Supporting Information

Glycofullerene-AuNPs as Multivalent Ligands of DC-SIGN and Bacterial lectin FimH: Tuning Nanoparticle size and Ligand density

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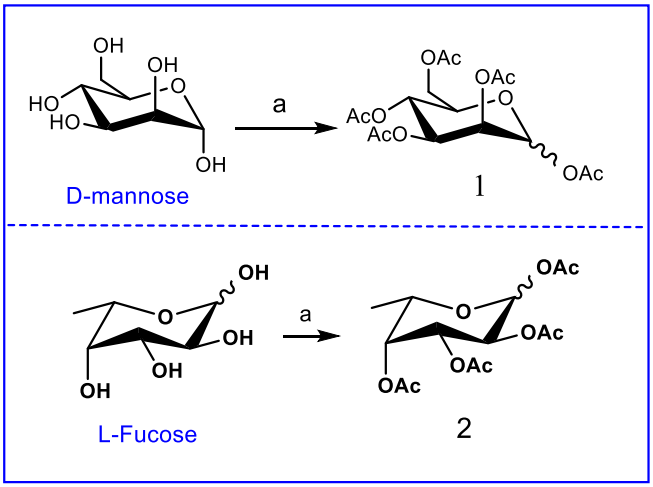
S1. General Information General methods and materials

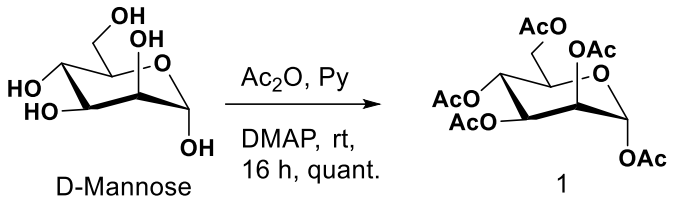
The solvents used for chromatography were purchased in industrial grade and further distilled before use. Dry dichloromethane was refluxed over calcium hydride (CaH_2). Reagents and chemicals were purchased from Sigma-Aldrich or Acros at ACS grade and were used without purification. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck aluminum roll silica gel 60-F254 using UV light and a phosphomolybdic acid solution as revelator. Merck silica gel (60, particle size 40-63 µm) was employed for flash column chromatography. IR spectra (cm^{-1}) were measured on a PerkinElmer Series FI-IR instrument. NMR spectra were recorded on a JEOL ECX 400 or 500 with solvent peaks as reference. All compounds were characterized by ^{1}H and ^{13}C NMR as well as by ^{1}H-^{1}H and ^{1}H-^{13}C correlation experiments when necessary. The abbreviations used to define the multiplicities are: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet and br = broad. Chemical shifts (δ) are reported in ppm and referenced indirectly to residual solvent signals. High resolution mass spectra (HRMS) were carried out on a Bruker MicroTOF-Q II XL spectrometer and MALDI-TOF-LD^{+} were recorded using waters QTOF1 spectrometer.

S2. Synthesis of ligands

S2.1. Synthesis of peracetylated carbohydrates



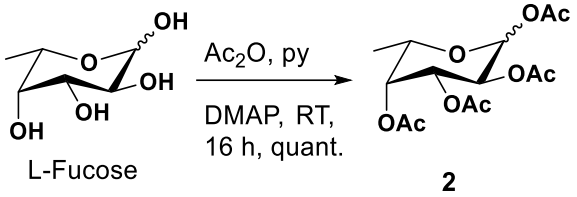
Reagents and conditions. a) Ac_2O, DMAP, Py, r.t, overnight, quant.



1,2,3,4,6-Penta-*O*-acetyl-α-D-mannopyranose 1. DMAP (0.85g, 6.99 mmol, 0.1 eq) was added slowly to a solution of **D-Mannose** (12.6 g, 69.94 mmol, 1 eq) and Ac_2O (49.5 mL, 524.53 mmol, 7.5 eq) in dry pyridine (100 mL). The reaction mixture was stirred overnight at room temperature under argon. Then the reaction mixture was diluted in ethyl acetate (120 mL), washed with aqueous HCl (1M, 50 mL×3), saturated aqueous NH_4Cl (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness to afford the desired peracetylated mannose **1** (28.75 g, quant.) as a sticky colorless oil. The analytical data of **1** were in complete agreement with literature data.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.06 (s, 1 H, H-1), 5.33 (m, 2 H, H-3, H-4), 5.26 (d, $J_{2,3}$ = 2.3 Hz, 1 H, H-2), 4.24 (m, 1 H, H-6a), 4.09-4.06 (m, 2 H, H-6b, H-5), 2.15 (s, 3H, CH_3), 2.15 (s, 3 H, CH_3), 2.07 (s, 3H, CH_3), 2.03 (s, 3 H, CH_3), 1.99 (s, 3H, CH_3).

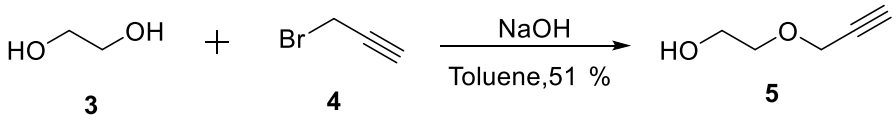
^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7 (CO), 170.0 (CO), 169.9 (CO), 169.6 (CO), 168.1(CO), 90.6 (C-1), 70.7 (C-5), 68.8 (C-3), 68.4 (C-2), 68.2 (C-2), 65.5 (C-4), 62.2 (C-6), 20.9 (CH_3), 20.8 (CH_3), 20.8 (CH_3), 20.7 (CH_3), 20.6 (CH_3).



1,2,3,4-tetra-*O*-acetyl-α-L-fucopyranose 2. DMAP (0.744 g, 6.09 mmol, 0.1 eq) was added slowly to a solution of L-Fucose (10 g, 60.92 mmol, 1 eq) and Ac_2O (42.83 mL, 456.88 mmol, 7.5 eq) in dry pyridine (150 mL). The reaction mixture was stirred overnight at room temperature under argon. Then the reaction mixture was diluted in ethyl acetate (120 mL), washed with aqueous HCl (1M, 50 mL×3), saturated aqueous NH_4Cl (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness to afford the desired peracetylated fucose **2** (21.2 g, quant.) as a sticky colorless oil. The analytical data of **3** were in complete agreement with literature data.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.36 (d, *J* = 2.8 Hz, 1 H, H-1α), 5.37-5.32 (m, 3 H, H-2, H-3, H-4), 4.30 (q, *J* = 6.6 Hz, 1 H, H-5), 2.18-2.02 (4 × s, 12 H, 4 × CH_3), 1.15 (d, *J* = 6.6 Hz, 3 H, H-6).

S2.2. Synthesis of alkyne-linker (2-Propargyloxyethoxy) 5



2-propargyloxyethoxy 5. A solution of propargyl bromide (22.5ml, 80% in toluene, 225 mmol) and ethylene glycol (225 ml, 252.5mmol) was cooled to 0°C and stirred for 30min under argon. Powdered NaOH (10.8 g, 96.25mmol) was added and the reaction mixture was stirred at 45 °C for 3 h. The precipitate was filtered and washed with DCM. After evaporation of the solvent, the crude product was purified using silica gel column chromatography (Cy/EtOAc, 2/1) to afford 11.5 g (51 %) of 2-propargyloxyethoxy **5** as a yellow oil. The analytical data of **6** were in complete agreement with literature data.[3]

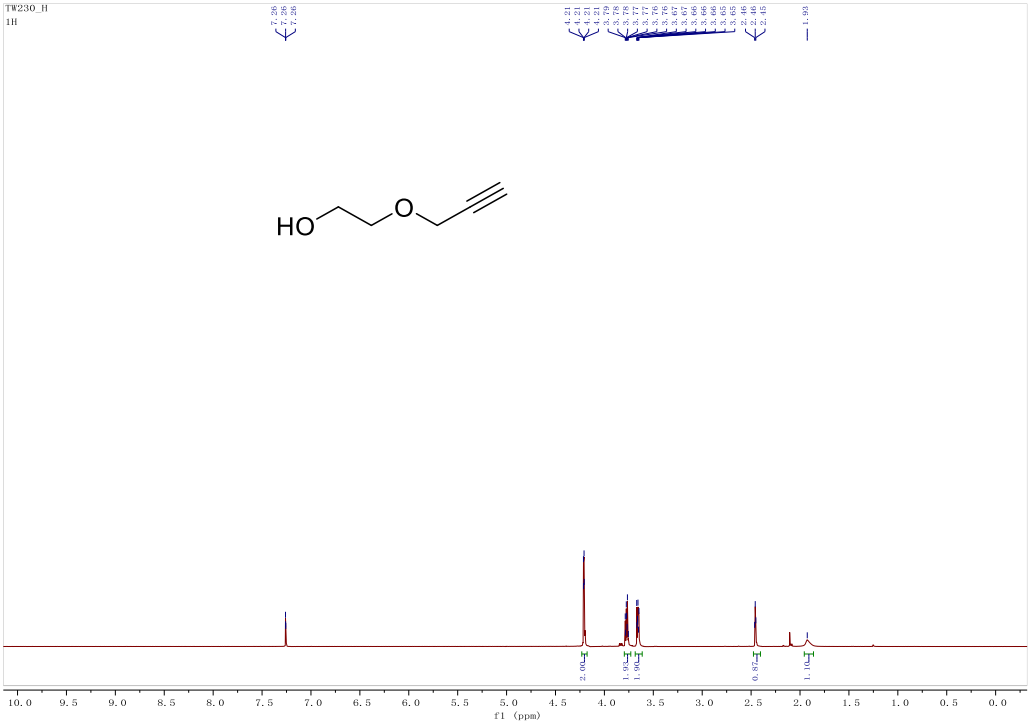
Formula: $C_5H_8O_2$

Mw: 100.12 g/mol;

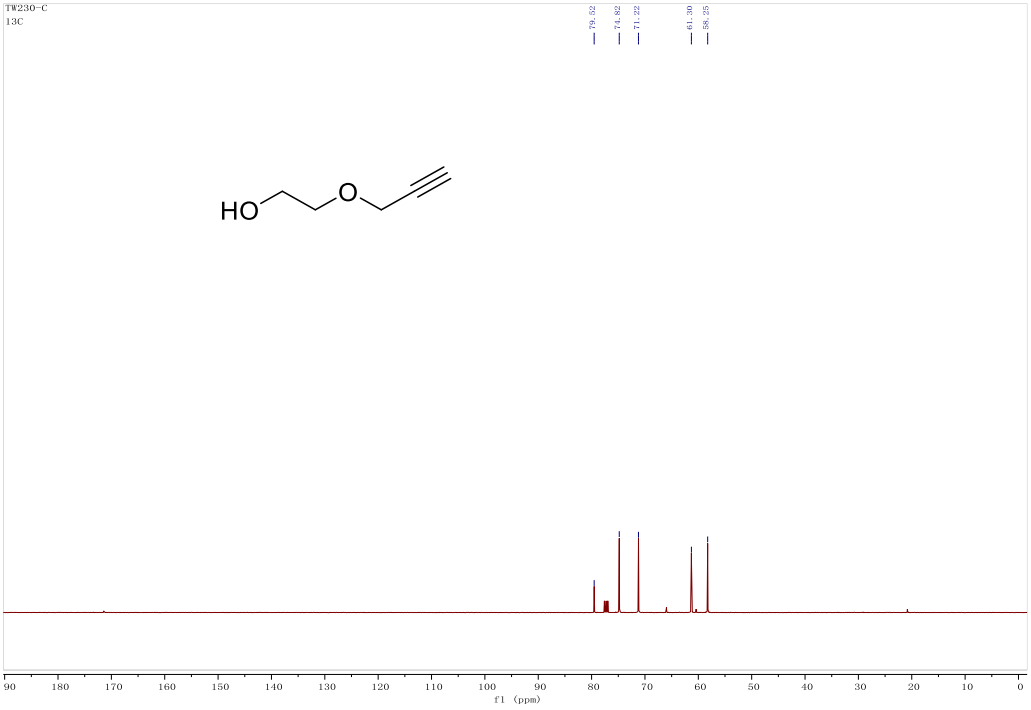
^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.21 (d, *J* = 2.4, Hz, 2H, C*H*$_2$CCH), 3.79-3.76 (m, 2H, C*H*$_2$O), 3.67-3.65 (m, 2H, C*H*$_2$OH), 2.46 (t, *J* = 2.4 Hz, 1H, CC*H*), 1.93 (s, 1H, O*H*).

^{13}C NMR (100 MHz, $CDCl_3$) δ= 79.52 (CH_2*C*CH), 74.82 (CH_2C*C*H), 71.22 (*C*H$_2$O), 61.30 (*C*H$_2$OH), 58.25 (*C*H$_2$CCH).

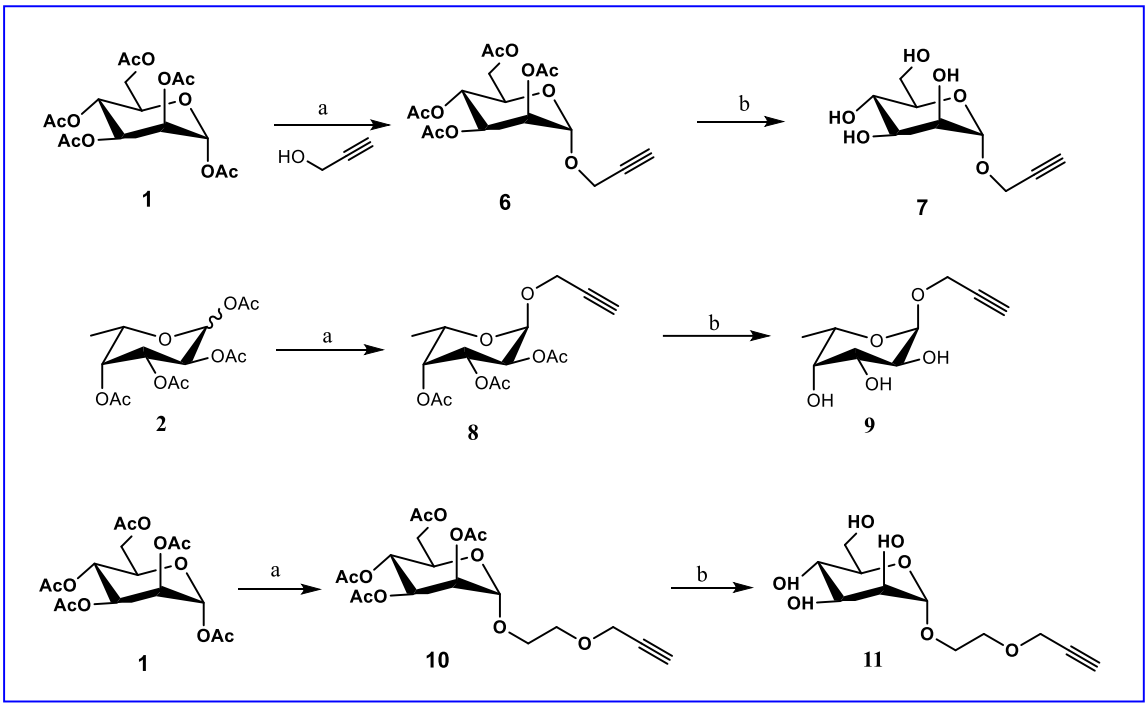
^{1}H NMR (400 MHz, $CDCl_3$)



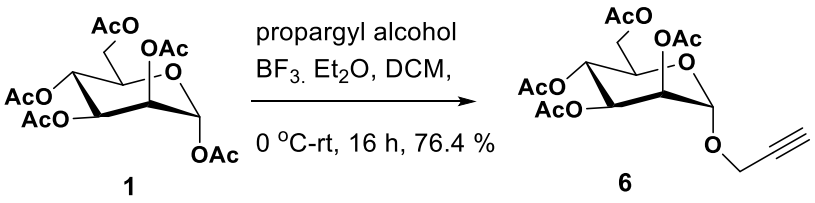
^{13}C **NMR** (100 MHz, $CDCl_3$)



S2.3. Synthesis of monosaccharides bearing on alkynylated linker at the anomeric position



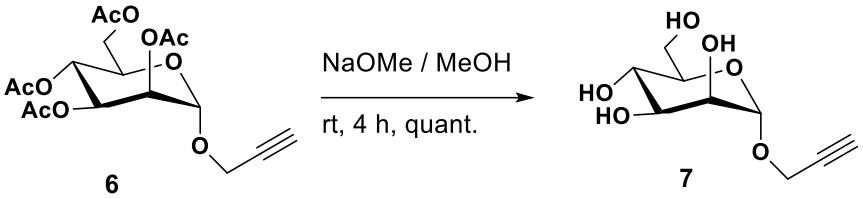
Reagents and conditions. a) $BF_3.Et_2O$, CH_3CN, r.t; b) NaOMe, MeOH.



1-***O*-propargyl-2,3,4,6-tetra-*O*-acetyl-*α*-D-mannopyranoside 6.** To an ice-cold solution of mannose peracetate **1** (2.7 g, 6.93 mmol,1 eq) and propargyl alcohol (1.62 mL, 27.71 mmol, 4 eq) in dry acetonitrile (60 mL) under argon atmosphere was added dropwise boron trifluoride diethyl etherate (4.27 mL, 34.64 mmol, 5 eq). The reaction mixture was allowed to warm to room temperature and then stirred overnight under argon. The solution was quenched with $NaHCO_3$ (5 g), stirred for 30 min and filtered through Celite®. The solid phase was washed with CH_2Cl_2. The liquid phase was concentrated under vacuum. Purification of the crude residue by flash chromatography on silica gel (Cy/EtOAc 7/3) afforded the desired Propargylated mannoside **6** (2.04 g, 76.4 %) as a white powder. The analytical data of **6** were in complete agreement with literature data.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.28 (dd, $J_{2,3}$ = 3.2 Hz, 1 H, H-3), 5.25 (m, 1 H, H-4), 5.24 (dd, $J_{1,2}$ = 1.8 Hz, J 2,3 = 3.2 Hz, 1 H, H-2), 4.98 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H-1), 4.22 (m, 1 H, H-6a), 4.24 (d, $J_{a,b}$ = 2.5 Hz, 2 H, SugO*CH*$_2$), 4.06 (dd, $J_{5,6b}$ = 2.5 Hz, $J_{6a,6b}$ = 12.4 Hz, 1 H, H-6b), 4.00 (m, 1 H, H-5), 2.45 (t, *J* = 2.3 Hz, 1 H, C*CH*), 2.15 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3).

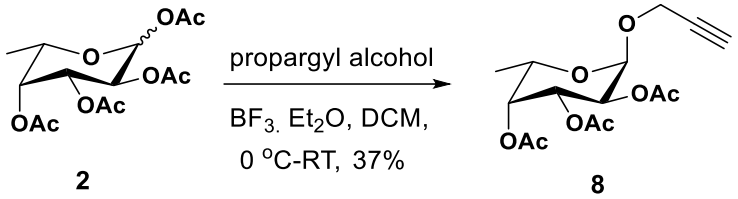
^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8-169.2 (4 × CO), 95.6 (C-1), 77.8 (*C*CH), 75.6 (C*CH*), 68.7, 68.5, 68.4, 65.3 (C-2, C-3, C-4, C-5), 61.7 (C-6), 54.3 (SugO*CH*$_2$), 20.1-20.0 (4 × CH_3).



1-***O*-propargyl-α-D-mannopyranoside 7.** To a solution of **6** (0.58 g, 1.574 mmol, 1 eq) in dry MeOH (10 mL) under argon atmosphere was added sodium methoxide (0.17 g, 3.149 mmol, 2 eq). The reaction mixture was then stirred at room temperature under argon for 3 h. The solution was neutralized by adding Dowex® 50WX8-200 (H^+ form). The resin was washed with MeOH (10 mL). The fractions containing the product were concentrated under reduced pressure to afford the desired product **7** (288 mg, quant.) as a colorless oil. The analytical data of **7** were in complete agreement with literature data.[2]

^{1}H NMR (400 MHz, D_2O) δ = 4.96 (d, $J_{1,2}$= 1.4 Hz, 1 H, H-1), 4.24-4.15 (ABX, *J* = 2.6 Hz, *J* = 25.5 Hz, 1 H, SugO*CH*$_2$), 4.18-4.12 (ABX, *J* = 2.6 Hz, *J* = 25.5 Hz, 1 H, SugO*CH*$_2$), 3.88-3.58 (m, 6 H, H-3, H-4, H-5, H-6a, H-6b), 2.84 (t, *J* = 2.6 Hz, 1 H, C*CH*).

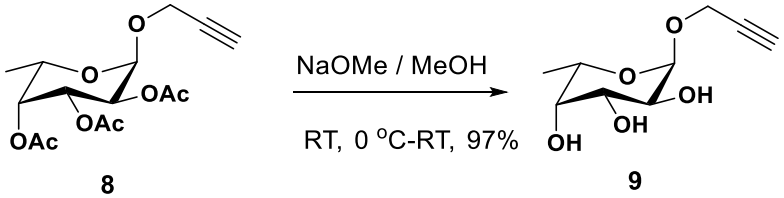
^{13}C NMR (100 MHz, D_2O): δ = 98.8 (C-1), 78.7 (*C*CH), 76.4 (C*CH*), 73.2, 70.4, 69.9 (C-2), 66.7, 60.7 (C-6), 54.5 (*CH*$_2$CCH).



1-***O*-propargyl-2,3,4-tri-*O*-acetyl-α-L-fucopyranoside 8.** To an ice-cold solution of fucose peracetate **2** (3 g, 9.03 mmol,1 eq) and propargyl alcohol (2.1 mL, 36.11 mmol, 4 eq) in dry acetonitrile (60 mL) under argon atmosphere was added dropwise boron trifluoride diethyl etherate (6.4 mL, 36.11 mmol, 5 eq). The reaction mixture was allowed to warm to room temperature and then stirred overnight under argon. The solution was quenched with $NaHCO_3$ (5g), stirred for 30 min and filtered through Celite®. The solid phase was washed with CH_2Cl_2. The liquid phase was concentrated under vacuum. Purification of the crude residue by flash chromatography on silica gel (Cy/EtOAc, 8:2) afforded the desired galactoside **8** (1.1 g, 37 %) as a white powder. The analytical data of **8** were in complete agreement with literature data.[4]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.37 (dd, *J* = 10.9, 3.7 Hz, 1H, H-3), 5.32 – 5.30 (m, 1H, H-4), 5.25 (d, *J* = 3.8 Hz, 1H, H-1), 5.16 (dd, *J* = 10.9, 3.8 Hz, 1H, H-2), 4.26 (d, *J* = 2.4 Hz, 2H, H-7), 4.21 (dd, *J* = 6.6, 0.6 Hz, 1H, H-5), 2.44 (t, *J* = 2.4 Hz, 1H, H-9), 2.17 (s, 3H, O*CH*$_3$), 2.08 (s, 3H, O*CH*$_3$), 1.98 (s, 3H, O*CH*$_3$), 1.14 (d, *J* = 6.6 Hz, 3H, *CH*$_3$).

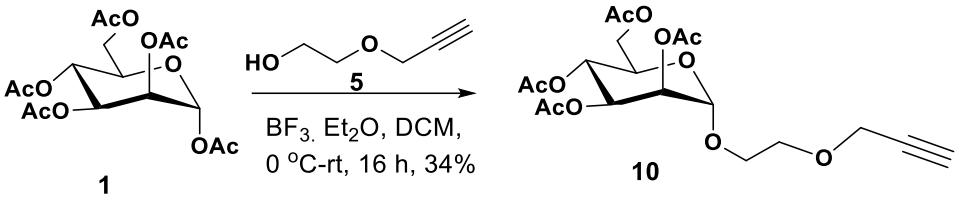
^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.7, 170.5, 170.1 (CO), 95.1 (C-1), 78.7 (C-8), 75.0 (C-8), 71.4 (C-2), 67.9, 67.9 (C-4, C-3), 65.2 (C-5), 55.3 (C-7), 21.0, 20.8, 20.8 (O*CH*$_3$), 15.9 (C-6).



1-*O*-propargyl-α-L-fucopyranoside 9. To a solution of **8** (0.69 g, 2.1 mmol, 1 eq) in dry MeOH (15 mL) under argon atmosphere was added sodium methoxide (0.17 g, 3.15 mmol, 2 eq). The reaction mixture was then stirred at room temperature under argon for 3 h. The solution was neutralized by adding Dowex® 50WX8-200 (H^+ form). The resin was washed with a solution of MeOH (10 mL). The fractions containing the product were concentrated under reduced pressure to afford the desired product **9** (990 mg, 97 %.) as a white powder. The analytical data of **9** were in complete agreement with literature data.[2]

^{1}H NMR (400 MHz, D_2O) δ = 4.95 (d, $J_{1,2}$ = 3.2 Hz, 1 H, H-1), 4.20 (s, 2 H, CH_2CCH), 3.96 (q, J5,6 = 6.4 Hz, 1 H, H-5), 3.71 (m, 3 H, H-2, H-3, H-4), 1.09 (d, $J_{5,6}$ = 6.6 Hz, 3 H, H-6).

^{13}C NMR (100 MHz, D_2O): δ = 98.1 C-1), 72.1, 69.8, 68.1 (3 C), 67.2 (C-5), 55.6 (CH_2CCH), 15.6 (C-6).



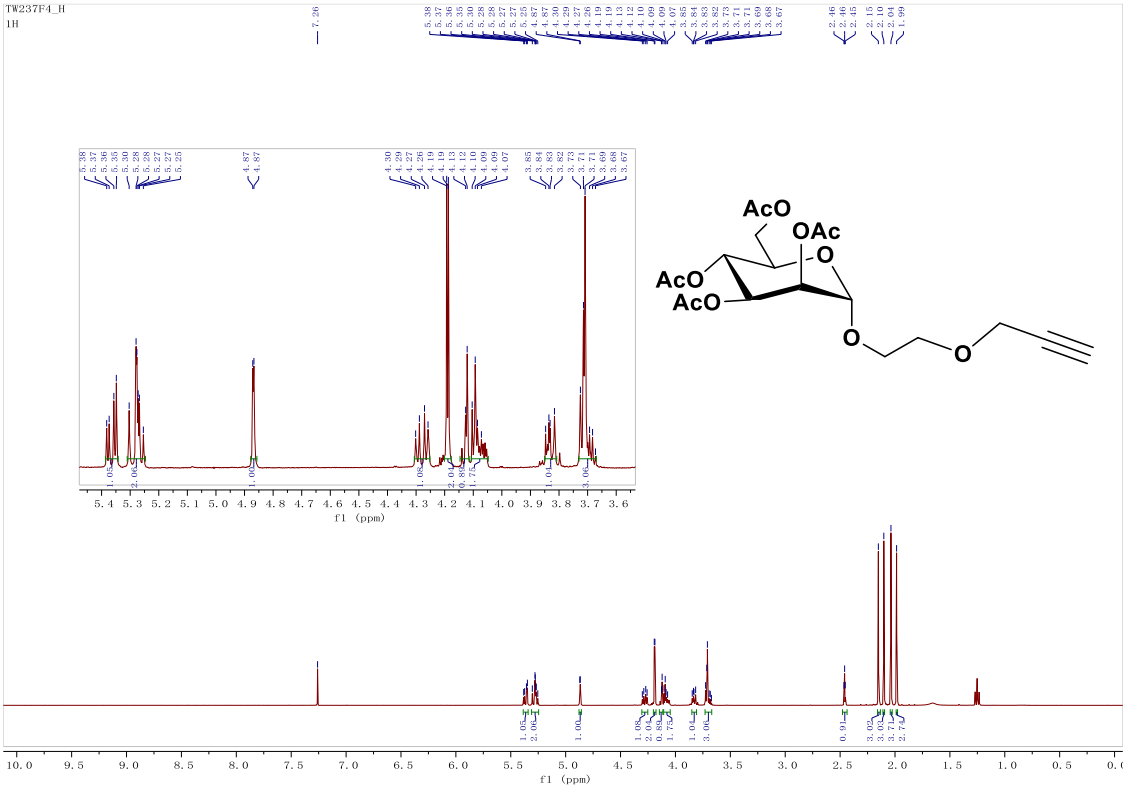
2-Propargyloxyethoxy ethanol-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside 10. To an ice-cold solution of fucose peracetate **1** (3.4 g, 8.75 mmol, 1 eq) and linker **5** (2.6 g, 26.24 mmol, 3 eq) in dry acetonitrile (25 mL) under argon atmosphere was added dropwise boron trifluoride diethyl etherate (4.96 mL, 34.98 mmol, 4 eq). The reaction mixture was allowed to warm to room temperature and then stirred overnight under argon. The solution was quenched with $NaHCO_3$ (5g), stirred for 30 min and filtered through Celite®. The solid phase was washed with CH_2Cl_2. The liquid phase was concentrated under vacuum. Purification of the crude residue by flash chromatography on silica gel (Cy/EtOAc, 3:1) afforded the desired mannoside **10** (1.2 g, 34 %) as a white powder. The analytical data of **10** were in complete agreement with literature data.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.37 (dd, *J* = 10.0, 3.5 Hz, 1H, H-3), 5.30-5.25 (m, 2H, H-2, H-4) 4.87 (d, *J* = 1.6 Hz, 1H, H-1), 4.28 (dd, *J* = 12.2, 5.2 Hz, 1H, H-6b), 4.19 (d, *J* = 2.4 Hz, 2H, CH_2CCH), 4.12 (dd, *J* = 12.2, 5.2 Hz, 1H, H-6a), 4.09 (m, 1H, H-5), 3.85-3.82 (m, 1H), 3.73-3.67 (m, 3H), 2.46 (t, *J* = 2.4 Hz, 1H, CH_2CCH), 2.15 (s, 3H), 2.10 (s, 3H), 2.04 (s, 4H), 1.99 (s, 3H).

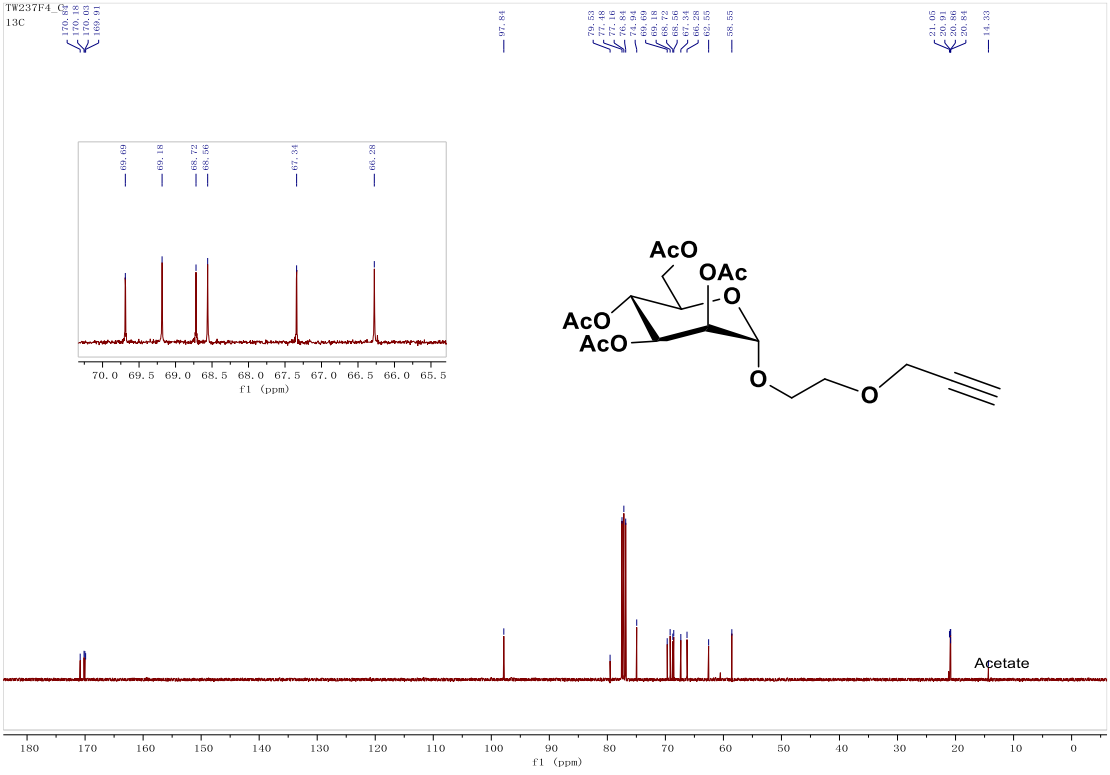
^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.84 (CO), 170.18 (CO), 170.03 (CO), 169.91 (CO), 97.84 (C-1), 79.53 (CH_2CCH, 74.94 (CH_2CCH)), 69.69, 69.18, 68.72, 68.56, 67.34, 66.28 (C-4), 62.55 (C-6), 58.55 (CH_2CCH), 21.05, 20.91, 20.86, 20.84 (4 × CH_3).

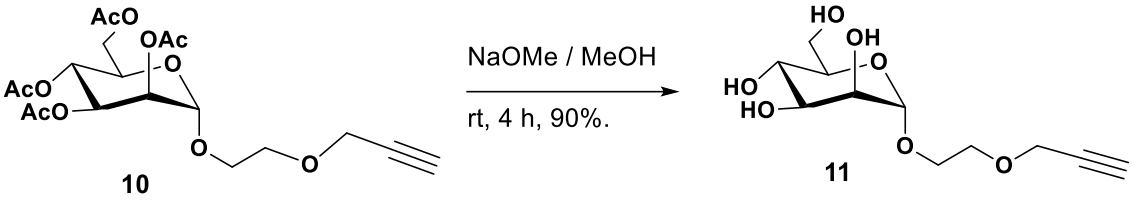
HRMS: (ESI^+-MS, m/z) calcd for $C_{19}H_{26}NaO_{11}$ $[M+Na]^+$: 453.1373, found: 453.1367.

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)





2-Propargyloxyethoxy-α-D-mannopyranoside 11. To a solution of **10** (0.65 g, 1.22 mmol, 1 eq) in dry MeOH (10 mL) under argon atmosphere was added sodium methoxide (0.13 g, 2.45 mmol, 2 eq). The reaction mixture was then stirred at room temperature under argon for 3 h. The solution was concentrated under reduced pressure and the residue was purified by ion-exchange with Dowex® 50WX8-200 (H^+ form). The resin was washed with MeOH (10 mL). The fractions containing the product were concentrated under reduced pressure to afford the desired product **11** (440 mg, 90 %.) as a white powder. The analytical data of **11** were in complete agreement with literature data.[5]

Formula: $C_{11}H_{18}O_7$

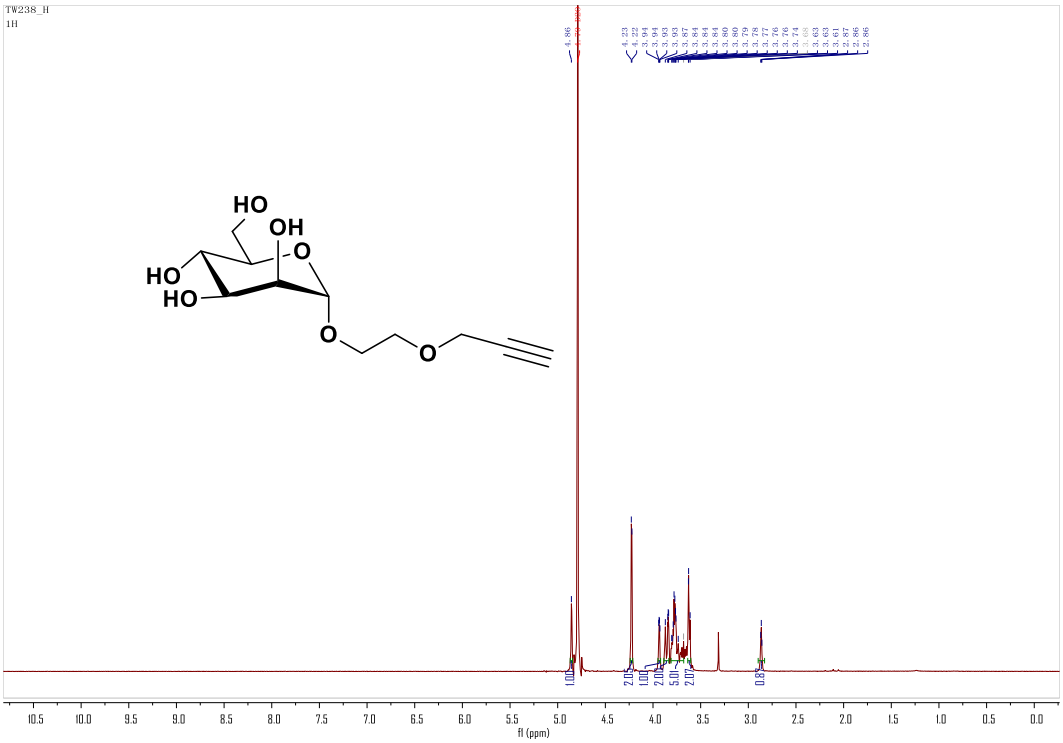
Mw: 262.26 g/mol;

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.86 (s, 1H, H-1), 4.22 (d, J = 2.1, 2H, *CH*$_2$CCH), 3.94 – 3.93 (m, 1H), 3.87 – 3.84 (m, 2H), 3.80 – 3.74 (m, 5H), 3.63 – 3.61 (m, 2H), 2.86 (t, J = 1.9, 1H, CH$_2$CC*H*).

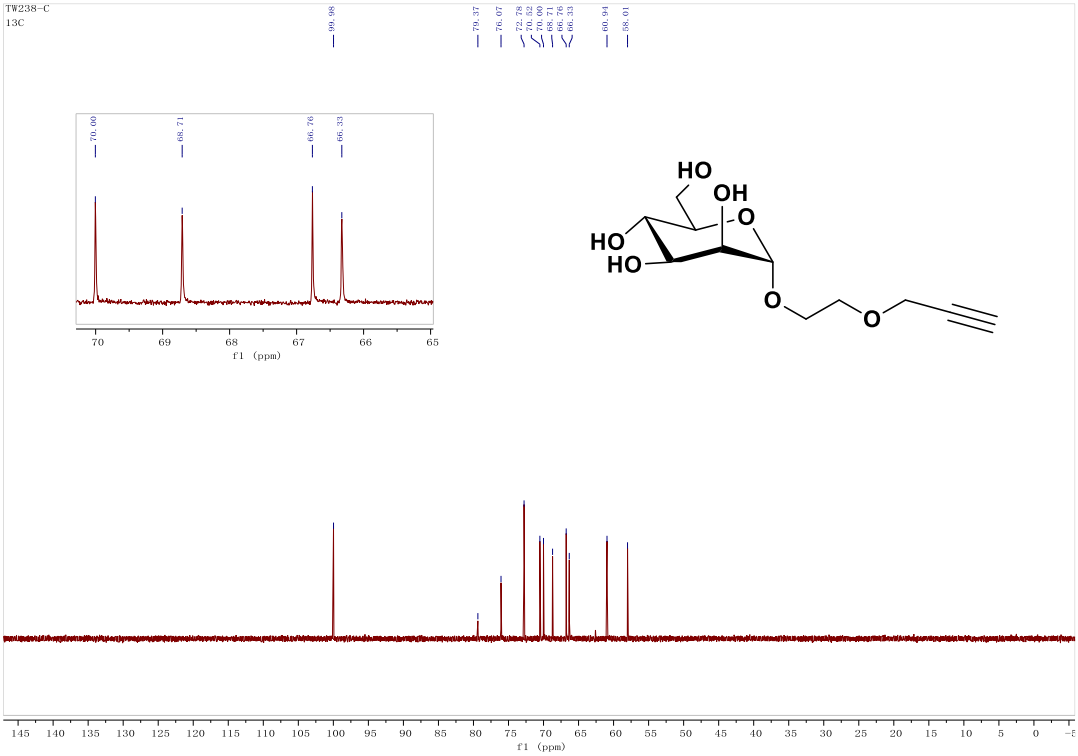
^{13}C NMR (100 MHz, D_2O) δ= 99.98 (C-1), 79.37 (C-10), 76.07 (C-11), 72.78 (C-5), 70.52 (C-3), 70.00 (C-2), 68.71 (C-7), 66.76 (C-4), 66.33 (C-8), 60.94 (C-6), 58.01 (C-9).

HRMS: (ESI$^+$-MS, m/z) calcd for $C_{11}H_{19}O_7$ $[M+H]^+$: 263.1131, found: 263.1125.

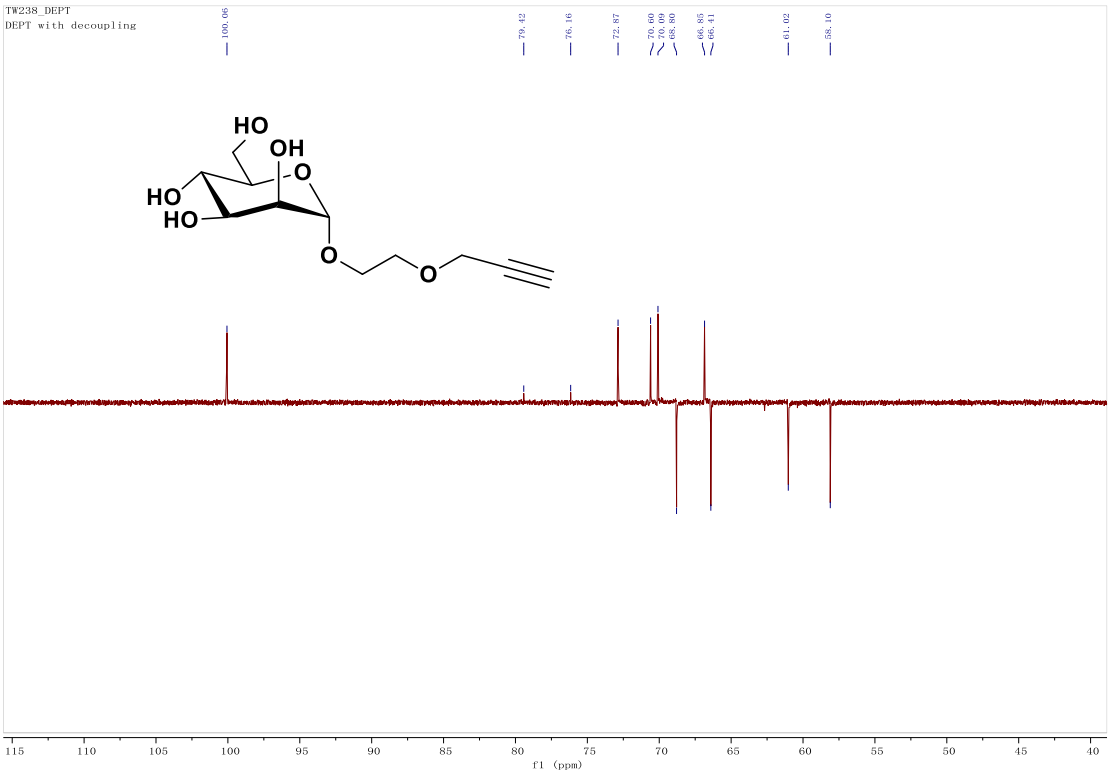
^{1}H NMR (400 MHz, $CDCl_3$)



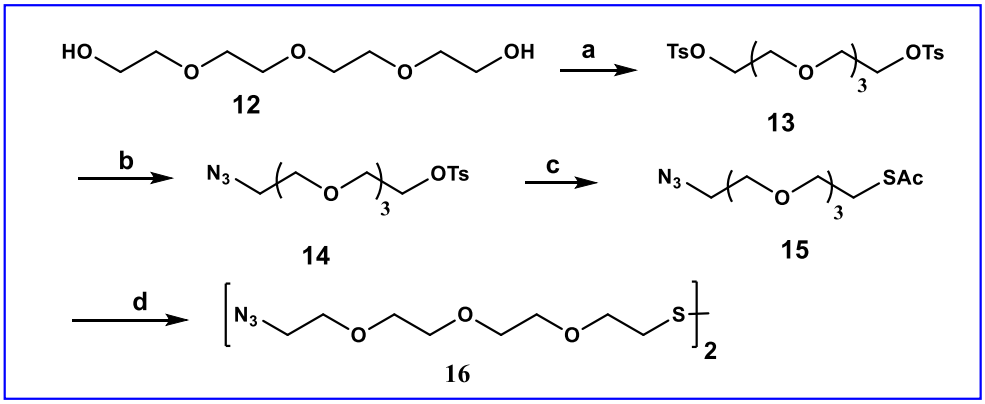
^{13}C NMR (100 MHz, D_2O)



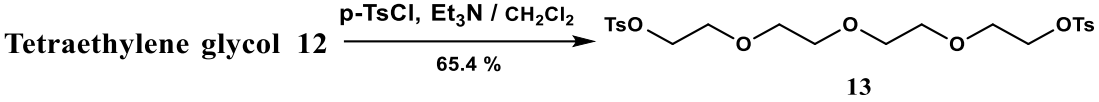
DEPT 135 (100 MHz, D_2O)



S2.4. Synthesis of the disulfide linker



Reagents and conditions. a) p-TsCl, Et_3N, DCM, r.t; b) NaN_3, DMF, 75 ^oC; c) KSAc, Acetone, 50 ^oC; d) NaOMe, DMSO, MeOH, r.t.

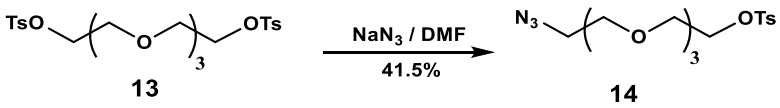


Tetraethylene glycol ditosylate 13. To a solution of tetraethylene glycol **12** (4.4 mL, 26 mmol, 1 eq) in dry CH_2Cl_2 (400 mL) was added Et_3N (9 mL, 65 mmol, 2.5 eq) at 0 ºC. Then p-TsCl (11.4 g, 60 mmol, 2.3 eq) was added and the solution was allowed to warm to room temperature. The reaction mixture was stirred at room temperature under argon for 6 h. After, it was washed with H_2O (1 × 200 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Cy/EtOAc, 6:4) to afford the desired bis-tosylate **13** (8.55g, 65.4%) as a yellow oil. The analytical data of **13** were in complete agreement with literature data.[6]

Formula: $C_{22}H_{30}S_2O_9$
Mw: 502.59 g/mol
***Rf*:** 0.4 (Cy/EtOAc 4:6)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.0 Hz, 4 H, *CH*Ar), 7.32 (d, *J* =8.0 Hz, 4 H, *CH*Ar), 4.15 (t, *J* = 4.8 Hz, 4 H, 2 × *CH*$_2$O), 3.67 (t, *J* = 4.0 Hz, 4 H, 2 × *CH*$_2$O), 3.56 (m, 8 H, 4 × *CH*$_2$O), 2.44 (s, 6 H, 2 × *CH*$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.6 (*C*-Ar), 132.8 (*C*-Ar), 129.6 (*CH*-Ar),127.7 (*CH*-Ar), 70.5 (*CH*$_2$O), 70.3 (*CH*$_2$O), 69.0 (*CH*$_2$O), 68.5 (*CH*$_2$O), 21.4 (*CH*$_3$)



Tetraethylene glycol tosylate mono-azidation 14. To a solution of compound **13** (8.55 g, 17.01 mmol, 1 eq) in dry DMF (90mL) was added NaN_3 (1.11mg, 17.01 mmol, 1 eq) and the mixture was stirred at 75 ºC under argon for 18 h. Then, it was poured into sat. NH_4Cl (200 mL) and extracted with EtOAc (3 × 120 mL). The organic layers were combined, washed with H_2O (1 × 100 mL) and sat. NaCl (1 × 100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Acetone/Cy, 1:3) affording the desired compound **14** (2.635g, 41.5%) as a clear oil. The analytical

data of **23** were in complete agreement with literature data.[6]

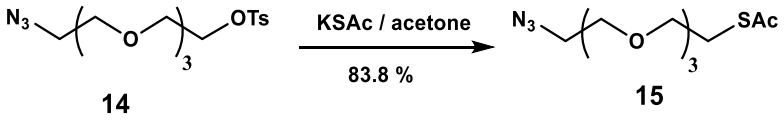
Formula: $C_{15}H_{23}N_3SO_6$;

Mw: 373.42 g/mol;

***Rf*:** 0.38 (Acetone/Cy 1:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 7.23 (d, *J* = 8.0 Hz, 2 H, CH_{Ar}), 4.14 (t, *J* =4.0 Hz, 2 H, CH_2O), 3.67-3.59 (m, 12 H, 6 × CH_2O), 3.25 (t, *J* = 5.2 Hz, 2 H, CH_2N), 2.44 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.9 (*C*-Ar), 133.0 (*C*-Ar), 130.1(*CH*-Ar), 127.6 (*CH*-Ar), 70.76 (CH_2O), 70.69 (CH_2O), 70.63 (CH_2O), 70.07 (CH_2O), 69.3 (CH_2O), 68.7 (CH_2O), 68.3 (CH_2O), 50.7 (CH_2N), 21.6 (CH_3)



S-[2-[2-(2-azidoethoxy)ethoxy]ethyl] ethanethioate 15. Compound **14** (2.635 g, 7.056 mmol, 1 eq) was dissolved in dry acetone (40 mL). KSAc (1.01 g, 1.239 mmol, 1.25 eq) was added and the mixture was stirred at 50 ºC under argon for 20 h. Then, the solvent was concentrated under reduced pressure and it was dissolved in CH_2Cl_2 (50 mL). The mixture was filtrated through Celite® and the collected crude was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Cy/Acetone, 3:1) to afford the desired compound **15** (1.644 g, 83.8 %) as a yellow oil. The analytical data of **15** were in complete agreement with literature data.[6]

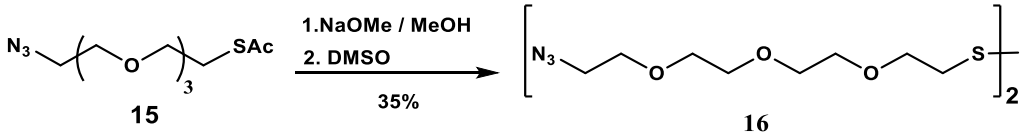
Formula: $C_{10}H_{19}N_3O_4S$;

Mw: 277.34 g/mol;

***Rf*:** 0.37 (Cy/Acetone 3:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.67-3.64 (m, 12 H, 6 × CH_2O), 3.40 (t, *J* = 4.0 Hz, 2 H, CH_2N), 3.01 (t, *J* = 4.8 Hz, 2 H, CH_2S), 2.33 (s, 3 H, CH_3).

^{13}CNMR (100 MHz, $CDCl_3$) δ = 195.3 (*C*=O), 70.6 (2 × CH_2O), 70.5 (CH_2O), 70.2(CH_2O), 69.9 (CH_2O), 69.6 (CH_2O), 50.5 (CH_2N), 30.4 (CH_2S), 28.7 (CH_3).



Tetraethylene glycol disulfide 16. To a solution of compound **15** (1.644 g, 5.928 mmol, 1 eq) in dry MeOH (37 mL) was added NaOMe (0.64g, 11.86 mmol, 2 eq) and the mixture was stirred at room temperature under argon for 2 h. Then, DMSO (0.89 mL) was added and the reaction mixture was stirred at room temperature under argon for 20 h. The solution was neutralized by adding Amberlyst 15 to reach pH 7 and then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Cy/Acetone, 3:1) to afford the desired disulfide **16** (0.97 g, 35 %) as a clear oil. The analytical data of **16** were in complete agreement with literature data.[6]

Formula: $C_{16}H_{32}N_6O_6S_2$

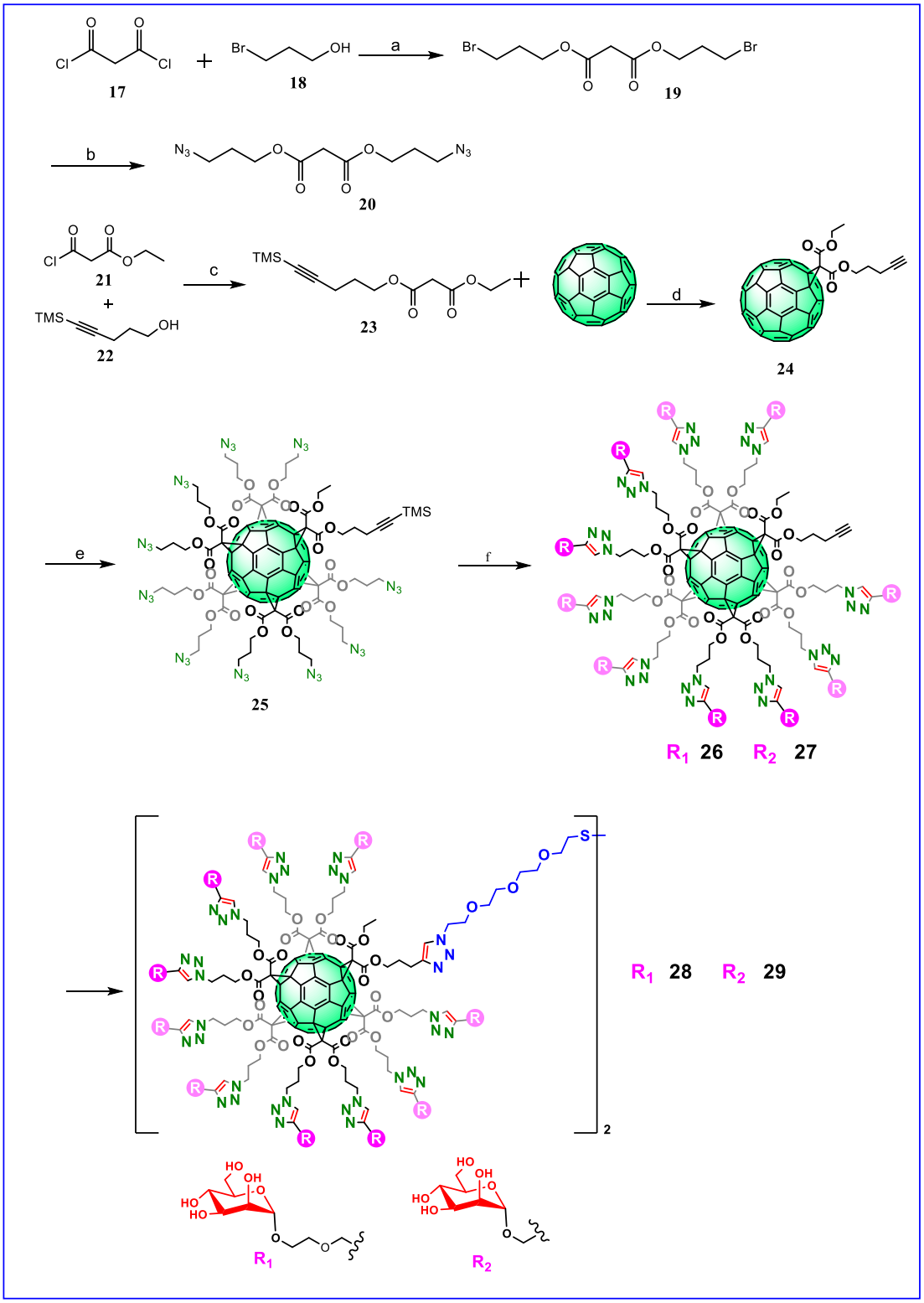
Mw: 468.59 g/mol

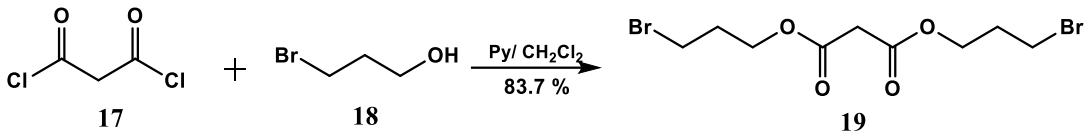
***Rf*:** 0.82 (Cy/Acetone 4:6)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69 (t, *J* = 6.8 Hz, 4 H, 2 × CH_2CH_2N), 3.68-3.65 (m, 20 H, 10 × CH_2O), 3.39 (t, *J* = 5.2 Hz, 4 H, 2 × CH_2N), 2.89 (t, *J* = 6.4Hz, 4 H, 2 × CH_2S).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 70.85 (CH_2O), 70.83 (CH_2O), 70.78 (CH_2O), 70.54 (CH_2O), 70.20 (CH_2O), 69.77 (CH_2O), 50.83 (CH_2N), 38.53 (CH_2S).

S2.5. Synthesis of thiolate glycofullerenes





17 18 19

Bis (3-bromopropyl) malonate 19. 3-bromopropanol (1.95 mL, 21.6 mmol, 2.3 eq) and pyridine (1.74 mL, 21.6 mmol, 2.3 eq) were dissolved in dry CH_2Cl_2 (150 mL) and malonyl dichloride (0.91 mL, 9.3831 mmol, 1eq) was added to this solution dropwise at 0 °C under argon. The mixture was allowed to warm to room temperature and stirred for 18 h, filtered through a short SiO_2 pad and concentrated under reduced pressure. Purification of the residue by column chromatography (Cy/EtOAc, 8:2) provided **19** (2.994 g, 83.7 %) as a colorless oil. The analytical data of **19** were in complete agreement with literature data.[6]

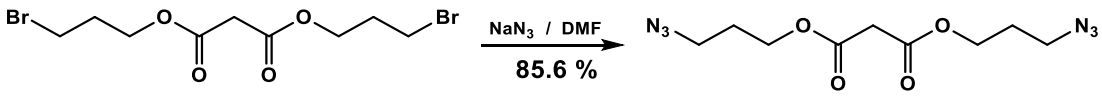
Formula: $C_9H_{14}O_4Br_2$;

Mw: 346.04 g/mol

***Rf*:** 0.64 (DCM)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.31 (t, *J* = 6 Hz, 4 H, 2 × *CH*$_2$O), 3.47 (t, *J* = 6.6 Hz, 4 H, 2 × *CH*$_2$Br), 3.41 (s, 2 H, *CH*$_2$COO), 2.19 (q, *J* = 6.2 Hz, 4 H, *CH*$_2$CH$_2$Br).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.4 (CO), 63.4 (*CH*$_2$O), 41.5 (*CH*$_2$COO), 31.6 (*CH*$_2$Br), 29.2 (*CH*$_2$CH$_2$Br).



19 20

Bis (3-bromopropyl) malonate 19. Malonate **20** (6.248 g, 18.1 mmol, 1 eq) was dissolved in dry DMF (90 mL) and sodium azide (4.694 g, 72.22 mmol, 4 eq) was added to this solution, which was stirred at room temperature under argon for 17 h. The reaction mixture was diluted in diethyl ether (150 mL) and washed with NH_4Cl (100 mL), H_2O (140 mL × 2). The aqueous phase was extracted with diethyl ether (300 mL × 3) and the joined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by Silica gel chromatography (Cy/EtOAc, 9:1) to afforded **20** (4.171 g, 85.6 %) as a colorless oil. The analytical data of **20** were in complete agreement with literature data.[6]

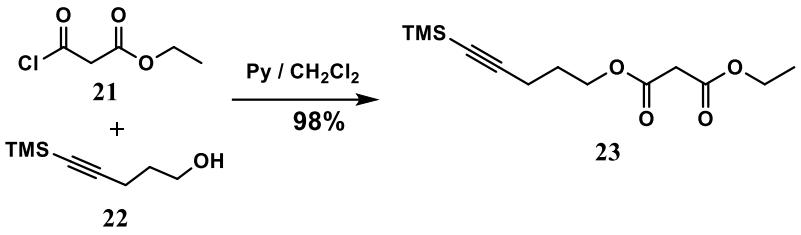
Formula: $C_9H_{14}O_4N_6$**;**

Mw: 270.27 g/mol;

Rf: 0.45

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.26 (t, *J* = 6.2 Hz, 4 H, 2 × *CH*$_2$O), 3.40 (m, 6 H, *CH*$_2$N, *CH*$_2$COO), 1.94 (q, *J* = 6.4 Hz, 4 H, *CH*$_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.1 (CO), 62.3 (*CH*$_2$O), 47.8 (*CH*$_2$N), 41.2 (*CH*$_2$COO), 27.8 (*CH*$_2$).



Ethyl (5-(trimethylsilyl)pent-4-yn-1-yl) malonate 23. Pyridine (1.54 mL,19.06 mmol, 1.2 eq) was added to solution of 5-(trimethylsilyl)pent-4-yn-1-ol (3.4 mL, 19.06 mmol, 1.2 eq) in dry CH_2Cl_2 (100 mL) and this mixture was colded to 0 ºC. Then ethyl malonyl chloride (2 mL, 15.89 mmol, 1 eq) was added dropwise and the reaction mixture was stirred at room temperature under argon for 16 h. The solution was filtrated through a SiO_2 pad, washed with 500 mL of CH_2Cl_2 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Cy/EtOAc, 7:3) affording the desired product **23** (4.457 g, 98 %) as a clear yellow oil. The analytical data of **23** were in complete agreement with literature data.[6]

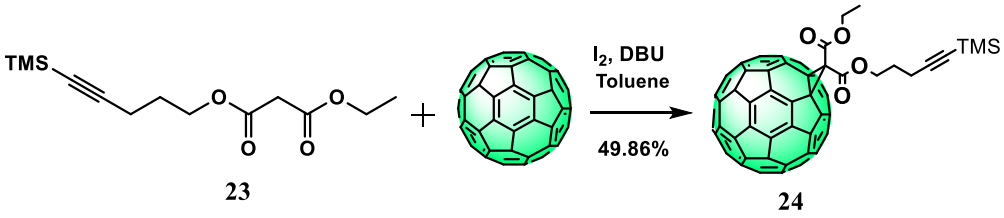
Formula: $C_{13}H_{22}SiO_4$;

Mw: 270.40 g/mol;

***Rf*:** 0.82 (Cy/DCM 6:4)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.21 (m, 4 H, 2 × C*H*$_2$O), 3.67 (s, 2 H, C*H*$_2$), 2.31 (t, $J_{a,b}$ =6.6 Hz, 2 H, C*H*$_2$), 1.86 (m, 2 H, C*H*$_2$), 1.28 (t, $J_{a,b}$ = 6.0 Hz, 3 H, C*H*$_3$), 0.12 (s, 9H, 3 × C*H*$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.4 (2 × CO), 105.4 (*C*≡C-Si), 85.4 (C≡*C*-Si), 64.0 (*C*H$_2$O), 61.5 (*C*H$_2$O), 41.5 (*C*H$_2$), 27.4 (*C*H$_2$C≡C), 16.4 *C*H$_2$), 14.0 (*C*H$_3$), 0.02 (Si*C*H$_3$).



Ethyl (5-(trimethylsilyl)pent-4-yn-1-yl) malonyl–[1,0]–mono–1,2–dihydro[60]–fullerene 24. Fullerene C_{60} (135.9 mg, 0.1886 mmol, 1 eq), I_2 (71.8 mg, 0.2829 mmol, 1.5 eq) and **23** (51mg, 0.1886 mmol, 1 eq) were dissolved in freshly distilled toluene (135 mL) and stirred for 30 min at room temperature. Then DBU (0.071 mL, 0.4715 mmol, 2.5 eq) was added dropwise and the mixture was stirred under argon for 12 h at room temperature. After this, it was filtered through a SiO_2 pad (eluted with cyclohexane to remove impurities and then with dichloromethane to recover the crude product) and concentrated under reduced pressure. Silica gel chromatography (Cy / DCM, 35:65) gave **24** (93mg, 49.9 %) as a red glassy product. The analytical data of **24** were in complete agreement with literature data.[6]

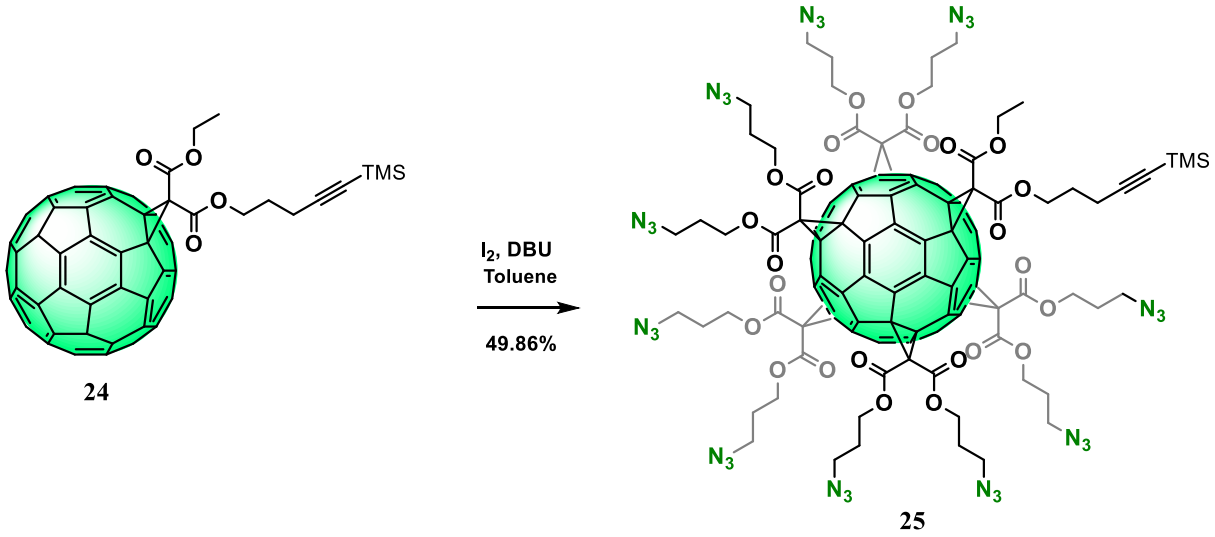
Formula: $C_{73}H_{20}SiO_4$

Mw: 989.06 g/mol;

***Rf*:** 0.45 (Cy / DCM 65:35)

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.58 (m, 4 H, 2 × *CH*$_2$O), 2.45 (t, *J* = 7.2 Hz, 2 H, *CH*$_2$C), 2.06 (m, 2 H, *CH*$_2$), 1.50 (t, *J* = 6.8 Hz, 3 H, *CH*$_3$), 0.17 (s, 9H, 3 × *CH*$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.7 (CO), 145.4, 145.3, 144.8, 144.7, 144.0, 143.2, 142.4, 141.1, 105.2 (*C*≡C-Si), 86.4 (C≡*C*-Si), 71.7 (Cq), 65.9, 63.7 (2 × *CH*$_2$O), 27.8 (*CH*$_2$C), 16.7 (*CH*$_2$), 14.4 (*CH*$_3$), 0.2 (*CH*$_3$).



24 25

Fullerene [5:1] scaffold 25. Fullerene mono-adduct **24** (700 mg, 0.708 mmol, 1 eq), CBr_4 (23.50 g, 70.77 mmol, 100 eq) and malonate **20** (1.92 g, 7.08 mmol, 10 eq) were dissolved in 1,2-dichlorobenzene (140 mL) and the mixture was stirred for 30 min at room temperature. Then DBU (2.11 mL, 14.2 mmol, 20 eq) was added dropwise and the mixture was stirred for 72 h at room temperature, filtered through a short SiO_2 pad (eluted with cyclohexane to remove impurities and then with DCM/EtOAc 1:1 to recover the crude 18 product) and concentrated under reduced pressure. Silica gel chromatography (Cy/EtOAc 8:2) gave **25** as a red glassy product (1.06 g, 64 %). The product was stored in dichloromethane at -20 °C. The analytical data of **25** were in complete agreement with literature data.[6]

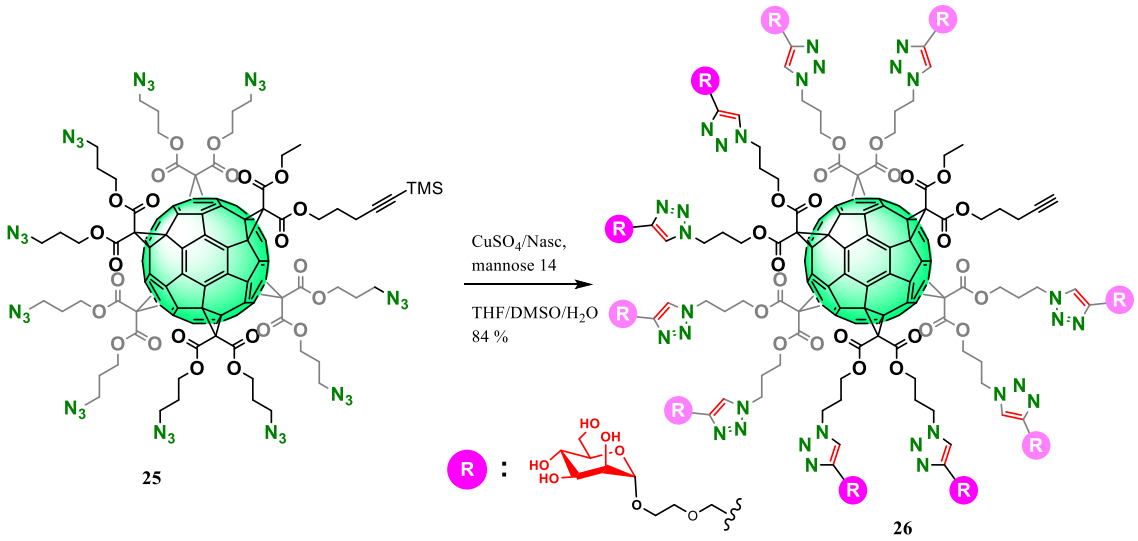
Formula: $C_{118}H_{80}N_{30}SiO_{24}$.

Mw: 2330.17 g/mol.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.31 (t, 24 H, *CH*$_2$O), 3.35 (t, *J* = 5.96 Hz, 24 H, *CH*$_2$N), 2.32 (m, 2 H, *CH*$_2$C), 1.88 (t, *J* = 5.72 Hz, 24 H, *CH*$_2$), 1.31 (t, *J* = 6.88 Hz, 3 H, *CH*$_3$), 0.07 (s, 9H, *CH*$_3$Si).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.7 (CO), 145.6 ($C_{sp}2$), 140.7 ($C_{sp}2$), 104.8

(*C*≡C-Si), 85.6 (C≡*C*-Si), 68.7, 65.2 (*CH*$_2$O), 63.4 (*CH*$_2$O), 62.9 (*CH*$_2$O), 47.4 (*CH*$_2$N), 44.9, 27.9 (*CH*$_2$), 26.7 (*CH*$_2$), 16.2 (*CH*$_2$C), 13.8 (*CH*$_3$), 0.2 (*CH*$_3$Si).



Fullerene [5:1] scaffold 26. Fullerene [5:1] **25** (146.5 mg, 0.063 mmol, 1 eq) was dissolved in THF (0.5 mL) and propargylated mannose **11** (247.3 mg, 0.943 mmol, 15 eq) was added, previously dissolved in DMSO (0.2 mL). A mixture of $CuSO_4$ (5 mg, 0.03 mmol, 0.5 eq) and NaAsc (18.7 mg, 0.094 mmol, 1.5 eq) in H_2O (0.2 mL) was added and the reaction mixture was stirred at room temperature under argon for 30 min. Then the reaction mixture was stirred under microwave irradiation at 80 ºC for 4 h. THF was then removed by evaporation and the product was precipitated by addition of acetone (10 mL) and washed/centrifuged with acetone (10 mL × 3). The crude was passed through size exclusion chromatography on Sephadex G-25 (elution with H_2O/MeOH, 1:1) to remove the excess of mannoside and the fractions containing the product were lyophilized to obtain **26** (260 mg, 84 %) as a dark orange solid.

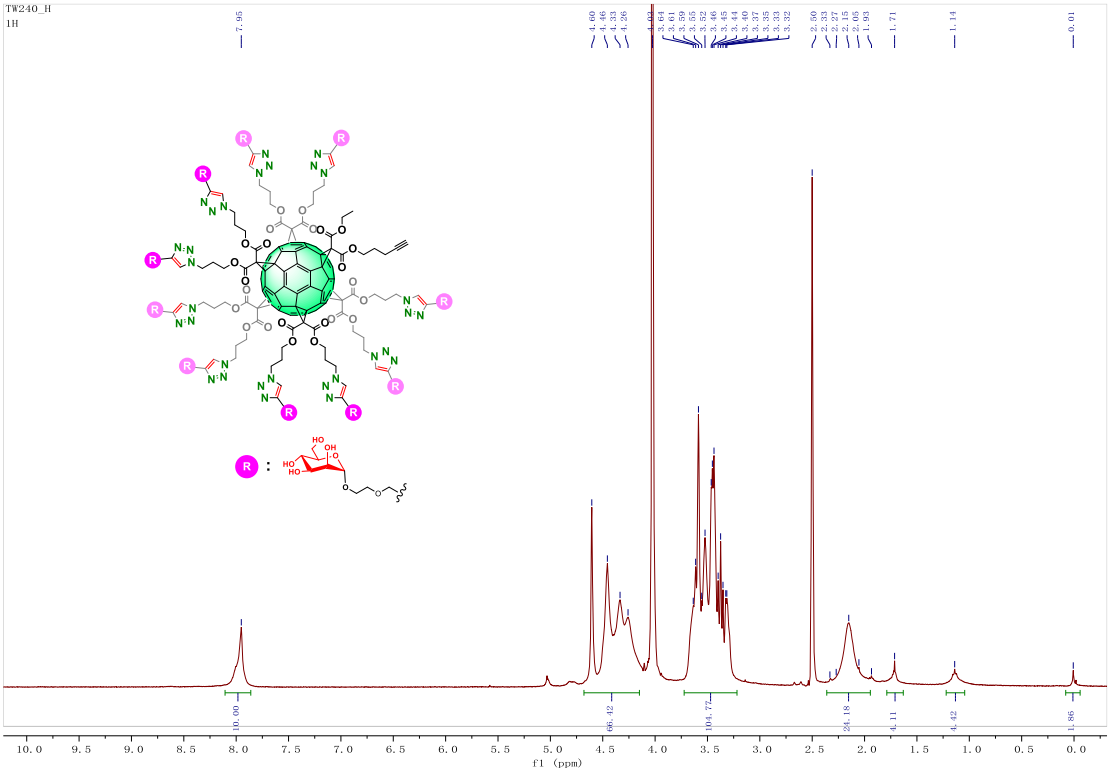
Formula: $C_{225}H_{252}N_{30}O_{94}$

Mw: 4880.90 g/mol;
^{1}H NMR (500 MHz, DMSO-d$_6$) δ = 7.95 (s, 10 H, H$_{arom}$), 4.60-4.26 (m), 3.64-3.32 (m), 2.33-1.93 (m), 1.71 (s, 4H), 1.14 (s, 4H), 0 (s, 1H).

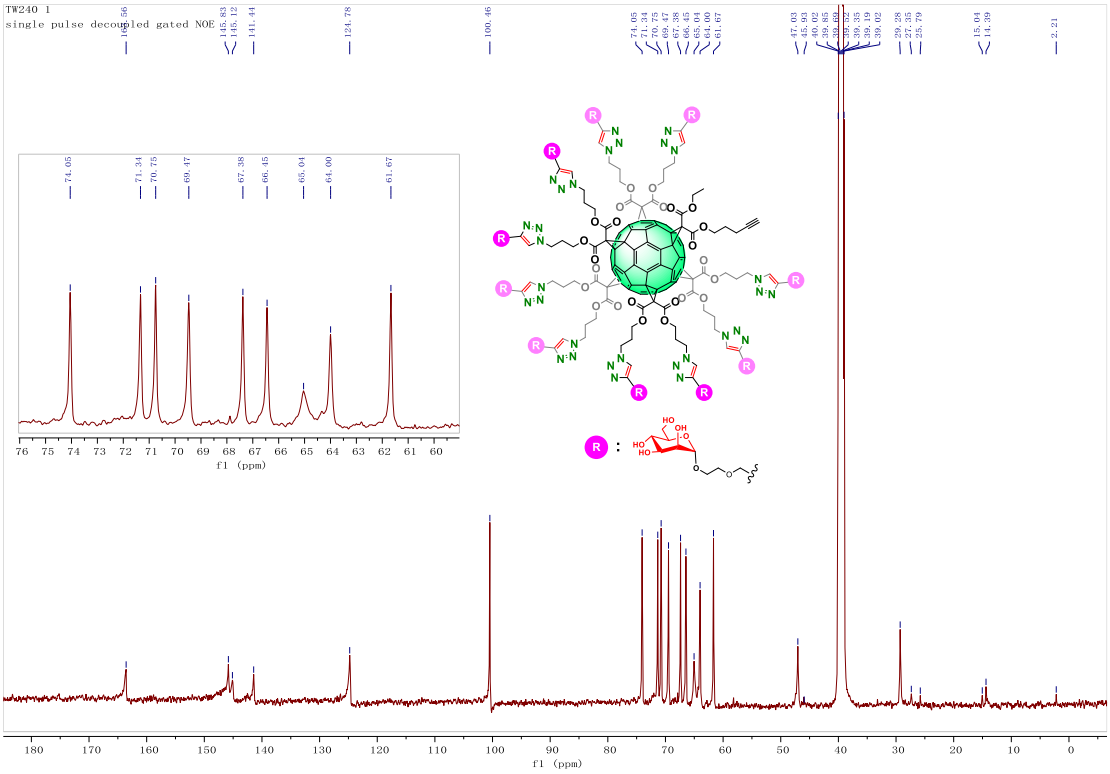
^{13}C NMR (125 MHz, DMSO-d$_6$) δ = 163.56 (C=O), 145.85 (C$_{arom}$), 145.12 (C$_{arom}$), 141.44 (C$_{arom}$), 124.78 (C$_{arom}$), 100.46 (C-1), 74.05, 71.34, 70.75, 69.47, 67.38, 66.45, 65.04, 64.00, 61.67 (C-2, C-3, C-4, C-5, C-6, CH$_2$O), 47.03 (*CH$_2$*N), 45.93 (C$_q$), 29.28 (*CH$_2$*), 27.35 (*CH$_2$*), 25.79 (*CH$_2$*), 15.04 (*CH$_2$*), 14.39 (*CH$_3$*), 0 (TMS).

HRMS: (TOF-MS-LD$^+$): m/z: 4903.6 [M+Na]$^+$, 4680.4 [M-C$_8$H$_{15}$O$_7$+Na]$^+$, 4546.45 [M-C$_{16}$H$_{25}$N$_3$O$_9$+2Na]$^+$, 4545. 4[M-C$_{14}$H$_{24}$N$_3$O$_8$+4H+2Na]$^+$.

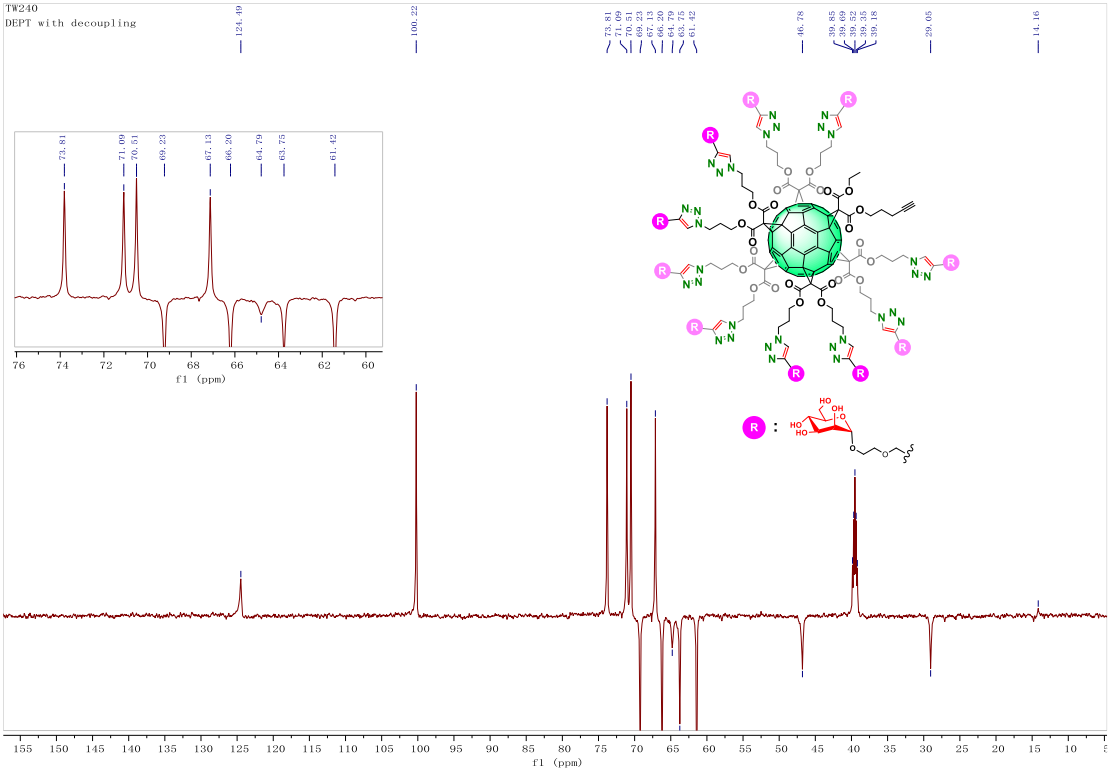
^{1}H NMR (500 MHz, DMSO-d_6)



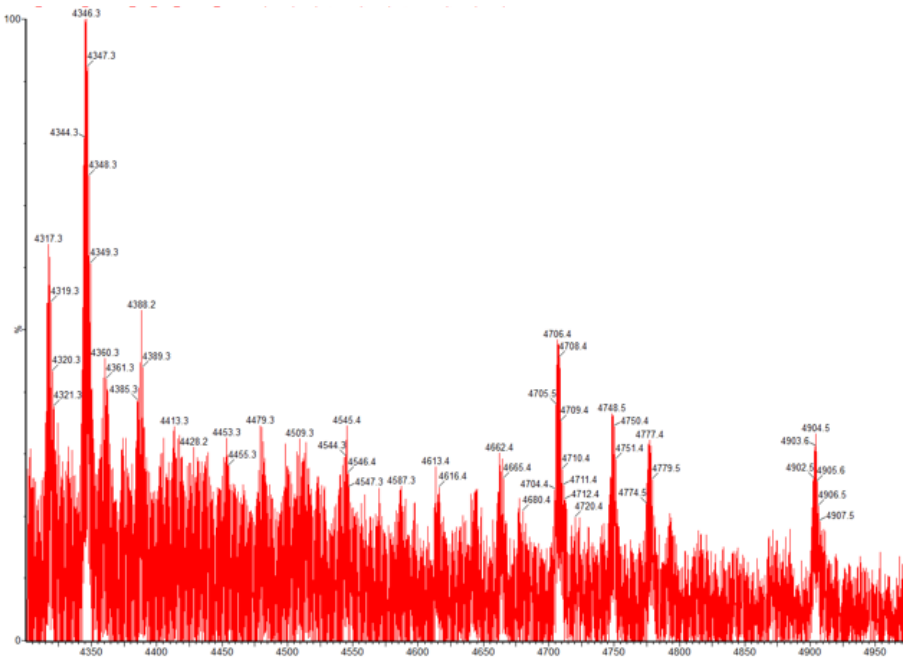
^{13}C NMR (125 MHz, DMSO-d_6)

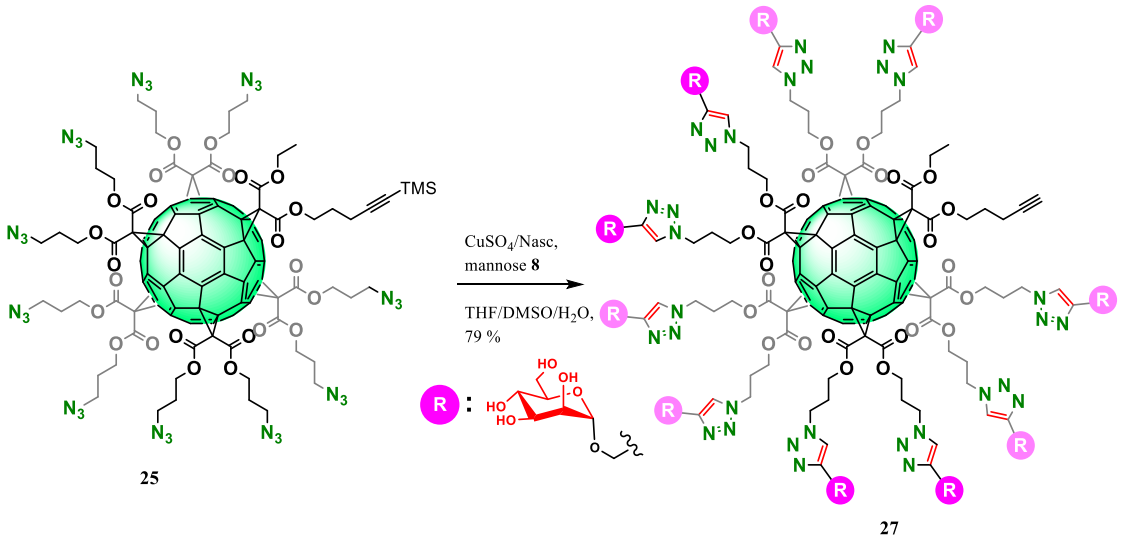


DEPT 135 (125 MHz, DMSO-d_6)



HRMS (TOF-MS-LD$^+$)





Fullerene [5:1] scaffold 27. Fullerene [5:1] **25** (83 mg, 0.036 mmol, 1 eq) was dissolved in THF (0.3 mL) and propargylated heptyl mannose **7** (116.6 mg, 0.534 mmol, 15 eq) in DMSO (0.2 mL) was added. A mixture of $CuSO_4$ (2.84 mg, 0.0178 mmol, 0.5 eq) and NaAsc (10.7 mg, 0.0543 mmol, 1.5 eq) in H_2O (0.1 mL) was added and the reaction mixture was stirred at room temperature under argon for 30 min. Then the reaction mixture was stirred under microwave irradiation at 80 ºC for 4 h. THF was then removed by evaporation and the product was precipitated by addition of acetone (10 mL) and washed/centrifuged with acetone (10 mL × 3). The crude was passed through a size-exclusion chromatography colunm (Sephadex G-25, elution with H_2O/MeOH, 1:1) to remove the excess of mannoside and the fractions containing the product were lyophilized to obtain **27** (125 mg, 79 %) as a dark orange solid.[6]

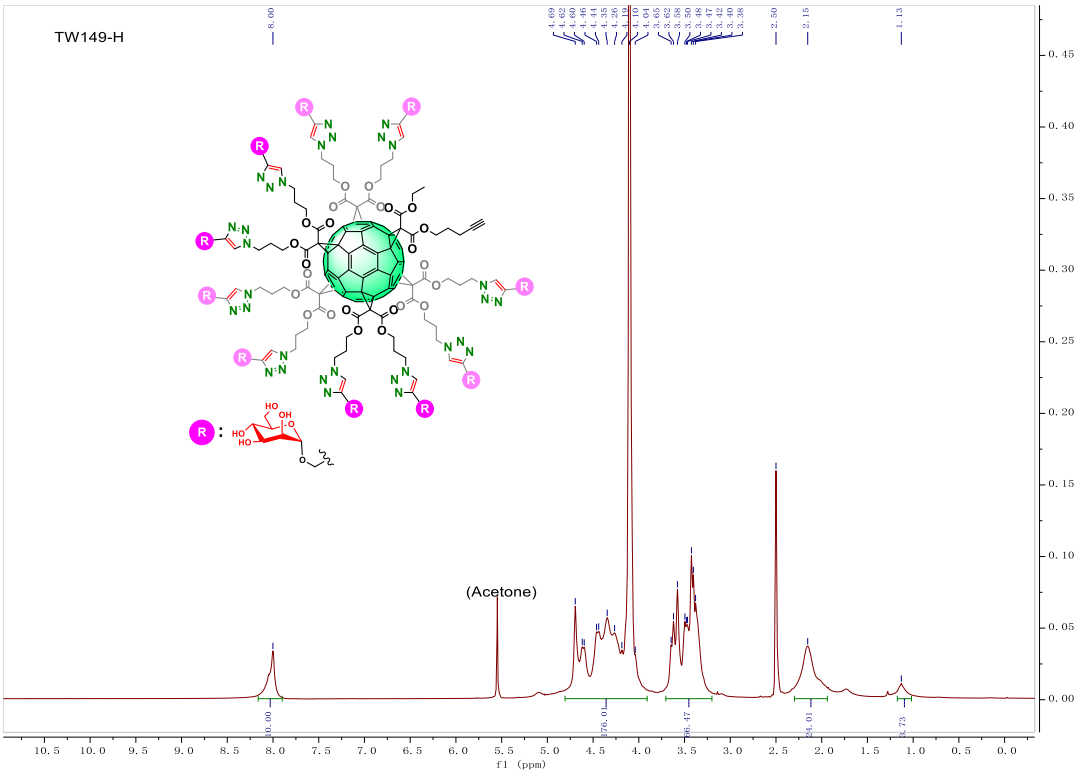
Formula: $C_{205}H_{212}N_{30}O_{84}$

Mw: 4440.37 g/mol

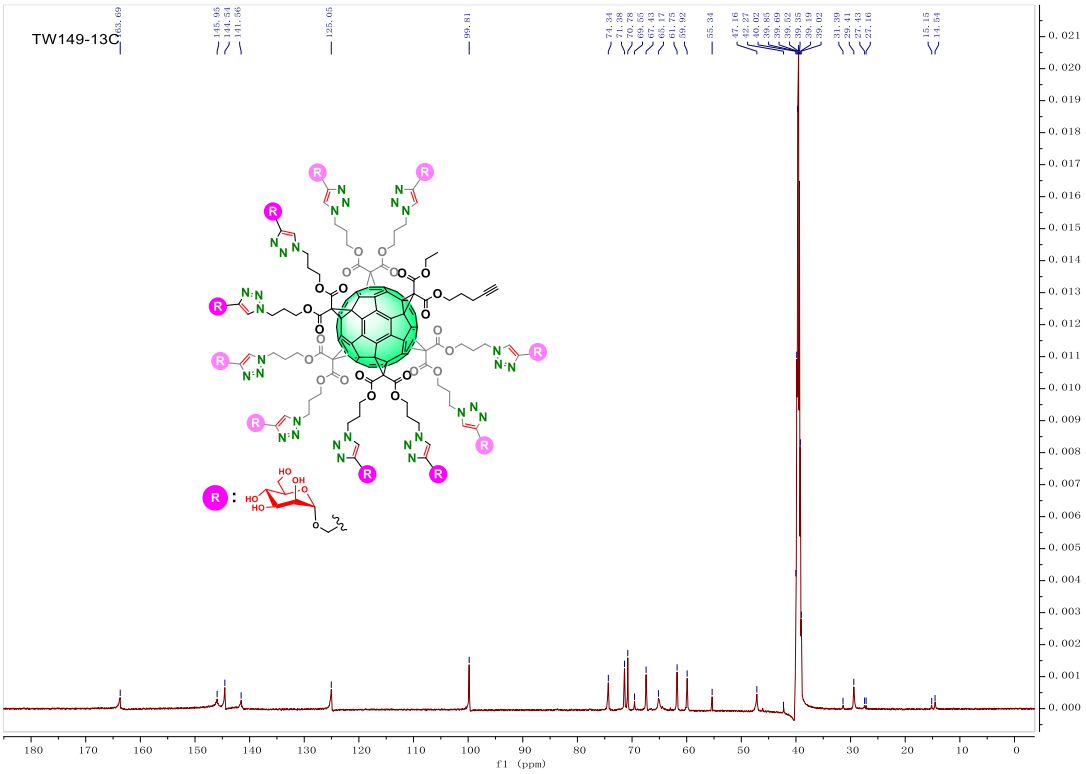
^{1}H NMR (500 MHz, DMSO-*d*$_6$: D_2O 5:1) δ = 8.02 (s, 10 H, H_{arom}), 4.69-4.04 (m), 3.68-3.38 (m), 2.15 (s, 24 H, 12 x CH_2), 1.13 (s, 4H).

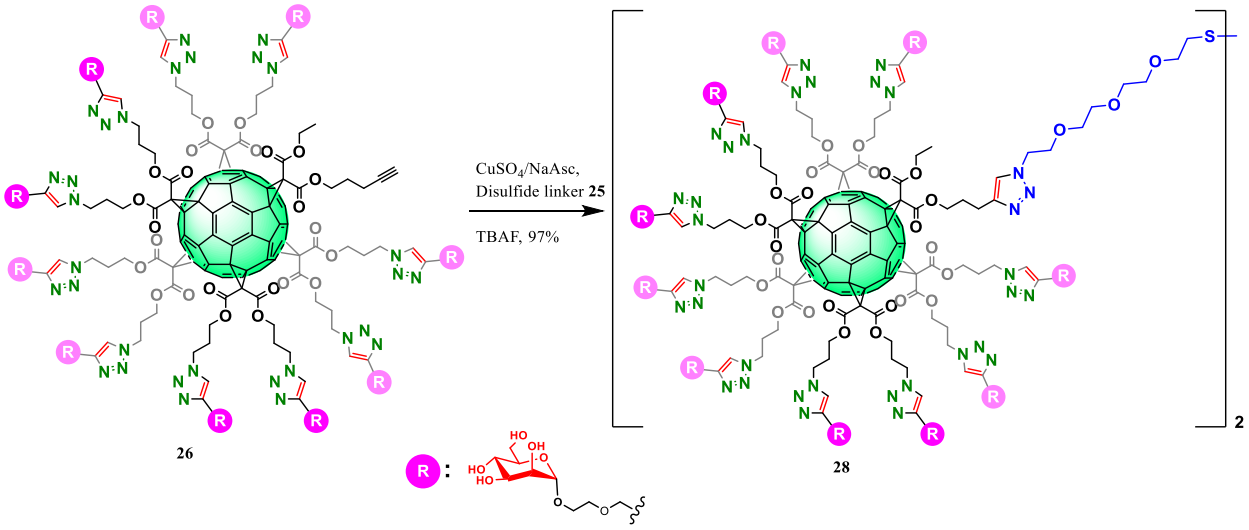
^{13}C NMR (125 MHz, DMSO-*d*$_6$: D_2O 5:1) δ = 163.69 (C=O), 145.95 (C_{arom}), 144.54 (C_{arom}), 141.56 (C_{arom}), 125.09 (C_{arom}), 99.81 (C-1), 74.34, 71.38, 70.78, 69.55, 67.43, 65.17, 61.75, 59.92 (C-2, C-3, C-4, C-5, C-6, *C*H_2O), 47.16 (*C*H_2N), 29.41 (*C*H_2), 27.43 (*C*H_2), 14.48 (*C*H_2), 14.54 (*C*H_3).

^{1}H NMR (500 MHz, DMSO-*d*$_6$: D_2O 5:1)



^{13}C NMR (125 MHz, DMSO-d_6 : D_2O 5:1)





Bis-disulfide glycofullerene 28. Glycofullerene **27** (180 mg, 0.0369 mmol, 2.2 eq) a was dissolved in H_2O (2 mL) and added into the azidated disulfide linker **16** (7.8 mg, 0.017 mmol, 1 eq) were dissolved in THF (0.1 mL), and a mixture of $CuSO_4$ (2.7 mg, 0.0168 mmol, 1 eq) and NaAsc (9.5 mg, 0.050 mmol, 3 eq) in H_2O (0.1 mL) was added. Then, TBAF 1M in THF (0.03 mL, 0.037 mmol, 2.2 eq) was added and the reaction mixture was stirred at room temperature under argon for 16 h. THF was removed by evaporation and the copper scavenger QuadrasilMP (10 mg) was added. The solution was stirred for 2 h at room temperature and filtered. Then the product was passed through a size-exclusion chromatography column (Sephadex G-25, elution with H_2O) and the fractions containing the product were lyophilized to afford **28** (180 mg, 97 %) as a dark orange solid.

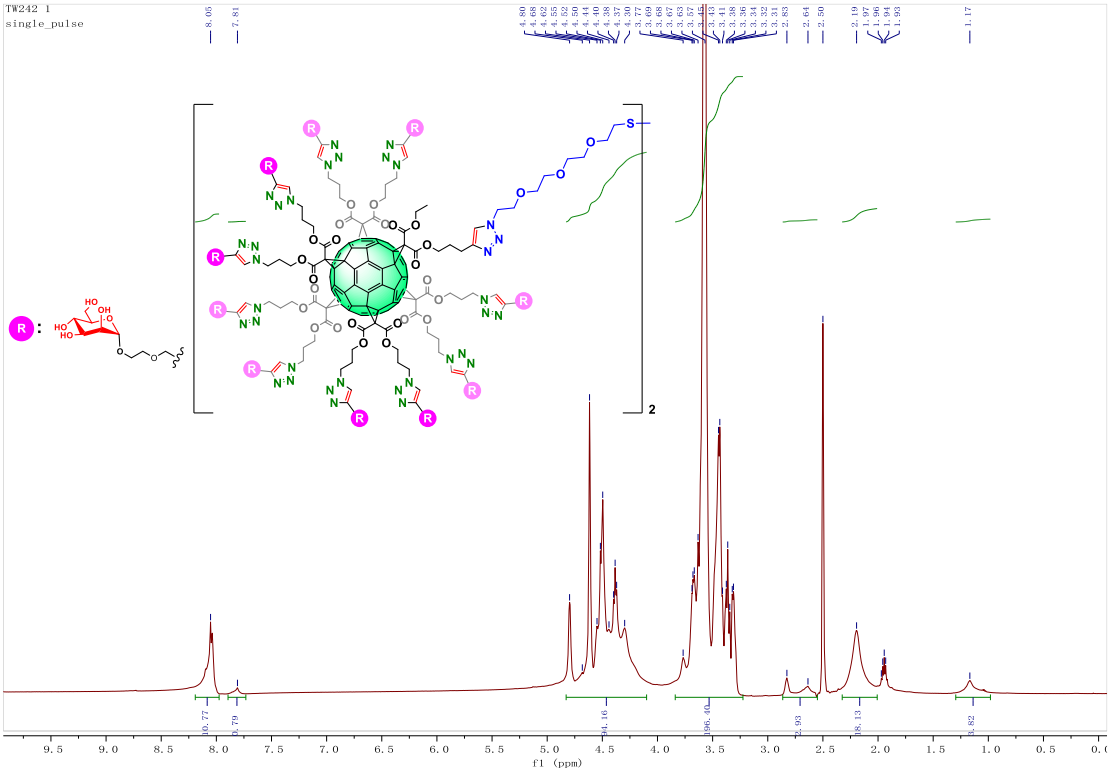
Formula: $C_{466}H_{536}N_{66}O_{194}S_2$

Mw: 10229.8 g/mol

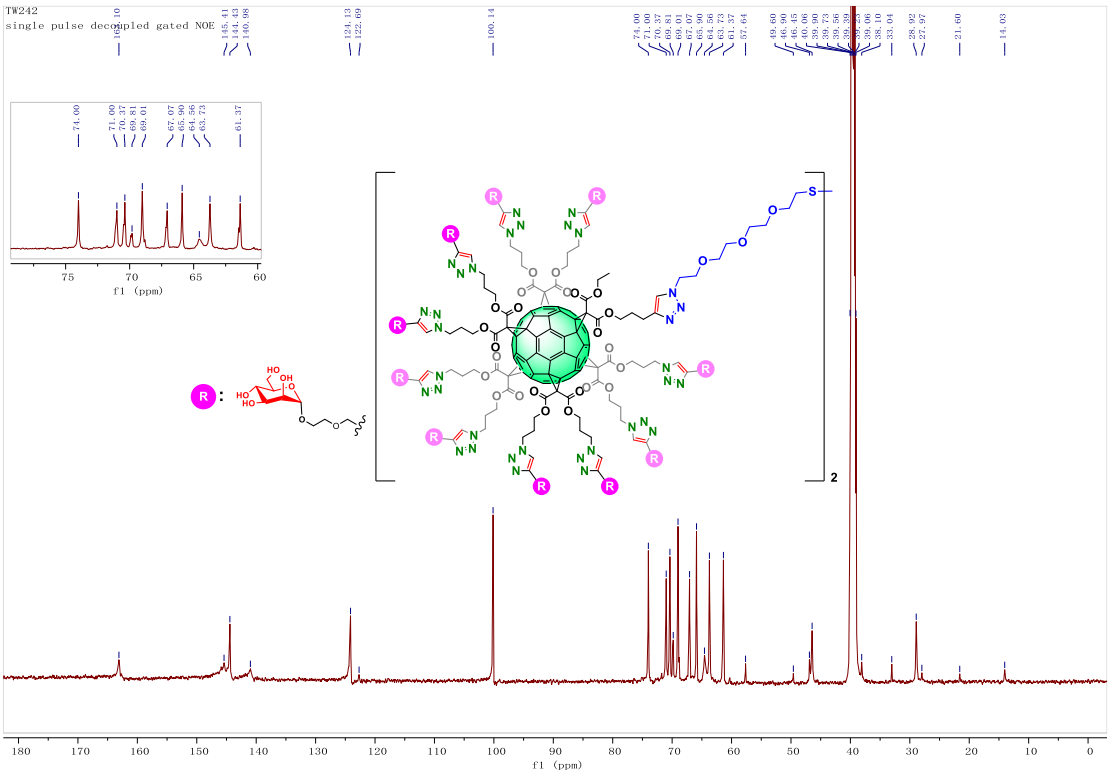
^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.05 (s, 10 H, $CH_{triazole}$), 7.81 (s, 1H, $CH_{triazole}$), 4.8-4.3 (m), 3.77-3.31 (m), 2.19 (m, 18H, 12 × CH_2), 1.17 (s, 3 H).

^{13}C NMR (125 MHz, DMSO) δ = 163.1 (C=O), 145.41 (C_{arom}), 144.43 (C_{arom}), 140.98 (C_{arom}), 124.13 (C_{arom}), 122.69 (C_{arom}), 100.14 (C-1), 74.0 (C-4), 71.0 (C-3), 70.37 (C-2), 69.81 (C, *CH_2*O), 69.01 (*CH_2*O), 67.07 (C-5), 65.9 (*CH_2*O), 64.56 (*CH_2*O), 63.73 (*CH_2*O), 61.37 (C-6), 49.6 (*CH_2*N), 46.9 (*CH_2*N), 46.45 (C_q), 38.1 (*CH_2*S), 28.92 (*CH_2*), 27.97 (*CH_2*), 21.6 (*$CH_2C_{triazole}$*), 14.03 (*CH_3*).

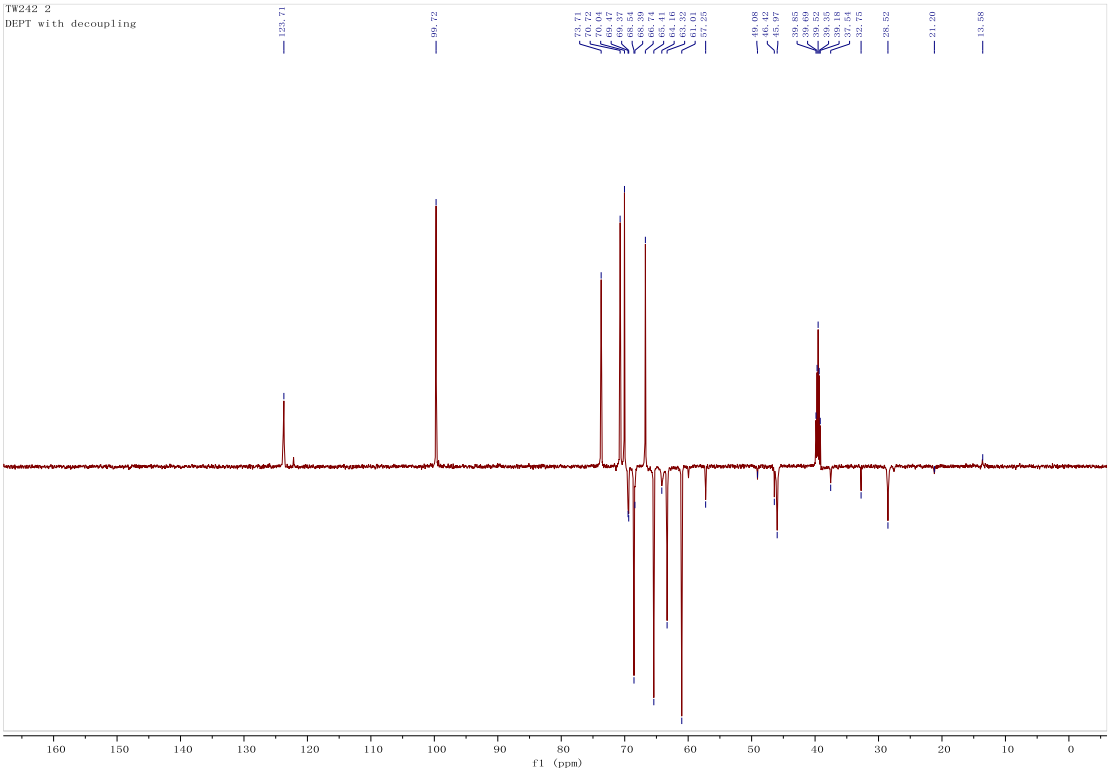
^{1}H NMR (500 MHz, DMSO-d_6)

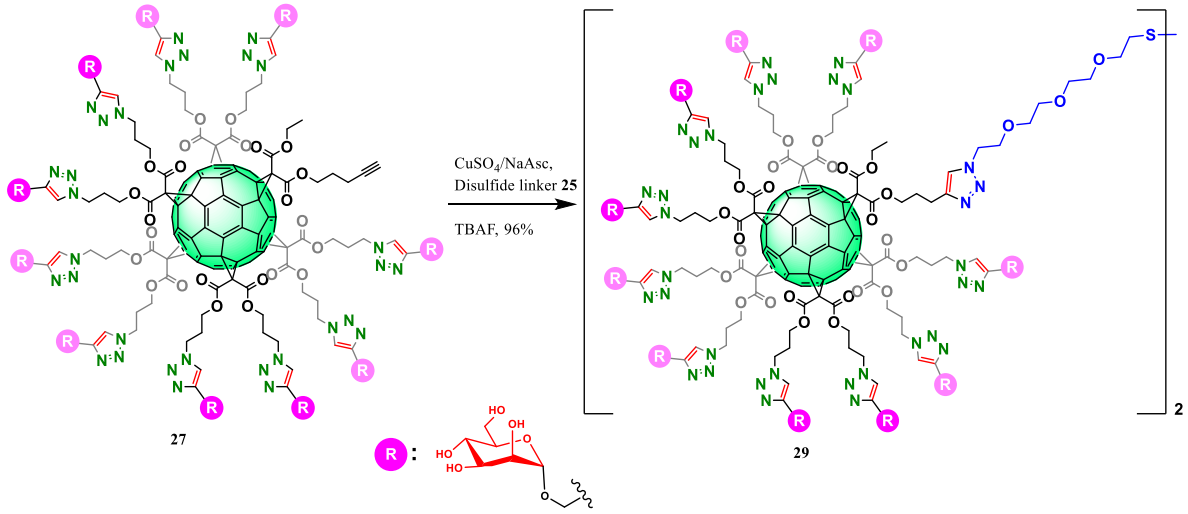


^{13}C NMR (125 MHz, DMSO-d_6)



DEPT 135 (125 MHz, DMSO-d_6)





Bis-disulfide glycofullerene 29. Glycofullerene **27** (254.4 mg, 0.0573 mmol, 2.2 eq) was dissolved in H_2O (2 mL) and added into the azidated disulfide linker **16** (12.2 mg, 0.0260 mmol, 1 eq) dissolved in THF (0.1 mL). And a mixture of $CuSO_4$ (6.7 mg, 0.0260 mmol, 1 eq) and NaAsc (12.2 mg, 0.0768 mmol, 3 eq) in H_2O (0.1 mL) was added. Then, TBAF 1M in THF (0.05 mL, 0.0512 mmol, 2.2 eq) was added and the reaction mixture was stirred at room temperature under argon for 16 h. After this, THF was removed by evaporation and the copper scavenger QuadrasilMP (10 mg) was added. The solution was stirred for 2 h at room

temperature and filtered. Then the product was passed through a size-exclusion chromatography column (Sephadex G-25, elution with H_2O) and the fractions containing the product were lyophilized to afford **29** (240 mg, 96 %) as a dark orange solid.[6]

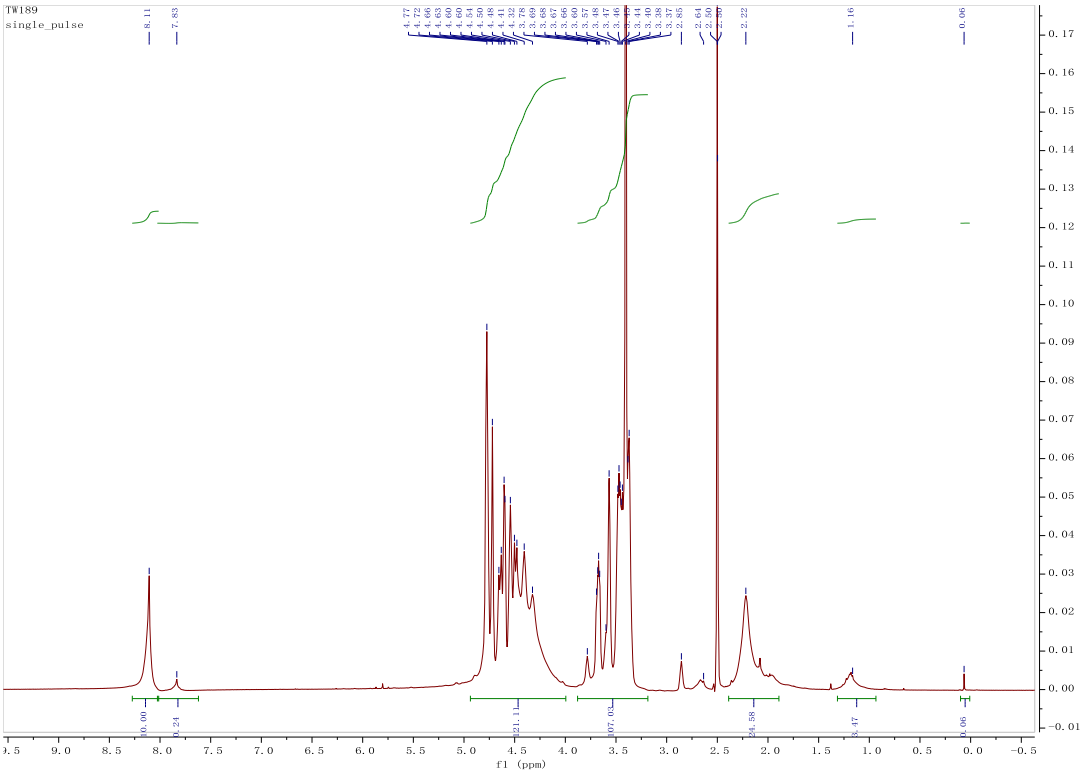
Formula: $C_{426}H_{454}N_{66}O_{174}S_2$

Mw: 9348.63 g/mol

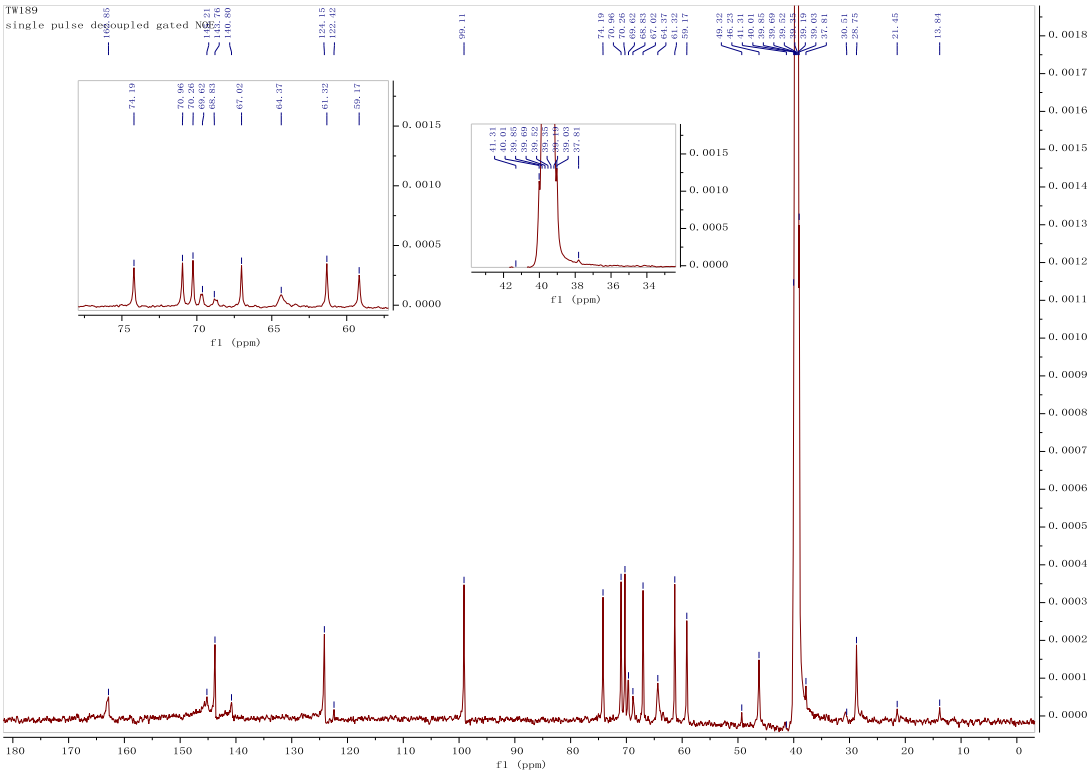
^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.11 (s, 10 H, *CH*$_{triazole}$), 7.83 (s, 1H, *CH*$_{triazole}$), 4.77-4.32 (m), 3.78-3.37 (m), 2.22 (m, 24 H, 12 x *CH*$_2$).

^{13}C NMR (125 MHz, DMSO-d_6) δ = 162.85 (C=O), 145.21 (C_{Ar}), 143.76 (C_{Ar}), 140.8 (C_{Ar}), 124.15 (*CH*$_{Ar}$), 122.42 (*CH*$_{Ar}$), 99.11 (C-1), 74.19 (C-5), 70.96 (C-2), 70.26 (C-3), 69.62 (C, *CH*$_2$O), 68.83 (*CH*$_2$O), 67.02 (C-4), 64.37 (*CH*$_2$O), 61.36 (C-6), 59.17 (*CH*$_2$O), 46.17 (*CH*$_2$N), 37.79 (*CH*$_2$S), 30.53 (CH_2), 28.75 (CH_2), 21.45 (*CH*$_2$C$_{triazole}$), 13.84 (CH_3).

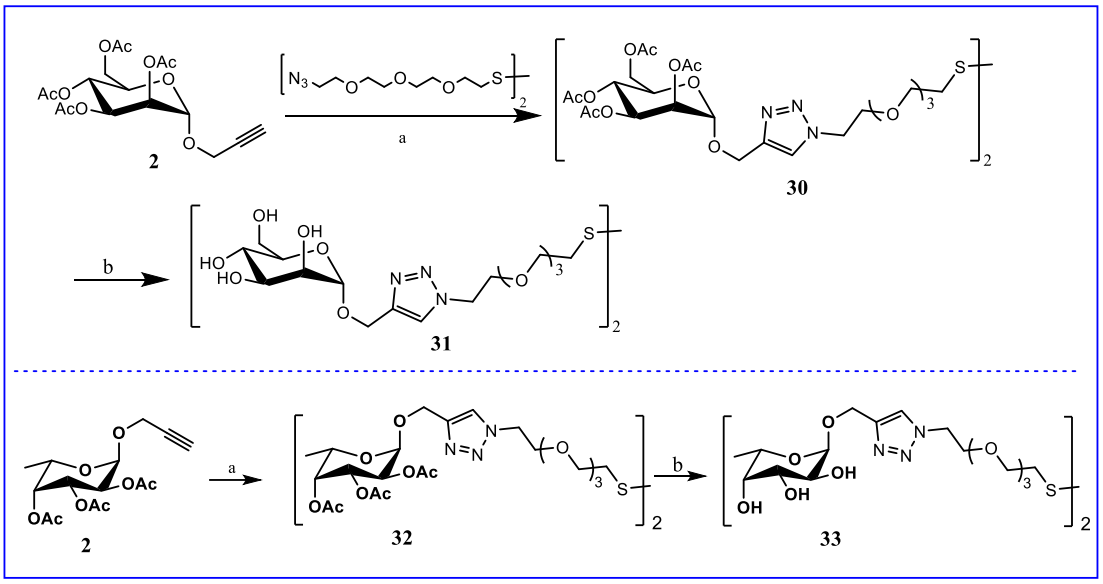
^{1}H NMR (500 MHz, DMSO-d_6)



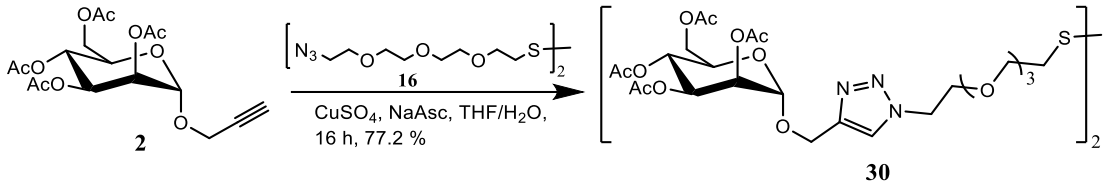
^{13}C NMR (125 MHz, DMSO-d_6)



S2.6. Synthesis of disulfide mannosides



a) $CuSO_4$, NaAsc, THF/H_2O; b) NaOMe / MeOH.



Bis-disulfide acetyl-α-D-mannosopyranoside 30. Molecule **2** (861 mg, 2.337 mmol, 3.5 eq) and disulfide linker **16** (312.9 mg, 0.668 mmol, 1 eq) was dissolved in THF (10 mL). A mixture of $CuSO_4$ (10.7 mg, 0.067 mmol, 0.1 eq) and NaAsc (79.3 mg, 0.401 mmol, 0.3 eq) in H_2O (0.2 mL) was added and the reaction mixture was stirred at room temperature under argon for 16 h. Then the THF was removed by evaporation. After the reaction mixture The residue was was extracted with DCM (100 mL × 3), washed sequence with NH_4Cl (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness. purified by column chromatography on silica gel (AcOEt/Cy/MeOH 30/10/0.1) affording the desired compound **30** (640 mg, 77.2 %) as a white powder.

Formula: $C_{50}H_{76}N_6O_{26}S_2$.

Mw: 1241.3 g/mol.

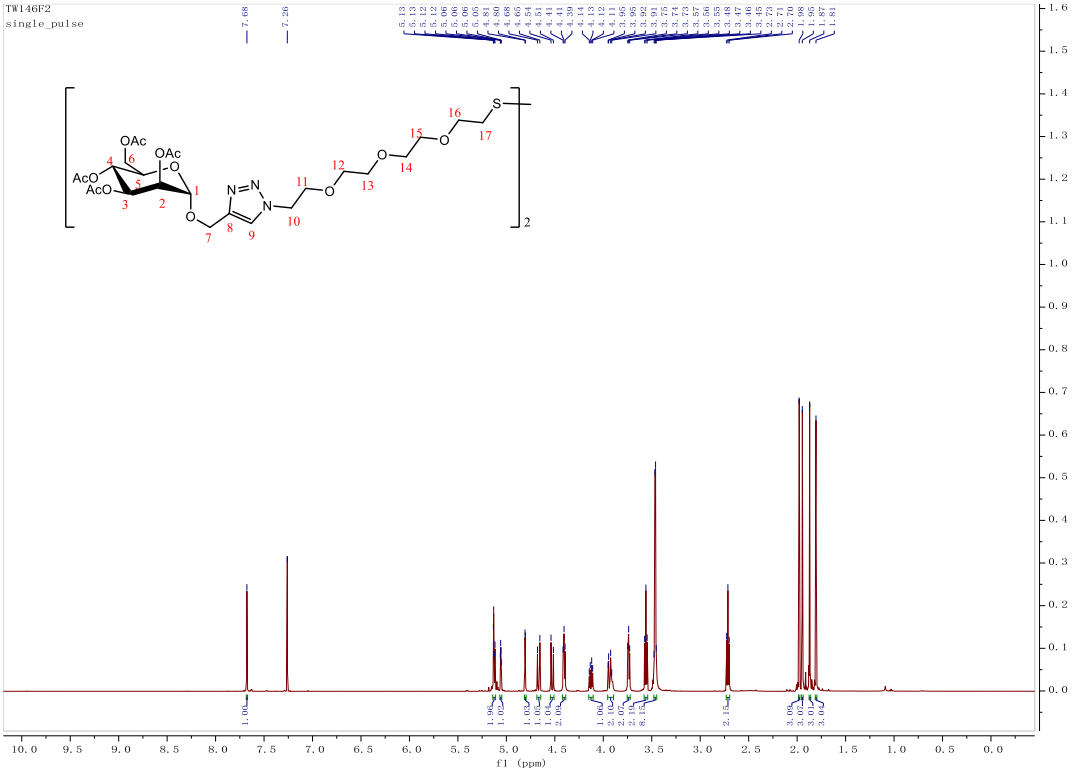
***R_f*:** 0.24 ($CHCl_3$/ MeOH 50:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.68 (s, 1H, H_{arom}), 5.14 – 5.11 (m, 2H, H-3, H-4), 5.07 – 5.05 (m, 1H, H-2), 4.81 (d, $J_{1,2}$ = 1.6 Hz, 1H, H-1), 4.67 (d, $J_{6a,6b}$ = 12.2 Hz, 1H, H-6a), 4.53 (d, $J_{6a,6b}$ = 12.3 Hz, 1H, H-6b), 4.42 – 4.39 (t, 2H, H-7), 4.15 – 4.10 (m, 1H, H-5), 3.95 – 3.89 (m, 2H, H-10), 3.75 – 3.72 (m, 2H, H-11), 3.56 (t, $J_{16,17}$ = 6.6 Hz, 2H, H-16), 3.46 (t, 8H, H-12, H-13, H-14, H-15), 2.71 (t, $J_{16,17}$ = 6.6 Hz, 2H, H-17), 1.98 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 1.87 (s, 3H, CH_3), 1.81 (s, 3H, CH_3).

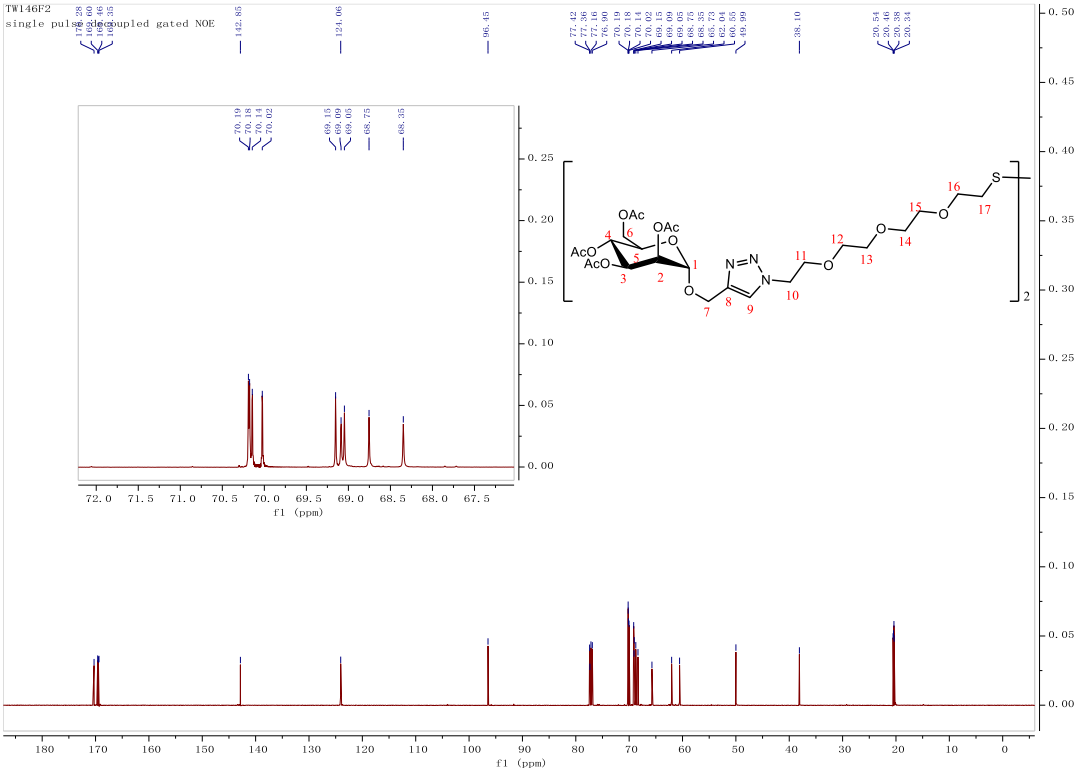
^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.28 (CO), 169.60 (CO), 169.46 (CO), 169.35 (CO), 142.85 (C_{arom}), 124.06 (C_{arom}), 96.45 (C-1), 70.18 (C-2), 70.14 (C-3), 70.02 (*CH_2*), 69.15 (*CH_2*), 69.09 (*CH_2*), 69.05 (*CH_2*), 68.75 (*CH_2*), 68.35 (C-4), 65.73 (C-5), 62.04 (C-6), 60.55 (C-7), 49.99 (C-10), 38.10 (C-17), 20.54, 20.46, 20.38, 20.34 (4 × *CH_3*).

HRMS: (ESI^+-MS, m/z) calcd for $C_{50}H_{77}N_6O_{26}S_2$ $[M+H]^+$: 1241.4329, found: 1241.4323.

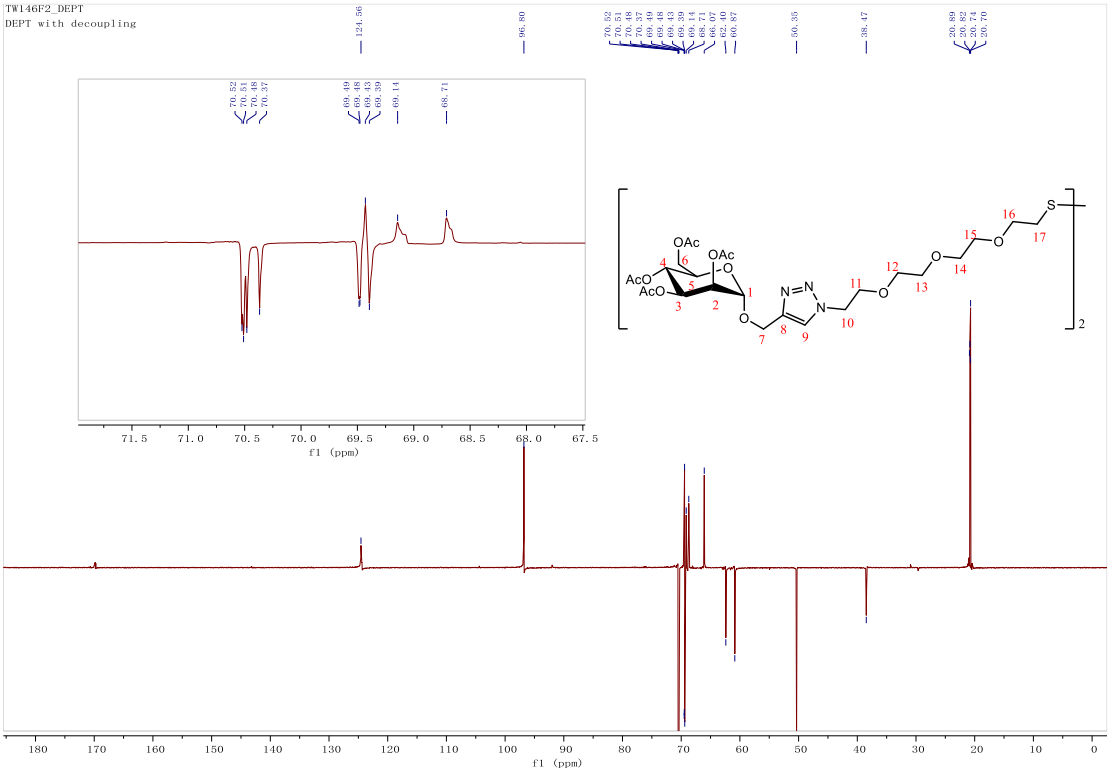
^{1}H NMR (500 MHz, $CDCl_3$)

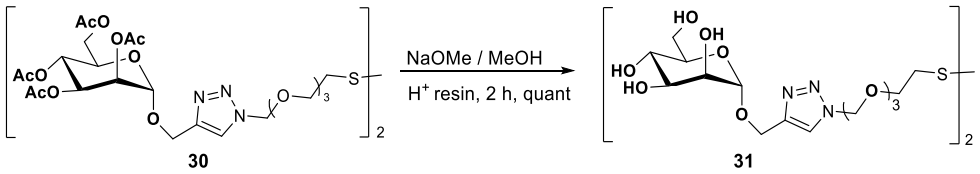


^{13}C NMR (125 MHz, $CDCl_3$)



DEPT 135 (125 MHz, $CDCl_3$)





Bis-disulfide α-D-mannosopyranoside 31. To a solution of **30** (630 mg, 0.5333 mmol, 1 eq) in dry MeOH (15 mL) under argon atmosphere was added sodium methoxide (86.4 mg, 1.6 mmol, 3 eq). The reaction mixture was then stirred at room temperature under argon for 2 h. The solution was concentrated under reduced pressure and the residue was purified by Dowex® 50WX8-200 (H^+ form). The resin was washed with a solution of MeOH (10 mL). The fractions containing the product were concentrated under reduced pressure to afford the desired product **31** (410 mg, quant.) as a white solid.

Formula: $C_{34}H_{60}O_{18}N_6S_2$

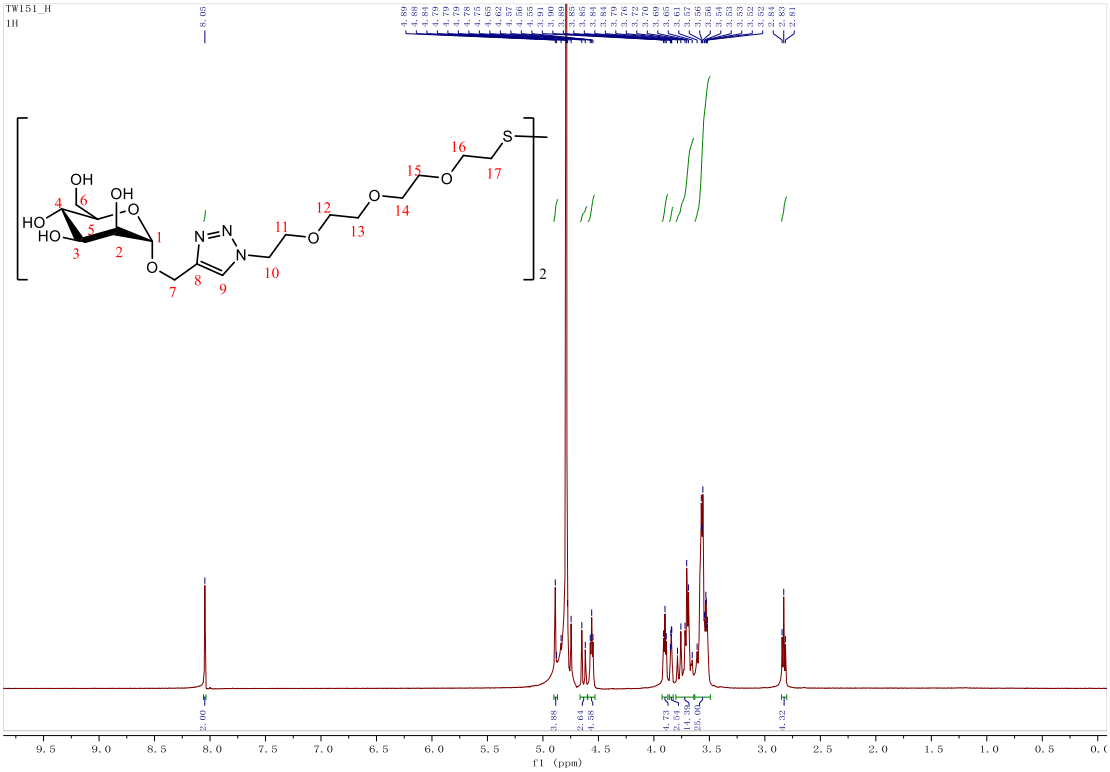
Mw: 904.35 g/mol

^{1}H NMR (500 MHz, D_2O) δ 8.05 (s, 2H, H_{arom}), 4.89 (d, *J* = 12.6 Hz, 2H, H-1), 4.61 (d, *J* = 12.6 Hz, 2H, H-2), 4.56 (m, 4H, H-3, H-4), 3.90-3.52 (m, 44H, H-5, H-6, *CH*$_2$), 2.80 (t, *J* = 6.3 Hz, 6H, 2×*CH*$_2$S).

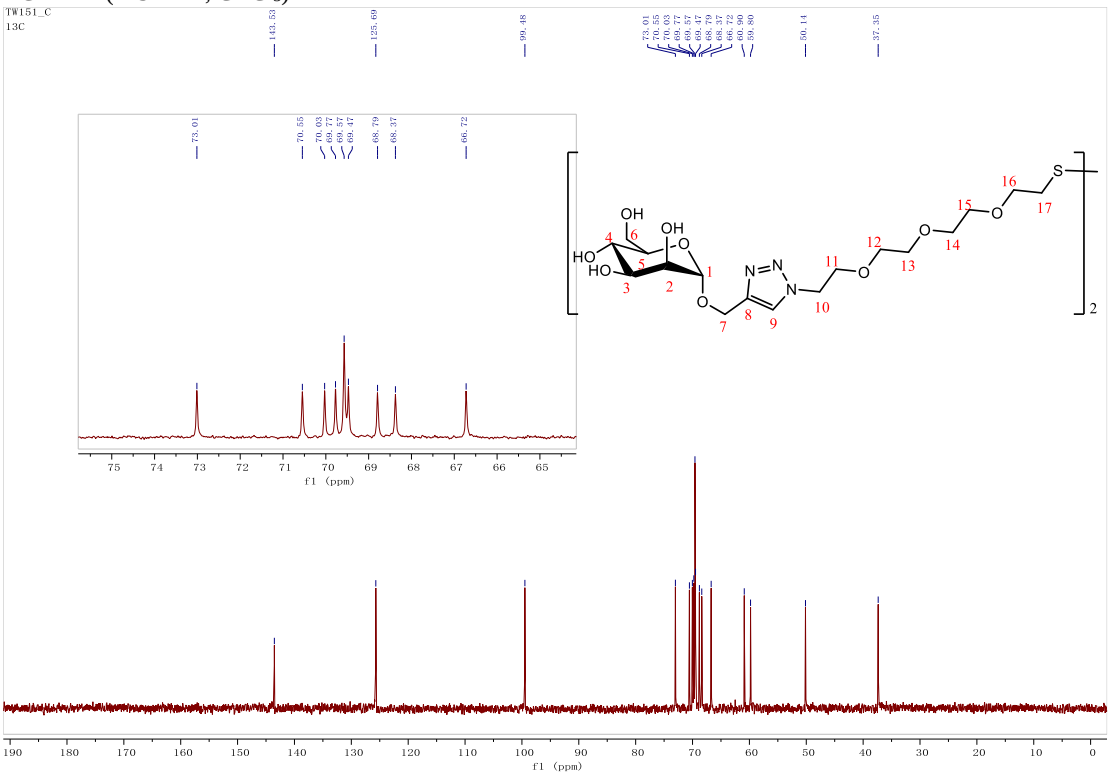
^{13}C NMR (125 MHz, D_2O) δ = 143.52 (C_{arom}), 125.69 (C_{arom}), 99.48 (C-1), 73.01 (C-2), 70.55 (C-3), 70.03 (*CH*$_2$), 69.77 (*CH*$_2$), 69.57 (*CH*$_2$), 69.47 (*CH*$_2$), 68.79 (*CH*$_2$), 68.37 (C-4), 66.72 (C-5), 60.90 (C-6), 59.80 (C-7), 50.14 (C-10), 37.35 (C-17).

HRMS: (ESI$^+$-MS, m/z) calcd for $C_{34}H_{61}N_6O_{18}S_2$ $[M+H]^+$: 905.3484, found: 905.3478.

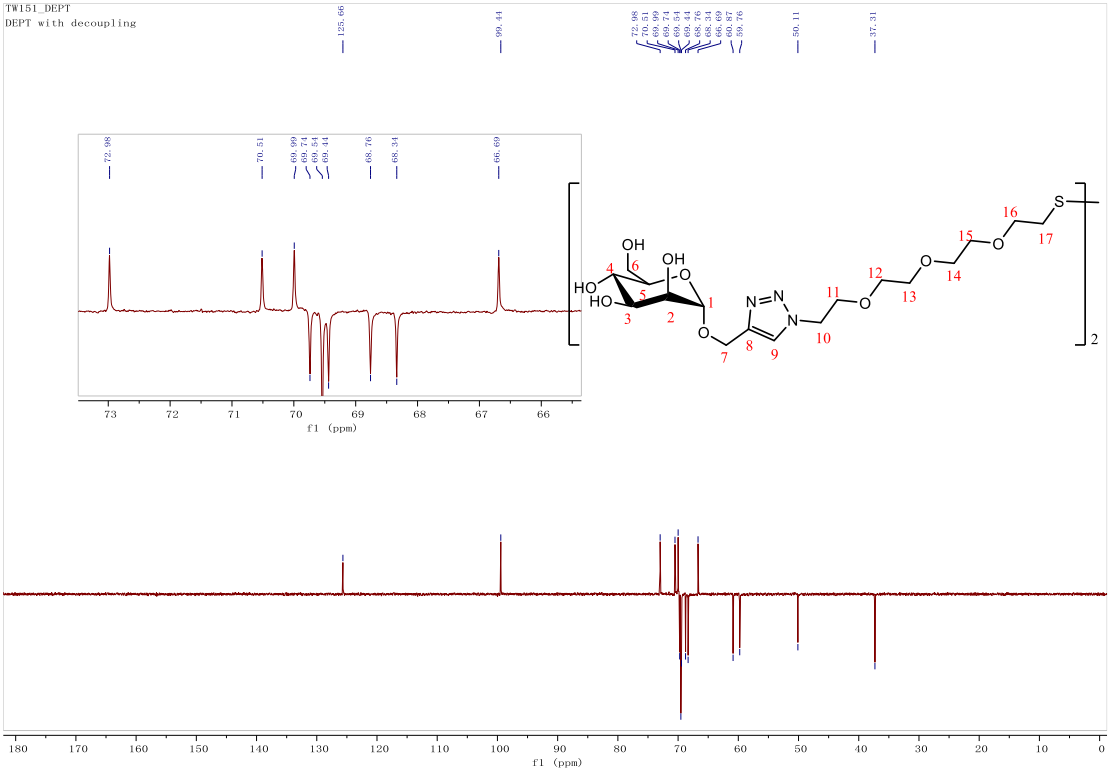
^{1}H NMR (500 MHz, D_2O)

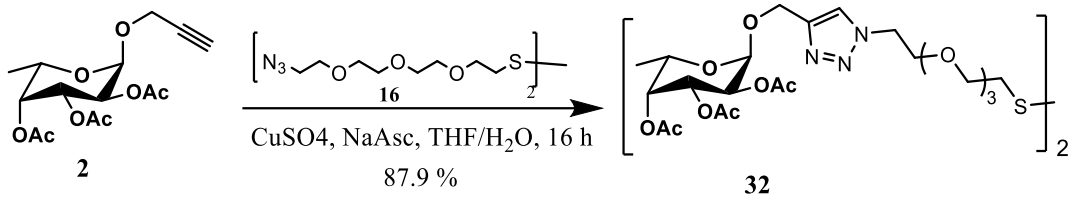


^{13}C NMR (125 MHz, $CDCl_3$)



DEPT 135 (125 MHz, $CDCl_3$)





Bis-disulfide 2,3,4-tri-*O*-acetyl-α-L-fucosopyranoside 32. Molecule 12 (879.4 mg, 2.6785 mmol, 3 eq) and disulfide linker **16** (418.37 mg, 0.8928 mmol, 1 eq) was dissolved in THF (10 mL). A mixture of $CuSO_4$ (14.25 mg, 0.08928 mmol, 0.1 eq) and NaAsc (106.26 mg, 0.53569 mmol, 0.3 eq) in H_2O (0.2 mL) was added and the reaction mixture was stirred at room temperature under argon for 16 h. Then the THF was removed by evaporation. After the reaction mixture was extracted with DCM (100 mL ×3), washed sequence with NH_4Cl (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residue was purified by column chromatography on silica gel (AcOEt/Cy/MeOH 30/1/0.1) affording the desired compound **32** (800 mg, 87.9 %) as a white powder.

Formula: $C_{46}H_{72}N_6O_{24}S_2$

Mw: 1125.22 g/mol;

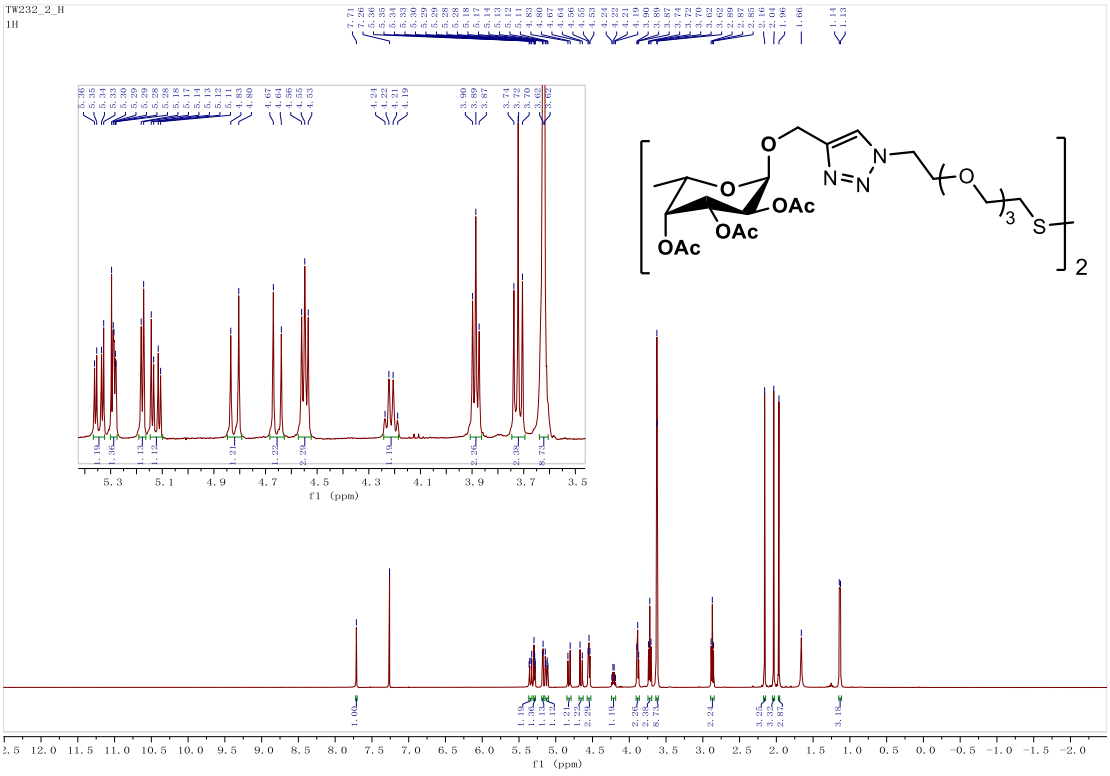
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H, H_{arom}), 5.34 (dd, J = 10.8, 3.4 Hz, 1H, H-3), 5.29 (m, 1H, H-4), 5.18 (d, J = 3.7 Hz, 1H, H-1), 5.12 (dd, J = 10.8, 3.7 Hz, 1H, H-2), 4.82 (d, J = 12.4 Hz, 1H, H_{6a}), 4.65 (d, J = 12.4 Hz, 1H, H_{6b}), 4.55 (m, 2H, H-7), 4.21 (q, J = 7.0, 6.5 Hz, 1H, H-5), 3.89 (t, J = 5.1 Hz, 2H, H-10), 3.72 (t, J = 6.6 Hz, 2H, H-16), 3.62 (d, J = 1.9 Hz, 8H, H-11, H-

12, H-13,H-14, H-15), 2.87 (t, J = 6.6 Hz, 2H, H-17), 2.16 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 1.96 (s, 3H, CH_3), 1.14 (d, J = 6.5 Hz, 3H, CH_3).

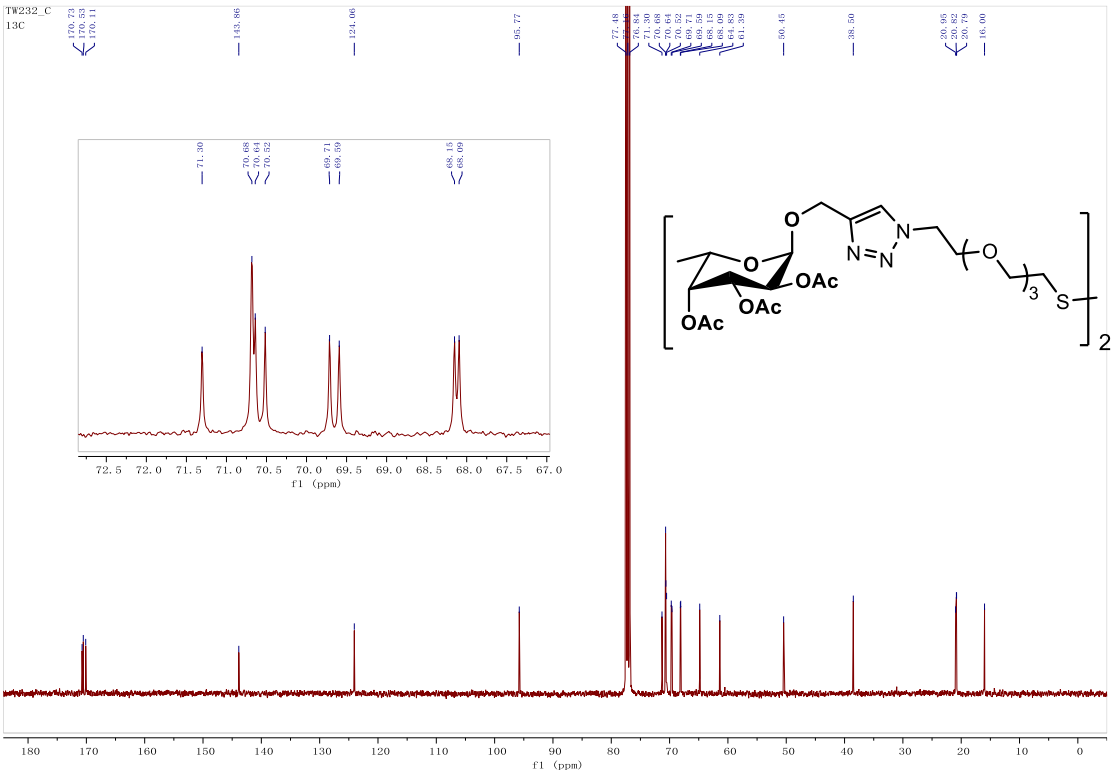
^{13}C NMR (100 MHz, $CDCl_3$) δ= 170.73 (CO), 170.53 (CO), 170.11 (CO), 143.86 (C_{arom}), 124.06 (C_{arom}), 95.77 (C-1), 71.30 (C-2), 70.68, 70.64, 70.52, 69.71, 69.59, 68.15, 68.09 (C-3), 64.83 (C-4), 61.39 (C-5), 50.45 (C-10), 38.50 (C-17), 20.95, 20.82, 20.79, 16.00 (4×*CH_3*).

HRMS: (ESI^+-MS, m/z) calcd for $C_{46}H_{73}N_6O_{22}S_2$ $[M+H]^+$: 1125.4219, found: 1125.4214.

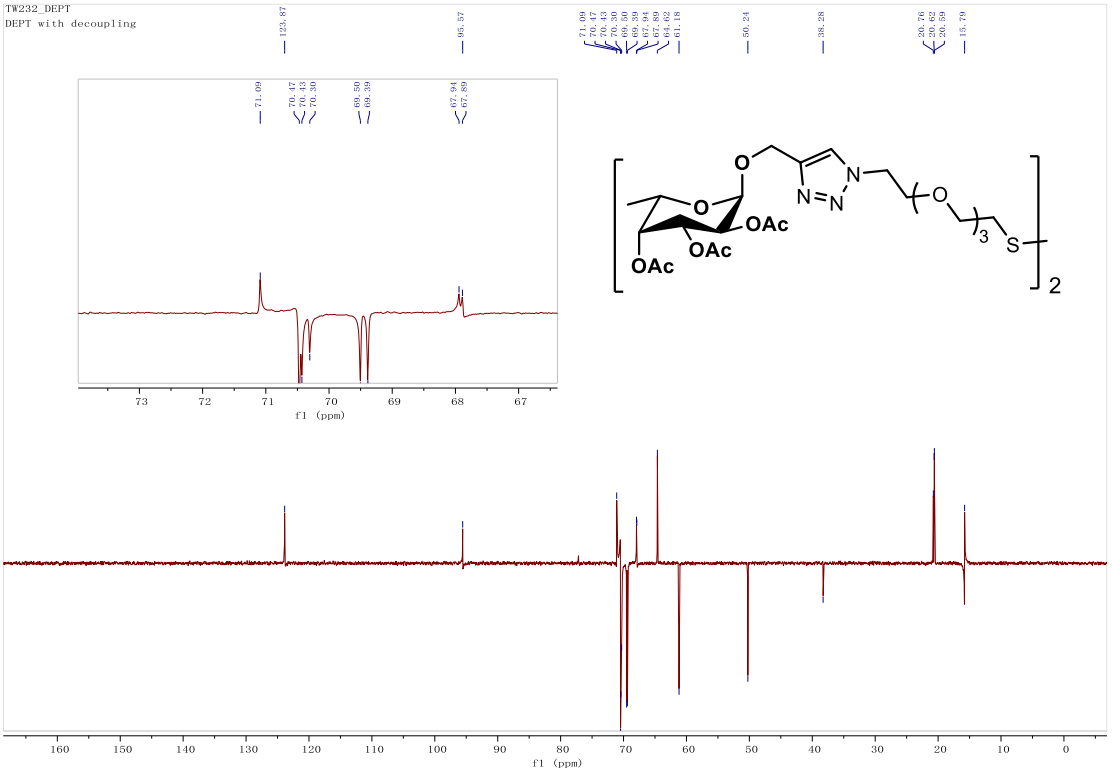
^{1}H NMR (400 MHz, $CDCl_3$)

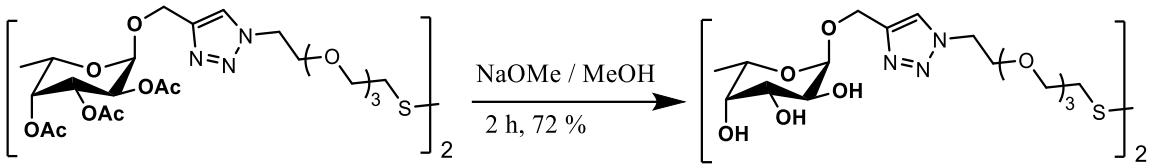


^{13}C NMR (100 MHz, $CDCl_3$)



DEPT 135 (100 MHz, $CDCl_3$)





32 **33**

Bis-disulfide α-L-fucosopyranoside 33. To a solution of **32** (839.6 mg, 0.7461 mmol, 1 eq) in dry MeOH (15 mL) under argon atmosphere was added sodium methoxide (80.6 mg, 1.4923 mmol, 3 eq). The reaction mixture was then stirred at room temperature under argon for 2 h. The solution was concentrated under reduced pressure and the residue was purified by Dowex® 50WX8-200 (H^+ form). The resin was washed with a solution of MeOH (10 mL). The fractions containing the product were concentrated under reduced pressure to afford the desired product **33** (470 mg, 72 %) as a white solid.

Formula: $C_{34}H_{60}N_6O_{16}S_2$

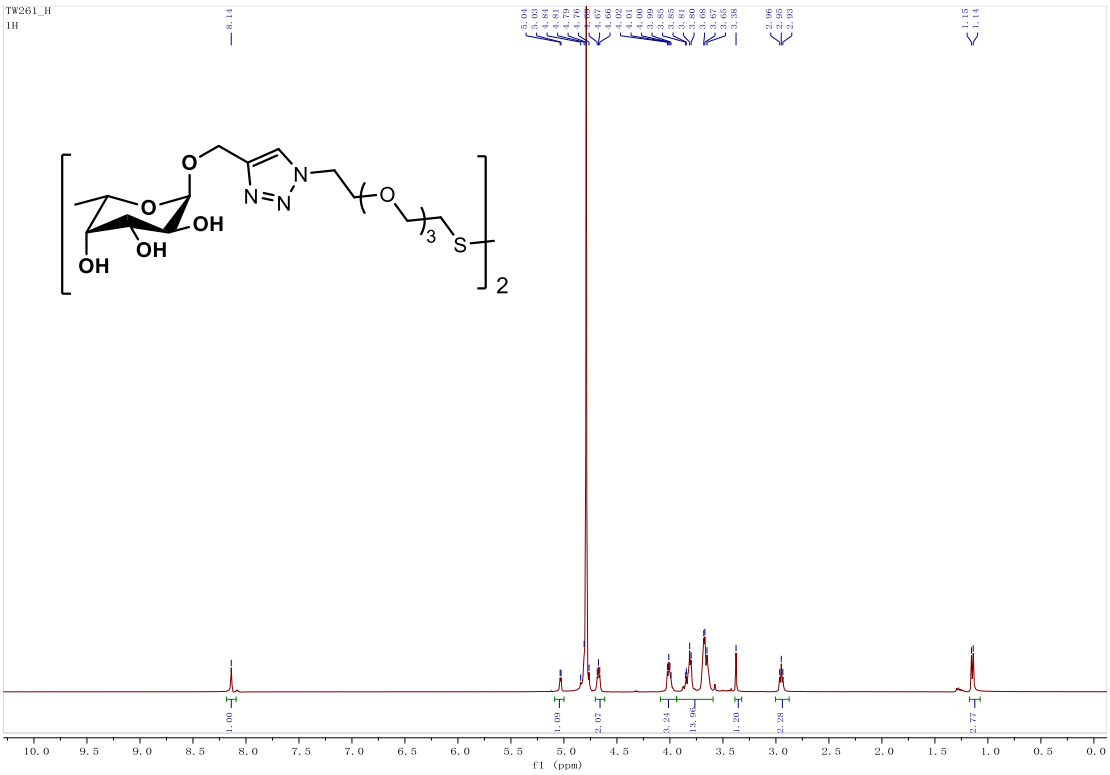
Mw: 873 g/mol;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, H_{arom}), 5.04 (dd, *J* = 10.8, 3.4 Hz, 1H, H-3), 4.67 (m, 1H, H-4), 4.01 (d, *J* = 3.7 Hz, 1H, H-1), 5.12 (dd, *J* = 10.8, 3.7 Hz, 1H, H-2), 4.82 (d, *J* = 12.4 Hz, 1H, H_{6a}), 4.65 (d, *J* = 12.4 Hz, 1H, H_{6b}), 4.55 (m, 2H, H-7), 4.21 (q, *J* = 7.0, 6.5 Hz, 1H, H-5), 3.89 (t, *J* = 5.1 Hz, 2H, H-10), 3.72 (t, *J* = 6.6 Hz, 2H, H-16), 3.62 (d, *J* = 1.9 Hz, 8H, H-11, H-12, H-13,H-14, H-15), 2.87 (t, *J* = 6.6 Hz, 2H, H-17), 2.16 (s, 3H, *CH*$_3$), 2.04 (s, 3H, *CH*$_3$), 1.96 (s, 3H, *CH*$_3$), 1.14 (d, *J* = 6.5 Hz, 3H, *CH*$_3$).

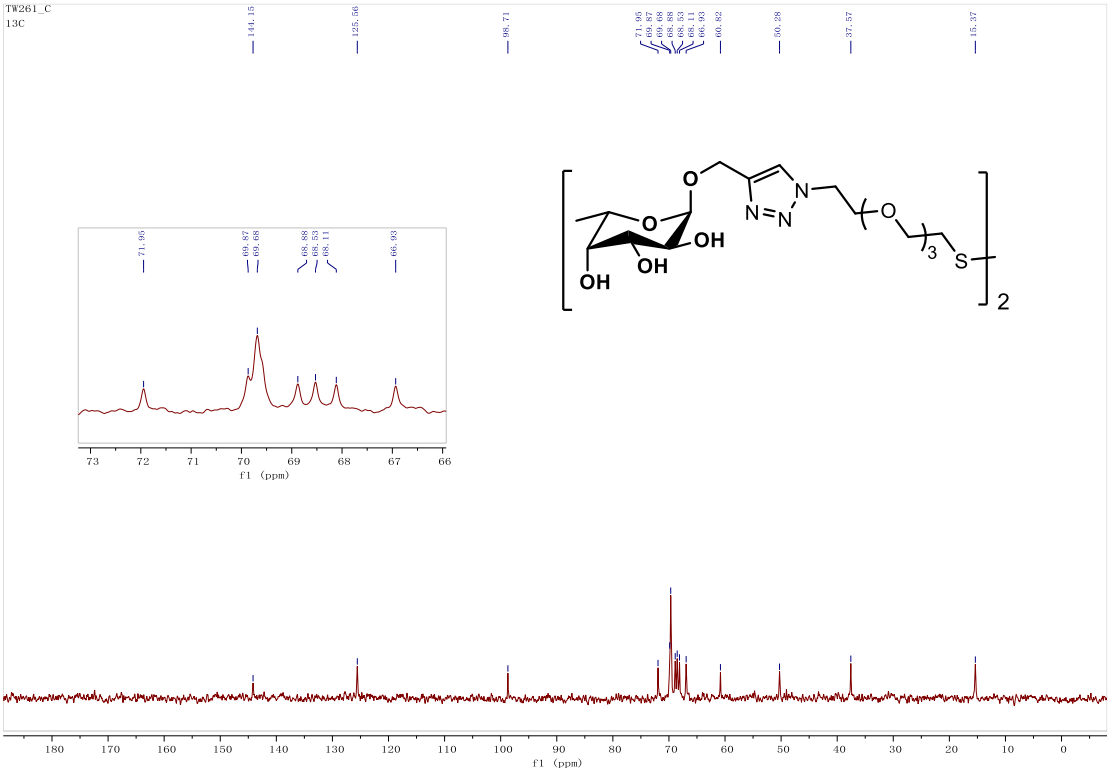
^{13}C NMR (100 MHz, D_2O) δ = 144.15 (C_{arom}), 125.56 (C_{arom}), 98.71 (C-1), 71.95, 69.87, 69.68, 68.88, 68.53, 68.11, 66.93, 60.82 (C-7), 50.28 (C-10), 37.57 (C-17), 15.37 (C-6).

HRMS: (ESI^+-MS, m/z) calcd for $C_{34}H_{61}N_6O_{16}S_2$ $[M+H]^+$: 873.3585, found: 873.3580.

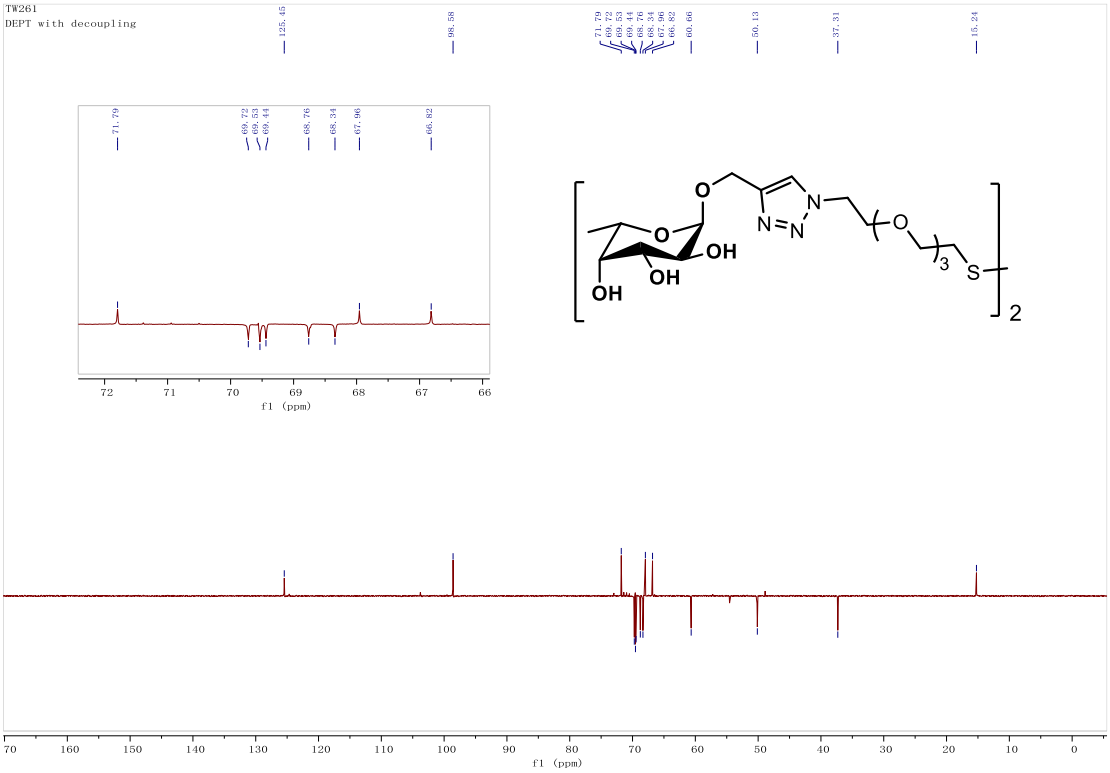
^{1}H NMR (400 MHz, D_2O)



^{13}C NMR (100 MHz, D_2O)



DEPT 135 (100 MHz, D_2O)



S3. Synthesis of Gold Nanoparticles

Materials and Reagents

Hydrogen tetrachloroaurate(III) tetrahydrate ($HAuCl_4 \cdot 3H_2O$, 99.99 %) was obtained from Sigma as well as citric acid and hydroquinone. Ultra-pure water was prepared by Milli-QA (Molsheim, France).

Instrumentation

Ultraviolet-visible (UV-Vis) absorption spectra were obtained using a Varian Cary 50 spectrophotometer (CA, USA). XPS analysis was obtained by X ray photoelectron spectroscope (XPS) from Thermo Fisher Scientific (East Grinstead, UK). Transmission electron microscopic images were obtained using TECNAI 10 transmission electron microscope (TEM) from JEOL (Tokyo, Japan). the hydrodynamic size of the generated NPs was determined using the NanoPlus HD system (Brea, CA, USA.).

S3.1. Preparation of Citrate stabilised 20 nm gold nanoparticles

20 nm AuNPs were prepared by a classical citrate reduction method following a reported protocol.[7] Briefly, 1000 mL of 0.01% (w/v) $HAuCl_4 \cdot 3H_2O$ solution was heated to ebullition and 27 mL of 1% (w/v) sodium citrate solution was quickly added under vigorous stirring, and maintained under reflux during 30 min (time after which the color of the solution did not change). Then, the solution was allowed to cool down to room temperature with stirring. The concentration of the resulting 20 nm AuNP solution was calculated according to the Haiss equation from the measured UV spectrum.

S3.2. Preparation of Citrate-stabilised 15 nm gold seed nanoparticles

15 nm gold seed nanoparticles were synthesized using the reported citrate reduction method.[8] Briefly, 1 mL of 1% (w/v) $HAuCl_4 \cdot 3H_2O$ solution in 100 mL Milli-Q water was heated to reflux and 3 mL of 1% (w/v) sodium citrate solution was quickly added under vigorous stirring. The resulting solution was refluxed for 15 to 30 minutes. Then, the solution was allowed to cool down to room temperature with stirring. Finally, the 15 nm gold nanoparticles were kept as the seed solution to prepare the 60 nm and 90 nm gold nanoparticles.

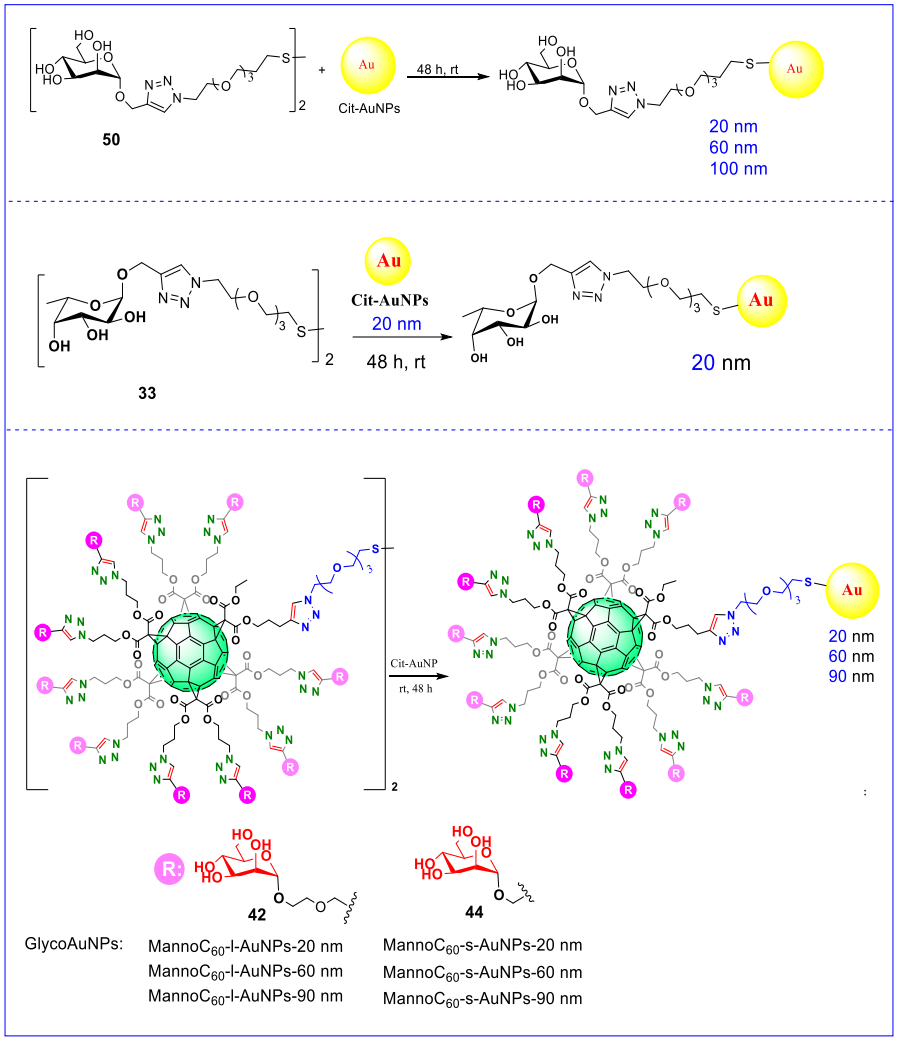
S3.3. Preparation of 60 nm gold nanoparticles

The 60 nm gold nanoparticles were synthesized by surface-assisted reduction of ionic gold by hydroquinone.[8-9] Briefly, 9 mL of a 1% (w/v) $HAuCl_4 \cdot 3H_2O$ solution was added to 869 mL Milli-Q water. 12.86 mL of particle seeds were then added and the reaction mixture was vigorously stirred at room temperature. Sodium citrate (15 mM, 9 mL) was then added, immediately followed by 9 mL of 25 mM hydroquinone. The reaction solution was stirred overnight at room temperature to complete the reduction of ionic gold and particle growth.

S3.4. Preparation of 90 nm gold nanoparticles

The 90 nm gold nanoparticles were synthesized by surface-assisted reduction of ionic gold by hydroquinone.[8-9] Briefly, 9 mL of a 1% (W/V) $HAuCl_4 \cdot 3H_2O$ solution was added to 868 mL Milli-Q water. 3.76 mL of particle seeds were then added to the above solution and the reaction mixture was vigorously stirred at room temperature. 9 mL of 15 mM sodium citrate was then added, immediately followed by 9 mL of 25 mM hydroquinone. The reaction solution was stirred overnight at room temperature to complete the reduction of ionic gold and particle growth.

S4. Synthesis of Gold Glyconanoparticles



S4.1. GlycoAuNPs-20 nm

Each disulfide ligand (10 mg) was dissolved in 1 mL of Milli-Q water and the pH was adjusted to 9 using 0.1 M NaOH. Then, the 5 mL of stock AuNP (diameter 20 nm, 20 nM) was added and continuously stirred at room temperature for 48 h. The solution was centrifuged through a centrifugal filter (Amicon, 5000 RPM, 30 kD, 4 ℃, 30 min). The residue was washed five times with Tris buffer (20 mM, pH=7.4, 10 ml each time) and centrifuged. After, the residue was washed with milliQ water and centrifuged to remove the Tris buffer. The residue was dissolved in 1 mL Milli-Q water and lyophilized.

S4.2. GlycoAuNPs-60 nm

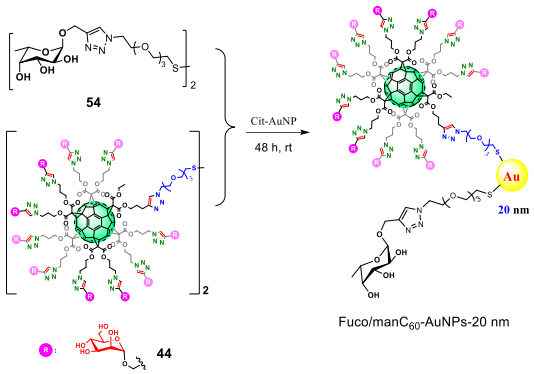
The disulfide ligand (10 mg) was dissolved in 1 mL of Milli-Q water using 0.1 M NaOH to adjust pH to 9. Then, 5 mL of stock AuNP (diameter 60 nm, 5 nM) was added and continuously stirred at room temperature for 48 h. The solution was centrifuged (3500 RPM, 4 ℃, 45 min). The residue was washed three times with Tris buffer (20 mM, pH=7.4, 10 ml each time). After, the

residue was washed with milliQ water and centrifuged to remove the Tris buffer. The residue was dissolved in 1 mL Milli-Q water and lyophilized.

S4.3 GlycoAuNPs-90 nm

The disulfide galactoside ligand (10 mg) was dissolved in 1 mL of Milli-Q water using 0.1 M NaOH to adjust pH to 9. Then, 5 mL of stock AuNP (diameter 20 nm, 20 nM) was added and continuously stirred at room temperature for 48 h. The solution was centrifuged (2000 RPM, 30 kD, 4 ℃, 30 min). The residue was washed three times with Tris buffer (20 mM, pH=7.4, 10 ml each time) and centrifuged. Then, the residue was washed with milliQ water and centrifuged to remove the Tris buffer. The residue was dissolved in 1 mL Milli-Q water and lyophilized.

S4.4 Heteromultivalent glycoAuNPs



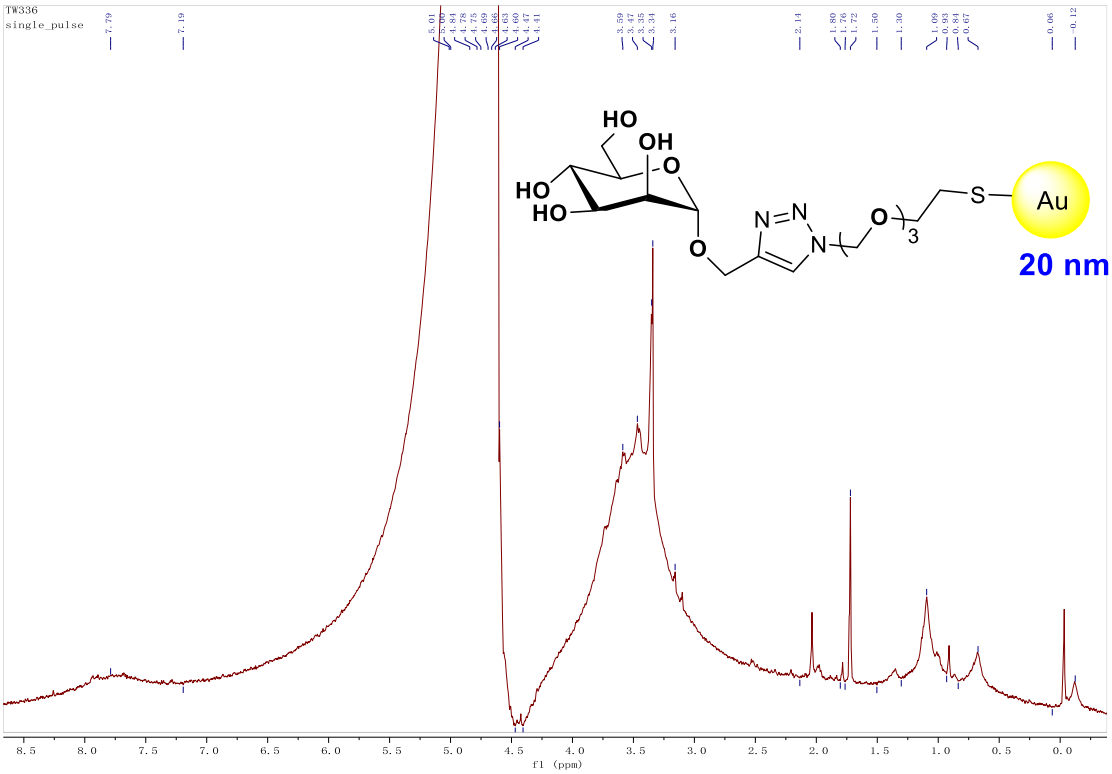
Disulfide fucoside **54** (1.86 mg) and disulfide mannofullerene **44** (20 mg) were mixed (equimolar ratio) and the pH was adjusted to 9-10 with a 0.5M K_2CO_3 solution. The resulting solution was added to the 20 nm cit-AuNPs and continuously stirred at room temperature for 48 h. The solution was centrifuged through a centrifugal filter (After, 5000 RPM, 30 kD, 4 ℃, 30 min). The residue was washed three times with Tris buffer (20 mM, pH=7.4, 10 mL each time) and centrifuged. The fourth time, milliQ water was used to remove the Tris buffer. The residue was dissolved in 1 mL Milli-Q water and lyophilized, to afford the desired glycoAuNPs as brown powder.

S5. Characterization of AuNPs and glycoAuNPs

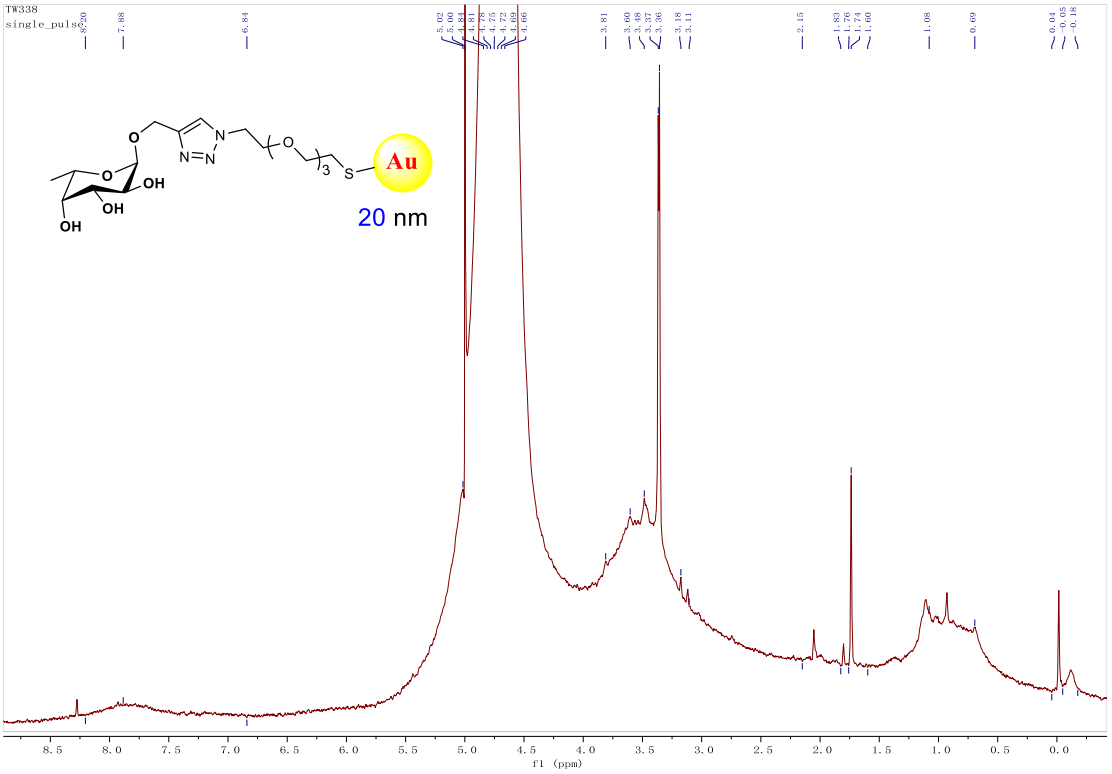
S5.1. Sample preparation for ^{1}H NMR

The produced glycoAuNPs were solubilized in deuterated water (D_2O), and were analyzed using a 500 MHz Jeol NMR spectrometer.

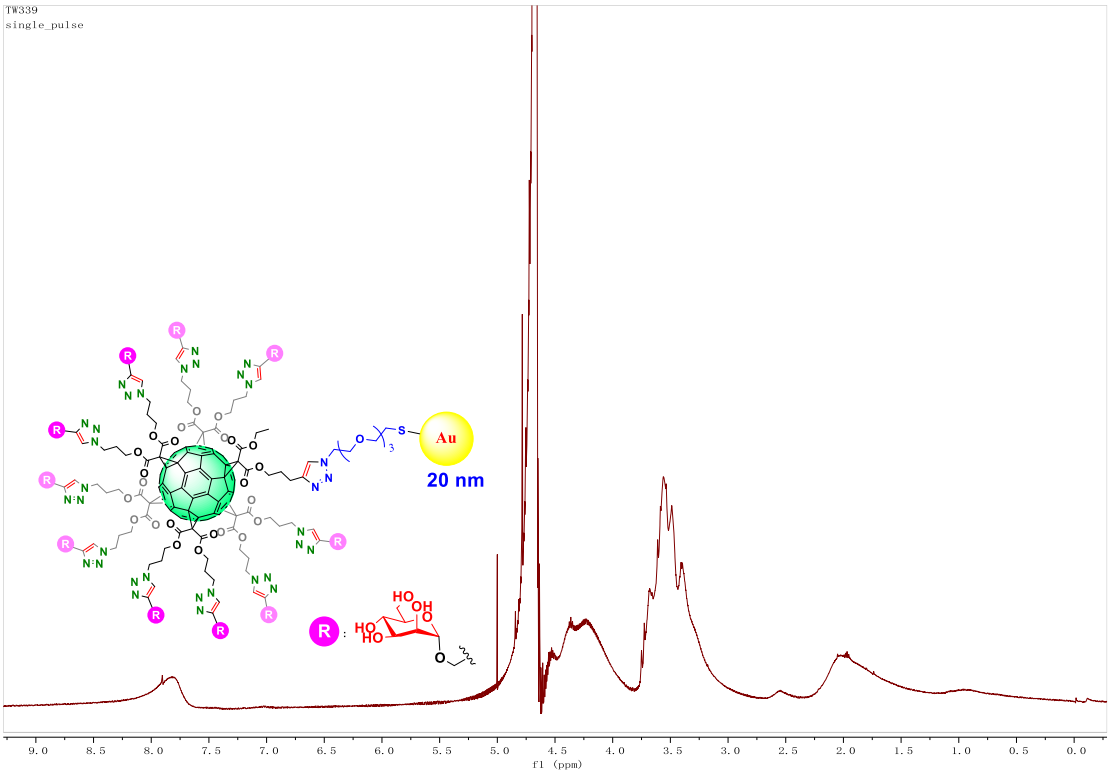
^{1}H NMR (500 MHz, D_2O) Manno-AuNPs-**20** nm



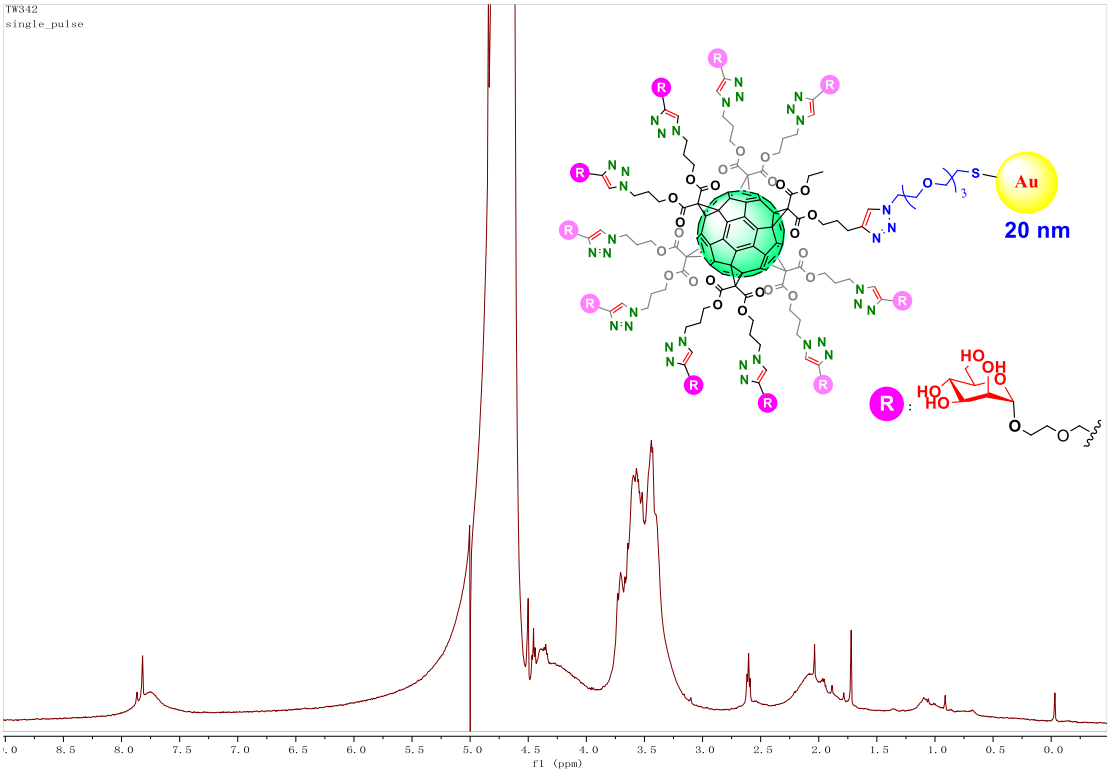
^{1}H NMR (500 MHz, D_2O) Fuco-AuNPs-20 nm



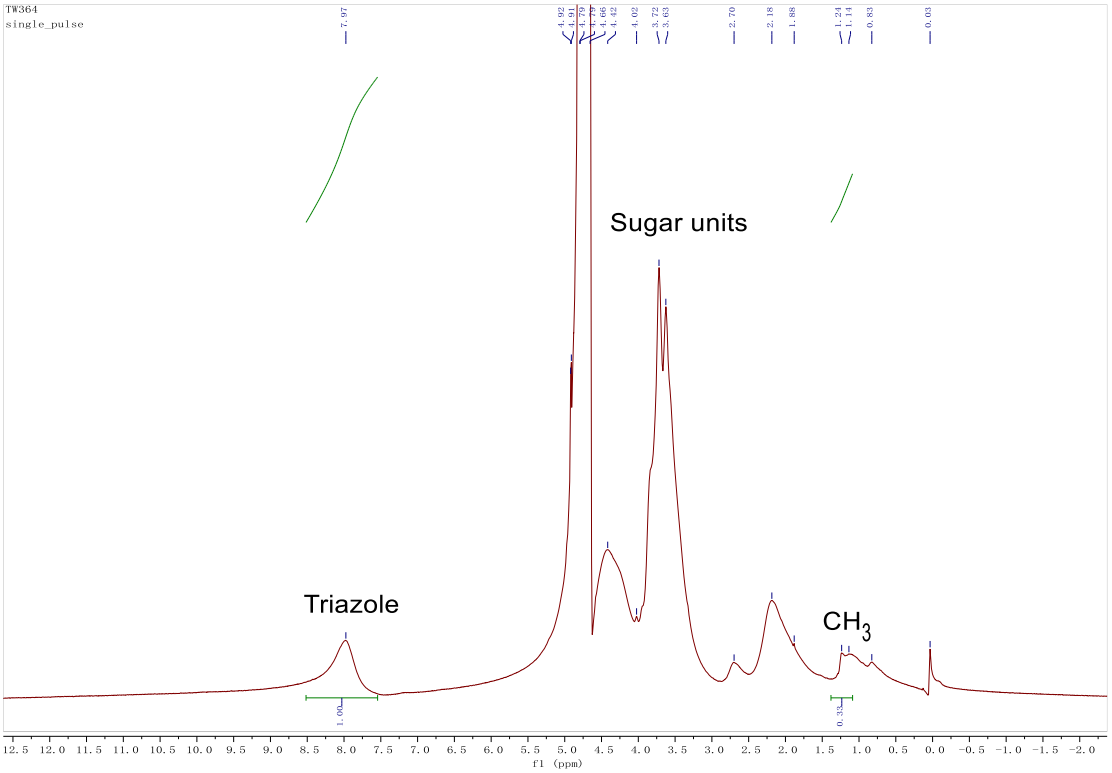
^{1}H NMR (500 MHz, D_2O) MannoC$_{60}$-s-AuNPs-**20** nm



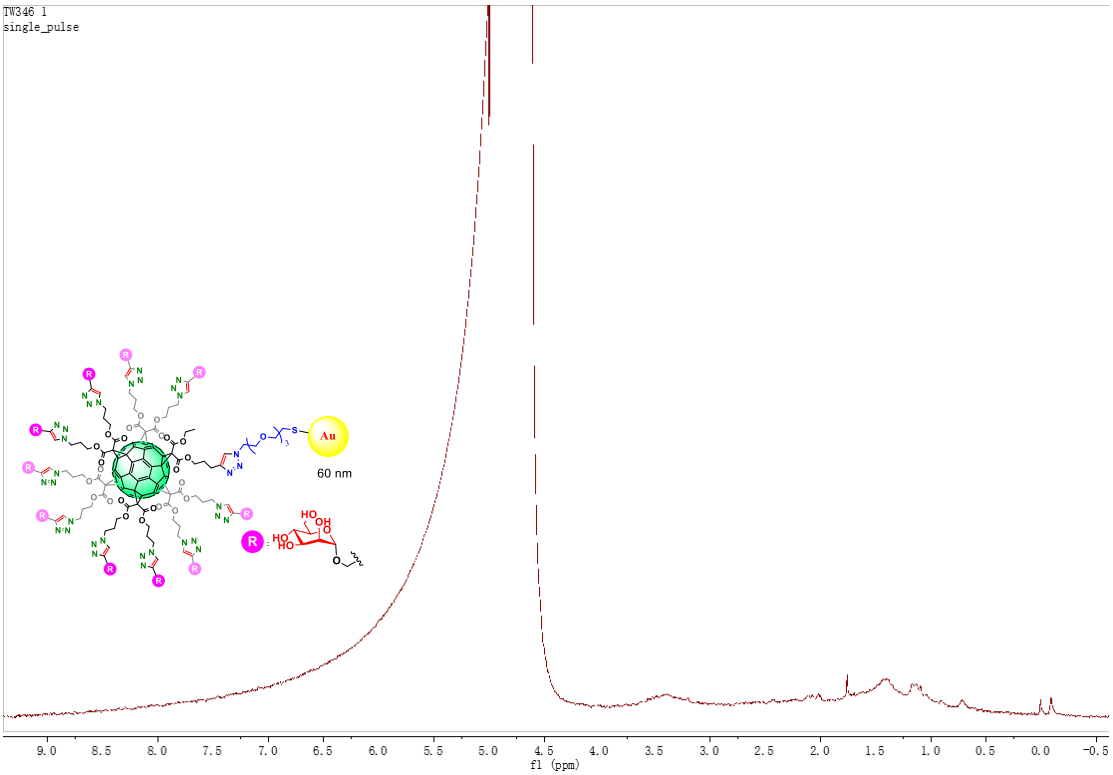
^{1}H NMR (500 MHz, D_2O) MannoC$_{60}$-l-AuNPs-**20** nm



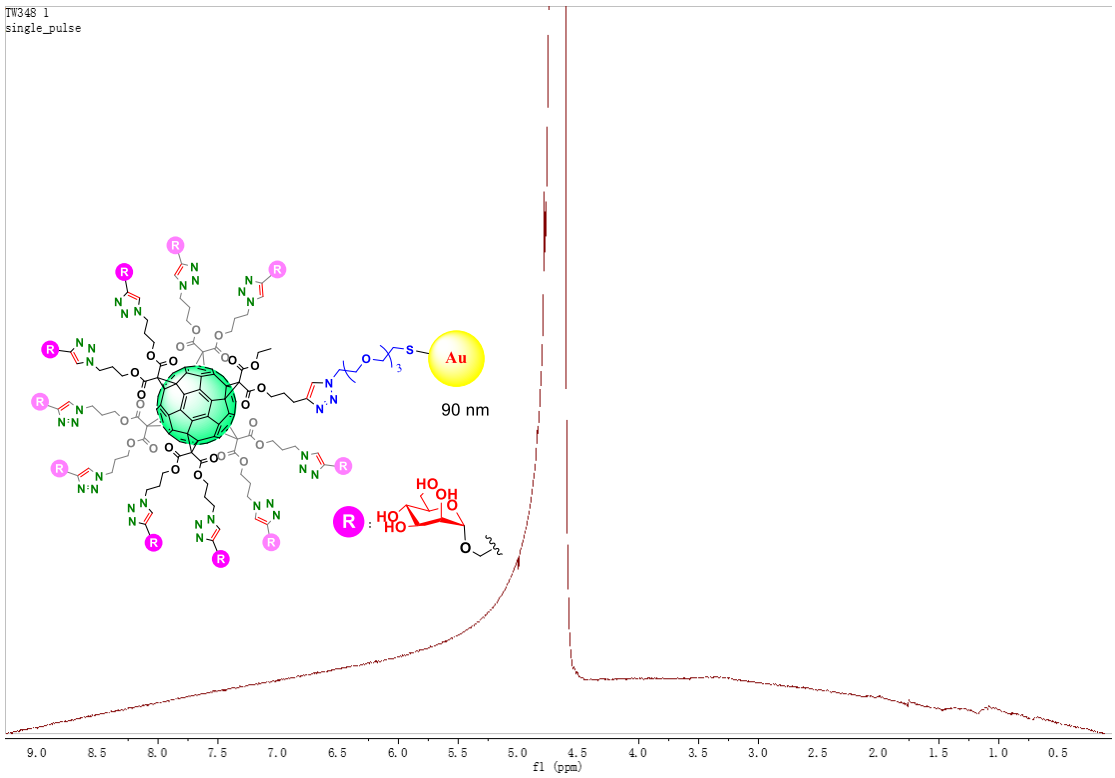
^{1}H NMR (500 MHz, D_2O) Fuco/ManC_{60}-AuNPs-20 nm



^{1}H NMR (500 MHz, D_2O) MannoC_{60}-s-AuNPs-**60** nm



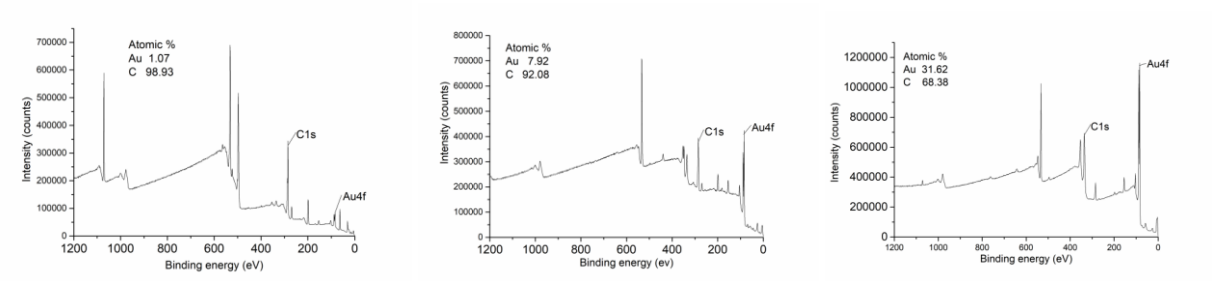
^{1}H NMR (500 MHz, D_2O) MannoC$_{60}$-s-AuNPs-**90** nm



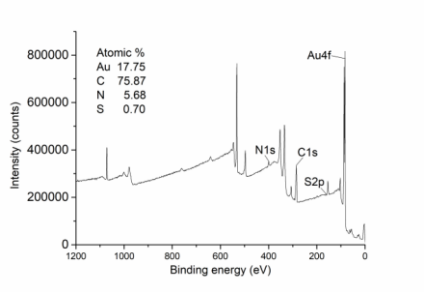
S5.2. Characterization of glycoAuNPs by XPS

Preparation of the glycoAuNPs samples for XPS analysis: aqueous solutions of glyco-AuNPs (1 mg/mL, 2 µL) were deposited on a silicon wafer that had been previously washed by a piranha solution consisting of the mixture of sulfuric acid (H_2SO_4, 95 %) and hydrogen peroxide (H_2O_2, 35 %) (3:1, v/v). The sample on the wafer was dried in a drying cabinet at room temperature. The procedure was repeated 10 times.[10-11] X-ray photoelectron spectroscopy (XPS) characterization was carried out with a Thermo Fisher ESCALAB 250 Xi instrument with a monochromatic Al Kα x-ray source (1486.6 eV).

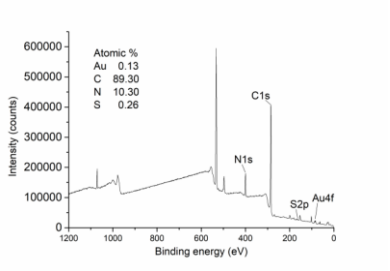
XPS graph show the atomic % of C, N and Au of glycoAuNPs



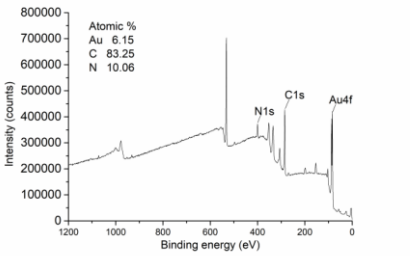
20 nm cit-AuNPs **60 nm cit-AuNPs** **100 nm cit-AuNPs**



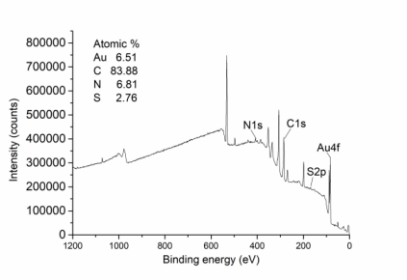
Manno-AuNPs-**20** nm



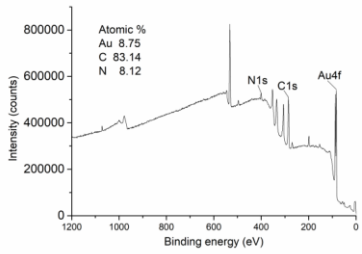
MannoC$_{60}$-s-AuNPs-**20** nm



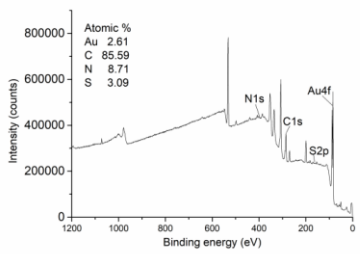
MannoC$_{60}$-l-AuNPs-**20** nm



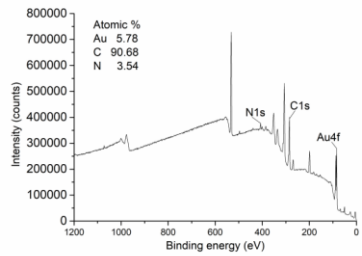
Manno-AuNPs-**60** nm



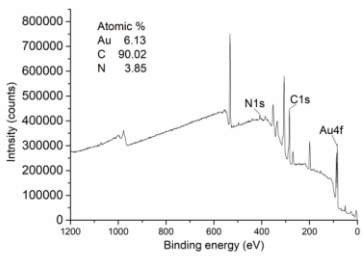
MannoC$_{60}$-s-AuNPs-**60** nm



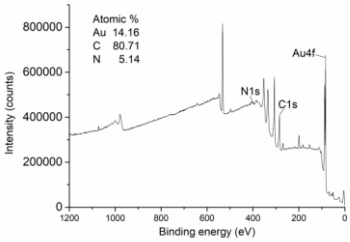
Manno-AuNPs-**100** nm



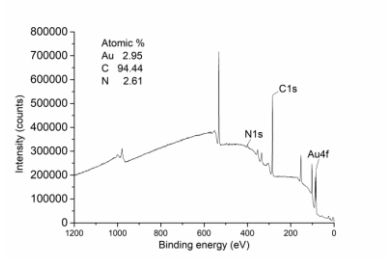
MannoC$_{60}$-s-AuNPs-**100** nm



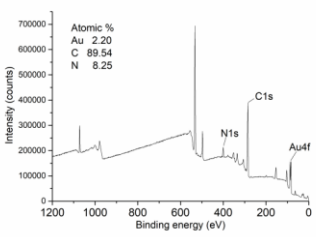
MannoC$_{60}$-l-AuNPs-**60** nm



MannoC$_{60}$-l-AuNPs-**100** nm

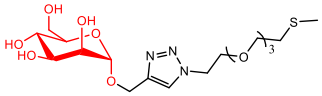
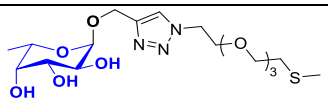
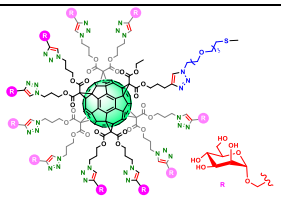
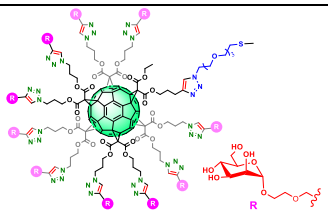
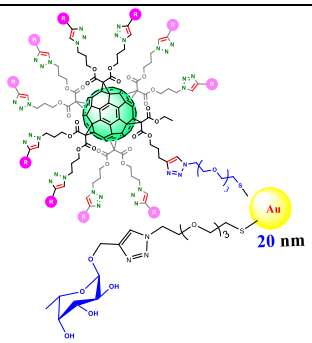


ManC$_{60}$-Fuco-AuNPs-**20** nm



Fuco-AuNPs-**20** nm

Table 1. Summary the ratio of N to Au for glycoAuNPs as determined by the relative integrations of the XPS AuNPs and N1s peaks.

Entries	Structure of ligands	GlycoAuNPs	N:Au	S 2p signa
1		Manno-AuNPs-**20** nm Manno-AuNPs-**60** nm Manno-AuNPs-**100** nm	0.32:1 1.05:1 3.34:1	Yes Yes Yes
2		Fuco-AuNPs-20 nm	3.75:1	No
3		MannoC_{60}-s-AuNPs-**20** nm MannoC_{60}-s-AuNPs-**60** nm MannoC_{60}-s-AuNPs-**100** nm	79.23:1 0.93:1 0.61:1	Yes No No
4		MannoC_{60}-l-AuNPs-**20** nm MannoC_{60}-l-AuNPs-**60** nm MannoC_{60}-l-AuNPs-**100** nm	1.65:1 0.63:1 0.36:1	No No No
5		ManC_{60}/Fuco-AuNPs-**20** nm	0.88:1	No

In addition, the surface density of ligands in AuNPs can be estimated using reported methods.[12-13] The gold atom are close-packed and form (Face Centred Cubic) in NPs.[14] The number of gold atoms,

$N_{Au} = (V_{NP} \times APF)/V_{Au} = (4\pi r_{NP}^3/3 \times 0.37405)/(4\pi r_{NP}^3/3) = (d_{NP}/2nm)^3 \times 0.74505/(0.144)^3$

$= (d_{NP}/nm)^3 \times 31$

where V_{NP} is the volume of a shere gold NP, V_{Au} is the volume of a gold atom, APF is the atomic packing factor, r_{NP} and d_{NP} are the radius and the diameter of a sphere gold NP (measured by TEM), and r_{Au} is the radius of a gold atom.

The number N_S of thiolate ligands per particle, $N_s = N_{Au} \times X$, X is the molar ratio of S to Au in NPs, M is the number ratio of N to S in each ligand molecule.[12-13] In our project, The number N_l of ligands per particle can be deduced by the molar ratio of N to Au, $N_l = N_{Au} \times X/M$, X is the molar ratio of N to Au in NPs, M is the number ratio of N to S in each ligand molecule (**Table 2**).

Table 2. The number of gold atoms and ligands per NP.

Samples	Size (TEM)	Au atoms per NP	Ligands per NP
Manno-AuNPs-**20** nm	16.6	141,803	15,125
MannoC_{60}-s-AuNPs-**20** nm	16.8	146,990	520,361
MannoC_{60}-l-AuNPs-**20** nm	15.5	115,440	5,842
Manno-AuNPs-**60** nm	63.6	7,975,043	2,791,265
MannoC_{60}-s-AuNPs-**60** nm	67.8	9,661,638	272,283
MannoC_{60}-l-AuNPs-**60** nm	65.3	8,631,797	164,789
Manno-AuNPs-**100** nm	104.7	35,579,655	39,612,016
Galacto-AuNPs-**100** nm	95.2	26,746,843	1,126,498
MannoC_{60}-s-AuNPs-**100** nm	100.2	31,186,372	576,475
MannoC_{60}-l-AuNPs-**100** nm	101.9	32,800,785	357,827
Fuco-AuNPs-20 nm	13.7	79,712	99,640

S5.3. Sample preparation for UV-vis analysis

The obtained glycoAuNPs (10 μg/ mL) were suspended in milliQ water for Ultraviolet-visible (UV-vis) absorption spectra that were obtained using a Varian Cary 50 spectrophotometer (CA, USA). The experimental results see Table 3.

Table 3. Summary of UV-vis absorbance and DLS data.

GlycoAuNPs	λ_{max} (UV-vis[a], nm)	D_H (DLS[b], nm)	PDI (DLS)
Manno-AuNPs-**20** nm	523	55.7	0.116
Manno-AuNPs-**60** nm	548	96.6	0.178
Manno-AuNPs-**100** nm	572	126.1	0.17
MannoC_{60}-s-AuNPs-**20** nm[c]	528	47.2	0.131
MannoC_{60}-s-AuNPs-**60** nm	549	99.9	0.173
MannoC_{60}-s-AuNPs-**100** nm	577	116.1	0.104
MannoC_{60}-l-AuNPs-**20** nm[d]	529	80.1	0.105
MannoC_{60}-l-AuNPs-**60** nm	549	95.3	0.102
MannoC_{60}-l-AuNPs-**100** nm	574	127.7	0.125
ManC_{60}-Fuco-AuNPs-**20** nm	529	46.8	0.129
Fuco-AuNPs-**20** nm	256	111.5	0.163

a. UV spectra recorded at RT, 10 μL of glycoAuNPs (1mg/mL) were diluted into 500 μL of milliQ water.

b. DLS analysis at a concentration of 10, 5 and 15 μg/mL for 20, 60 and 100 nm AuNPs, respectively, recorded at 25 ℃.

c. "s" indicates short linker.

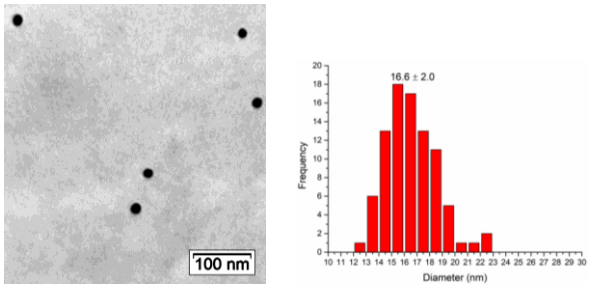
d. "l" indicates long linker.

S5.4 Sample preparation for DLS analysis

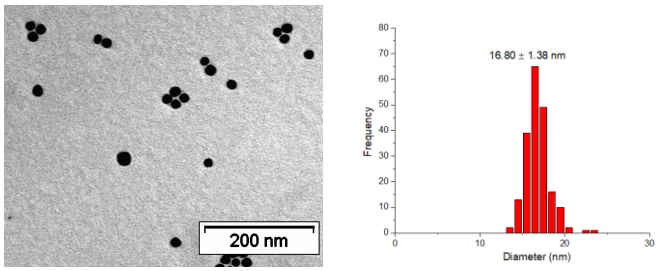
The obtained glycoAuNPs (20 µg/ mL, 5 µg/ mL, 2 µg/ mL corresponding to 20 nm, 60, 90 nm, respectively) were suspended in milliQ water for the hydrodynamic size measurement by a NanoPlus HD system (Brea, CA, USA.) operating at 633 nm with a 173º scattering angle. Measurements were made in a 1 cm path-length round quartz cell maintained at 25°C. Solution samples were filtered through nylon Acrodisc syringe filters (Pall Life Sciences) with 0.2 µm pore size. Each measurement was for 5 scans, each of 25 seconds duration. The mean particle hydrodynamic diameters were calculated from intensity based particle size distribution. The experimental results see Table 3.

S5.5. Sample preparation for TEM analysis

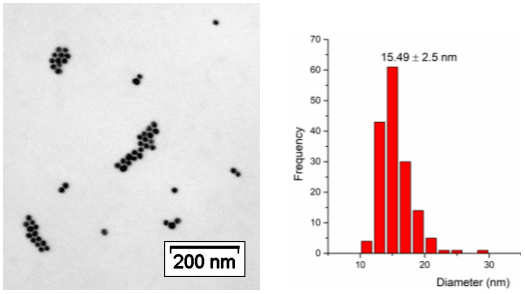
The generated glycoAuNPs (1 mg/mL)were two fold diluted with deionized water followed by depositing glycoAuNPs (2 µL) on a copper grid disk. The copper disk was dried in the oven for 12 h to remove water prior to TEM analysis. Transmission electron microcopy (TEM) images of the samples were recorded on microgrid copper mesh by using a TECNAI 10 at an acceleration voltage of 80 kV. Nanoparticles size (*d*) was estimated using the formula $d = 2(A/\pi)^{1/2}$, where A is the cross-sectional area of a particle measured by Image J.[9, 15]



Manno-AuNPs-20 nm



MannoC_{60}-s-AuNPs-20 nm



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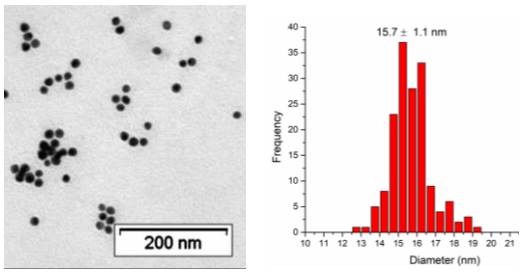

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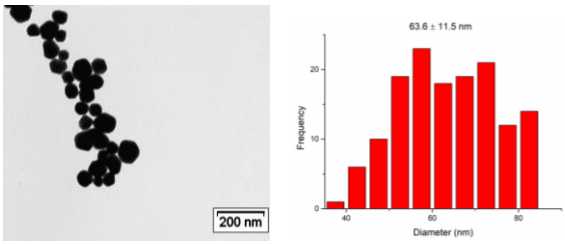

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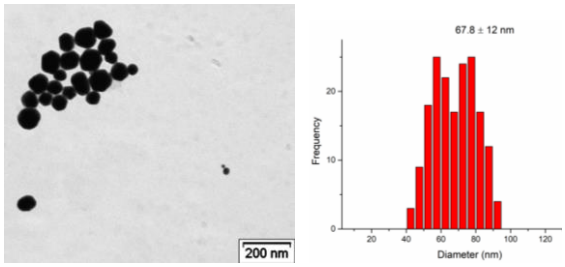

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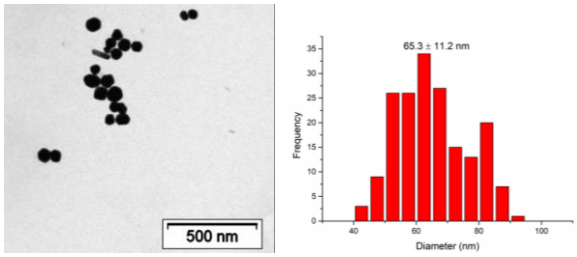

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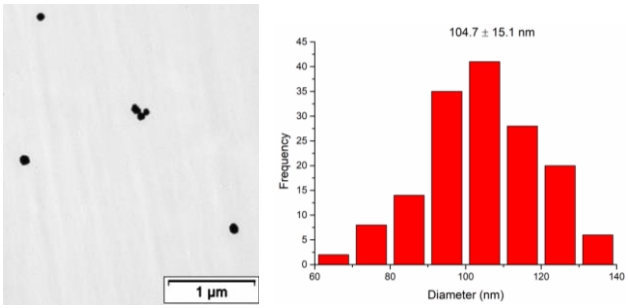
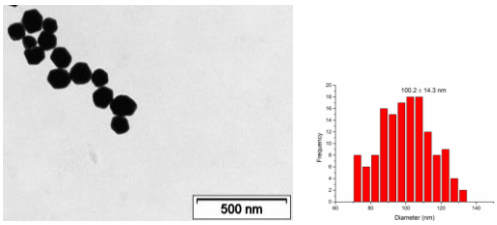
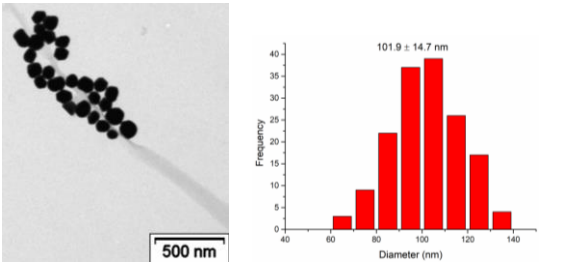


Manno-AuNPs-100 nm



MannoC_{60}-s-AuNPs-100 nm



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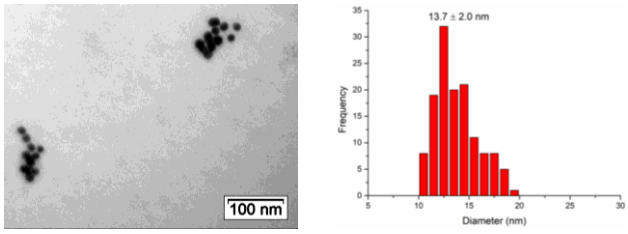


Fuco-AuNPs-20 nm

S6. Quantitation of the amount of carbohydrates on the AuNPs

The carbohydrates' quantitaion was realized by the phenol-sulfuric acid assay.[16] Briefly, 30 µL of ice-cold standard sample solutions (with the corresponding ligand) were mixed with 100 µL of concentrated sulfuric acid in microplate wells. 20 µL of aqueous 5% phenol solution was then added into each well. The plate was floated uncovered on near boiling (>90 ºC) water bath for 5 min for color development, followed by cooling on ice for another 5 min. A microplate reader (Spectramax iD3 microplate reader) was used to record the absorbance of each well at 490 nm. The concentration of standard solution was plotted with the absorbance of each solution. The corresponding AuNPs in sulfuric acid Spectramax were used as controls.

The amount of sugar was thus evaluated thanks to the calibration curve.

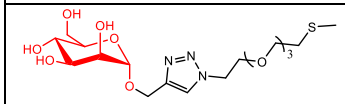
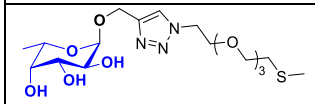
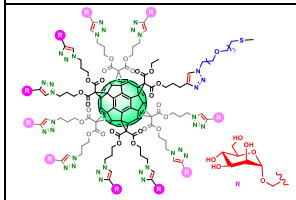
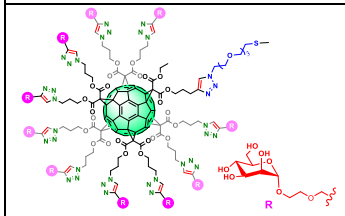
The ligand density on the nanoparticles were calculated by the following equations:[17]

$$N_{Au} = d_{NP}^3 \times 31,\ m_{Au} = N_{Au} \times 196.97,\ m_L = m_{Au} \times (\text{wt\% of L/wt\% of Au})$$

$$N_L = m_L/M_L,\ S_{NP} = 4\pi r^2,\ \sigma = N_L/S_{NP}$$

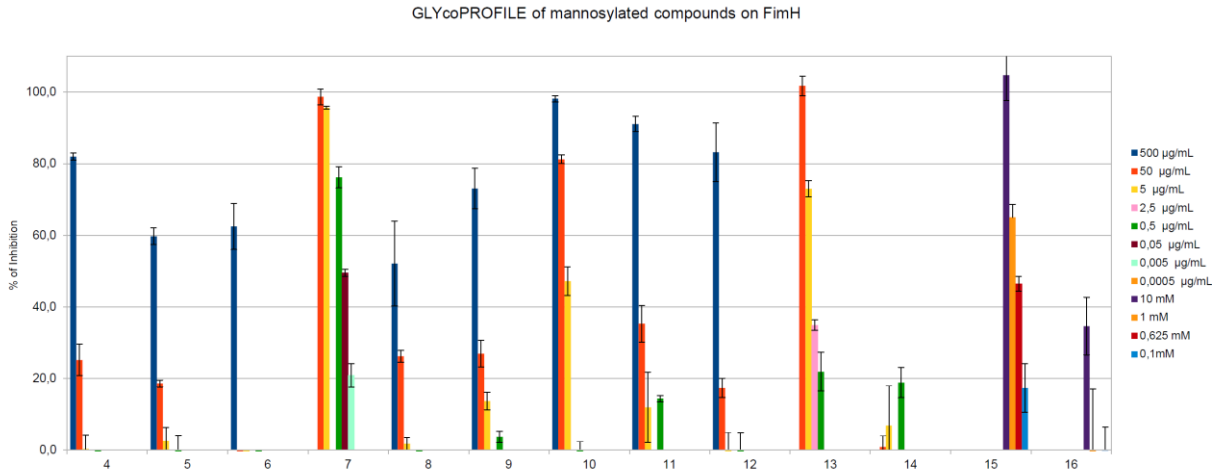
where N_{Au} is the number of Au atoms, d_{NP} is the diameter of AuNPs, m_{Au} the mass of the Au atom in the NP, m_L mass of the ligand in the NP, M_L is the molecular mass of ligand. N_L the number of ligands per NP. r is the particles radius (nm), S_{NP} (nm^2) is surface area of per AuNP, σ (ligands/nm^2) is the lignad density. The wt% of L/wt% of Au can be obtained from phenol-H_2SO_4. The results are gathered in Table 4.

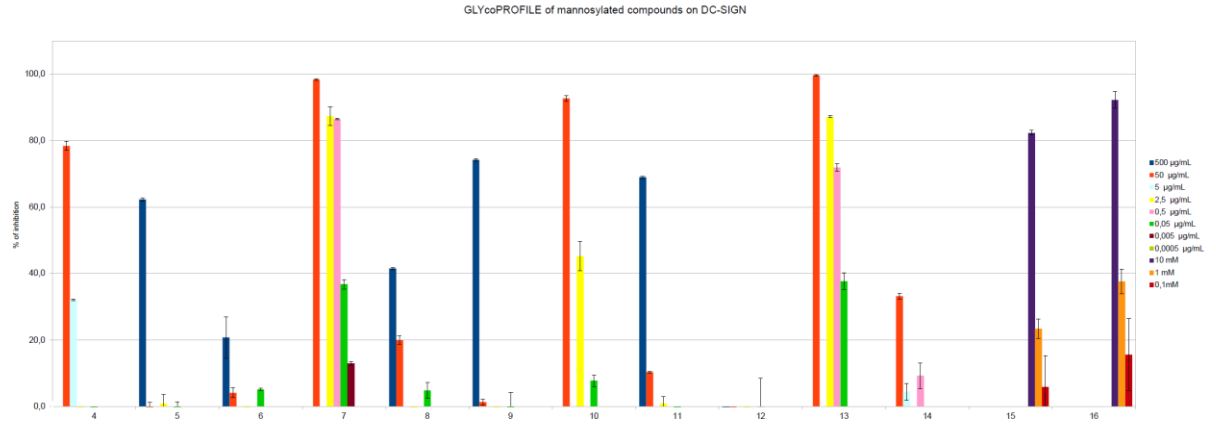
Table 4. Number of ligands per nanoparticle.

Structure of ligands	GlycoAuNPs	Amount of ligand on 1 mg of NPs (µg/mg)	N_{Au}	Wt% of L	Wt% of Au	No. of ligand per NP	S_{NP} (nm^2)	Ligand Density (ligands/nm^2)
	Manno-AuNPs-**20** nm Manno-AuNPs-**60** nm Manno-AuNPs-**100** nm	107.6 32.4 45.5	141803 7975043 35579655	10.76 3.24 4.55	89.24 96.74 95.45	7,449 116,351 738,815	865.26 12,701.17 34,420.96	8.6 9.2 21.5
	Fuco-AuNPs-**20** nm	33.6	79712	3.36	96.64	1,250	589.35	2.1
	MannoC_{60}-s-AuNPs-**20** nm MannoC_{60}-s-AuNPs-**60** nm MannoC_{60}-s-AuNPs-**100** nm	346.7 89.7 56.9	146990 9661638 31186372	34.67 8.97 5.69	65.33 91.03 94.31	3,287 42,232 83,464	886.23 14,434.08 31,525.73	3.7 2.9 2.6
	MannoC_{60}-l-AuNPs-**20** nm MannoC_{60}-l-AuNPs-**60** nm MannoC_{60}-l-AuNPs-**100** nm	352.8 36.3 162.9	115440 8631797 32800785	35.28 3.63 16.29	64.72 96.37 83.71	2,539 13,103 257,589	754.39 13,389.24 32,604.54	3.4 1 7.9

S7. GLYcoPROFILE

The GLYcoPROFILE is the interaction profile of a product with a range of lectins. The study was carried out on 2 lectins (FimH and DC-SIGN). The interaction profiles of each compound were determined through an indirect method based on the inhibition by the sample of the interaction between a specific couple lectin-glycan. FimH LEctPROFILE® plates and DC-SIGN LEctPROFILE® plates were used to perform these analyses. Briefly, a mix of the biotinylated neoglycoprotein functionalized with mannose (Ref: NeoM, GLYcoDiag) (fixed concentration) and the inhibitor (range of concentrations, see Figure and Table) prepared in PBS supplemented with 1 mM $CaCl_2$ and 0.5 mM $MgCl_2$ is deposed in each well (100 µl) in triplicates and incubated two hours at room temperature. After washing with PBS buffer, the conjugate streptavidin-DTAF was added (50 µL) and the plate was incubated 30 min more. The plate was washed again with PBS. Finally, 100 µL of PBS was added for the readout, performed with a fluorescence reader (λex = 485 nm, λem = 530 nm Fluostar, BMG labtech, Offenburg, Germany). The signal intensity is inversely correlated with the capacity of the inhibitor to be recognized by the lectin and expressed as inhibition percentage with comparison with the corresponding tracer ligand alone. Glycoprofiles for glycoAuNPs have been realized on the inhibition of the interaction using at least three different concentrations of glycoAuNPs. Each experiment has been set in duplicate.[18]





S8. Hemagglutination inhibition Assays (HIA)

Hemagglutination assays were performed using 96-well round bottom microtiter plates. Red blood cells (from Guinea Pig, RBCs) were purchased from Envigo RMS B.V and directly used without further treatment. RBCs were diluted to 5 % in a cold phosphate buffer solution (PBS, 17 mM KH_2PO_4, 150 mM NaCI). PBS buffer was used for all experiments. Bacterial growth: a bacteria inoculation loop was used to transfer the bacterial strain UTI89 (clinical isolate engineered for continuous type-1 fimbriation) to 10 mL of LB liquid medium kept static at 37 ℃ for 24 hours. Then, the bacteria were centrifuged and washed in cold PBS (10 mL, 3000 RPM, 4 ℃). This process was repeated three times. The hemagglutination unit, which is the minimal concentration of bacteria required to agglutinate the red blood cells, was obtained by constant addition of 50 µL of the 5 % RBCs solution to 50 µL aliquots of sequential 2-fold dilution of *E.coli*. The hemagglutination unit was recorded after 1 hour incubation at 4 ℃. A bacterial concentration of twice the determined hemagglutination titer was kept constant in the hemagglutination inhibition assays.

The inhibition assays were carried out by adding 25 µL of 2-fold dilution solution of the glycoAuNPs (starting from 250 mg/mL for each sample) to a fixed volume of 25 µL of bacteria and 50 µL of 5 % RBCs. The final volume was 100 µL in each well. The microplates were incubated at 4 ℃ for 1 hour before read-out. The minimum inhibitory concentration (MIC) for each sample was recorded for each triplicate.[19-20]

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