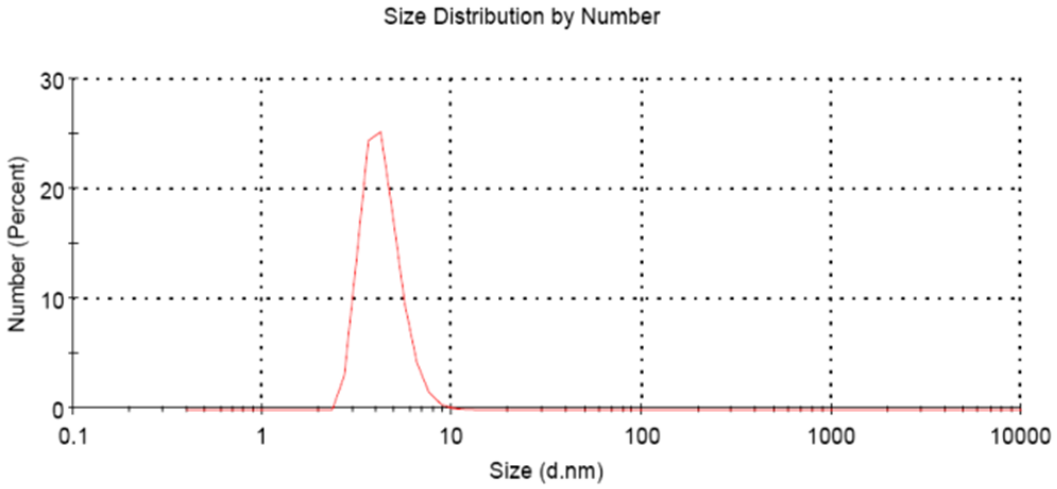


Figure S16. DLS size distribution of dendrimer **3** in methanol at 25°C.

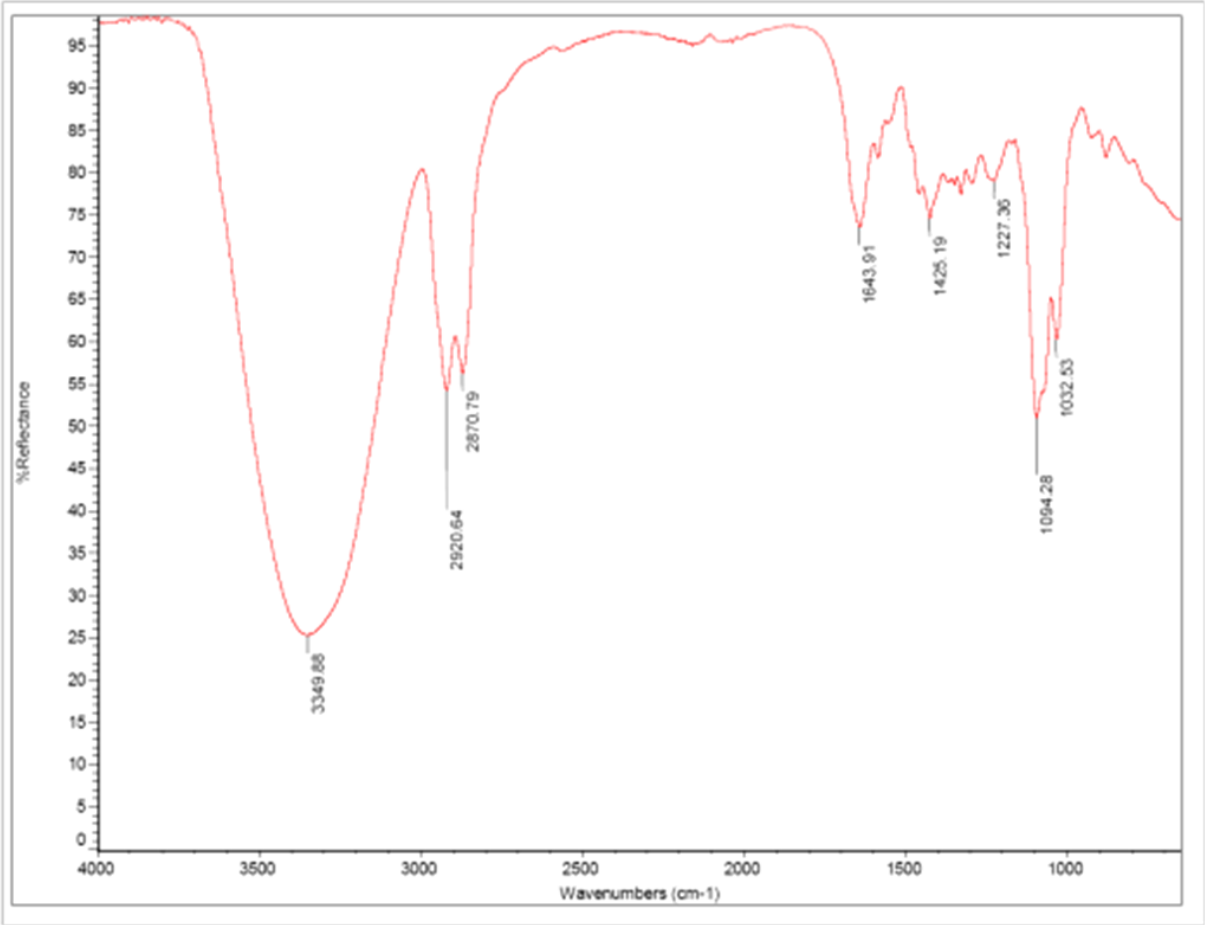
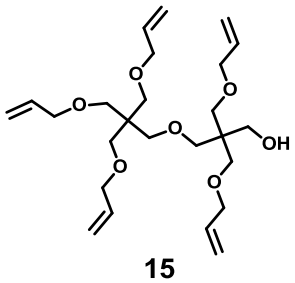


Figure S17. IR spectrum of compound **3**.



15

Synthesis of compound 15: Dipentaerythritol **14** (1.5 g, 5.9 mmol) was suspended in DMSO (22 ml) followed by addition of Sodium hydroxide solution (40% in water, 16 ml) slowly. The mixture was stirred at room temperature for 30 minutes. Allyl bromide (5.2 ml, 57.3 mmol) was added drop wise. The reaction mixture was stirred at room temperature for 16 h. It was diluted with diethyl ether (150 ml), washed with water (25 ml) and brine (25 ml), and dried over $MgSO_4$. The solvent was evaporated and the crude was passed through a column of silica gel with hexane-ethyl acetate mixtures (0-30% ethyl acetate) as eluent to obtain pure pentaallyl dipentaerythritol **15** in 40% yield along with tetraallyl derivative in 49% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, *J* = 22.6, 10.6, 5.4 Hz, 5H), 5.34 – 5.09 (m, 10H), 4.03 – 3.89 (m, 10H), 3.71 (d, *J* = 6.3 Hz, 2H), 3.48 (s, 4H), 3.44 (d, *J* = 6.2 Hz, 10H), 3.04 (t, *J* = 6.3 Hz, 1H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 135.17, 134.90, 116.43, 72.42, 71.11, 70.69, 69.63, 66.18, 45.40, and 45.10 .

I.R (cm^{-1}) 3502, 3079, 2979, 2866, 1754, 1646, 1478, 1420, 1350, 1265, 1089, 991, 922.

HRMS (ESI$^+$) m/z calc, 454.5968; found, 455.30 [*M* + H]$^+$.

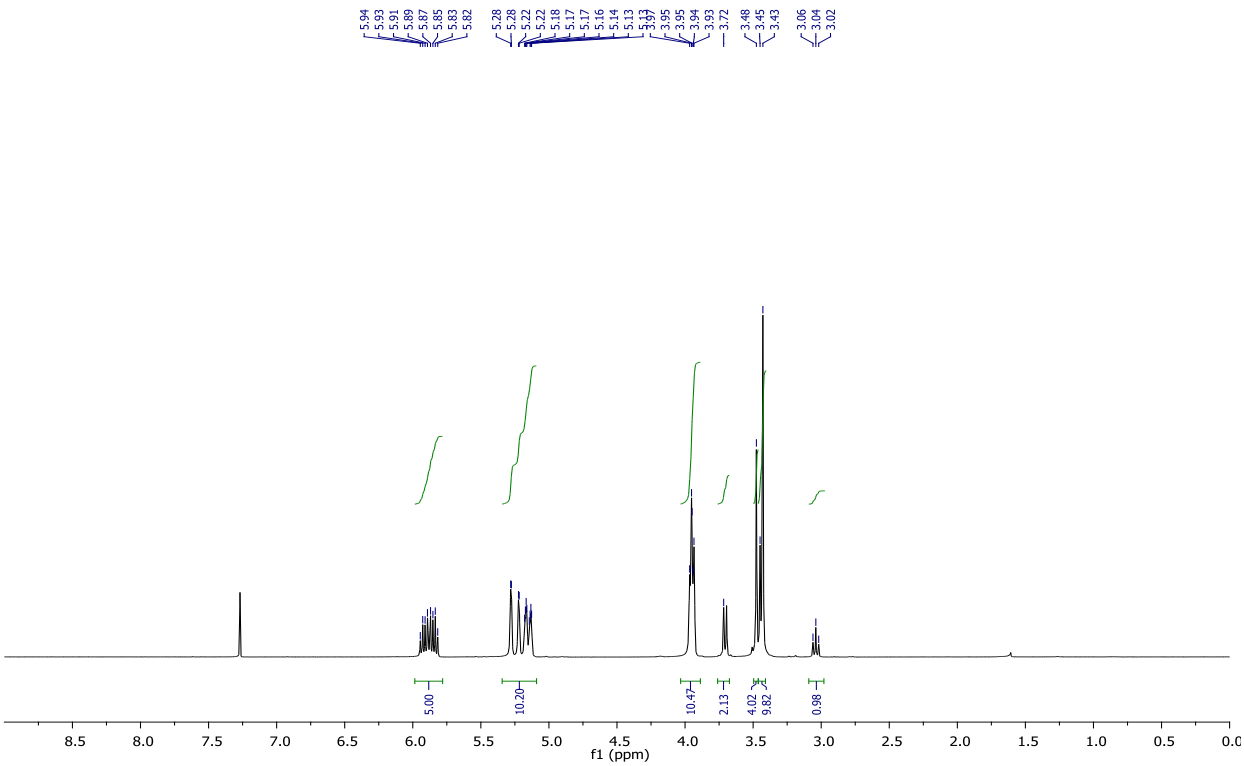


Figure S18. ^{1}H NMR spectrum of compound **15** ($CDCl_3$, 300 MHz).

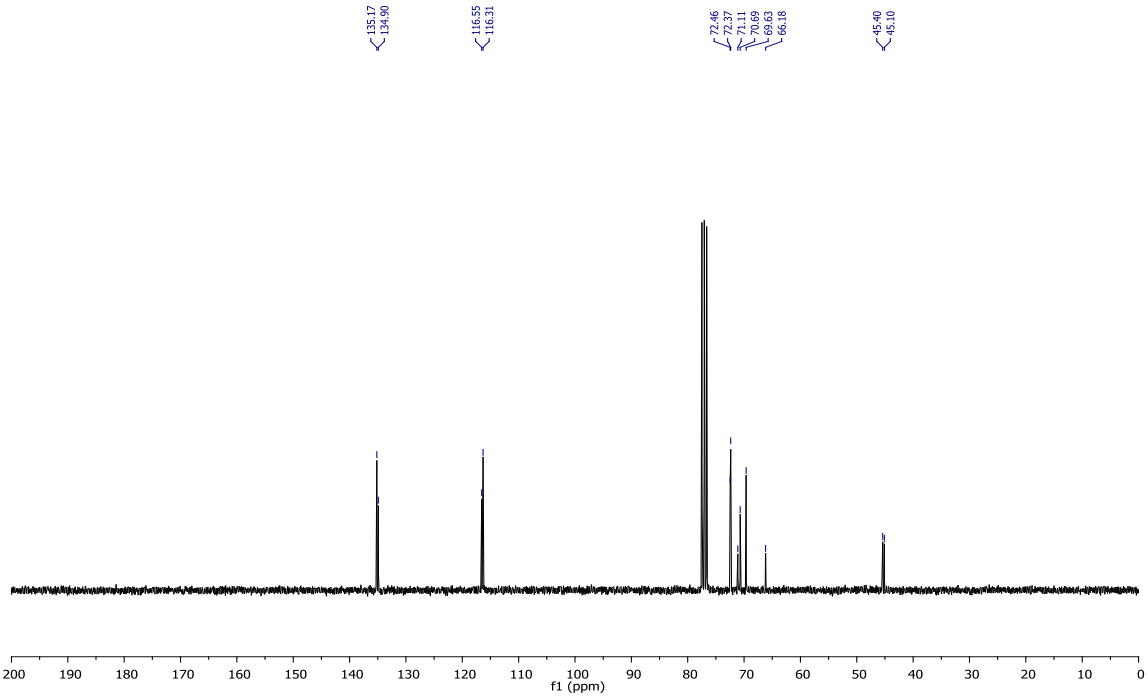


Figure S19. ^{13}C {^{1}H} NMR of compound **15** ($CDCl_3$, 75 MHz).

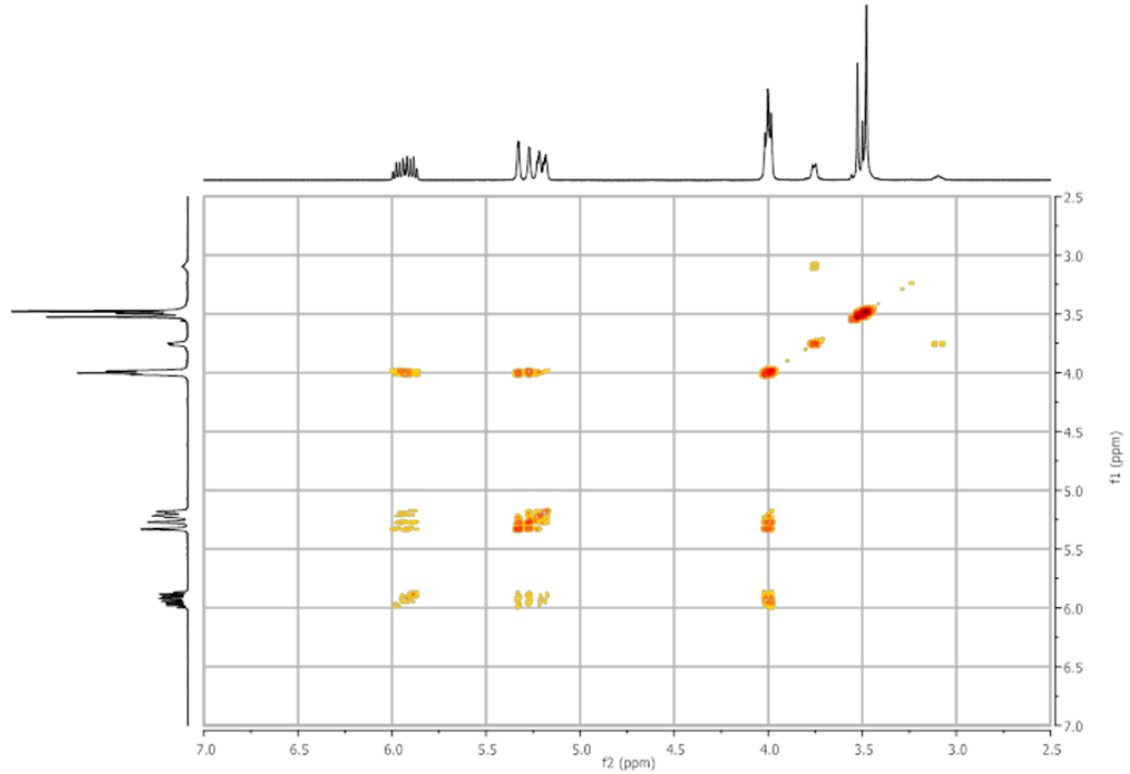


Figure S20. COSY spectrum of compound **15.**

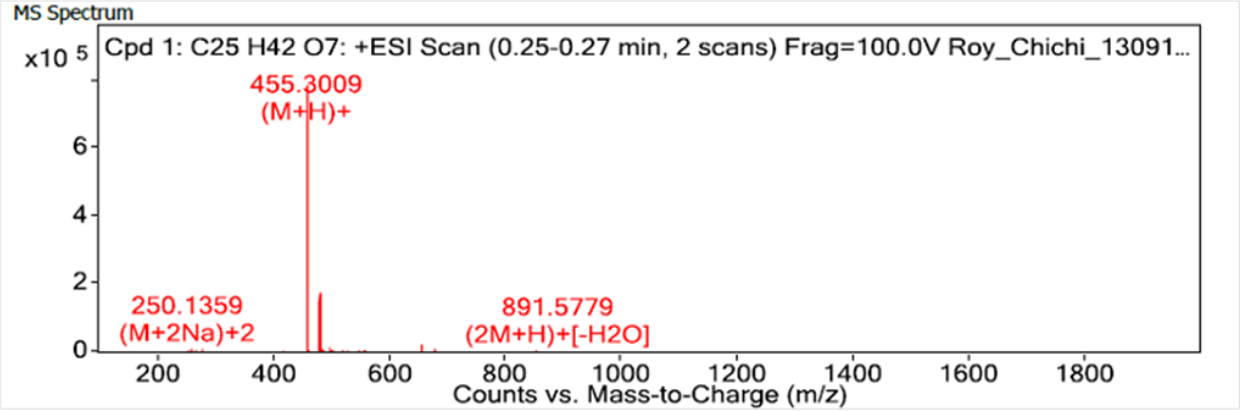


Figure S21. HRMS (ESI^+) spectrum of compound **15.**

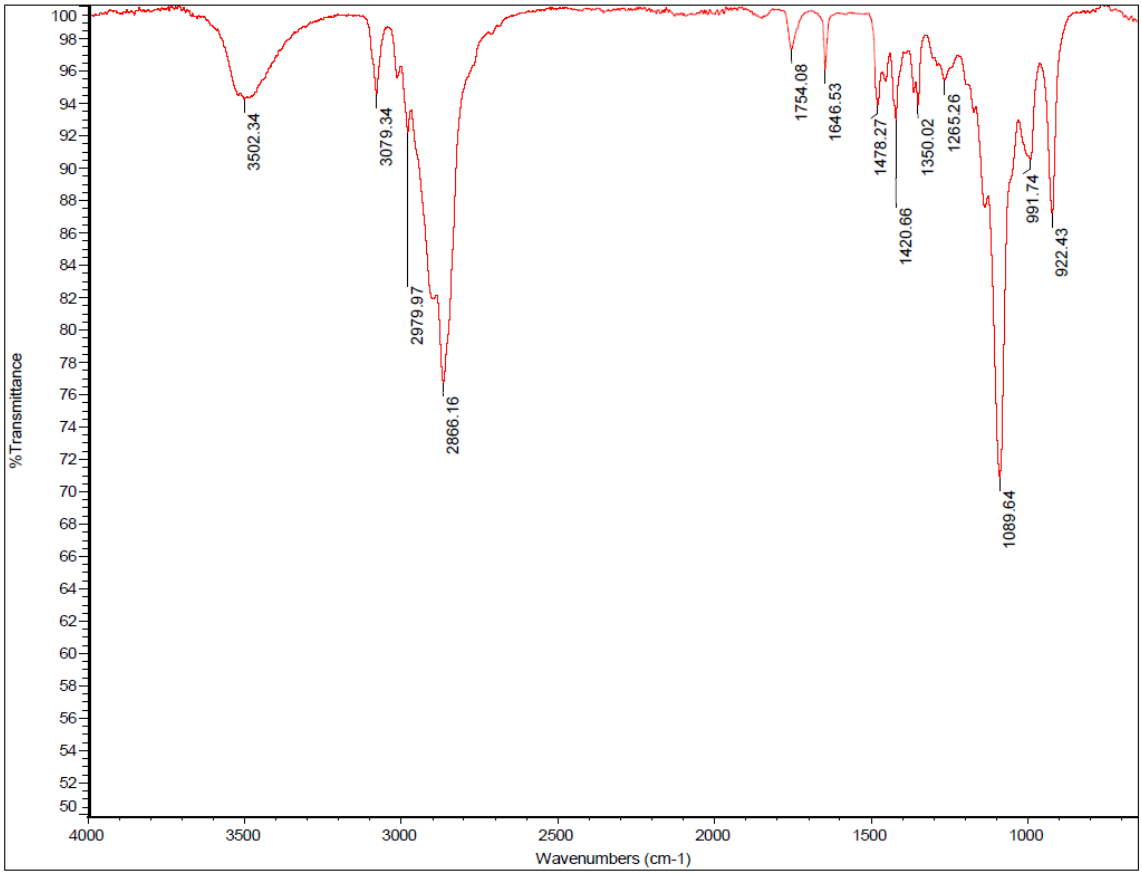
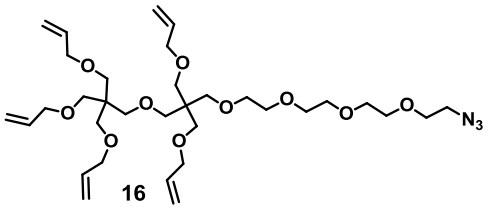


Figure S22. IR spectrum of compound **15**.



16

Synthesis of compound 16: To a solution of 3-(allyloxy)-2-((3-(allyloxy)-2,2-bis((allyloxy)methyl)propoxy)methyl)-2-((allyloxy)methyl)propan-1-ol (**15)** (800 mg, 1.76 mmol) in DMF (10ml) at 0^{o}C sodium hydride (60% in oil, 500 mg, 12.5 mmol) was added. The mixture was stirred at 0^{o}C for 15 min followed by addition of 2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (**12)** (8.54 mg, 2.29 mmol) dissolved in DMF (2ml). The mixture was stirred at 0^{o}C for 1 h and RT for 10 minutes. Reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc (50 ml) followed with brine wash. The organic layer was separated, dried and crude mixture was purified with column chromatography. Desired compound **16** was obtained using 25% EtOAc: hexane as eluent in 68% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96 – 5.80 (m, 5H), 5.19 (ddd, *J* = 13.8, 11.4, 1.3 Hz, 10H), 4.02 – 3.88 (m, 10H), 3.67 (d, *J* = 5.4 Hz, 10H), 3.64 – 3.53 (m, 4H), 3.47 – 3.37 (m, 18H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 135.1, 115.9, 72.1, 70.9, 70.5, 70.2, 70.1, 69.9, 69.3, 50.5, 45.5, 45.4.

HRMS (ESI^{+}) *m/z* calc. For $C_{33}H_{57}N_3O_{10,}$ 655.8198; Found, 656.4104 $[M + H]^{+}$, 673.4368 $[M + NH_4]^{+}$.

I.R (cm^{-1}) 2865, 2102, 1646, 1478, 1452, 1420, 1349, 1288, 1085, 989, 919.

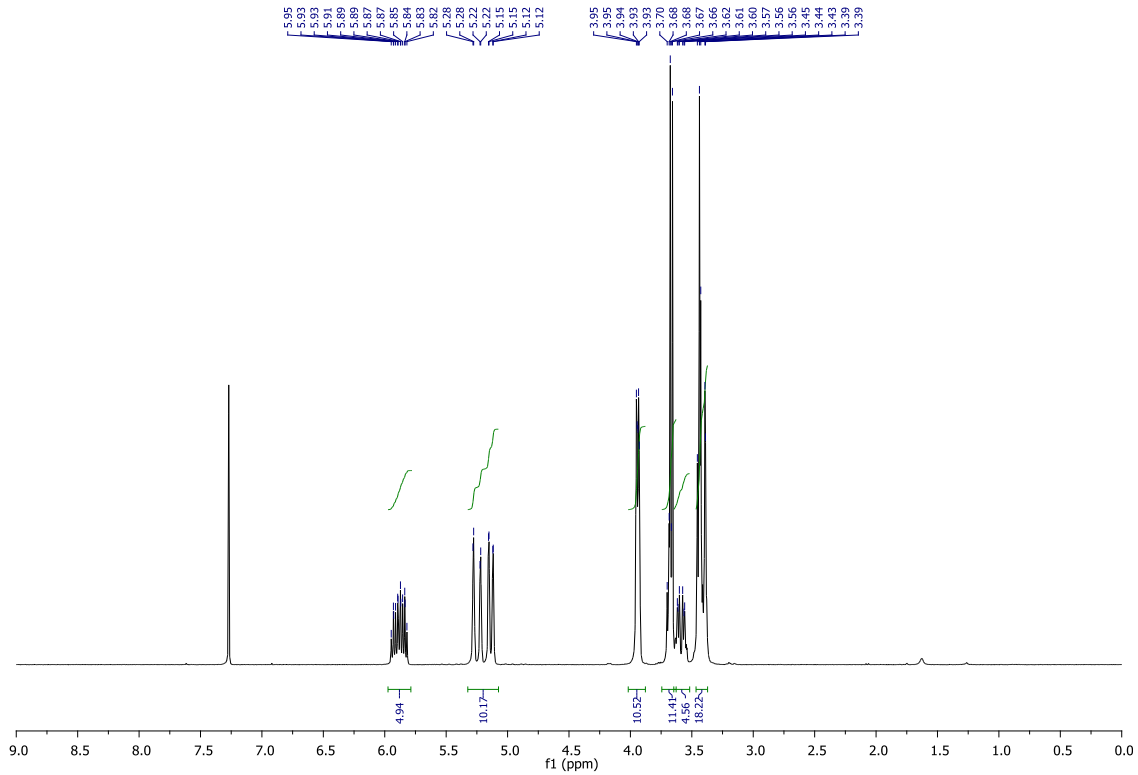


Figure S23. ^{1}H NMR spectrum of compound **16** ($CDCl_3$, 300 MHz).

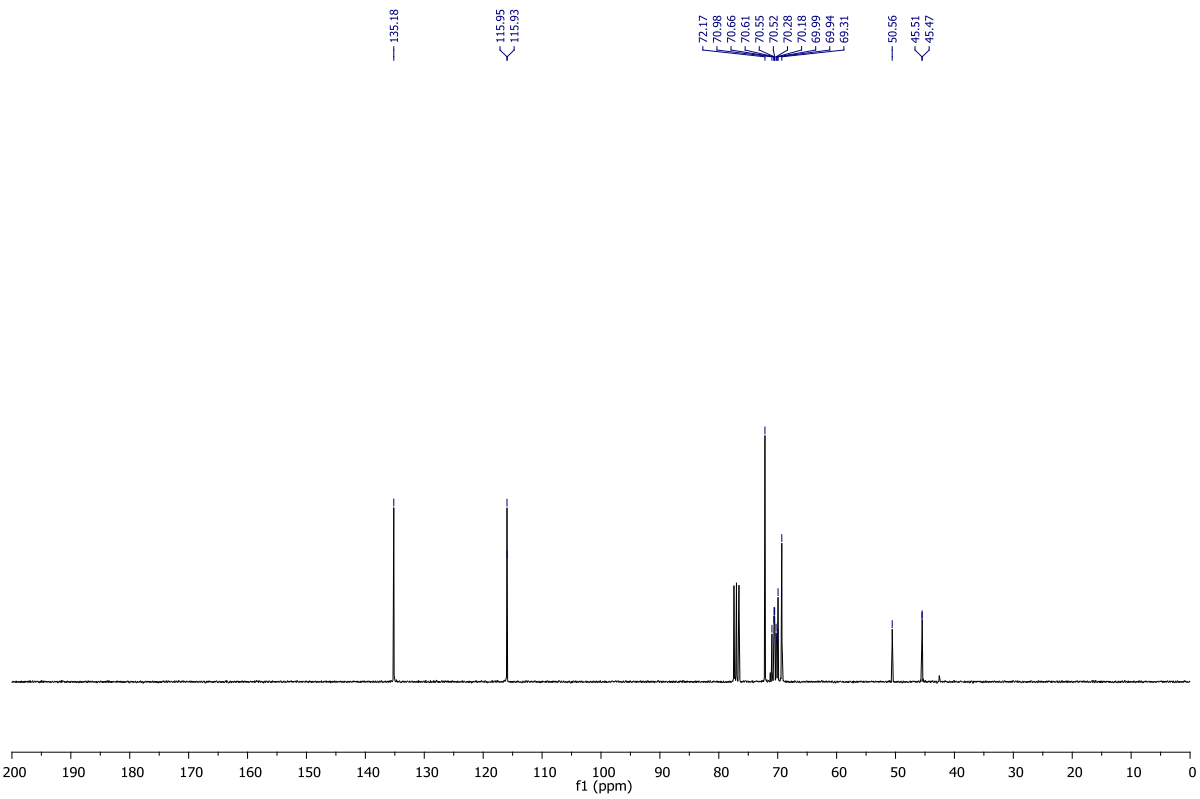


Figure S24. ^{13}C {^{1}H} NMR of compound **16** ($CDCl_3$, 75 MHz).

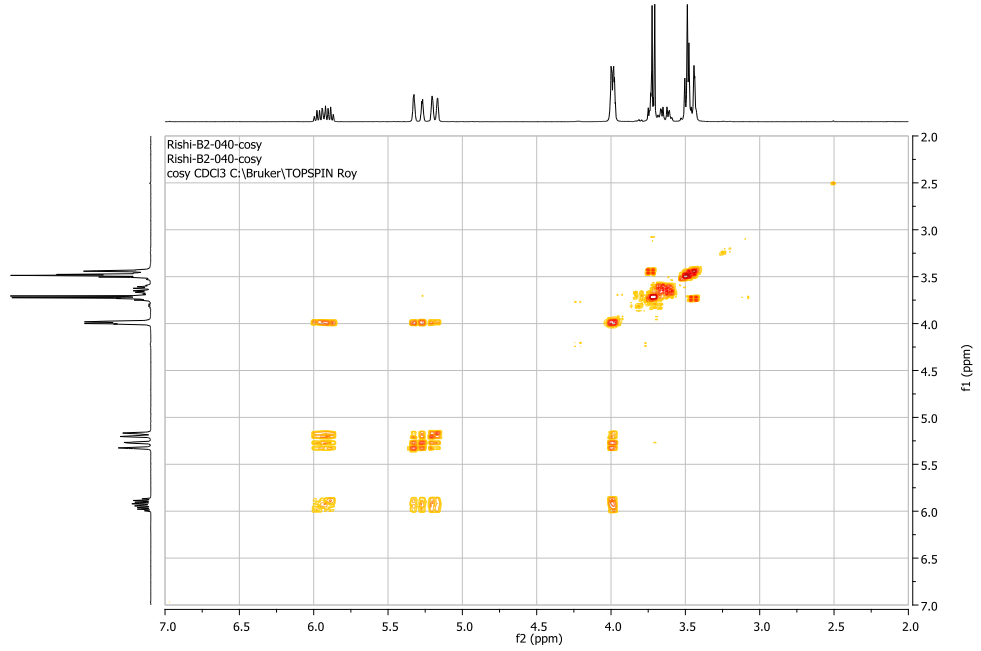


Figure S25. COSY spectrum of compound **16.**

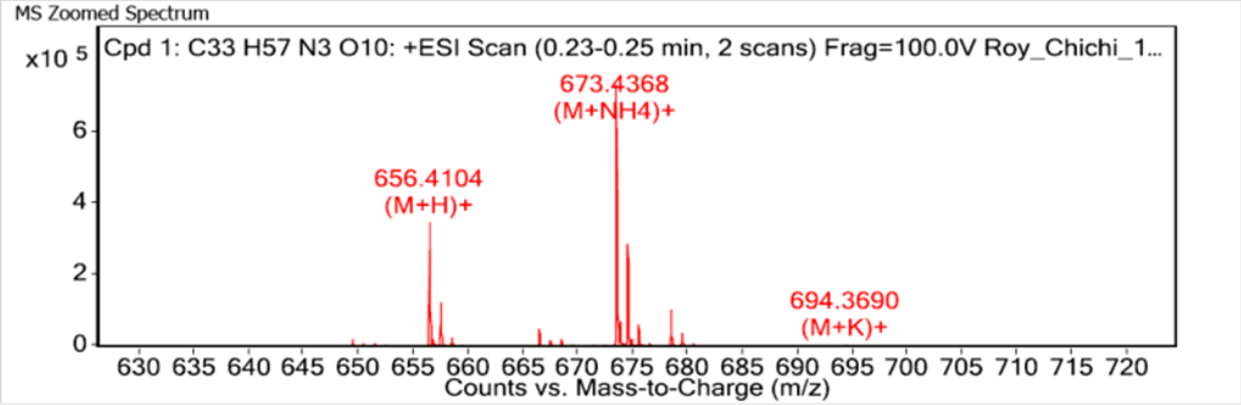


Figure S26. HRMS (ESI^+) spectrum of compound **16**.

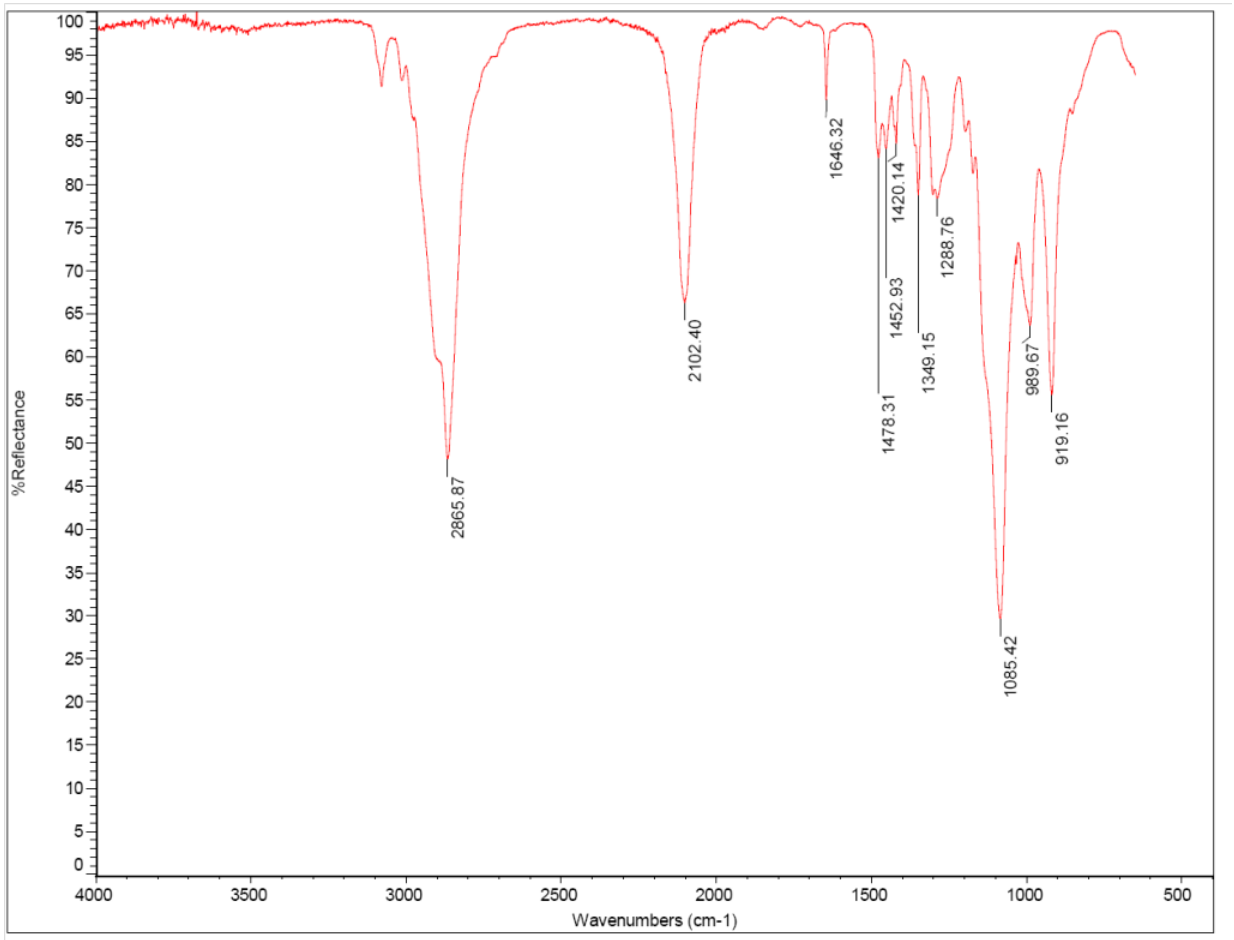
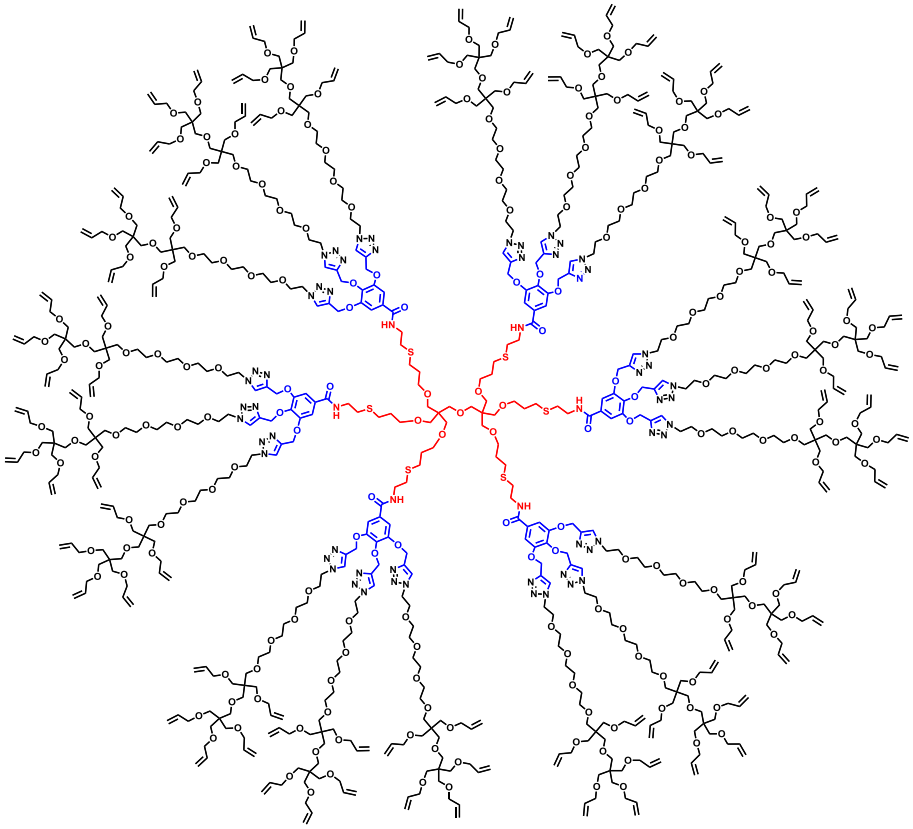


Figure S27. IR spectrum of compound **16**.



4

Synthesis of compound 4: Propargyl terminated dendrimer **1** (30 mg, 0.0117 mmol, 1eq), compound **16** (207 mg, 0.31 mmol, 27 eq.), $CuSO_4.5H_2O$ (26 mg, 0.1053 mmol, 9 eq.) and sodium ascorbate (21 mg, 0.1053 mmol, 9 eq.) were reacted together following the procedure A and was purified by column chromatography (4% MeOH in DCM as eluent) to yield compound **4** as a colourless oil in 71% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (s, 12H), 7.84 (s, 6H), 7.24 (s, 12H), 5.94 – 5.80 (m, 90H), 5.28 – 5.25 (m, 45H), 5.22 – 5.19 (m, 40H), 5.15 – 5.09 (m, 110H), 4.60 – 4.43 (m, 36H), 3.95 – 3.86 (m, 220H), 3.64 – 3.52 (m, 244H), 3.45 – 3.34 (m, 315H), 2.77 (s, 12H), 2.65 (s, 12H), 2.10 – 1.76 (m, 24H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$): δ166.7, 152, 144, 143.2, 140.2, 135.2, 130.1, 124.7, 124.6, 124.4, 116, 107.1, 72.2, 70.9, 70.9, 70.5, 70.4, 70.3, 70.02, 70, 69.7, 69.30, 66.2, 62.9, 50.1, 49.9, 45.5, 45.3, 39.6, 31.3, 29.7, 28.5.

I.R (cm^{-1}) 3800, 3664, 3647, 2980, 2971, 2929, 1462, 1381, 1250, 1151, 1077, 956.

(MALDI-TOF) m/z: calculated for $C_{730}H_{1174}N_{60}O_{211}S_6$: 14359.7980, found: 14385.100 $[M+Na]^+$

GPC ($CHCl_3$): M_n= 14490 g/mol. M_w/M_n= 1.20

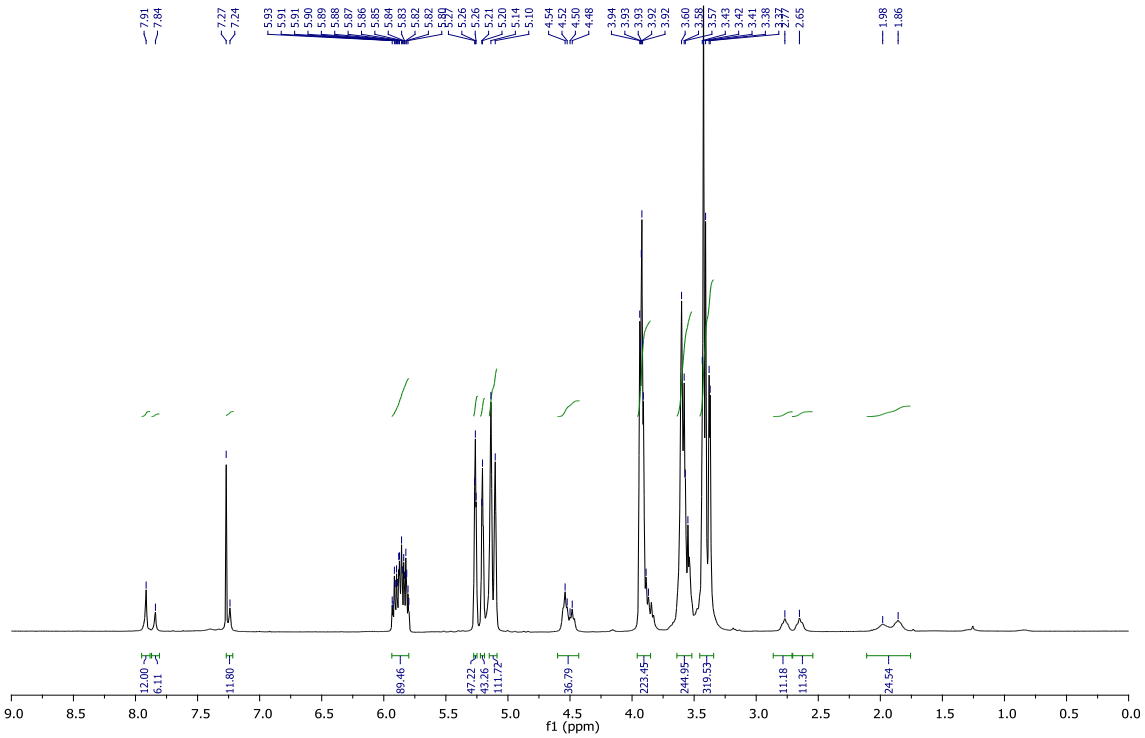


Figure S28. ^{1}H NMR spectrum of compound **4** ($CDCl_3$, 300 MHz).

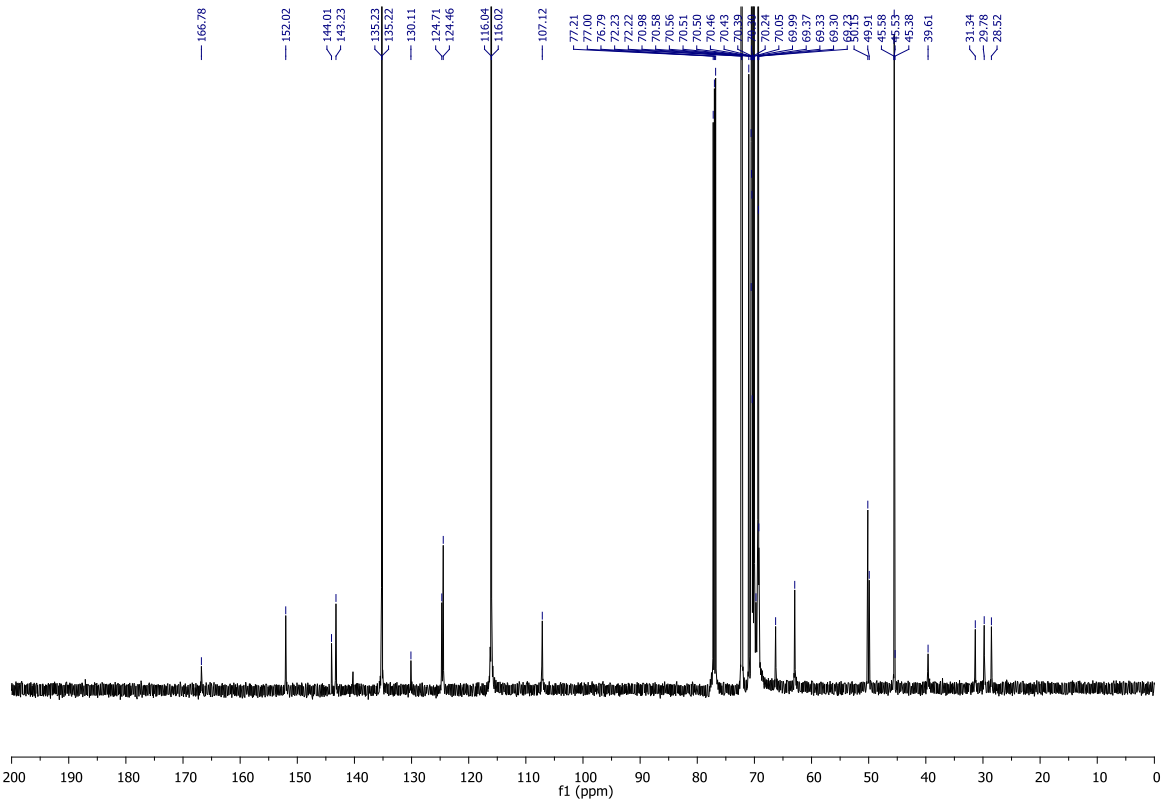


Figure S29. $^{13}C\{^{1}H\}$ NMR of compound **4** ($CDCl_3$, 151 MHz).

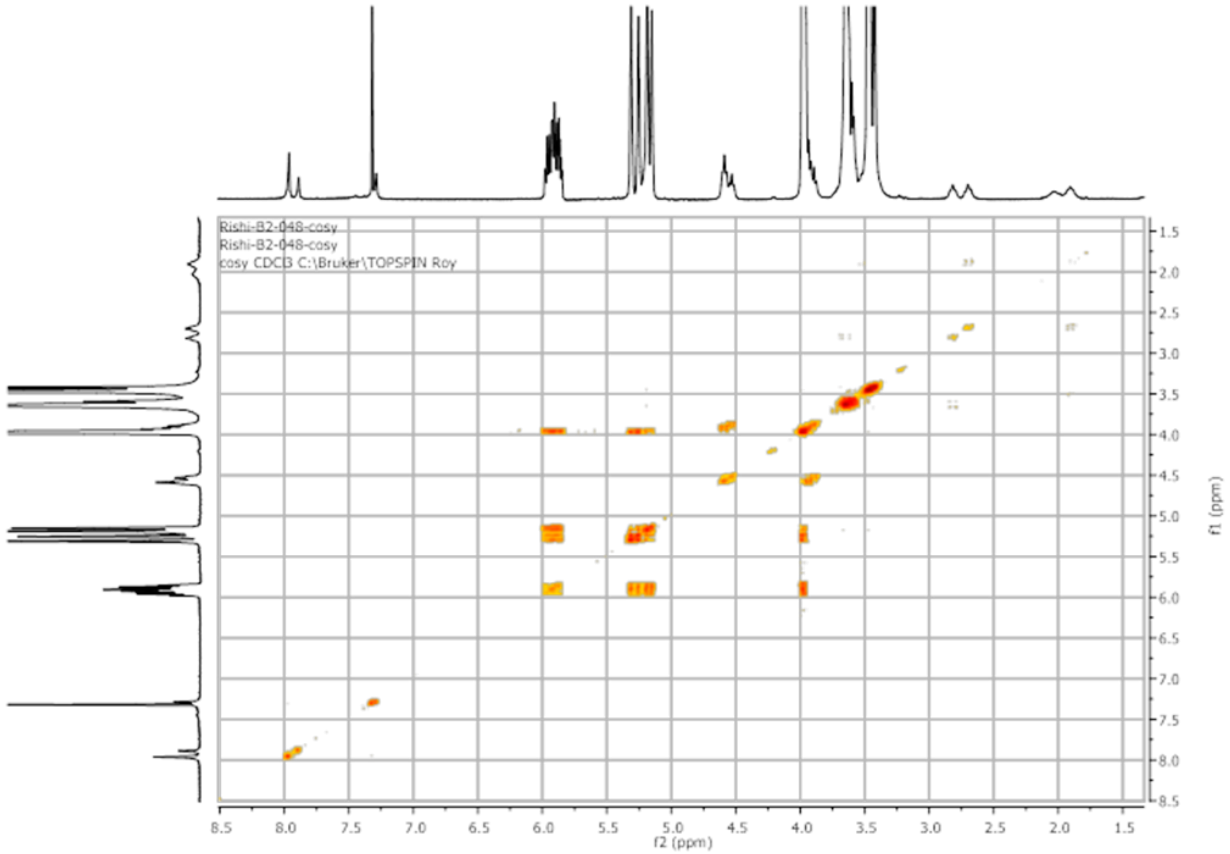


Figure S30. COSY spectrum of compound **4.**

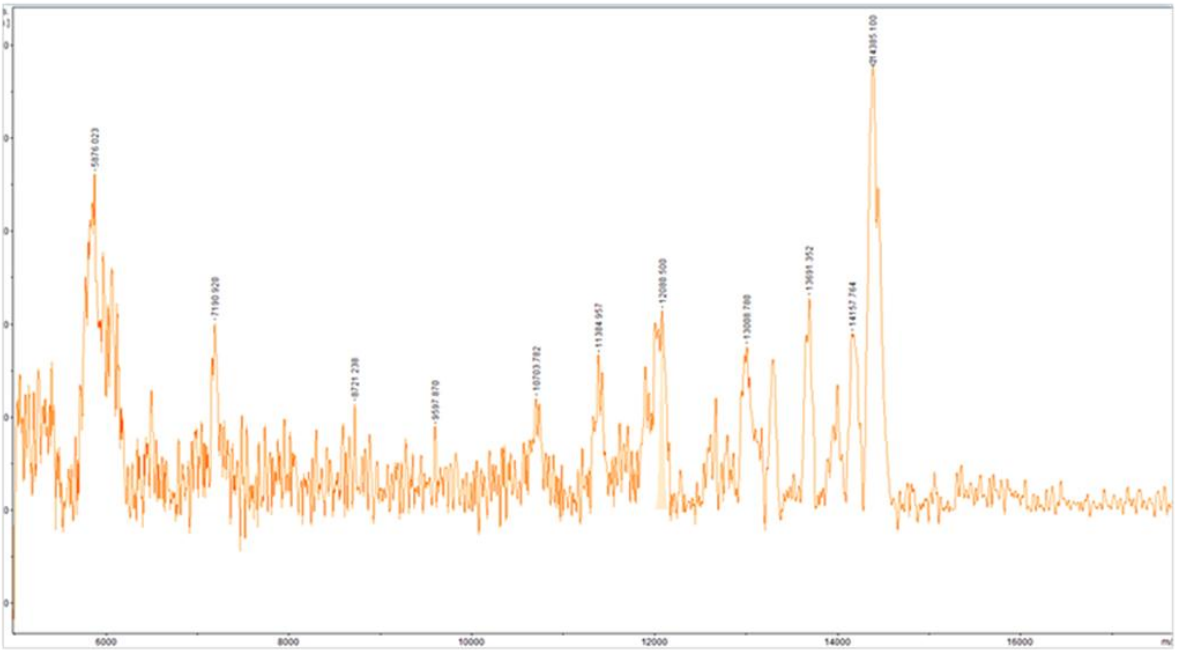
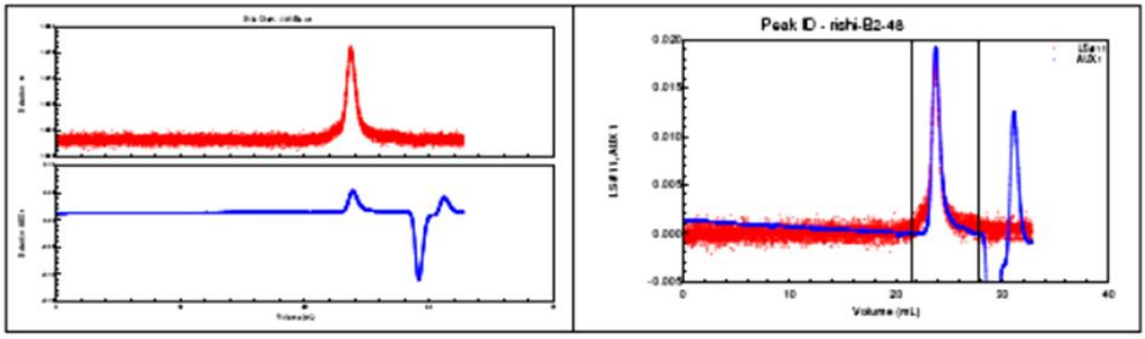


Figure S31. MALDI-TOF spectrum of compound **4**.



COLLECTION INFORMATION

Collection time	:	Thu Jun 06, 2002 03:32 AM Est (heure d'été)
Instrument type	:	DAWN EOS
Cell type	:	K5
Laser wavelength	:	690.0 nm
Solvent name	:	chloroform
Solvent RI	:	1.439
Calibration constants		
DAWN	:	8.7600e-06
» AUX1	:	2.7500e-04
AUX2	:	1.0000e-04
Flow rate	:	1.000 mL/min
Collection interval	:	0.250 sec
Number of slices	:	7863
Volume (mL)	:	21.392 - 27.704
Slices (used)	:	1516 (1152)
A2 (mol mL/g^2)	:	0.000e+00
Fit degree	:	1
Injected Mass (g)	:	1.1920e-04
dn/dc (mL/g)	:	0.092
Polydispersity(Mw/Mn)	:	1.203±0.245 (20%)
Polydispersity(Mz/Mn)	:	4.487±4.867 (108%)

Molar Mass Moments (g/mol)

Mn	:	1.449e+04 (10%)
Mw	:	1.743e+04 (17%)
Mz	:	6.500e+04 (107%)

R.M.S. Radius Moments (nm)

Rn	:	18.4 (124%)
Rw	:	21.6 (101%)
Rz	:	32.7 (67%)

Figure S32. GPC traces of compound **4**.

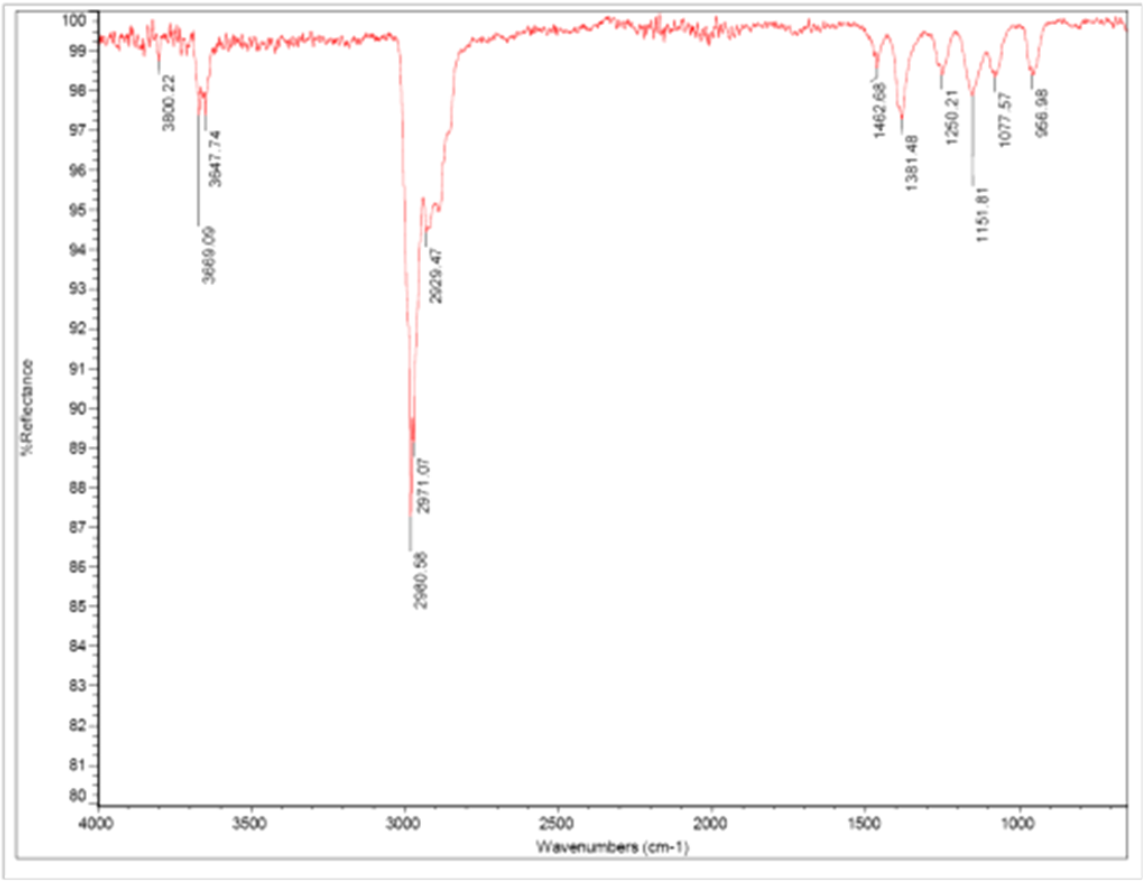
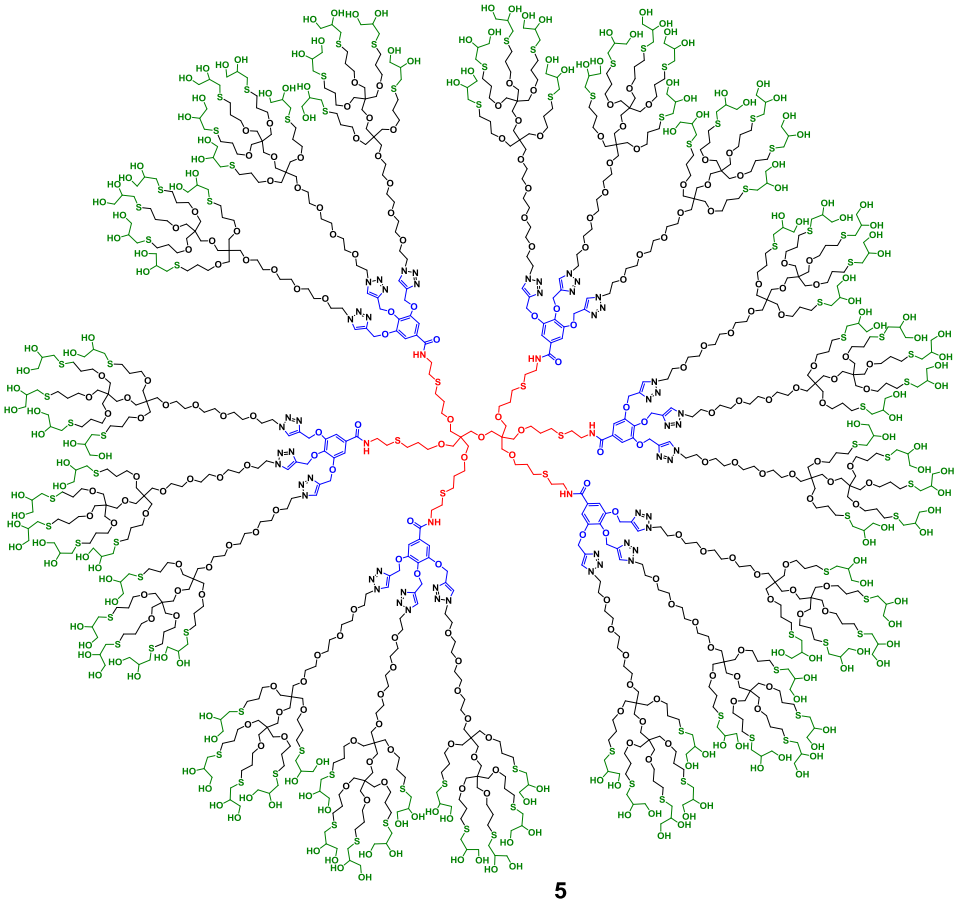


Figure S33. IR spectrum of compound **4**.



5

Synthesis of compound 5: Allyl terminated dendrimer **4** (35 mg, 0.0024 mmol, 1eq), 1-thioglycerol (0.093 ml, 1.08 mmol, 450 eq.), and AIBN (7mg, 0.043, 18 eq.) were reacted together following the procedure B and was purified by dialysis to yield compound as a colourless oil in 82% yield.

^{1}H NMR (300 MHz, CD_3OD) δ 8.18 (br s, 12H), 7.92 (br s, 6H), 7.36 (br s, 12H), 5.18 (d, *J* = 30.4 Hz, 40H), 4.59 (d, *J* = 28.8 Hz, 30H), 3.99 – 3.36 (m, 1068H), 2.75 – 2.53 (m, 370H), 1.91 – 1.76 (m, 180H).

^{13}C {^{1}H} NMR (151 MHz, CD_3OD) δ168.7, 153.5, 145.2, 144.4, 141.5, 131.2, 126.5, 108.4, 77.7, 73.8, 73.2, 72.8, 72.3, 71.9, 71.7, 71.6, 71.5, 71.3, 70.9, 70.4, 69.9, 66.0, 64.4, 63.8, 51.5, 51.4, 47.0, 41.2, 36.3, 35.2, 35.1, 33.0, 32.1, 31.5, 31.0, 30.8, 30.7, 30.5, 29.7, 23.7, 19.3, 14.4.

I.R (cm^{-1}) 3707, 3680, 3396, 2980, 2966, 2936, 2922, 2865, 1101, 1056, 1032, 1015.

HRMS (ESI^{+}) *m/z* calc. for $C_{1001}H_{1898}N_{60}O_{391}S_{96}$: 24110.1882, found: 24124.9040

Differential light scattering Hydrodynamic diameter: 8.221 (nm)

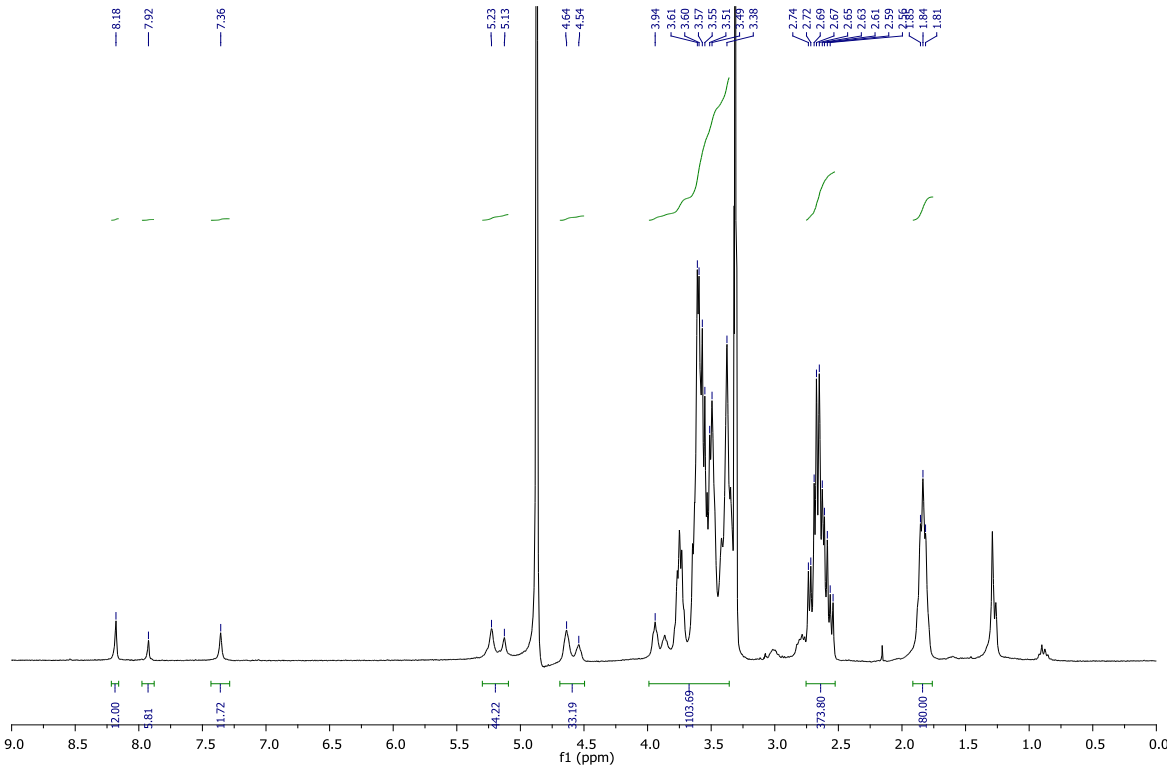


Figure S34. ^{1}H NMR spectrum of compound **5** (CD_3OD, 300 MHz).

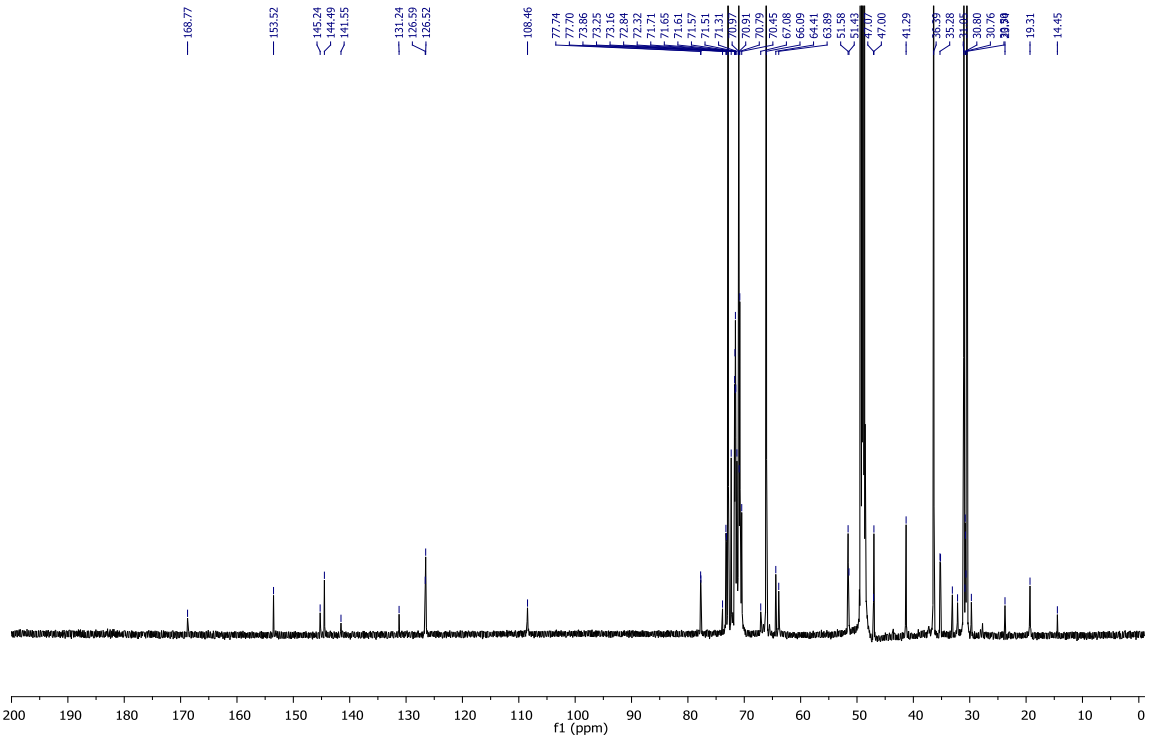


Figure S35. ^{13}C {^{1}H} NMR of compound **5** (CD_3OD, 151 MHz).

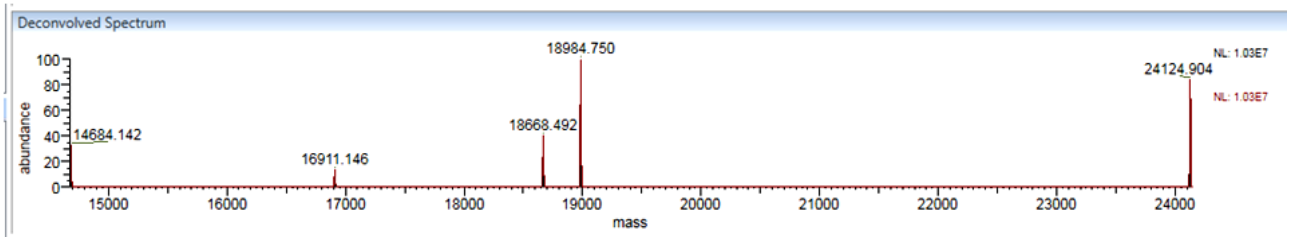


Figure S36. HRMS (ESI^+) spectrum of compound **5.**

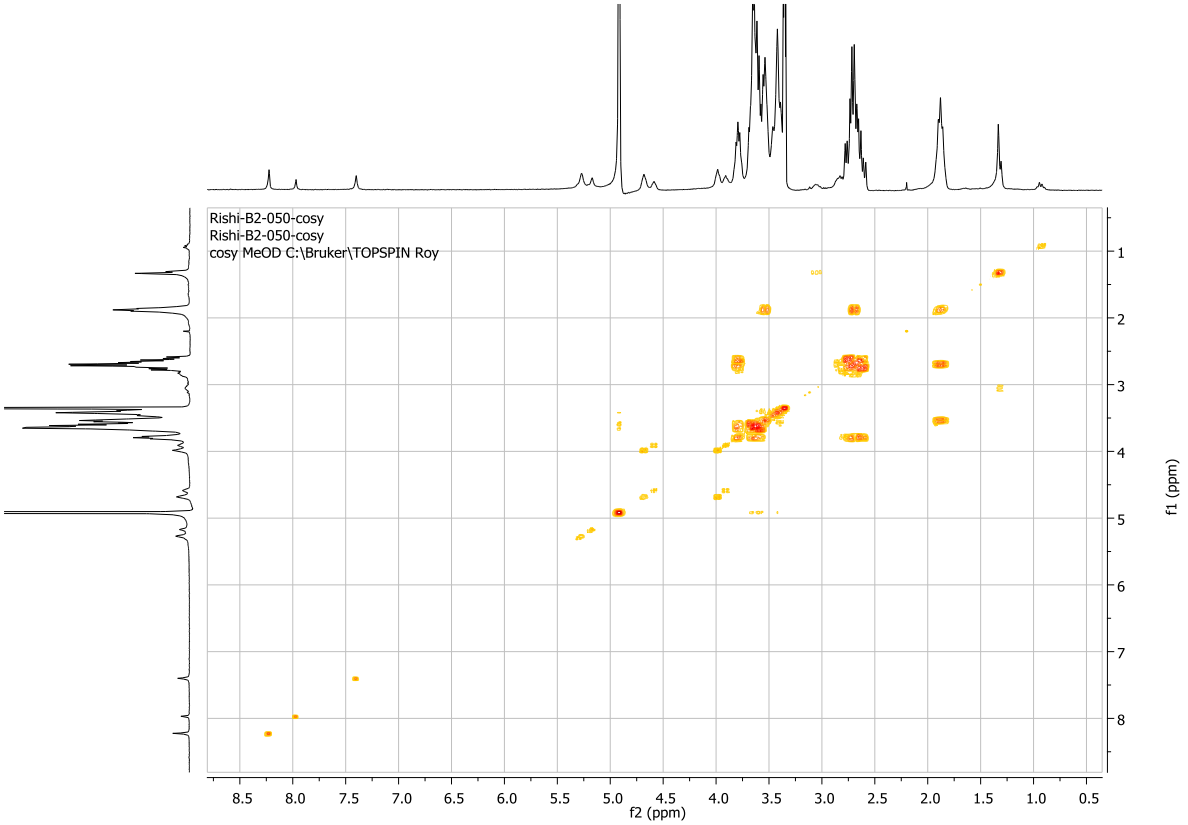


Figure S37. COSY spectrum of compound **5.**

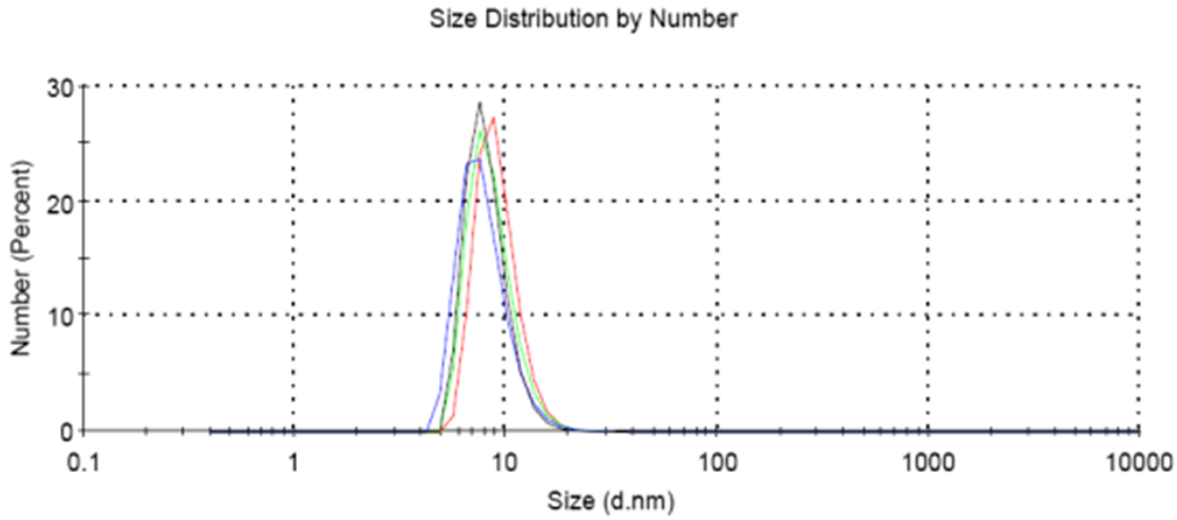


Figure S38. DLS size distribution of dendrimer **5** in methanol at 25^{o}C

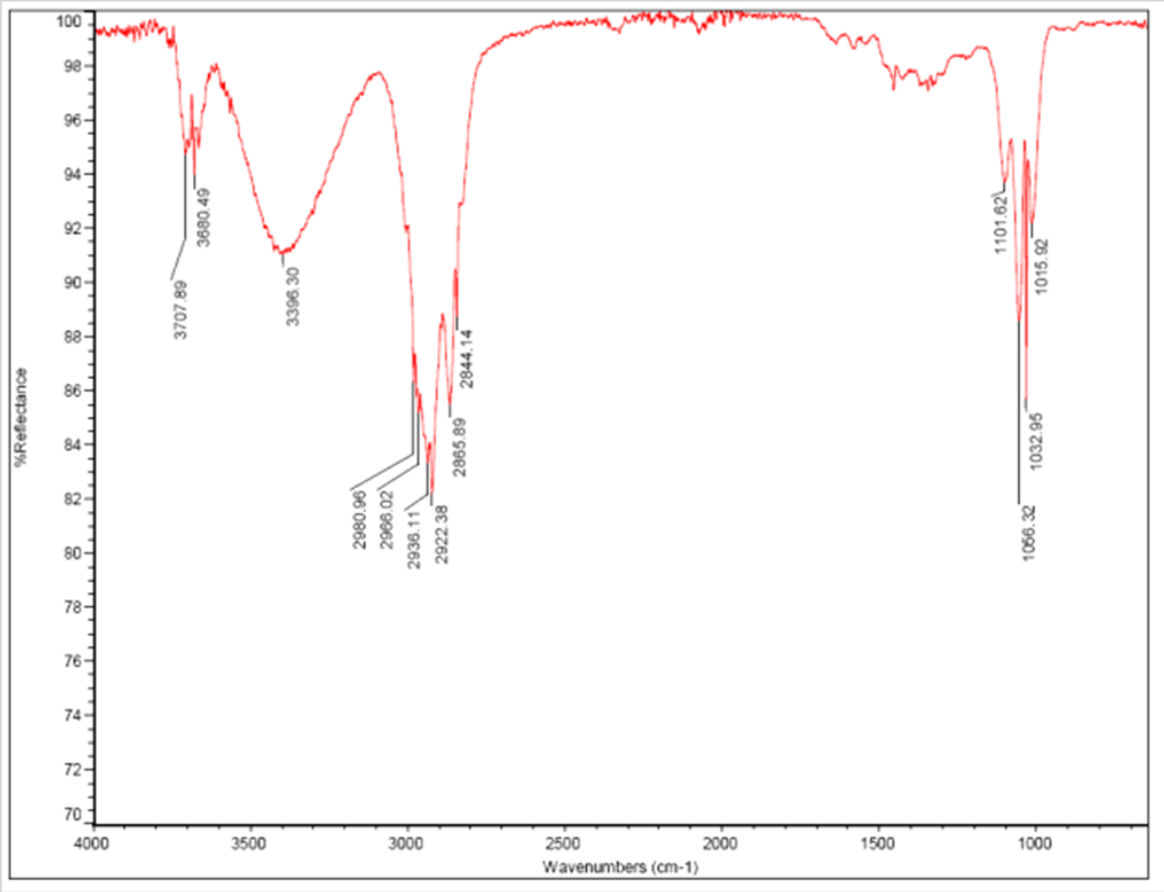
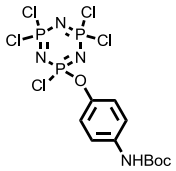


Figure S39. IR spectrum of compound **5.**



19

Synthesis of compound 19: Recrystallized hexachlorocyclotriphosphazene **17** (200.0 mg, 0.0575 mmol, 2.0 eq.) and Boc protected p-aminophenol **18** (60.2 mg, 0.0287 mmol, 1.0 eq.) were dissolved in 25 ml of anhydrous THF. Under nitrogen atmosphere, CS_2CO_3 (187.4 mg, 0.5750 mmol, 2.0 eq.) was added and the mixture was stirred at reflux temperature (66°C) for 6 hours. The solution was filtered and washed with DCM. The filtrate was concentrated under reduced pressure. Column chromatography on silica (DCM/Hexanes 1:9 to 7:3) afforded the desired compound **19** (75.0 mg, 0.0144 mmol, 50%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ ppm 7.40 (d, 2H, J = 9.0 Hz,), 7.18 (d, 2H, J = 9.0 Hz,), 6.62 (s, 1H,), 1.52 (s, 9H,).

^{13}C {^{1}H} NMR ($CDCl_3$, 75 MHz): δ ppm 152.5, 144.4, 137.0, 121.8, 119.5, 80.9, 28.3.

^{31}P NMR ($CDCl_3$, 121.5 MHz): δ ppm 22.4 (d, 2P, 2J (P,P) = 59.3 Hz, PCl_2), 12.8 (t, 1P, 2J(P,P) = 59.3 Hz, P-O).

HRMS (ESI^{+}) *m/z* calc. for $C_{11}H_{14}C_{l5}N_4O_3P_3$ = 540.8614 $[M+Na]^{+}$; found 540.8628.

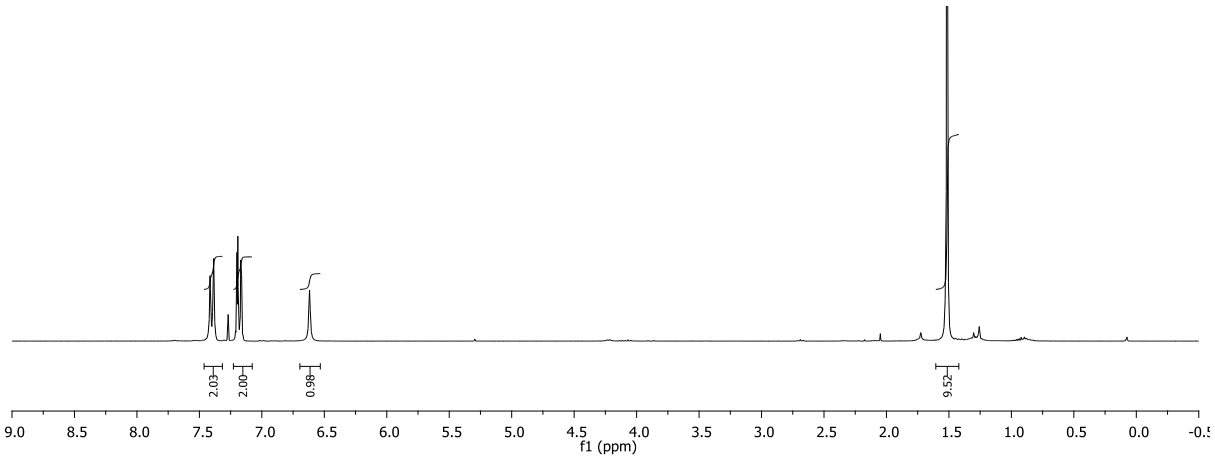


Figure S40.^{1}H NMR spectrum of compound **19** ($CDCl_3$, 300 MHz).

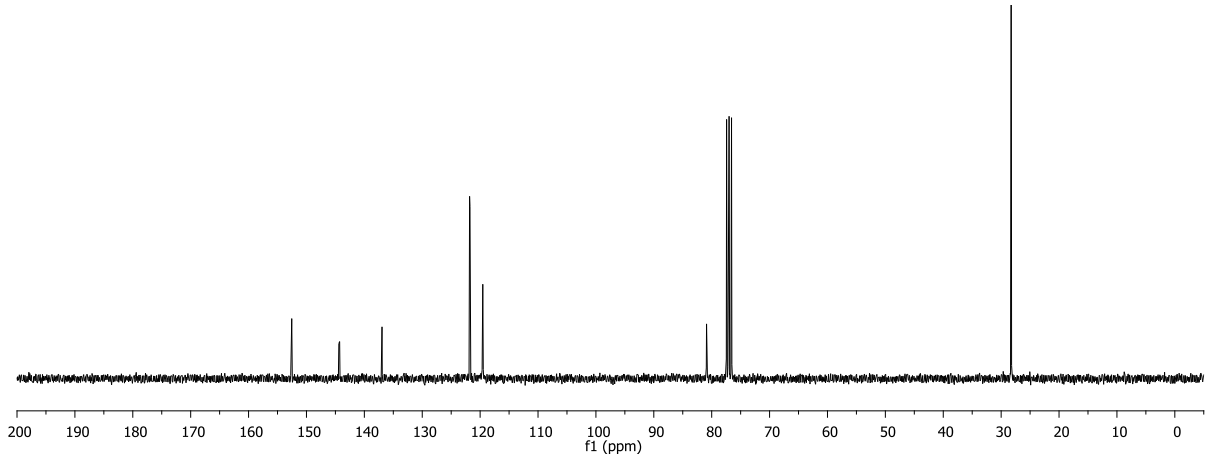


Figure S41. $^{13}C\{^{1}H\}$ NMR of compound **19** ($CDCl_3$, 75 MHz).

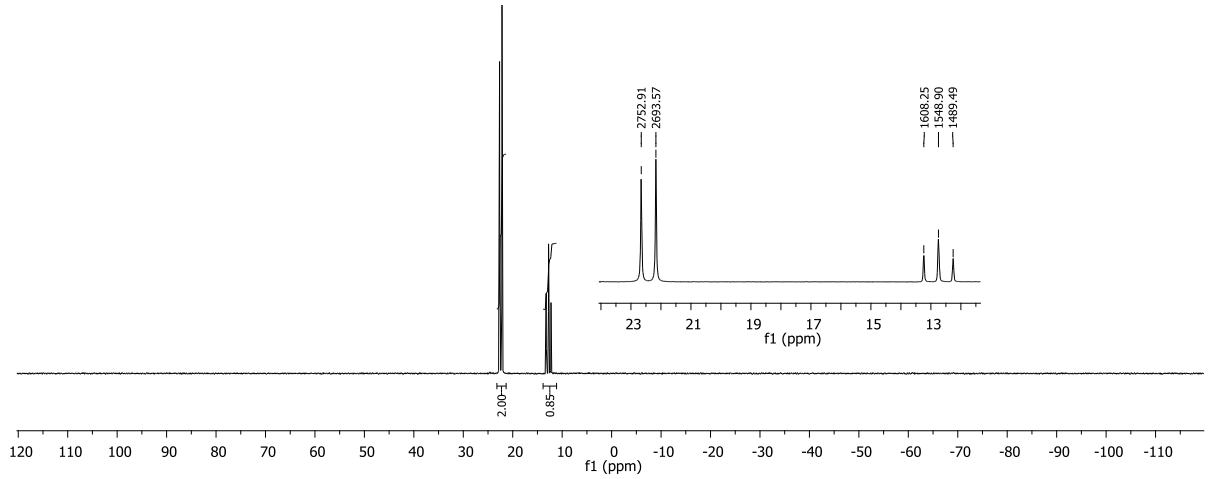
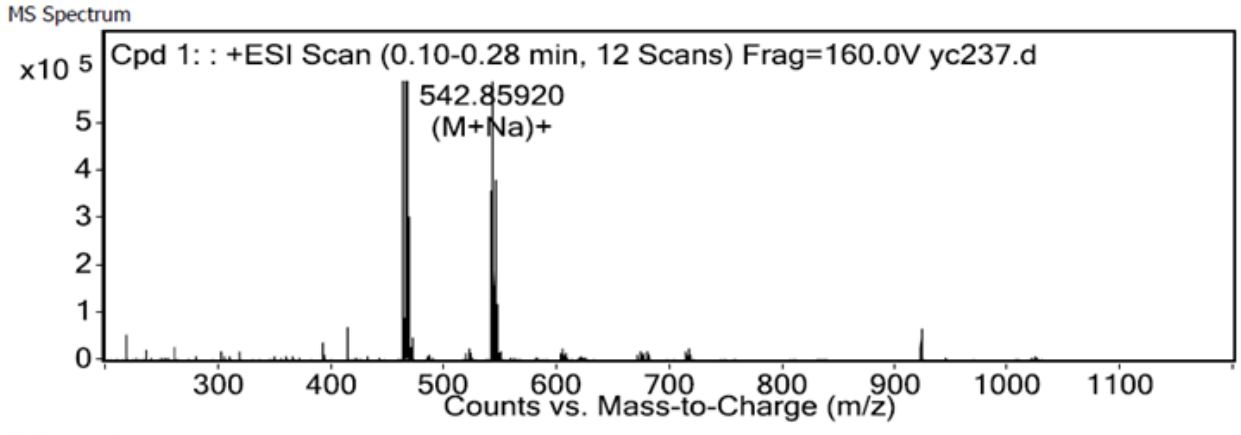
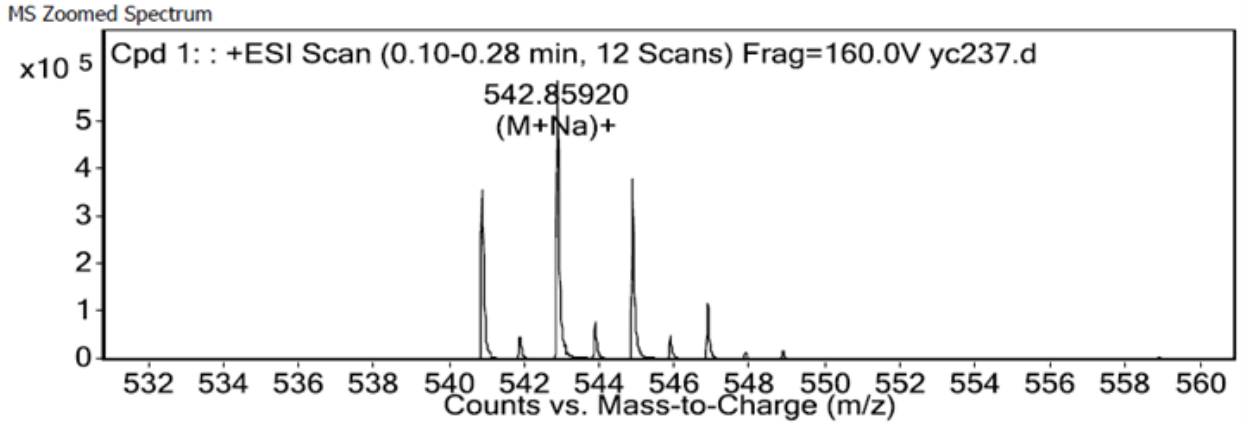


Figure S42. ^{31}P NMR spectrum of compound **19** ($CDCl_3$, 122 MHz).

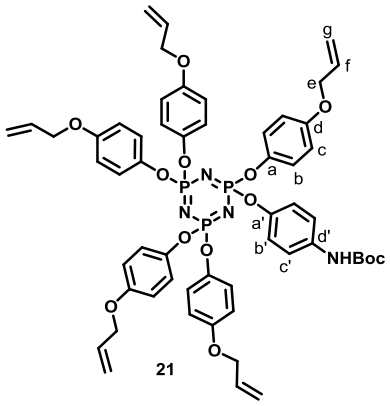




MS Spectrum Peak List

Ion	Ion Formula	Abund	*Expe. m/z*	*Calc. m/z*	Diff(ppm)
(M+Na)+	C11H14Cl5N4NaO3P3	366441.2	540.86277	540.86136	2.61

Figure S43. HRMS (ESI^+) spectrum of compound **19**.



Synthesis of compound 21: To Boc protected amine monofunctionalized cyclotriphosphazene (**19**) (240 mg, 0.46 mmol, 1 eq) and p-allyloxyphenol **20** (692.1 mg, 4.6 mmol, 10 eq) in THF (40 ml) was added dry cesium carbonate (2.3 g, 6.9 mmol, 15 eq). The solution was stirred and refluxed for 16h. Upon completion, reaction mixture was diluted with EtOAc (50 ml) and washed with brine and water. The mixture was dried with anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. Silica gel column chromatography was performed (Hexane/AcOEt 5% to 25%) to obtain pure desired compound **21** in 88% yield.

Rf= 0.57, Hex/AcOEt65:35
^{1}H NMR ($CDCl_3$, 300 MHz,**) :** δ 7.16 (d, 2H, $^{3}J_{c',b'}$=8.9 Hz, H-c'), 6.84-6.79 (m, 12H, H-b', H-c), 6.71-6.67 (m, 10H, H-b), 6.41 (s, 1H, NH), 6.11-5.97 (m, 5H, H-f), 5.44-5.37 (m, 5H, H-g) 5.30-5.26 (m, 5H, *J*=1.3 Hz,*J*=10.5 Hz, H-g), 4.49-4.45 (m, 10H, H-e), 1.51(s, 9H, Boc) ppm.
^{13}C {^{1}H} NMR ($CDCl_3$, 75 MHz): δ 155.6, 152.7, 144.4, 135.2, 133.3, 133.2, 121.9, 121.5, 119.5, 117.8, 115.2, 80.6, 76.7, 69.2, 28.4.
^{31}P NMR ($CDCl_3$, 75 MHz)**:** 9.89 (t, *J* = 15.9 Hz, 3P).
HRMS (ESI^{+}) *m/z* calc. for $C_{56}H_{59}N_4O_{13}P_3$, 1089.3364 $[M+H]^+$, found 1089.3372.

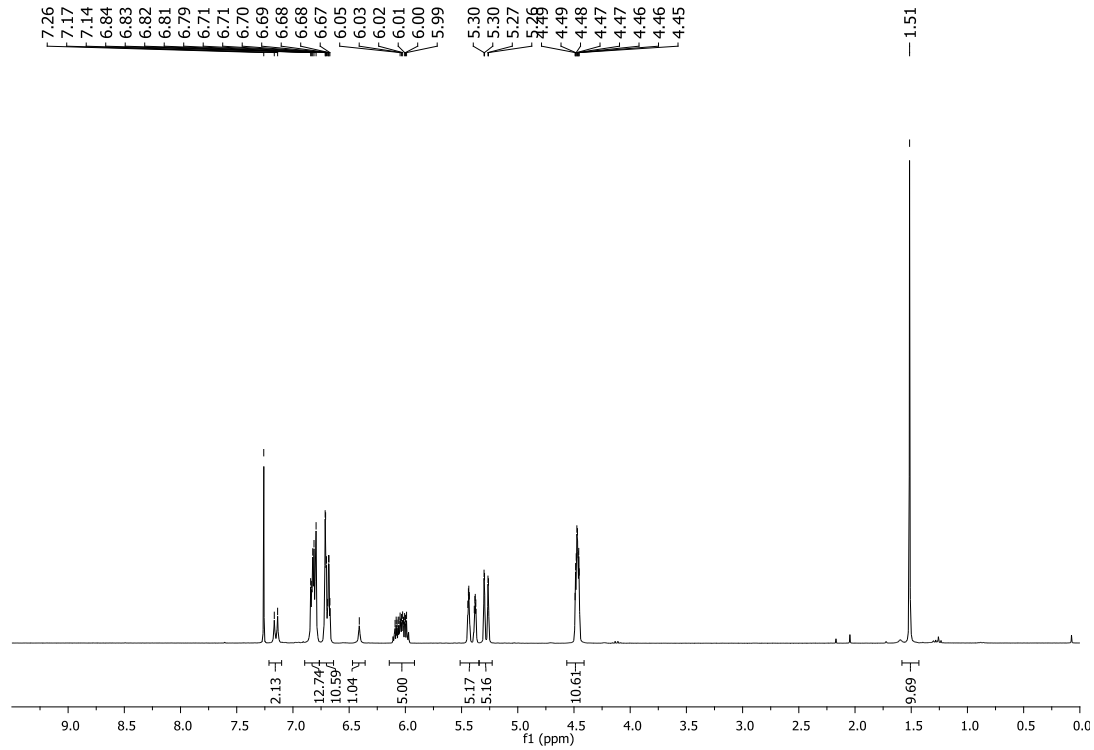


Figure S44. ^{1}H NMR spectrum of compound **21**($CDCl_3$, 300 MHz).

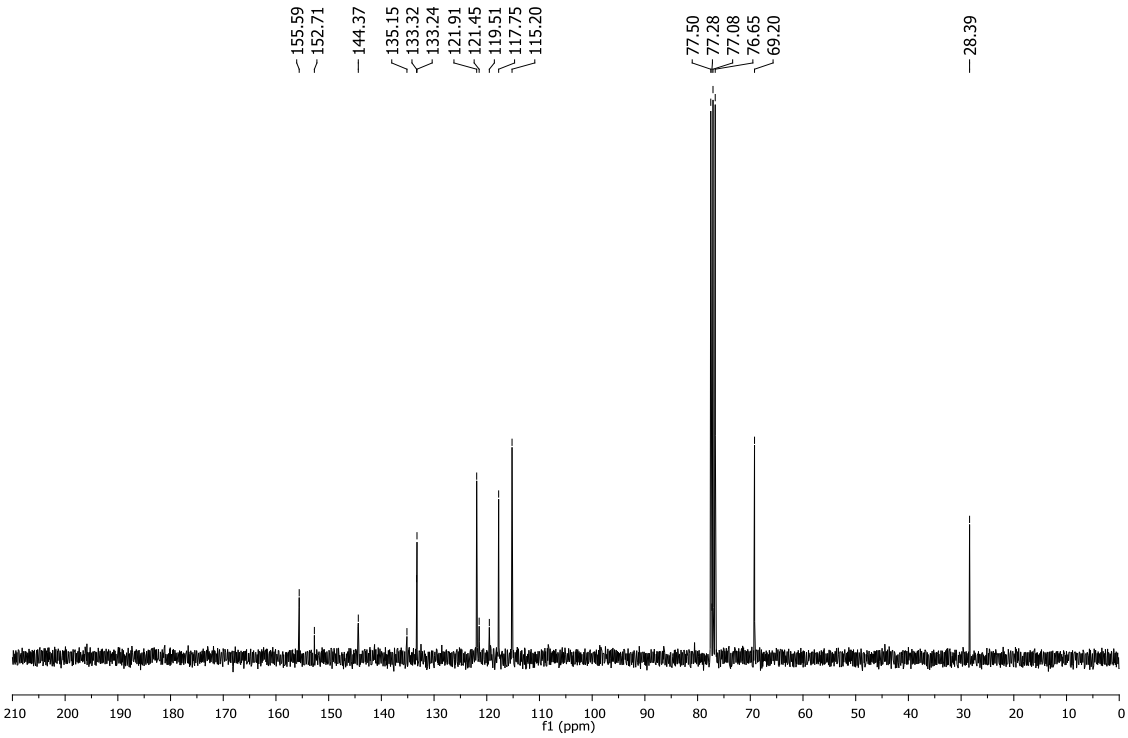


Figure S45. $^{13}C\{^{1}H\}$ NMR of compound **21** ($CDCl_3$, 75 MHz).

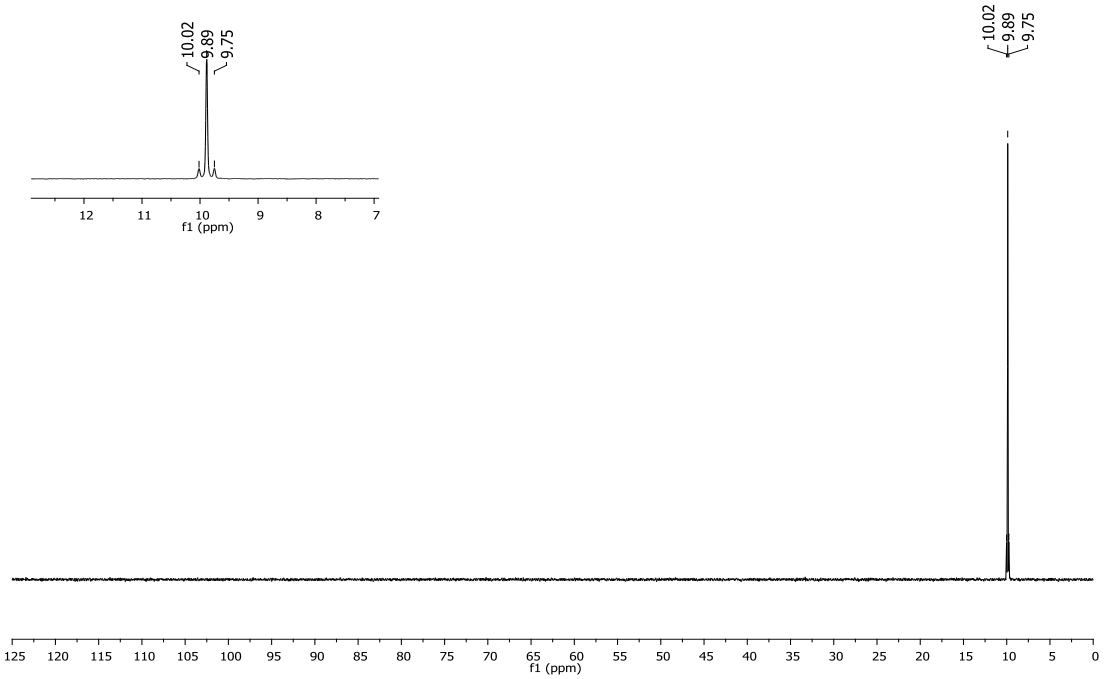


Figure S46. ^{31}P NMR spectrum of compound **21** ($CDCl_3$, 122 MHz).

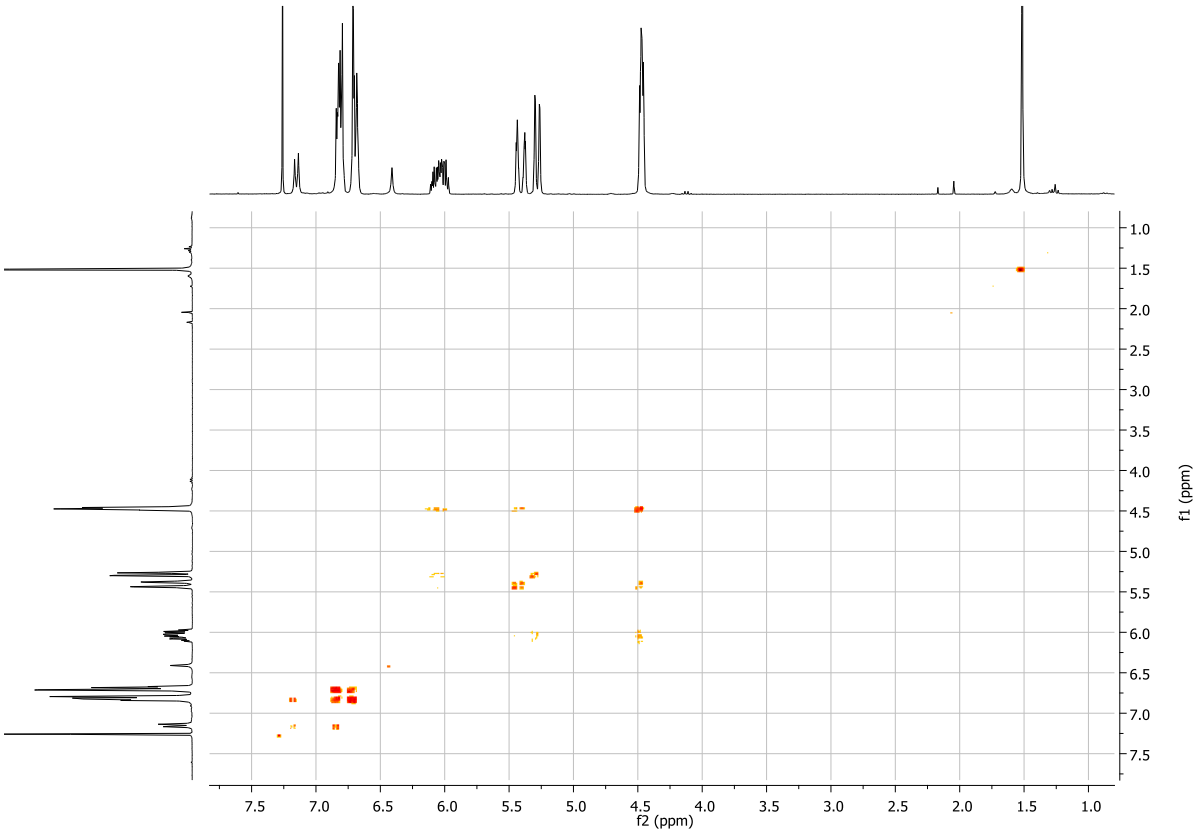


Figure S47. COSY spectrum of compound **21.**

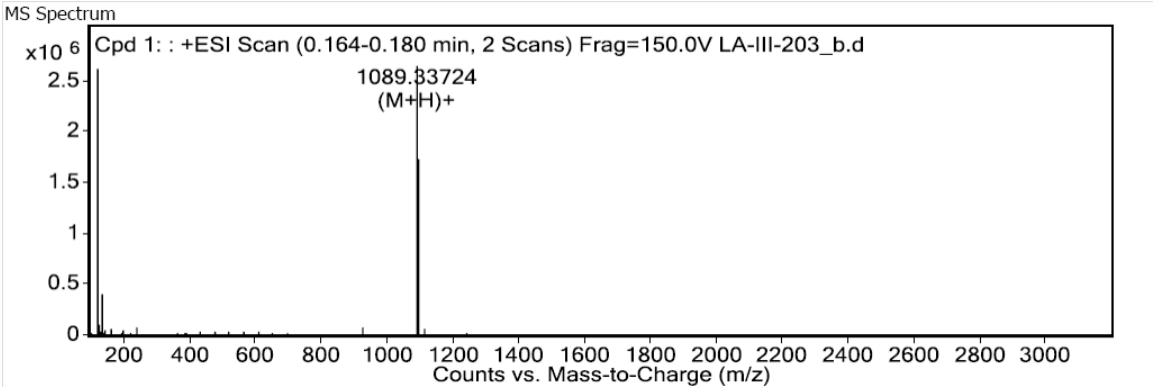
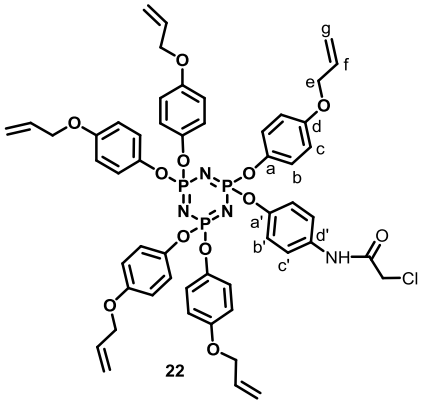


Figure S48. HRMS (ESI^+) spectrum of compound **21**.



Synthesis of compound 22: To a stirring solution of compound **21** (294 mg, 0.27 mmol) in 3ml DCM at 0^oC was added TFA (4ml) and the reaction mixture was stirred for 4h at room temperature. Upon completion solvent was removed followed by co-evaporation with toluene 3-4 times. Reaction mixture was dried under vacuum. To the TFA salt was added DIPEA (, 1.3 mmol, 4.8 eq) and DCM (3 ml) followed by addition of chloroacetyl chloride (85 µL, 1.1 mmol, 4 eq) slowly. The solution was stirred at room temperature overnight. After 16 h, the reaction mixture was evaporated, diluted with EtOAc (50 ml) and washed with HCl (1M) and water. The mixture was dried with anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. Purification by silica gel column (Hexane/ EtOAc 10% to 40%) afforded desired compound **22** (220.8 mg, 76%).

Rf= 0.32, Hex/AcOEt65:35

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.19 (s, 1H, NH),7.36 (d, 2H, $^3J_{c',b'}$=8.9 Hz, H-c'), 6.92-6.81 (m, 12H, H-b', H-c), 6.75-6.70 (m, 10H, H-b), 6.10-5.99 (m, 5H, H-f), 5.45-5.39 (dd, 5H,*J*=1.9 Hz, *J*=10 Hz, H-g)5.31-5.28 (dd, *J*=1.4 Hz, *J*=17.2 Hz, 5H, H-g), 4.49-4.47 (m, 10H, H-e), 4.18 (s, 2H, $C\underline{H}_2Cl$) ppm.

^{13}C {^{1}H } NMR ($CDCl_3$, 75 MHz): δ =163.7, 155.7, 147.8, 144.3, 133.3, 133.2, 121.9, 121.6, 121.2, 117.8, 115.3, 115.2, 76.7, 69.2, 69.2, 42.9.

^{31}P NMR ($CDCl_3$, 121.5 MHz): 9.89 (t, *J* =19.9 Hz, 3P).

HRMS (ESI^+) *m/z* calc. for $C_{53}H_{52}ClN_4O_{12}P_3$, 1065.2556 $[M+H]^+$, found 1065.2561, $[M+Na]^+$, 1087.2388 found.

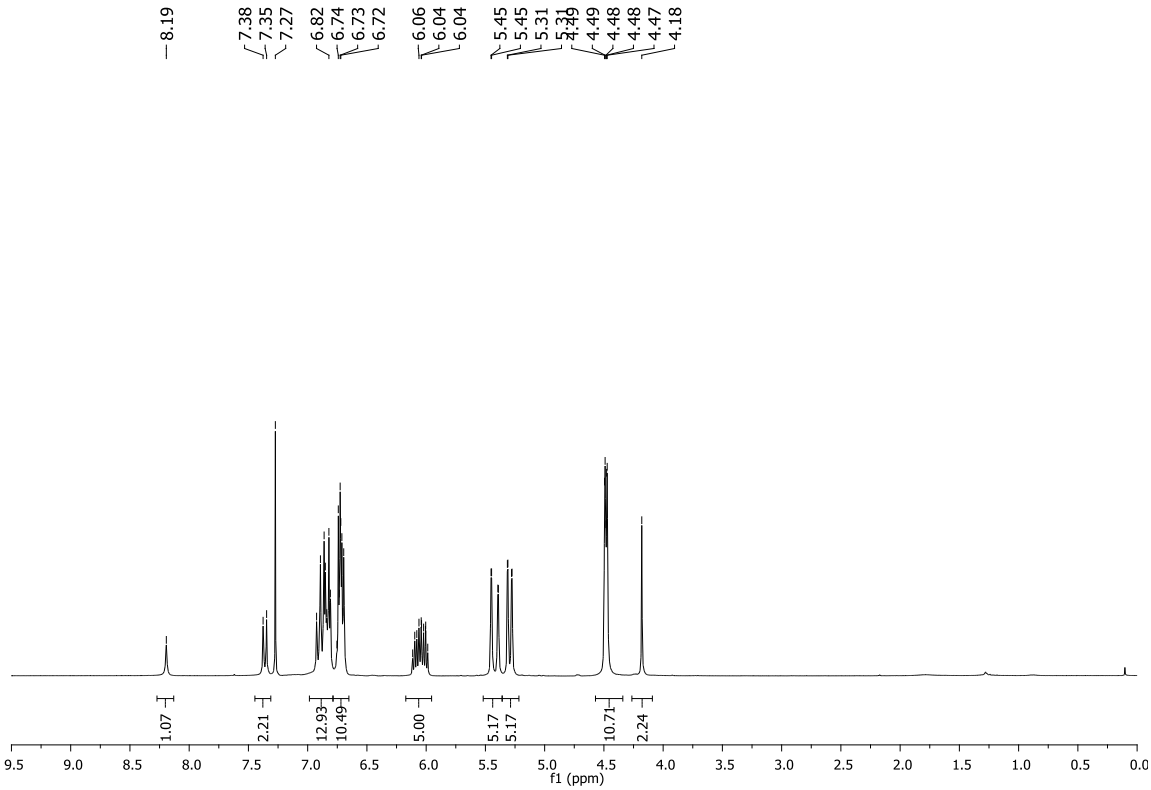


Figure S49. ^{1}H NMR spectrum of compound **22** ($CDCl_3$, 300 MHz).

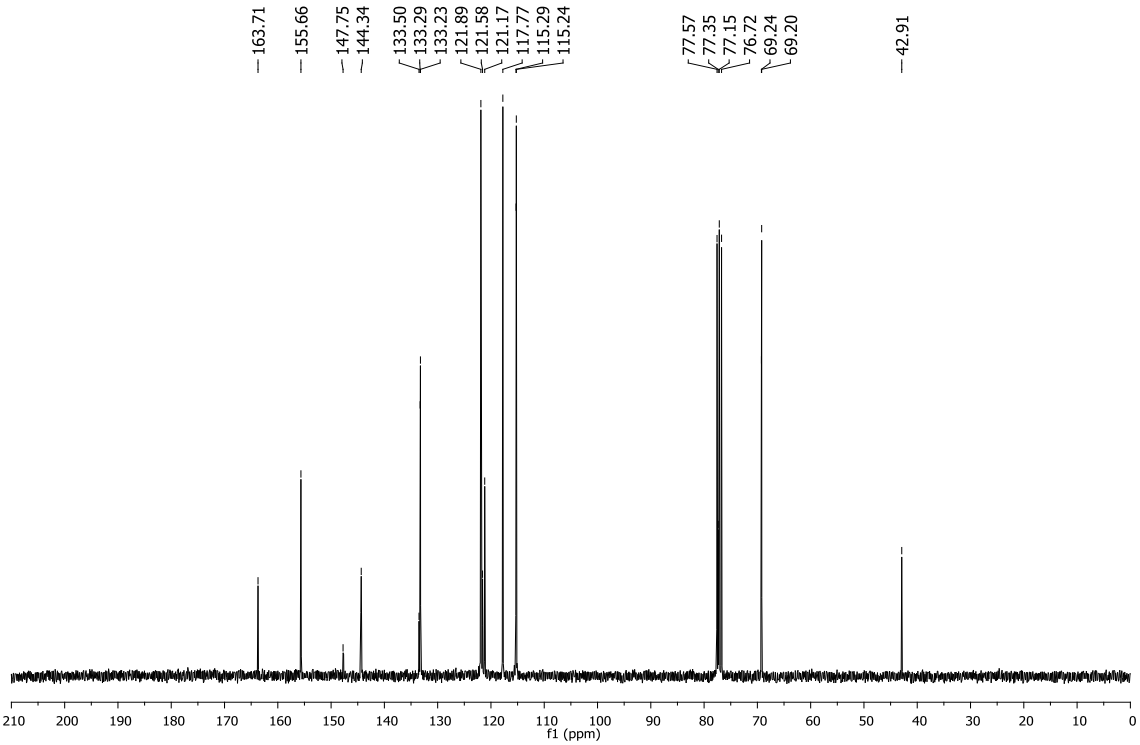


Figure S50. ^{13}C {^{1}H} NMR of compound **22** ($CDCl_3$, 75 MHz).

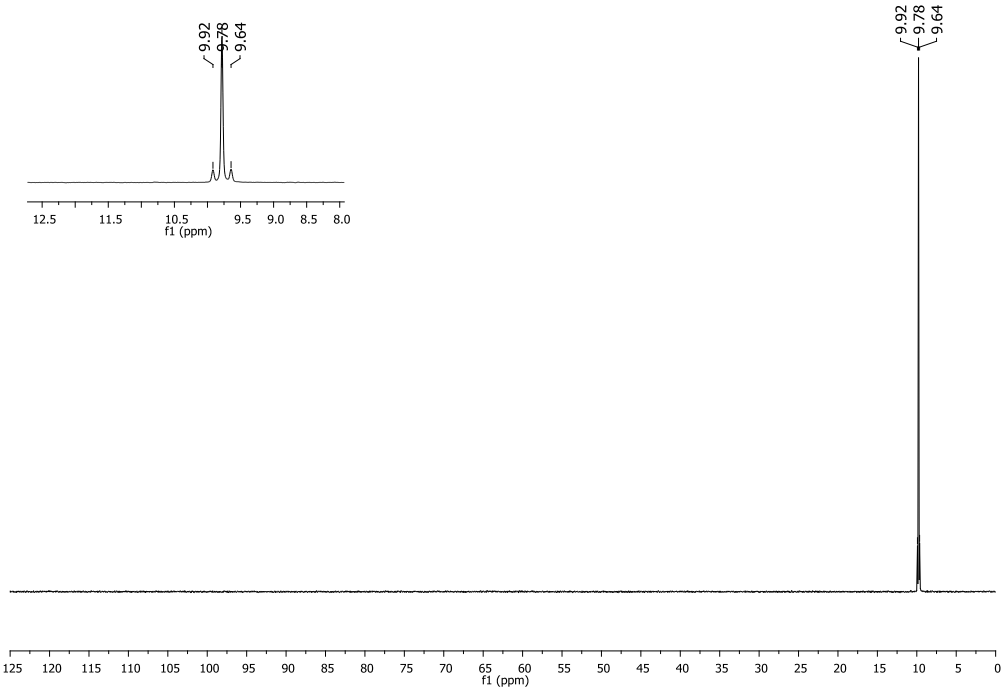


Figure S51. ^{31}P NMR spectrum of compound **22** ($CDCl_3$, 122 MHz).

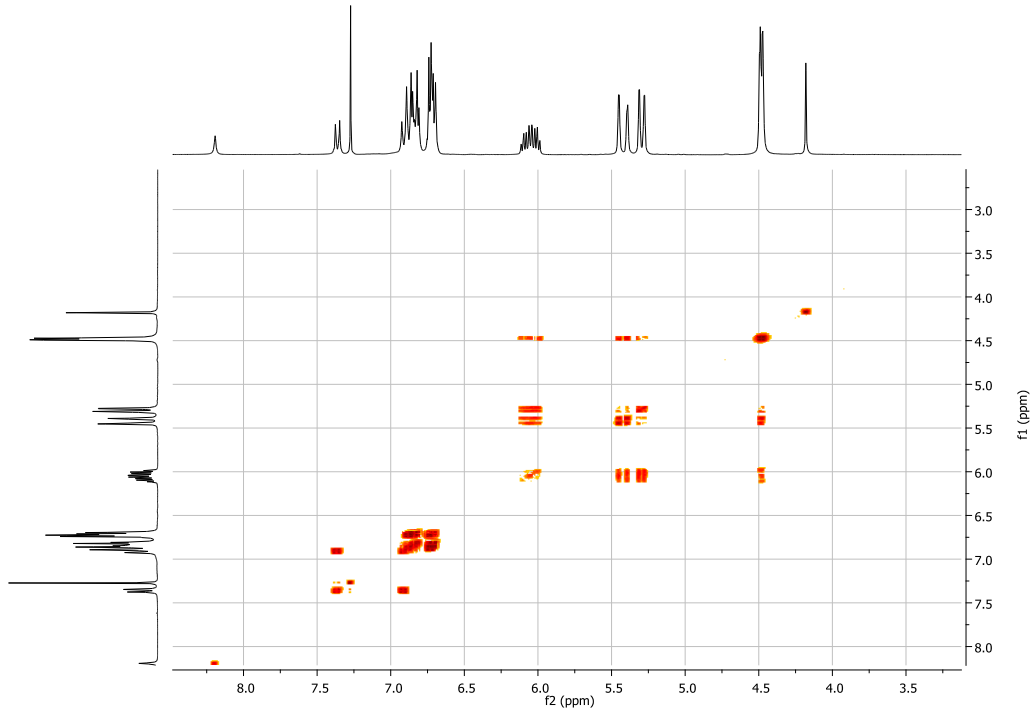
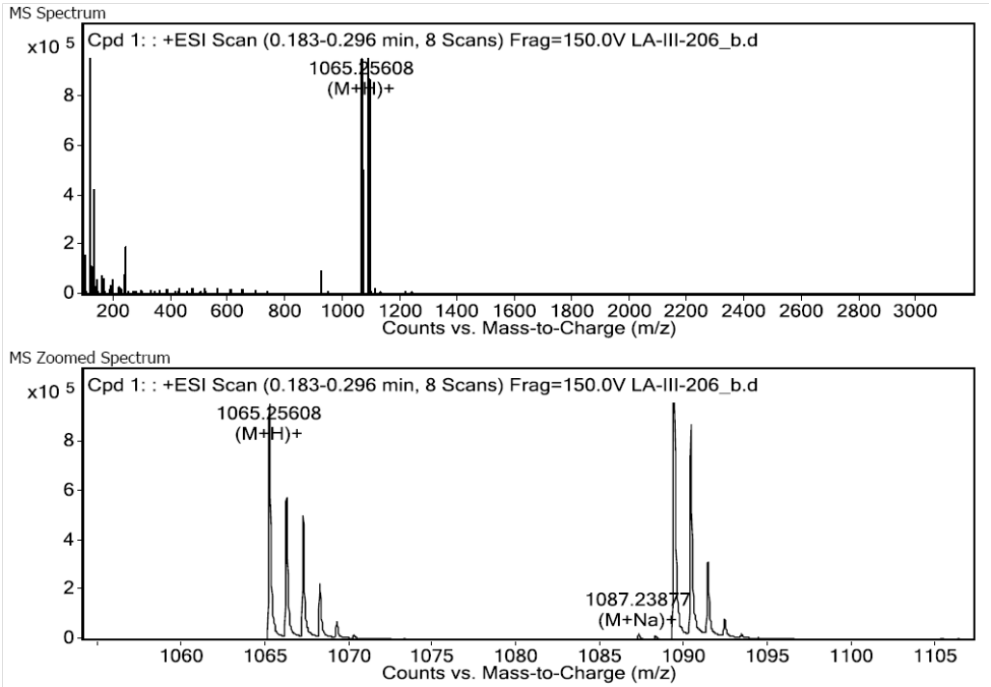


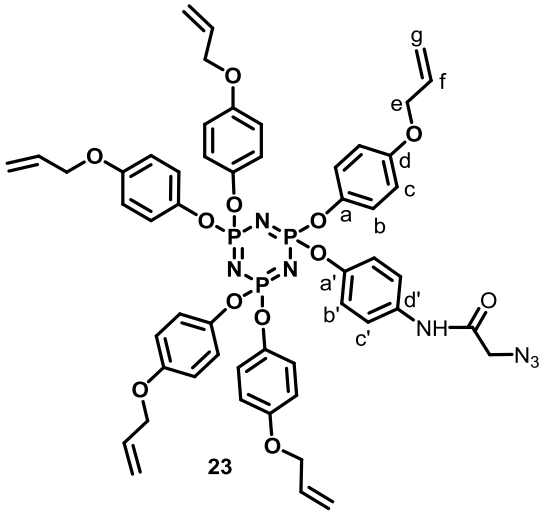
Figure S52. COSY spectrum of compound **22.**



MS Spectrum Peak List

Ion	Ion Formula	Abund	*Expe. m/z*	*Calc. m/z*	Diff(ppm)
(M+H)+	C53H53ClN4O12P3	953097.6	1065.25608	1065.25559	0.46
(M+Na)+	C53H52ClN4NaO12P3	25132.6	1087.23877	1087.23753	1.14

Figure S53. HRMS (ESI^+) spectrum of compound **22**.



Synthesis of compound 23: To a solution of compound **22** (220 mg, 0.21 mmol, 1.0 eq) in DMF (3 ml) under nitrogen atmosphere were added sodium azide (40.3 mg, 0.62 mmol, 3.0 eq) and sodium iodide (6.2 mg, 0.04 mmol, 0.2 eq). The suspension was stirred and heated at 50-60 °C overnight. After 12 h, the solvent was removed under vacuum. The reaction mixture was diluted with EtOAc (50 ml) and washed with water (4 × 40 ml) dried and evaporated. Crude mixture was purified using silica gel column chromatography (hexane/AcOEt 10% to 70%) afforded desired compound **23** (109.3 mg, 81%).

Rf= 0.84, DCM/MeOH96:4

^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.97 (s, 1H, NH), 7.35 (d, 2H,*J*=8.9 Hz, H-c'), 6.90-6.79 (m, 12H, H-b', H-c), 6.74-6.68 (m, 10H, H-b), 6.09-5.99 (m, 5H, H-f), 5.45-5.38 (m, 5H,H-g) 5.30-5.26 (dd, *J*=1.1 Hz, *J*=10.3 Hz, 5H, H-g), 4.48-4.46 (m, 10H, H-e), 4.12 (s, 2H, $C\underline{H}_2N_3$).

^{13}C {^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.4, 155.6, 147.4, 144.3, 133.5, 133.3, 133.2, 121.8, 121.5, 121.0, 117.7, 115.2, 76.7, 69.2, 69.1, 52.9.

^{31}P NMR ($CDCl_3$, 121.5 MHz)**:** 9.89 (t, *J* =19.9 Hz, 3P).

HRMS (ESI^{+}) *m/z* calc. for $C_{53}H_{52}ClN_4O_{12}P_3$, 1072.2960 $[M+H]^{+}$, found 1072.2971.

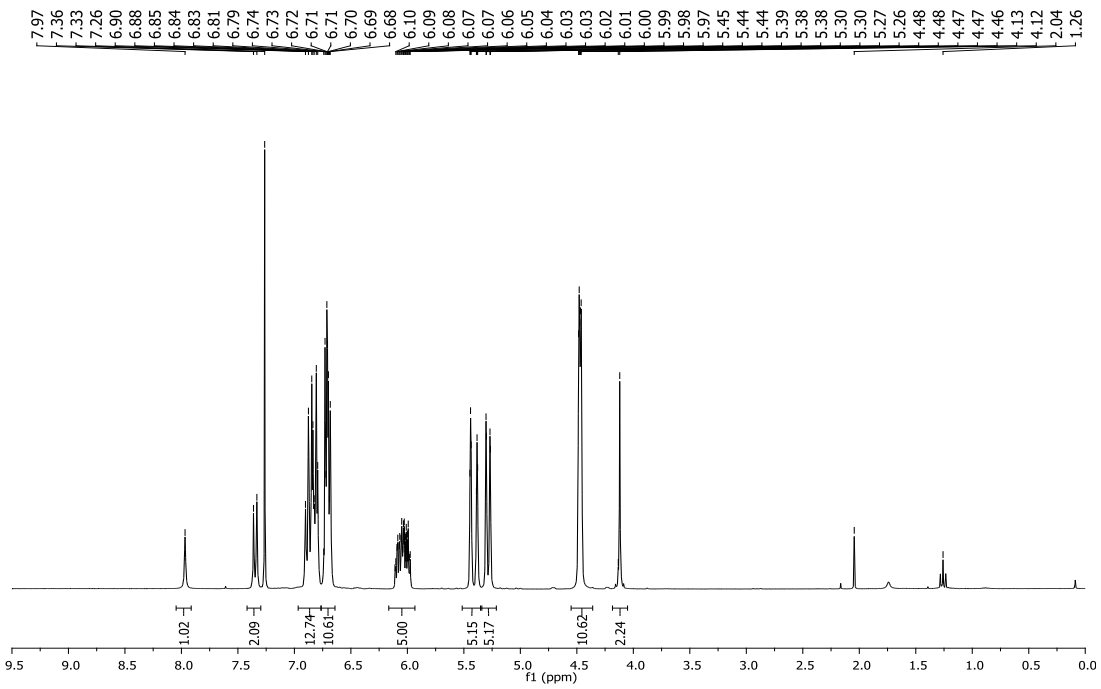


Figure S54. ^{1}H NMR spectrum of compound **23** ($CDCl_3$, 300 MHz).

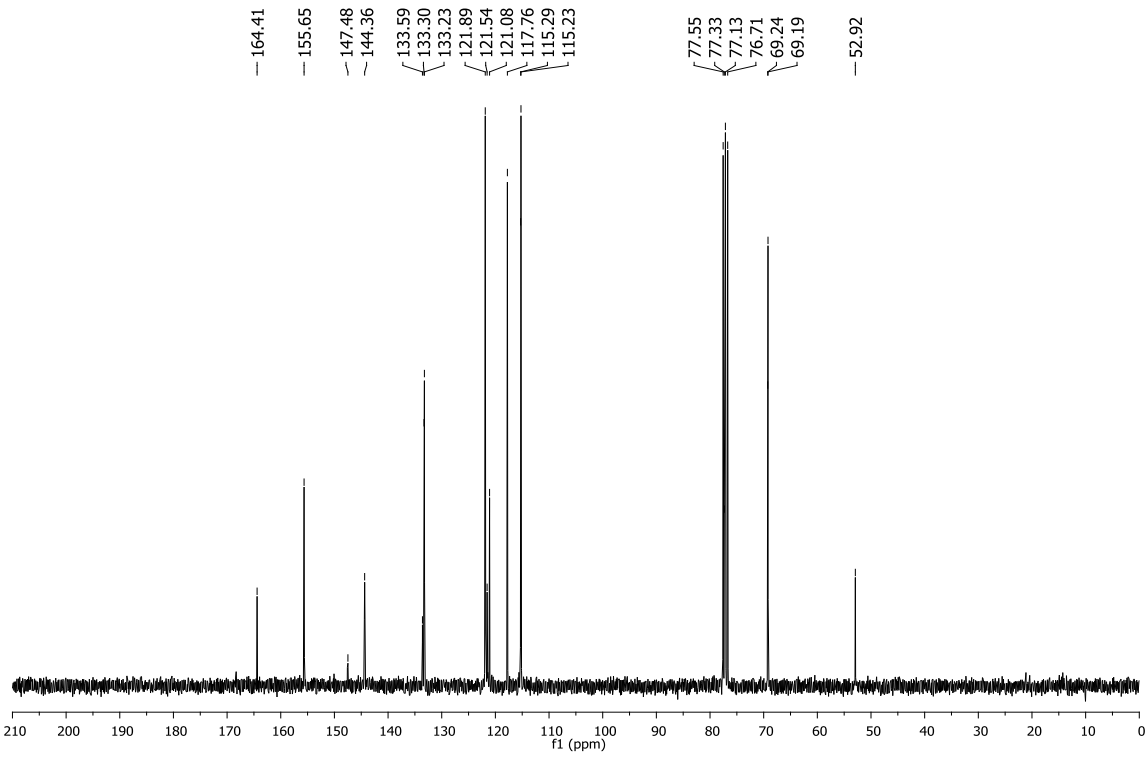


Figure S55. ^{13}C {^{1}H} NMR spectrum of compound **23** ($CDCl_3$, 75 MHz).

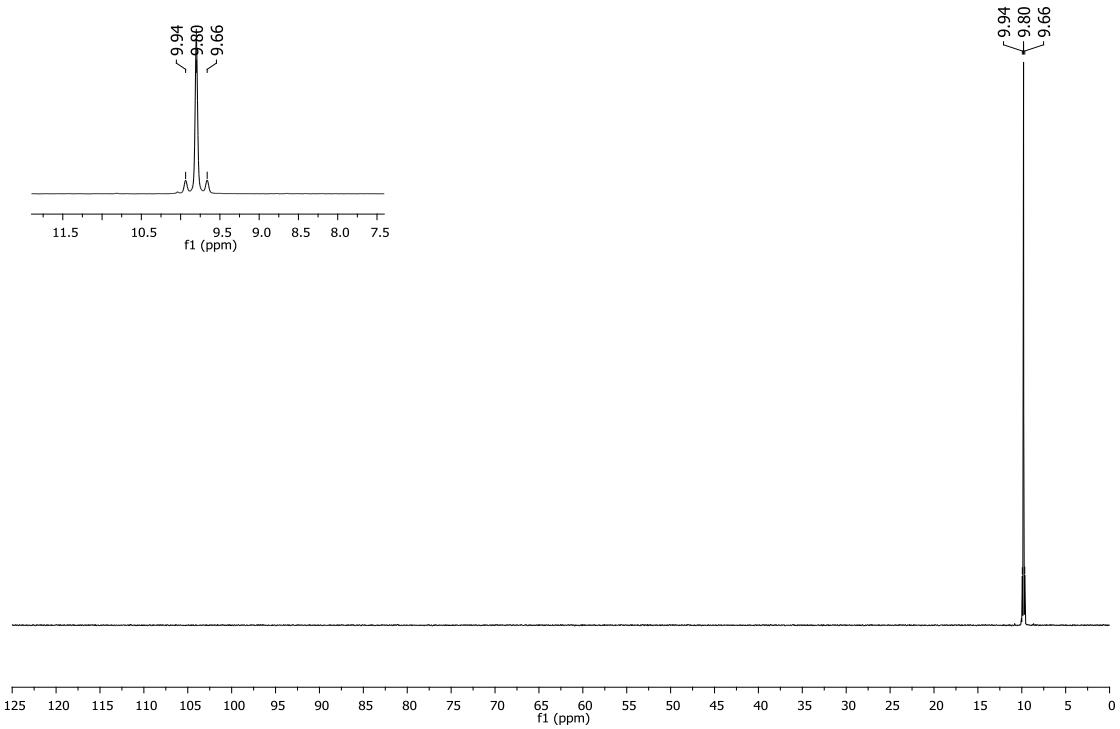


Figure S56. ^{31}P NMR spectrum of compound **23** ($CDCl_3$, 122 MHz).

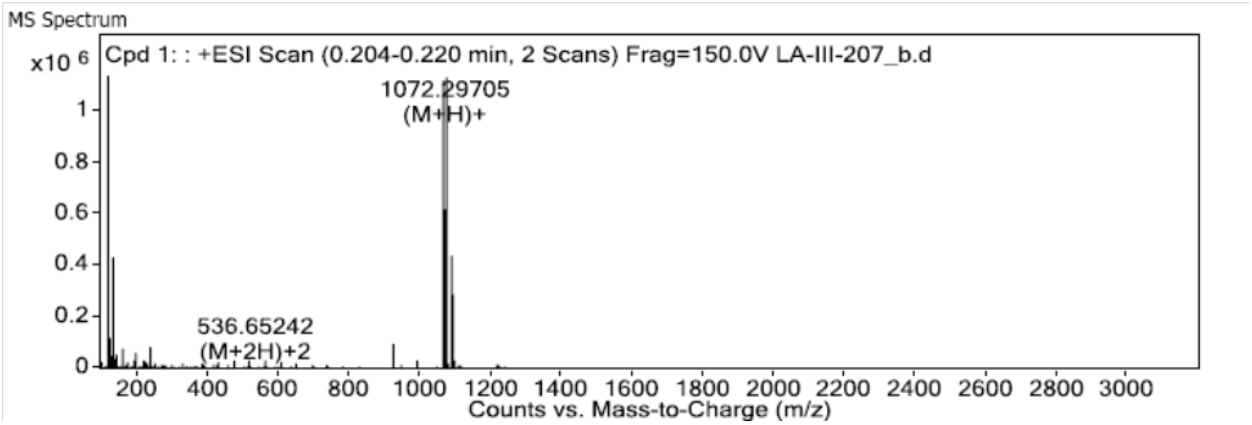


Figure S57. HRMS (ESI^+) spectrum of compound **23**.

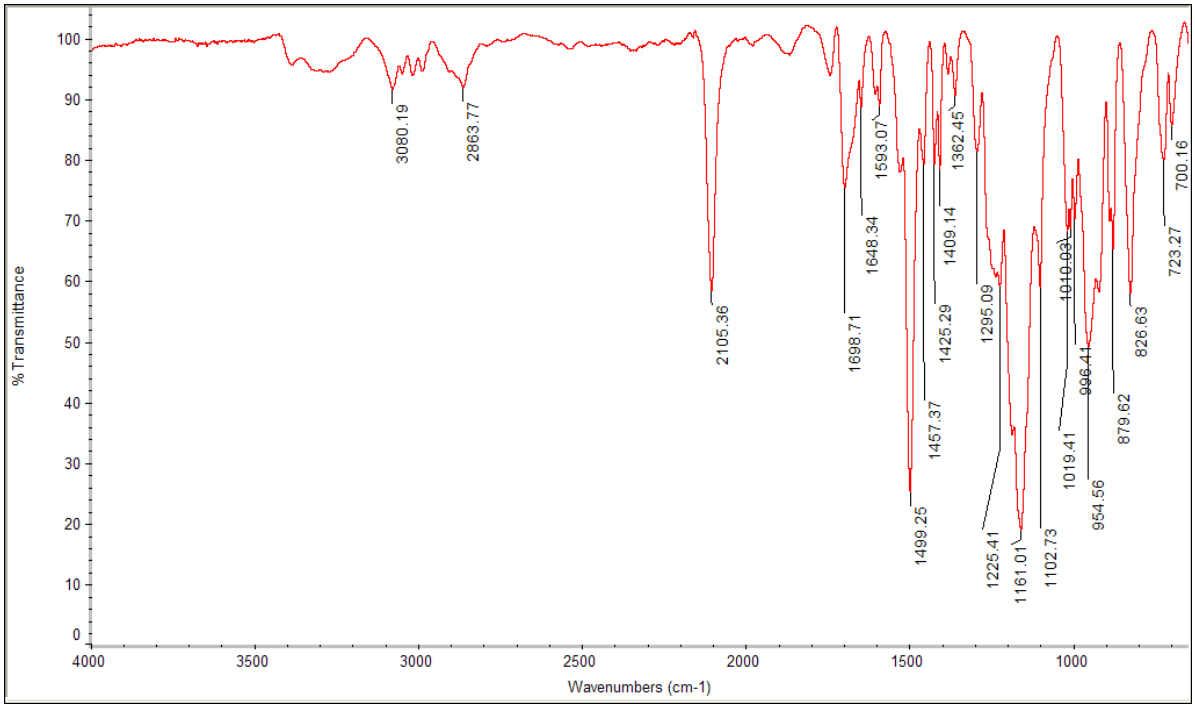
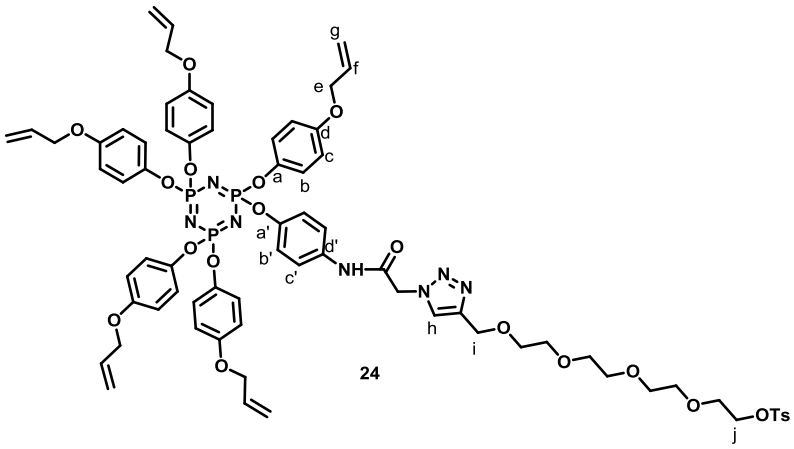


Figure S58. IR spectrum of compound **23**.



Synthesis of compound 25: 3,6,9,12-tetraoxapentadec-14-yn-1-yl 4-methylbenzenesulfonate **24** (75.0 mg, 0.19 mmol, 1.3 eq.) and compound **23** (160.3 mg, 0.15 mmol, 1.0 eq) were dissolved in a THF/H_2O 1:1 mixture (3 mL). Sodium ascorbate (88.7 mg, 0.45 mmol, 3.0 eq) and $CuSO_4$ $5H_2O$ (111.8 mg, 0.45 mmol, 3.0 eq) were added. The solution was stirred and heated at 55 °C overnight. The reaction mixture was diluted with EtOAc (50 ml) and washed twice with saturated aqueous ammonium chloride (2 × 75 ml) and water (50 ml). The mixture was dried with anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. Crude reaction mixture was purified using silica gel column (DCM/MeOH 100:0 to 94:6) which afforded desired compound **25** (139.6 mg, 64%).
Rf= 0.31, DCM/MeOH 96:4

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.73 (s, 1H, NH), 7.81 (s, 1H, H-triazole), 7.73 (d, 2H,*J*=8.3 Hz, H-c'), 7.37 (d, 2H,*J*=8.9 Hz, H-aromTos) 7.26 (d, 2H, *J*=8.1 Hz, H-aromTos), 6.90-6.64 (m, 22H, H-b', H-c, H-b), 6.08-5.93 (m, 5H, H-f), 5.42-5.33 (m, 5H,H-g) 5.28-5.18 (m, 7H, H-g, C$\underline{H_2}$-triazole), 4.65 (s,2H, H-i), 4.45-4.42 (m, 10H, H-e), 4.11-4.07 (m, 2H, H-j), 3.68-3.52 (m, 14H, OC$\underline{H_2}$C$\underline{H_2}$O), 2.38 (s, 3H, C$\underline{H_3}$).
^{13}C {^{1}H} NMR ($CDCl_3$, 75 MHz,) **:** δ 163.4, 155.7, 155.6, 147.4, 145.3, 145.0, 144.3, 134.3, 133.3, 133.2, 132.8, 130.0, 128.0, 124.9, 121.9, 121.4, 121.1, 117.7, 115.3, 115.2, 76.8, 70.7, 70.6, 70.6, 70.5, 70.5, 69.8, 69.4, 69.2, 68.8, 64.5, 53.2, 21.7.
^{31}P NMR ($CDCl_3$, 121.5 MHz)**:** 9.76 (t, *J* =18.1 Hz, 3P).
HRMS (ESI+) *m/z* calc. for $C_{71}H_{78}N_7O_{19}P_3S$, 1458.4359 $[M+H]^+$, found 1458.4384.

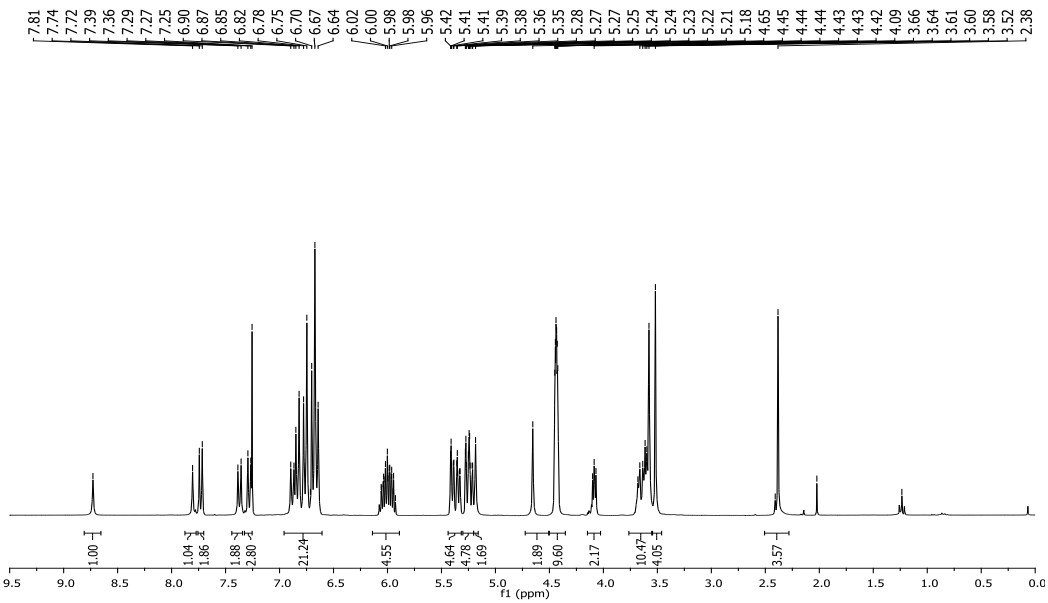


Figure S59. ^{1}H NMR spectrum of compound **25** ($CDCl_3$, 300 MHz).

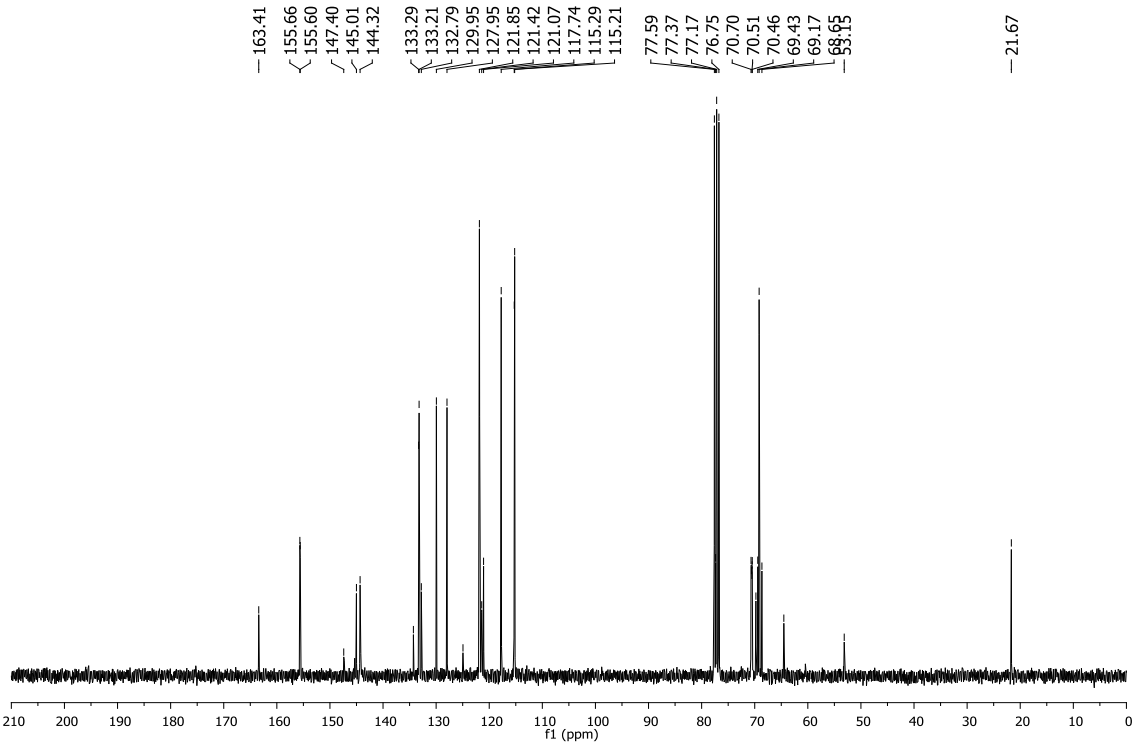


Figure S60. ^{13}C {^{1}H} NMR of compound **25** ($CDCl_3$, 75 MHz).

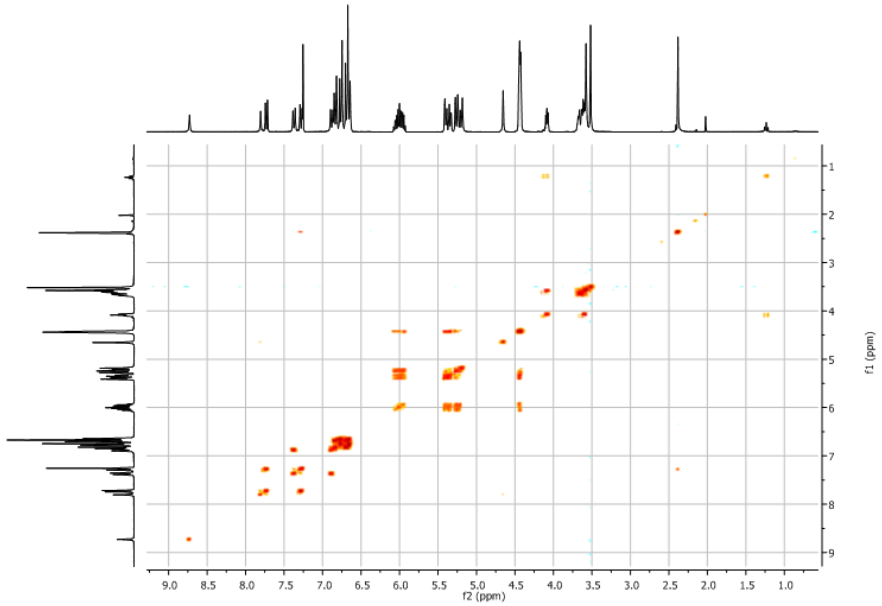


Figure S61. COSY spectrum of compound **25**.

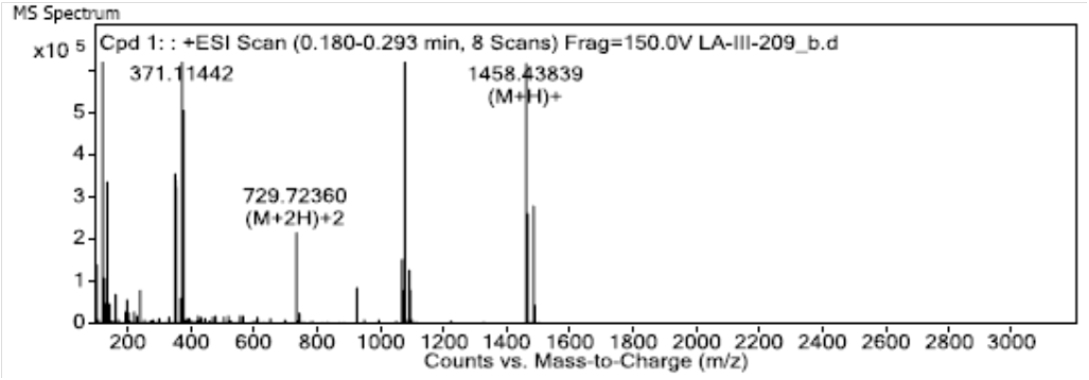


Figure S62. HRMS (ESI^+) spectrum of compound **25.**

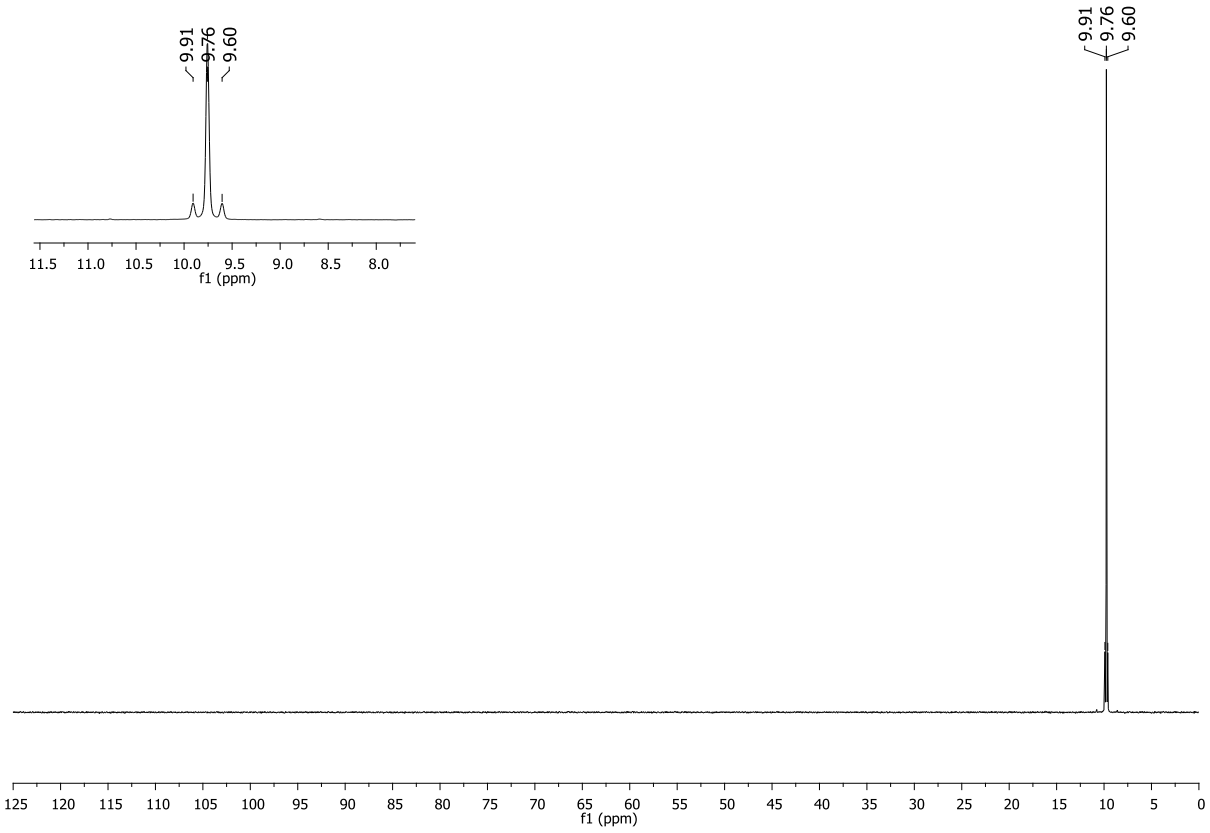
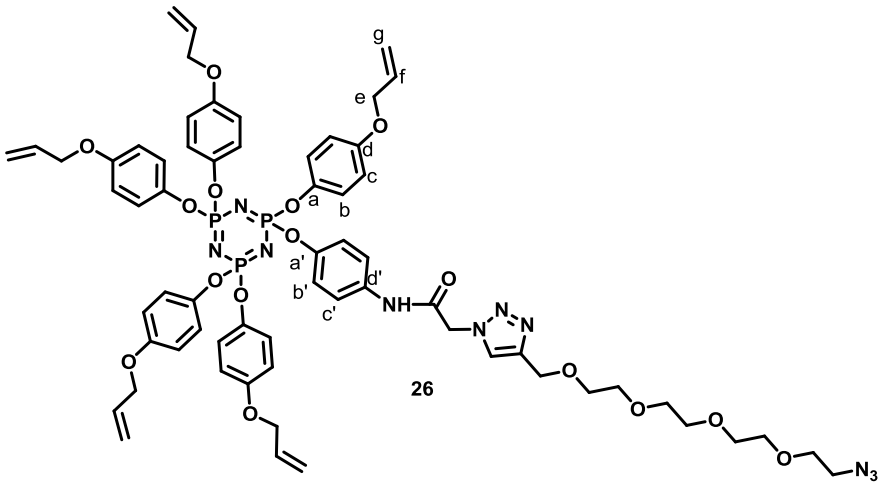


Figure S63. ^{31}P NMR spectrum of compound **25** ($CDCl_3$, 122 MHz).



Synthesis of compound 26: To a solution of compound **25** (139.6 mg, 0.10 mmol, 1.0 eq) in DMF (2 ml) under nitrogen atmosphere were added sodium azide (18.7 mg, 0.29 mmol, 3.0 eq) and sodium iodide (1.4 mg, 0.01 mmol, 0.1 eq). The suspension was stirred and heated at 50-60 °C overnight. After 12 h, the solvent was removed under vacuum. The reaction mixture was diluted with EtOAc (50 ml) and washed with water (4 × 40 ml). Crude mixture was purified using silica gel column (DCM/MeOH 99:1 to 98:2) which afforded desired compound **26** in 86% yield.

Rf= 0.31, DCM/MeOH 96:4

^{1}H NMR (300 MHz, $CDCl_3$) : δ 8.91 (s, 1H, NH), 7.75(s, 1H, H-triazole), 7.38 (d, 2H,*J*=8.9 Hz, H-c'), 6.92-6.65 (m, 22H, H-b', H-c, H-b), 6.06-5.93 (m, 5H, H-f), 5.42-5.34 (m, 5H,H-g) 5.28-5.25 (m, 5H, H-g) 5.17 (s, 2H, C$\underline{H_2}$-triazole), 4.64 (s,2H, H-i), 4.45-4.43 (m, 10H, H-e), 3.69-3.55 (m, 14H, OC$\underline{H_2}$C$\underline{H_2}$O), 3.29 (t, 2H,*J*=5.2 Hz, H-j).

^{13}C {^{1}H }NMR (75 MHz, $CDCl_3$) δ 163.4, 155.7, 155.6, 147.3, 145.2, 144.4, 144.3, 134.3, 133.3, 133.2, 124.9, 121.8, 121.5, 121.1, 117.8, 115.3, 115.2, 76.8, 70.6, 70.6, 70.0, 69.9, 69.2, 69.2, 64.5, 53.1, 50.6.

^{31}P NMR (121.5 MHz, $CDCl_3$) 9.75 (t, *J* =18.0 Hz, 3P).

HRMS (ESI^{+}) *m/z* calc. for $C_{64}H_{71}N_{10}O_{16}P_3$, 1329.4335 $[M+H]^{+}$, found 1329.4361.

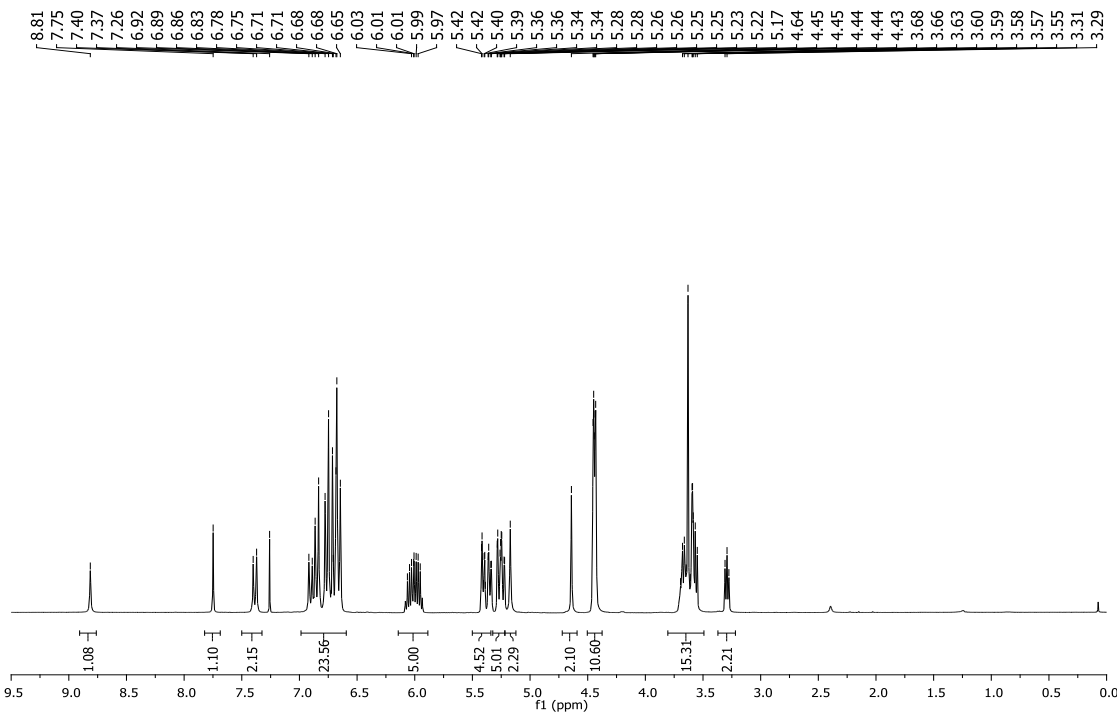


Figure S64. ^{1}H NMR spectrum of compound **26** ($CDCl_3$, 300 MHz).

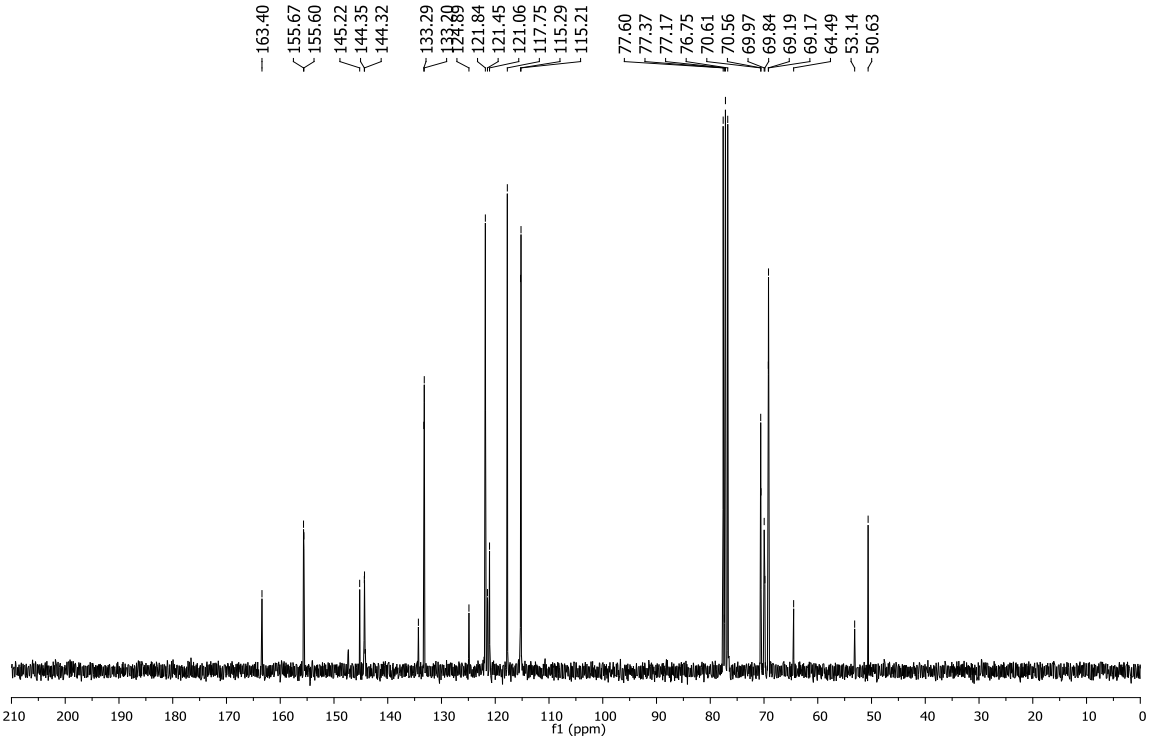


Figure S65. ^{13}C {^{1}H} NMR of compound **26** ($CDCl_3$, 75 MHz).

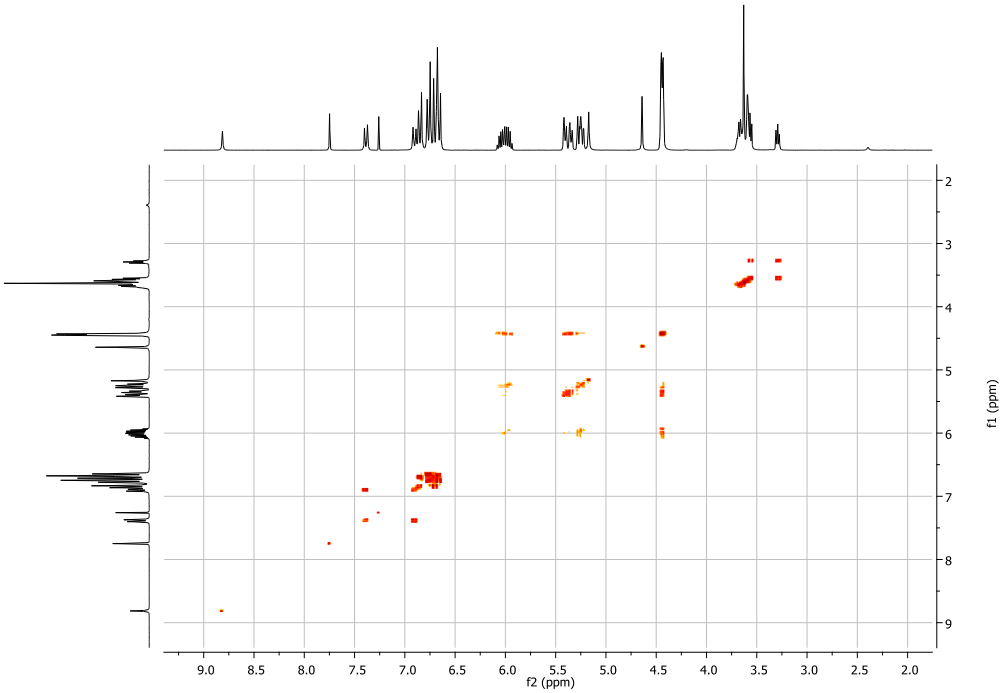


Figure S66. COSY spectrum of compound **26.**

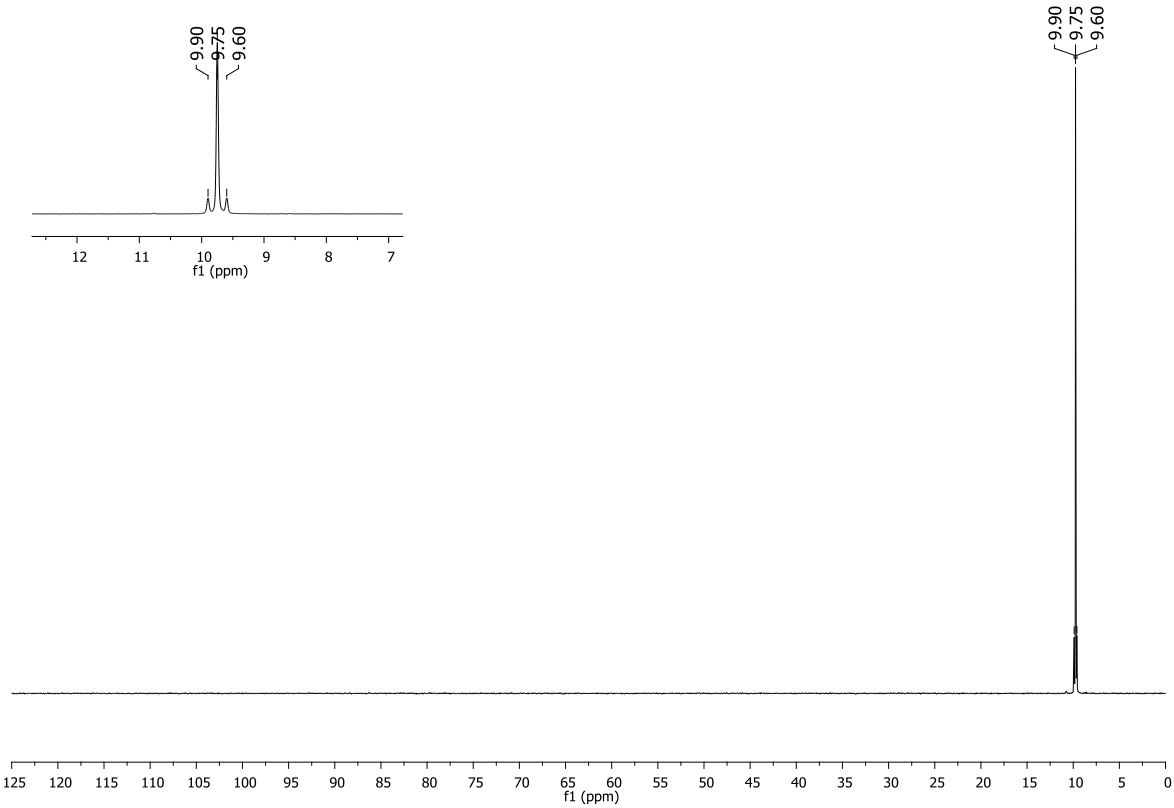


Figure S67. ^{31}P NMR spectrum of compound **26** ($CDCl_3$, 122 MHz).

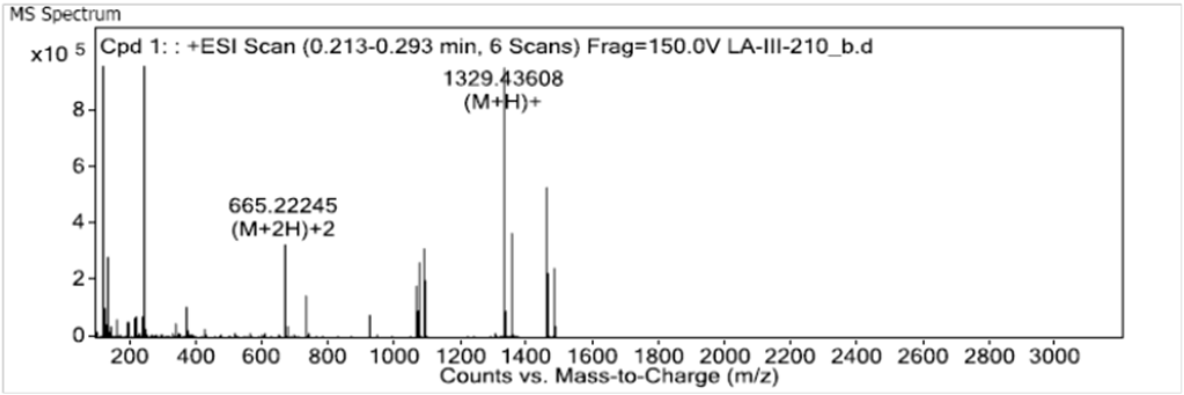
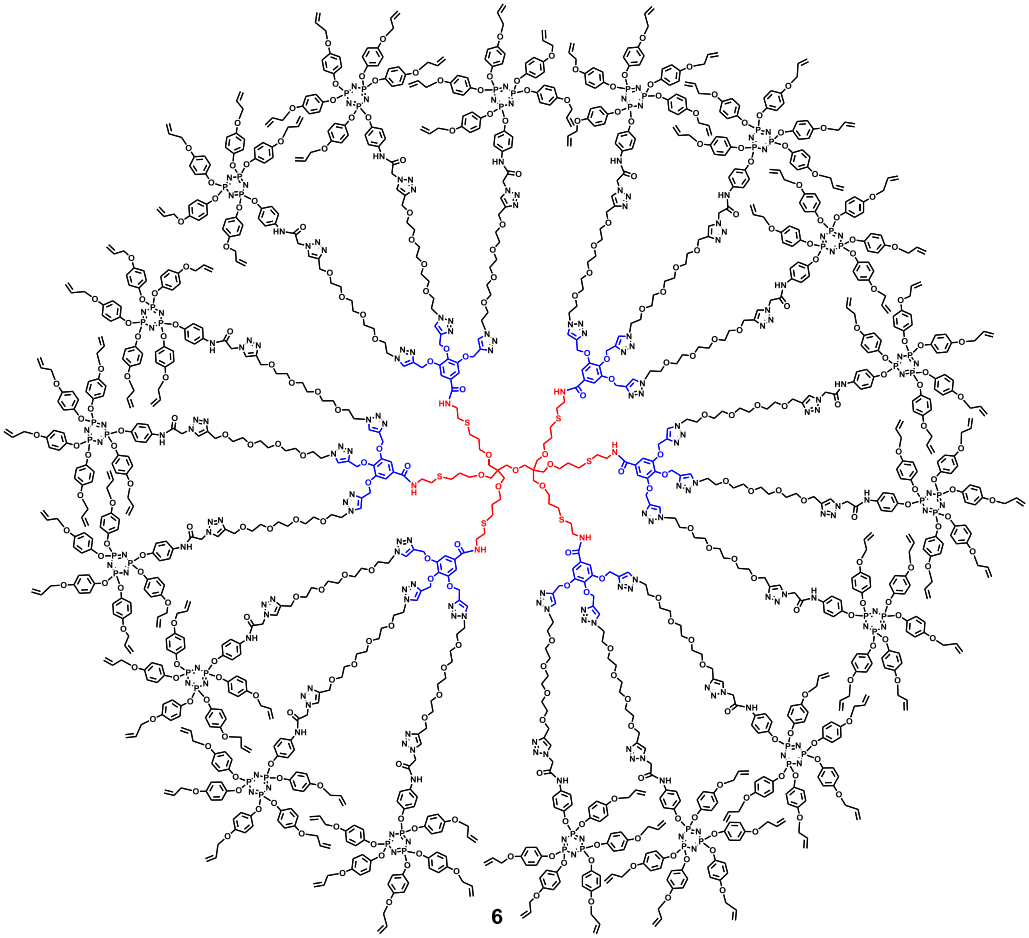


Figure S68. HRMS (ESI$^+$) spectrum of compound **26.**

Figure S69. IR spectrum of compound **26.**



6

Synthesis of compound 6: Propargyl terminated dendrimer **1** (5 mg, 0.0019 mmol, 1eq), compound **26** (94 mg, 0.070 mmol, 36 eq.), $CuSO_4.5H_2O$ (9 mg, 0.0351 mmol, 18 eq.) and sodium ascorbate (7 mg, 0.0351 mmol, 18 eq.) were reacted together following the procedure A and was purified by column chromatography (4% MeOH in DCM as eluent) to yield compound **6** as a colourless oil in 50% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.63 (s, 12H), 7.88 (d, *J* = 29.3 Hz, 18H), 7.73 (s, 18H), 7.56 – 7.42 (m, 36H), 7.07 – 6.44 (m, 396H), 6.10 – 5.88 (m, 90H), 5.52 – 4.94 (m, 244H), 4.67 – 4.13 (m, 260H), 3.80 – 3.20 (m, 302H), 2.71 (d, *J* = 41.5 Hz, 30H), 1.79 (s, 12H).

^{13}C {^{1}H } NMR (151 MHz, $CDCl_3$) δ 167.6, 163.7, 155.5, 147.1, 144.6, 144.2, 134.7, 130.8, 128.7, 125.0, 121.7, 121.2, 120.9, 117.6, 117.5, 115.2, 115.1, 106.9, 71.3, 70.3, 69.6, 69.0, 68.1, 64.1, 52.8, 50.2, 38.7, 31.9, 30.3, 29.6, 28.9, 23.7, 22.9, 22.6, 20.3, 14.0, 10.9.

^{31}P NMR (122 MHz, $CDCl_3$) δ 9.70 (s).

I.R (cm^{-1}) 3708, 3680, 2980, 2922, 2865, 2844, 1702, 1552, 1501, 1455, 1426, 1295, 1262, 1189, 1170, 1103, 1054, 1032, 1011, 953, 884, 834.

MALDI-TOF m/z: calculated for $C_{1288}H_{1426}N_{186}O_{319}P_{54}S_6$: 26481.1320, found: 26249.7870.

GPC (THF): M*n*= 26350 g/mol. M*w/Mn*= 1.03

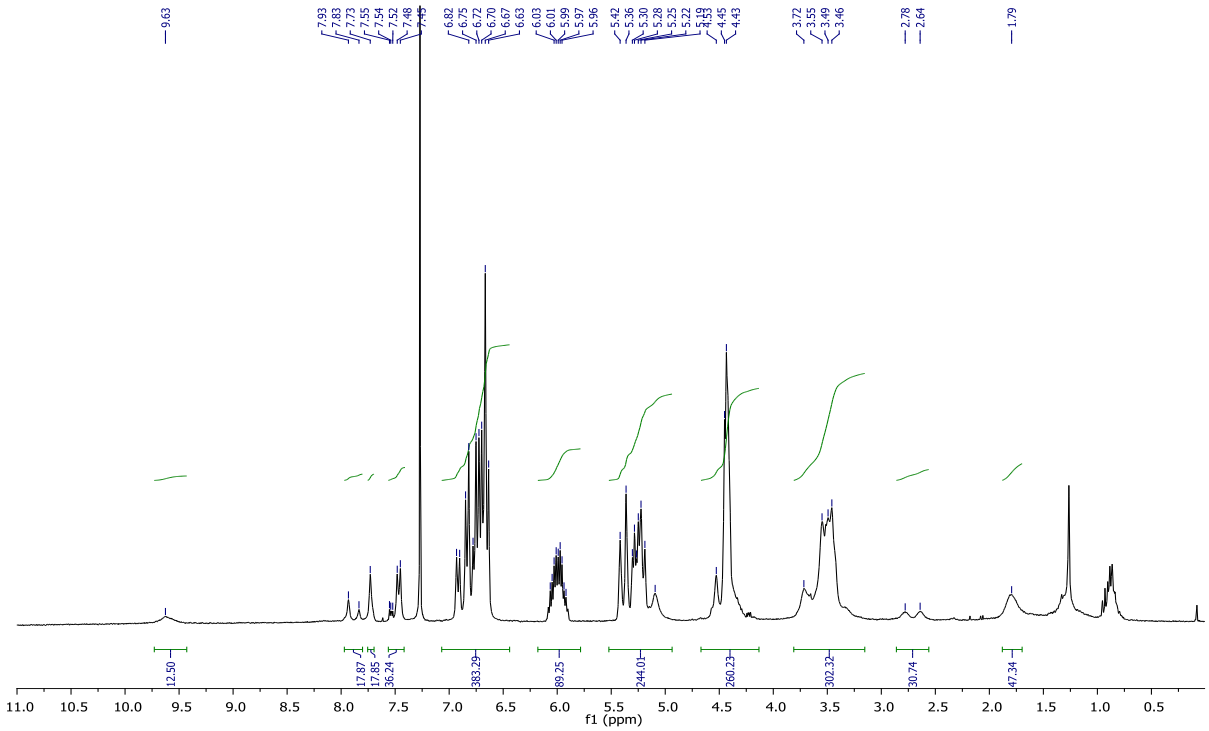


Figure S70. ^{1}H NMR spectrum of compound **6** ($CDCl_3$, 300 MHz).

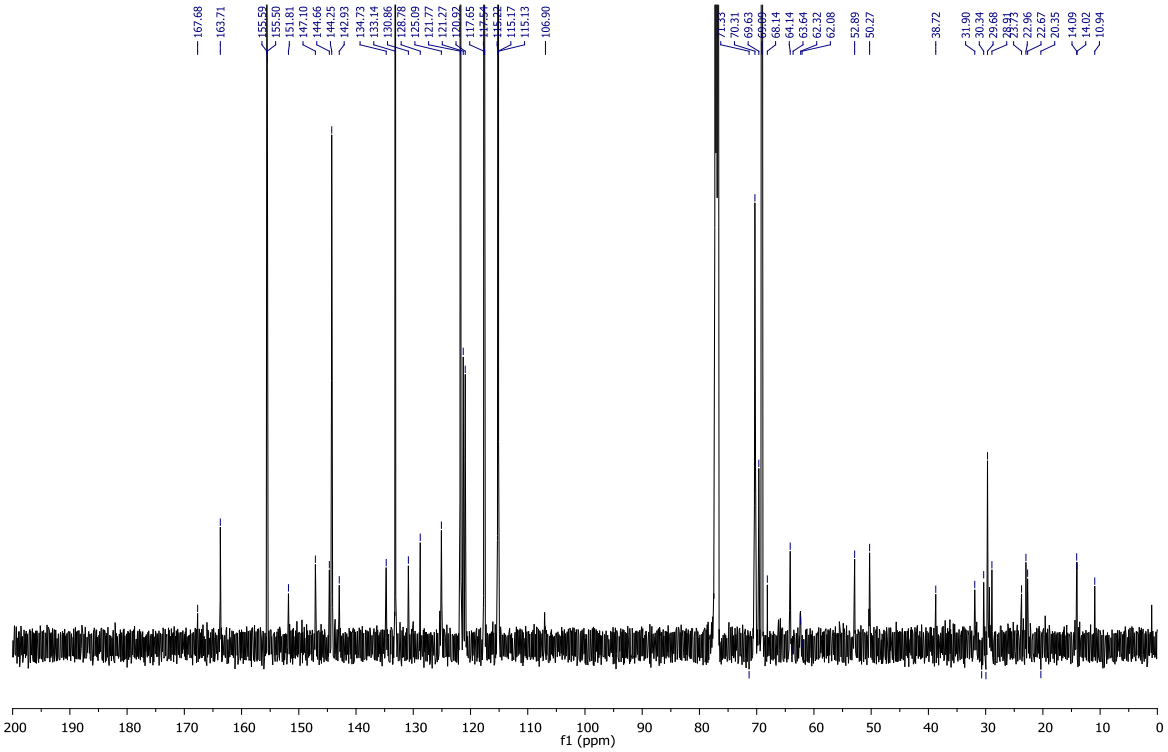


Figure S71. ^{13}C {^{1}H} NMR of compound **6** ($CDCl_3$, 151 MHz).

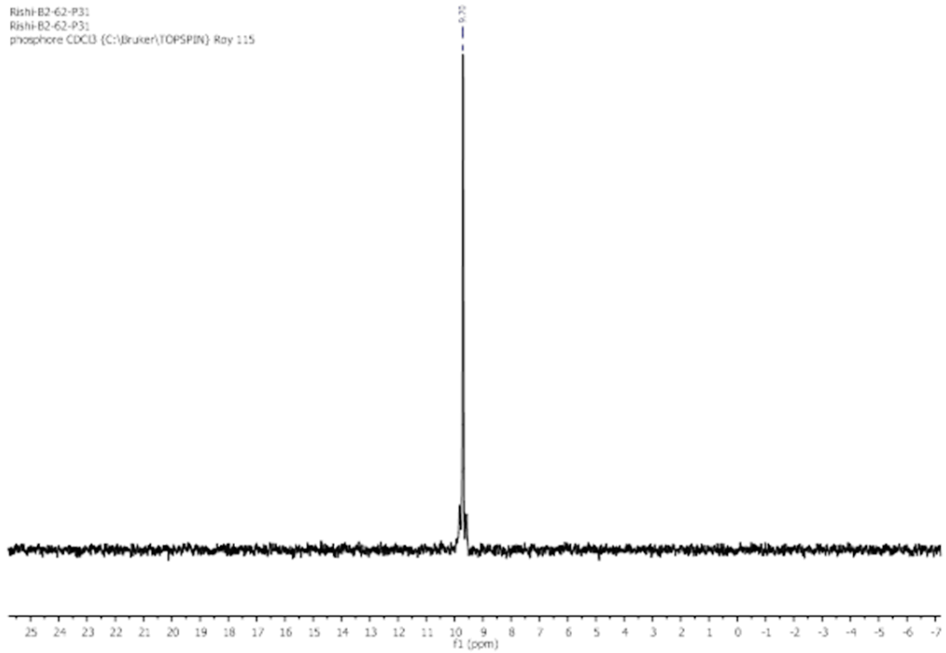


Figure S72. ^{31}P NMR spectrum of compound **6** ($CDCl_3$, 122 MHz).

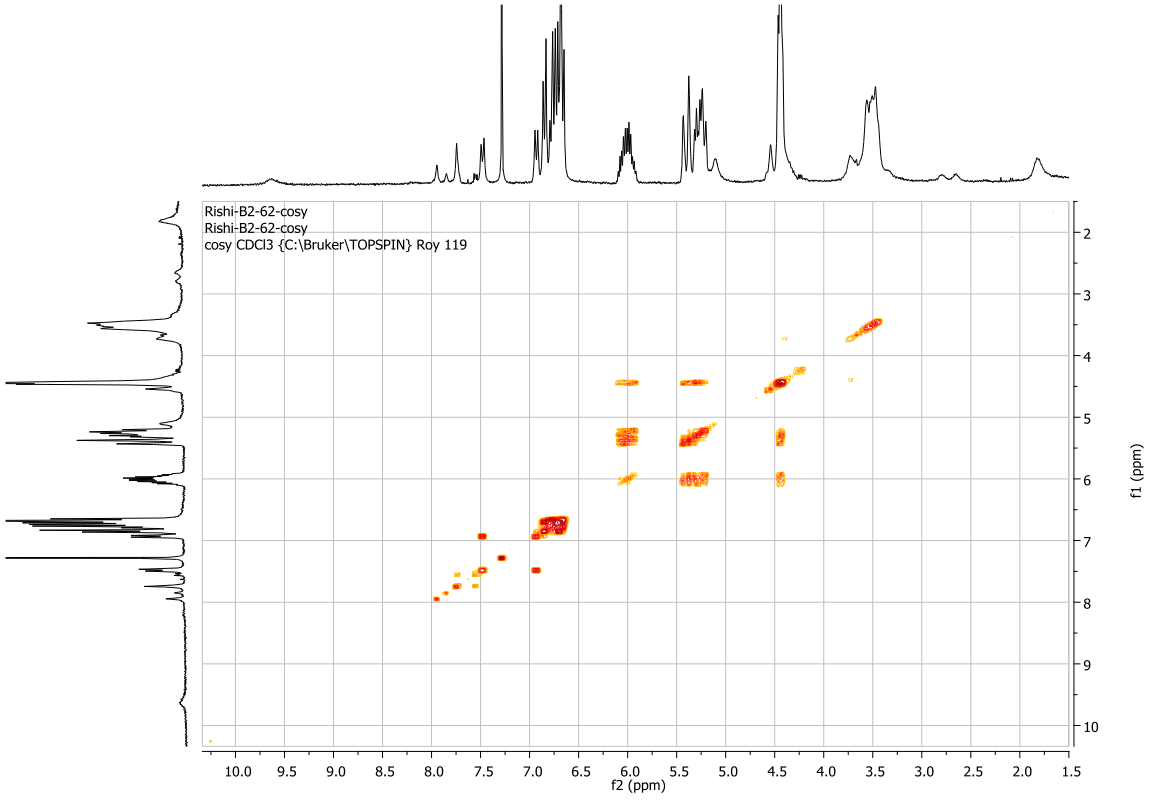


Figure S73. COSY spectrum of compound **6.**

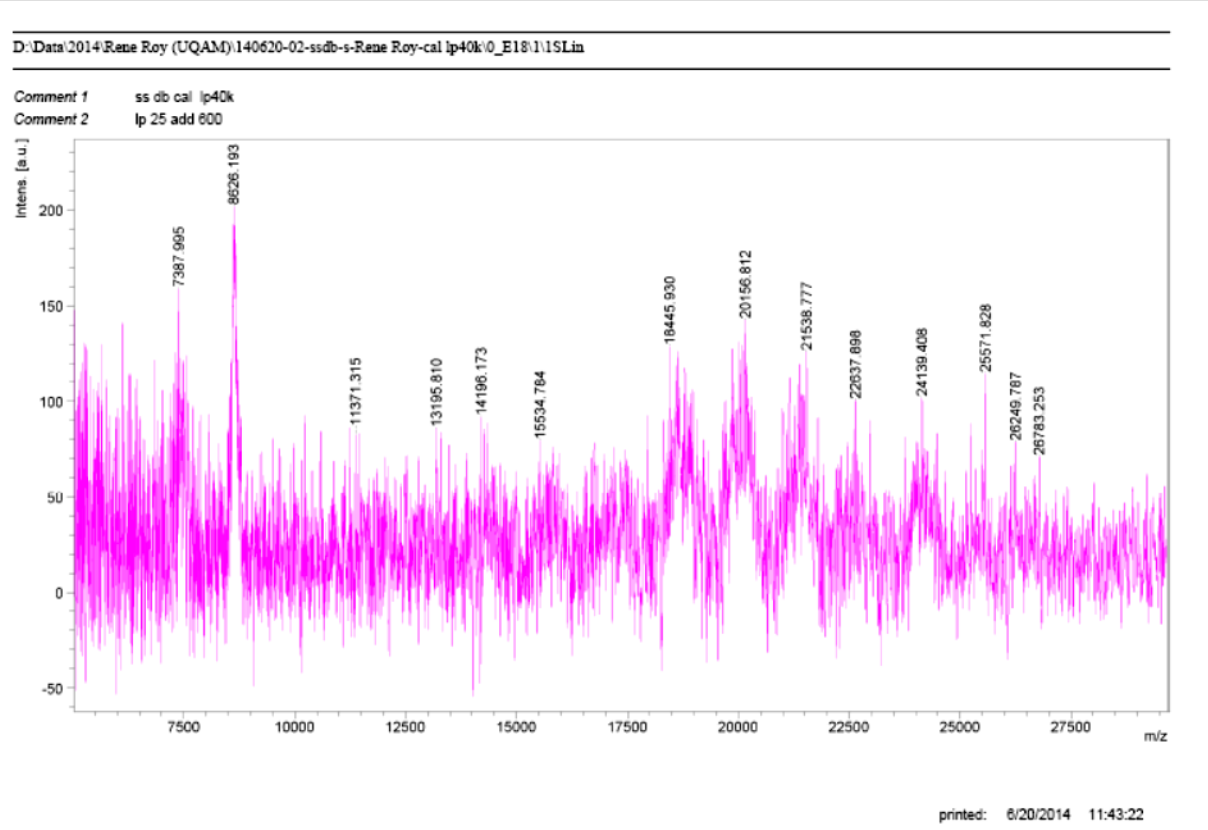
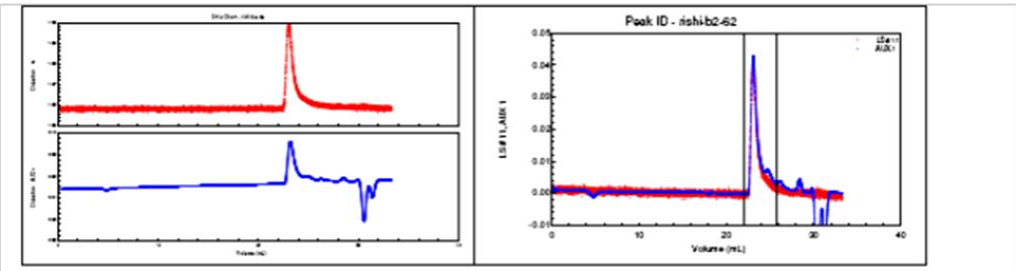


Figure S74. MALDI-TOF spectrum of compound **6**.



COLLECTION INFORMATION

Collection time	:	Wed May 08, 2002 04:28 PM Est (heure d'été)
Instrument type	:	DAWN EOS
Cell type	:	K5
Laser wavelength	:	690.0 nm
Solvent name	:	thf
Solvent RI	:	1.401
Calibration constants		
DAWN	:	8.7600e-06
» AUX1	:	2.8000e-04
AUX2	:	1.0000e-04
Flow rate	:	1.000 mL/min
Collection interval	:	0.250 sec
Number of slices	:	7989

Volume (mL)	:	22.104 - 25.725
Slices (used)	:	870 (767)
A2 (mol mL/g²)	:	0.000e+00
Fit degree	:	1
Injected Mass (g)	:	1.1100e-04
dn/dc (mL/g)	:	0.098
Polydispersity(Mw/Mn)	:	1.030±0.132 (13%)
Polydispersity(Mz/Mn)	:	1.058±0.237 (22%)

Molar Mass Moments (g/mol)

Mn	:	2.635e+04 (9%)
Mw	:	2.713e+04 (9%)
Mz	:	2.787e+04 (20%)

Figure S75. GPC traces of compound **6**.

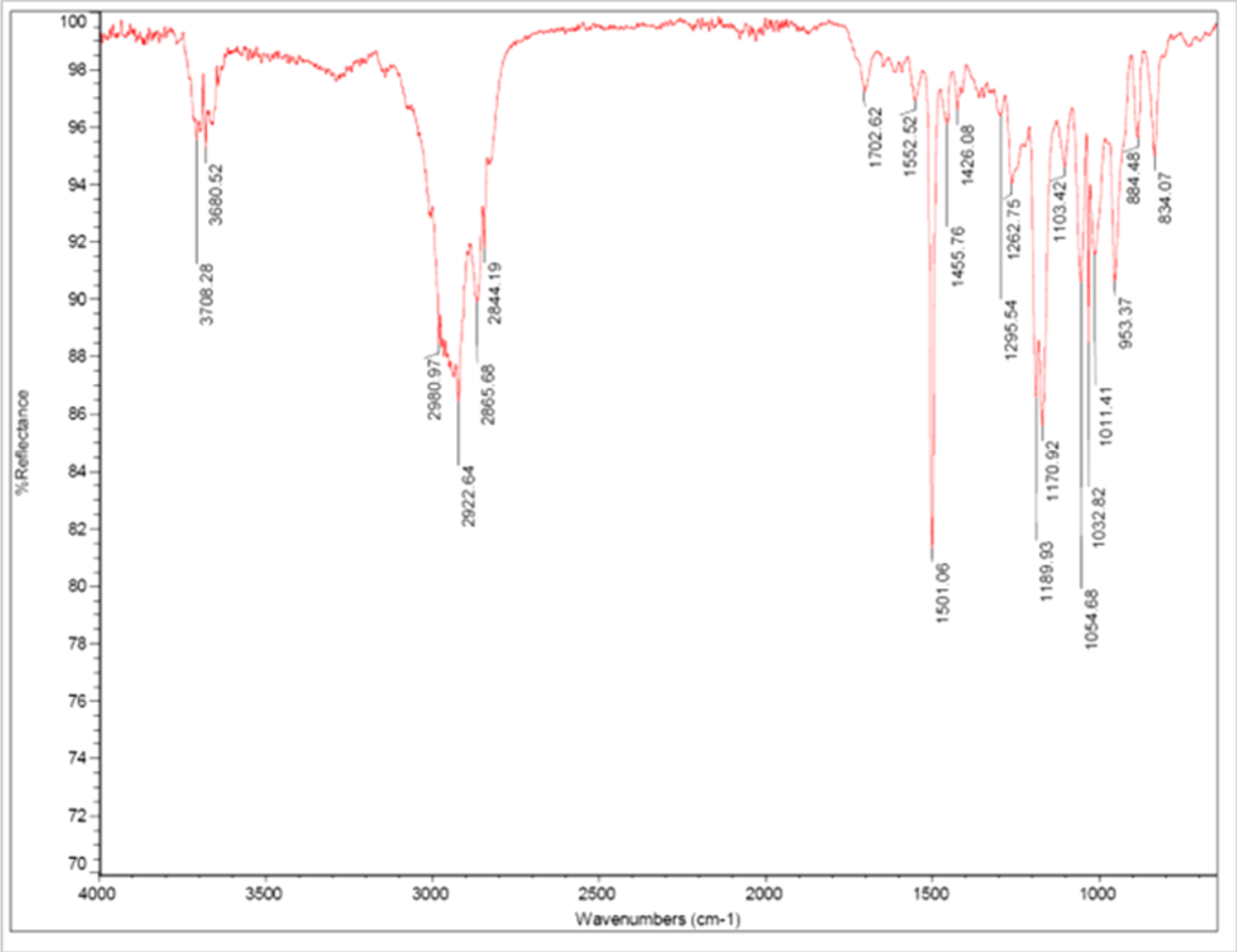
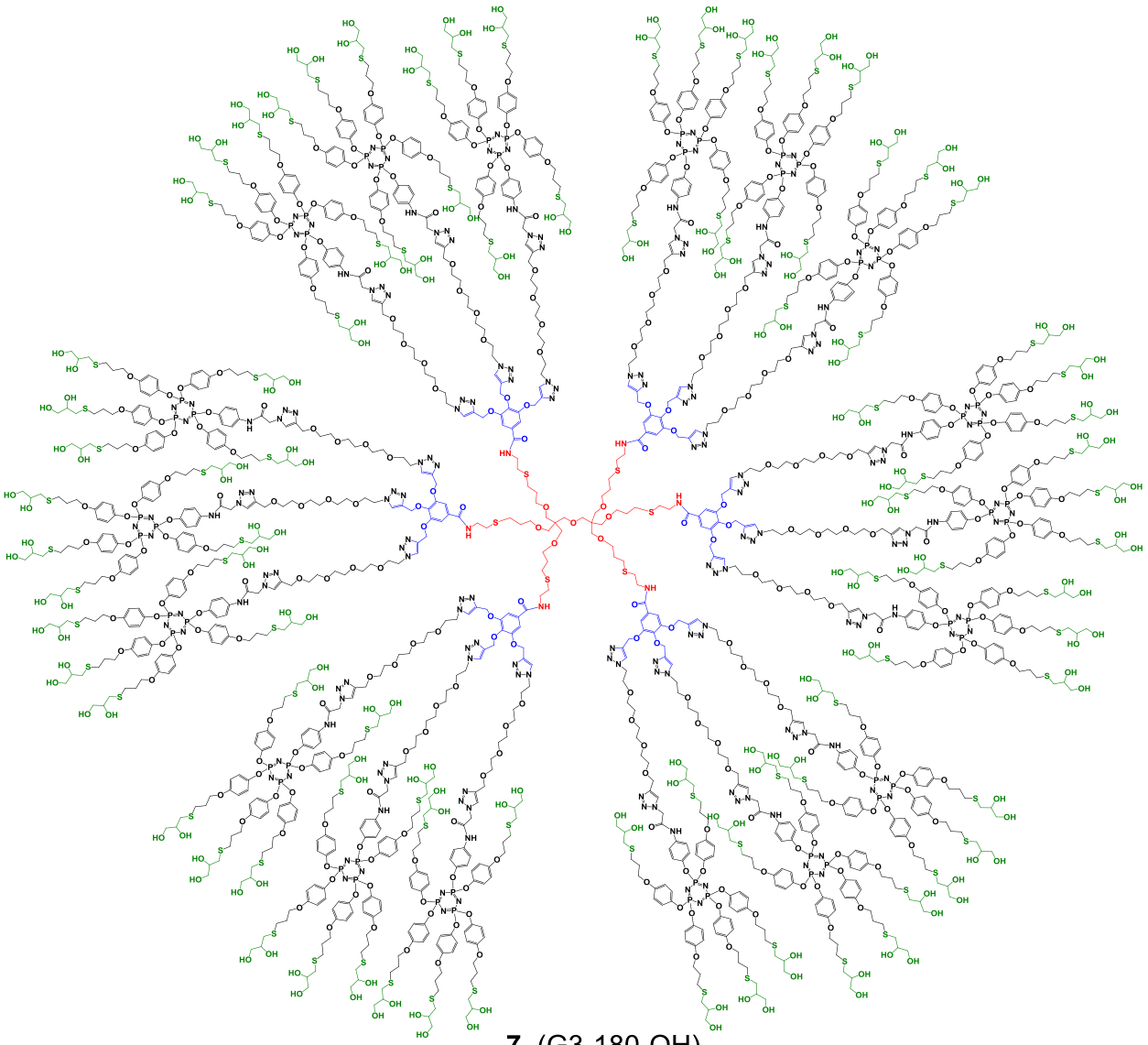


Figure S76. IR spectrum of compound **6**.



7 (G3-180-OH)

Synthesis of compound 7: Alkene terminated dendrimer **6** (20 mg, 0.00075 mmol, 1eq), 1-thioglycerol (0.040 ml, 0.4725 mmol, 630 eq.), and AIBN (3.7 mg, 0.0225, 30 eq.) were reacted together following the procedure B and was purified by dialysis to yield compound **7** as a colourless oil in 75% yield.

^{1}H NMR (300 MHz, MeOD): δ 7.94 – 7.84 (m, 36H), 7.50 – 7.40 (m, 36H), 6.73 (s, 396H), 5.25 (d, *J* = 36.8 Hz, 460H), 4.55 (brs, 233H), 3.9 – 2.6 (m, 793), 2.07 (s, 192H).

^{13}C {^{1}H} NMR (151 MHz, MeOD): δ 185.2, 157.4, 145.2, 122.9, 122.6, 122.4, 122.3, 120.7, 116.9, 116.2, 81.4, 72.9, 72.8, 72.7, 71.9, 67.8, 65.9, 64.5, 63.6, 54.1, 53.8, 50.5, 50.4, 44.2, 41.7, 39.6, 39.2, 38.5, 37.3, 37.0, 36.8, 36.2, 35.9, 34.7, 33.6, 33.5, 30.6, 30.5, 30.1, 28.2, 23.6.

^{31}P NMR (243 MHz, MeOD): δ 10.39, 10.34, 10.24, 10.19.

MALDI-TOF m/z: calculated for $C_{1558}H_{2146}N_{186}O_{499}P_{54}S_{96}$: 36215.4798, found: 37226.6720.

Differential light scattering Hydrodynamic diameter: 1.955nm

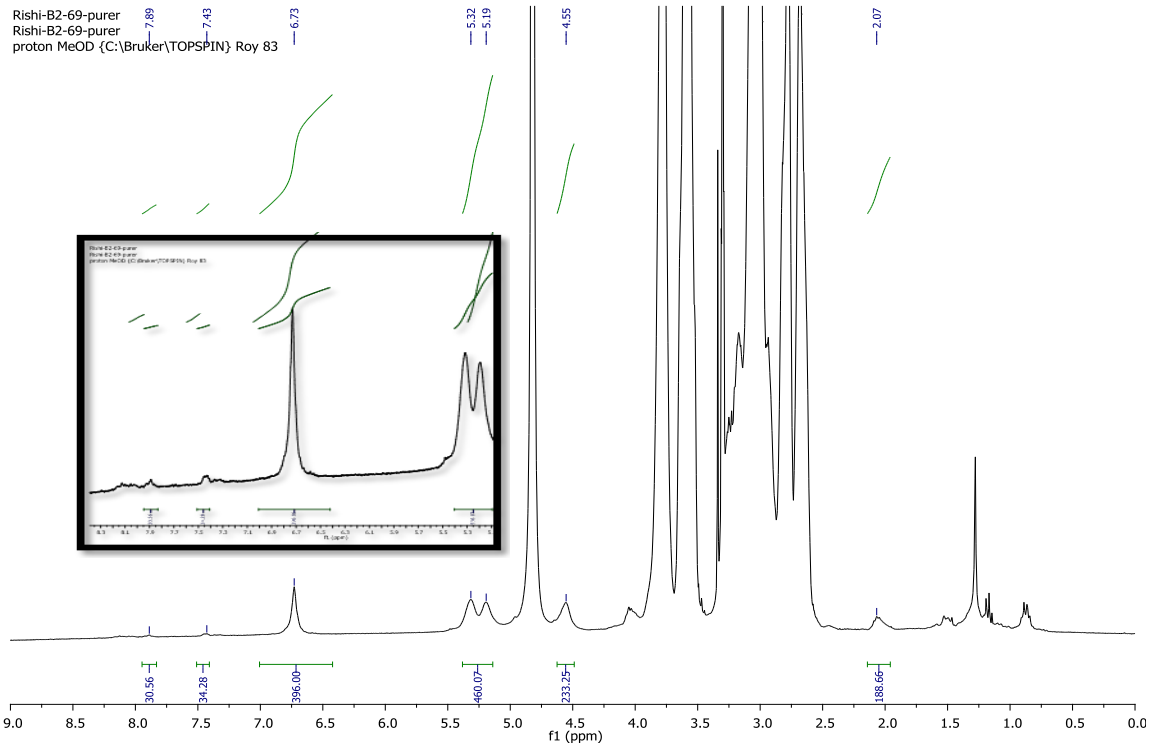


Figure S77. ^{1}H NMR spectrum of compound **7** (CD_3OD, 300 MHz).

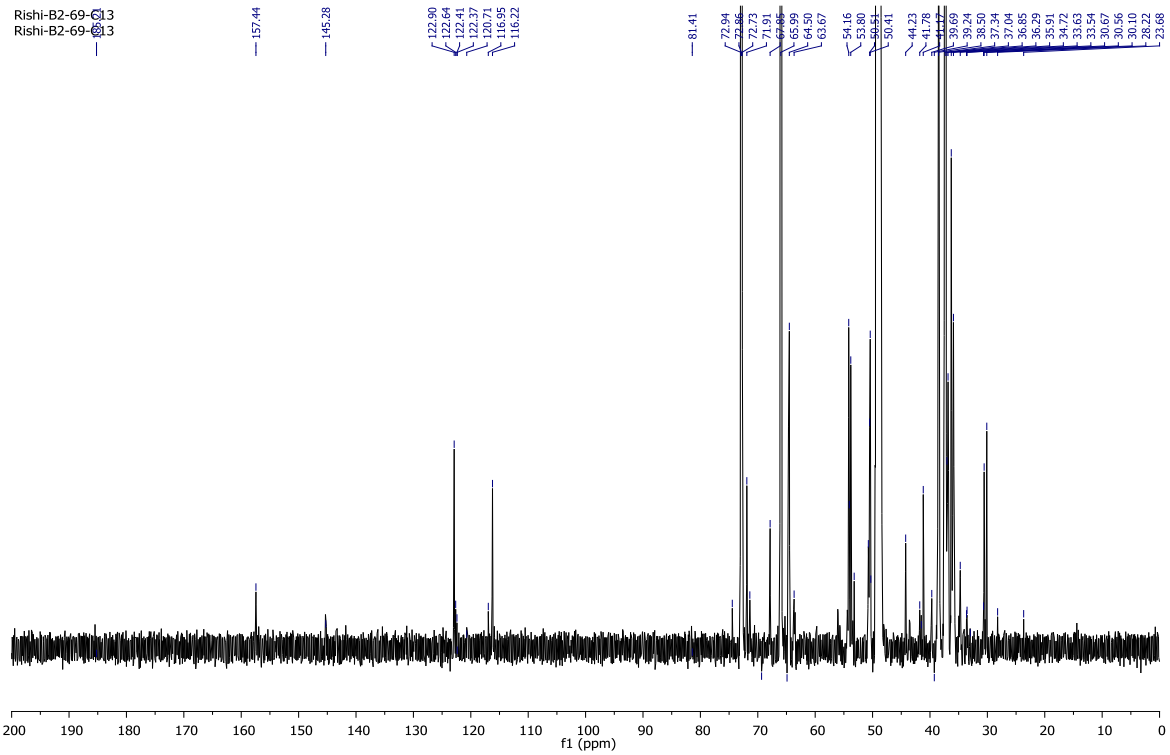


Figure S78. ^{13}C {^{1}H} NMR of compound **7** (CD_3OD, 151 MHz).

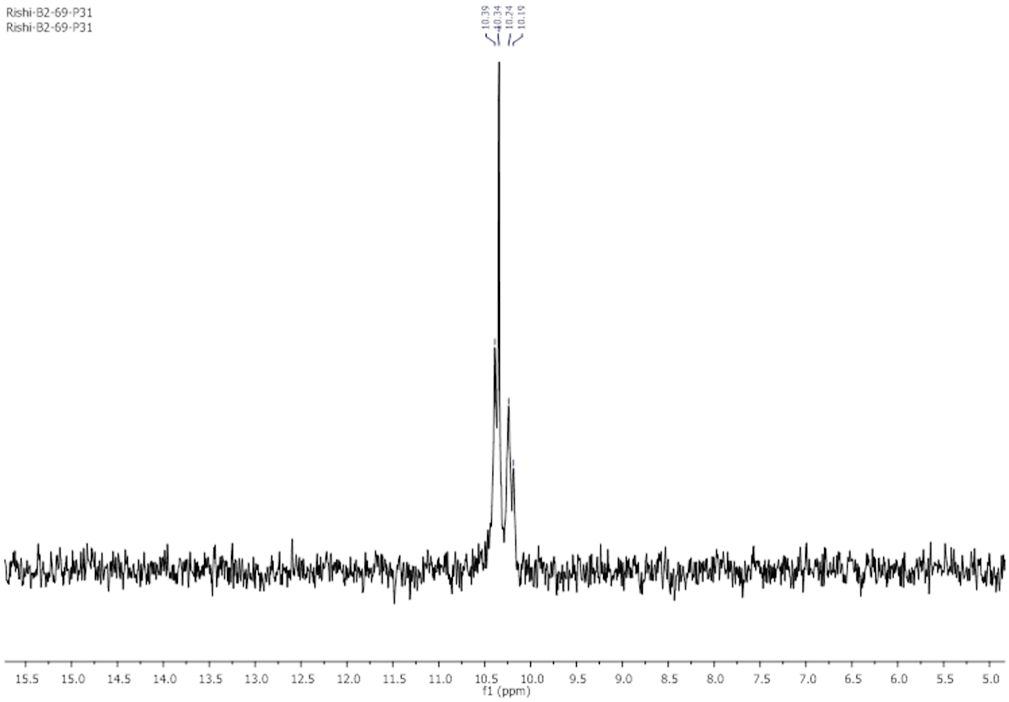


Figure S79 ^{31}P NMR spectrum of compound **7** (CD_3OD, 243 MHz).

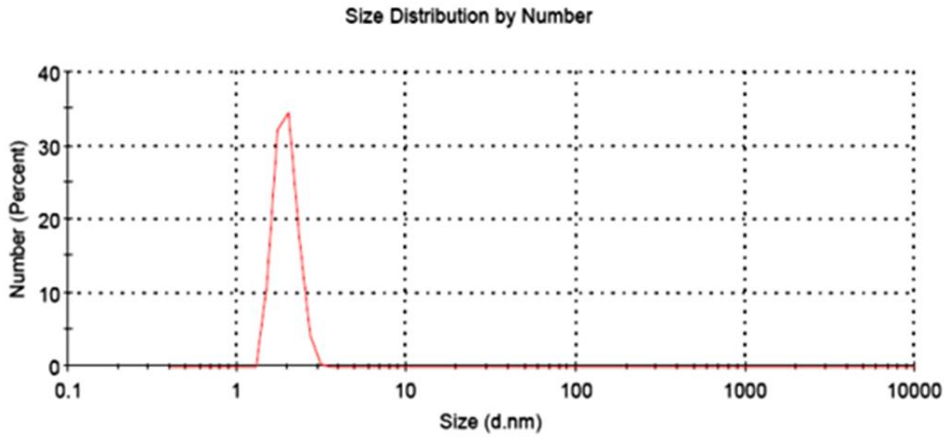


Figure S80. DLS size distribution of dendrimer **7** in methanol at 25^{o}C

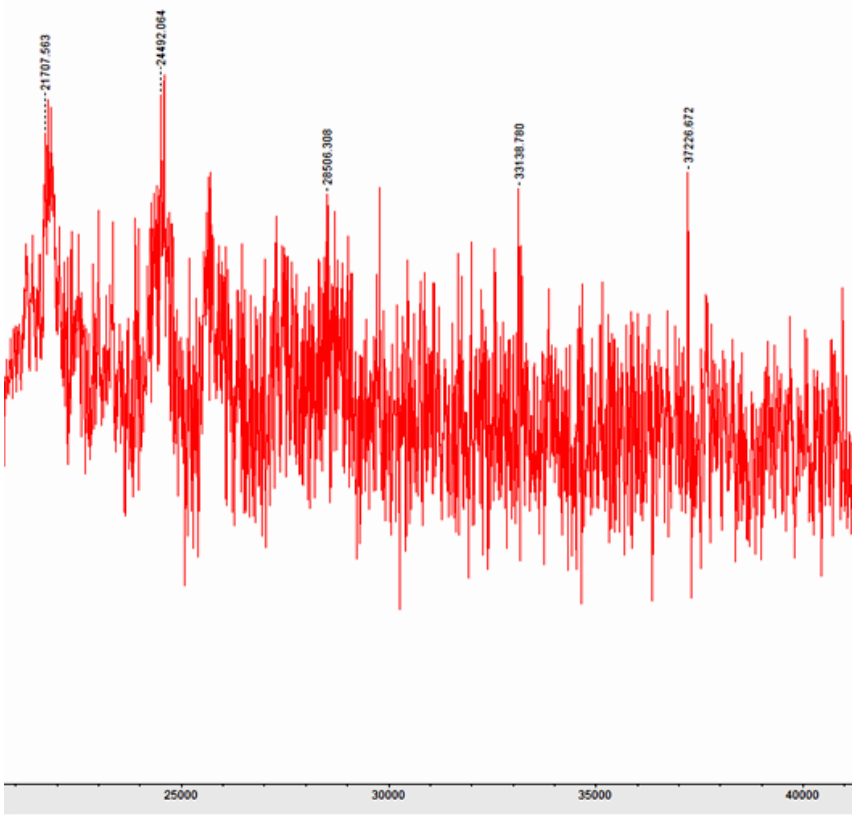
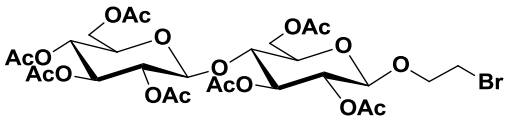


Figure S81. MALDI-TOF spectrum of compound **7**.



28

Synthesis of compound 28: Cellobiose octaacetate **27** (1.5g, 0.0021 moles) was dissolved in DCM (20 ml) followed by the addition of 2- bromoethanol (0.31 ml, 0.0044 moles). The reaction mixture was cooled to 0^{o}C and BF_3.etherate (0.8 ml, 0.0064 moles) was added dropwise. The mixture was then stirred at 0^{o}C for 4 h. It was allowed to come to room temperature and stirred for additional 2 h. The mixture was diluted with DCM (100 ml) and washed with aq. $NaHCO_3$ (3X30ml) and brine. The organic layer was dried and evaporated. The crude was purified by flash chromatography over silica gel (eluent hexane: DCM: Toluene: Ethyl acetate, 1:1:1:2) to provide **28**. (Yield: 43%).

^{1}H NMR (600 MHz, CDCl3) δ 5.22 – 5.10 (m, 2H), 5.06 (t, J = 9.7 Hz, 1H), 4.92 (t, J = 9 Hz 2H), 4.52 (dt, J = 15.1, 4.5 Hz, 3H), 4.36 (dd, J = 12.4, 4.3 Hz, 1H), 4.12- 4.01 (m, 2H), 4.04 (dd, J = 12.4, 1.4 Hz, 1H), 3.85 – 3.73 (m, 2H), 3.65 (ddd, J = 9.9, 3.8, 1.9 Hz, 1H), 3.60 (dd, J = 9.9, 4.9 Hz, 1H), 3.48-3.39 (m, 2H), 2.14 – 1.95 (m, 21H).

^{13}C {^{1}H} NMR (151 MHz, CDCl3) δ 170.44 (s), 170.4, 170.2, 170.1, 169.7, 169.6, 169.2, 168.9, 100.8, 100.7, 76.3, 72.8, 72.7, 72.2, 71.9, 71.5, 71.2, 69.7, 67.6, 61.4, 29.8, 20.8, 20.7, 20.6, 20.5.

HRMS (ESI^{+}) *m/z* calc. For $C_{28}H_{39}BrO_{18,}$ 743.5025 found, 762.1631 $[M + NH_4]^{+}$.

I.R (cm^{-1}) 3712, 3705, 3680, 3667, 2981, 2972, 2892, 2865, 2843, 2825, 1743, 1365, 1261, 1216, 1052, 1032, 1017.

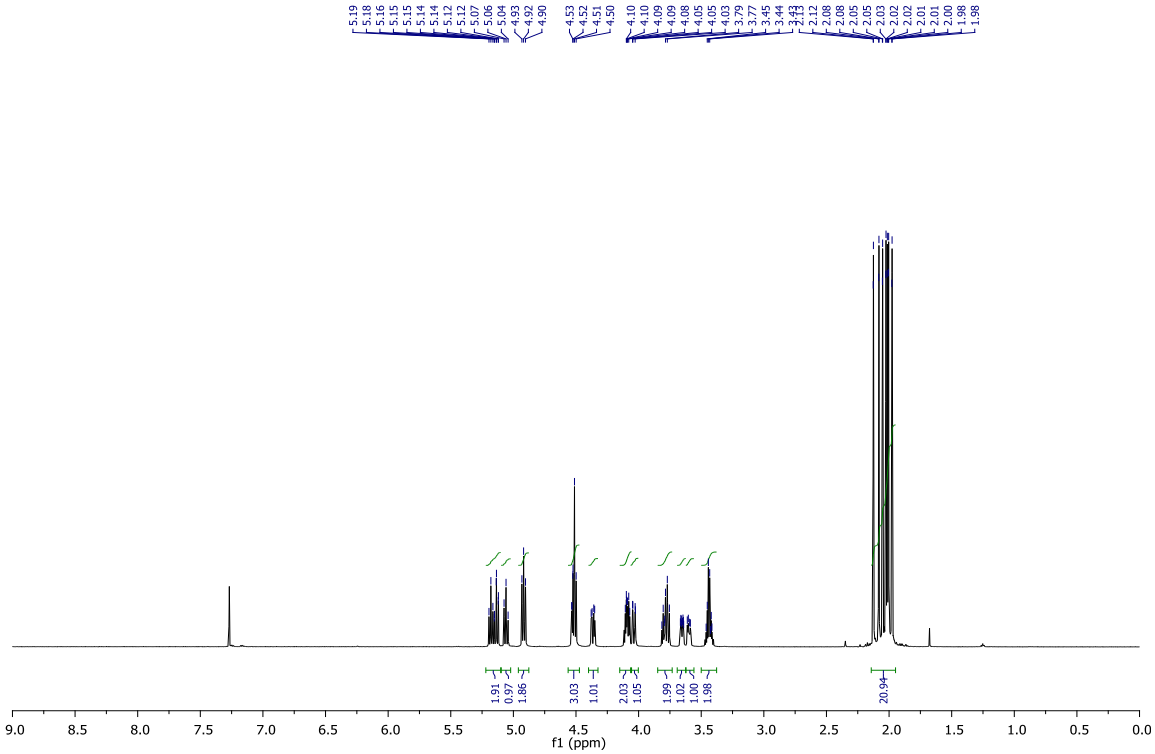


Figure S82. ^{1}H NMR spectrum of compound **28** ($CDCl_3$, 300 MHz).

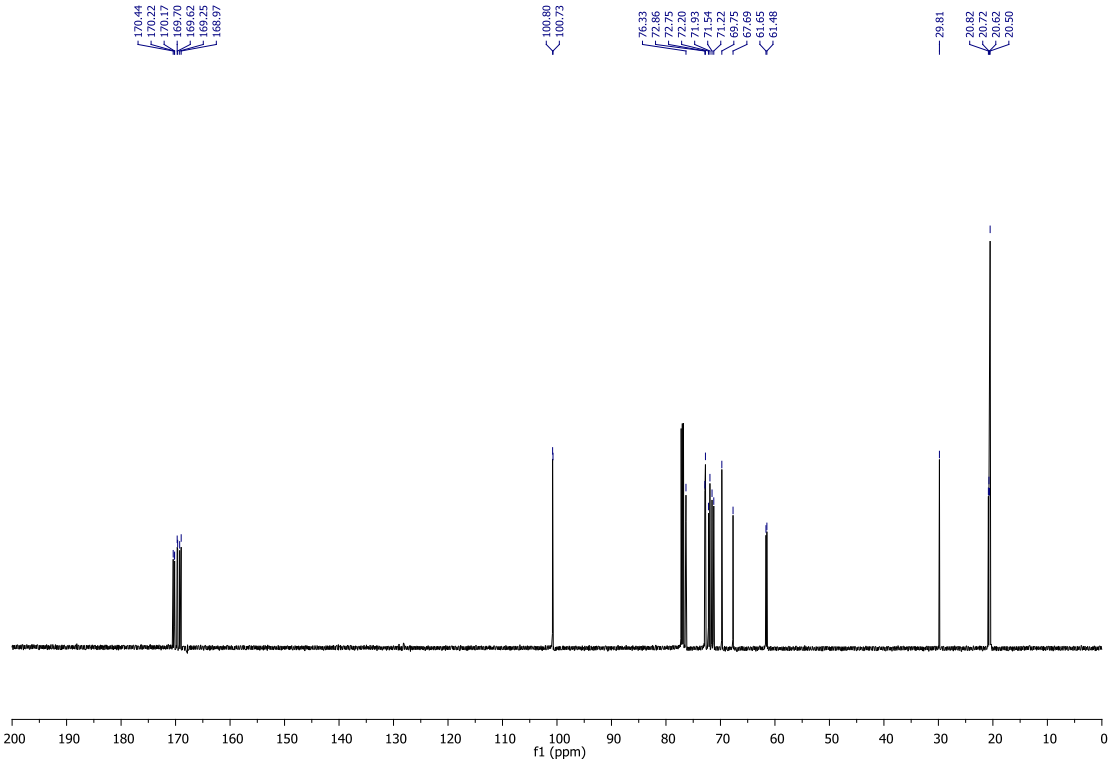


Figure S83. ^{13}C {^{1}H} NMR of compound **28** ($CDCl_3$, 151 MHz).

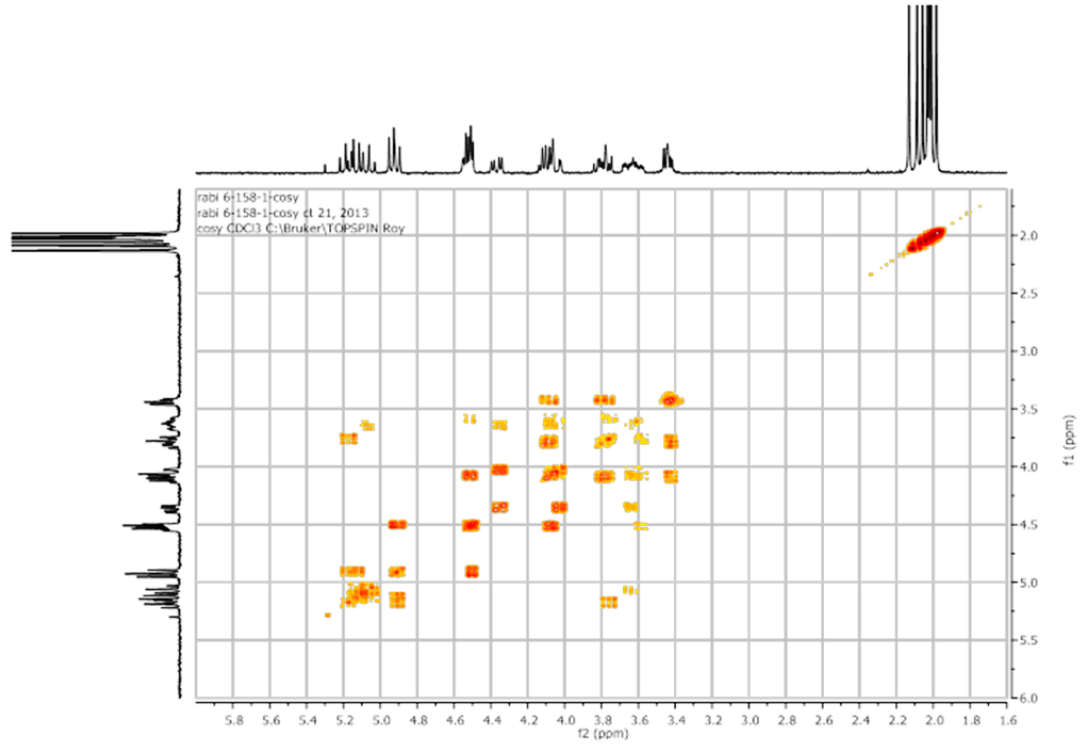


Figure S84. COSY spectrum of compound **28.**

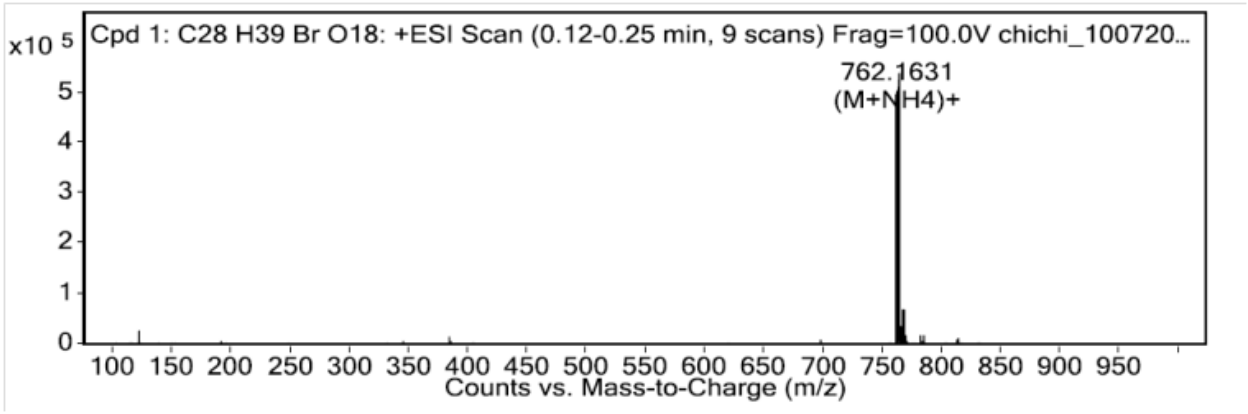


Figure S85. HRMS (ESI^+) spectrum of compound **28**.

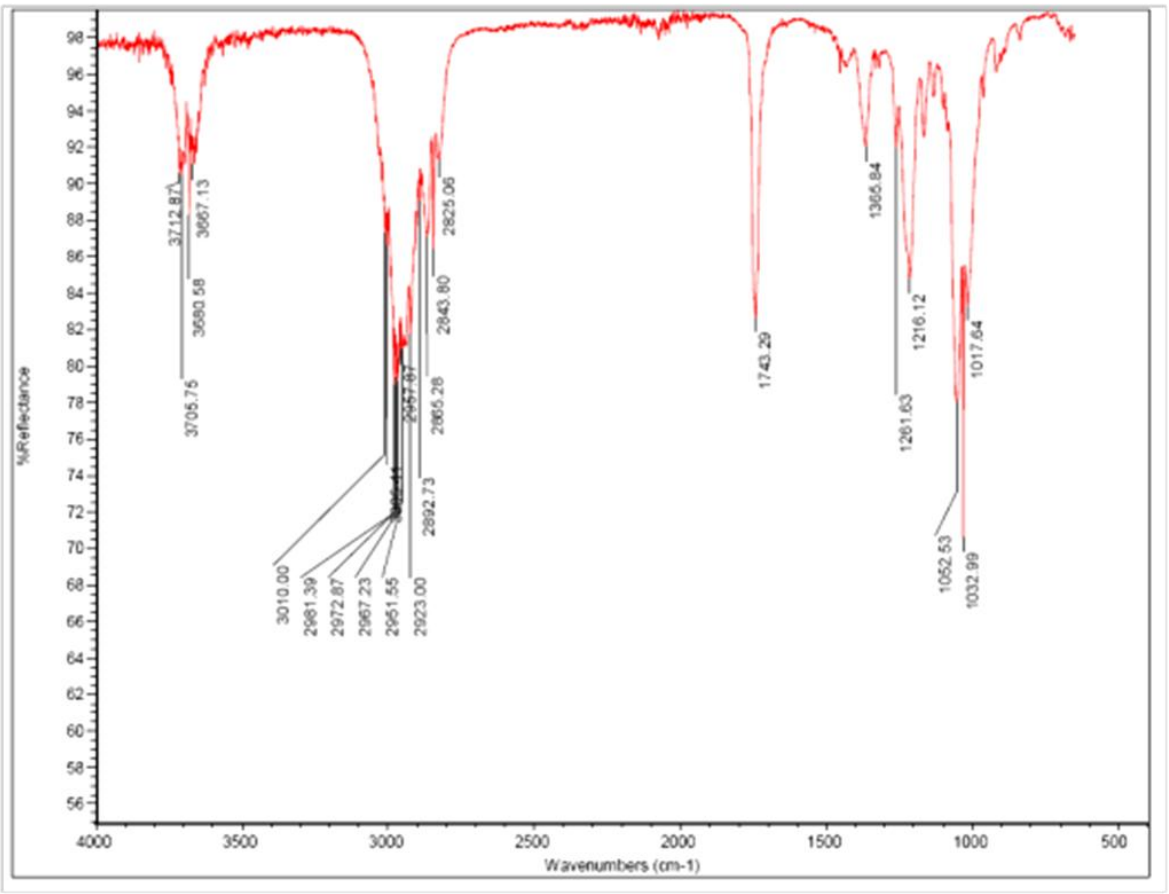
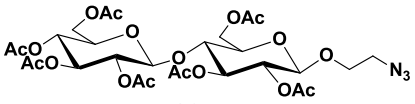


Figure S86. IR spectrum of compound **28**.



29

Synthesis of compound 29: A mixture of heptaacetyl-1(2-bromoethyl)- cellobiose **28** (500 mg, 0.67 mmol,) and sodium azide (152 mg, 2.33 mmol) in DMF (5ml) was kept at 70^{o}C for 4 hrs. The mixture was cooled, diluted with EtOAc, washed with H_2O (2X10ml) and brine. The organic layer was dried with anhydrous sodium sulphate, filtered and evaporated. The crude was recrystallized from DCM: hexane mixture and pure azide **29** was obtained in 92% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.22 – 5.13 (m, 2H), 5.08 (t, *J* = 9, 1H), 4.98 – 4.90 (m, 2H), 4.60 – 4.50 (m, 3H), 4.38 (dd, *J* = 12.5, 3.3 Hz, 1H), 4.13 – 4.02 (m, 2H), 4.03 – 3.96 (m, 1H), 3.80 (t, *J* = 9.5 Hz, 1H), 3.71 – 3.64 (m, 2H), 3.61 (dd, *J* = 9.9, 4.7 Hz, 1H), 3.52 – 3.44 (m, 1H), 3.27 (dt, *J* = 13.4, 3.4 Hz, 1H), 2.17 – 1.96 (m, 21H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.4, 170.24, 169.7, 169.6, 169.2, 169, 100.7, 100.5, 76.3, 72.9, 72.7, 72.4, 71.9, 71.5, 71.3, 68.6, 67.7, 61.6, 61.5, 50.4, 20.8, 20.6, 20.5.

HRMS (ESI^{+}) *m/z* calc. For $C_{28}H_{39}N_3O_{18,}$ 705.6186; found, 723.2585 $[M + NH_4]^{+}$.

I.R (cm^{-1}) 2963, 2105, 1432, 1366, 1165, 1130, 1035, 906, 731.

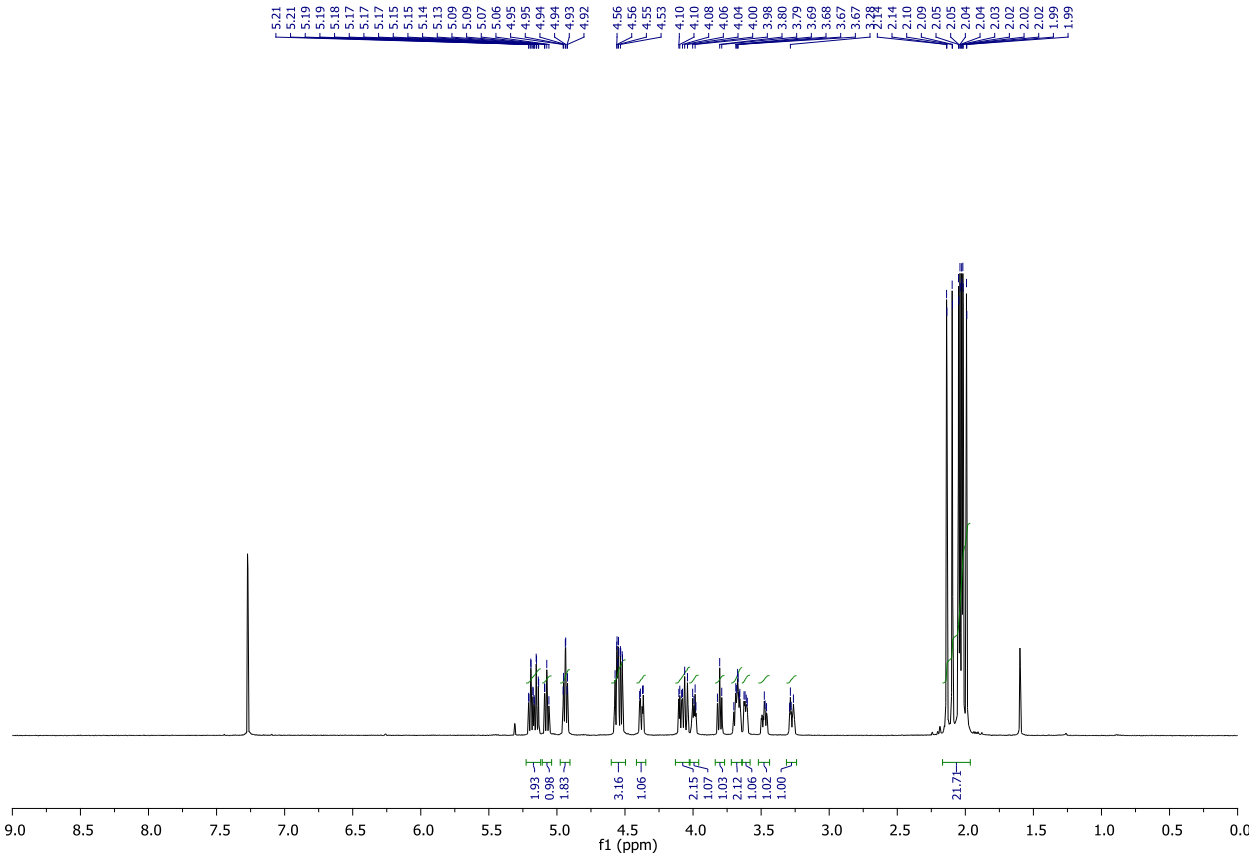


Figure S87. ^{1}H NMR spectrum of compound **29** ($CDCl_3$, 300 MHz).

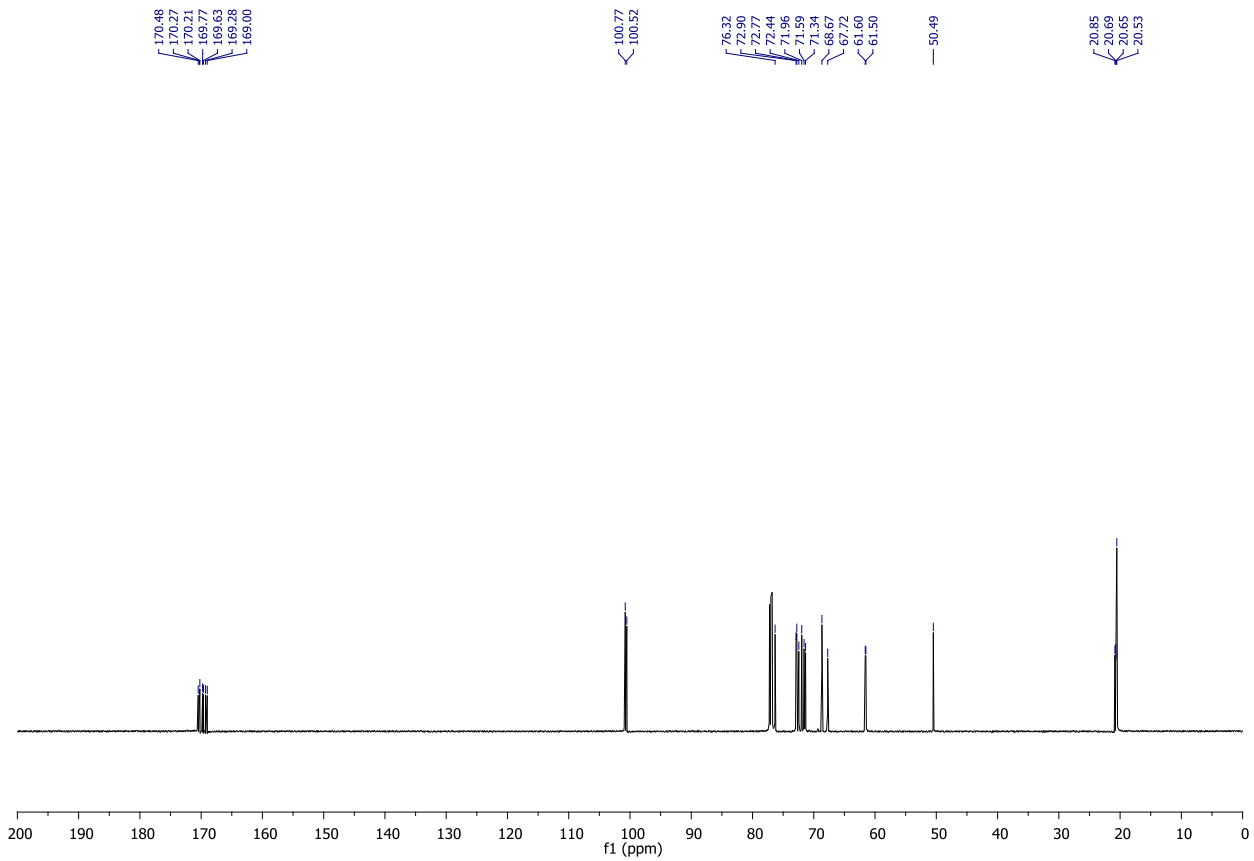


Figure S88. ^{13}C {^{1}H} NMR of compound **29** ($CDCl_3$, 151 MHz).

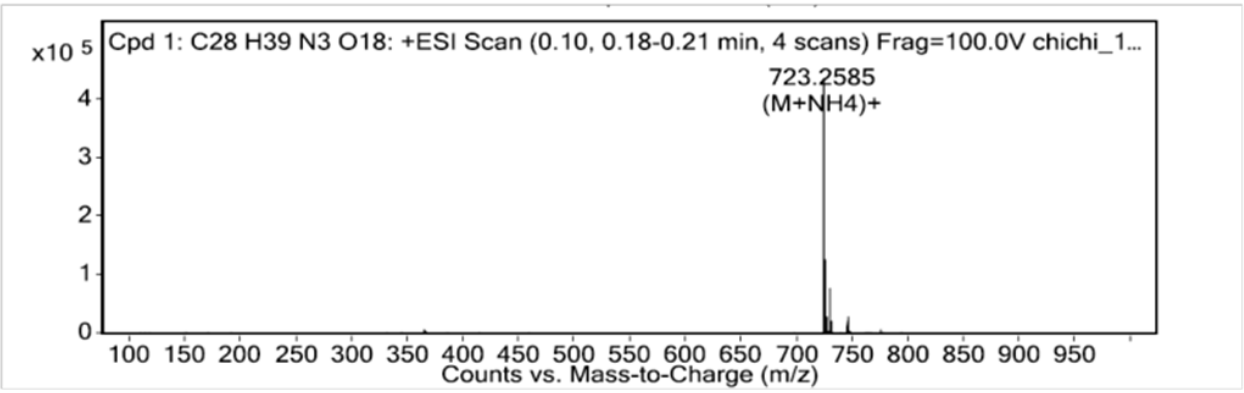


Figure S89. HRMS (ESI^+) spectrum of compound **29**.

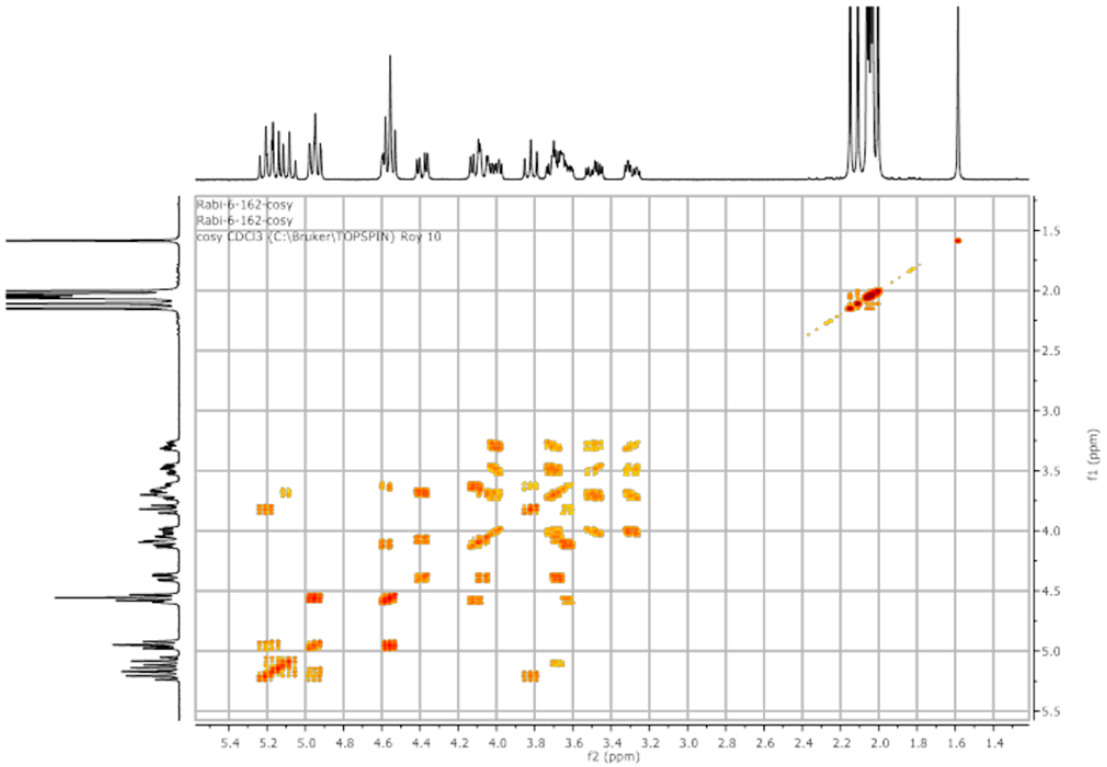


Figure S90. COSY spectrum of compound **29.**

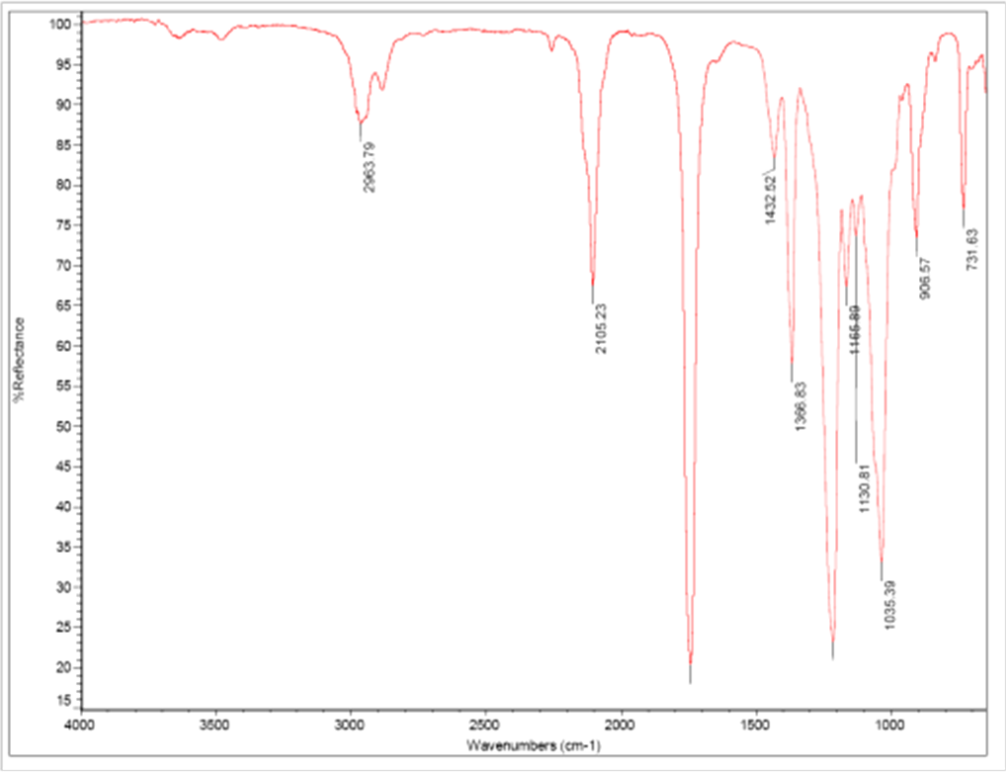
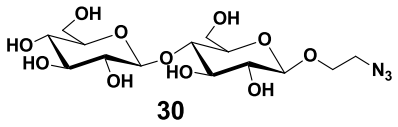


Figure S91. IR spectrum of compound **29**.



30

Synthesis of compound 30: To a solution of heptaacetyl-1(2-azidoethyl) cellobioside **29** (520 mg, 0.74 mmol) in methanol was added 1M NaOMe until pH 9-10 was reached. It was allowed to stir at room temperature for 5h. Acidic resin (IR-120) was added to make pH 5-6 and solution was filtered through cotton bed and evaporated to yield **30** in 90% yield.
^{1}H NMR (300 MHz, D_2O**)** δ 4.53 (dd, *J* = 7.9, 5.9 Hz, 2H), 4.11 – 3.23 (m, 16H).
^{13}C {^{1}H} NMR (75 MHz, D_2O) δ 110.4, 103.2, 102.8, 79.2, 76.6, 76.1, 75.4, 74.92, 73.8, 73.5, 70.1, 69.2, 61.2, 60.6, 51.1.
HRMS (ESI^{+}) *m/z* calc. For $C_{14}H_{25}N_3O_{11,}$ 411.3618; found, 434.1396 $[M + Na]^{+}$.
I.R (cm^{-1}) 3345, 2114, 1639, 1032.

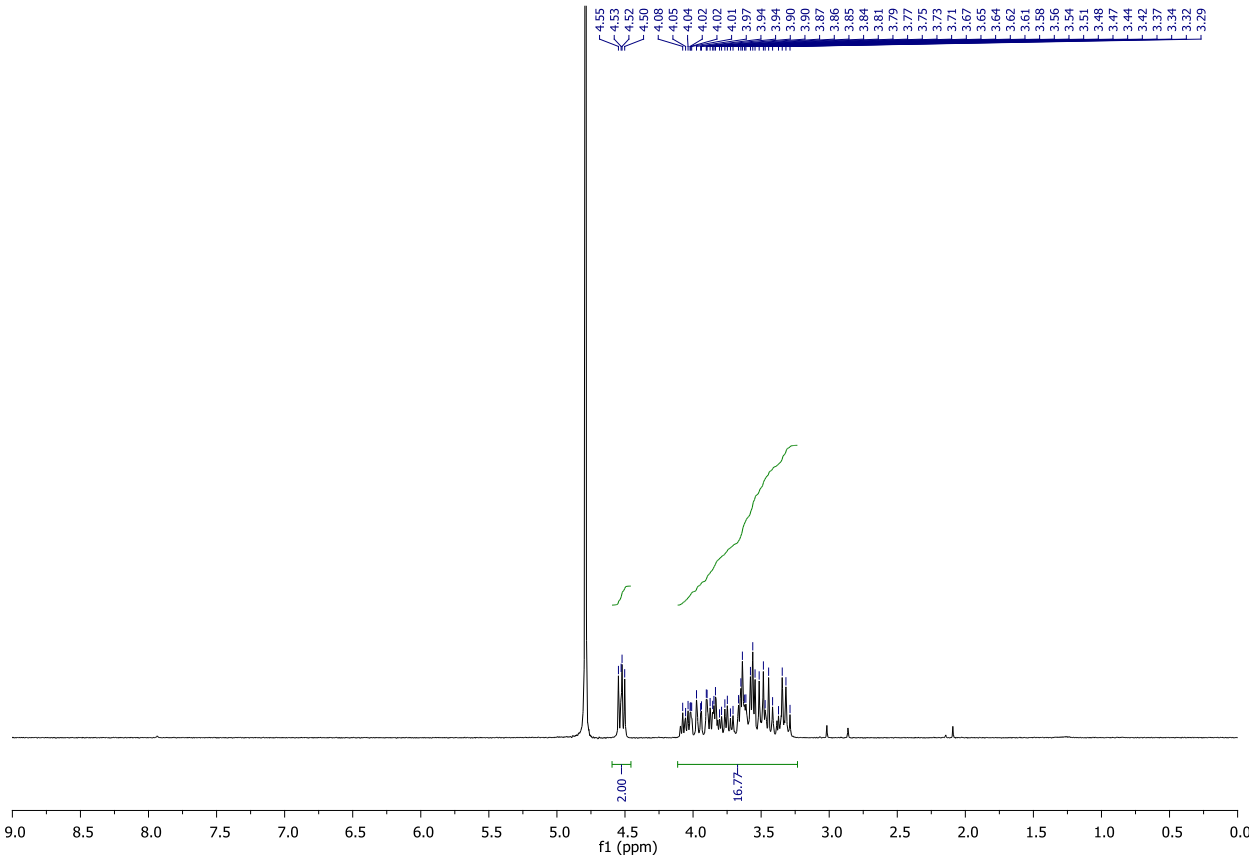


Figure S92. ^{1}H NMR spectrum of compound **30** (D_2O, 300 MHz).

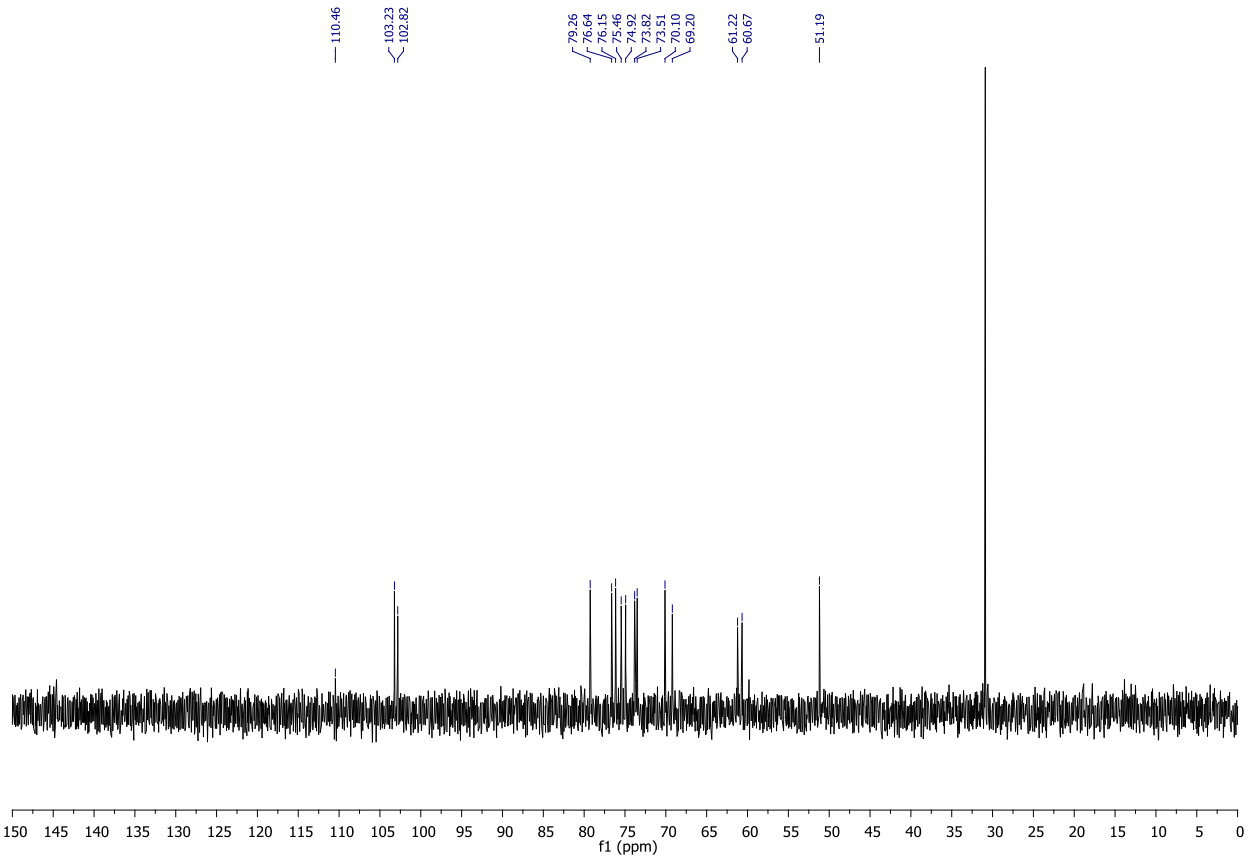


Figure S93. ^{13}C {^{1}H} NMR of compound **30** (D_2O, 75 MHz).

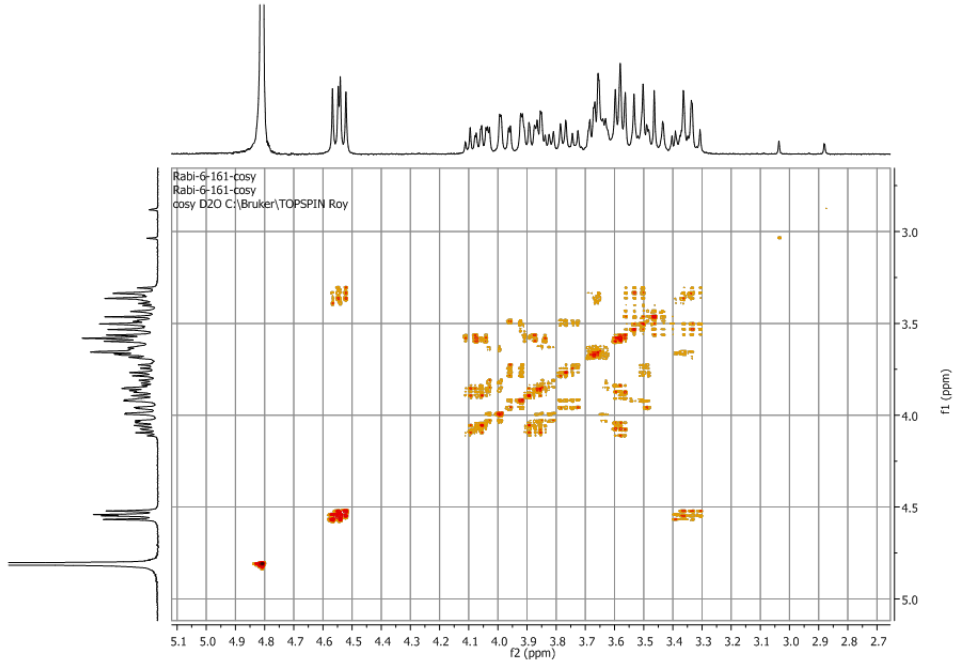


Figure S94. COSY spectrum of compound **30**.

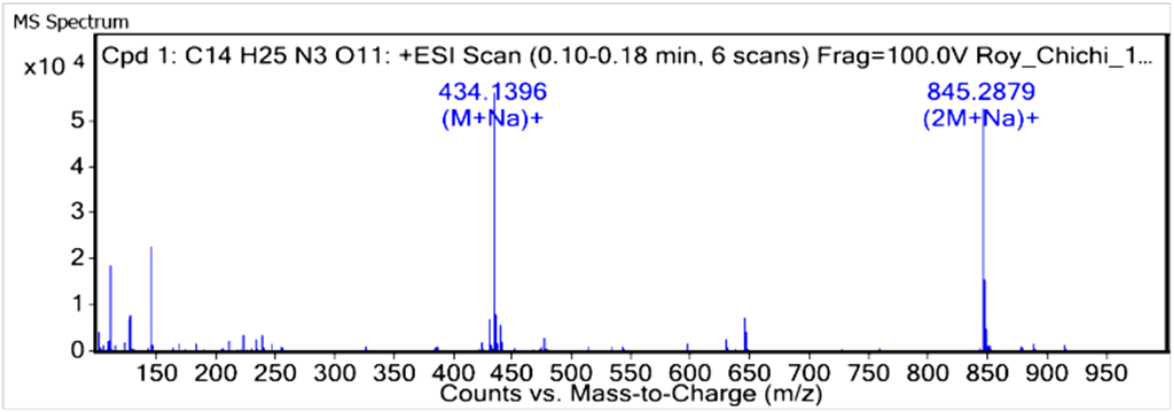


Figure S95. HRMS (ESI$^+$) spectrum of compound **30**.

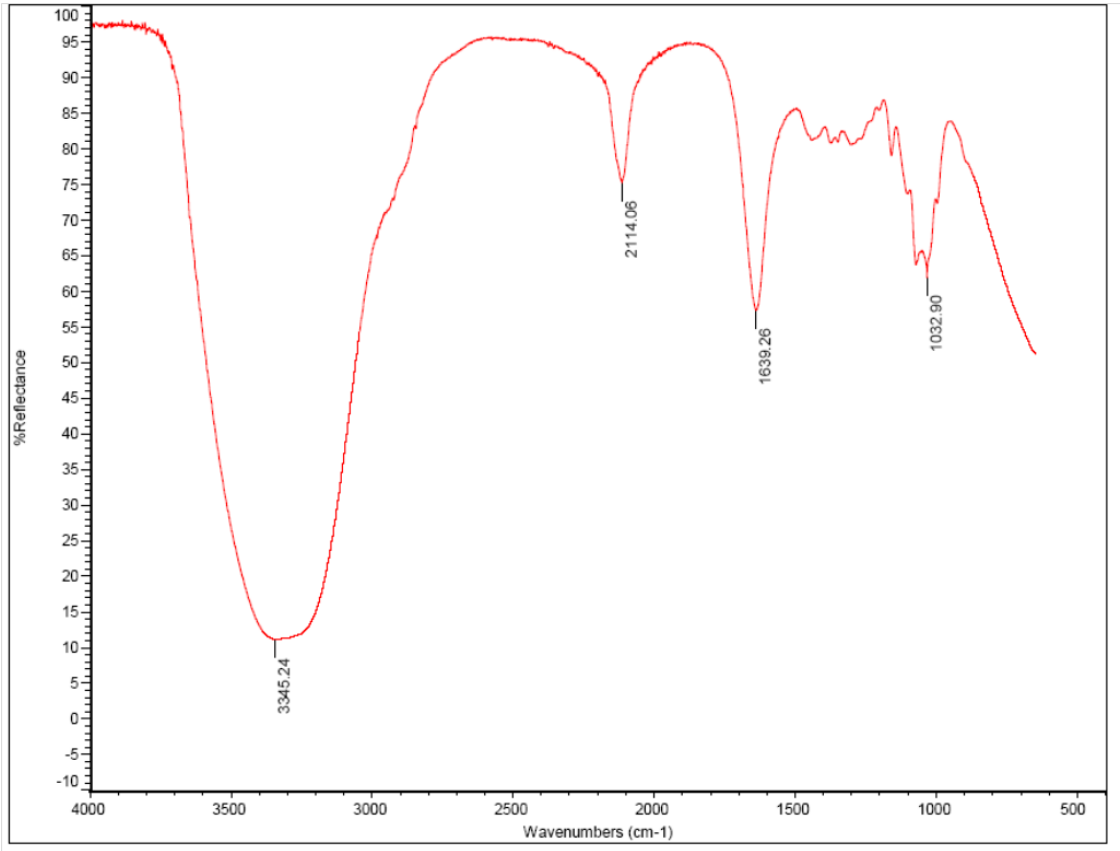
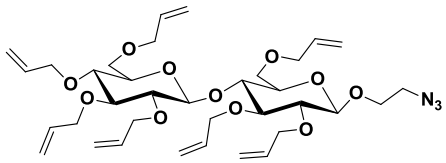


Figure S96. IR spectrum of compound **30**.



31

Synthesis of compound 31: To a solution of 1-(2-azidoethyl) cellobioside **30** (268 mg, 0.387 mmol) in DMF (10ml) at 0^{o}C sodium hydride (60% in oil, 500 mg, 12.5 mmol) was added. The mixture was stirred at 0^{o}C for 15 min followed by addition of allyl bromide (1.4 ml, 16.2 mmol) dropwise. The mixture was stirred at 0^{o}C for 1 h and at RT for 10 minutes. Reaction was quenched with saturated NH_4Cl sol. and extracted with EtOAc (50 ml) followed with brine wash. The organic layer was separated, dried and evaporated. The crude mixture was purified with column chromatography. The desired compound **31** was obtained using 20% EtOAc: hexane as eluent in 89% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.07 – 5.79 (m, 7H), 5.35 – 5.04 (m, 14H), 4.49 – 3.89 (m, 17H), 3.85 – 3.58 (m, 6H), 3.56 – 3.19 (m, 8H), 3.17 – 3.07 (t, J = 18 Hz, 1H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 136, 135.2, 135.1, 135, 134.9, 134.8, 134.6, 116.8, 116.7, 116.6, 116.4, 116.3, 115.7, 84.4, 82.4, 81.8, 81, 77.3, 77.2, 75, 74.7, 74.2, 74, 73.8, 73.7, 73.5, 72.3, 72.1, 68.6, 68.1, 68, 50.9

HRMS (ESI^{+}) *m/z* calc. For $C_{35}H_{53}N_3O_{11,}$ 691.8088; found, 709.4022 $[M + NH_4]^{+}$, 730.3342 $[M + K]^{+}$.

I.R (cm^{-1}) 3680, 3078, 2919, 2866, 2103, 1646, 1457, 1420, 1346, 1305, 1120, 994, 918.

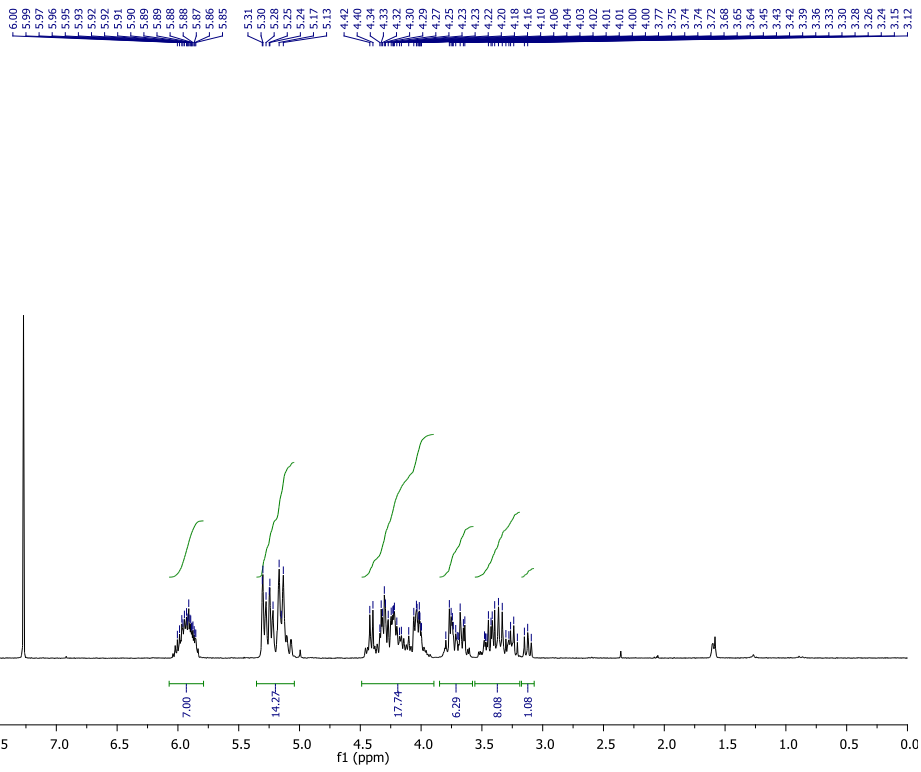


Figure S97. ^{1}H NMR spectrum of compound **31** ($CDCl_3$, 300 MHz).

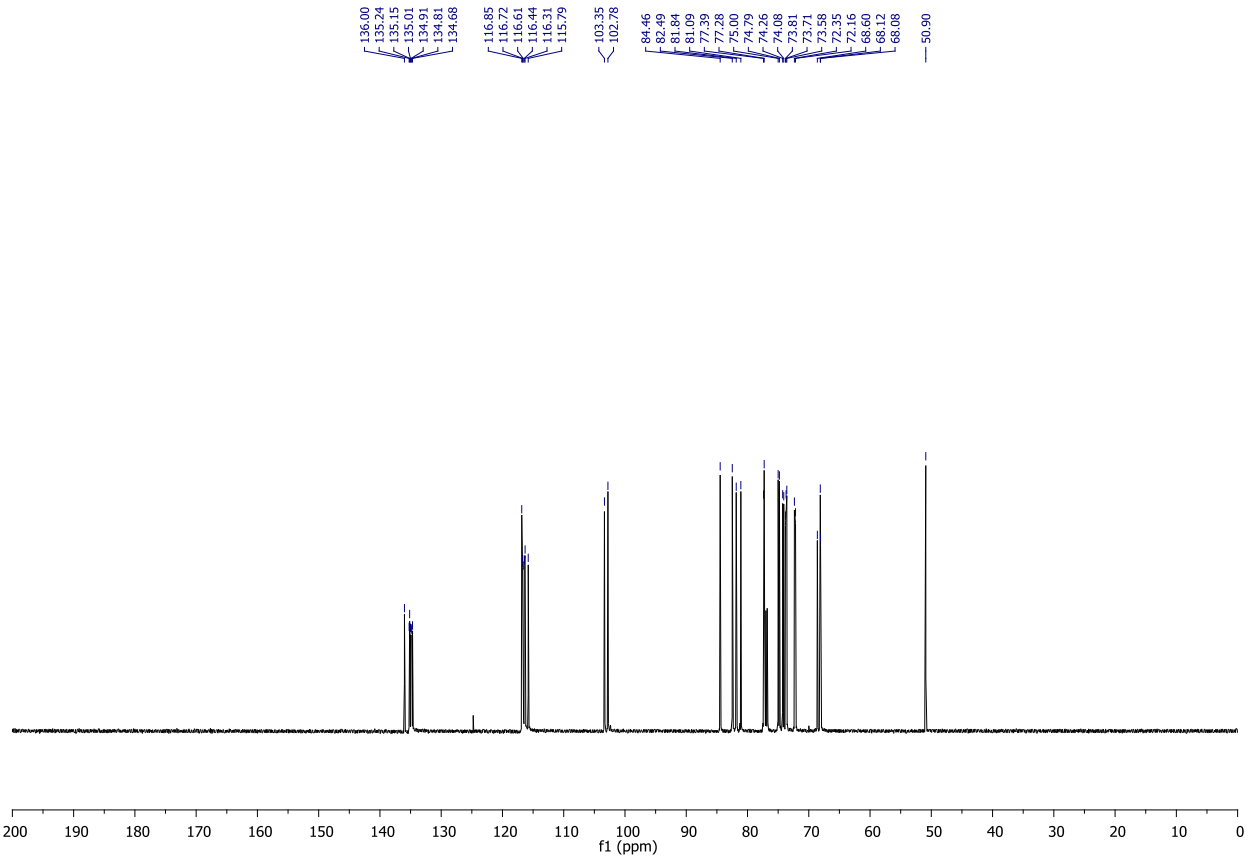


Figure S98. ^{13}C {^{1}H} NMR of compound **31** ($CDCl_3$, 151 MHz).

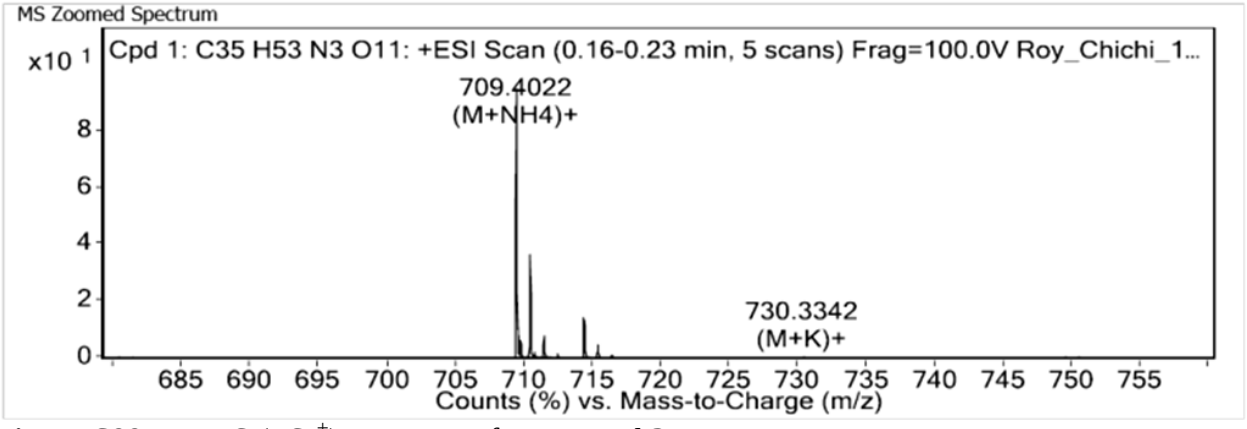


Figure S99. HRMS (ESI^{+}) spectrum of compound **31**.

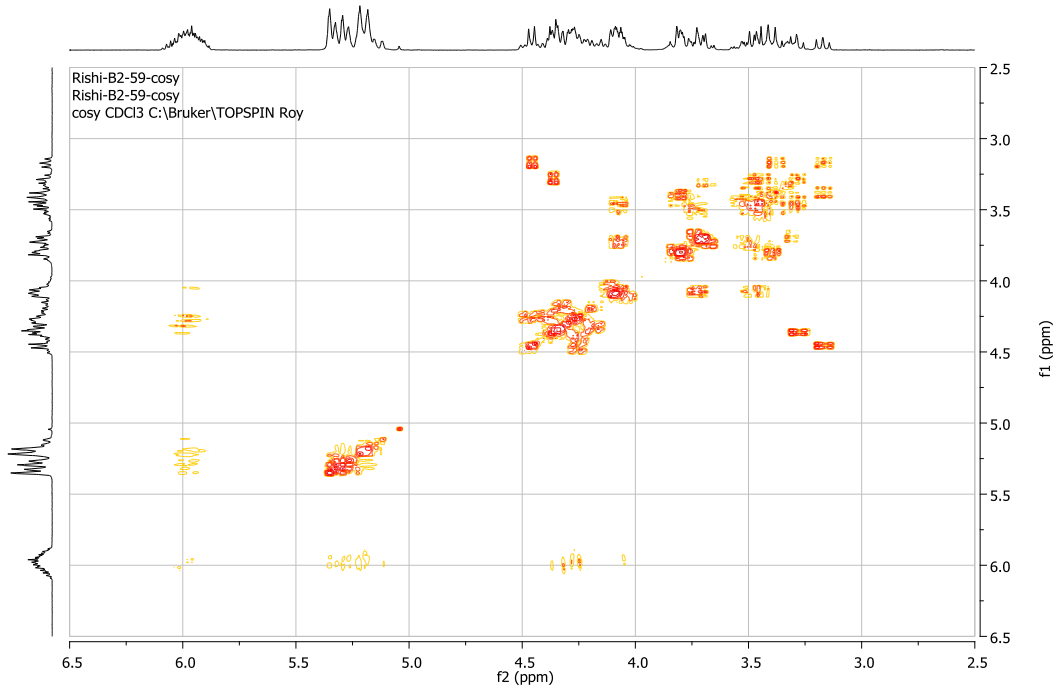


Figure S100. COSY spectrum of compound **31.**

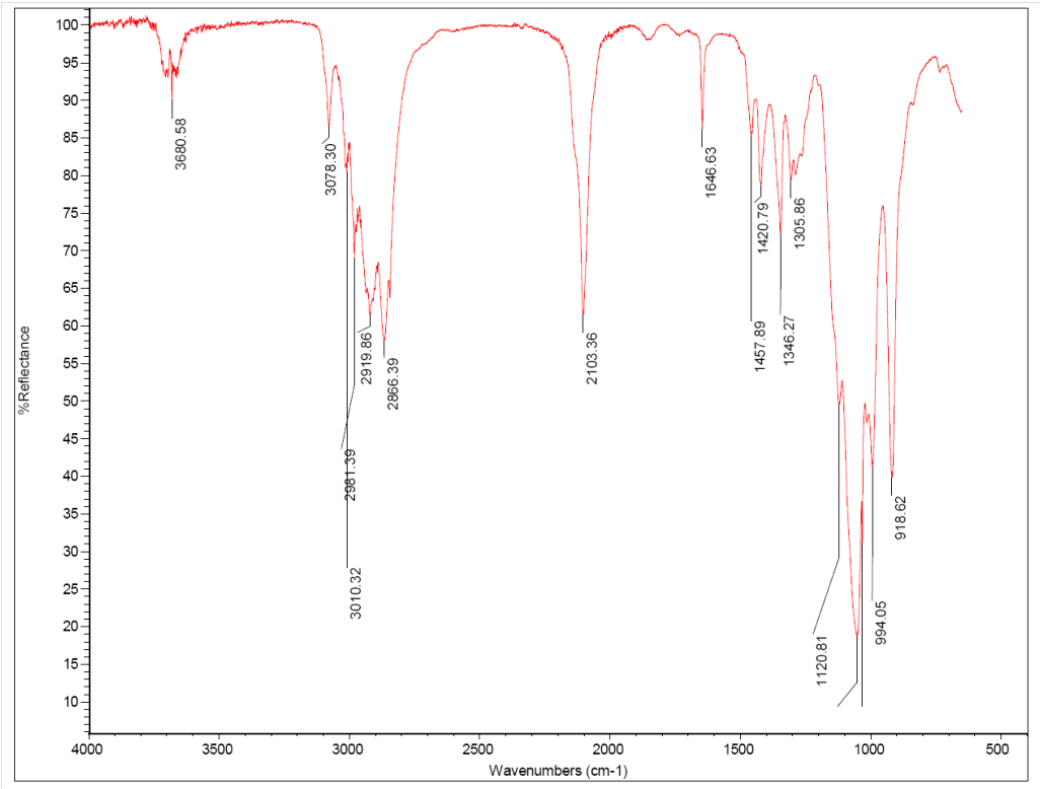
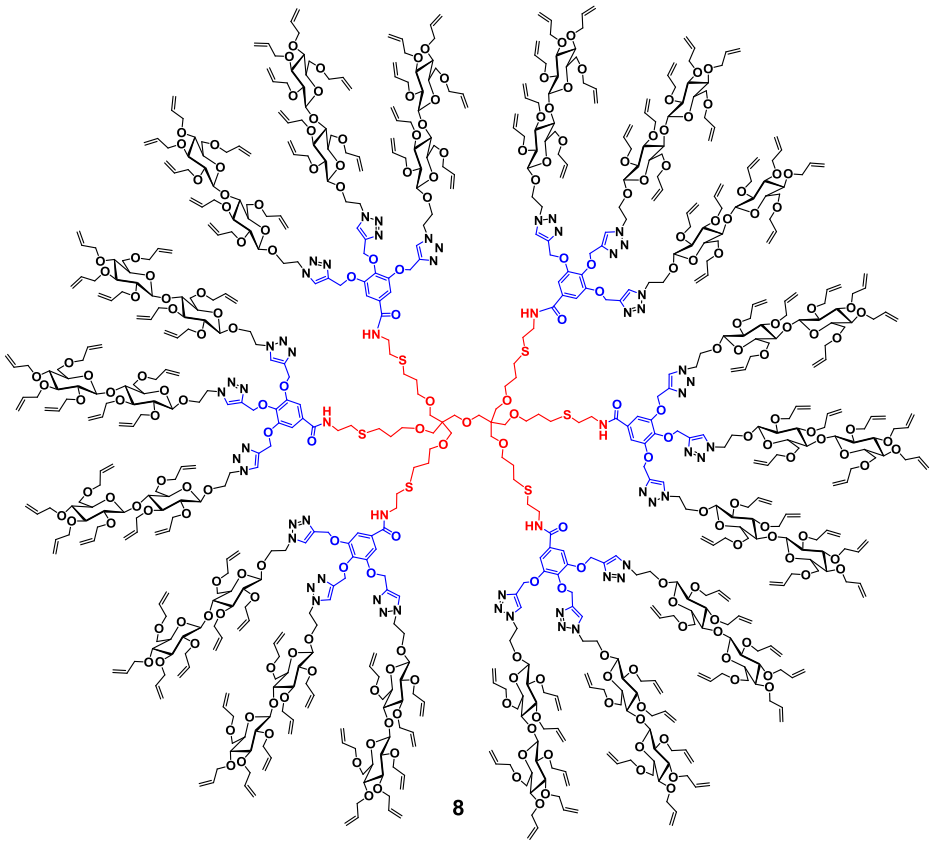


Figure S101. IR spectrum of compound **31**.



8

Synthesis of compound 8: Propargyl terminated dendrimer **1** (10 mg, 0.0039 mmol, 1eq), compound **31** (72 mg, 0.105 mmol, 27 eq.), $CuSO4.5H_2O$ (9 mg, 0.0351 mmol, 9 eq.) and sodium ascorbate (7 mg, 0.0351 mmol, 9 eq.) were reacted together following the procedure A and was purified by column chromatography (4% MeOH in DCM as eluent) to yield compound **8** as a colourless oil in 76% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 – 7.88 (m, 18H), 7.30 (br s, 12H), 6.04 – 5.69 (m, 126H), 5.32 – 4.98 (m, 272H), 4.68 – 3.03 (m, 638H), 2.85 (br s, 12H), 2.70 (br s, 12H), 1.87 (br s, 12H).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ 166.6, 151.8, 144.0, 143.3, 135.9, 135.2, 134.9, 134.8, 134.5, 129.9, 124.6, 116.8, 116.7, 116.5, 116.3, 115.8, 115.7, 107.1, 103.0, 102.7, 84.4, 82.4, 81.8, 80.7, 74.9, 74.7, 74.2, 74.0, 73.6, 73.5, 73.4, 72.3, 72.0, 68.6, 68.4, 68.0, 67.9, 67.5, 62.5, 50.2, 45.5, 39.3, 34.6, 31.5, 29.6, 25.2, 22.5, 14.0, 11.3.

I.R (cm^{-1}) 3648, 3403, 3080, 2980, 2971, 2918, 1647, 1459, 1379, 1261, 1072, 925.

MALDI-TOF m/z: calculated for $C_{766}H_{1102}N_{60}O_{229}S_6$: 15007.6007, found: 15011.0180

GPC ($CHCl_3$): M*n*= 15140 g/mol. M*w/Mn*= 1.07

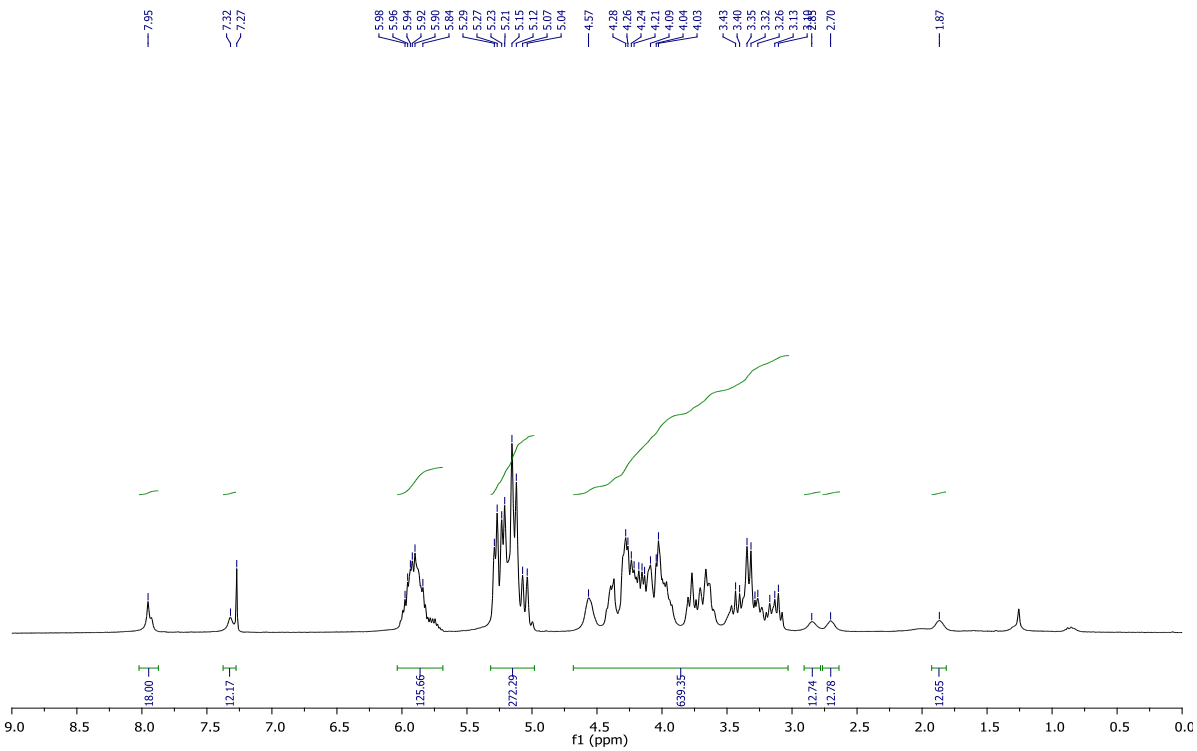


Figure S102. ^{1}H NMR spectrum of compound **8** ($CDCl_3$, 300 MHz).

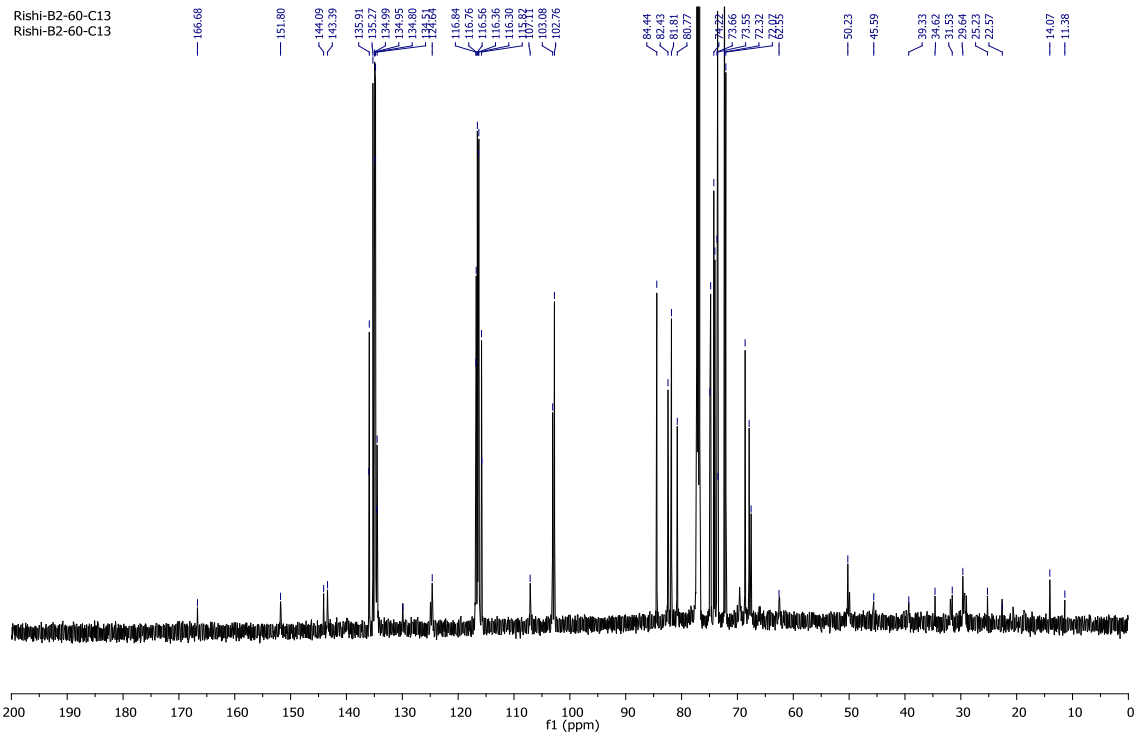


Figure S103. ^{13}C {^{1}H} NMR of compound **8** ($CDCl_3$, 151 MHz).

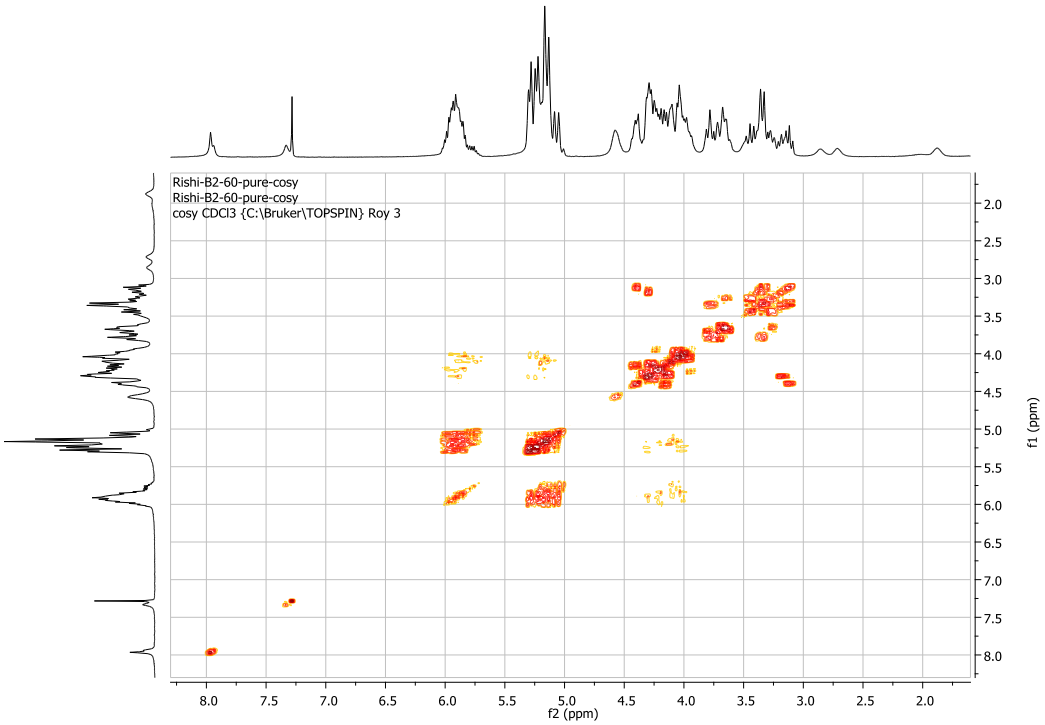


Figure S104. COSY spectrum of compound **8.**

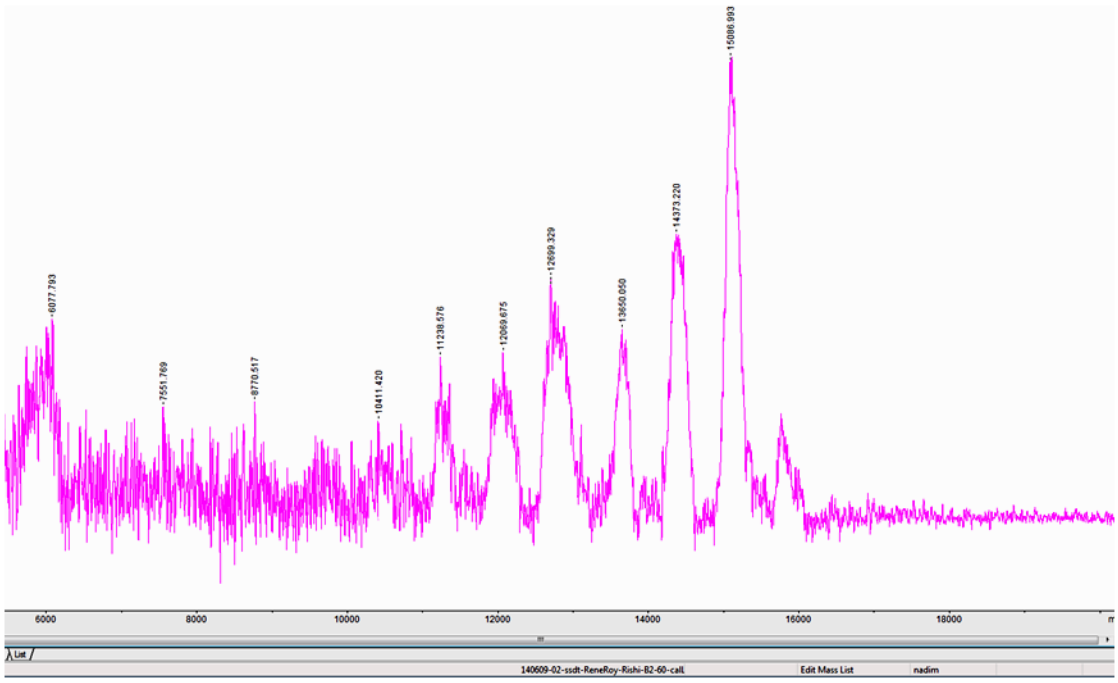


Figure S105. MALDI-TOF spectrum of compound **8**.

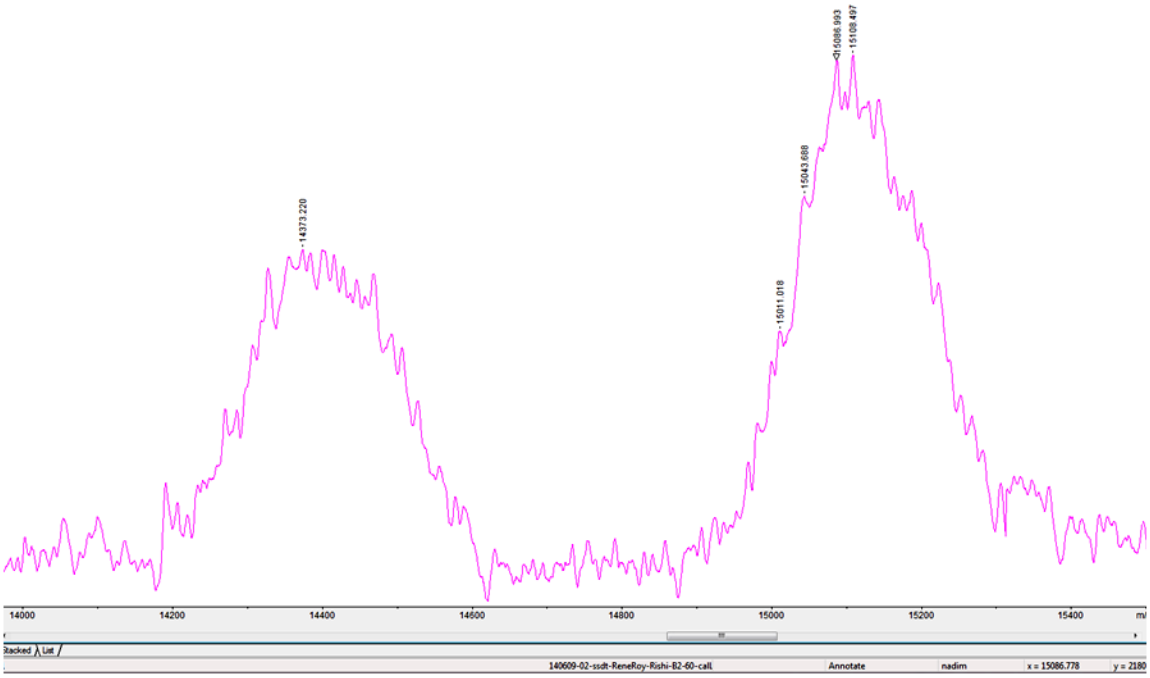
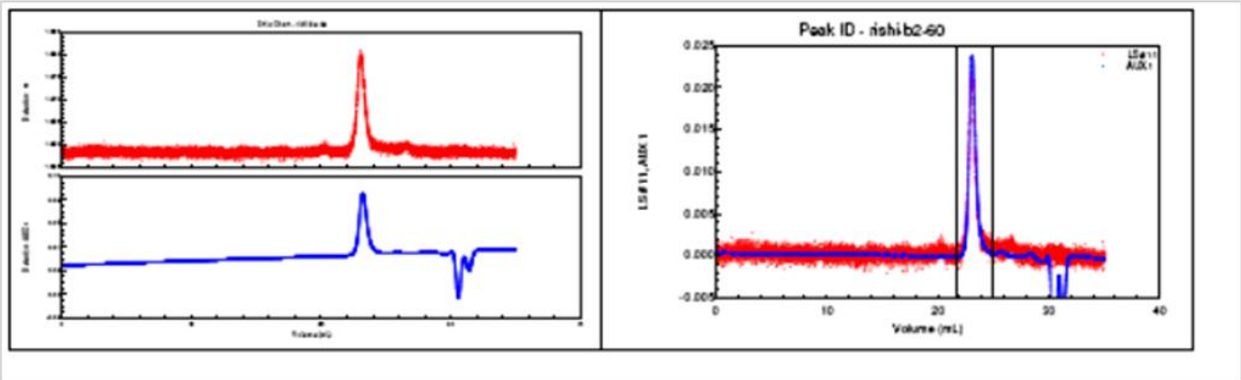


Figure S106. MALDI-TOF expanded spectrum of compound **8**.



Volume (mL)	:	21.587 - 24.971
Slices (used)	:	813 (698)
A2 (mol mL/g^2)	:	0.000e+00
Fit degree	:	1
Injected Mass (g)	:	1.3600e-04
dn/dc (mL/g)	:	0.079
Polydispersity(Mw/Mn)	:	1.074±0.152 (14%)
Polydispersity(Mz/Mn)	:	1.400±0.490 (35%)
Molar Mass Moments (g/mol)		
Mn	:	1.514e+04 (9%)
Mw	:	1.626e+04 (10%)
Mz	:	2.120e+04 (33%)
R.M.S. Radius Moments (nm)		
Rn	:	23.2 (73%)
Rw	:	23.8 (72%)
Rz	:	25.8 (70%)

COLLECTION INFORMATION		
Collection time	:	Wed May 08,
Instrument type	:	DAWN EOS
Cell type	:	K5
Laser wavelength	:	690.0 nm
Solvent name	:	Chcl3
Solvent RI	:	1.446
Calibration constants		
DAWN	:	8.7600e-06
» AUX1	:	2.8000e-04
AUX2	:	1.0000e-04
Flow rate	:	1.000 mL/min
Collection interval	:	0.250 sec
Number of slices	:	9400

Figure S107. GPC traces of compound **8**.

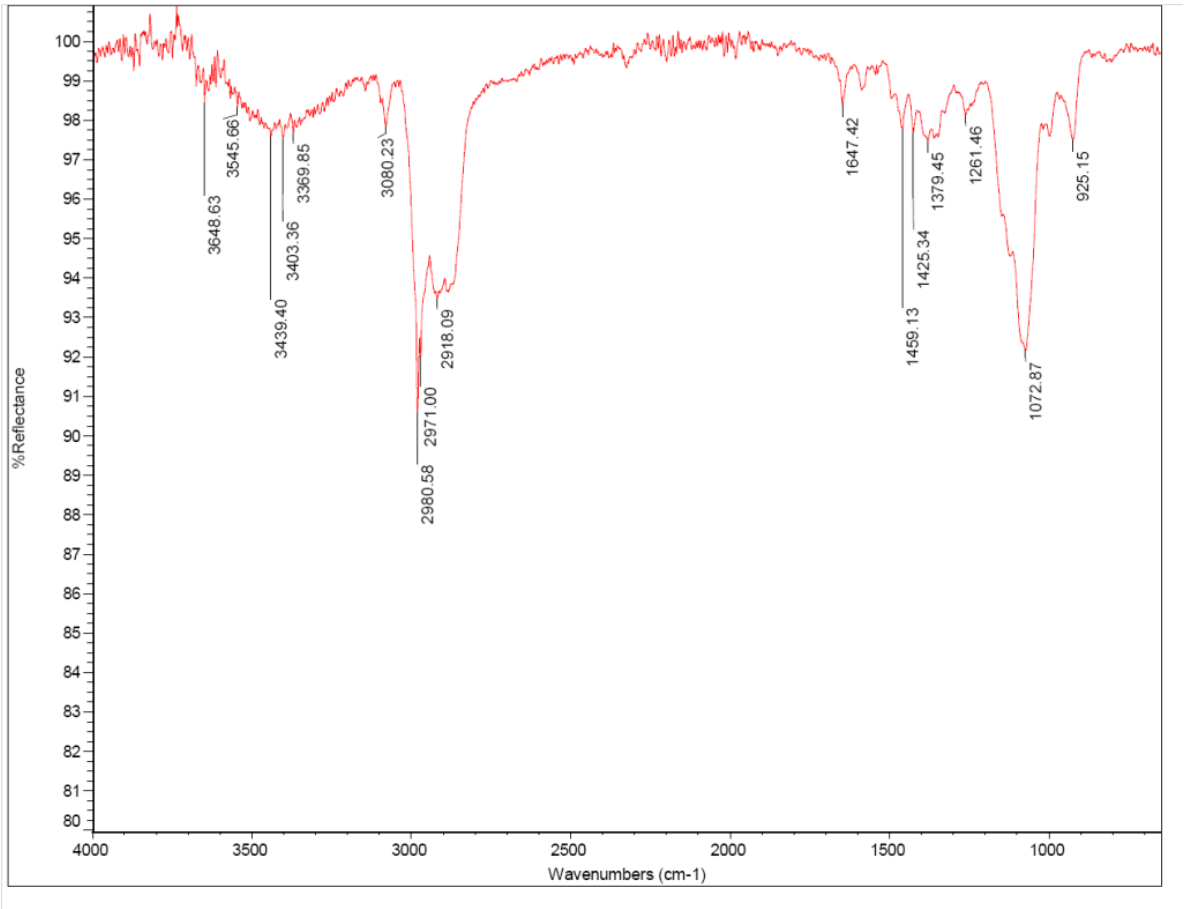
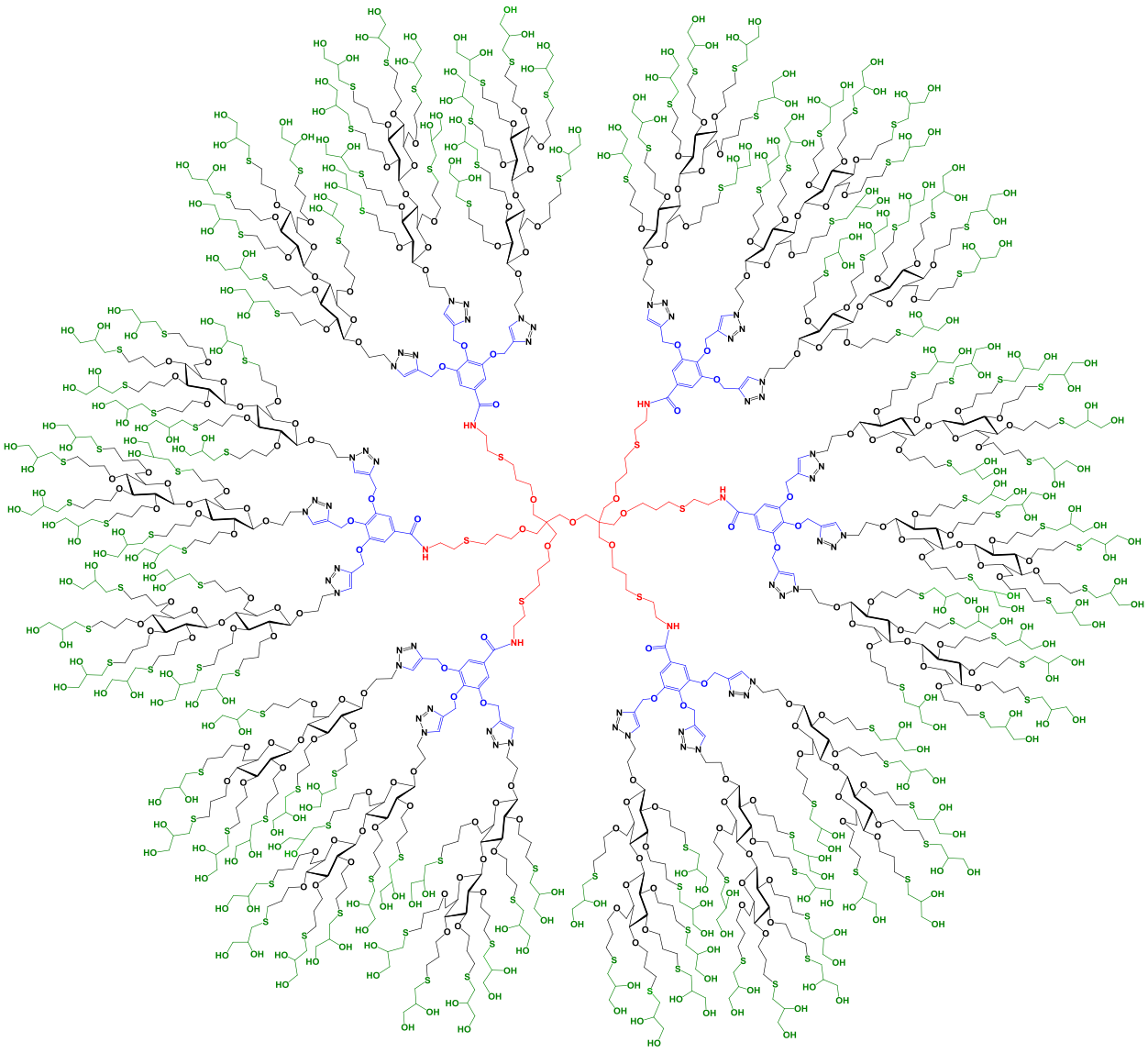


Figure S108. IR spectrum of compound **8**.



Synthesis of compound 9: Allyl terminated dendrimer **8** (25 mg, 0.0016 mmol, 1eq), 1-thioglycerol (0.096 ml, 1.4mmol, 882 eq.), and AIBN (4 mg, 0.020, 12.6 eq.) were reacted together following the procedure B and was purified by dialysis to yield compound **9** as a colourless oil in 85% yield.

^{1}H NMR (600 MHz, MeOD) δ 8.16 (br s, 12H), 7.92 (br s, 6H), 7.30 (br s, 6H), 5.35 – 4.95 (m, 48H), 4.69 – 4.47 (m, 40H), 4.43 – 2.17 (m, 1308H), 2.07 – 1.40 (m, 208H), 1.35 – 1.05 (m, 34H).

^{13}C {^{1}H} NMR (151 MHz, MeOD) δ 153.5, 144.3, 126.4, 104.4, 103.8, 86.2, 83.9, 82.8, 79.3, 77.6, 76.2, 73.2, 72.8, 71.9, 71.0, 70.9, 66.1, 65.3, 49.4, 49.2, 49.0, 48.8, 48.7, 48.5, 43.5, 36.3, 36.3, 31.8, 31.5, 31.0, 30.5, 30.4, 23.7, 21.2, 19.3, 17.9.

I.R (cm^{-1}) 3707, 3694, 3680, 3377, 2981, 2937, 2922, 2866, 2843, 1050, 1033, 1013.

(MALDI-TOF) m/z: calculated for $C_{1146}H_{2118}N_{60}O_{481}S_{132}$: 28667.7725, found: 28690.0370. $[M+Na]^{+}$.

Differential light scattering Hydrodynamic diameter: 6.41nm

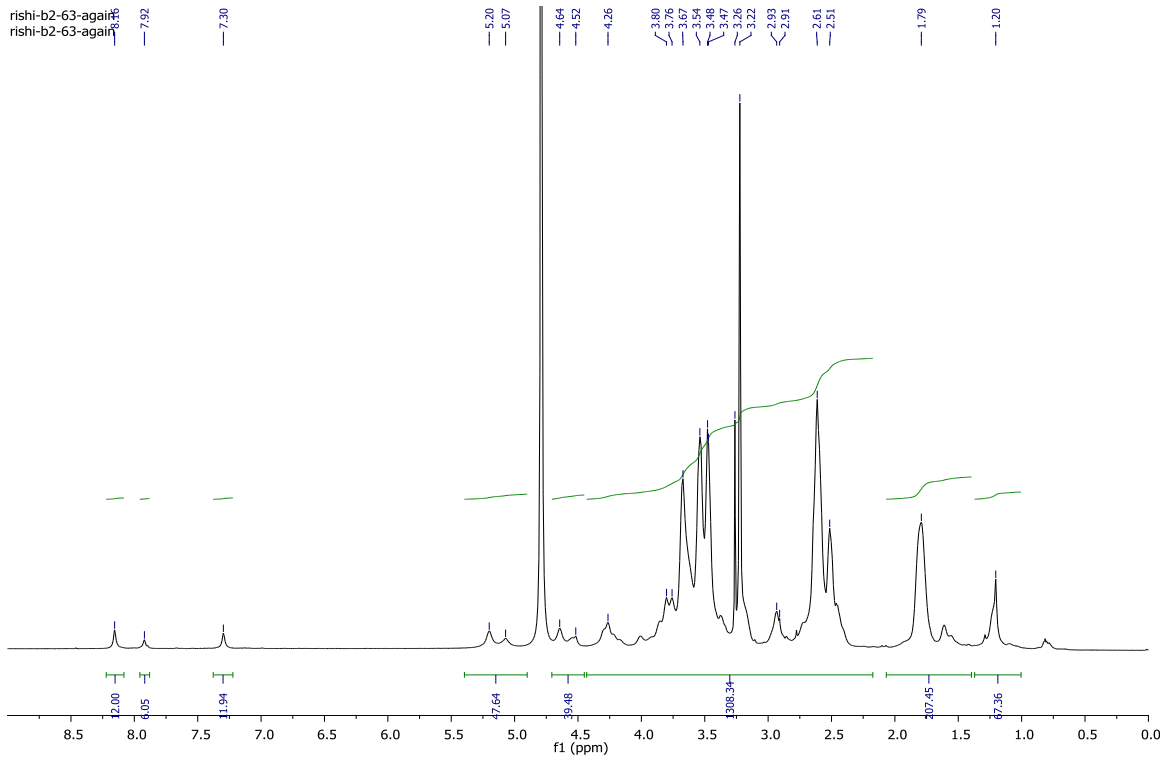


Figure S109. ^{1}H NMR spectrum of compound **9** (CD_3OD, 300 MHz).

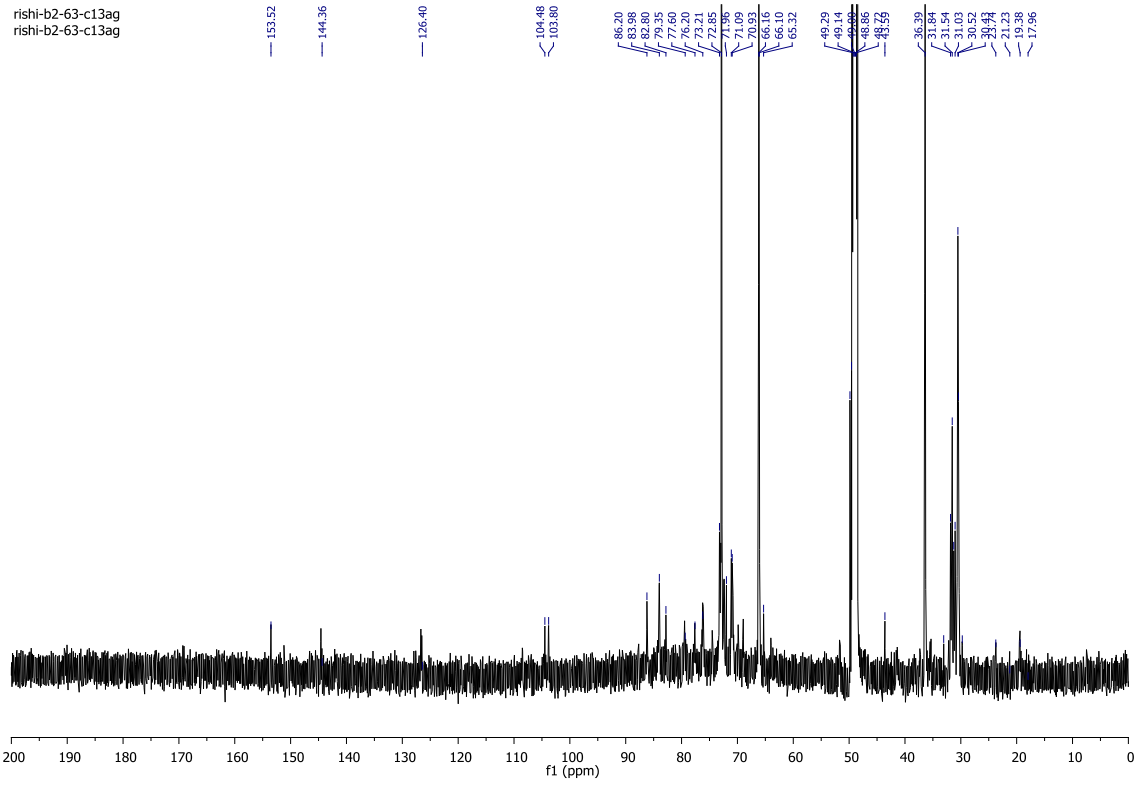


Figure S110. ^{13}C {^{1}H} NMR of compound **9** (CD_3OD, 151 MHz).

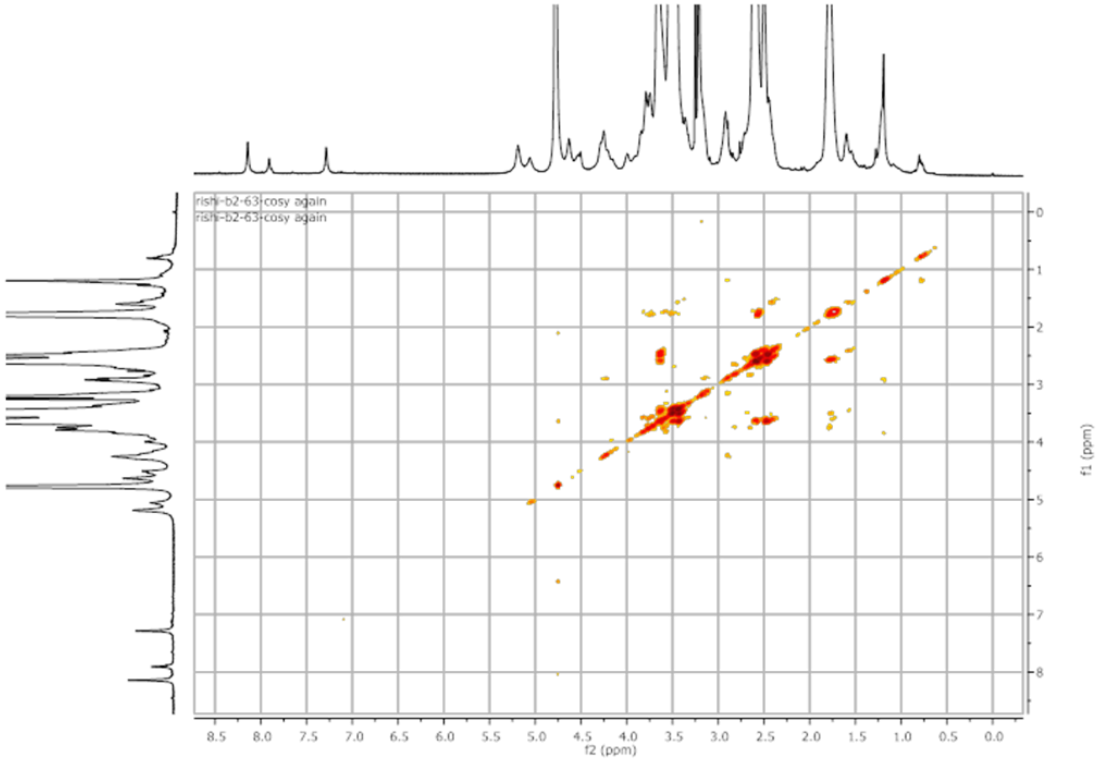


Figure S111. COSY spectrum of compound **9.**

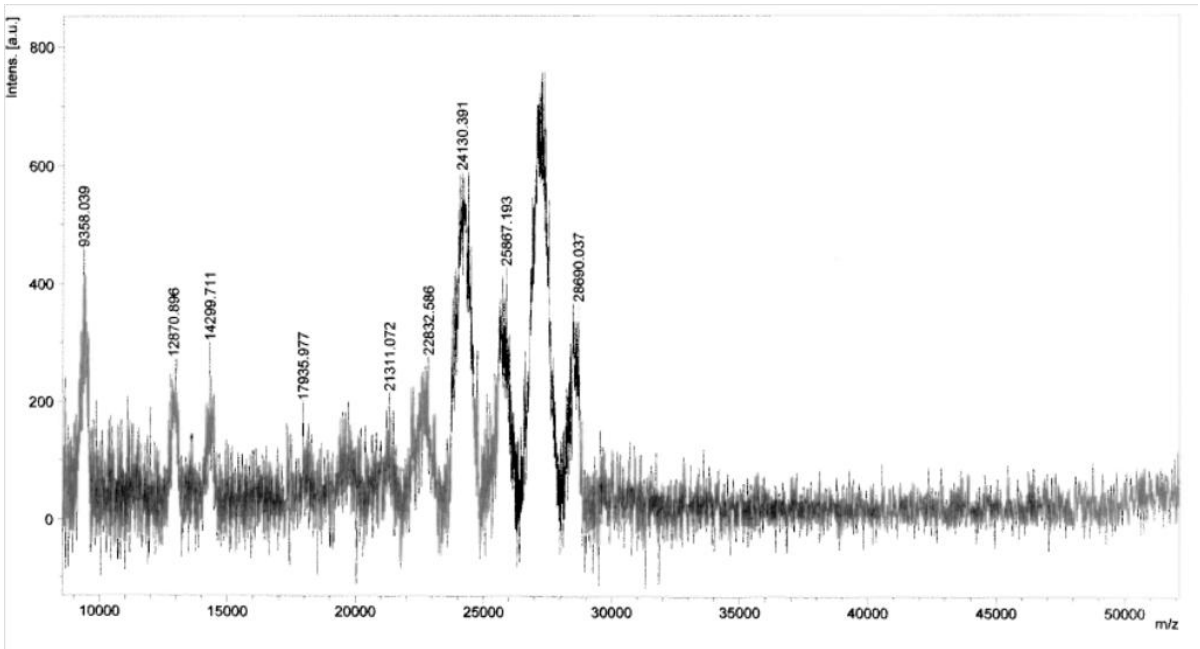


Figure S112. MALDI-TOF expanded spectrum of compound **9.**

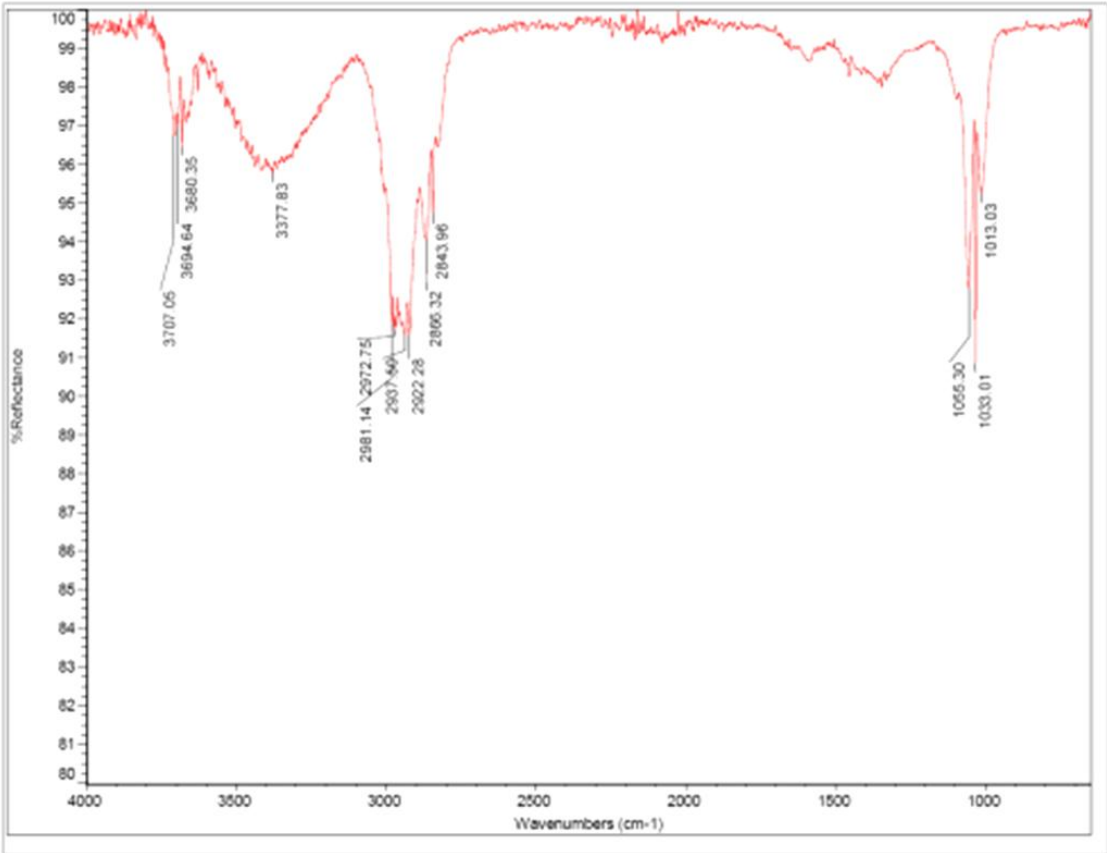


Figure S113. IR spectrum of compound **9**.

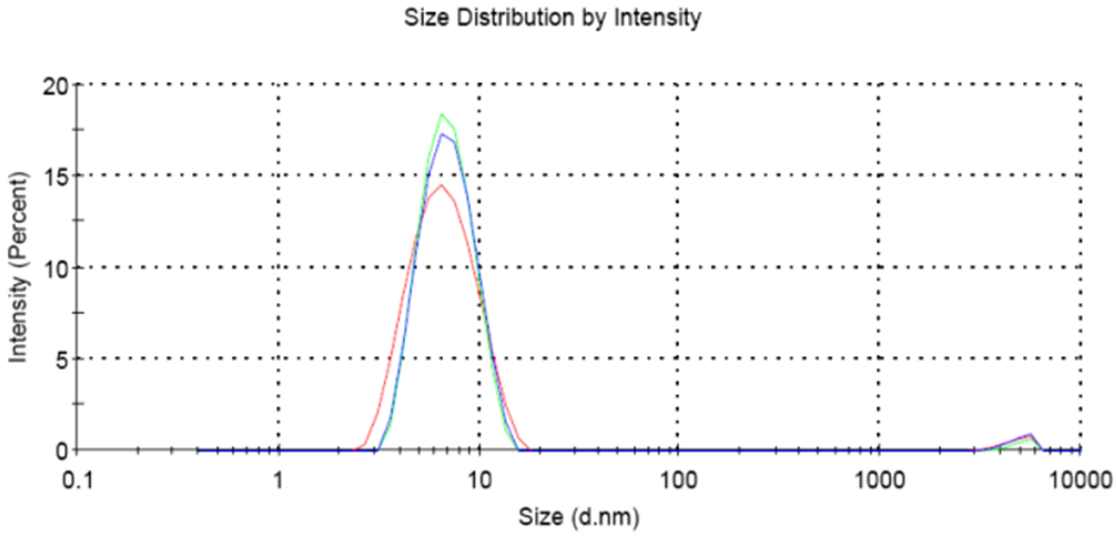


Figure S114. DLS size distribution of dendrimer **9** in methanol at 25^{o}C

3. Biological Experiments:

Cell culture and treatment. The HepG2, U251N and MCF-7 human cell lines were originally obtained from the American Type Culture Collection. HepG2 cells were cultured in Minimum Essential Medium (Invitrogen); U251N and MCF-7 cells were cultured in Dulbecco's Modified Eagle's Medium (Invitrogen). All media were supplemented with 10% (v/v) fetal bovine serum (Invitrogen), 2 mM L-glutamine, 100 IU/mL penicillin, 100 μg/mL streptomycin (Invitrogen), and 1% non-essential amino acids. Cells were maintained at 37°C with 5% CO_2.

Confluent HepG2, U251N and MCF-7 cells cultures were detached using 0.05% trypsin-EDTA (Invitrogen), seeded at 20,000 cells per well in 96-well plates (Sarstedt), and cultured for 24h before treatment. Cells were treated with dendrimers at increasing concentrations (1 nM, 10 nM, 50 nM, 100 nM, 500 nM, 1 μM, 5 μM, and 10 μM) for 24h. Dendrimers were dissolved in dimethyl sulfoxide (DMSO; Sigma-Aldrich), and in-well DMSO concentrations were kept below 0.3%. Vehicle controls were included in each experiment.

MTT assay. After treatment, media was refreshed with serum-deprived media, and thiazolyl blue tetrazolium (Sigma-Aldrich) was added for an in-well concentration of 0.5 mg/mL. Cells were incubated for 30 minutes at 37°C to allow for the formation of formazan crystals, following which the medium was removed and 100 μL/well of DMSO was added to dissolve the formazan. Absorbance was measured at 595 nm using an Asys UVM 340 microplate reader (Biochrom).

Cell viability assay. After treatment, media was removed and cells were washed twice with phosphate buffered saline (PBS). Cells were fixed using 4% paraformaldehyde for 15 minutes, labelled with 10 μM Hoechst 33342 (Sigma-Aldrich) for 10 minutes, then washed and stored in PBS. Imaging of cell nuclei fluorescently labelled with Hoechst was performed using an Operetta high-throughput imaging platform (Perkin Elmer). Image analysis and cell counting was done in the Columbus Analysis platform (Perkin Elmer).

Statistical analysis. Each experiment was performed three times and each treatment was included in sixplicate. The student's *t*-test with Bonferroni correction was used to find significant differences between treatments (p values < 0.01 were considered significant).

Reference:

1 Diaz, M. D.; Berger, S. Carbohydr. Res. 2000, 329, 1−5.