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ELECTRONIC SUPPORTING INFORMATION

A Highly versatile convergent/divergent "onion peel" synthetic strategy toward potent multivalent glycodendrimers

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Contents

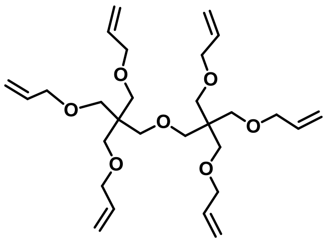
1. Materials and methods:

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. Water used for lyophilization of final dendrimers was nanopure grade, purified through Barnstead NANOPure II Filter with Barnstead MegOhm-CM Sybron meter. 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 of de-*O*-acetylated compounds), 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 THF as the eluent, at 40^oC 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 (M_n) and polydispersity index (M_w/M_n). 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 wavenumbers (cm^{-1}).

Accurate mass measurements (HRMS) were performed on a LC-MSD-ToF instrument from Agilent Technologies in positive electrospray mode. Low-resolution mass spectra were performed on the same apparatus or on a LCQ Advantage ion trap instrument from Thermo Fisher Scientific in positive electrospray mode (Mass Spectrometry Laboratory (Université de Montréal), or Plateforme analytique pour molécules organiques (Université du Québec à Montréal), Québec, Canada). 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). Samples were solubilized in H_2O for a final concentration of 6 mg/mL. Dihydroxybenzoic acid was used as the matrix. Cationization was eased by the use of the corresponding sodium salt (2 mg/mL).

2. Synthetic protocols and characterization:



Synthesis of compound 2: A flame dried two-neck round bottom flask (250mL) was charged with dipentaerythritol **1** (4.00g, 15.7mmol) and sodium hydride (3.77g, 157.4mmol). To this, DMF (60ml) was added slowly at 0^{o}C under nitrogen atmosphere. The reaction mixture was stirred for 20 minutes at 0^{o}C. It was followed by the addition of allyl bromide (16.3mL, 188.8mmol) and stirred for 5 hrs at room temp. The completion of reaction was monitored by TLC. The reaction mixture was then quenched with methanol at 0^{o}C. Solvent was evaporated and the residue was dissolved in ethyl acetate (100mL) and washed with water. Organic layer was separated, dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude compound was purified by column chromatography using 7% ethyl acetate in hexanes as eluent to afford desired compound **2** (6.22g, 12.6mmol) in 80% yield as light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddt, *J* = 17.1, 10.5, 5.3 Hz, 6H), 5.34–5.08 (m, 12H), 3.94 (dt, *J* = 5.2, 1.4 Hz, 12H), 3.46 (d, *J* = 7.9 Hz, 12H), 3.40 (s, 4H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 135.3, 116.0, 72.3, 70.1, 69.4, 45.6.
IR (cm^{-1}) 3079, 2980, 2903, 2867, 1646, 1478, 1420, 1349, 1269, 1173, 989, 920.
HRMS (ESI^{+}) for $C_{28}H_{46}O_7$ *m/z* calc for $C_{28}H_{46}O_7$, 495.3316 $[M+H]^+$; found: 495.3299.

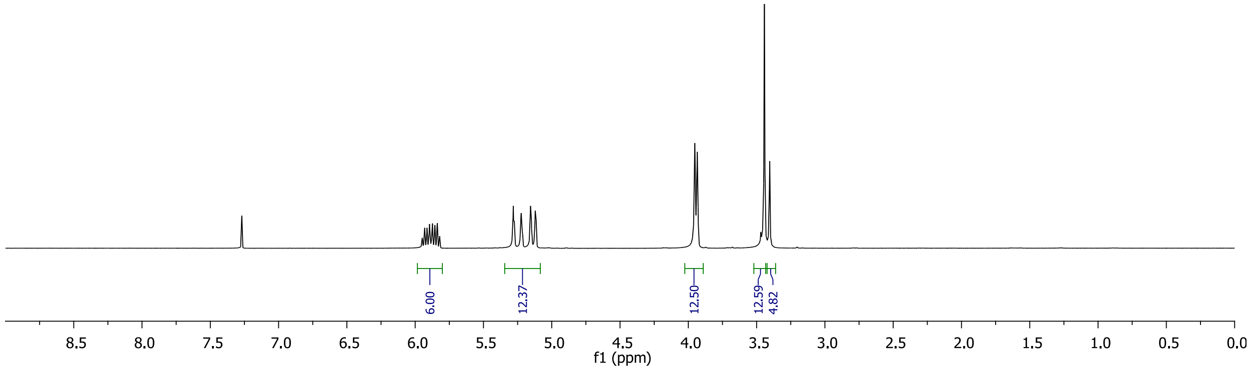


Figure S1. ^{1}H NMR spectrum of compound **2** ($CDCl_3$, 300 MHz).

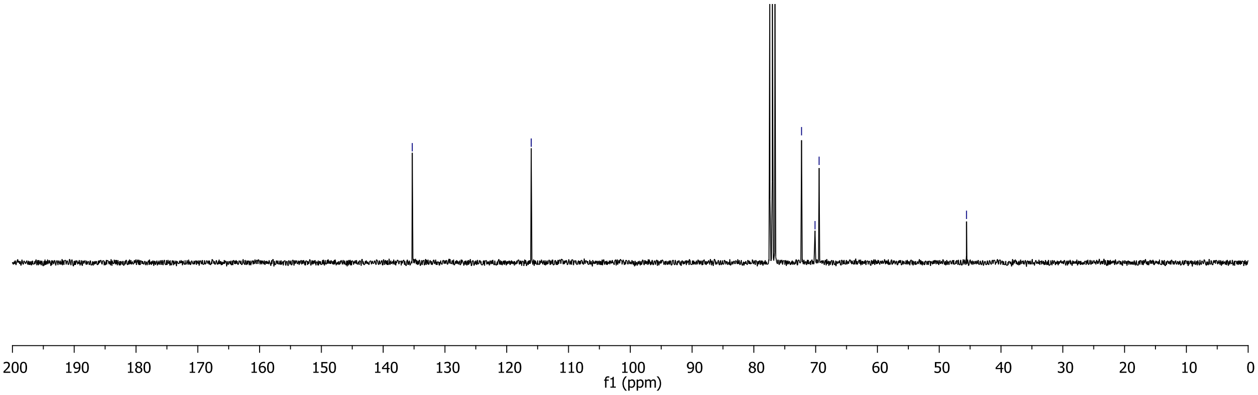


Figure S2. $^{13}C\{^{1}H\}$ NMR spectrum of compound **2** ($CDCl_3$, 75 MHz).

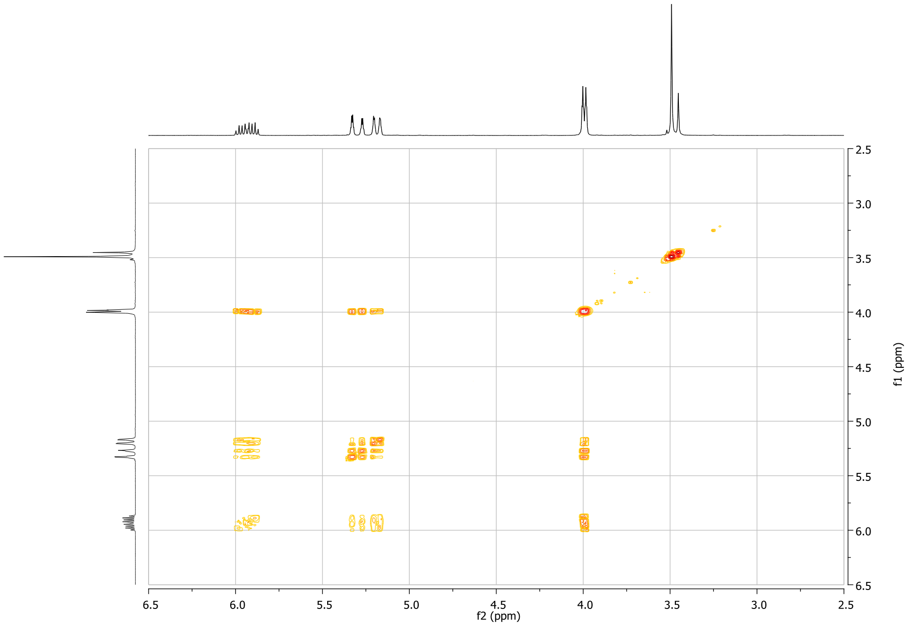


Figure S3. COSY spectrum of compound **2.**

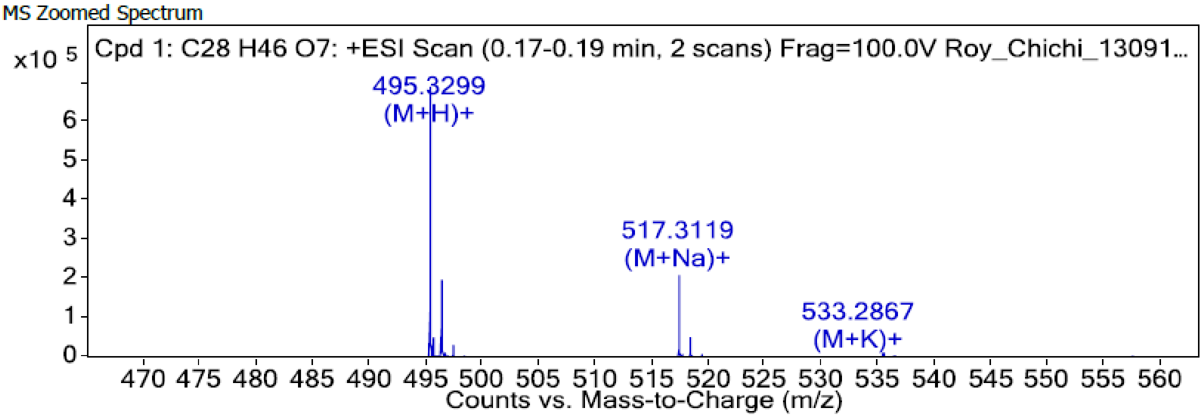


Figure S4. HRMS (ESI^{+}) spectrum of compound **2**.

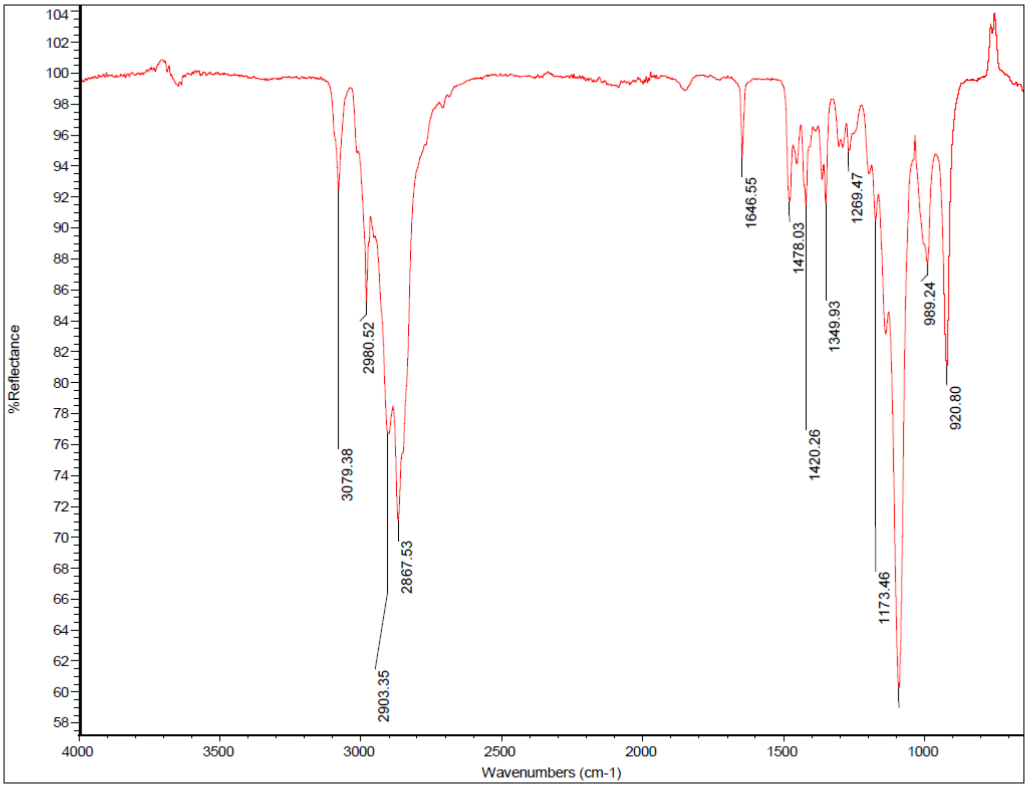
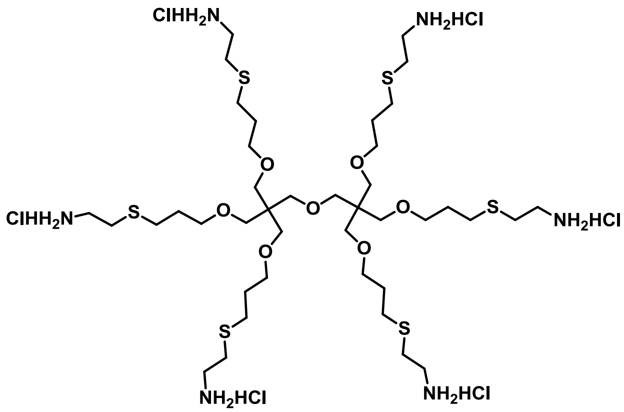


Figure S5. IR spectrum of compound **2**.



Synthesis of compound 3: To a stirring solution of hexa-allyl derivative **2** (300mg, 0.606mmol), 2,2'-dimethoxy-2-phenylacetophonone (DMPAP) (155mg, 0.606mmol) in dry DMF (3ml) was added cysteamine hydrochloride (1.03g, 9.07mmol) under nitrogen. The vial was then purged with N_2 for 10 min and irradiated for 4-6 hrs with UV lamp (365nm) at room temperature. Upon completion of the reaction, the contents of the vial were washed three times with diethyl ether to remove excess of thiol, affording a clear viscous liquid. It was further purified using dialysis bag (cut-off 1000 Da, spectrum). Dialysis bath water was changed 4-5 times in the span of 6 hrs to remove all the impurities. The compound was lyophilized to yield white hygroscopic solid **3** (534mg, 0.455mmol) in 75% yield.

^{1}H NMR (300 MHz, D_2O) δ 3.62 (t, *J* = 6.2 Hz,12H), 3.48 (s, 12H), 3.39 (s, 4H), 3.26 (t, *J* = 6.7 Hz, 12H), 2.90 (t, *J* = 6.8 Hz, 12H), 2.70 (t, *J* = 7.2 Hz, 12H), 1.98–1.83 (m, 12H).
^{13}C{^{1}H} NMR (75 MHz, D_2O) δ 70.5, 69.9, 45.8, 38.9, 28.8, 28.0.
IR (cm^{-1}) 3637, 2980, 2971, 2883, 1382, 1150, 1070, 954.
HRMS (ESI+) *m/z* calc. for $C_{40}H_{88}N_6O_7S_6$, 957.5112 [*M*+H]$^+$; found, 957.5134.

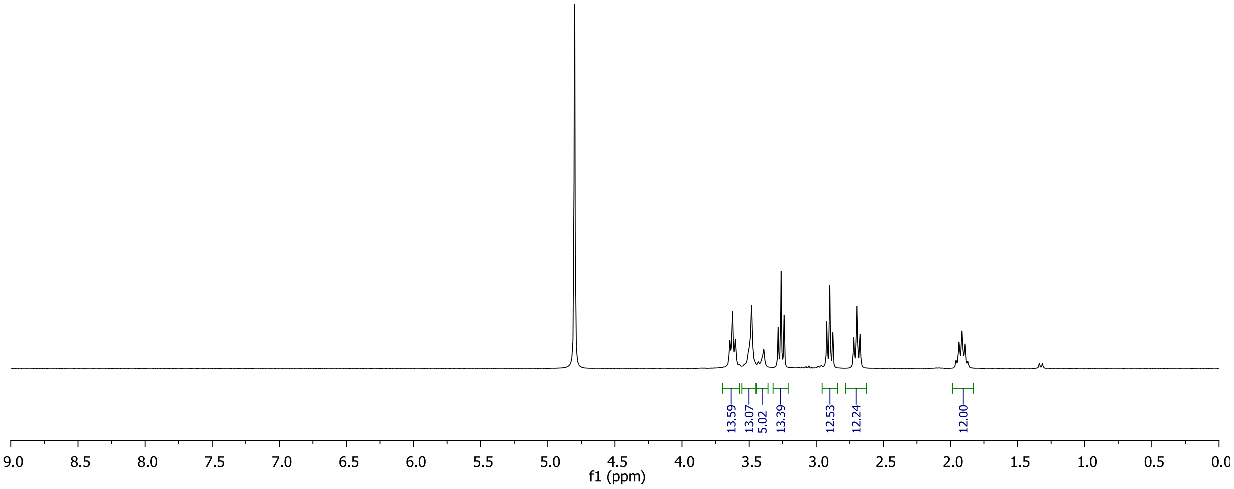


Figure S6. ^{1}H NMR spectrum of compound **3** (300 MHz, D_2O).

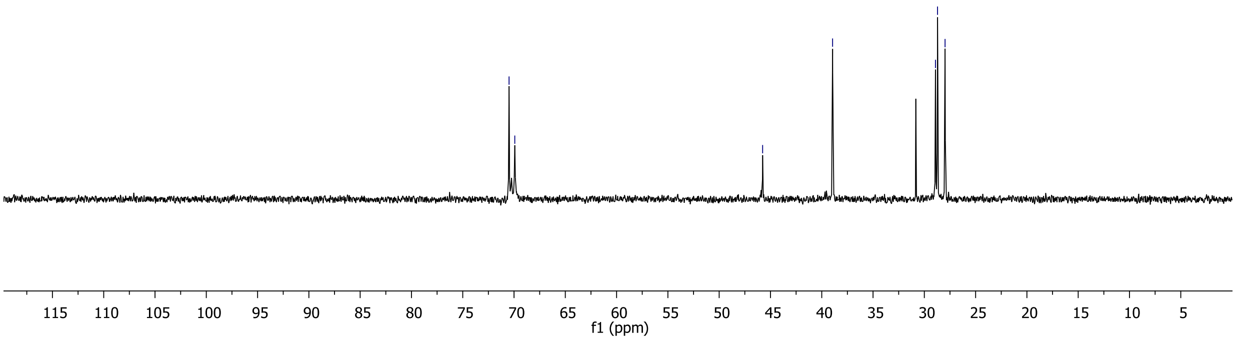


Figure S7. $^{13}C\{^{1}H\}$ NMR spectrum of compound **3** (75 MHz, D_2O).

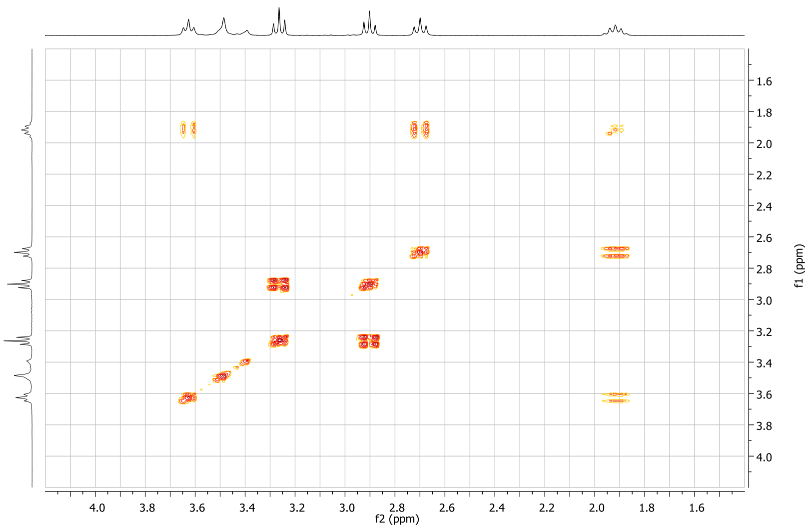


Figure S8. COSY spectrum of compound **3**.

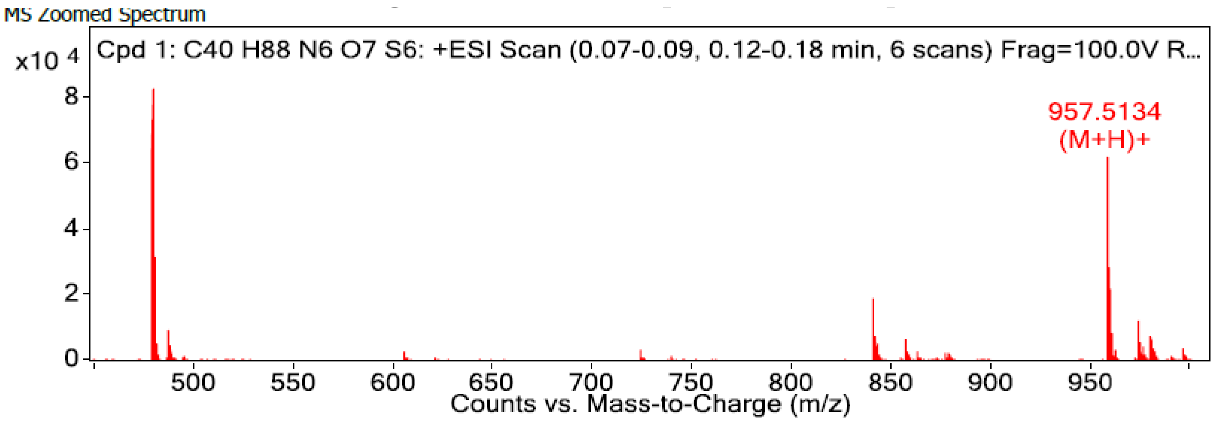


Figure S9. HRMS (ESI+) spectrum of compound **3**.

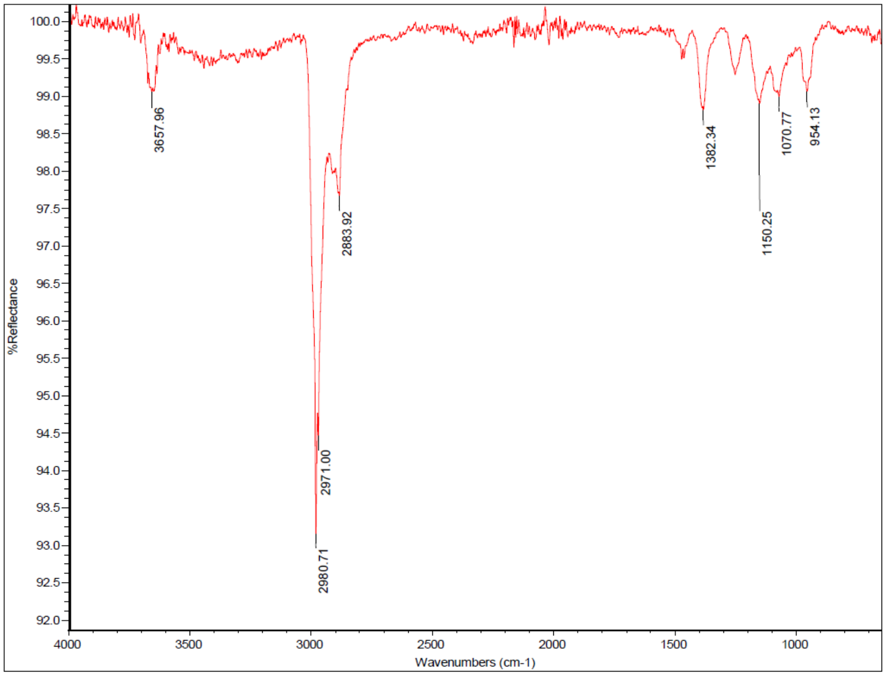
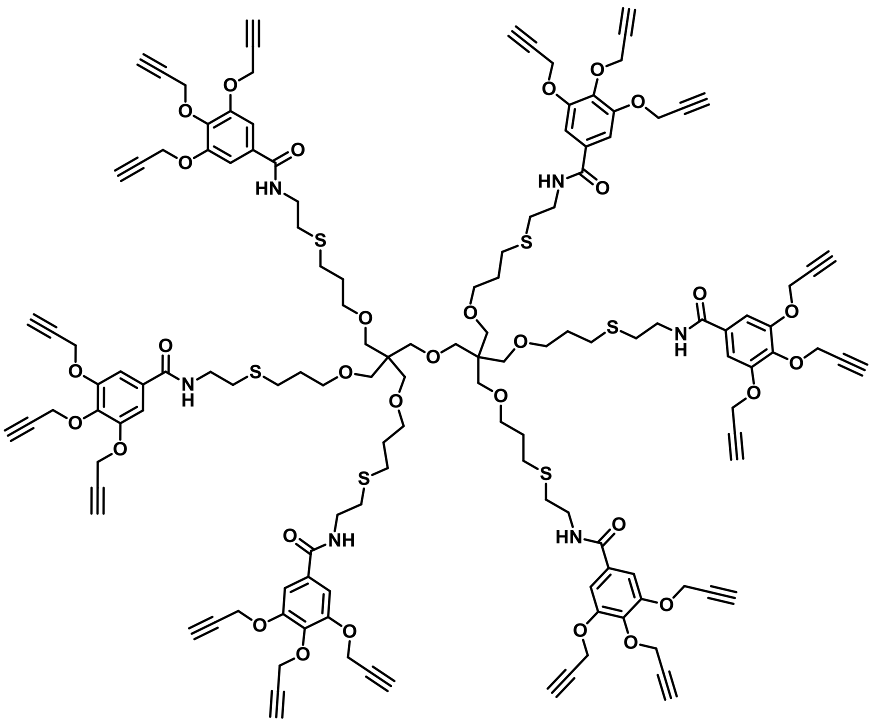


Figure S10. IR spectrum of compound **3**.



Synthesis of compound 5: A solution of hexa-amine hydrochloride **3** (150mg, 0.127mmol) and *N,N*-diisopropylethylamine (0.26ml, 1.48mmol) in DMF (2ml) was stirred for 30 minutes. In another two neck flask, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC.HCl) (243mg, 1.27mmol), and 4-(dimethylamino)pyridine (DMAP) (155mg, 1.27mmol) were added in DMF (4mL) and stirred for 10 minutes followed by the addition of tripropargylated gallic acid **4** (434mg, 1.53mmol). The free amine solution from first flask was then transferred to the reaction mixture of the second flask with the help of canula syringe and was heated at 50^{o}C for overnight. The completion of reaction was monitored by TLC. Upon completion, the reaction mixture was diluted with water (40mL) and extracted with ethyl acetate (3×40mL). The combined organic extracts were washed with 0.1 N HCl (3×15mL), followed by saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The crude mixture was then purified with the help of flash column chromatography using 80% EtOAc in hexanes as eluent. The desired compound **5** (232.5mg, 0.0910mmol) was achieved in 72% yield as light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27–7.23 (m, 12H), 7.07 (br s, 6H), 4.78 (dd, *J* = 2.3, 2.3 Hz, 36H), 3.60 (d, *J* = 6.0 Hz, 12H), 3.43 (t, *J* = 5.9 Hz, 12H), 3.31 (d, *J* = 8.1 Hz, 16H), 2.74 (t, *J* = 6.6 Hz, 12H), 2.59 (t, *J* = 7.2 Hz, 12H), 2.55 (t, *J* = 2.3 Hz, 12H), 2.48 (t, *J* = 2.4 Hz, 6H), 1.92–1.70 (m, 12H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 166.7, 151.5, 140.0, 130.2, 107.9, 78.7, 78.1, 76.4, 75.7, 69.6, 60.3, 57.3, 45.6, 39.2, 31.6, 29.8, 28.4.

IR (cm^{-1}) 3290, 3005, 2922, 2867, 2122, 1637, 1581, 1541, 1492, 1428, 1365, 1323, 1275, 1261, 1207, 1106, 1032, 992, 764, 750, 671.

HRMS (ESI^{+}) *m/z* for $C_{136}H_{148}N_6O_{31}S_6$, 1277.4329 [*M*+2H]$^{2+}$; found, 1277.4359, 2576.8406 [*M*+Na]$^{+}$; found 2575.8346.

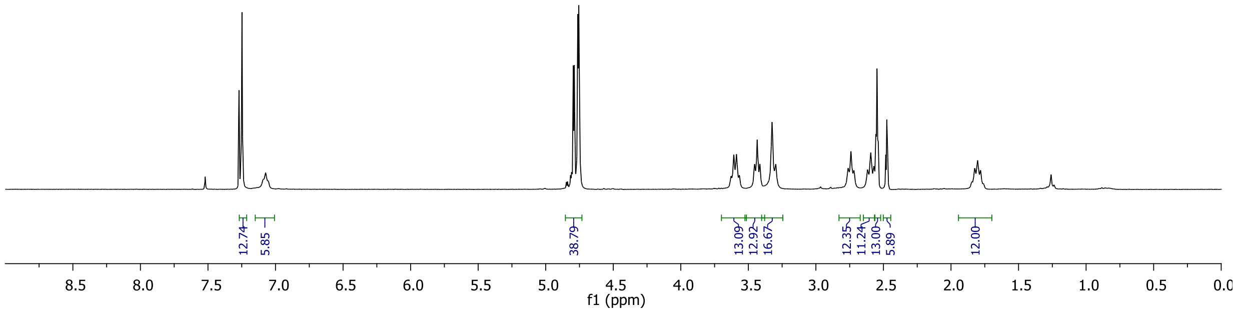


Figure S11. ^{1}H NMR spectrum of compound **5** (300 MHz, $CDCl_3$).

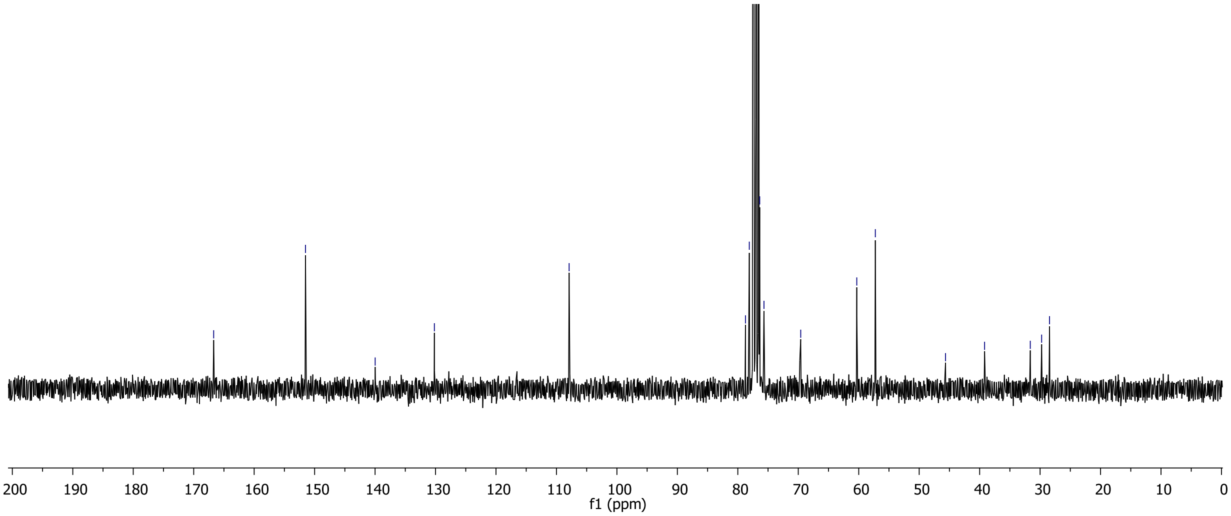


Figure S12. $^{13}C\{^{1}H\}$ NMR spectrum of compound **5** (75 MHz, $CDCl_3$).

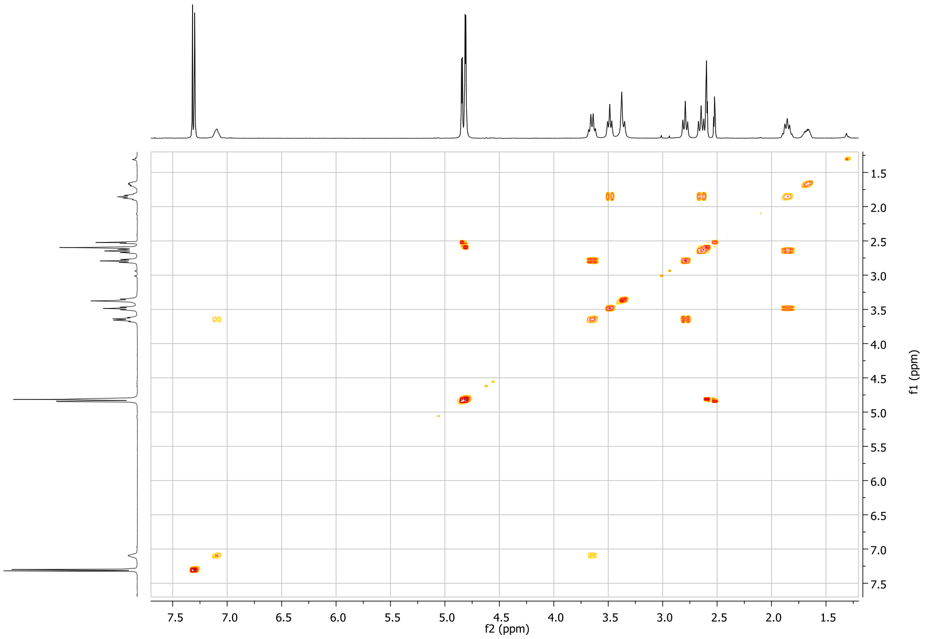


Figure S13. COSY spectrum of compound **5**.

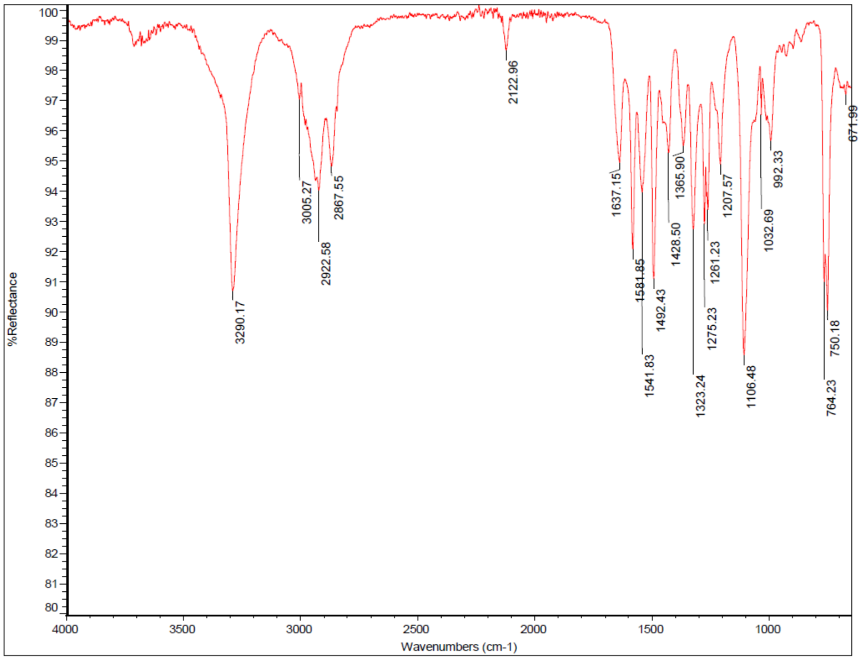
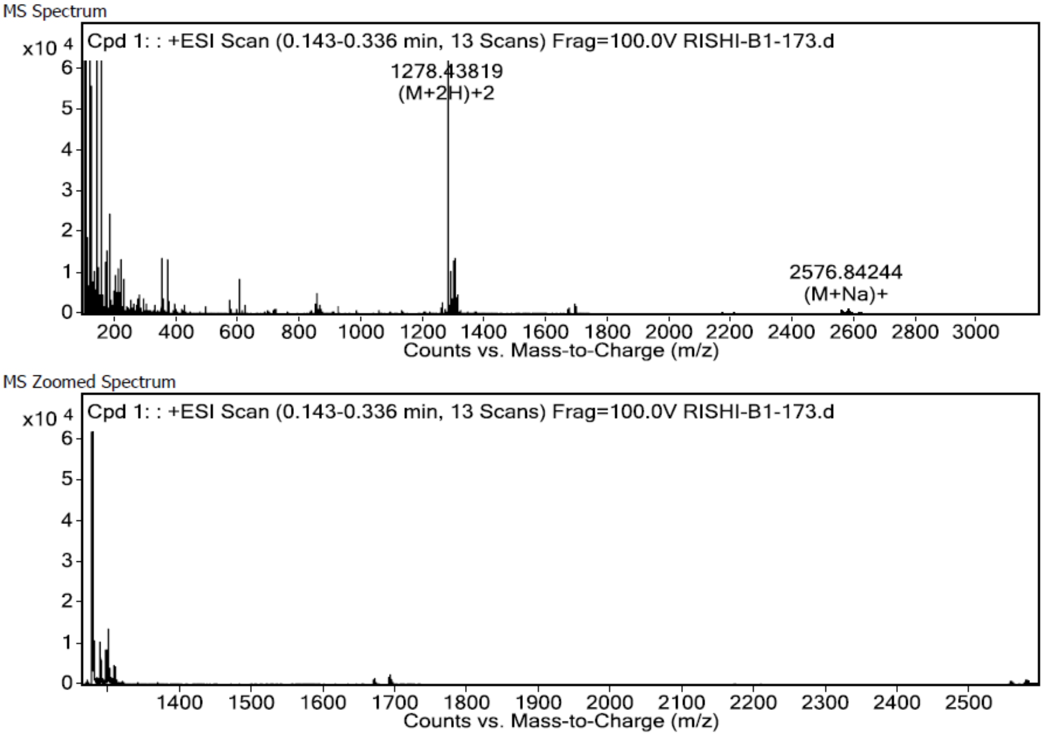


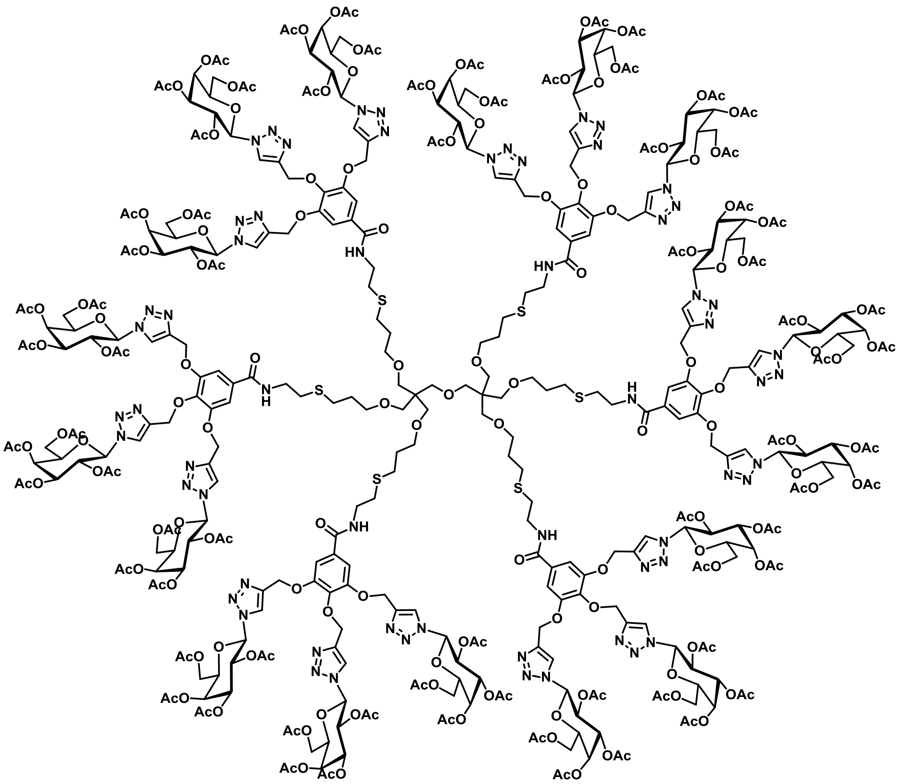
Figure S14. IR spectrum of compound **5**.



MS Spectrum Peak List

Ion	Ion Formula	Abund	*Expe. m/z*	*Calc. m/z*	Diff(ppm)
(M+2H)+2	C136H150N6O31S6	34035.5	1277.43589	1277.43294	2.31
(M+Na)+	C136H148N6NaO31S6	1046.2	2575.83462	2575.84055	-2.3

Figure S15. HRMS (ESI$^+$) spectrum of compound **5**.



Synthesis of compound 7: *Divergent approach*

To a solution of compound **5** (50.0mg, 0.0195mmol) in THF (3mL) was added azido derivative **6** (261mg, 0.702mmol) dissolved in THF (2mL), followed by the addition of sodium ascorbate (70.0mg, 0.351mmol). An aqueous solution of $CuSO_4 \cdot 5H_2O$ (88.0 mg, 0.351mmol) was then added to the reaction mixture. The final ratio of H_2O to THF was kept 1:1. The reaction mixture was stirred at 40^oC for 12 hrs. The progress of the reaction was monitored with the help of TLC. Upon completion, reaction mixture was diluted with EtOAc (25mL) and washed with a saturated solution of EDTA (2×15mL). Organic layer was washed with brine, dried over anhydrous $Na_2SO_{4,}$ filtered and concentrated under reduced pressure. Purification of the crude compound was achieved *via* flash column chromatography on silica gel using 2-4% MeOH in DCM as eluent gradient to afford desired compound **7** (146.5mg, 0.0158mmol) in 81% yield as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 6H), 8.09 (s, 12H), 7.19 (s, 12H), 5.94 (d, *J* = 9.2 Hz, 18H), 5.68 (t, *J* = 9.8 Hz, 6H), 5.56 (dd, *J* = 10.9, 6.9 Hz, 32H), 5.38–5.12 (m, 55H), 4.32 (t, *J* = 6.4 Hz, 18H), 4.27–4.06 (m, 38H), 3.58 (d, *J* = 5.5 Hz, 12H), 3.45 (s, 12H), 3.34 (s, 16H), 2.74 (t, *J* = 6.5 Hz, 12H), 2.63 (t, *J* = 6.9 Hz, 12H), 2.20 (s, 58H), 2.01 (d, *J* = 8.4 Hz, 118H), 1.77 (d, *J* = 18.0 Hz, 54H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.3, 170.3, 170.1, 170.1, 169.9, 169.8, 169.6, 169.0, 168.7, 166.7, 151.9, 144.6, 144.0, 140.1, 130.3, 123.3, 122.3, 107.2, 86.1, 85.7, 73.7, 73.5, 73.2, 71.0, 70.7, 69.7, 67.9, 67.7–67.5, 66.8, 66.1, 62.8, 61.0, 31.3, 29.8, 28.5, 20.5, 20.1.

IR (cm^{-1}): 3628, 2994, 2947, 1751, 1651, 1583, 1491, 1428, 1370, 1218, 1093, 1064, 923, 732, 667.

MALDI-TOF: *m*/*z* calc. for $C_{388}H_{490}N_{60}O_{193}S_{6,}$ 9274.7; found, 9296.4. [*M*+Na]$^+$; m/z calc. for $C_{388}H_{490}N_{60}O_{193}S_6$, 9274.7; found, 9312.05. [M+K]$^+$

GPC (THF): M$_n$= 9600 g/mol. M$_w$/M_n= 1.03

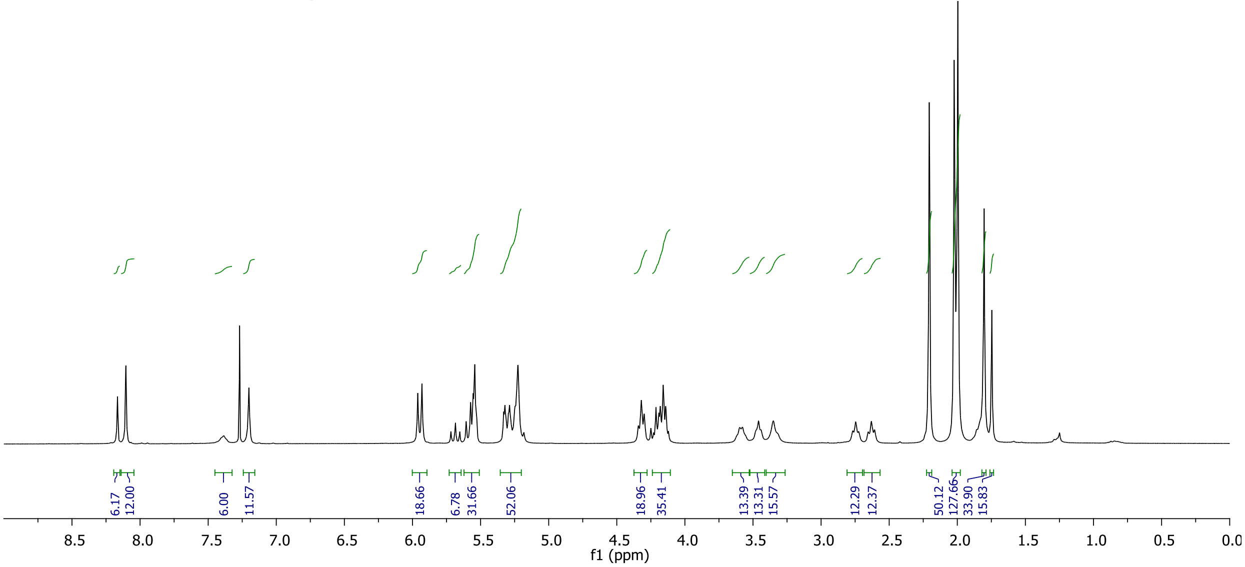


Figure S16. ^{1}H NMR spectrum of compound **7** (300 MHz, CDCl$_3$).

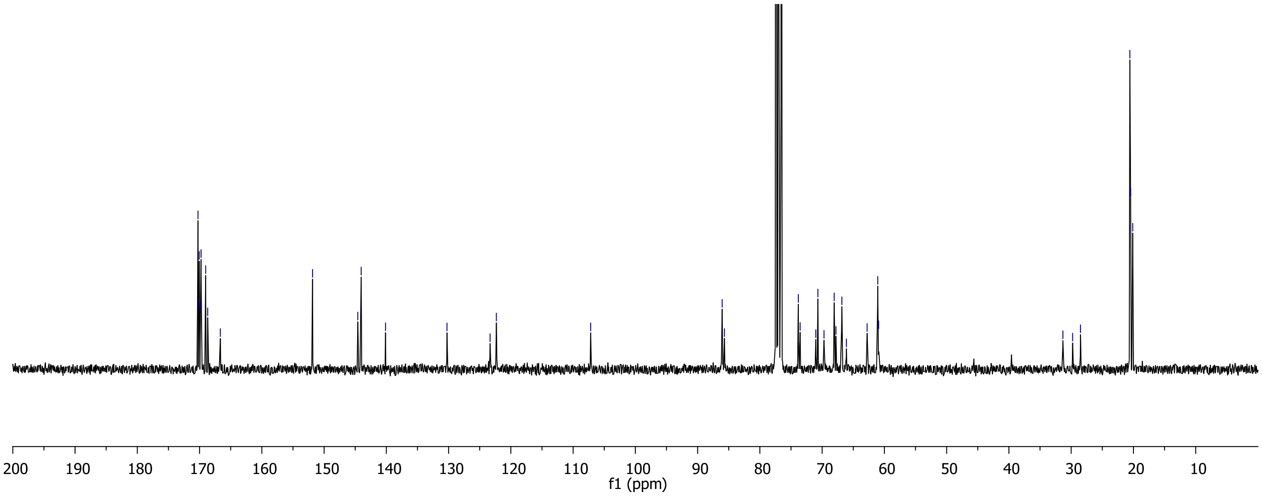


Figure S17. ^{13}C{^{1}H} NMR spectrum of compound **7** (75 MHz, CDCl$_3$).

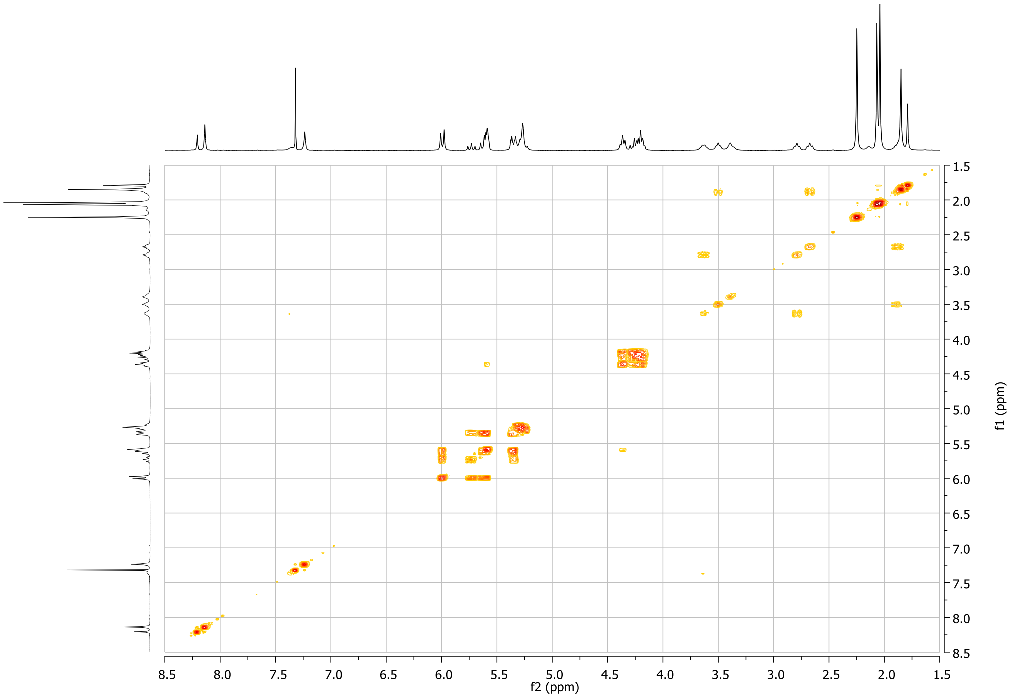
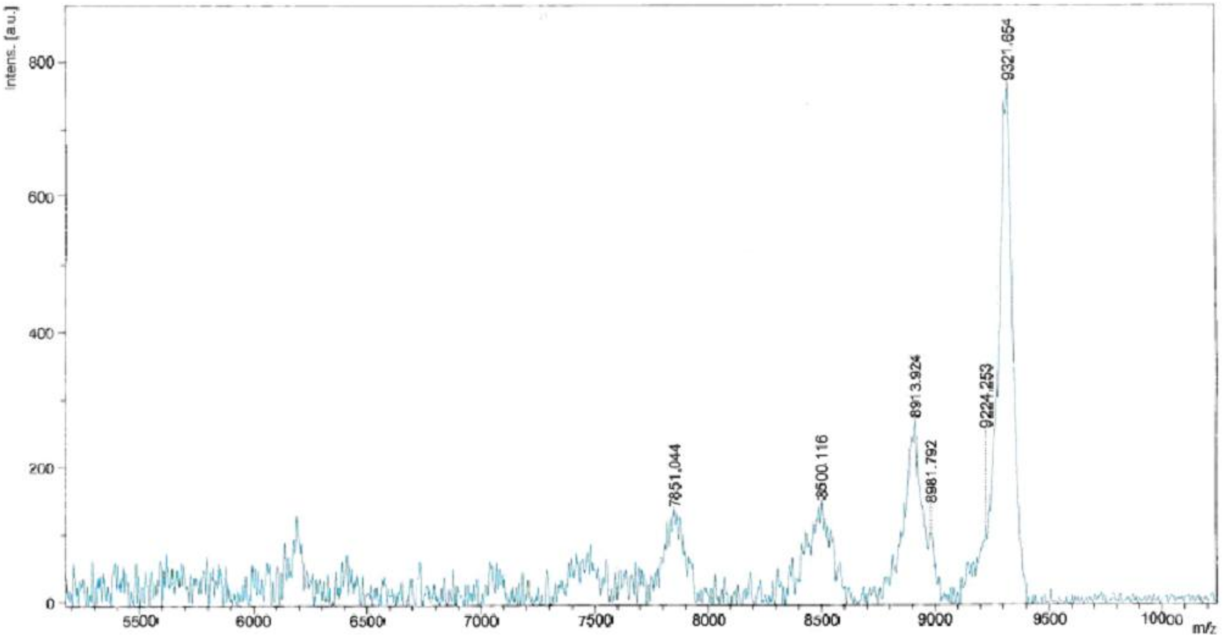


Figure S18. COSY spectrum of compound **7**.



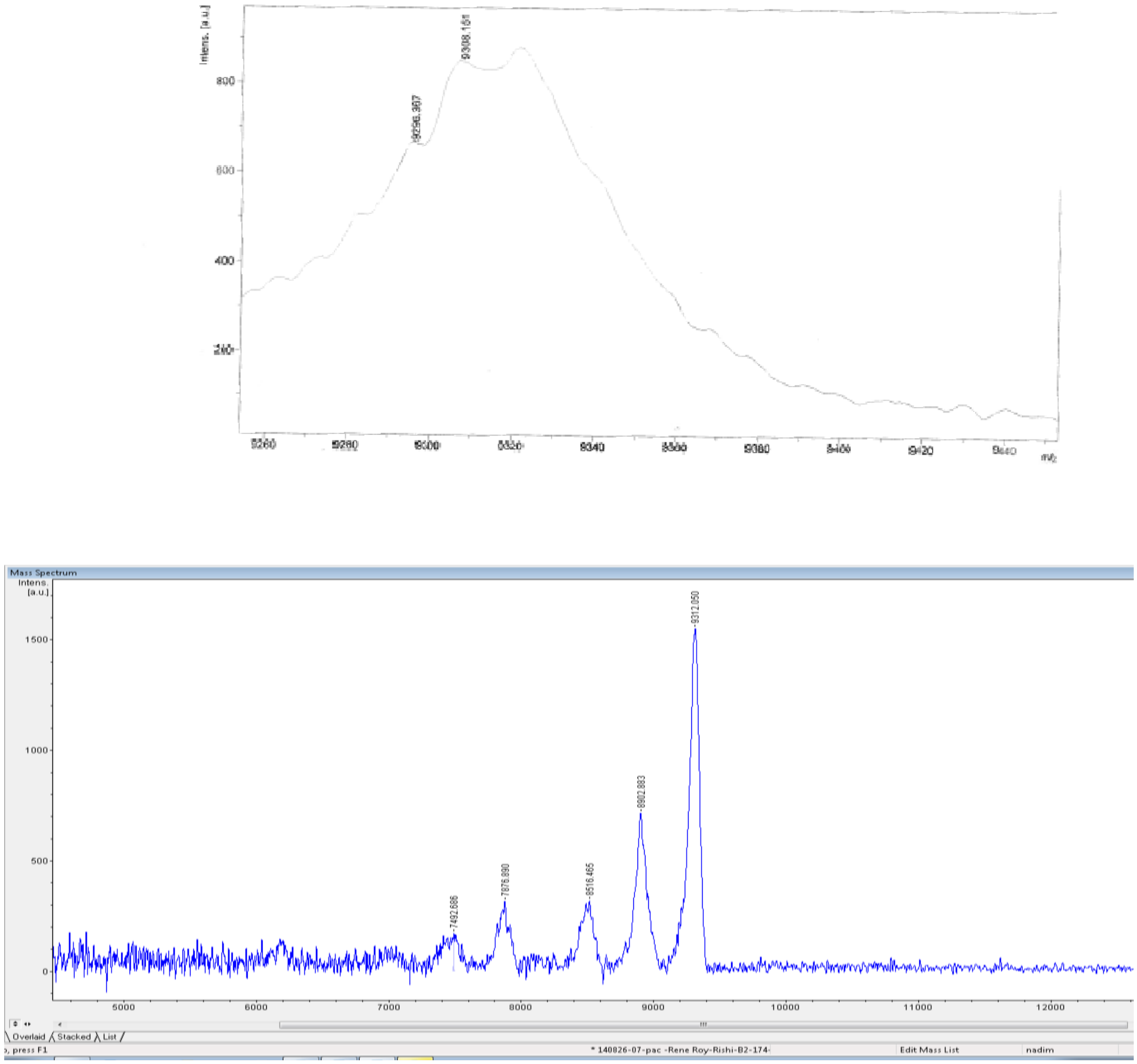


Figure S19. MALDI ToF spectrum of compound **7**.

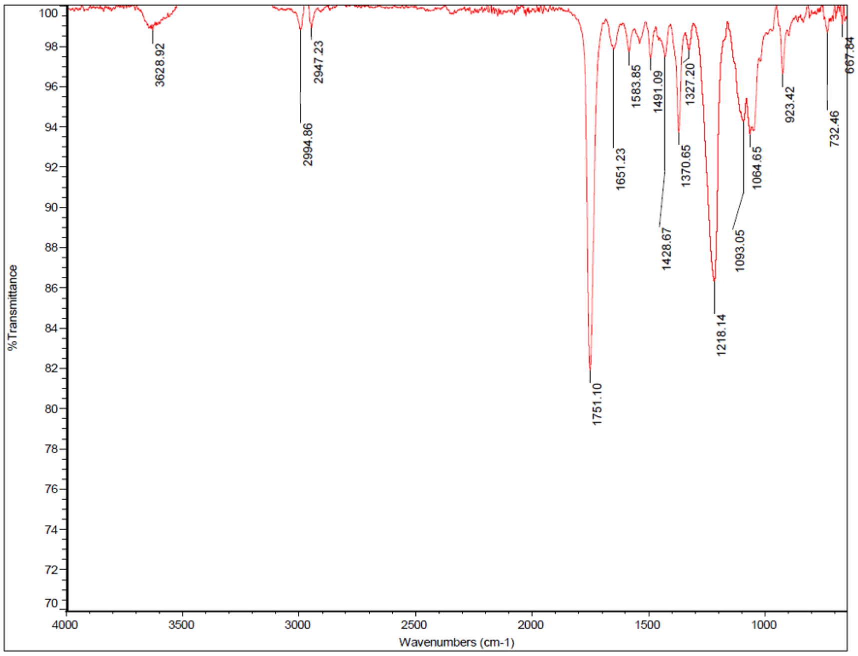


Figure S20. IR spectrum of compound **7**.

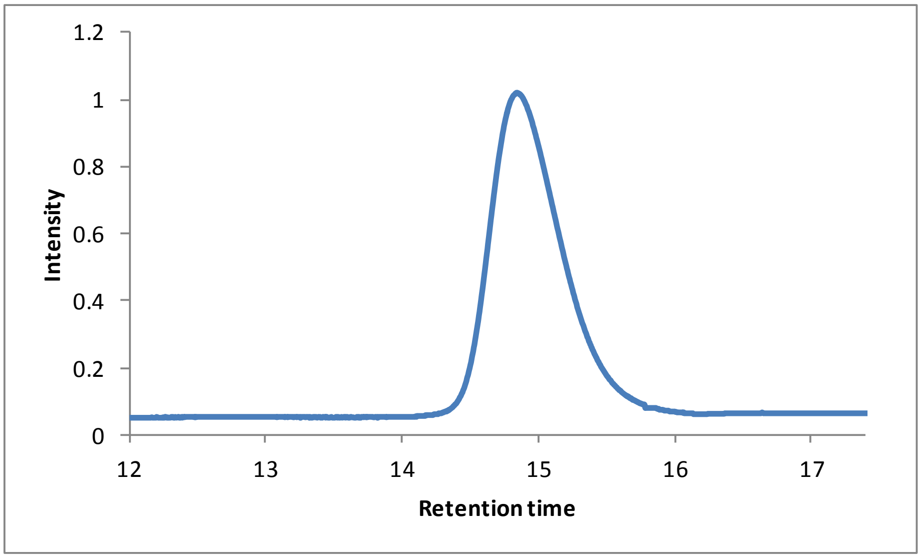
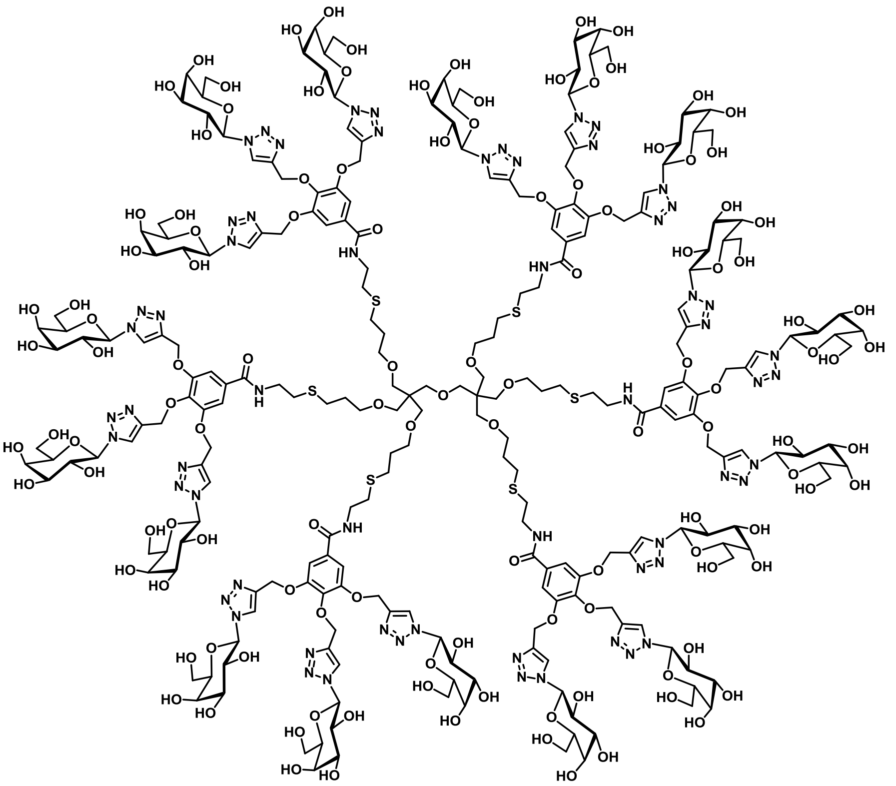


Figure S21. GPC profile of compound **7**.



Synthesis of compound 8: To a stirring solution of compound **7** (100mg, 0.0107mmol) in MeOH (3mL) was slowly added 1M solution of MeONa in MeOH to adjust the pH 9–10. Reaction mixture was left for overnight stirring at room temperature. The reaction pH was then adjusted with H$^+$ resin to pH 6. Solvent was evaporated and the residue was dissolved in 3mL of water and washed with diethyl ether (3×15mL) to remove impurities. Aqueous layer was finally lyophilized to yield **8** (58.8mg, 9.42μmol) as a white solid with a 88% yield.

^{1}H NMR (600 MHz, D$_2$O) δ 8.29 (s, 12H), 7.98 (s, 6H), 7.15 (s, 12H), 5.59 (d, *J* = 65.2 Hz, 18H), 5.04–4.79 (m, 112H), 4.29–3.22 (m, 150H), 2.68 (t, *J* = 56.2 Hz, 24H), 1.97–1.70 (m, 12H).
^{13}C{^{1}H} NMR (151 MHz, D$_2$O) δ 168.6, 152.2, 144.0, 143.7, 139.3, 130.6, 125.2, 124.5, 107.3, 88.8, 88.6, 78.8, 73.7, 70.3, 69.8, 69.2, 65.8, 62.7, 61.4, 40.5, 30.1, 28.9.
IR (cm^{-1}) 3350, 2879, 1637, 1583, 1494, 1428, 1327, 1233, 1095, 1057, 891, 825, 760, 703.
HRMS (ESI$^+$) *m*/*z* calc. for $C_{244}H_{346}N_{60}O_{121}S_{6}$, 1584.0165 ([*M*+4Na]$^{4+}$); found, 1584.0122.

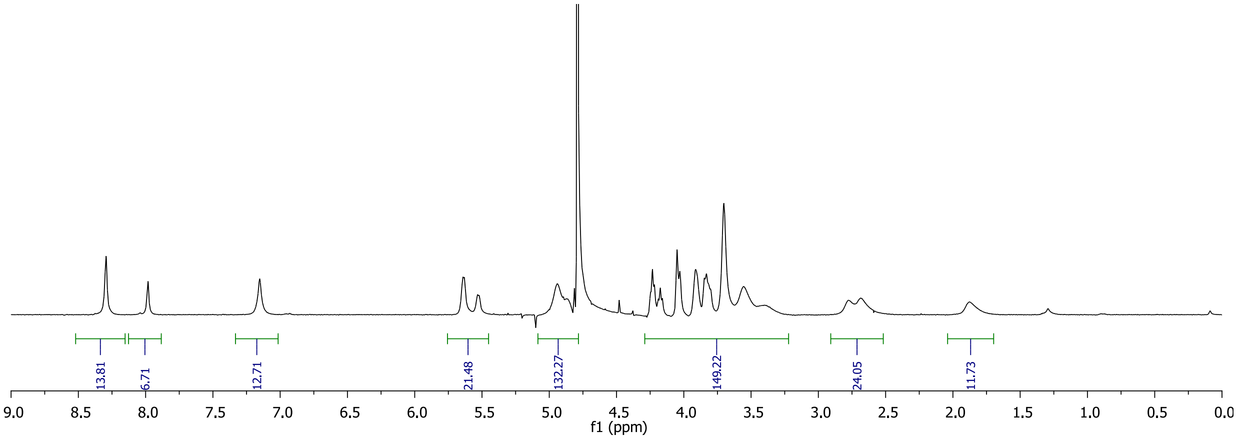


Figure S22. ^{1}H NMR spectrum of compound **8** (600 MHz, D_2O).

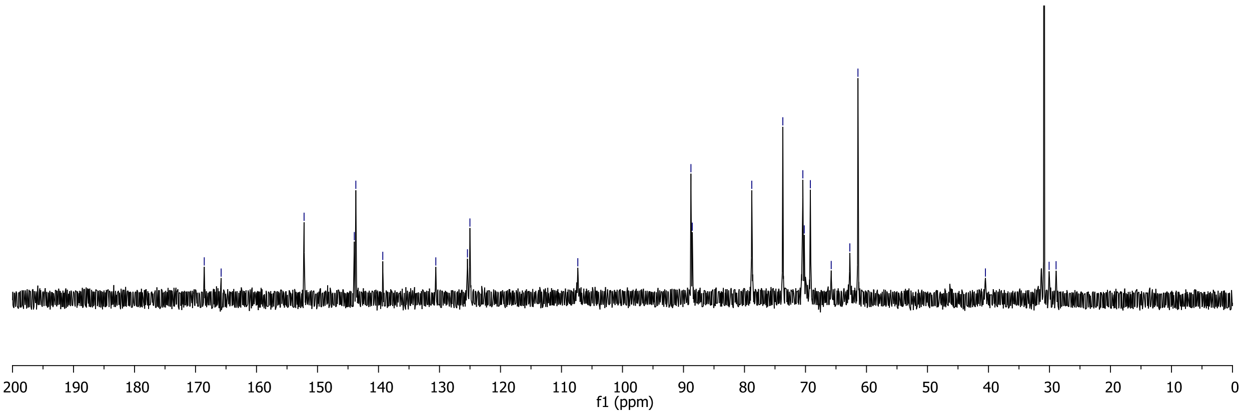


Figure S23. $^{13}C\{^{1}H\}$ NMR spectrum of compound **8** (151 MHz, D_2O).

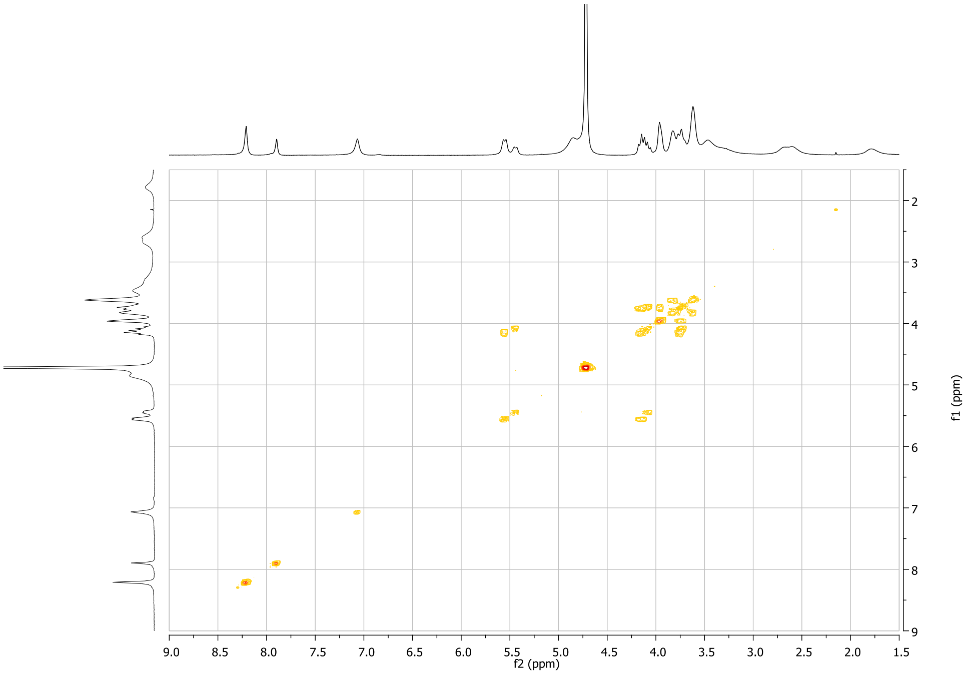
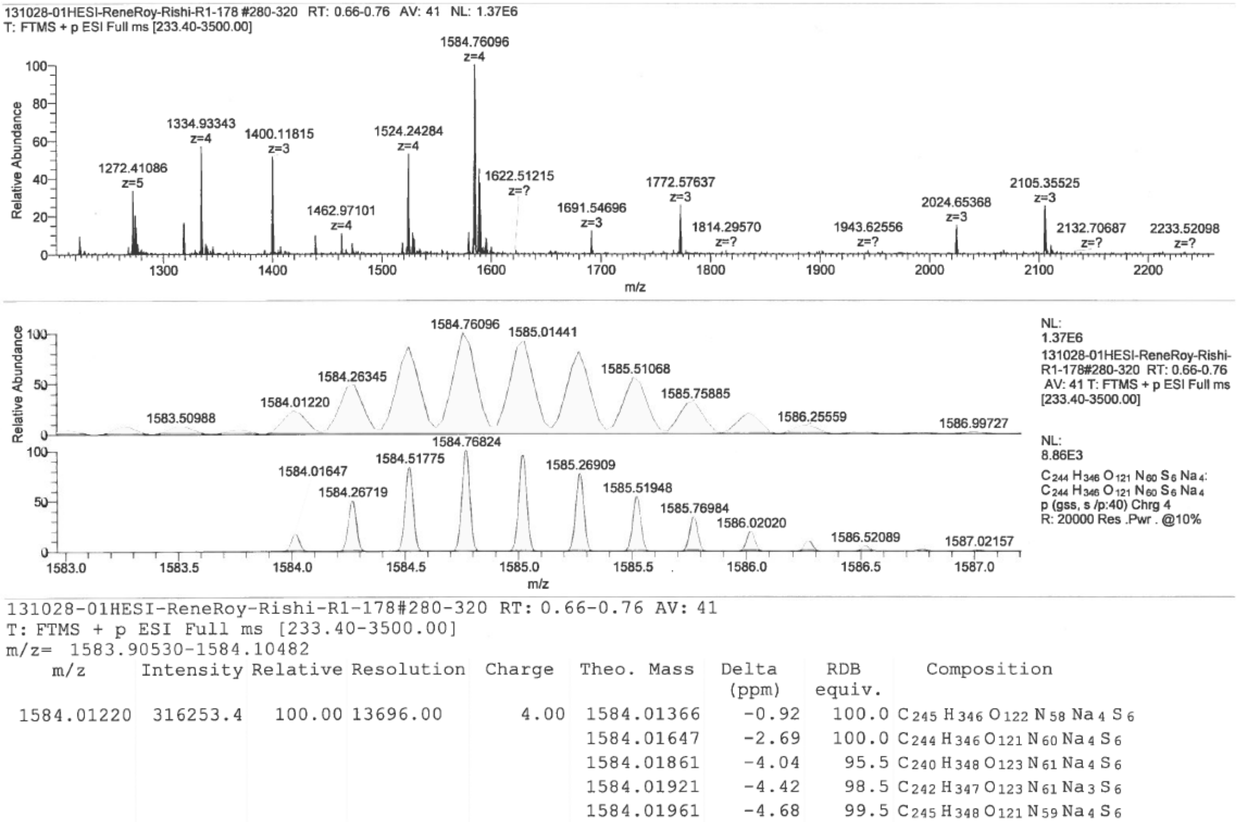


Figure S24. COSY spectrum of compound **8** (300 MHz, D_2O).



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131028-01HESI-ReneRoy-Rishi-R1-178#280-320 RT: 0.66-0.76 AV: 41
T: FTMS + p ESI Full ms [233.40-3500.00]
m/z= 1583.90530-1584.10482
      m/z    Intensity Relative Resolution  Charge  Theo. Mass   Delta     RDB      Composition
                                                                 (ppm)    equiv.
  1584.01220  316253.4   100.00 13696.00      4.00  1584.01366   -0.92    100.0 C245 H346 O122 N58 Na4 S6
                                                    1584.01647   -2.69    100.0 C244 H346 O121 N60 Na4 S6
                                                    1584.01861   -4.04     95.5 C240 H348 O123 N61 Na4 S6
                                                    1584.01921   -4.42     98.5 C242 H347 O123 N61 Na3 S6
                                                    1584.01961   -4.68     99.5 C245 H348 O121 N59 Na4 S6
```

Figure S25. HRMS (ESI$^+$) spectrum of compound **8**.

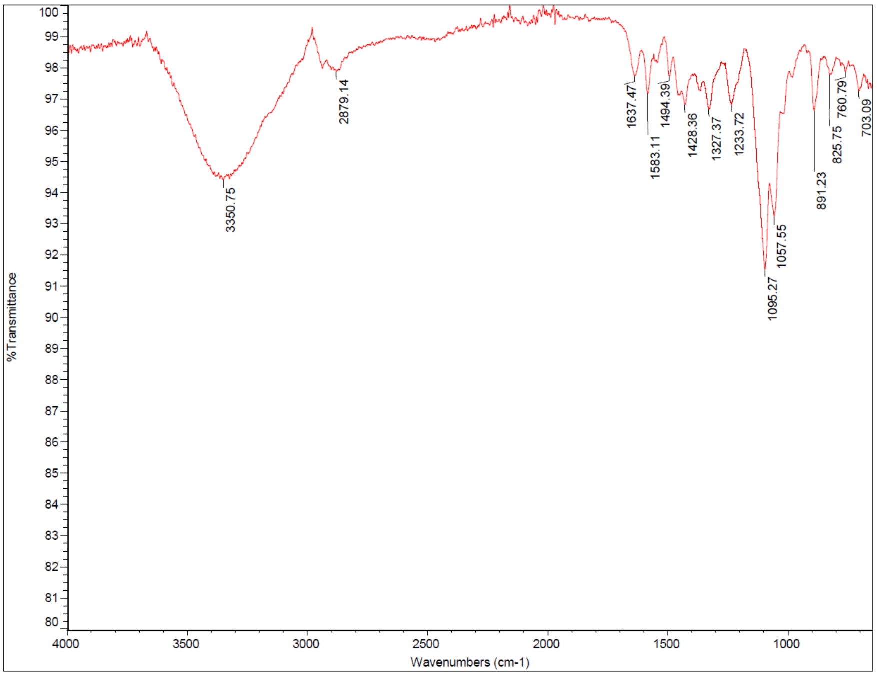
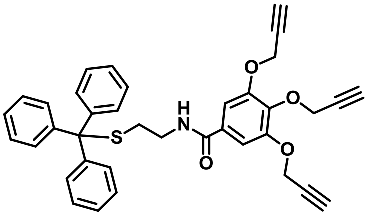


Figure S26. IR spectrum of compound **8**.



Synthesis of compound 10: To a stirring solution of tripropargyl gallic acid **4** (562mg, 1.98mmol) in DMF (3mL) were added EDC·HCl (529mg, 2.77mmol) and DMAP (290mg, 2.37mmol). The reaction mixture was stirred under nitrogen atmosphere for 15 minutes. Amine terminated compound **9** (600mg, 1.98mmol) was then added and the reaction mixture was stirred at 50°C for overnight. The completion of reaction was monitored by TLC. Upon completion, the reaction mixture was diluted with water (50mL) and extracted with ethyl acetate (3×30mL). The combined organic extracts were washed with 0.1N HCl (3×10mL), followed by saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous Na_2SO, filtered and evaporated under reduced pressure. The crude mixture was then purified by flash column chromatography using 2% MeOH in DCM as eluent to furnish **10** (905mg, 1.54mmol) in a 78% yield as an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 7.24–7.04 (m, 12H), 6.20 (s, 1H), 4.72 (dd, *J* = 2.4, 2.4 Hz, 6H), 3.20 (m, 2H), 2.46 (t, *J* = 6.2 Hz, 2H), 2.38 (t, *J* = 2.4 Hz, 1H), 2.32 (t, *J* = 2.3 Hz, 2H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 166.1, 151.1, 144.3, 139.4, 130.0, 129.2, 127.7, 126.5, 107.5, 78.52, 77.8, 76.2, 75.5, 66.5, 60.0, 56.9, 38.4, 31.7.

IR (cm^{-1}): 3284, 3057, 2937, 2121, 1750, 1647, 1582, 1537, 1489, 1444, 1427, 1368, 1323, 1214, 1106, 1063, 952, 923, 734, 700.

HRMS (ESI$^+$) *m/z* calc for $C_{37}H_{31}NO_4S$, 608.1866 [*M*+Na]$^+$; found, 608.1863.

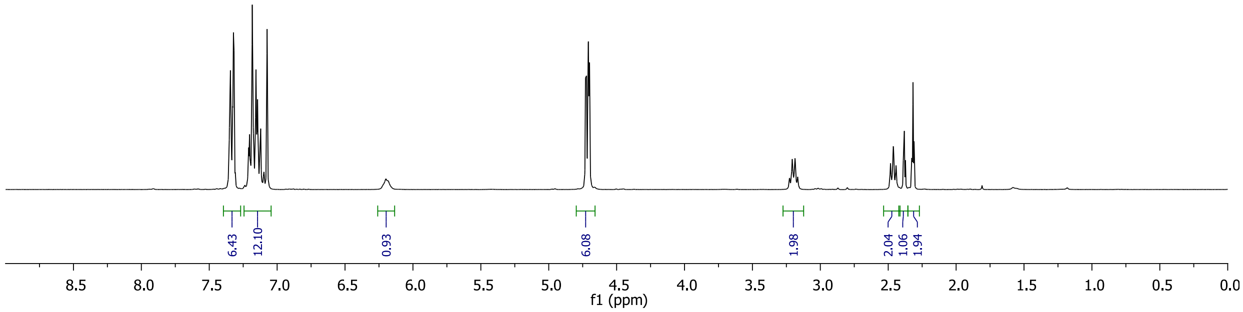


Figure S27. ^{1}H NMR spectrum of compound **10** (300 MHz, $CDCl_3$).

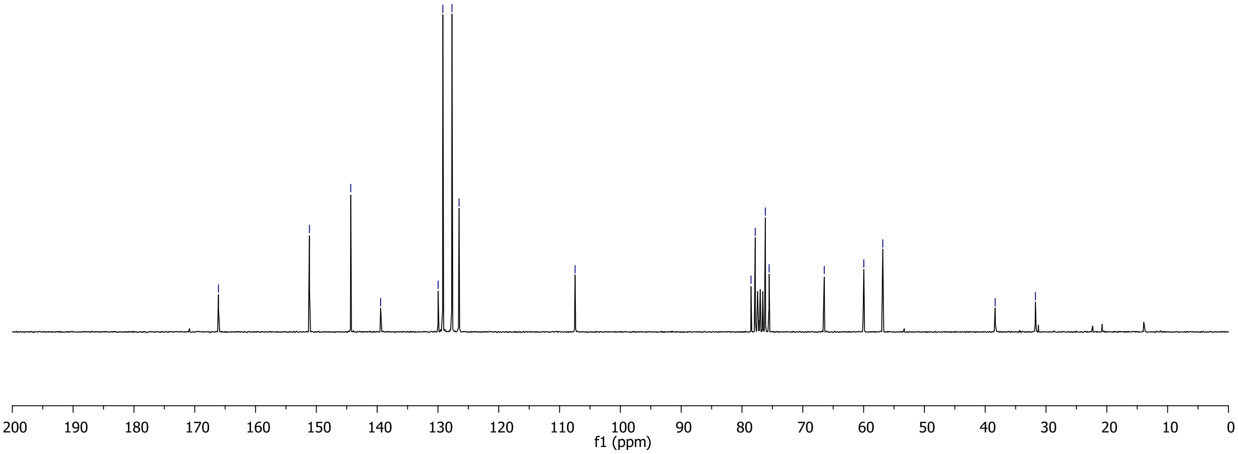


Figure S28. $^{13}C\{^{1}H\}$ NMR spectrum of compound **10** (75 MHz, $CDCl_3$).

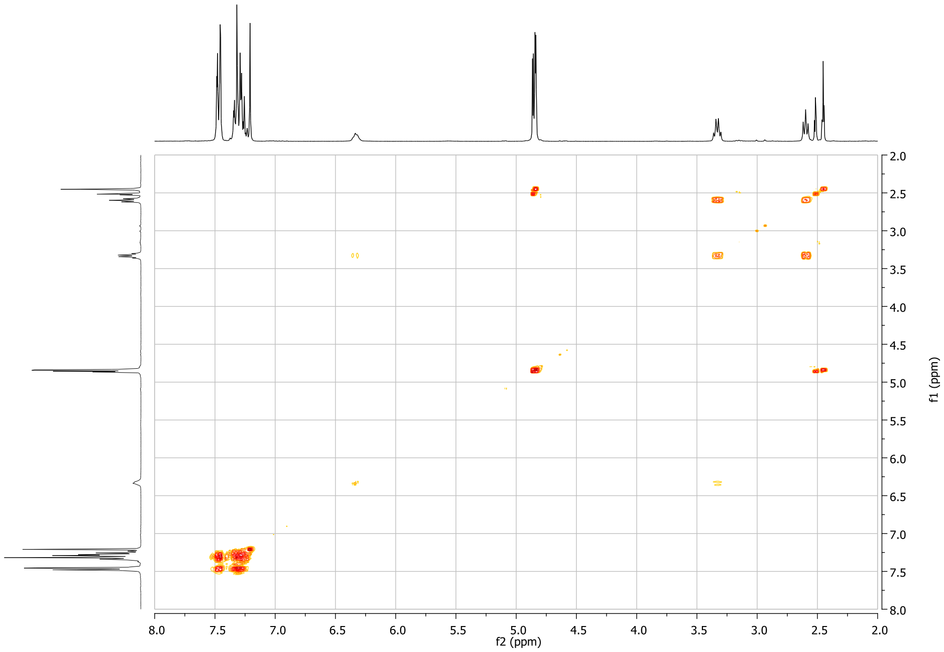


Figure S29. COSY spectrum of compound **10**.

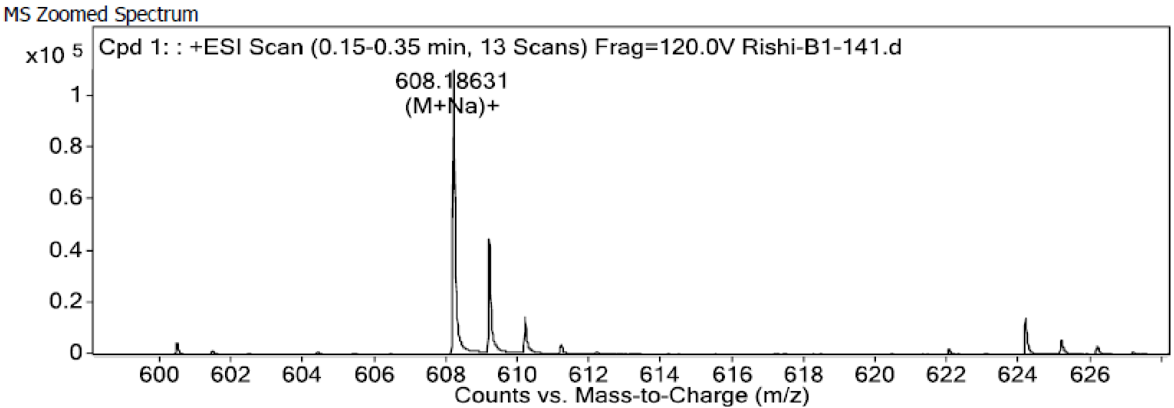


Figure S30. HRMS (ESI$^+$) spectrum of compound **10**.

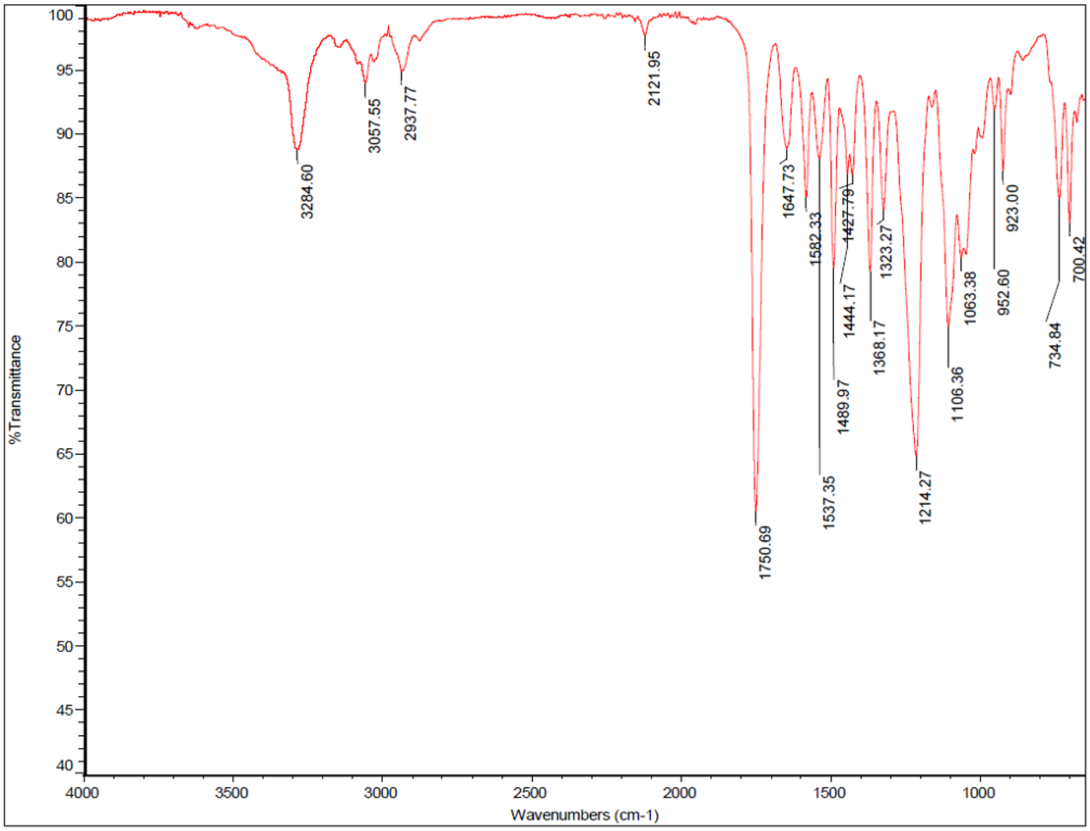
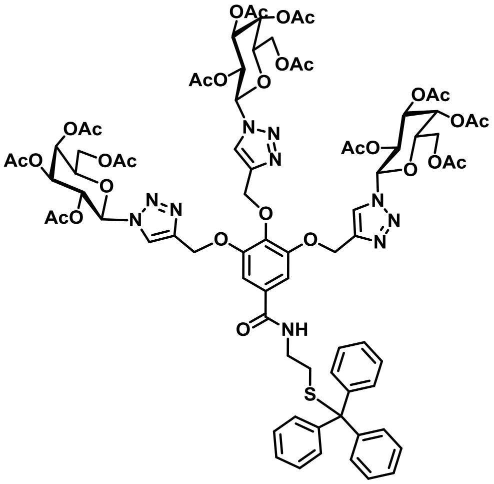


Figure S31. IR spectrum of compound **10.**



Synthesis of compound 11: To a solution of compound **10** (200mg, 0.341mmol) in THF (2mL) was added galactosyl azide **6** (442mg, 1.196mmol) dissolved in THF (3mL), followed by the addition of sodium ascorbate (67mg, 0.34mmol). An aqueous solution of $CuSO_4·5H_2O$ (85mg, 0.34mmol) was added and the final ratio of H_2O and THF was kept 1:1. The reaction mixture was stirred at 40^oC for 12 hrs. The progress of the reaction was monitored with the help of TLC. Upon completion, reaction mixture was diluted with EtOAc (25mL) and washed with saturated solution of EDTA (2×15mL). Organic layer was finally washed with brine solution, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue was achieved *via* flash column chromatography on silica gel using 2% MeOH in DCM as eluent to afford the desired compound **11** (488mg, 0.286mmol) in a 84% yield as an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.04 (s, 2H), 7.49–7.38 (m, 6H), 7.30–7.17(m, 15H), 7.09 (s, 2H), 6.47 (s, 1H), 5.90 (m, 3H), 5.69 (t, *J* = 9.8 Hz, 1H), 5.63–5.45 (m, 5H), 5.39–5.20 (m, 9H), 4.37–4.10 (m, 9H), 3.34–3.13 (m, 2H), 2.51 (t, *J* = 6.5 Hz, 2H), 2.22 (s, 9H), 2.08–1.98 (m, 18H), 1.82 (s, 6H), 1.77 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.1, 170.0, 169.9, 169.8, 169.4, 168.8, 168.5, 166.2, 151.6, 144.4, 143.8, 140.0, 130.0, 129.2, 127.7, 126.5, 122.9, 121.9, 107.1, 85.9, 85.5, 73.5, 70.8, 70.4, 67.8, 67.6, 66.6, 65.9, 62.7, 60.9, 38.7, 31.7, 20.3, 19.9.
IR (cm^{-1}) 2980, 1750, 1654, 1584, 1535, 1490, 1428, 1369, 1324, 1216, 1100, 1047, 953, 923, 733, 702.
HRMS (ESI$^+$) *m/z* calc for $C_{79}H_{88}N_{10}O_{31}S$, 1727.5230 $[M+Na]^+$; found, 1727.5256, 1705.5410 $[M+H]^+$; found 1705.5452.

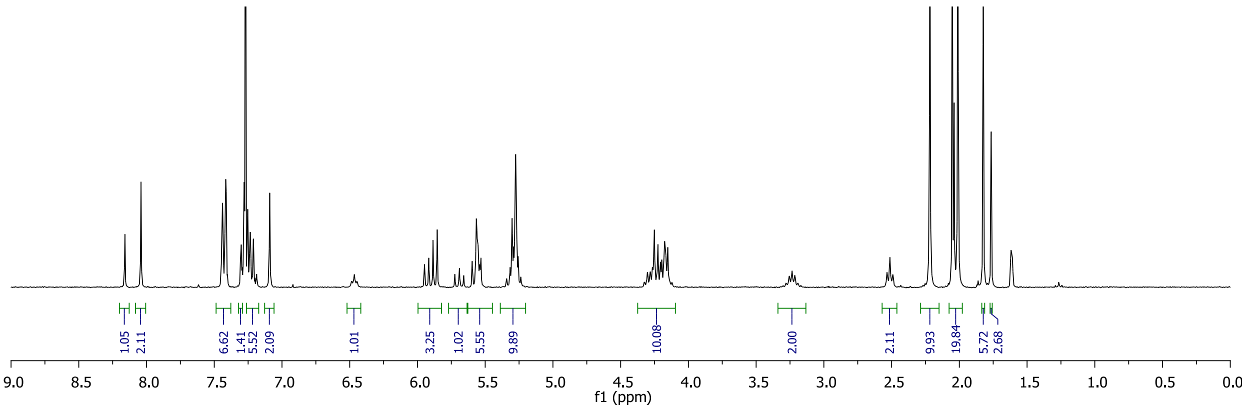


Figure S32. ^{1}H NMR spectrum of compound **11** (300 MHz, $CDCl_3$).

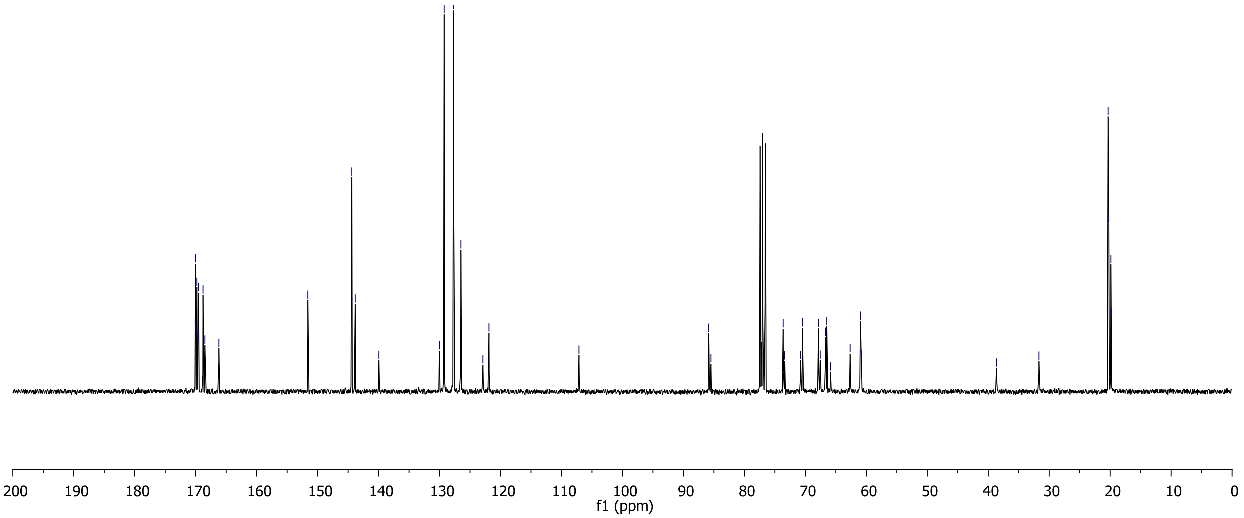


Figure S33. $^{13}C\{^{1}H\}$ NMR spectrum of compound **11** (75 MHz, $CDCl_3$).

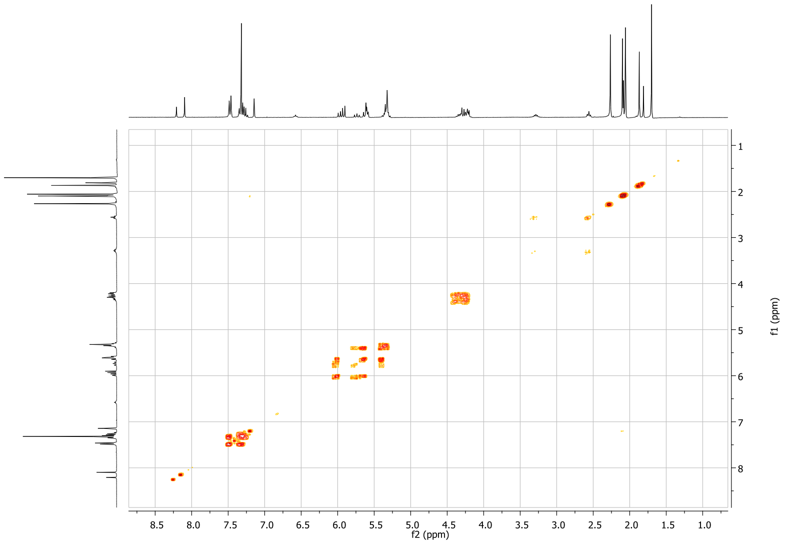


Figure S34. COSY spectrum of compound **11**.

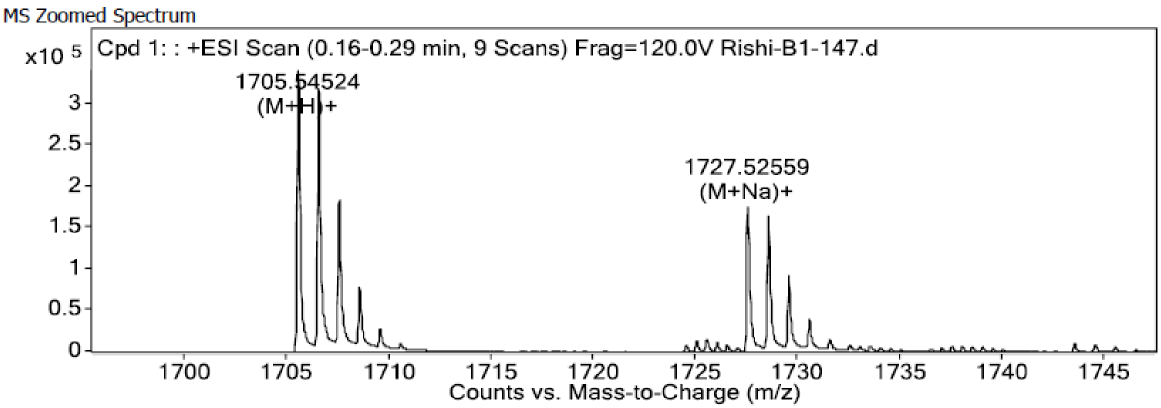


Figure S35. HRMS (ESI$^+$) spectrum of compound **11**.

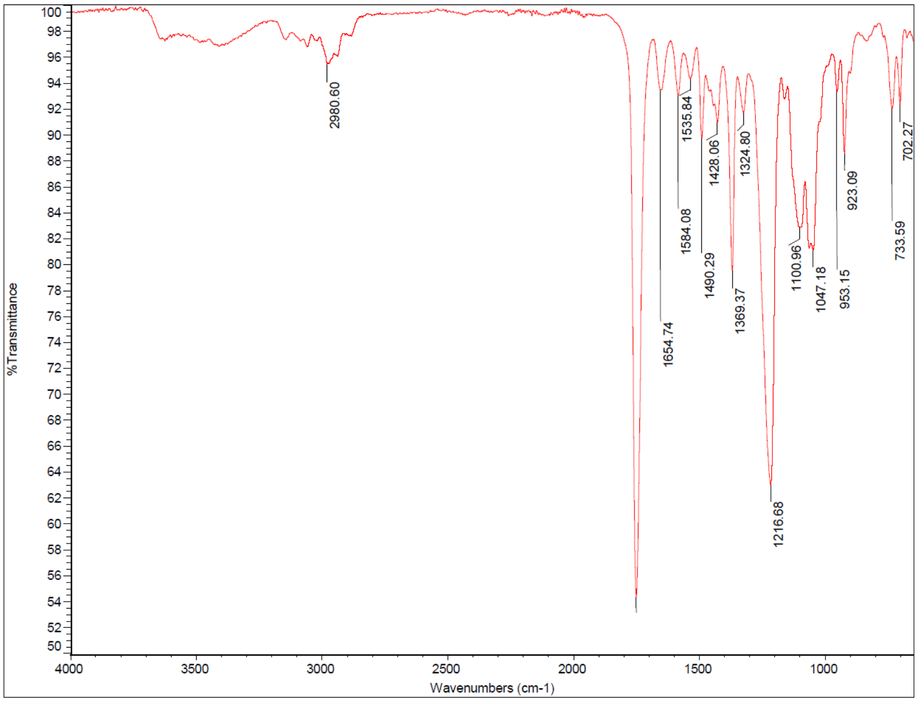
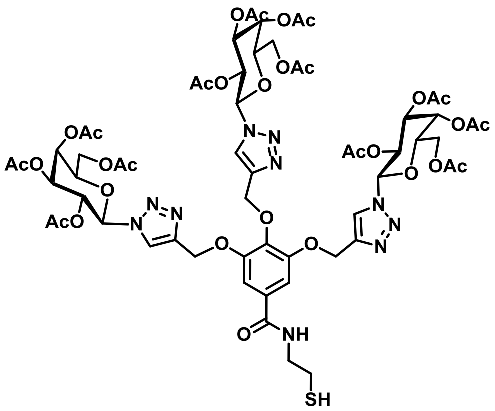


Figure S36. IR spectrum of compound **11**.



Synthesis of compound 12: To a stirring solution of 3% trifluoroacetic acid in DCM (1.5mL), was added a solution of **11** (300mg, 0.176mmol) in dichloromethane (1.5mL). Et_3SiH (28µL, 0.18mmol) was added to the orange solution. After 3 hrs, toluene (4mL) was added and the solvents were evaporated under vacuum. The addition of toluene and evaporation was repeated twice. The product **12** was isolated by quick flash chromatography using 3% MeOH in DCM in a 86% yield (221mg, 0.151mmol).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.04 (s, 2H), 7.16 (s, 2H), 6.91 (s, 1H), 5.91 (m, 3H), 5.67 (t, *J* = 9.8 Hz, 1H), 5.64–5.48 (m, 5H), 5.39–5.17 (m, 9H), 4.39–4.06 (m, 9H), 3.73–3.46 (m, 2H), 2.76 (dd, *J* = 14.9, 6.5 Hz, 2H), 2.22 (d, *J* = 2.3 Hz, 9H), 2.14–1.96 (m, 18H), 1.81 (d, *J* = 18.4 Hz, 9H), 1.48 (t, S***H***, *J* = 8.5 Hz, 1H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.3, 169.9, 169.2, 168.8, 151.9, 144.2, 107.4, 86.3, 74.0, 70.7, 68.2, 66.8, 62.9, 61.1, 43.0, 24.5, 20.6, 20.2.
IR (cm^{-1}) 3649, 2980, 2888, 1754, 1382, 1249, 1153, 1079, 955.
HRMS (ESI$^+$) *m/z* calc for $C_{60}H_{74}N_{10}O_{31}S$ 1463.4315 [*M*+H]$^+$; found, 1463.4317.

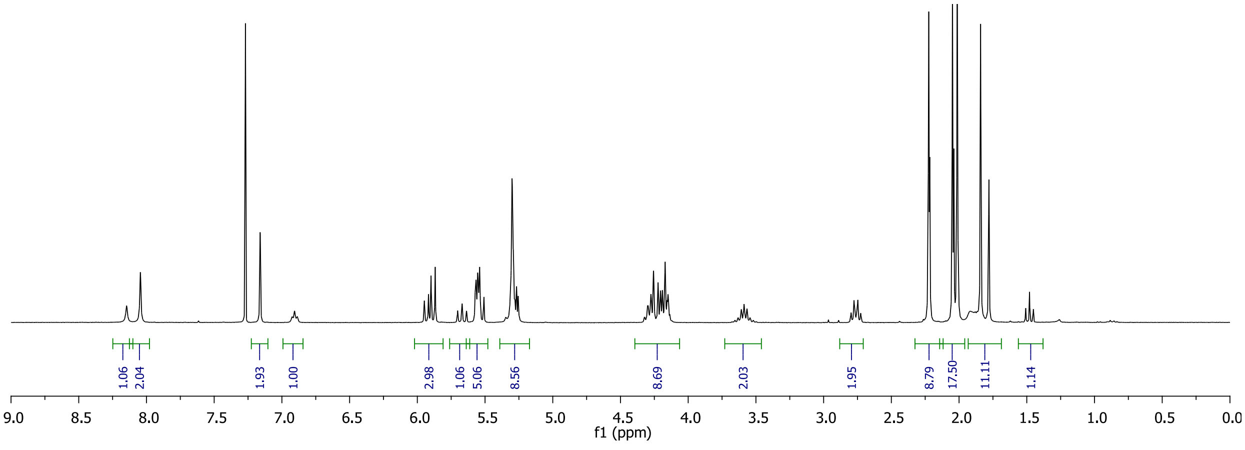


Figure S37. ^{1}H NMR spectrum of compound **12** (300 MHz, $CDCl_3$).

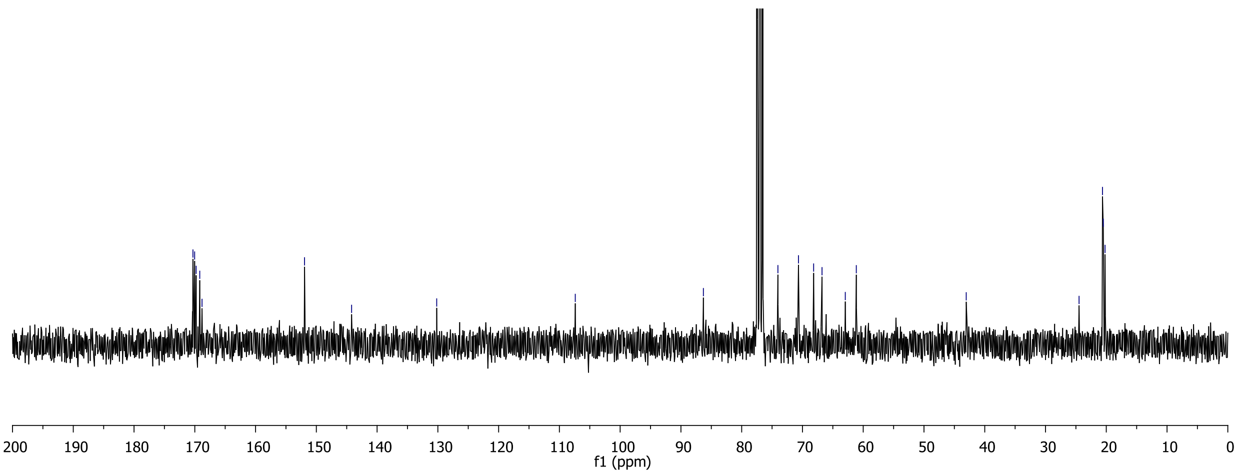


Figure S38. $^{13}C\{^{1}H\}$ NMR spectrum of compound **12** (75 MHz, $CDCl_3$).

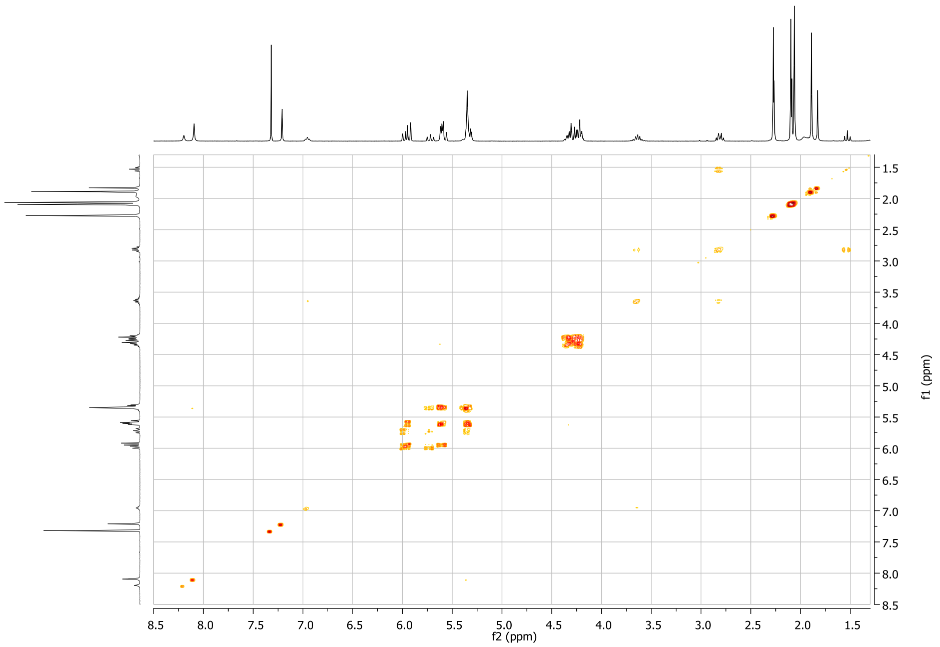


Figure S39. COSY spectrum of compound **12**.

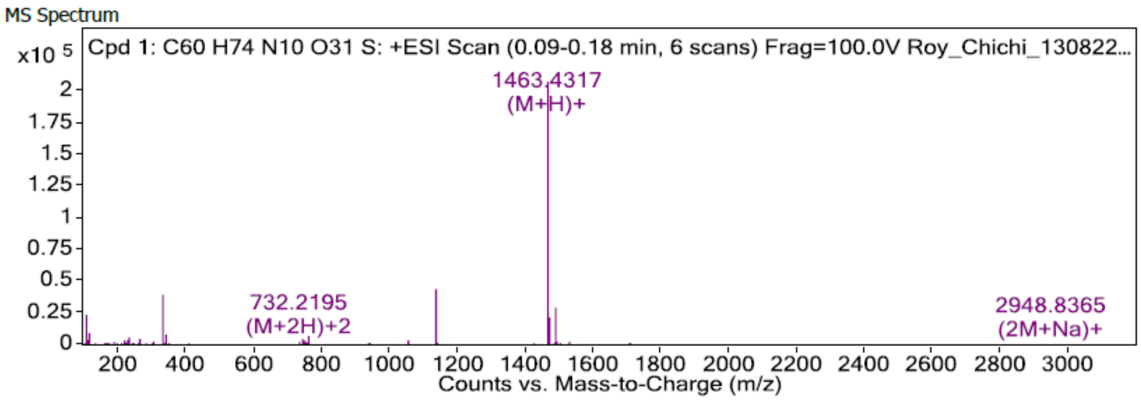


Figure S40. HRMS (ESI^{+}) spectrum of compound **12**.

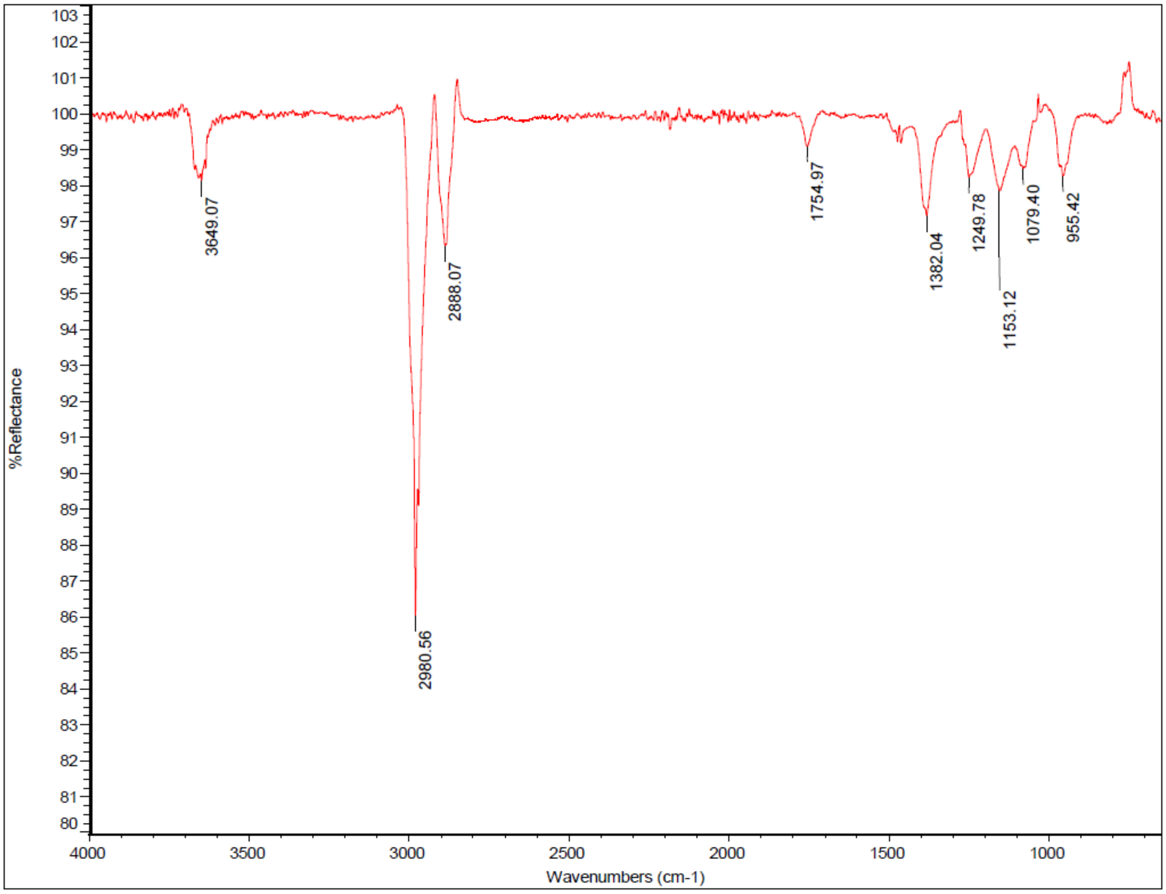
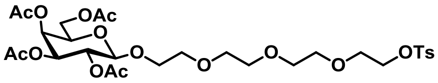


Figure S41. I.R spectrum of compound **12** (75 MHz, $CDCl_3$).

Synthesis of galactodendrimer 7 according to a convergent strategy

Compound **2** (3mg, 6µmol) and compound **12** (263mg, 0.180mmol, 5eq/alkene) were suspended in dioxane (1mL) in a 5 mL glass vial equipped with a small magnetic stirring bar. To this was added AIBN (1mg, 0.5µmol, 0.15eq/alkene), and the vial was tightly sealed with an aluminum/Teflon® crimp top. The mixture was then heated at 75°C for 5 hrs. After completion of the reaction, the vial was cooled to 25°C before it was opened. Dioxane was removed under vacuum. Purification of the crude compound was achieved *via* flash column chromatography on silica gel using 2-4% MeOH in DCM as eluent gradient to afford desired compound **7** (29.8mg, 3.22µmol) in 53% yield as a white solid. *Spectroscopic data for compound **7** obtained via convergent strategy are in full agreement with those of one originated from divergent approach.*



Synthesis of compound 15: *β*-D-Galactopyranose pentaacetate **13** (300mg, 0.769mmol) and monotosylated tetra(ethylene)glycol **14** (669mg, 1.92mmol) were mixed in dry DCM (5mL) and stirred for 1 hr with 4Å molecular sieves. The reaction mixture was then cooled to 0°C, followed by the addition of $BF_3{\cdot}Et_2O$ (660µL, 5.38mmol). The reaction mixture was stirred for 4 hrs at room temperature. Upon completion of reaction, the mixture was diluted with DCM (30mL), washed with water, saturated $NaHCO_3$ solution followed by brine. Drying over Na_2SO_4 and concentration under vacuum afforded crude compound that was purified by column chromatography (60% EtOAc in hexanes as eluent) to give **15** (287mg, 0.423mmol) colourless oil in 55% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 5.39 (d, *J* = 3.3 Hz, 1H), 5.21 (dd, *J* = 10.4, 8.0 Hz, 1H), 5.02 (dd, *J* = 10.5, 3.4 Hz, 1H), 4.57 (d, *J* = 7.9 Hz, 1H), 4.15 (dt, *J* = 15.5, 7.8 Hz, 4H), 4.05 – 3.87 (m, 2H), 3.82–3.53 (m, 13H), 2.46 (s, 3H), 2.15 (s, 3H), 2.06 (d, *J* = 1.9 Hz, 6H), 1.99 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.2, 170.1, 169.9, 169.3, 144.6, 132.8, 129.6, 127.7, 101.1, 77.2, 70.5, 70.4, 70.4, 70.3, 68.8, 66.9, 61.1, 21.4, 20.5, 20.5, 20.4.
IR (cm^{-1}) 2923, 1748, 1367, 1221, 1176, 1075.
HRMS (ESI$^+$) *m/z* calc for $C_{29}H_{42}O_{16}S$, 701.2086 $[M{+}Na]^+$; found, 701.2073.

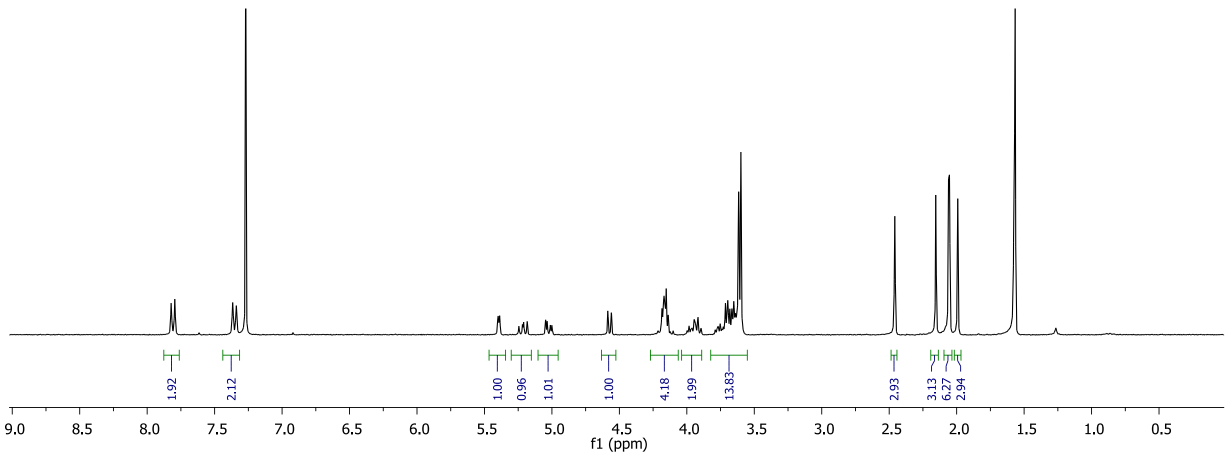


Figure S42. ^{1}H NMR spectrum of compound **15** (300 MHz, $CDCl_3$).

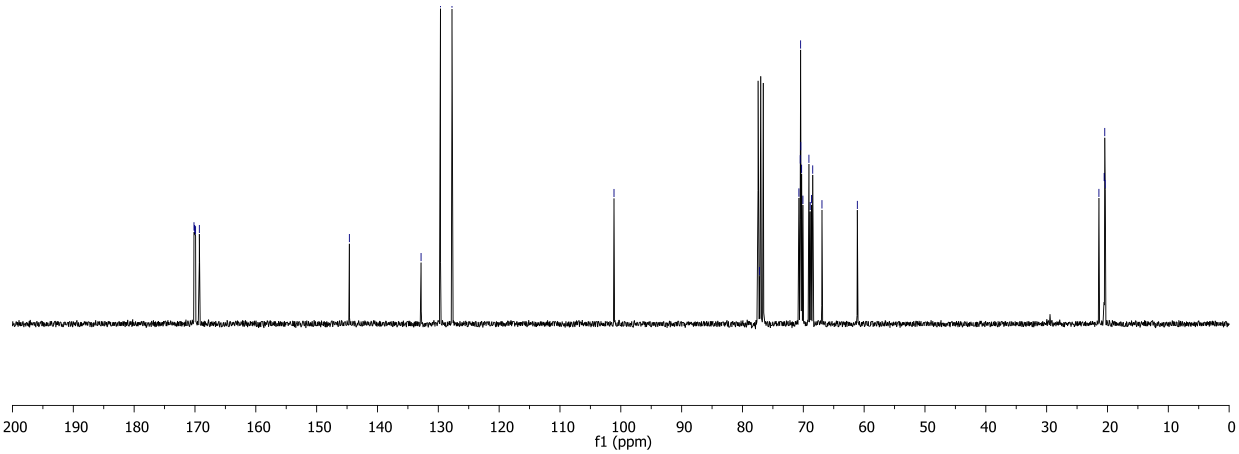


Figure S43. ^{13}C{^{1}H} NMR spectrum of compound **15** (75 MHz, $CDCl_3$).

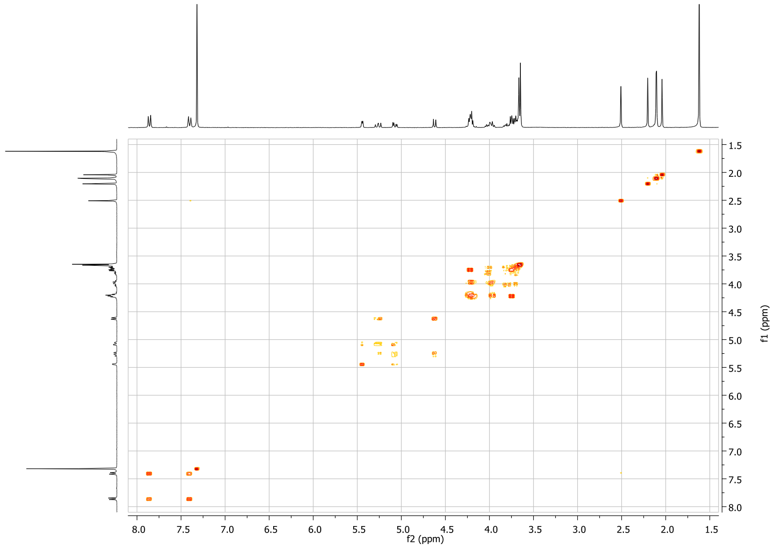


Figure S44. COSY spectrum of compound **15**.

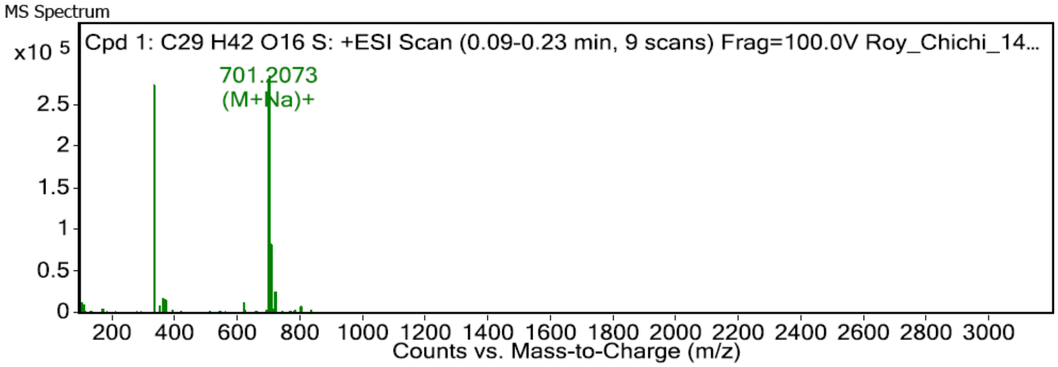


Figure S45. HRMS (ESI^+) spectrum of compound **15**.

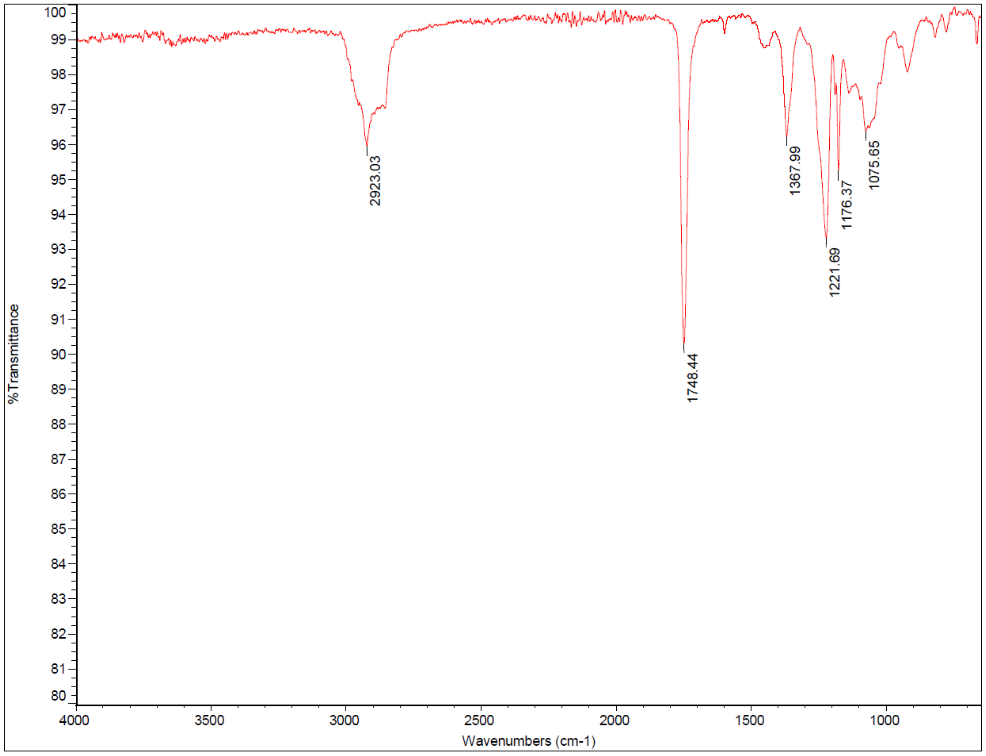
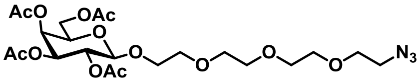


Figure S46. IR spectrum of compound **15**.



Synthesis of compound 16: Compound **15** (2.000g, 2.949mmol) and sodium azide (958mg, 15.0mmol) in dry DMF (20mL) were stirred at 80°C for 6 hrs. The solvent was evaporated under reduced pressure and crude was diluted with ethyl acetate (50mL), washed with water (2×30mL) and brine, dried over Na_2SO_4 and concenterated in *vacuo*. Column chromatography of the residual crude mixture was performed using 60% EtOAc in hexanes as eluent to give **16** (1.329g, 2.410mmol) as a yellowish oil in 82% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.42–5.35 (m, 1H), 5.24–5.15 (m, 1H), 5.00 (ddd, *J* = 10.5, 3.4, 1.7 Hz, 1H), 4.56 (dd, *J* = 8.0, 1.6 Hz, 1H), 4.14 (dddd, *J* = 25.6, 11.3, 6.7, 1.5 Hz, 2H), 4.01–3.87 (m, 2H), 3.80–3.70 (m, 1H), 3.72–3.58 (m, 12H), 3.38 (t, *J* = 4.3 Hz, 2H), 2.13 (d, *J* = 1.7 Hz, 3H), 2.11–2.00 (m, 6H), 1.97 (d, *J* = 1.7 Hz, 3H).
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.4, 170.2, 170.1, 169.5, 101.3, 70.9, 70.7, 70.6, 70.3, 70.0, 69.0, 68.8, 67.0, 61.3, 50.6, 20.7, 20.6, 20.6, 20.6.
IR (cm^{-1}) 2980, 2881, 2098, 1749, 1369, 1223, 1073.
HRMS (ESI$^+$) *m/z* calc for $C_{22}H_{35}N_3O_{13}$, 567.2508 [*M*+NH_4]$^+$; found, 567.2480, 588.1802 [*M*+K]$^+$; 588.1789.

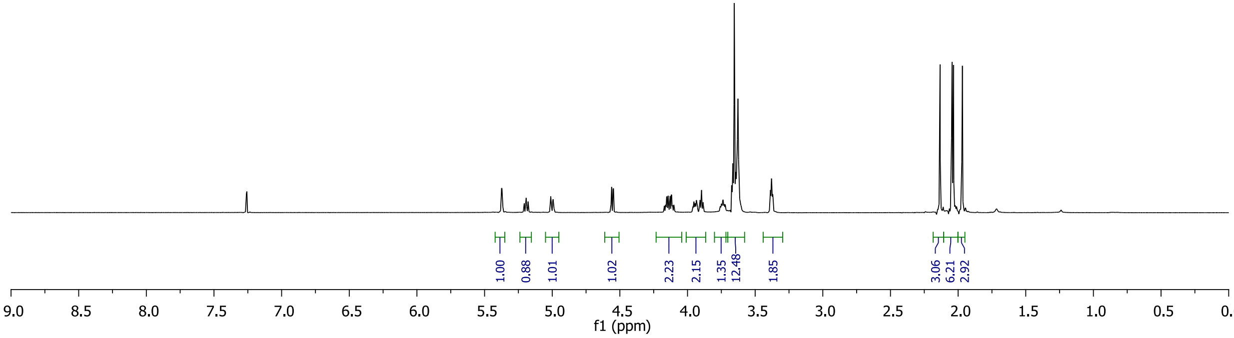


Figure S47. ^{1}H NMR spectrum of compound **16** (600 MHz, $CDCl_3$).

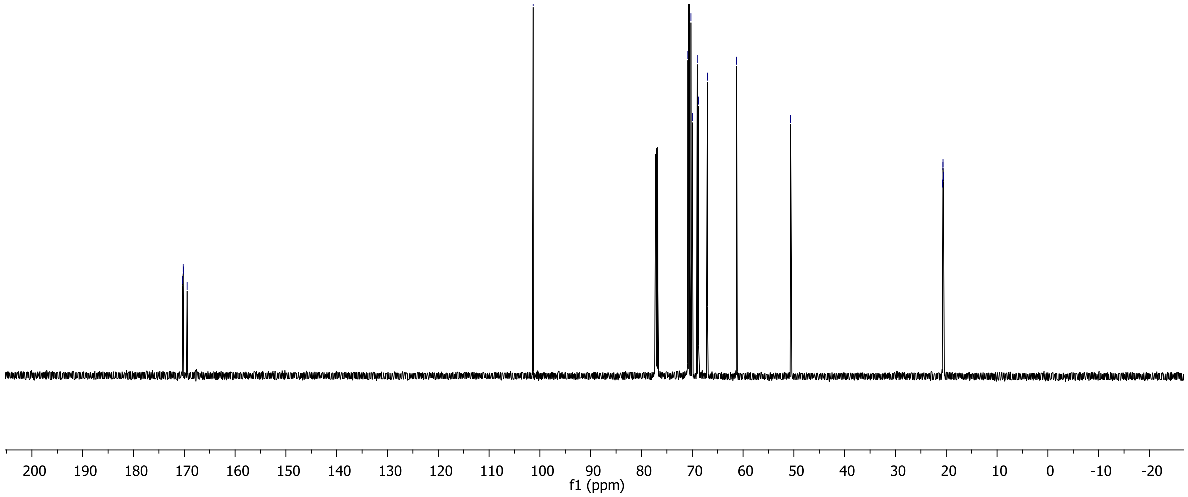


Figure S48. ^{13}C{^{1}H} NMR spectrum of compound **16** (151 MHz, $CDCl_3$).

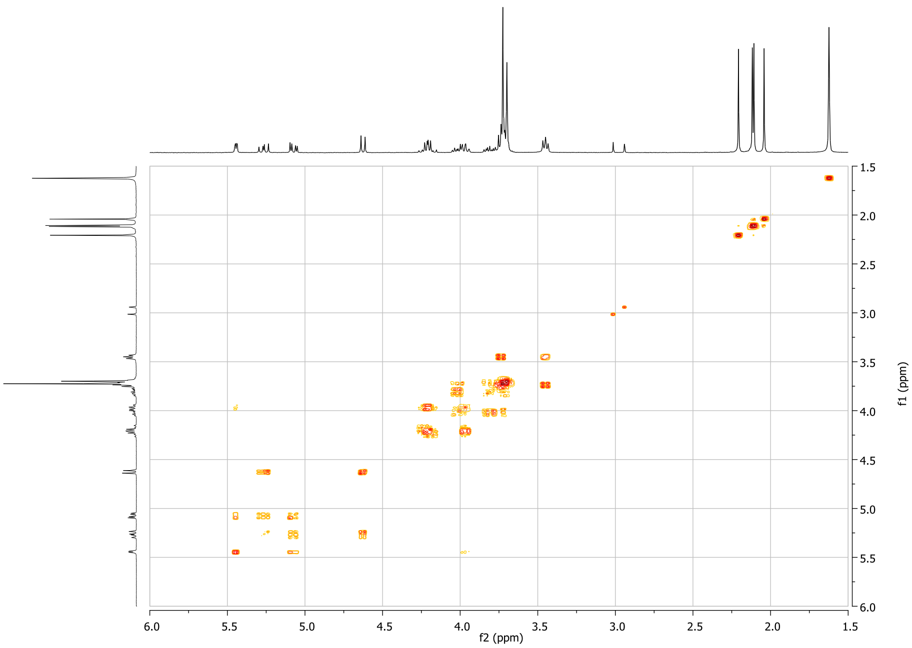


Figure S49. COSY NMR spectrum of compound **16**.

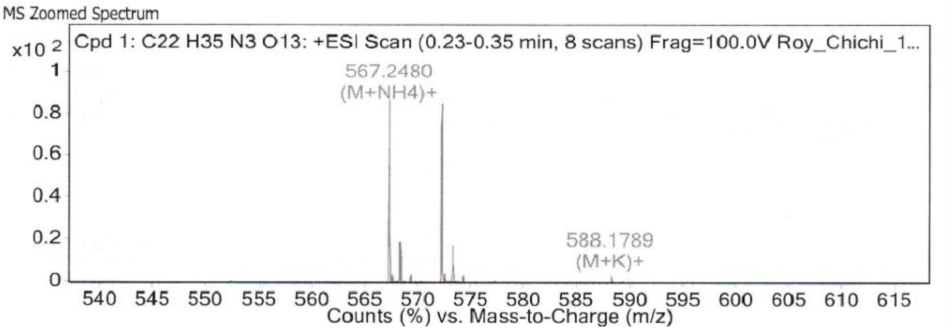


Figure S50. HRMS (ESI$^+$) spectrum of compound **16**.

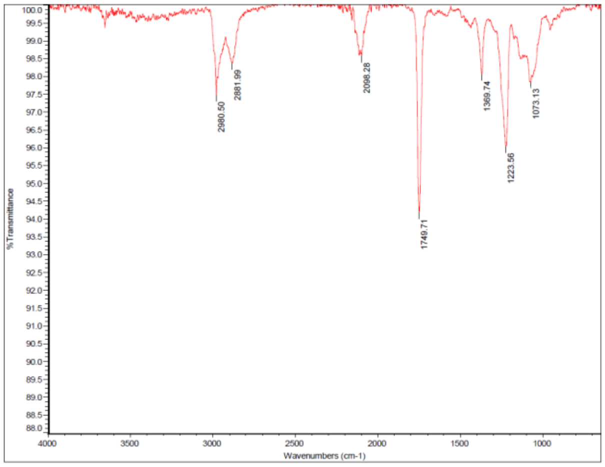
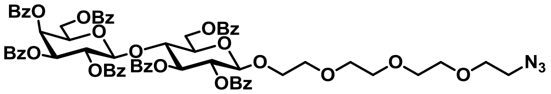


Figure S51. IR spectrum of compound **16**.



Synthesis of compound 17: To a solution of per-*O*-acetylated lactose (β anomer,[1] 5.00g, 7.40mmol) and tetra(ethylene)glycol monotosylate (synthesized as previously described,[2] 8.10g, 22.1mmol) in dry DCM (60mL) under a nitrogen atmosphere and at 0°C was added dropwise $BF_3 \cdot Et_2O$ (2.7mL, 22.1mmol) over a 15 minutes period. After stirring overnight (12 hrs) at r.t., the solvent was removed and EtOAc was added, then the solution was washed successively with $NaHCO_3$ (40mL), water (40mL) and brine (40mL). The organic phase was then dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was directly re-dissolved in DMF (70mL) under a nitrogen atmosphere and sodium azide (962mg, 14.8mmol) together with sodium iodide (11.1mg, 0.11mmol) were added. After stirring overnight (16 h) at 70°C, the solvent was removed and EtOAc (100mL) was added, then the solution was washed successively with water (4×40mL) and brine (3×50mL). The organic phase was then dried over $MgSO_4$ and concentrated under reduced pressure. After a short flash column chromatography on silica (EtOAc/Hexanes 6:4 to 8:2), the crude was subjected to de-*O*-acetylation protocol and dissolved in MeOH (40mL). To this solution was slowly added 1M MeONa/MeOH to adjust the pH 9−10. Reaction mixture was left for stirring overnight. The reaction pH was then adjusted with H^+ resin to adjust pH to 6. Solvent was evaporated and the residue was benzoylated with benzoyl chloride (20.8g, 17.2mL, 148mmol) in pyridine (50mL) for overnight stirring at room temperature. Upon completion solvents were removed and reaction mixture was dissolved in DCM (100mL) and washed with 0.1N HCl (3×50 mL) followed by saturated solution of $NaHCO_3$ (3×75mL) and finally with brine. Organic layer was then dried with anhydrous sodium sulphate filtered and evaporated. Crude compound was then purified with the help of column chromatography using Hexane/Ethyl Acetate (1:1) as eluent. Desired compound **17** (5.93g, 4.66mmol) was isolated in a 63% overall yield as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12–7.94 (m, 10H), 7.94–7.87 (m, 2H), 7.77–7.69 (m, 2H), 7.69–7.29 (m, 17H), 7.18 (m, 4H), 5.87–5.68 (m, 3H), 5.53–5.41 (m, 1H), 5.37 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.86 (dd, *J* = 10.8, 7.9 Hz, 2H), 4.61 (d, *J* = 11.1 Hz, 1H), 4.49 (dd, *J* = 12.1, 4.0 Hz, 1H), 4.26 (t, *J* = 9.5 Hz, 1H), 3.87 (dd, *J* = 13.3, 8.1 Hz, 3H), 3.69 (ddd, *J* = 14.0, 10.4, 5.0 Hz, 5H), 3.62–3.48 (m, 6H), 3.47–3.33 (m, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 165.5, 165.4, 165.2, 165.1, 164.8, 133.5, 133.4, 133.2, 133.7, 130.0, 129.8, 129.7, 129.6, 129.6, 129.5, 129.4, 128.8, 128.7, 128.6, 128.5, 128.5, 128.31, 128.20, 101.2, 101.0, 76.0, 72.9, 72.9, 71.8, 70.6, 70.5, 70.5, 70.3, 69.9, 69.9, 69.2, 67.5, 62.4, 61.0, 50.6.
IR (cm^{-1}) 2980, 2883, 2104, 1728, 1601, 1451, 1314, 1267, 1176, 1094, 1069, 1027, 709.
HRMS (ESI$^+$) *m/z* calc for $C_{69}H_{65}N_3O_{21},$ 1294.4003 $[M{+}Na]^+$; found, 1294.4031

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[1] Wolfrom, M. L., Thompson, A. *Methods. Carbohydr. Chem.* **1963**, 211-215.

[2] Zhang, L.; Sun, L.; Cui, Z.; Gottlieb, R. L.; Zhang, B. *Bioconjugate Chem.* **2001**, *12*, 939-948.

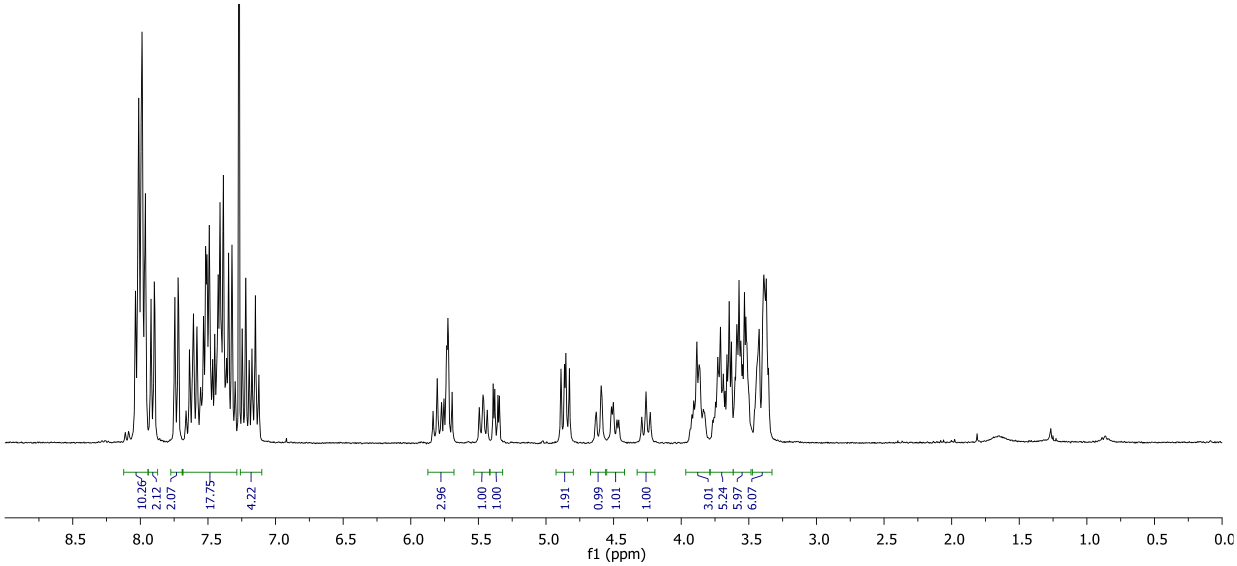


Figure S52. ^{1}H NMR spectrum of compound **17** (300 MHz, $CDCl_3$).

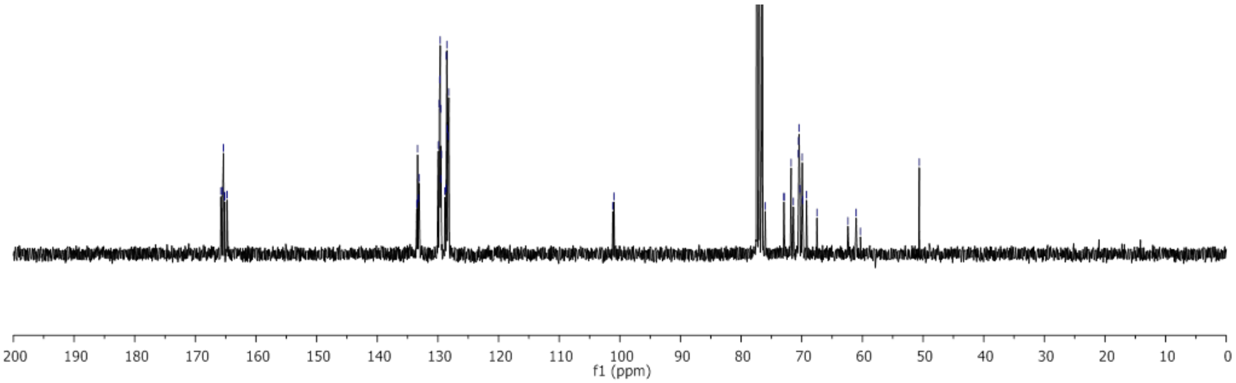


Figure S53. $^{13}C\{^{1}H\}$ NMR spectrum of compound **17** (300 MHz, $CDCl_3$).

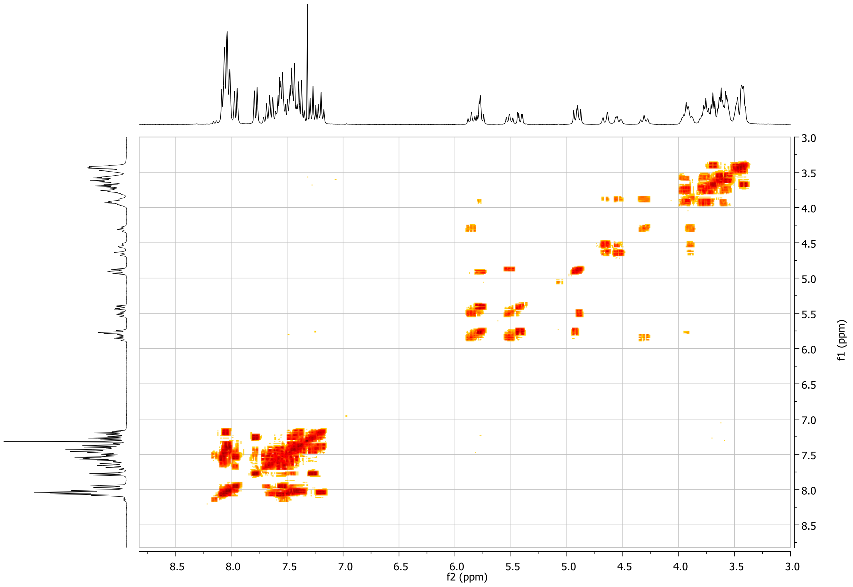


Figure S54. COSY spectrum of compound **17** (300 MHz, $CDCl_3$).

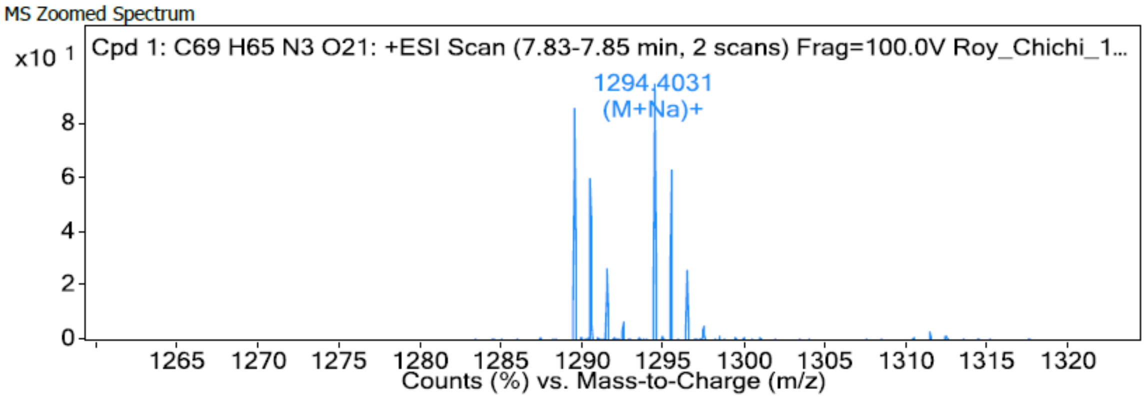


Figure S55. HRMS (ESI$^+$) spectrum of compound **17**.

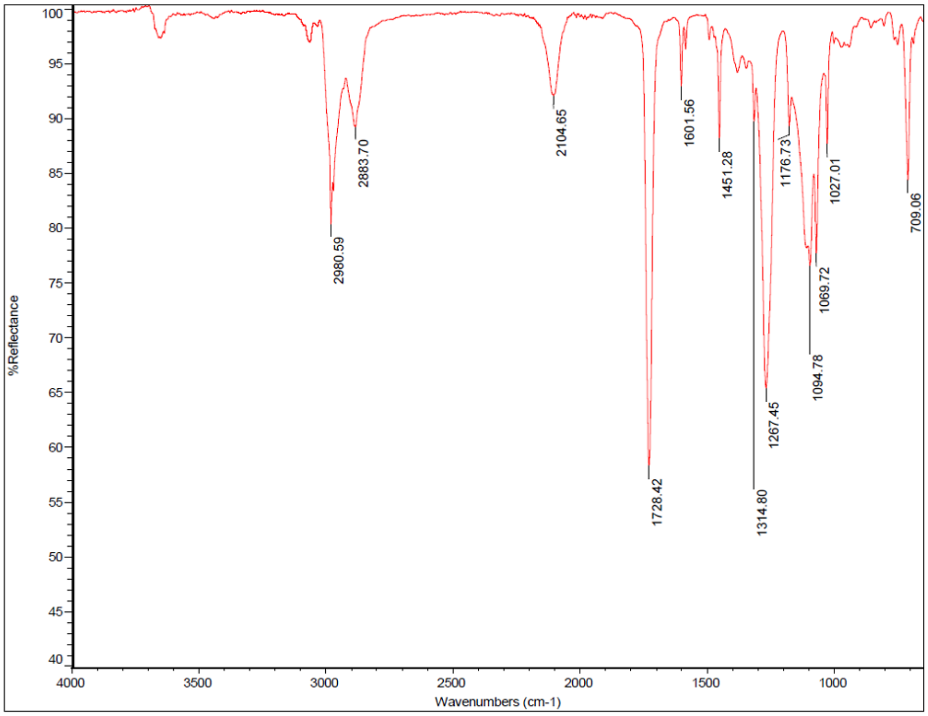
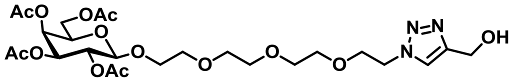


Figure S56. IR spectrum of compound **17**.



Synthesis of compound 19a: To a solution of azide terminated compound **16** (100mg, 0.181mmol) in THF (4mL), was added propargyl alcohol (0.021ml, 0.363mmol), followed by sodium ascorbate (36mg, 0.181mmol). An aqueous solution of $CuSO_4 \cdot 5H_2O$ (45mg, 0.181mmol) was added and the final ratio of H_2O to THF was kept 1:1. The reaction mixture was stirred at 40^oC for 12 hrs. Progress of the reaction was monitored with the help of TLC. Upon completion, reaction mixture was diluted with EtOAc (25mL) and washed with a saturated solution of EDTA (2×15mL). Organic layer was washed with brine solution, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the crude was achieved *via* flash coloumn chromatography on silica gel using 2% MeOH in DCM as eluent to afford acetylated compound **19a** (93.2mg, 0.154mmol) in a 85% yield as a yellowish oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 5.38 (d, *J* = 3.2 Hz, 1H), 5.19 (dd, *J* = 10.4, 7.9 Hz, 1H), 5.02 (dd, *J* = 10.5, 3.4 Hz, 1H), 4.79 (d, *J* = 5.0 Hz, 2H), 4.55 (dd, *J* = 6.3, 4.9 Hz, 3H), 4.25–4.06 (m, 2H), 4.04–3.82 (m, 4H), 3.78–3.51 (m, 11H), 2.14 (s, 3H), 2.04 (s, 6H), 1.98 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.4, 170.2, 170.2, 169.3, 70.8, 70.7, 70.6, 70.5, 70.5, 70.4, 70.2, 69.4, 69.1, 68.8, 67.0, 61.2, 56.6, 50.2, 20.7, 20.7, 20.6, 20.6.
IR (cm^{-1}): 3478, 2881, 1744, 1433, 1369, 1219, 1175, 1047, 954.
HRMS (ESI$^+$) *m/z* calc for $C_{25}H_{39}N_3O_{14}$ 606.2505 [*M*+H]$^+$; found, 606.2501.

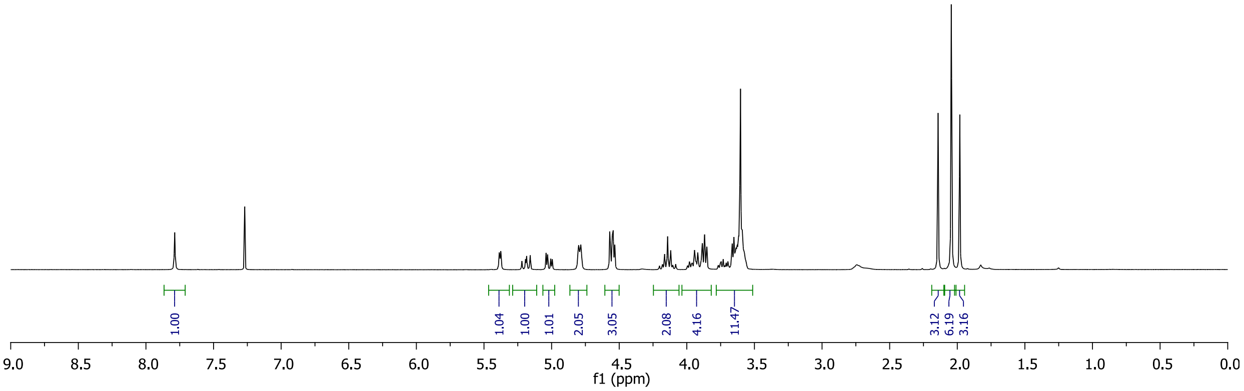


Figure S57. ^{1}H NMR spectrum of compound **19a** (300 MHz, $CDCl_3$).

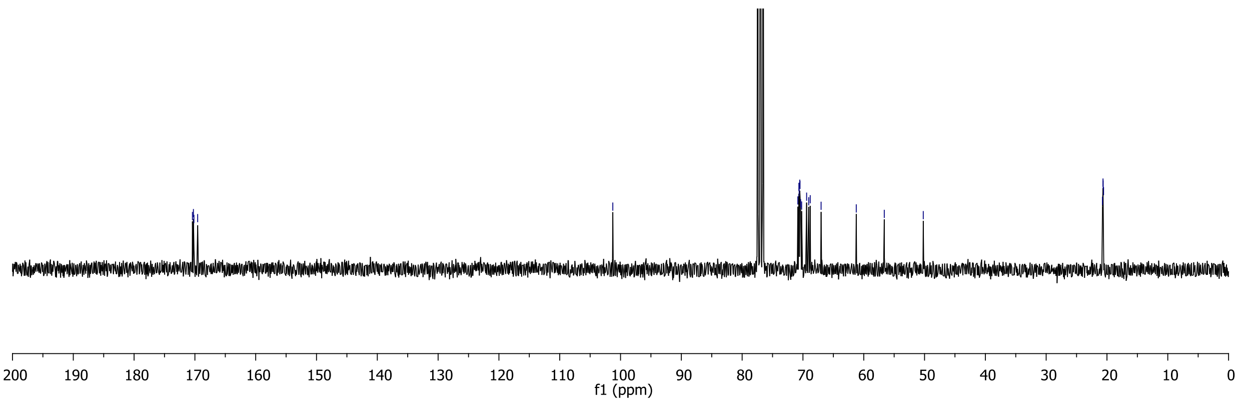


Figure S58. $^{13}C\{^{1}H\}$ NMR spectrum of compound **19a** (75 MHz, $CDCl_3$).

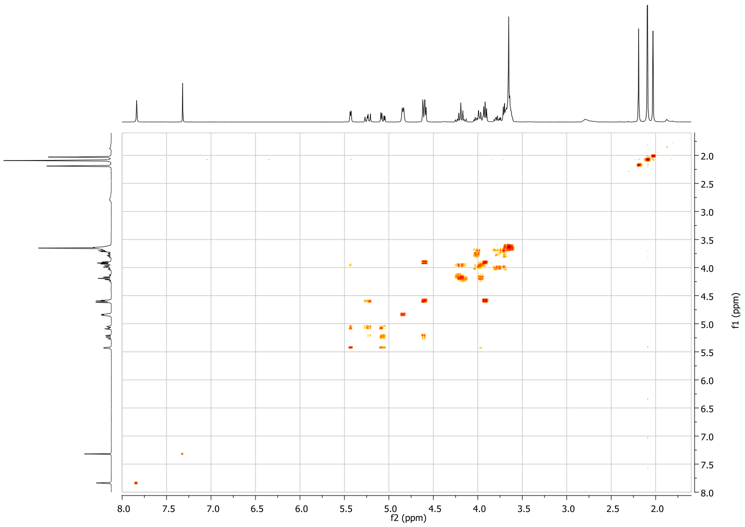


Figure S59. COSY spectrum of compound **19a**.

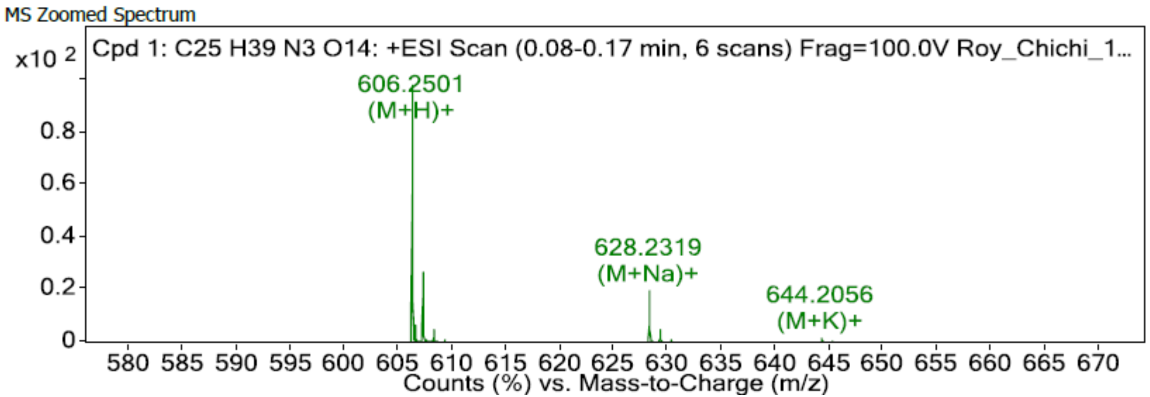


Figure S60. HRMS (ESI^+) of compound **19a**.

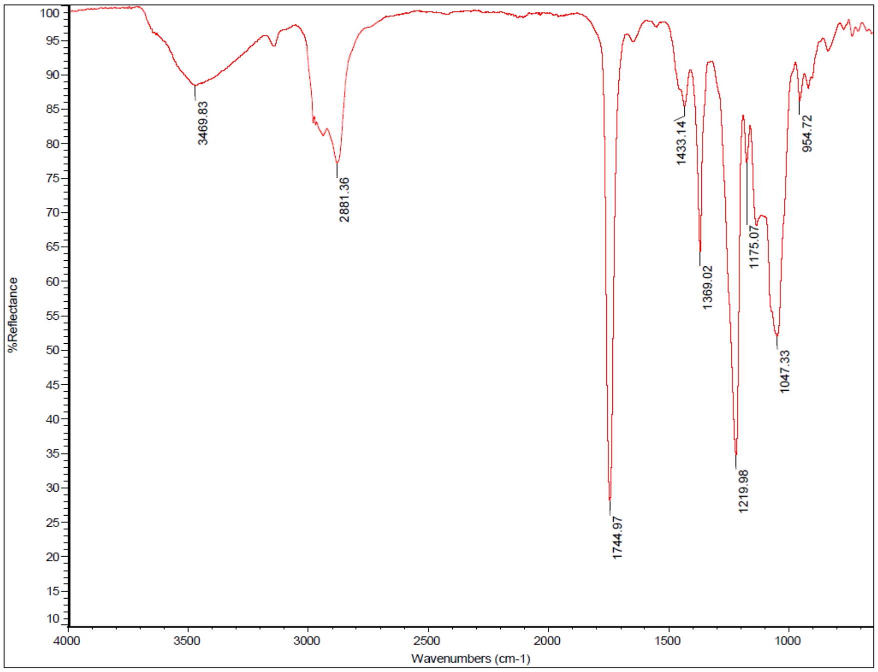
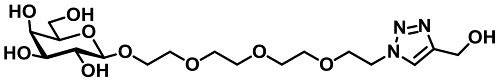


Figure S61. IR spectrum of compound **19a**.



Synthesis of compound 19: To a stirring solution of compound **19a** (100mg, 0.165mmol) in MeOH (3mL) was slowly added 1M MeONa/MeOH solution to adjust the pH to 9-10. Reaction mixture was left to stir overnight. The reaction pH was then adjusted to 6 with H^+ resin. The solvent was evaporated and the residue was dissolved in 3mL of water, and washed with diethyl ether (3×15mL) to remove impurities. Aqueous layer was lyophilized to provide **19** (65mg, 0.149mmol) as a white solid in a 90% yield.

^{1}H NMR (300 MHz, CD_3OD) δ 8.11 (br s, 1H), 4.74 (s, 2H), 4.63 (d, *J* = 4.7 Hz, 2H), 4.27 (d, *J* = 7.0 Hz, 1H), 4.09–3.97 (m, 1H), 3.93 (t, *J* = 5.0 Hz, 2H), 3.84 (d, *J* = 2.2 Hz, 1H), 3.79–3.57 (m, 13H), 3.57–3.44 (m, 3H).
^{13}C{^{1}H} NMR (75 MHz, CD_3OD) δ 105.0, 76.7, 74.8, 72.5, 71.4, 70.3, 70.2, 69.6, 62.5, 51.8.
IR (cm^{-1}) 3358, 2924, 2502, 1643, 1455, 1073.
HRMS (ESI$^+$) *m/z* calc for $C_{17}H_{31}N_3O_{10}$, 438.2082 [M+H]$^+$; found, 438.2107.

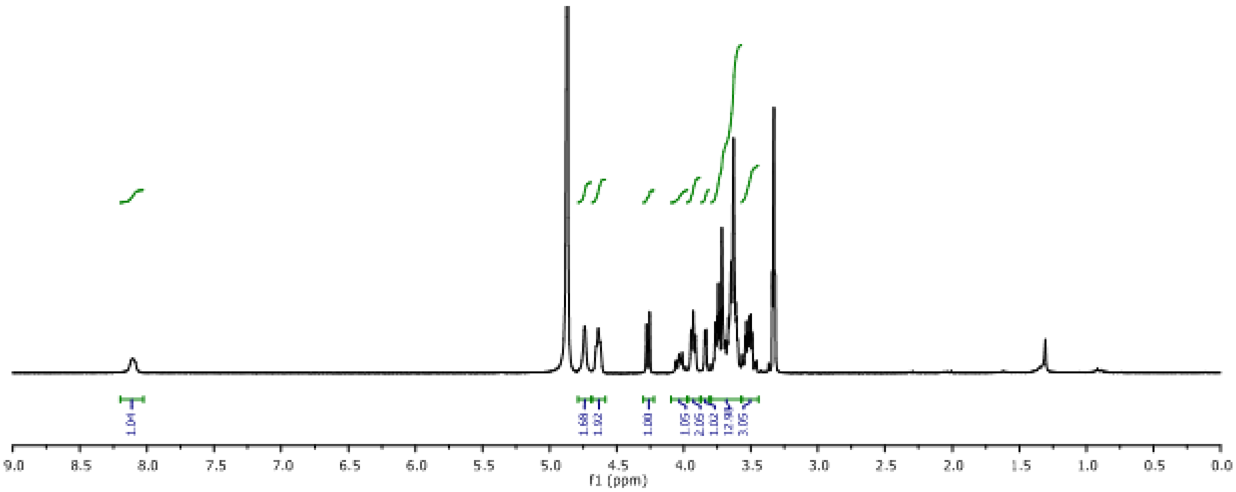


Figure S62. ^{1}H NMR spectrum of compound **19** (300 MHz, CD_3OD).

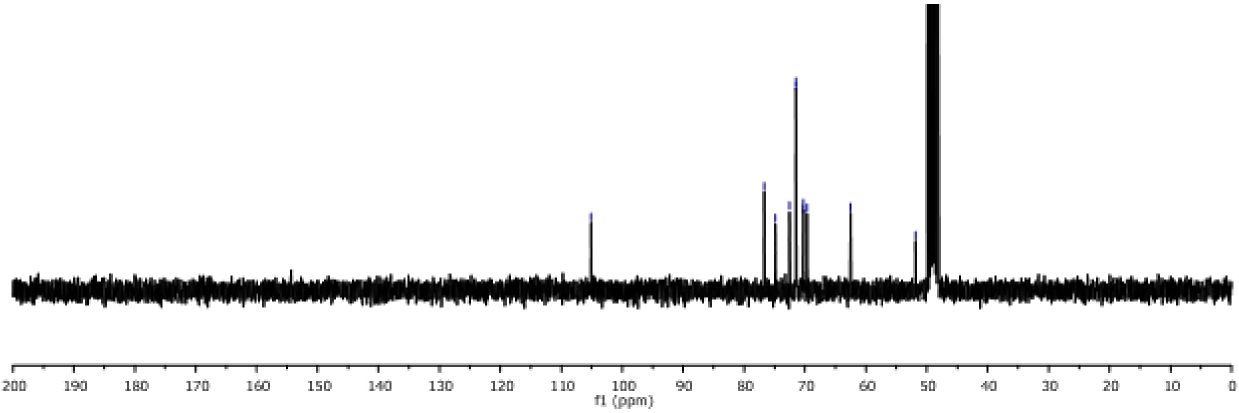


Figure S63. ^{13}C{^{1}H} NMR spectrum of compound **19** (75 MHz, CD_3OD).

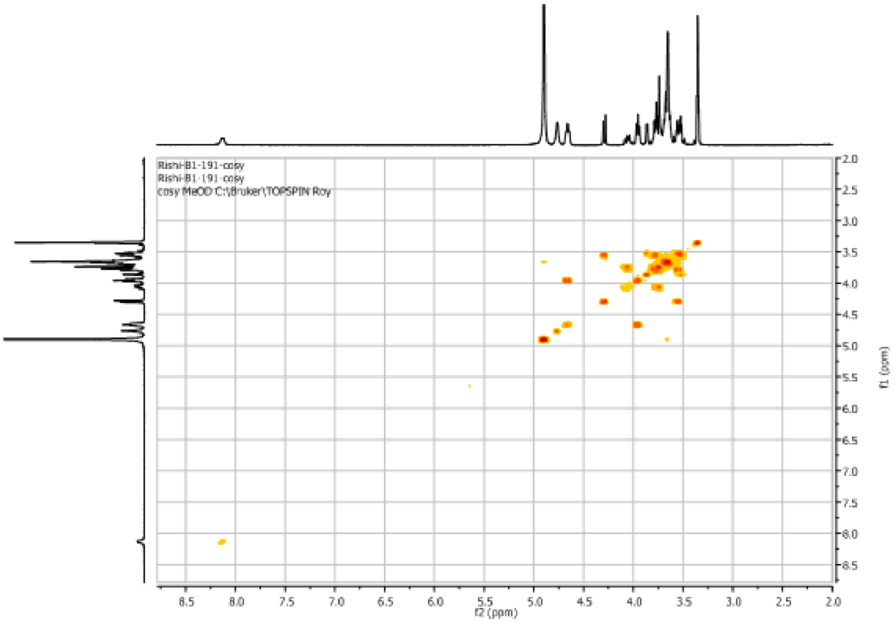


Figure S64. COSY spectrum of compound **19.**

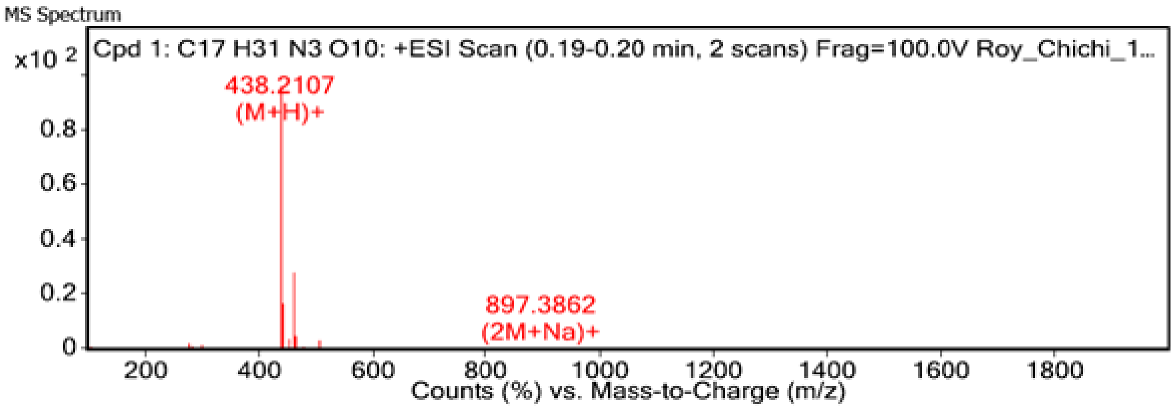


Figure S65. HRMS (ESI$^+$) of compound **19**.

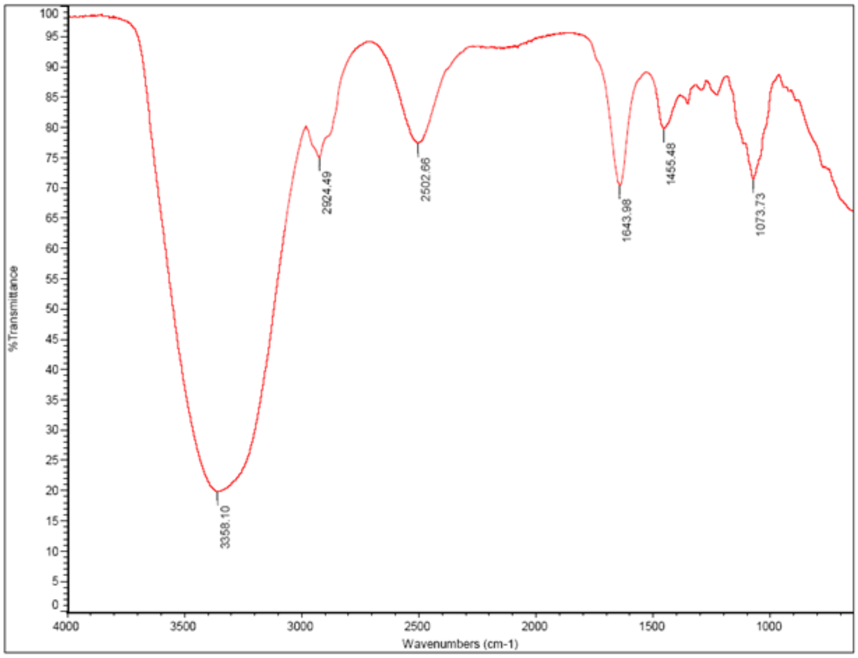
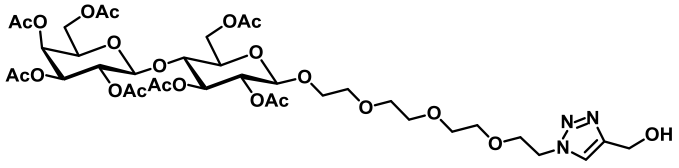


Figure S66. IR spectrum of compound **19**.



Synthesis of compound 20a: To a solution of per-*O*-acetylated galactose (100mg, 119µmol) in a 1:1 mixture of H_2O/THF_{anh} (5 mL), were added propargyl alcohol (29.1µL, 501µmol), $CuSO_4 \cdot 5H_2O$ (14.9mg, 59.7µmol) and sodium ascorbate (11.8mg, 59.7µmol). While stirring, the mixture was first heated at 50°C for 3 hrs and at room temperature for additional 18 hours. Ethyl acetate (15mL) was added and the solution was poured into a separatory funnel containing ethyl acetate (10mL), washed with saturated aqueous NH_4Cl (2×10mL), water (10mL) and brine (5mL). Organics were collected, dried over Na_2SO_4 and concentrated to dryness *in vacuo* with rotary evaporator. Purification by flash chromatography (SiO_2, DCM/MeOH 100:0 to 92:8) afforded desired multivalent compound **20a** (86.0mg, 96.6µmol) as a white foam in a 91% yield.

^{1}H NMR (600 MHz, $CDCl_3$, δ ppm): 7.75 (s, 1H), 5.29 (d_{app}, 1H), 5.14 (dd, $^3J_{4,3}$ = 9.4 Hz, $^3J_{3,2}$ = 9.1 Hz, 1H), 5.05 (dd, $^3J_{2,1}$ = 10.5 Hz, $^3J_{3,2}$ = 8.0 Hz, 1H), 4.93 (dd, $^3J_{2,3}$ = 10.5 Hz, $^3J_{3,4}$ = 3.4 Hz, 1H), 4.83 (dd, $^3J_{2,1}$ = 9.4 Hz, $^3J_{3,2}$ = 8.0 Hz, 1H), 4.73 (br s, 2H), 4.53 (d, $^3J_{1,2}$ = 9.4 Hz, 1H), 4.50 (t_{app}, 2H), 4.48 (dd, $^2J_{6a.6b}$ = 12.0 Hz, $^3J_{5.6a}$ = 2.1 Hz, 1H), 4.47 (d, $^3J_{1,2}$ = 7.9 Hz, 1H), 4.12–4.00 (m, 3H), 3.90-3.52 (m, 17H), 3.30 (br s, 1H), 2.15 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H), 2.04 (3s, 9H), 1.96 (s, 3H).
^{13}C NMR (150 MHz, $CDCl_3$, δ ppm): 170.3, 170.2, 170.0, 169.9, 169.7, 169.6, 169.0, 147., 122.9, 100.9, 100.4, 76.6, 72.6, 72.5, 71.5, 70.8, 70.5, 70.3, 70.3, 70.2, 70.2, 69.3, 69.0, 68.9, 66.5, 61.8, 60.7, 56.3, 50.0, 20.8, 20.8, 20.7, 20.6, 20.6, 20.6, 20.5.
HRMS (ESI$^+$) *m/z* for $C_{37}H_{55}N_3O_{22}$, 894.3350 $[M+H]^+$; found 894.3361, 916.3169 $[M+Na]^+$; found 916.3181.

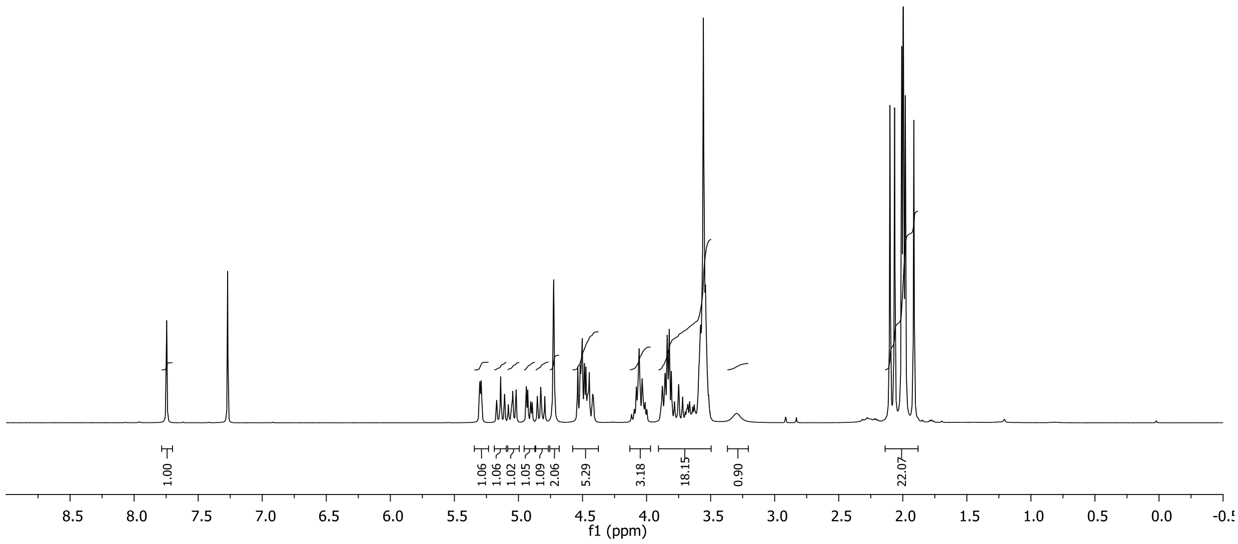


Figure S67. ^{1}H NMR spectrum of compound **20a** (600 MHz, $CDCl_3$).

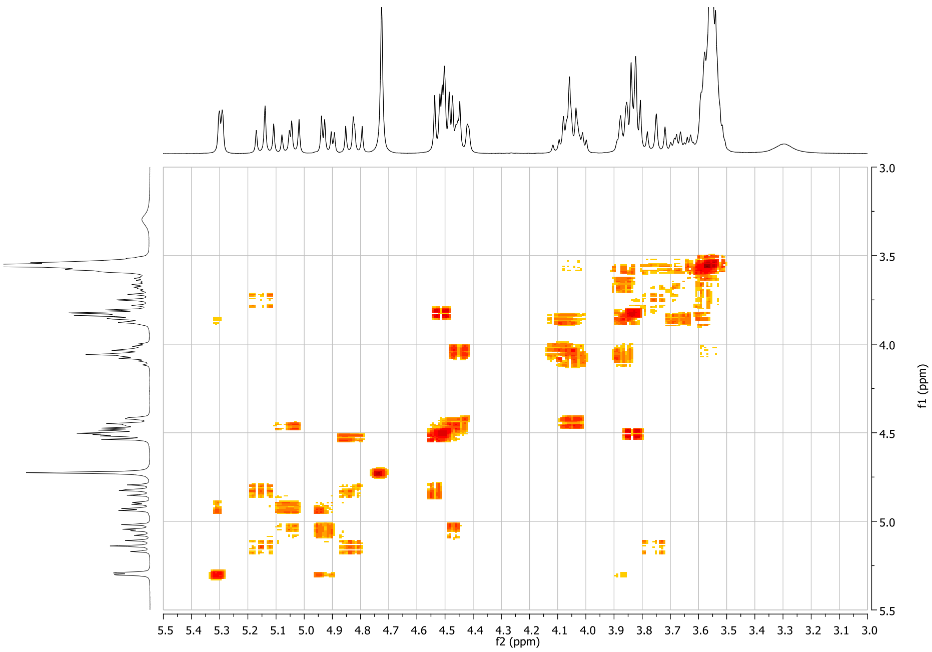


Figure S68. COSY spectrum of compound **20a**.

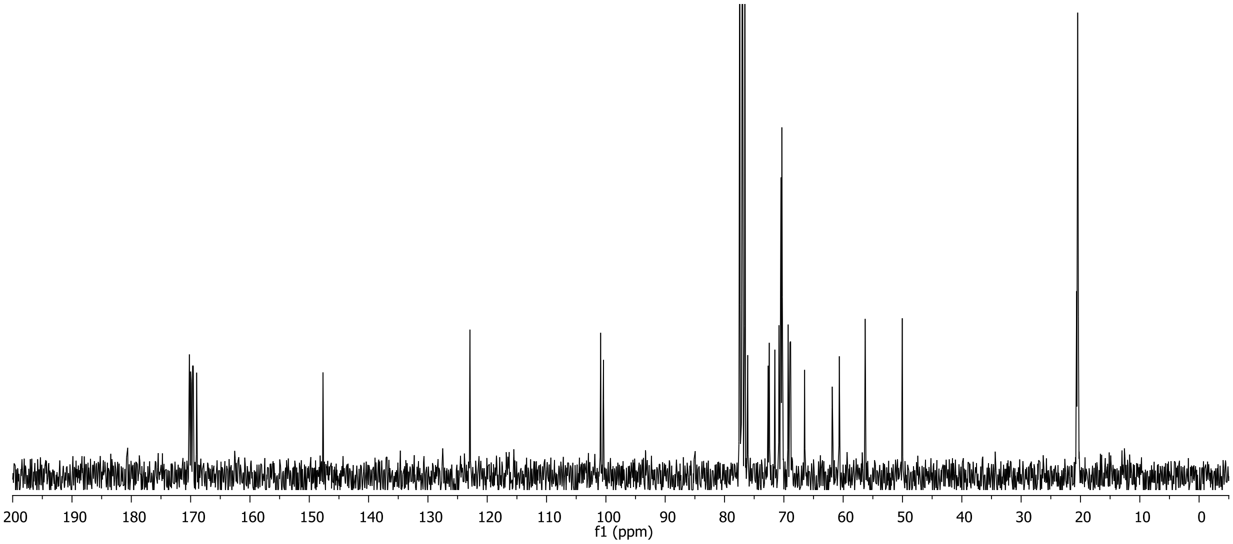
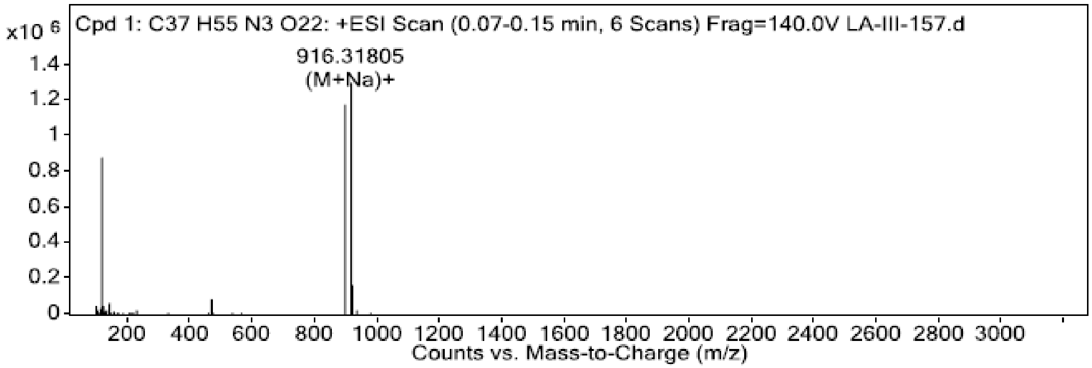
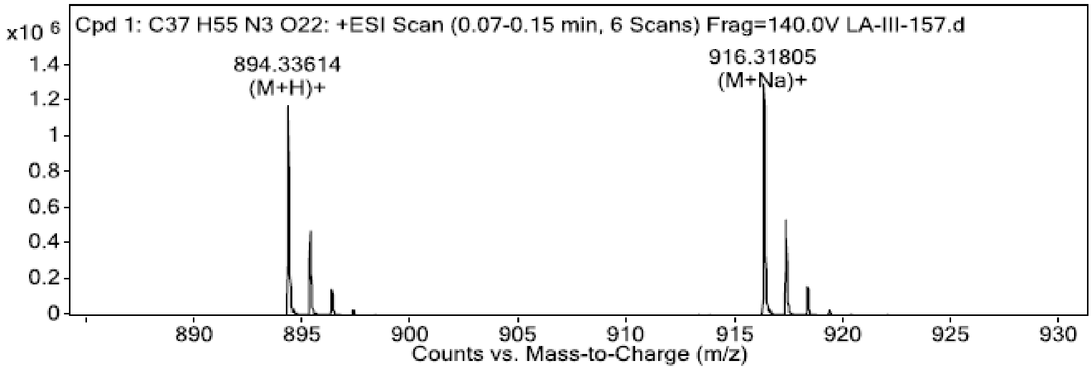


Figure S69. $^{13}C\{^{1}H\}$ NMR spectrum of compound **20a** (151 MHz, $CDCl_3$).

MS Spectrum



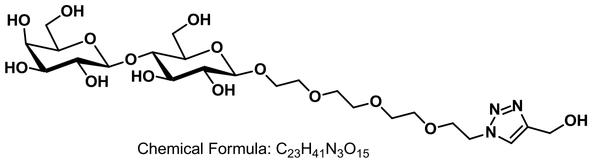
MS Zoomed Spectrum



MS Spectrum Peak List

Ion	Formula	Abund	Observed m/z	Calc m/z	Diff (ppm)
(M+H)+	C37H56N3O22	1193152.62	894.33614	894.335	1.27
(M+Na)+	C37H55N3NaO22	1308225.57	916.31805	916.31694	1.21

Figure S70. HRMS (ESI$^+$) of compound **20a**.



Chemical Formula: $C_{23}H_{41}N_3O_{15}$
Exact Mass: 599,25377
Molecular Weight: 599,58274

Synthesis of compound 20: Acetylated compound **20a** (86.0mg, 96.6μmol) was dissolved in dry MeOH (4mL) and a solution of sodium methoxide (1M in MeOH, 150 μL) was added until pH 9-10. The reaction mixture was stirred at room temperature for 24 hrs. The pH was adjusted to 6-7 with addition of ion-exchange resin (Amberlite IR 120 H^+). After filtration, the solvent was removed under *vacuum* with rotary evaporator, lyophilized to yield the fully deprotected reference **20** as a white solid (52.5mg, 87.6μmol) in a 91% yield.

^{1}H NMR (300 MHz, D_2O, δ ppm): 8.03 (s, 1H), 4.73 (s, 2H), 4.64 (t, *J* = 5.0 Hz, 2H), 4.52 (d, *J* = 7.9 Hz, 1H), 4.46 (d, *J* = 7.7 Hz, 1H), 4.08-3.53 (m, 25H), 3.36 (m, 6H).
^{13}C NMR (75 MHz, D_2O, δ ppm): 147.5, 125.1, 103.6, 102.7, 79.0, 76.0, 75.4, 75.0, 73.5, 73.2 (, 71.6, 70.3, 70.2, 70.1, 70.1, 69.4, 69.2, 61.7, 60.7, 55.3, 50.7.
HRMS (ESI$^+$) ***m/z*** for $C_{23}H_{41}N_3O_{15}$,600.2610 $[M+H]^+$; found 600.2618, 622.2430 $[M+Na]^+$; found 622.2438.

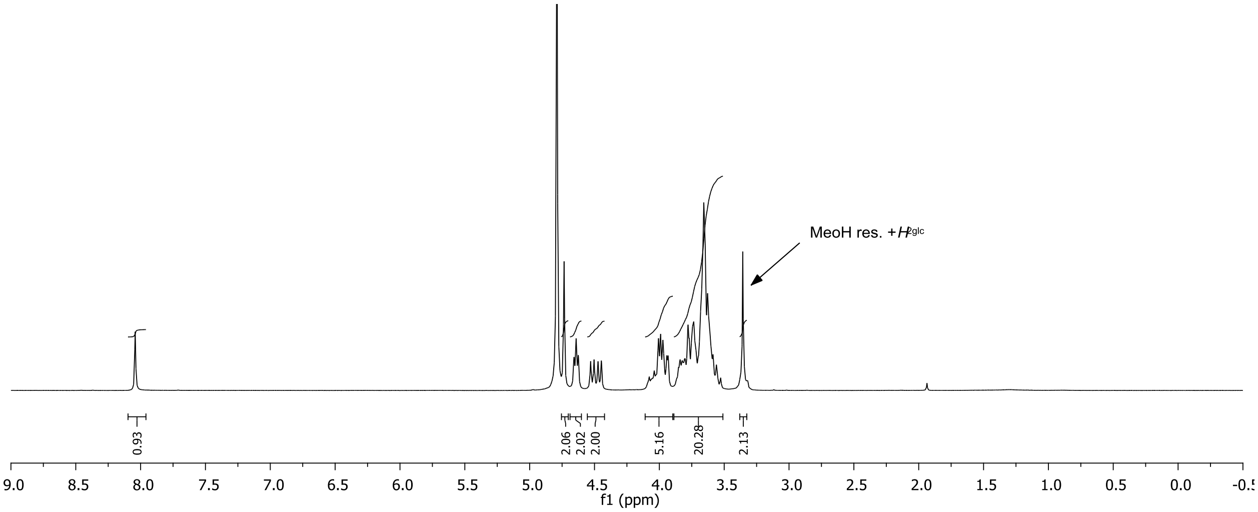


Figure S71. ^{1}H NMR spectrum of compound **20** (300 MHz, D_2O).

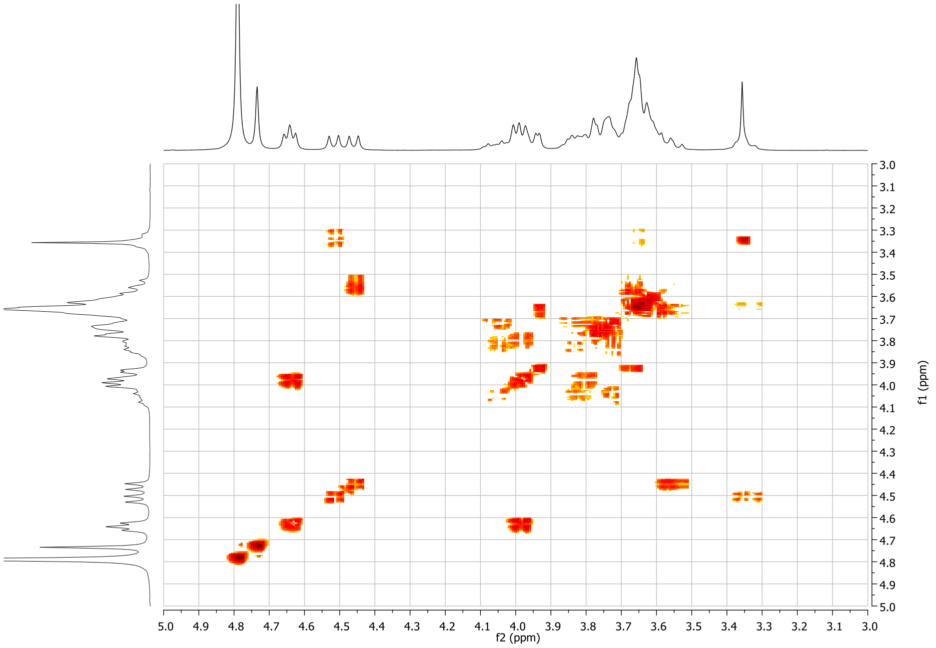


Figure S72. COSY spectrum of compound **20**.

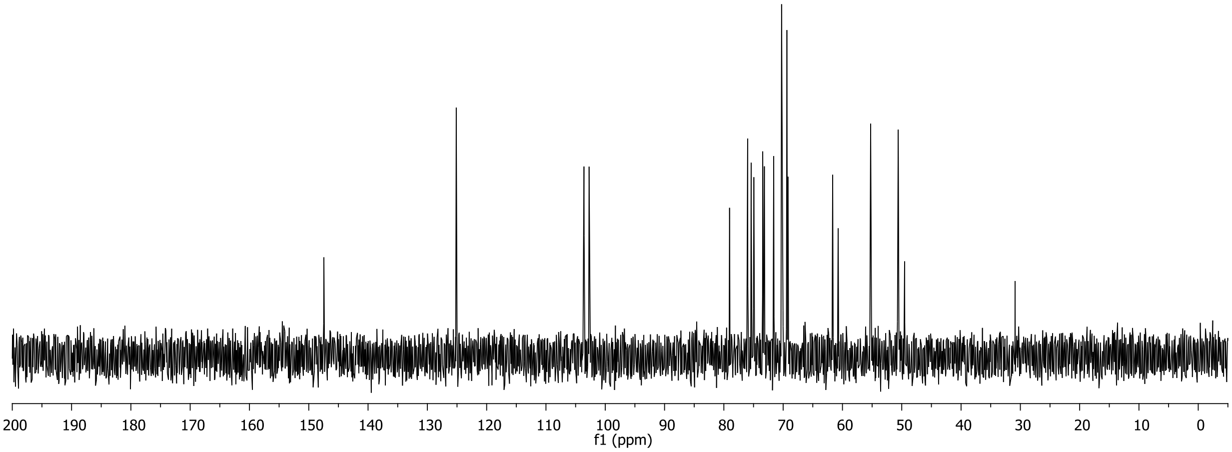
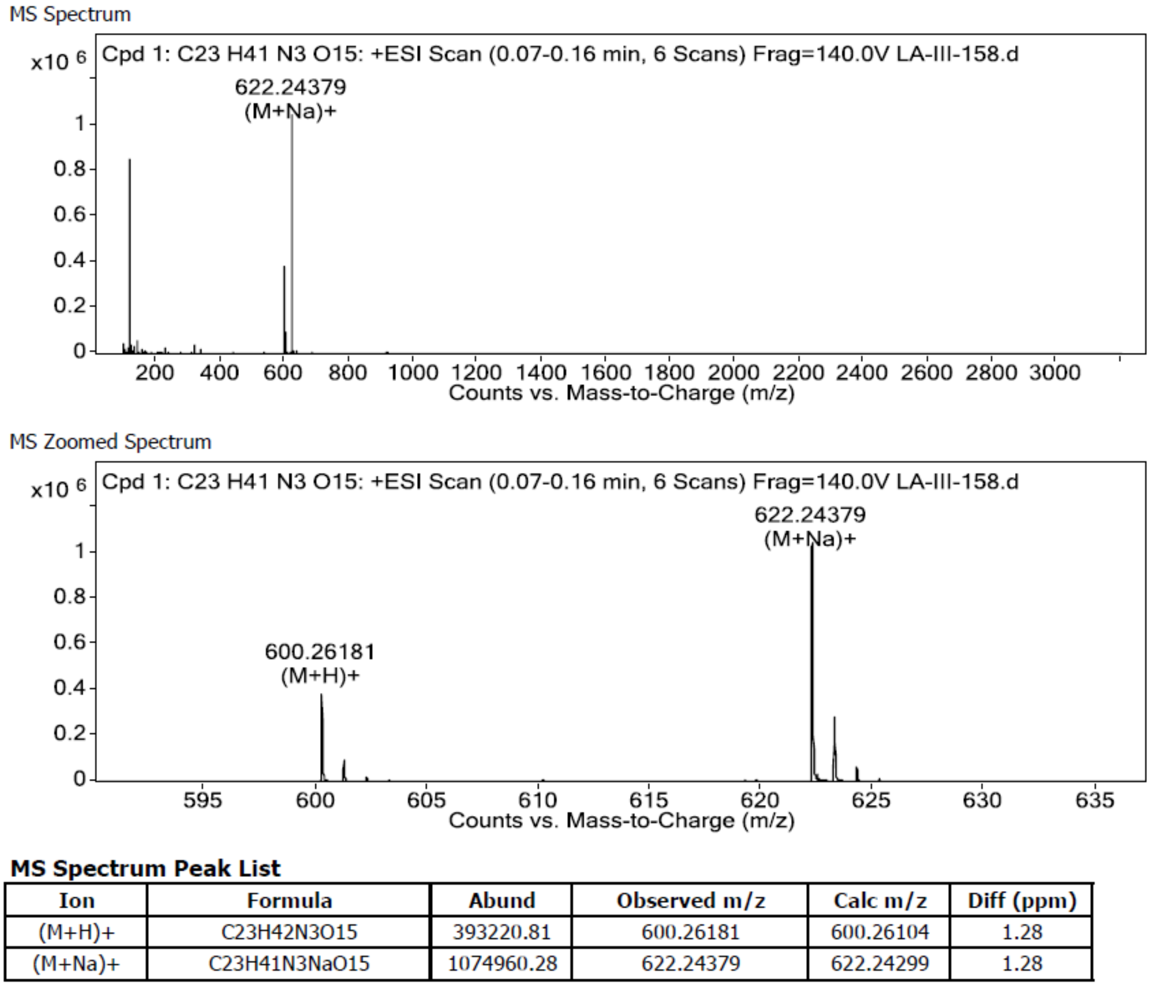


Figure S73. $^{13}C\{^{1}H\}$ NMR spectrum of compound **20** (75 MHz, $CDCl_3$).

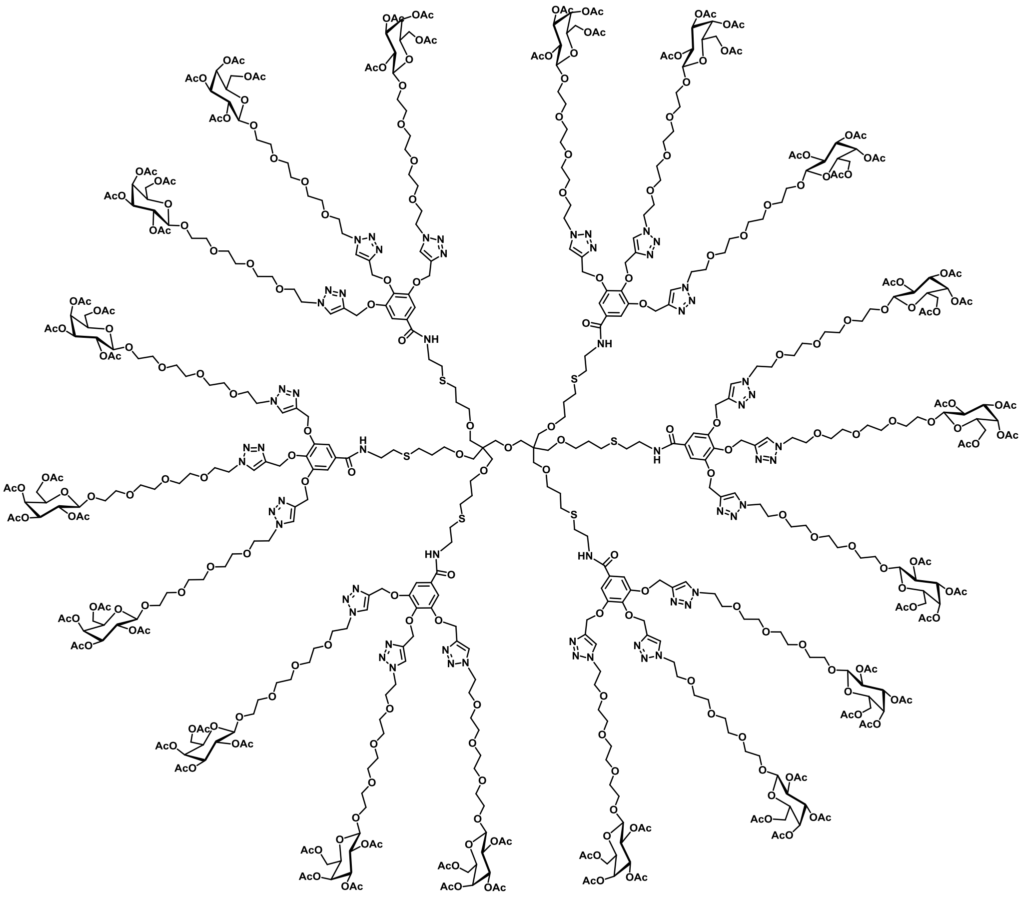

MS Spectrum

MS Zoomed Spectrum

MS Spectrum Peak List

Ion	Formula	Abund	Observed m/z	Calc m/z	Diff (ppm)
(M+H)+	C23H42N3O15	393220.81	600.26181	600.26104	1.28
(M+Na)+	C23H41N3NaO15	1074960.28	622.24379	622.24299	1.28

Figure S74. HRMS (ESI$^+$) of compound **20**.



Synthesis of compound 22: To a solution of propargylated scaffold **5** (55mg, 0.022mmol) in THF (5mL) was added galactoside **16** (354mg, 0.645mmol), followed by sodium ascorbate (68mg, 0.39mmol). An aqueous solution of $CuSO_4 \cdot 5H_2O$ (96mg, 0.39mmol) was added and the final ratio of H_2O to THF was kept 1:1. The reaction mixture was stirred at 40^{o}C for 24 hrs. The progress of the reaction was monitored with the help of TLC. Upon completion, the reaction mixture was diluted with EtOAc (25mL) and washed with saturated solution of EDTA (2×15mL). Organic layer was washed with brine solution, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the crude compound was achieved *via* flash column chromatography on silica gel using 5% MeOH in DCM as eluent to afford the desired compound **22** (208mg, 0.0167mmol)in 76% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (s,12H), 7.84 (s, 6H), 7.25-7.230 (m, 12H), 5.40–5.31 (m, 18H), 5.30–5.27 (m, 7H), 5.19–5.07 (m, 53H), 4.99 (dd, *J* = 10.5, 3.4 Hz, 19H), 4.52 (dd, *J* = 22.2, 19.3 Hz, 57H), 4.18–4.04 (m, 36H), 3.97–3.77 (m, 75H), 3.70 (ddd, *J* = 10.8, 6.9, 3.9 Hz,19H), 3.63–3.50 (m, 176H), 3.45 (br s, 18H), 3.34 (s, 18H), 2.75 (br s,1 2H), 2.63 (br s, 12H), 2.12 (d, *J* = 1.4 Hz, 52H), 2.04–1.93 (m, 164H), 1.83 (s, 12H).
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.2, 170.0, 170.0, 170.0, 169.3, 166.7, 152.0, 144.0, 143.2, 140.1, 130.1, 124.7, 124.4, 107.3, 101.2, 70.8, 70.6, 70.5, 70.5, 70.4, 70.4, 70.1, 69.7, 69.3, 69.2, 69.0, 68.8, 67.1, 66.3, 63.0, 61.2, 50.2, 39.6, 31.4, 29.7, 28.6.
IR (cm^{-1}) 2872, 1747, 1491, 1427, 1368, 1325, 1221, 1175, 1104, 1050, 732.
MALDI-TOF (DHB matrix) *m*/*z* calc. for $C_{532}H_{778}N_{60}O_{265}S_6$, 12446.5; found, 12446.0.
GPC *Mn*= 12500 g/mol. *Mw/Mn*= 1.06.

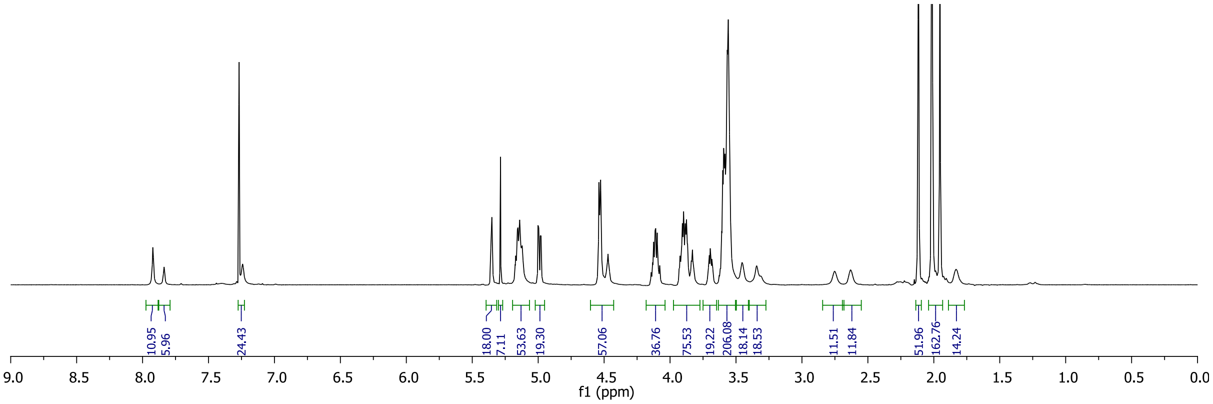


Figure S75. ^{1}H NMR spectrum of compound **22** (600 MHz, CDCl$_3$).

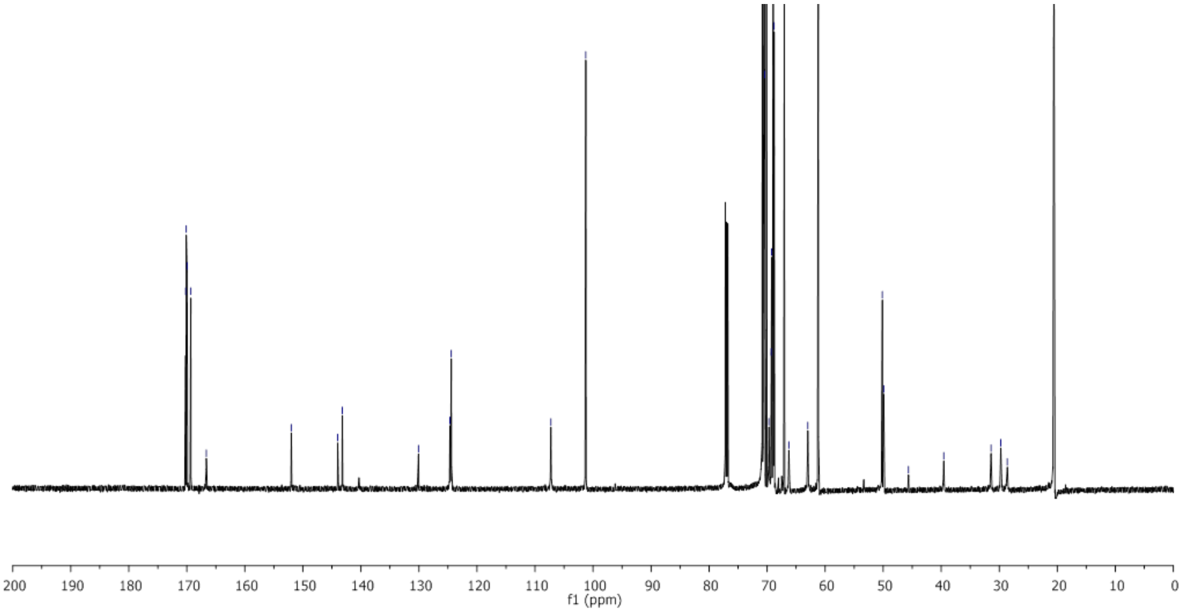


Figure S76. ^{13}C{^{1}H} NMR spectrum of compound **22** (151 MHz, CDCl$_3$).

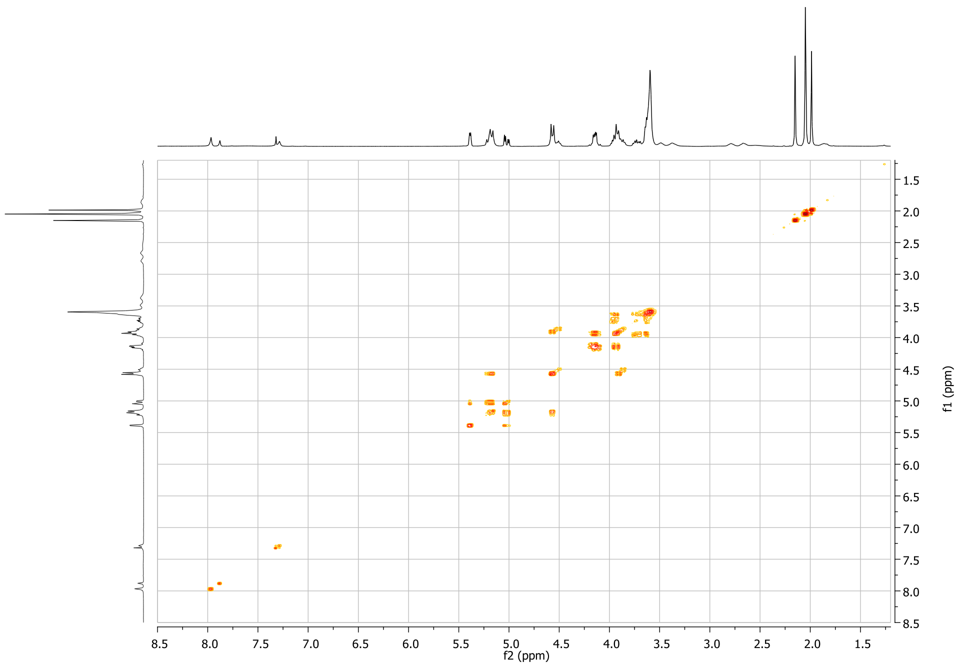
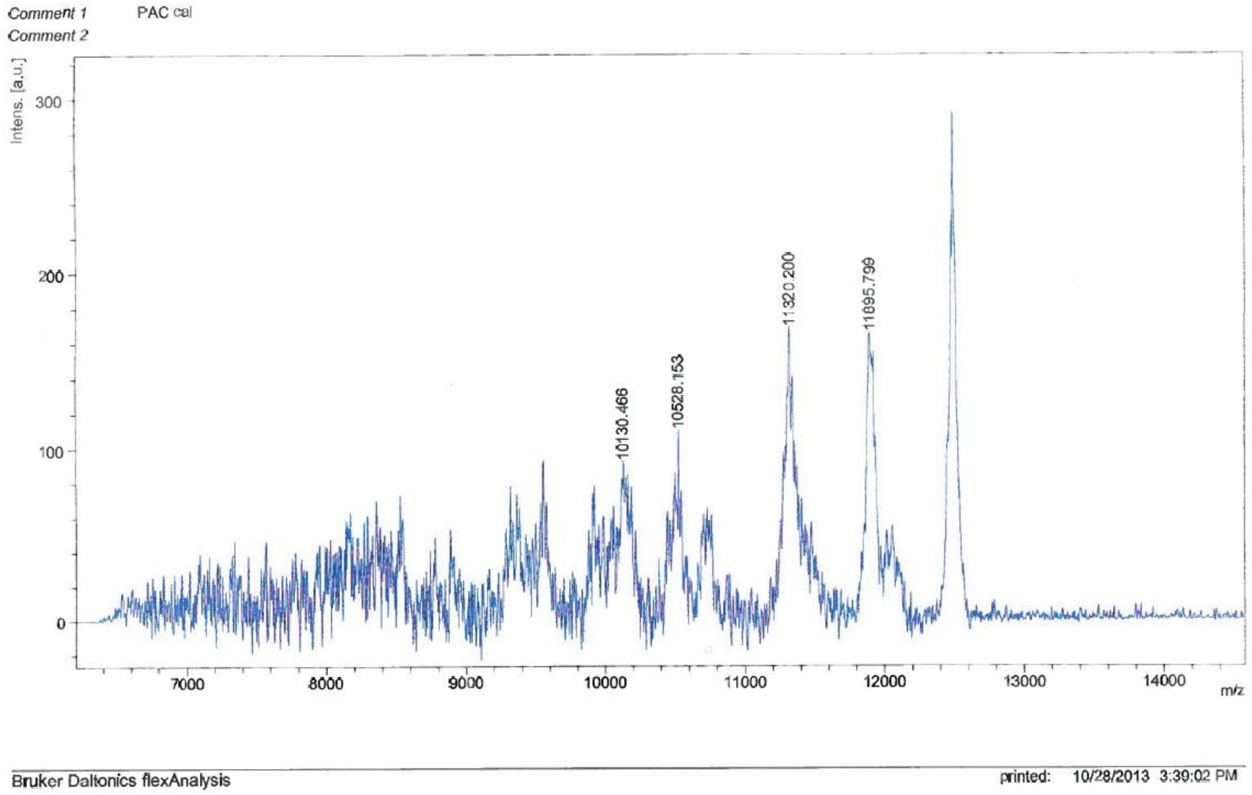


Figure S77. COSY spectrum of compound **22**.



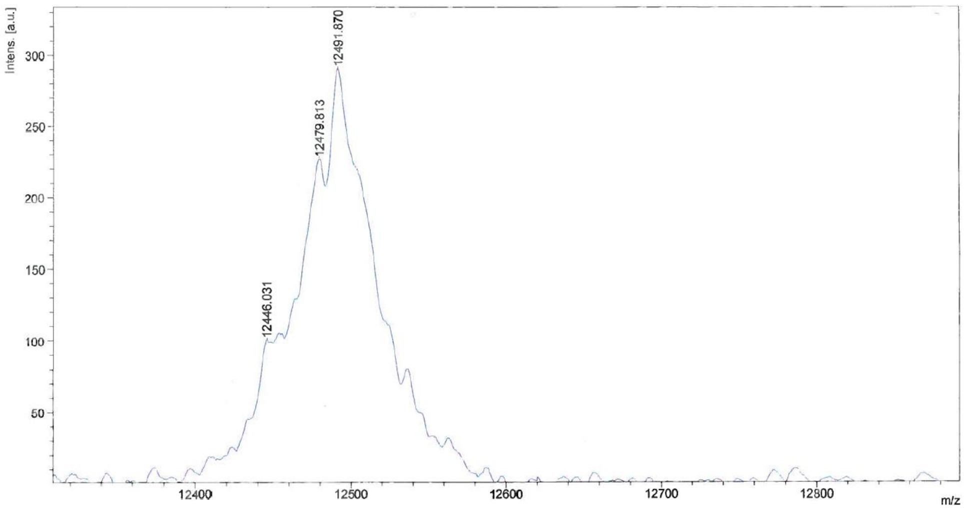


Figure S78. MALDI TOF spectrum of compound **22**.

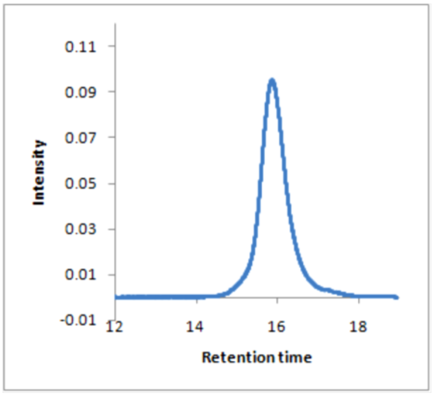


Figure S79. GPC traces of compound **22**.

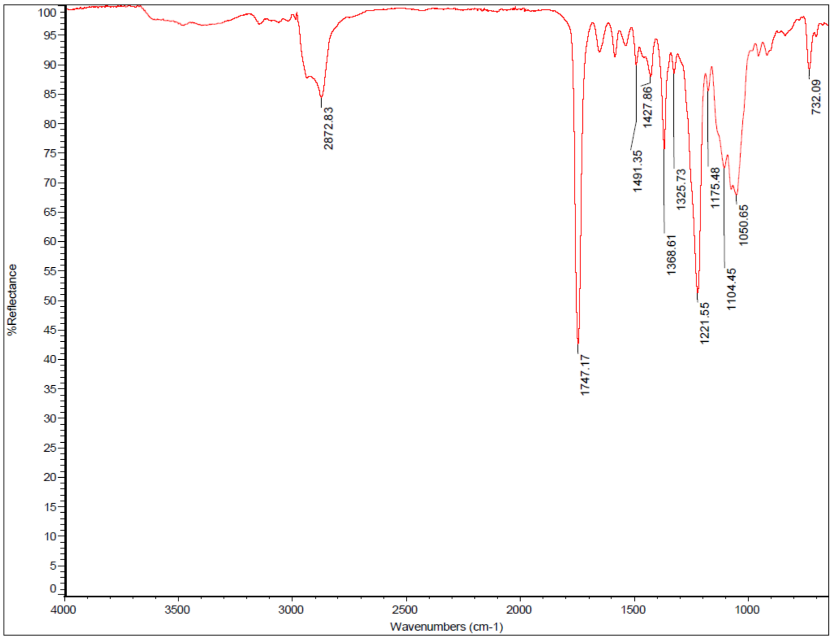
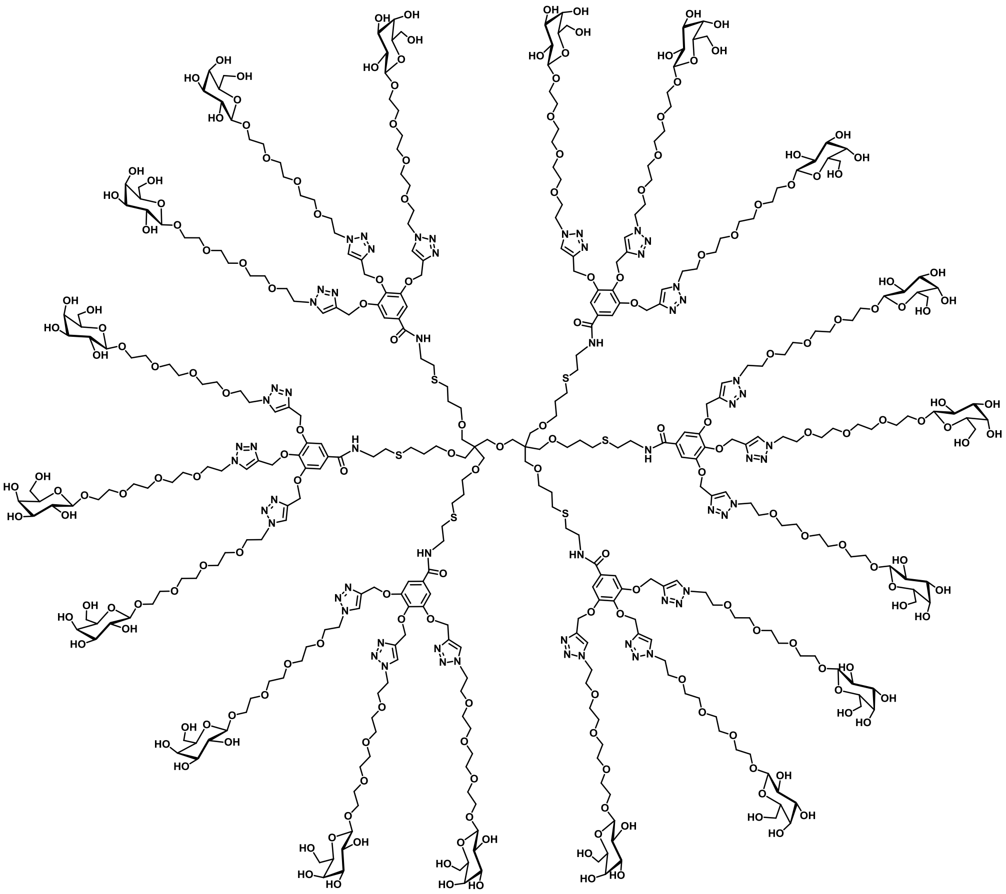


Figure S80. IR spectrum of compound **22**.



Synthesis of compound 23: To a stirring solution of compound **22** (100mg, 0.080mmol) in MeOH (3mL), was slowly added a 1M solution of MeONa/MeOH to adjust the pH to 9-10. The reaction mixture was left stirring overnight. The reaction pH was then adjusted to 6 with H^+ resin. Solvent was evaporated and the residue was dissolved in 3 mL of water and washed with diethyl ether (3x15ml) to remove impurities. Aqueous layer was finally lyophilized to yield **23** (68mg, 0.072mmol) as a white solid in 90% yield.

^{1}H NMR (600 MHz, D_2O) δ 8.40–7.80 (m, 18H), 7.28 (br s, 12H), 5.30-5.00 (m ,30H), 4.62–4.49 (m ,36H), 4.38 (d, *J* = 8.0 Hz, 15H), 4.02 (d, *J* = 11.4 Hz, 18H), 3.93 (d, *J* = 13.8 Hz, 39H), 3.88–3.82 (m, 12H), 3.80-3.71 (m , 54H), 3.69–3.61 (m, 75H), 3.62–3.49 (m, 165 H), 3.45–3.38 (m, 16H), 3.37–3.35 (m, 100H), 3.28–3.22 (m, 9H), 2.86–2.70 (m, 12H), 2.68–2.49 (m, 12H), 1.85–1.65 (m, 12H).
^{13}C{^{1}H} NMR (151 MHz, D_2O) δ 168.8, 152.7, 140.1, 130.7, 107.8, 103.9, 76.1, 73.7, 73.0, 71.7, 70.7, 70.6, 70.5, 70.5, 69.7, 69.6, 69.5, 63.5, 61.9, 61.4, 51.2, 40.5, 31.7, 29.9, 29.1 *(C and CH of triazole rings not visible)*.
IR (cm^{-1}) 3377, 2917, 1653, 1586, 1495, 1239, 1104.
MS (ESI$^+$) *m*/*z* calc for $C_{388}H_{634}N_{60}O_{193}S_6$, 9420.9 [*M*+H]$^+$; found (deconvoluted), 9414.0.

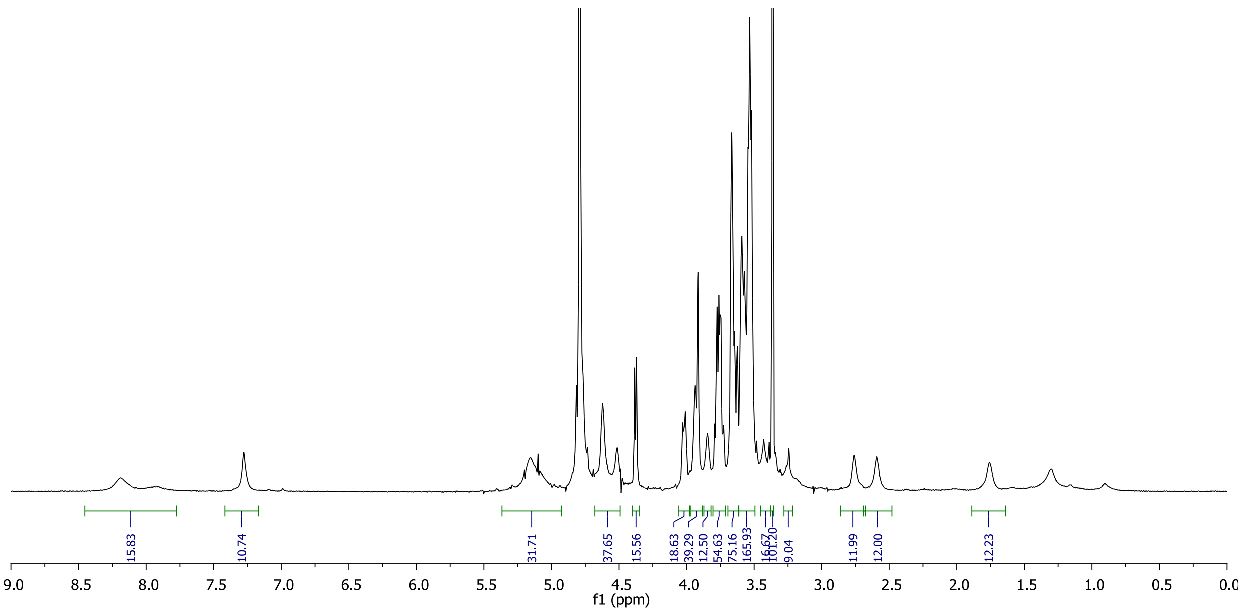


Figure S81. ^{1}H NMR spectrum of compound **23** (600 MHz, D_2O).

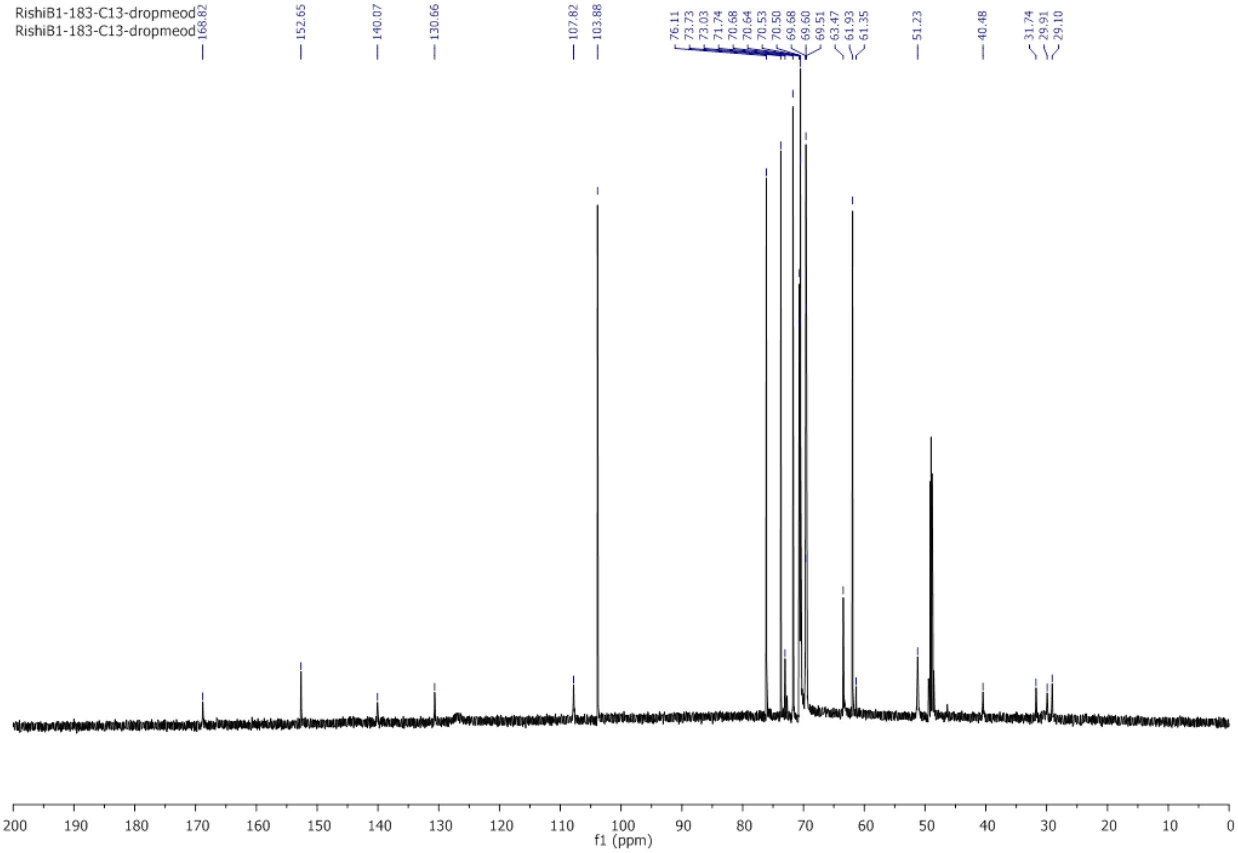


Figure S82. ^{13}C{^{1}H} NMR spectrum of compound **23** (151 MHz, D_2O).

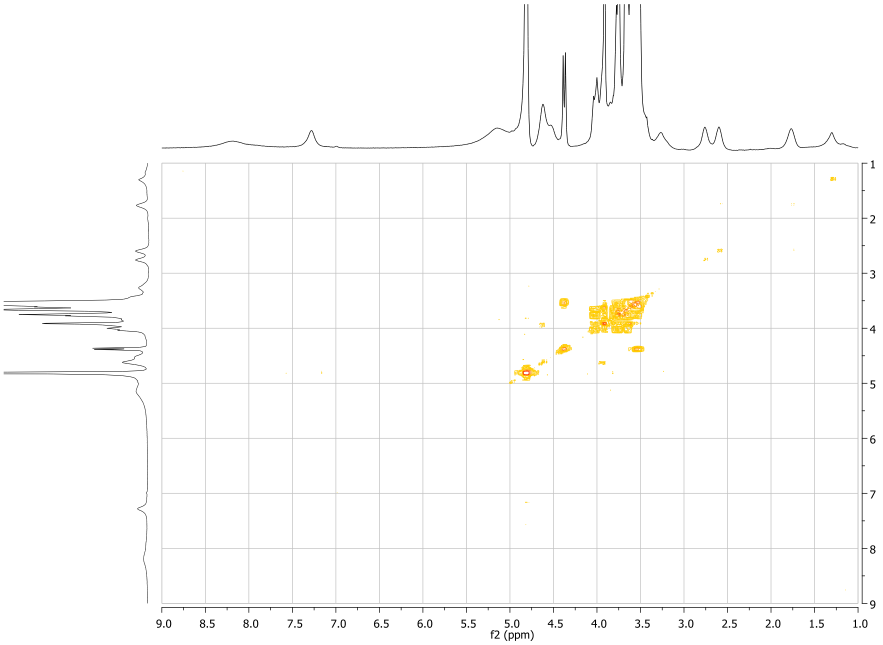
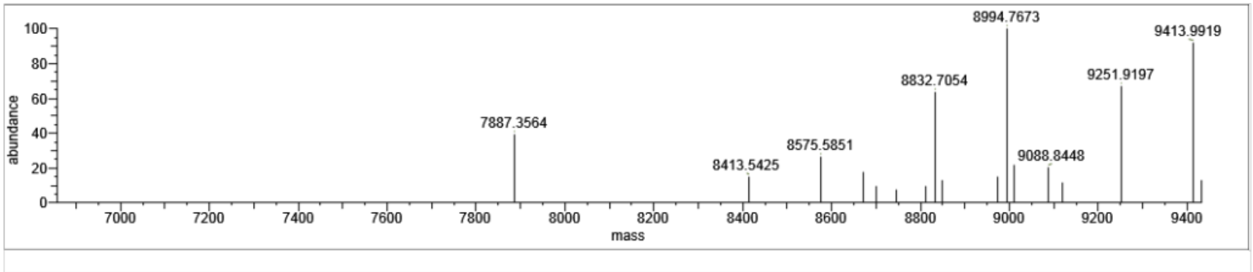
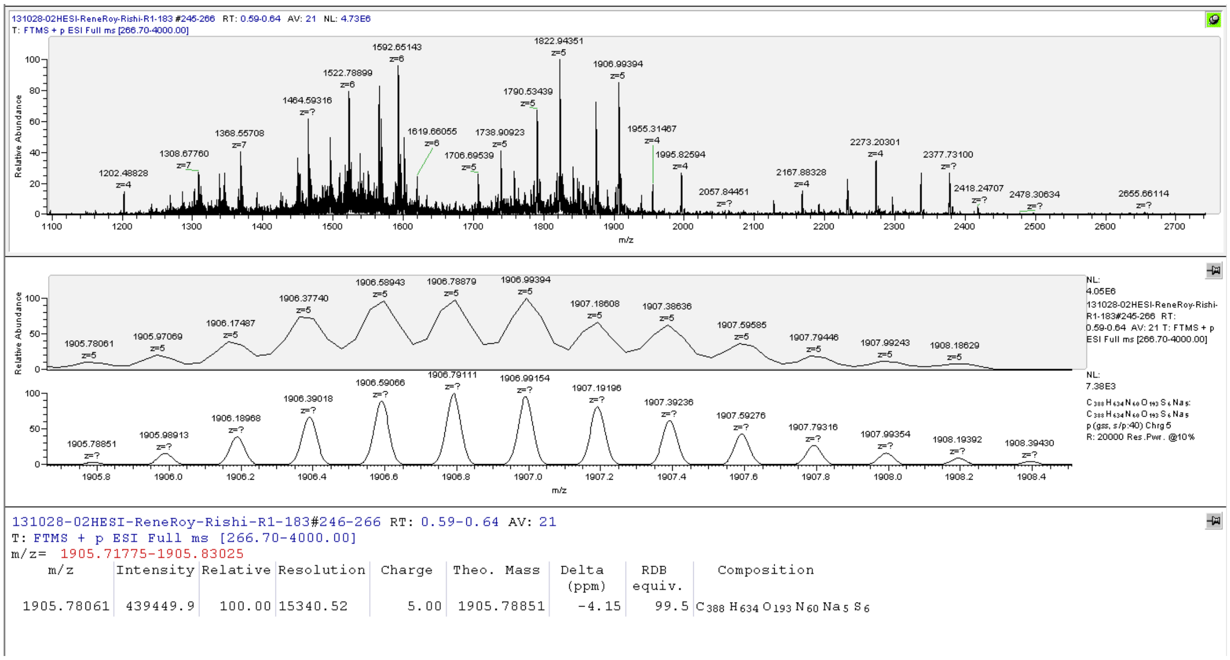


Figure S83. COSY spectrum of compound **23**.





```
131028-02HESI-ReneRoy-Rishi-R1-183#246-266 RT: 0.59-0.64 AV: 21
T: FTMS + p ESI Full ms [266.70-4000.00]
m/z= 1905.71775-1905.83025
     m/z     Intensity Relative Resolution  Charge  Theo. Mass   Delta     RDB     Composition
                                                                 (ppm)    equiv.

 1905.78061  439449.9    100.00 15340.52      5.00  1905.78851   -4.15     99.5 C388 H634 O193 N60 Na5 S6
```

Results

No.	Monoisotopic Mass	Sum Intensity	Number of Charge States	Average Charge	Delta Mass	Relative Abundance
1	8994.7673	12,682,989.07	4	5.31	0.00	100.0000
2	9413.9919	11,664,948.25	3	5.71	419.22	91.9732
3	9251.9197	8,508,868.28	3	5.62	257.15	67.0888
4	8832.7054	8,098,504.60	4	5.28	-162.06	63.8533
5	7887.3564	4,977,314.38	3	4.93	-1,107.41	39.2440

Figure S84. HRMS (ESI$^+$) spectrum of compound **23**.

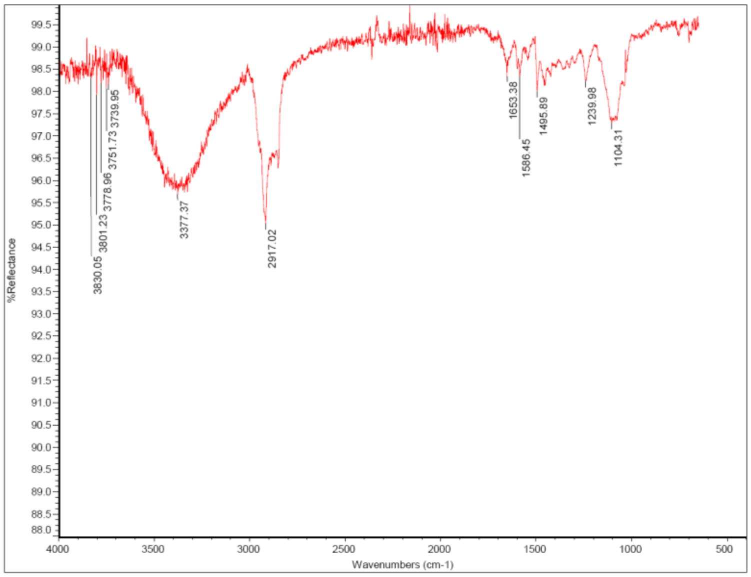
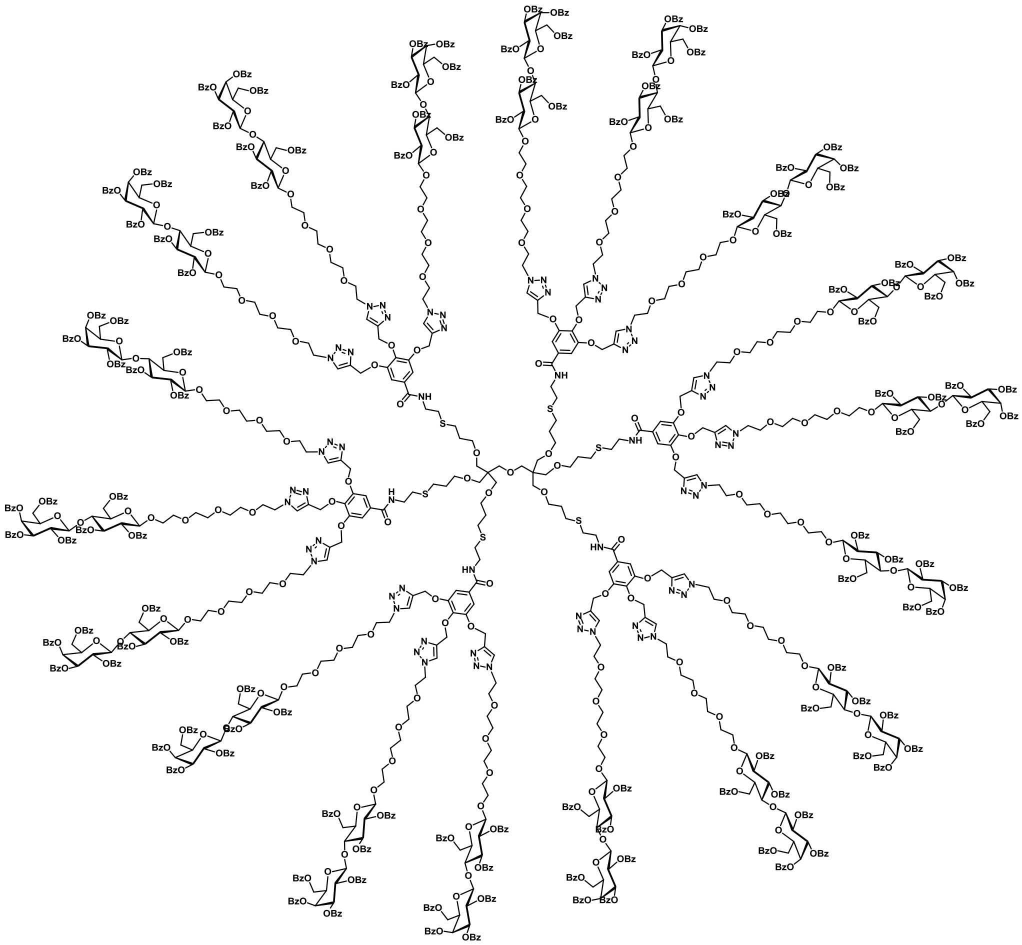


Figure S85. IR spectrum of compound **23**.



Synthesis of compound 24: To a solution of propargylated scaffold **5** (20mg, 7.8μmol) in THF (5mL) was added PEGylated lactoside **17** (302mg, 0.234mmol), followed by sodium ascorbate (28mg, 0.14mmol). An aqueous solution of $CuSO_4 \cdot 5H_2O$ (35mg, 0.14mmol) was added and the final ratio of H_2O to THF was kept 1:1. The reaction mixture was stirred at 40^{o}C for 24 hrs. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was diluted with EtOAc (25mL) and washed with sat. solution of EDTA (2×15mL). Organic layer was washed with brine solution, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue was achieved *via* flash coloumn chromatography on silica gel using 5% MeOH in DCM as eluent to afford desired compound **24** (153mg, 6.0μmol) as an off-white viscous solid in 77% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06–7.14 (m, 666H), 5.83–5.67 (m, 54H), 5.49–5.34 (m, 36H), 5.11 (s, 32H), 4.88 (d, *J* = 7.9 Hz, 18H), 4.80 (d, *J* = 7.8 Hz, 18H), 4.65–4.55 (m, 18H), 4.53–4.38 (m, 54H), 4.26 (t, *J* = 9.4 Hz, 18H), 3.95–3.20 (m, 368H), 2.85–2.50 (m, 24H), 1.82 (br s, 12H).
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ *166.7*, 165.8, 165.5, 165.4, 165.2, 165.1, 164.8, *152.0*, *144.6*, *140.0*, 133.5, *130.2*, 133.4, 133.3, 129.7, 129.6, 129.5, 129.3, 128.6, 128.6, 128.5, 128.4, 128.2, *107.9*, 101.2, 101.0, 76.0, *75.7*, 70.5, 69.9, *69.6*, 67.5, 62.4, 61.0, *60.3*, *57.3*, *45.6*, *39.2*, *31.6*, *29.8*, *28.4* (Signals corresponding to *C*ONH, C_{ar}H, CH_2 and C_q (*in italic*) located in inner positions are not visible in this case, even after 30000 scans).

IR (cm^{-1}): 2879, 1730, 1601, 1584, 1451, 1369, 1315, 1269, 1250, 1175, 1069, 1026, and 708. **MALDI-TOF** *m*/*z* calc. for $C_{1378}H_{1318}N_{60}O_{409}S_6$, 25478.7 [M+Na]$^+$; found, 25602.3.

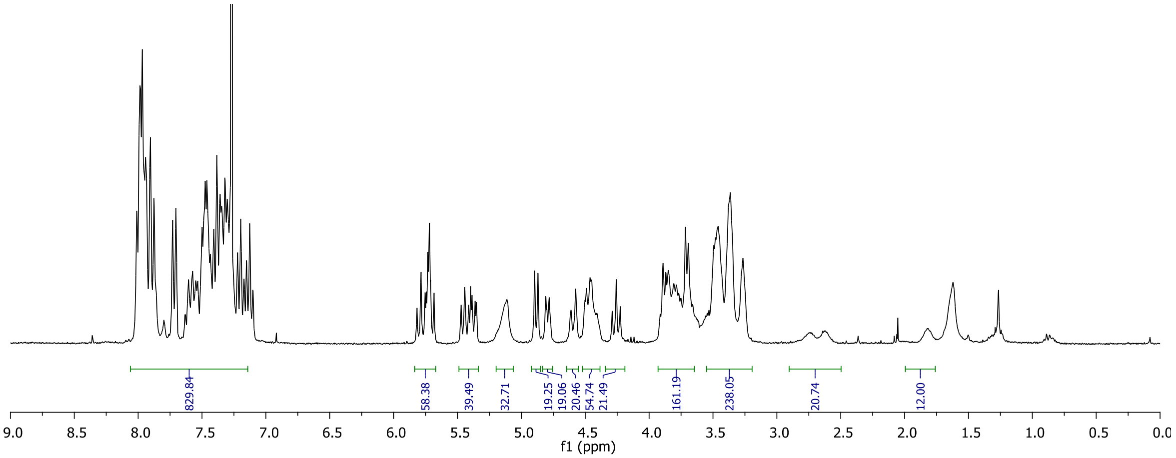


Figure S86. ^{1}H NMR spectrum of compound **24** (300 MHz, CDCl$_3$).

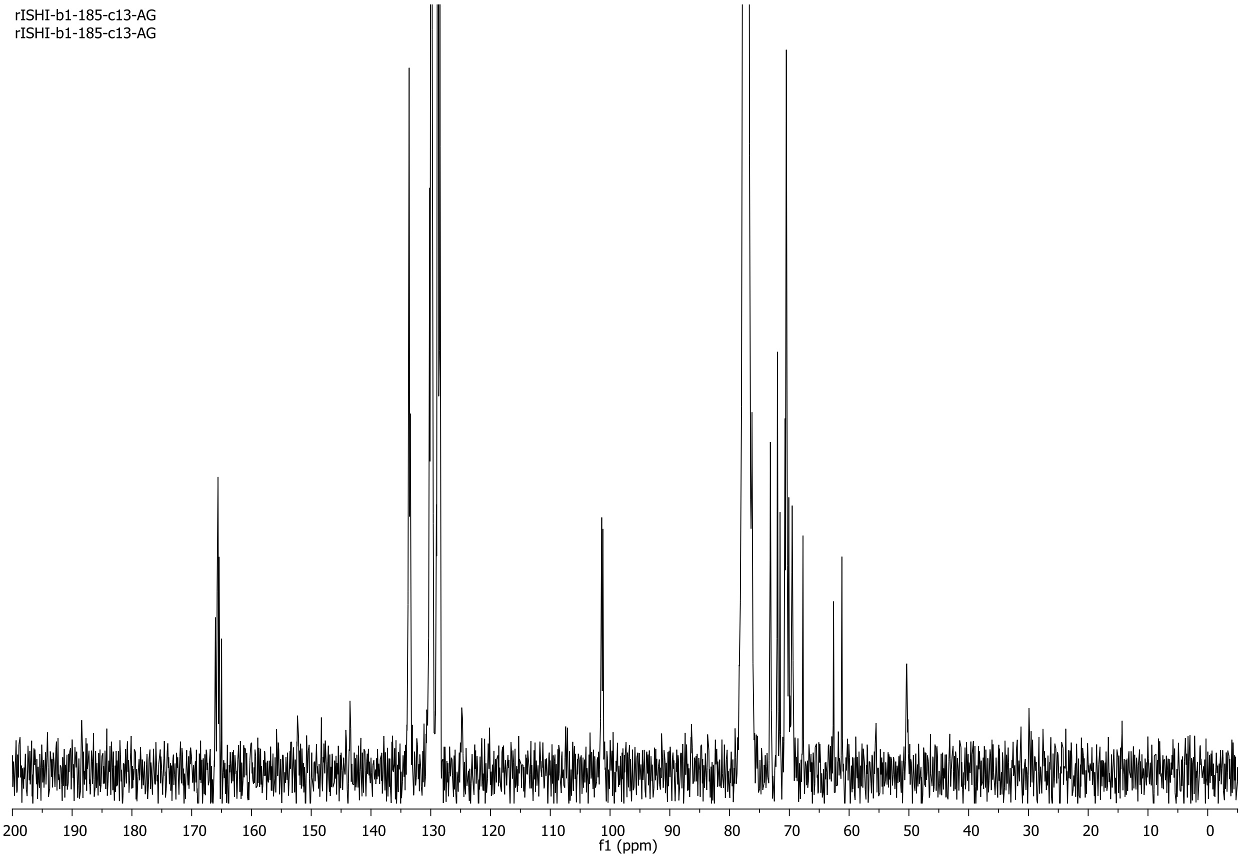


Figure S87. $^{13}C\{^1H\}$ NMR spectrum of compound **24** (151 MHz, CDCl$_3$).

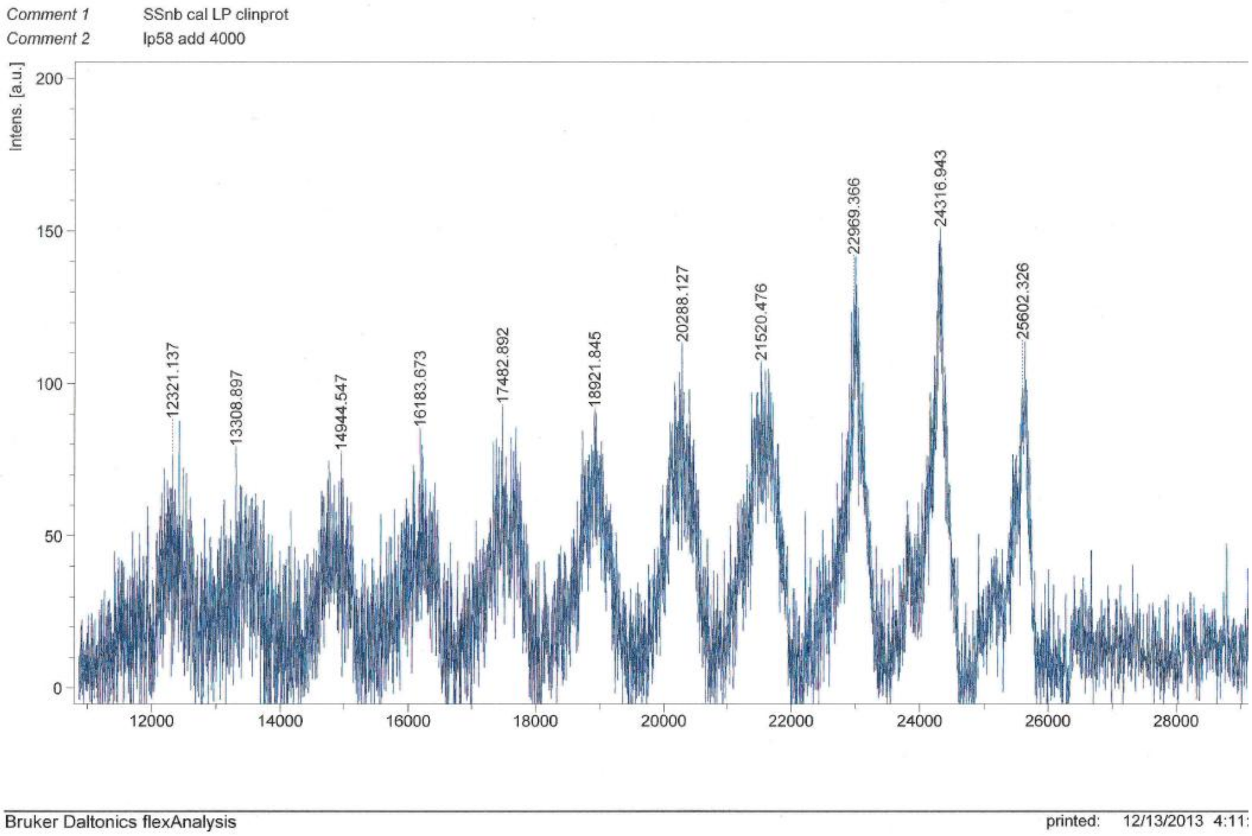


Figure S88. MALDI TOF spectrum of compound **24**.

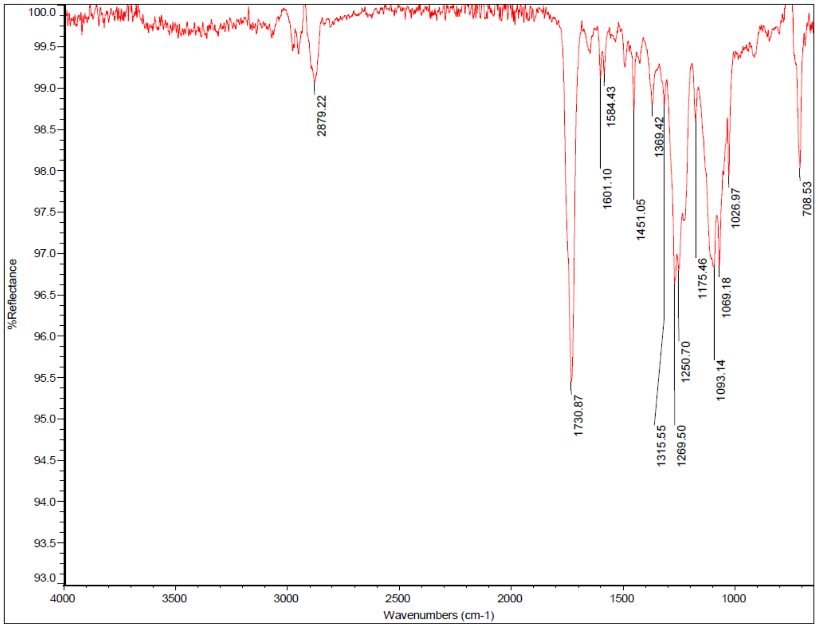
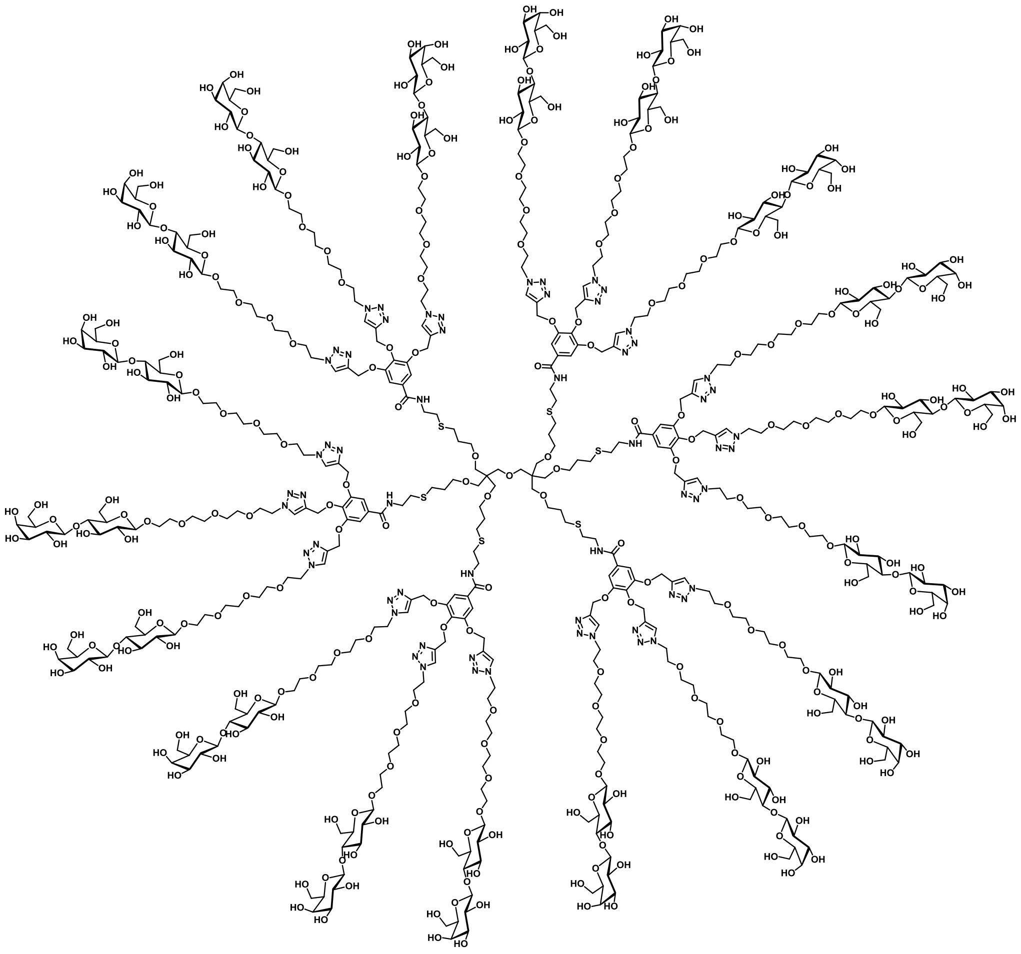


Figure S89. IR spectrum of compound **24**.



Synthesis of compound 25: To a stirring solution of compound **24** (100mg, 3.93μmol) in MeOH (3mL), was slowly added a 1M solution of MeONa/MeOH to adjust the pH to 9-10. The reaction mixture was left stirring overnight. The reaction pH was adjusted to 6 with H^+ resin and the solvent was evaporated. The residue was dissolved in 3mL of water and washed with diethyl ether (3×15ml) to remove the impurities. Aqueous layer was lyophilized to afford **25** (41mg, 3.3μmol) as a white solid in a 85% yield.

^{1}H NMR (600 MHz, D_2O) δ 8.16–7.70 (m, 18H), 7.25–71 (m, 12H), 5.15–4.83 (m, 18H), 4.56–4.20 (m, 36H), 4.37–4.20 (m, 67H), 3.86–3.06 (m, 627H), 2.67–2.47 (br s,12H), 2.45–2.30 (br s, 12H), 1.75–1.45 (br s, 12H).
^{13}C{^{1}H} NMR (151 MHz, D_2O) δ: 168.5, 152.3, 150.4, 139.7, 130.3, 126.4, 107.4, 103.6, 102.8, 79.1, 75.9, 75.3, 74.9, 73.4, 73.1, 72.6, 71.5, 70.2, 70.1, 70.1, 69.2, 69.1, 63.0, 61.6, 60.7, 51.0, 45.9, 40.0, 31.3, 29.4, 28.6.
IR (cm^{-1}): 3695, 3384, 2937, 2843, 1646, 1429, 1347, 1055, and 1032.
MALDI-TOF *m*/*z* calc for $C_{496}H_{814}N_{60}O_{283}S_6$, 12361.4 [*M*+Na]$^+$; found, 12368.4, 12401.9 (Cu adduct); found 12403.5.

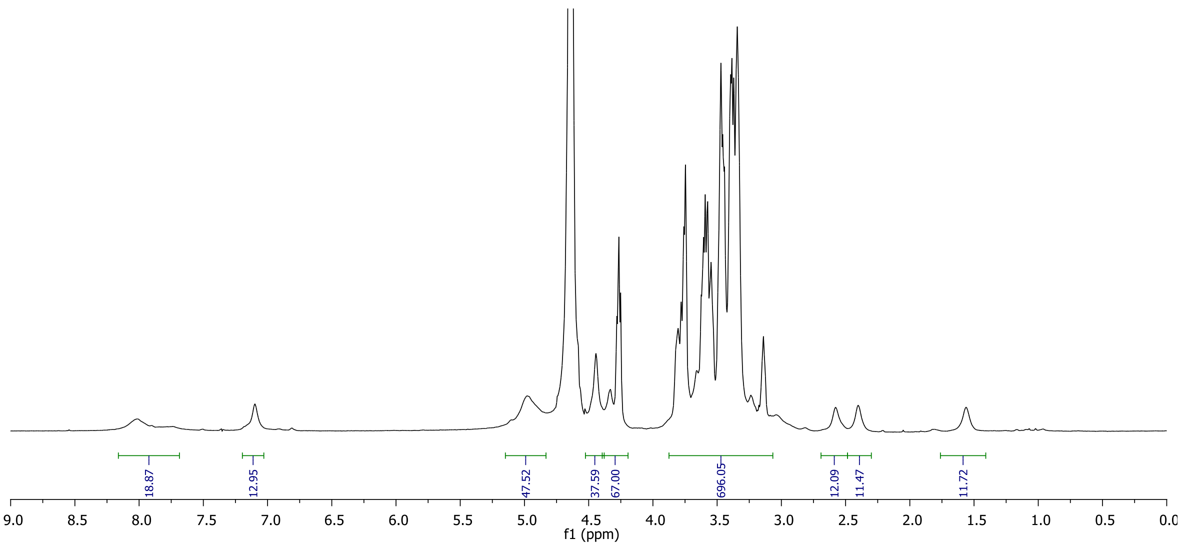


Figure S90. ^{1}H NMR spectrum of compound **25** (600 MHz, D_2O).

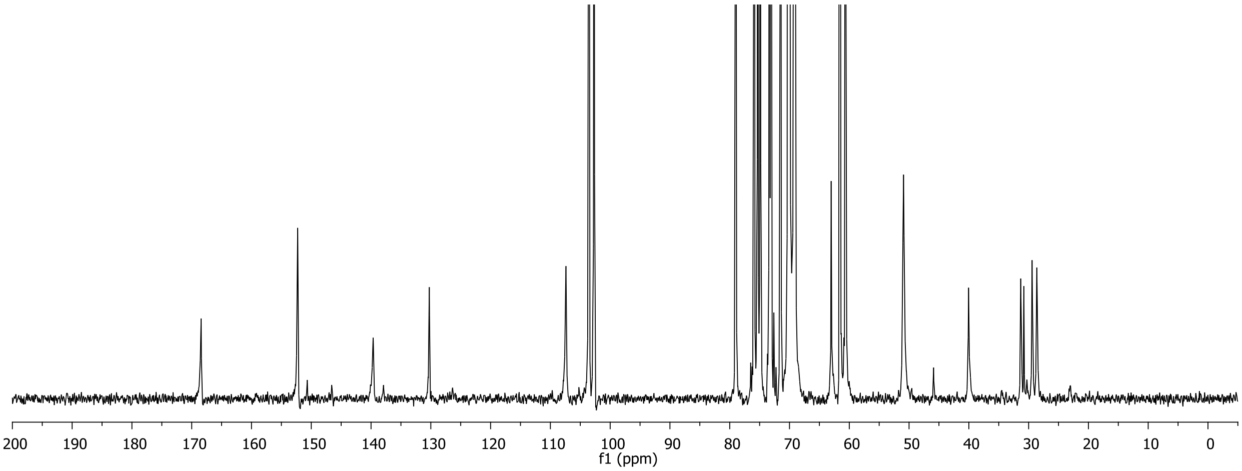


Figure S91. ^{13}C{^{1}H} NMR spectrum of compound **25** (151 MHz, D_2O).

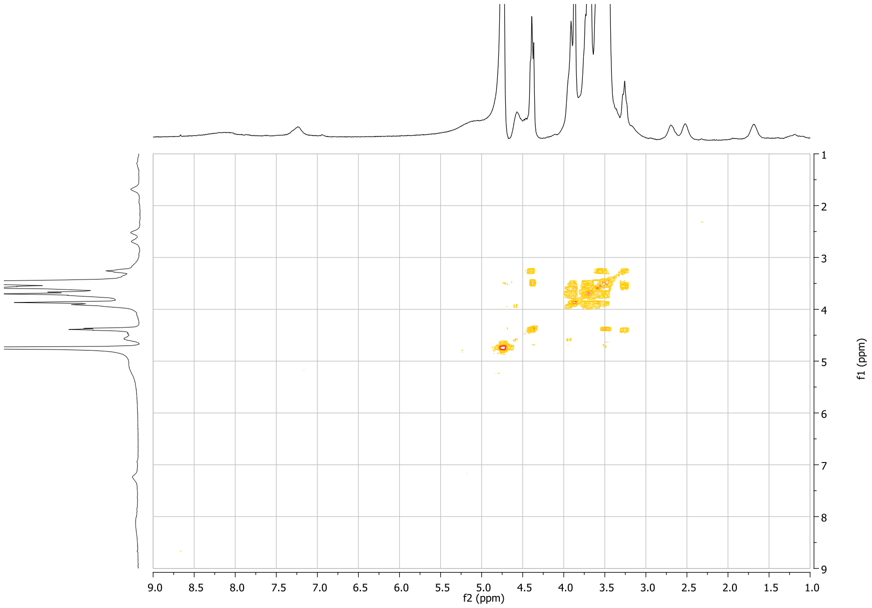
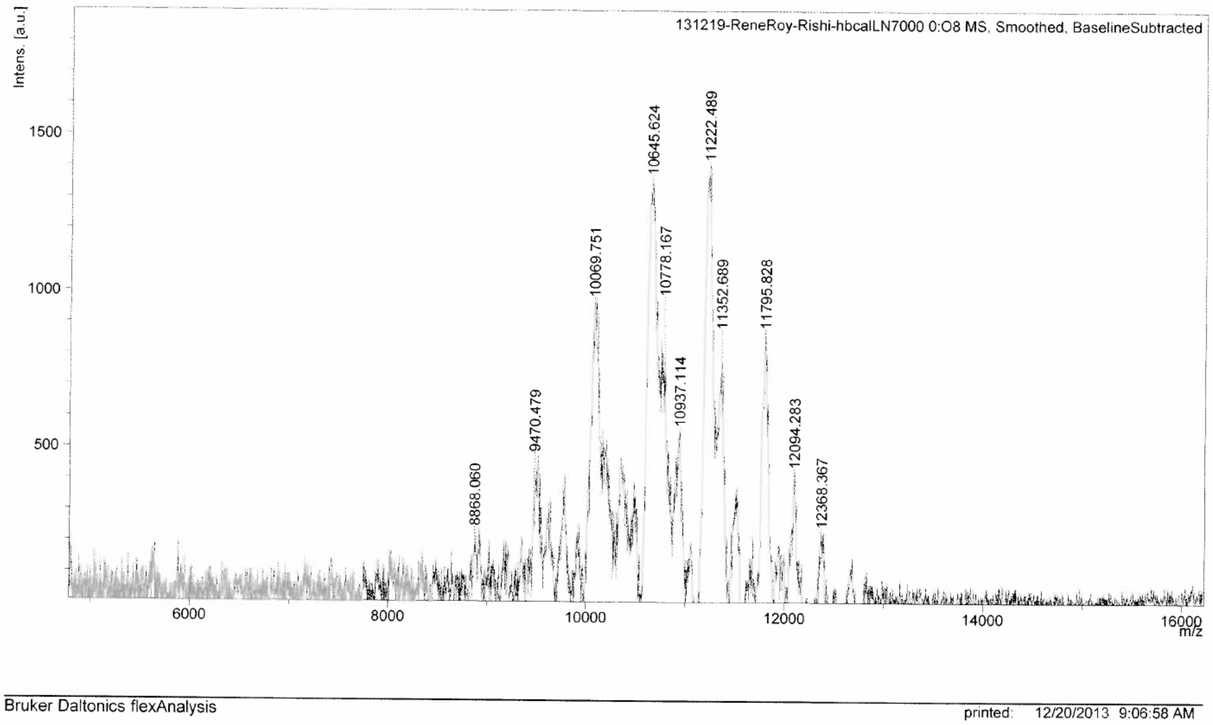
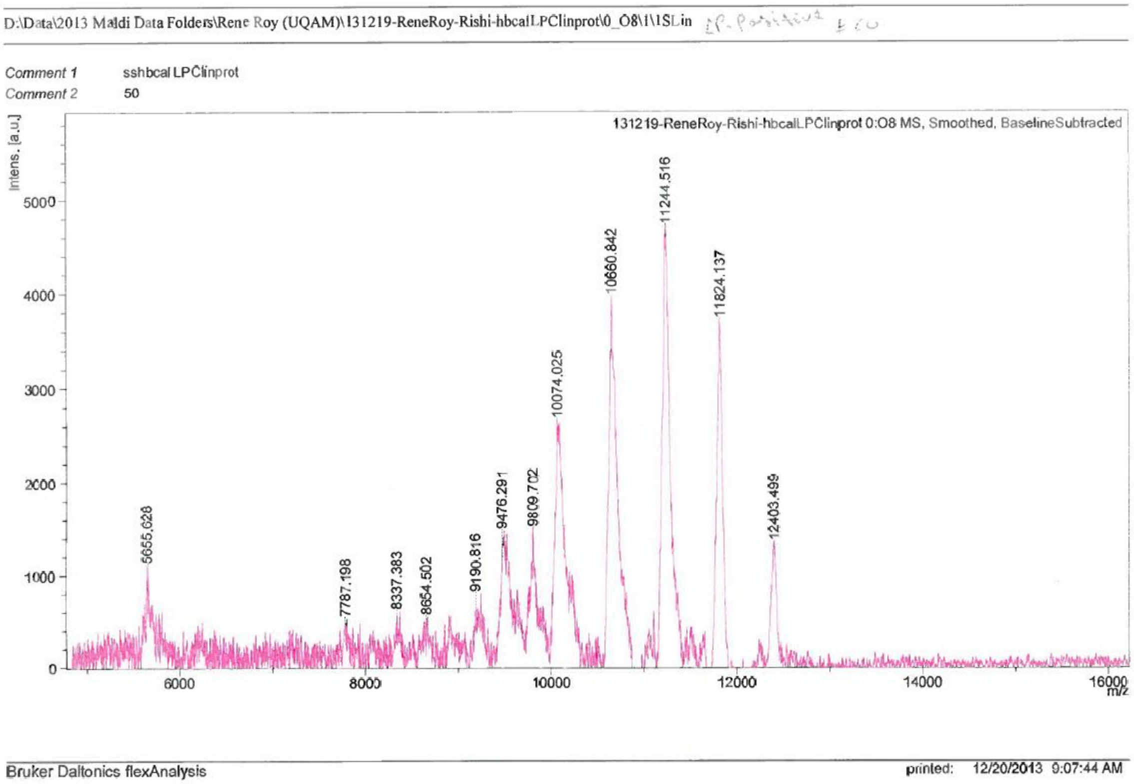


Figure S92. COSY spectrum of compound **25.**





D:\Data\2013 Maldi Data Folders\Rene Roy (UQAM)\131219-ReneRoy-Rishi-hbcalLPClinprot\0_O8\1\1SLin LP-Positive + Cu

Comment 1 sshbcal LPClinprot
Comment 2 50

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Figure S93. Top: MALDI TOF spectrum of compound **25**, bottom: MALDI-TOF spectrum of compound **25** (Positive mode with Cu)

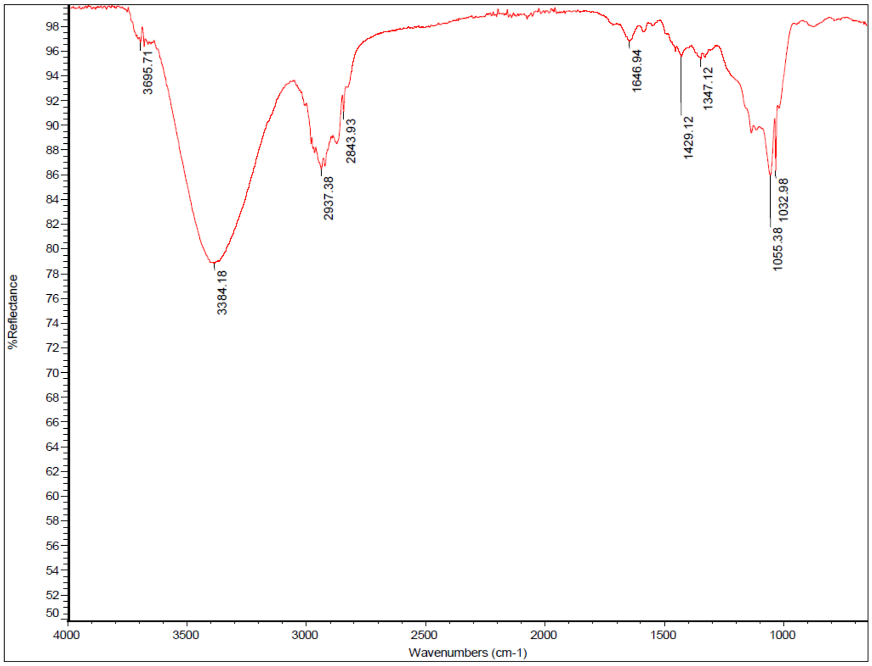
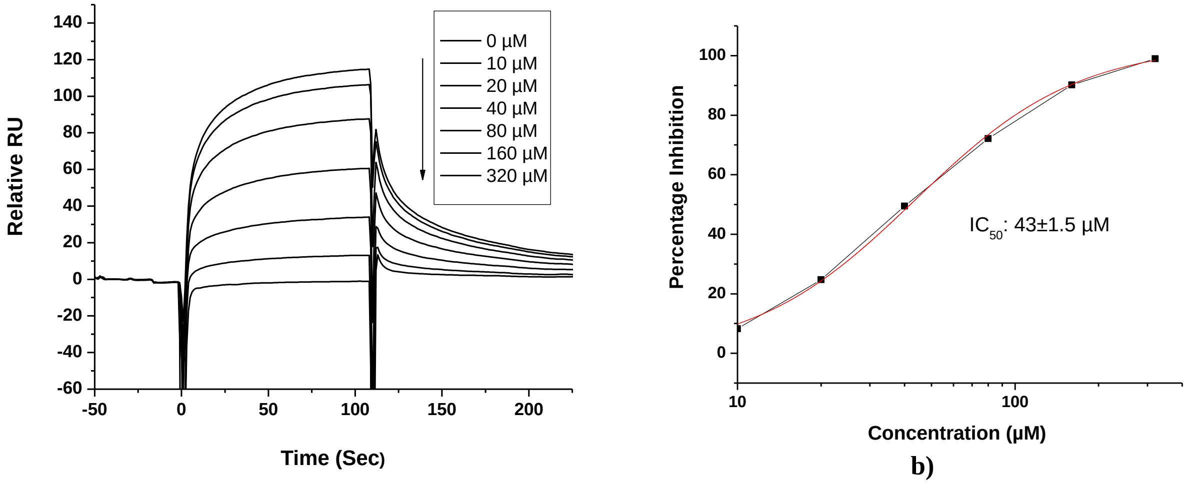


Figure S94. IR spectrum of compound **25**.

4. Surface plasmon resonance (SPR) studies:

The studies were conducted using a Biacore T200 SPR instrument with a CM5 sensor chip. A continuous flow of HEPES buffer (10 mm HEPES and 150 mm NaCl, 2 mM $CaCl_2$, pH 7.4) was maintained over the sensor surface at a flow rate of 10 µl/min. The CM5 sensor chip was activated with an injection of a solution containing *N*-ethyl-*N*′-(3-diethylaminopropyl) carbodiimide (EDC) (0.2M) and *N*-hydroxysuccinimide (NHS) (0.05M) for 7 minutes. Lactoside **21** (200 µg/mL) and Et_3N (1 mM) in NaOAc buffer (pH 4.5) was injected over the activated flow cell at flow rate of 10 µl/min for 2 minute to achieve a ~230 RU immobilization. The immobilization procedure was completed by an injection of ethanolamine hydrochloride (1M) (70 µL), followed by a flow of the buffer (100 µL/min.), in order to eliminate physically adsorbed compounds. Ethanol amine alone was used in one of the flow-cell as a reference. The solutions of pre-incubated (1 hr) mixtures of glycodendrimers or monomers (with the various concentrations) and a PA-IL lectin (1.5 µM) in running HEPES buffer are passed over flow cells of the galactoside and ethanol amine (Association: 3 min and dissociation: 3 min). The sensor chip was regenerated with the serial injections of D-lactose (0.25 M, 3 min), buffer (3 min), D-lactose (0.25 M, 3 min) and buffer (3 min). For each inhibition assay, PA-IL lectin (1.5 µM) without inhibitor was injected to observe the full adhesion of the lectin onto the sugar-coated surface (0% inhibition). Response units from the surface of lactoside were subtracted from the surface of ethanol amine to eliminate non-specific interactions, as well as, bulk change in RU due to variation in refractive index of the medium. The primary subtracted sensorgrams were analyzed by 1:1 Langmuir model fitting, using the BIAevaluation software. For IC_{50} evaluation, the response units at the equilibrium was considered as the amount of lectin bound to the sugar surface in the presence of a defined concentration of inhibitor. Inhibition curves were obtained by plotting the percentage of inhibition against the inhibitor concentration (on a logarithmic scale) by using Origin 7.0 software (OriginLab Corp.) and IC_{50} values were extracted from a sigmoidal fit of the inhibition curve.

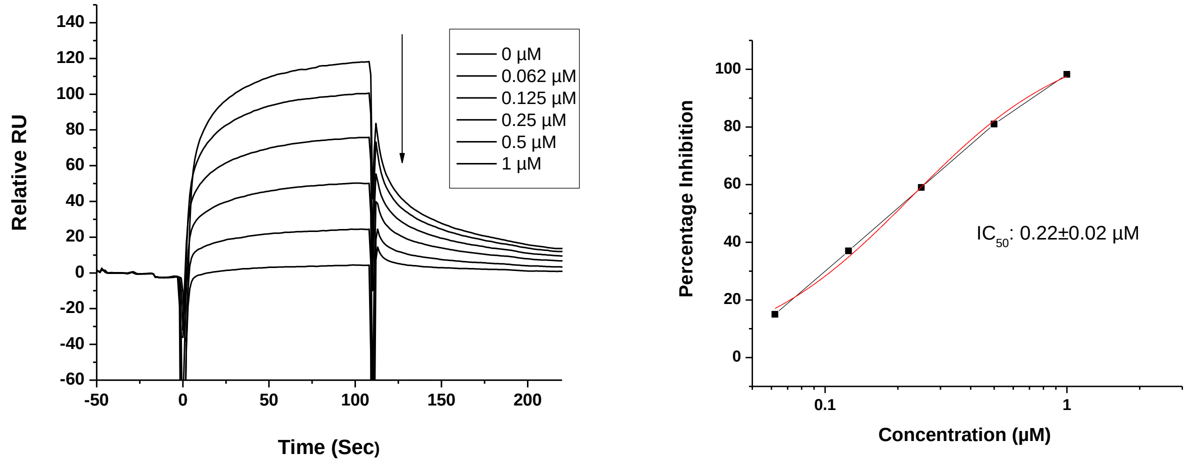
5. SPR Sensorgram:



b)

a)

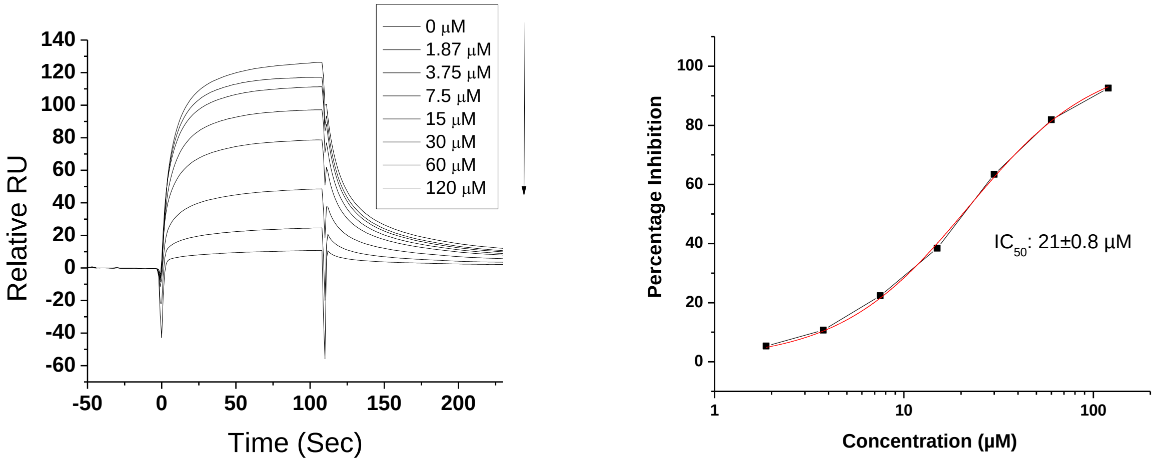
Figure S95. (a) Sensorgrams obtained by injection of PA-IL (1.5 µM) incubated with different concentrations of **18** varying from 10 µM (top curve) to 320 µM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for the **18**. IC_{50} value was extracted from the sigmoidal fit of the inhibition curve.



b)

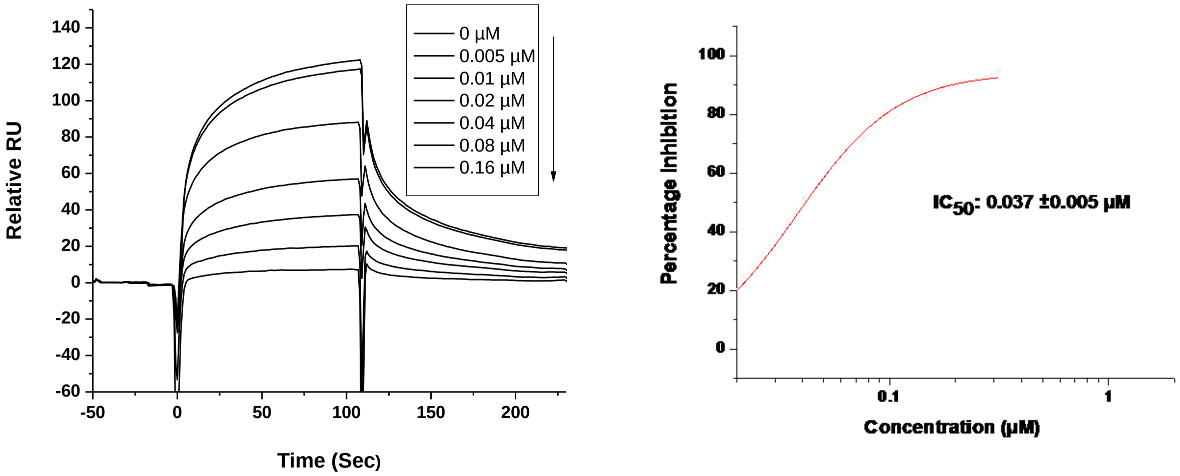
a)

Figure S96. (a) Sensorgrams obtained by injection of PA-IL (1.5 µM) incubated with different concentrations of dendrimer **8** varying from 0.062 µM (top curve) to 1 µM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for the dendrimer **8**. IC_{50} value was extracted from the sigmoidal fit of the inhibition curve.



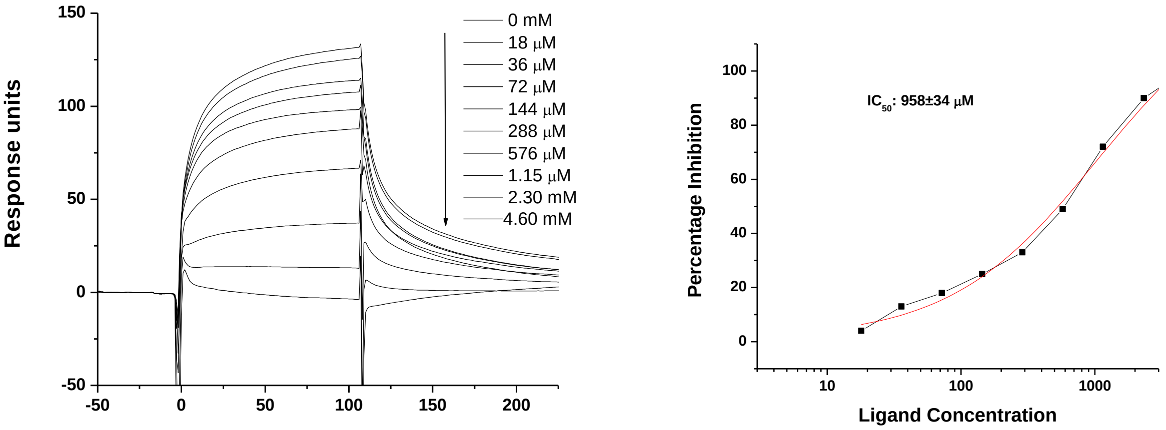
a) **b)**

Figure S97. (a) Sensorgrams obtained by injection of PA-IL (1.5 μM) incubated with different concentrations of **19** varying from 1.87 μM (top curve) to 120 μM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for the **19**. IC50 value was extracted from the sigmoidal fit of the inhibition curve.



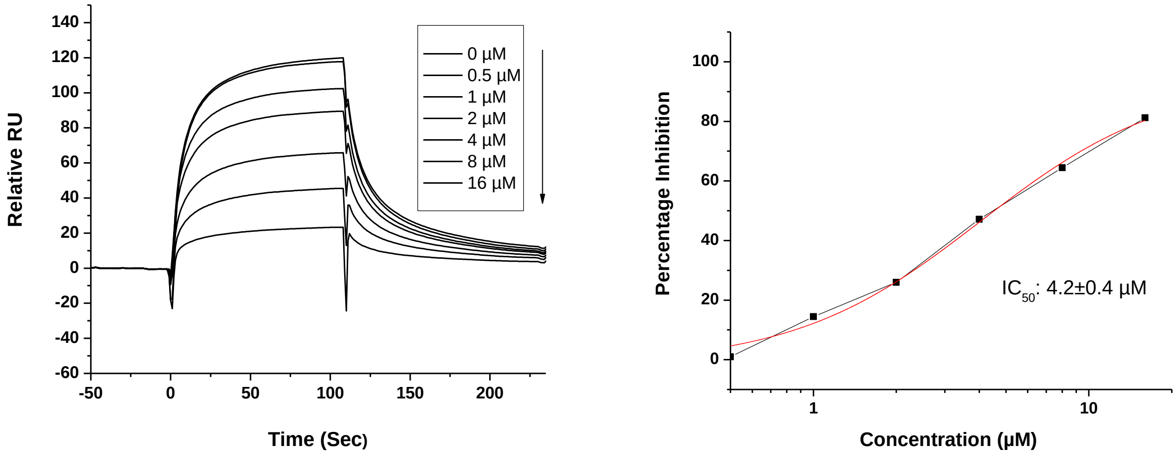
a) **b)**

Figure S98. (a) Sensorgrams obtained by injection of PA-IL (1.5 μM) incubated with different concentrations of glycodendrimer **23** varying from 0.005 μM (top curve) to 0.16 μM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for the glycodendrimer **23**. IC_{50} value was extracted from the sigmoidal fit of the inhibition curve.



a) b)

Figure S99. (a) Sensorgrams obtained by injection of PA-IL (1.5 μM) incubated with different concentrations of **20** varying from 18 μM (top curve) to 4.60 mM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for 20. IC50 value was extracted from the sigmoidal fit of the inhibition curve.



a) b)

Figure S100. (a) Sensorgrams obtained by injection of PA-IL (1.5 μM) incubated with different concentrations of dendrimer **25** varying from 0.5 μM (top curve) to 16 μM (bottom curve) on the surface of immobilized lactoside **21**. (b) The inhibitory curve for the dendrimer **25**. IC50 value was extracted from the sigmoidal fit of the inhibition curve.