Supporting Information

Surface mannosylation of dispersion polymerisation derived nanoparticles by copper mediated click chemistry

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1. Synthesis and characterisation of alkyne functional NPs

1.1 Synthesis of the hydrophilic macroinitiator

Procedure for the preparation of poly(PEGMA$_{18}$-*stat*-PgMA$_5$). In a Schlenk tube, PEGMA (5 ml, 0.28 mmol) and PgMA (0.13 ml, 0.002 mmol) and PMDETA (0.2 ml, 0.83 mmol) were dissolved in anisole (0.5 ml). The solution was degassed through freeze-pump-thaw cycles (× 4). EBiB ATRP initiator (77 µL, 0.4 mmol) was added after two cycles through a degassed needle. CuCl (52 mg, 0.4 mmol) was added after three cycles under a high nitrogen flux. The tube was immersed into a preheated oil bath at 60 °C and left reacting for 10 min. The reactive solution was quenched through exposure to atmospheric oxygen and cooling before dilution with THF and addition of Dowex ® Marathon™ C hydrogen resin to remove the spent Cu(I) catalyst. THF and anisole were removed under reduced pressure and the product was dissolved in deionised water. It was dialyzed against deionized water for 72 hours. The product was lyophilized and collected as a transparent viscous liquid (yield: 70%, 1.18 g).

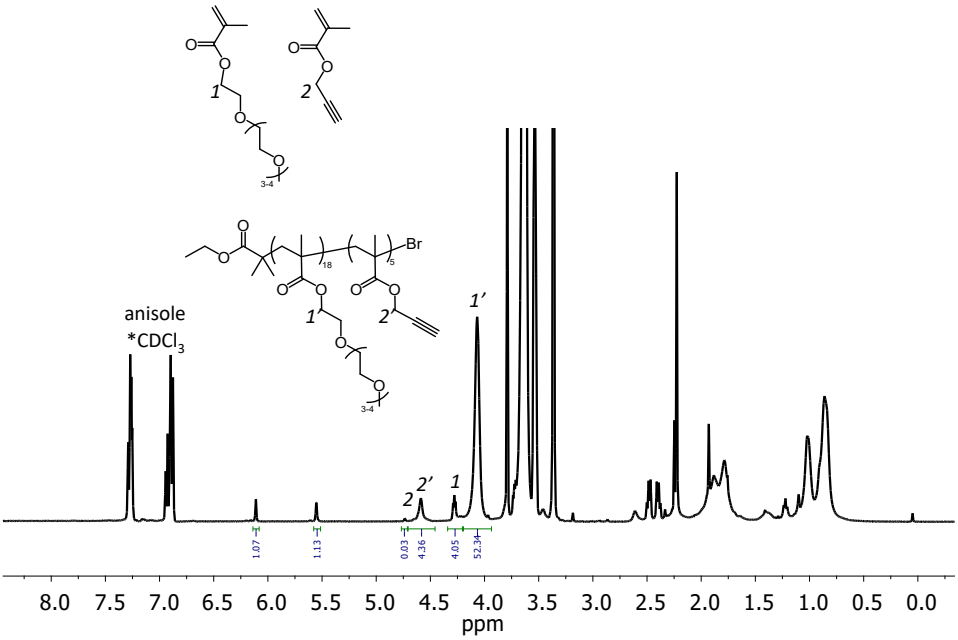


Figure S1. ^{1}H NMR spectrum of the crude polymerisation solution after 15 min. for the calculation of monomer conversion of PEGMA and PgMA ($CDCl_3$, 400 MHz). The conversion of the polymerisation was determined by comparing the CO-O-CH_2-C≡CH monomer peak at 4.75 ppm (2) to the analogues polymer peak at 4.59 ppm (2') in the case of PgMA monomer, and comparing PEGMA monomer peak R-CO-O-CH_2-R (1) peak at 4.28 ppm to poly(PEGMA) peak at 4.07 ppm (1').

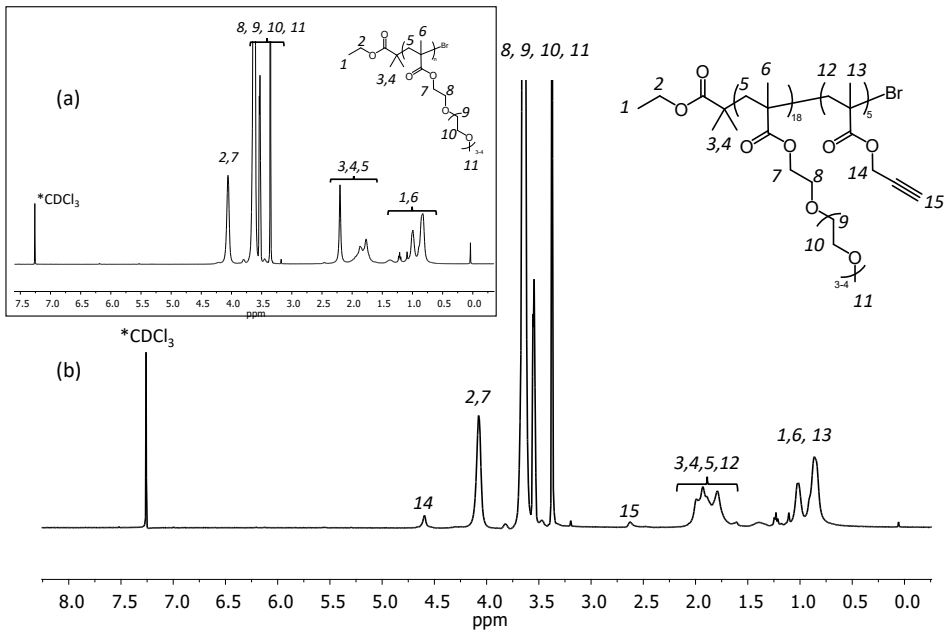


Figure S2: ^{1}H NMR spectrum of (a) poly(PEGMA) and (b) poly($PEGMA_{18}$-stat-$PgMA_5$) after purification ($CDCl_3$, 400 MHz).

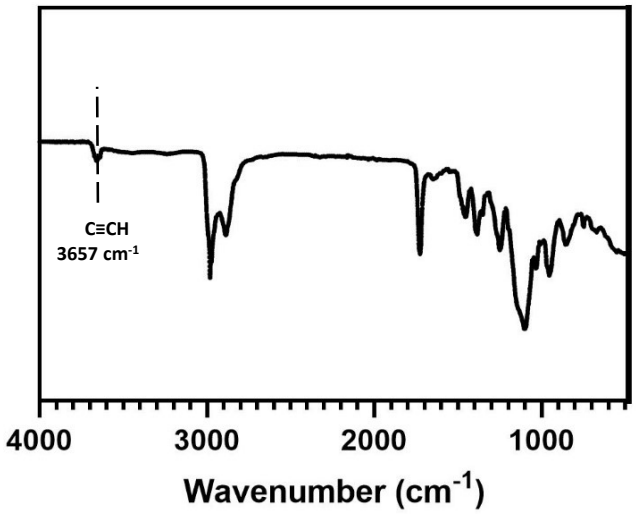


Figure S3. FT-IR spectrum of poly($PEGMA_{18}$-stat-$PgMA_5$).

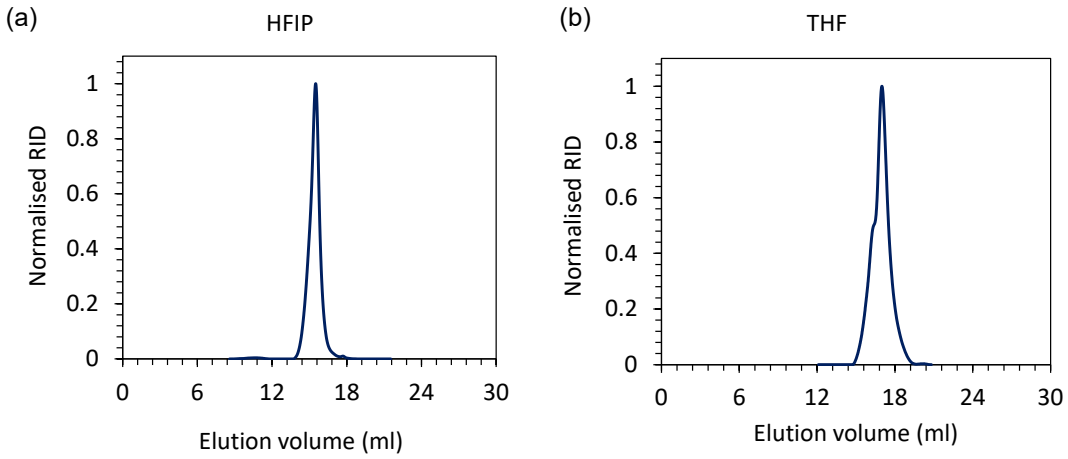


Figure S4. HFIP (a) and THF (b) gel permeation chromatography (GPC) (vs. PMMA standards) obtained for poly(PEGMA$_{18}$-stat-PgMA)$_5$ prepared by ATRP (dRI detector; flow rate 1 mL × min^{-1}).

1.2 Synthesis of nanoparticles

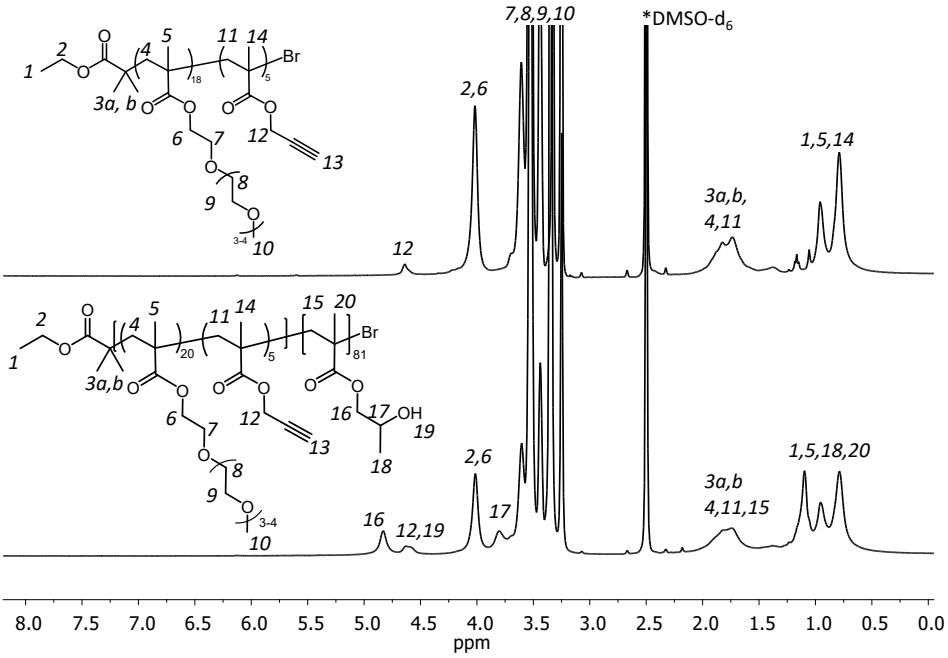


Figure S5. ^{1}H-NMR spectra of (a) poly(PEGMA$_{18}$-stat-PgMA$_5$) and (b) poly(PEGMA$_{18}$-stat-PgMA$_5$)-b-poly(HPMA) (400 MHz, DMSO-d6, 303 K).

Table S1. Feeds ratio for the fabrication of poly(PEGMA$_{18}$-*stat*-PgMA)$_5$-*b*-poly(HPMA)$_x$ NPs when targeting DP$_{HPMA}$=150, 300, 450

DP$_{HPMA}$	poly(PEGMA$_{18}$-*stat*-PgMA$_5$)	Me$_6$TREN	Na Asc	TBAB	SC (%)	H_2O (ml)	HPMA
150	150 mg (0.025 mmol)	136 µL (0.5 mmol)	7.19 mg (0.04 mmol)	40 mg (0.12 mmol)	10	7	0.52 g (3.63 mmol)
300	150 mg (0.025 mmol)	136 µL (0.5 mmol)	7.19 mg (0.04 mmol)	40 mg (0.12 mmol)	10	12	1.05 g (7.26 mmol)
450	150 mg (0.025 mmol)	136 µL (0.5 mmol)	7.19 mg (0.04 mmol)	40 mg (0.12 mmol)	10	17	1.57 g (10.89 mmol)

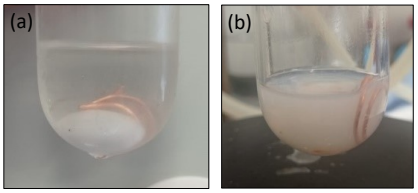


Figure S6. Images of the SET-LR-PISA reaction at (a) time zero and (b) end of the reaction (40 min).

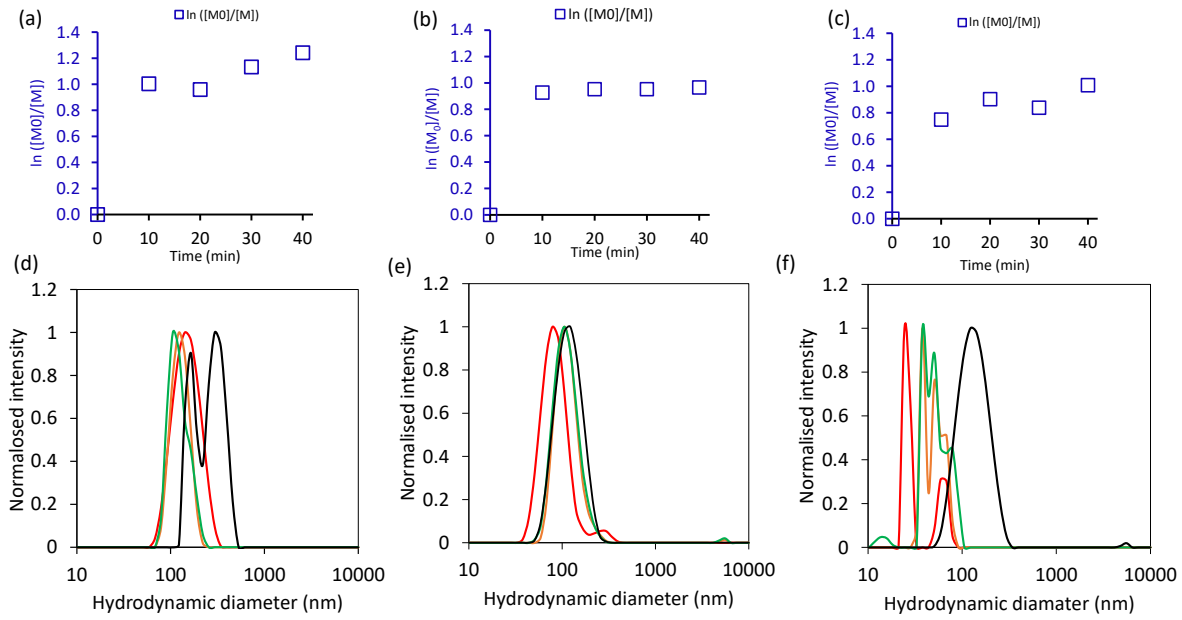


Figure S7. NP synthesis targeting DP$_{HPMA}$ = 150; three repeat experiments. Semilogarithmic plots (a, b, c) of monomer consumption and hydrodynamic diameter evolution by DLS (d, e, f) (e); colour code: red = 10 min., orange = 20 min., green = 30 min. and black = 40 min. Reaction condition: Cu(0) wire (10 cm, 0.5 mm), Me$_6$TREN (20 equiv.), NaAsc (1.5 equiv.), TBAB (5 equiv.), 30 °C, 10% SC.

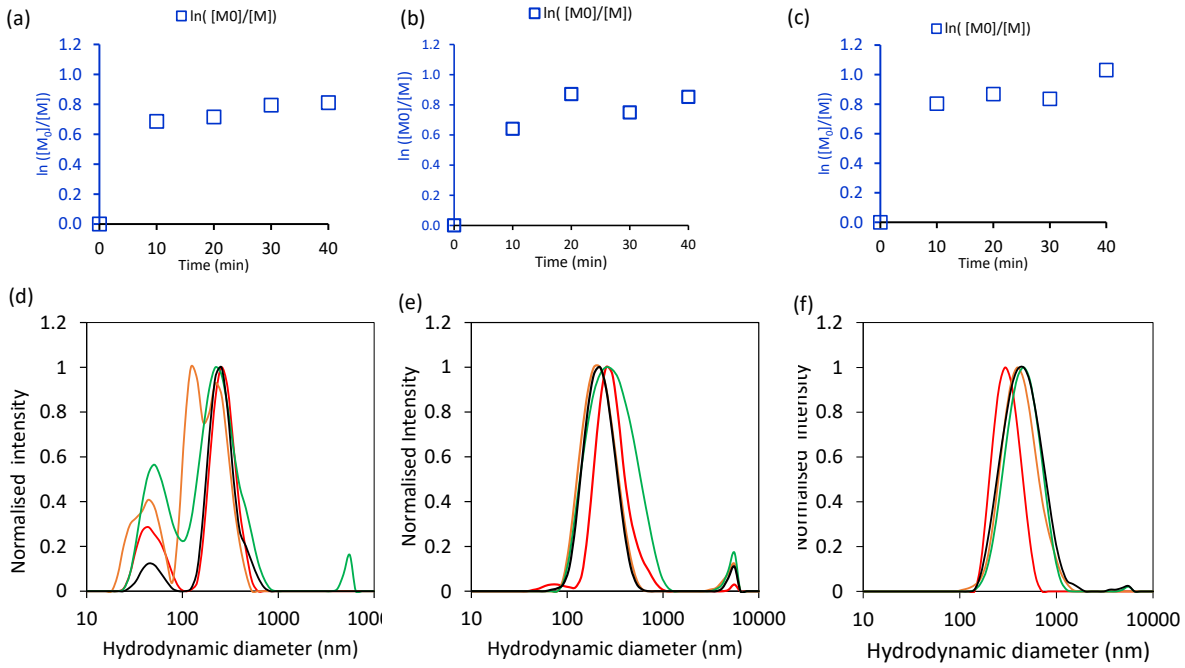


Figure S8. NP synthesis targeting DP_{HPMA} = 300; three repeat experiments. Semilogarithmic plots (a, b, c) of monomer consumption and hydrodynamic diameter evolution by DLS (d, e, f) (e); colour code: red = 10 min., orange = 20 min., green = 30 min. and black = 40 min. Reaction condition: Cu(0) wire (10 cm, 0.5 mm), Me_6TREN (20 equiv.), NaAsc (1.5 equiv.), TBAB (5 equiv.), 30 °C, 10% SC.

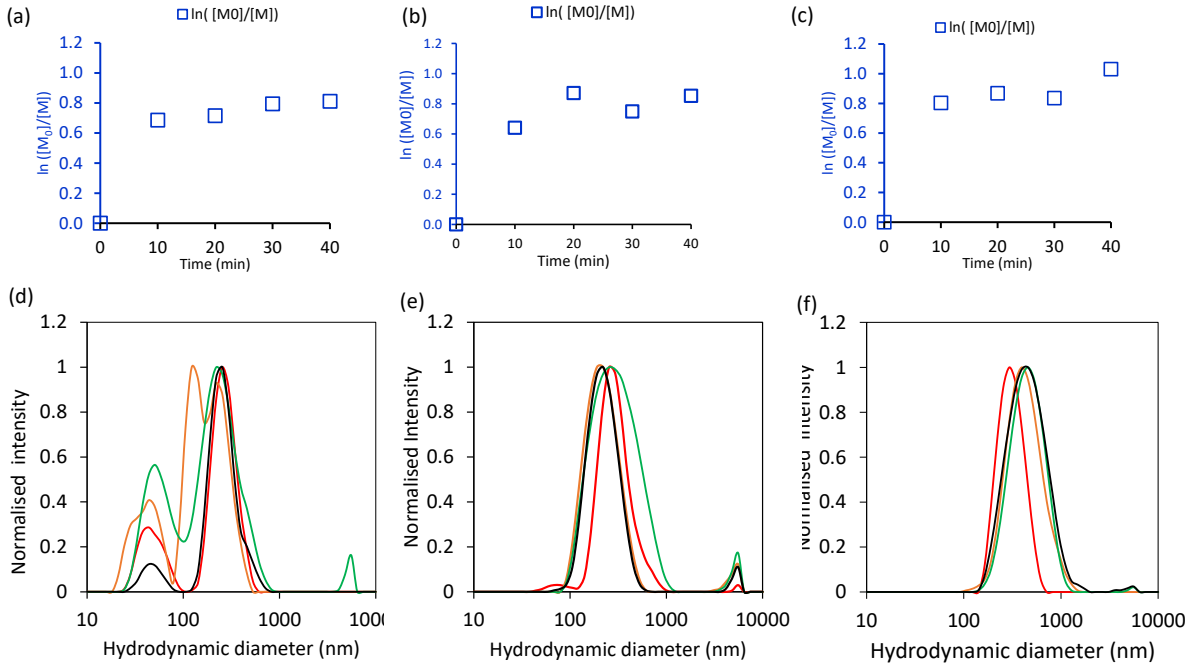


Figure S9. NP synthesis targeting DP_{HPMA} = 450; three repeat experiments. Semilogarithmic plots (a, b, c) of monomer consumption and hydrodynamic diameter evolution by DLS (d, e, f) (e); colour code: red = 10 min., orange = 20 min., green = 30 min. and black = 40 min. Reaction condition: Cu(0) wire (10 cm, 0.5 mm), Me_6TREN (20 equiv.), NaAsc (1.5 equiv.), TBAB (5 equiv.), 30 °C, 10% SC.

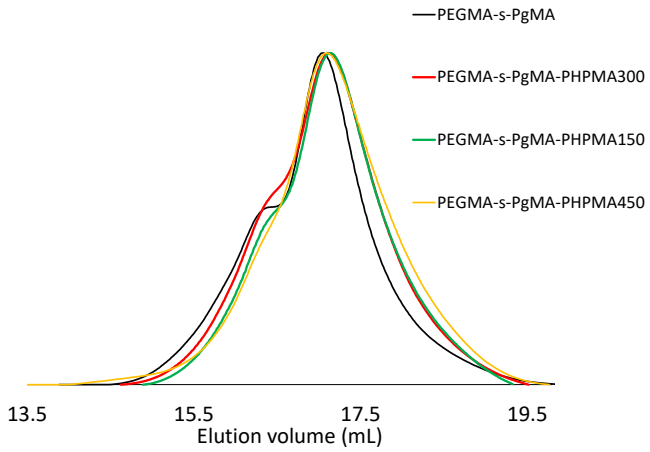


Figure S10: GPC traces of block copolymers after chain extension at different macroinitiator to HPMA ratios (DP = 150, DP = 300, DP = 450).

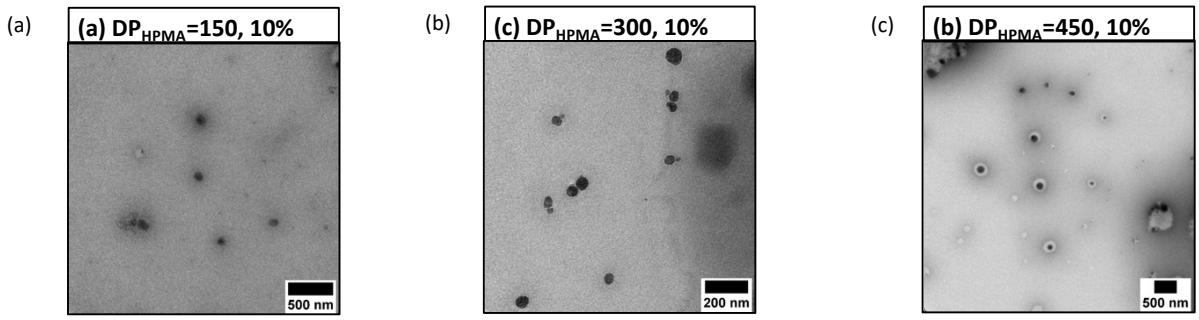


Figure S11: TEM images of the obtained NP at 10 % solid content of samples taken after 40 min.

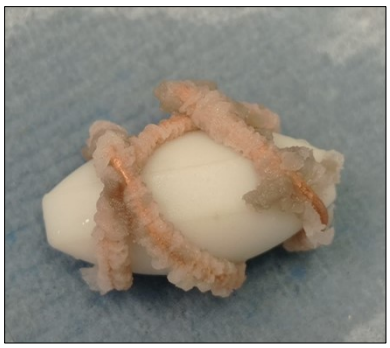


Figure S12: Image of the copper catalyst at the end of the SET-LR-PISA reaction when targeting DP_{HPMA}= 450. Gelation of the polymer around the copper wire catalyst was observed.

1.3 Functionalisation of nanoparticles with fluorescein

Procedure for the shell functionalisation by copper catalysed alkyne-azide cycloaddition (Cu AAc) for sample with targeted DP_{HPMA} = 300: To 3 ml aqueous colloidal solution containing ca. 0.5 g of purified poly($PEGMA_{18}$-*stat*-$PgMA_5$)-*b*-poly(HPMA)$_x$ NP, (±) sodium ascorbic acid (3 mg, 0.01 mmol) and fluorescein azide (0.8 mg, 0.75 mmol) were added. $CuSO_4$ 5 H_2O (0.8 mg, 0.005 mmol) in 100 µL H_2O

(note: this was performed using a stock solution of 80 mg in 10 mL of H_2O) was added and the reaction was left stirring overnight. Dowex® Marathon™ MSC hydrogen acidic resin was added to remove the copper, before being filtered off through glass wool and the solution was dialyzed for 3 days.

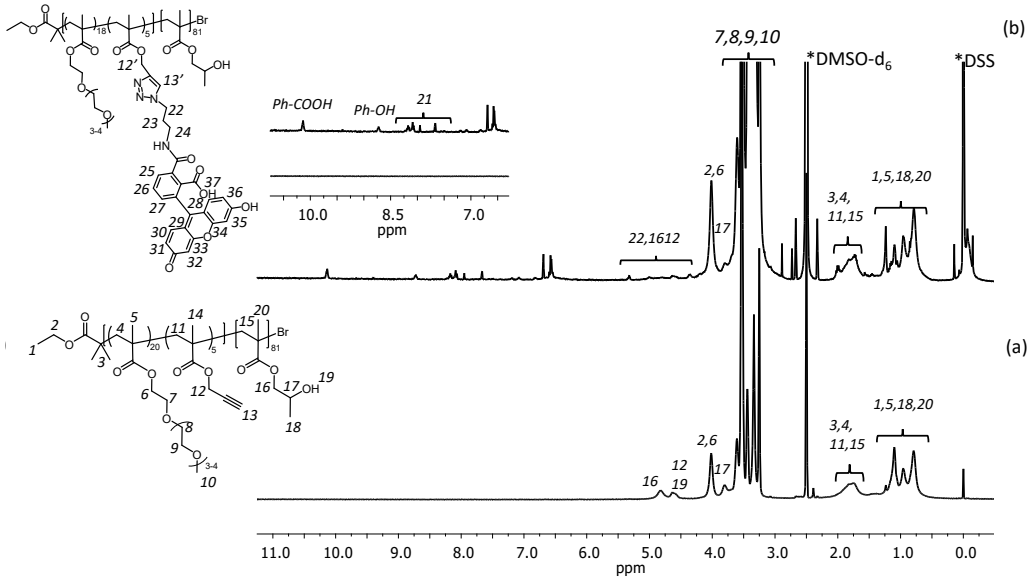


Figure S13. ^{1}H-NMR spectrum of poly(PEGMA$_{18}$-*stat*-PgMA$_5$)-*b*-poly(HPMA)$_{166}$ before (a) and after (b) the click reaction with fluorescein azide (400 MHz, DMSO-d6, 303K).

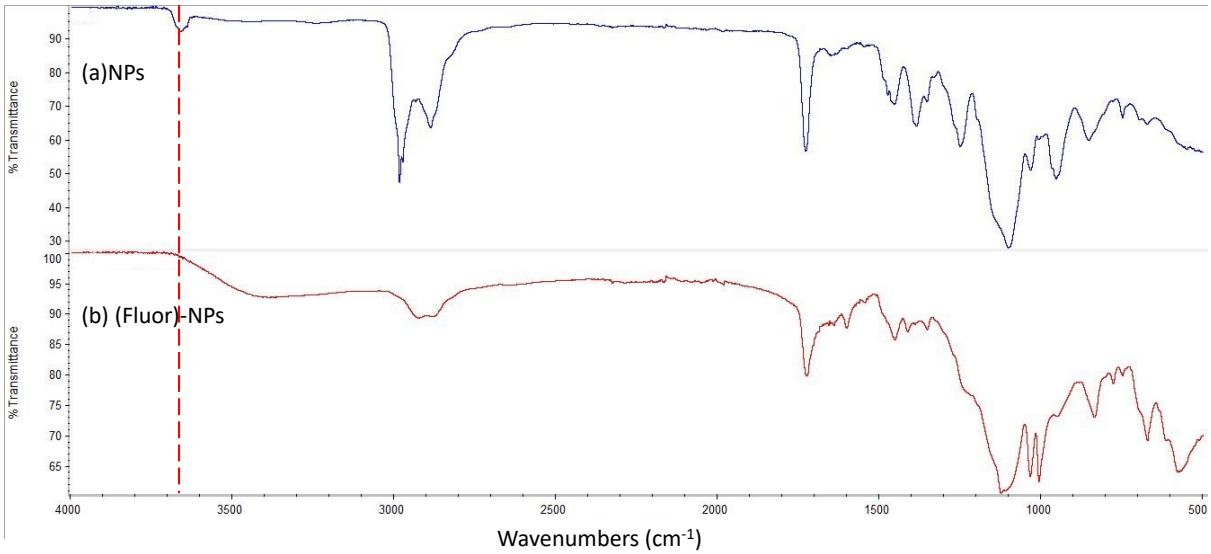


Figure S14: FT-IR spectrum of poly(PEGMA$_{18}$-stat-PgMA$_5$)-b-poly(HPMA) (targeted DP$_{HPMA}$ = 300) before (a) and after (b) functionalisation with fluorescein.

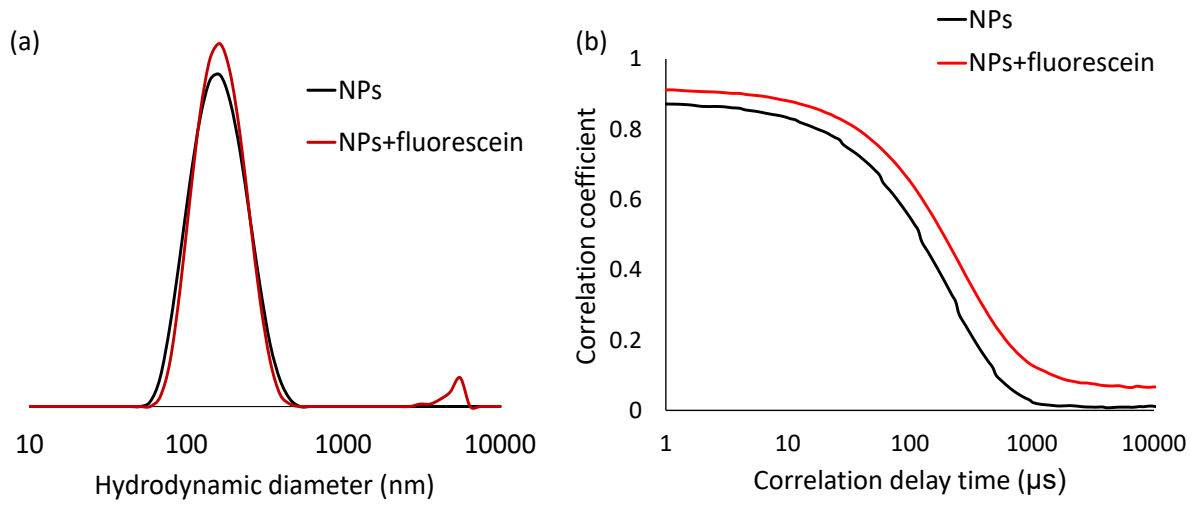
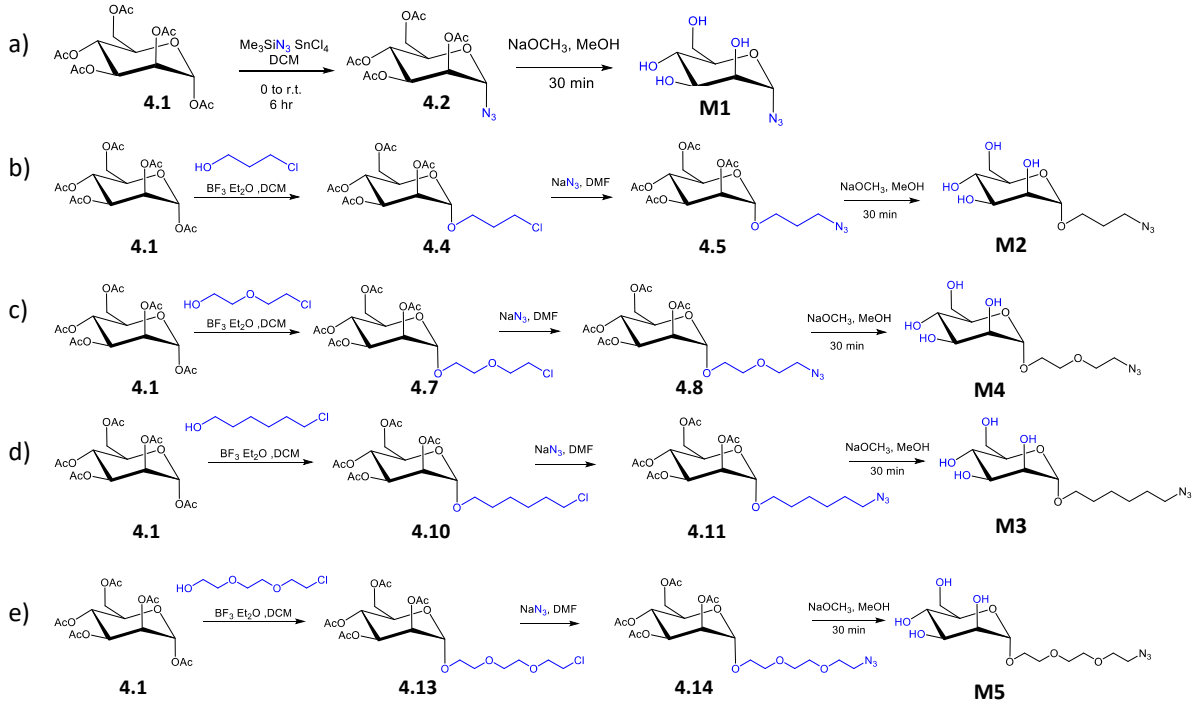


Figure S15. Comparison of the (a) hydrodynamic diameter and (b) correlogram of poly($PEGMA_{18}$-stat-$PgMA_5$)-b-poly(HPMA) (targeted DP_{HPMA} = 300) before and after the shell functionalization fluorescein.

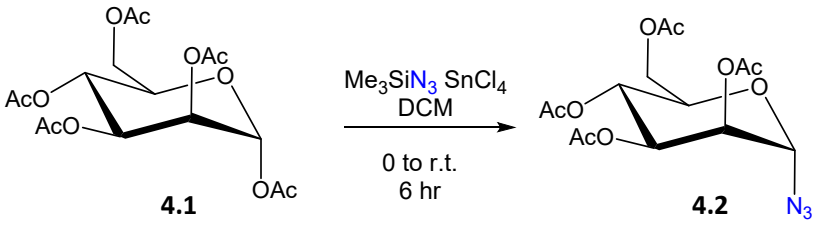
2 Synthesis of mannosides

2.1 Synthetic procedures

Scheme S1. Reaction scheme for the preparation of compounds M1-M5.



Synthesis of 1-azido-2,3,4,6-tetra-O-acetyl-α-D-mannopyranose (4.2).[1]



To a solution of penta-O-acetyl-mannopyranose (**4.1**) (2 g, 5.12 mmol) and $TMSN_3$ (2.71 ml, 9.28 mmol) in dry DCM (0.2 M), $SnCl_4$ (0.5 ml, 0.6 mmol) was added dropwise at 0 °C. The reaction was left reacting at r.t. for 6 h and monitored *via* TLC (EtOAc:Hex:Tol= 3:3:1). The reactive solution was then washed with a saturated solution of $NaHCO_3$ and brine, dried over $NaSO_4$ and the solvent was removed under reduce pressure. The product (**4.2**) was recovered as an oil (yield: 73%, 1.4 g). It was utilized in the next step without further purification procedure.

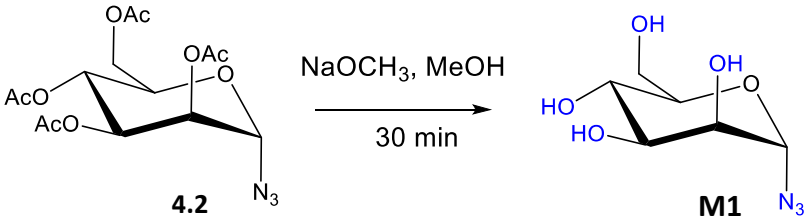
^{1}H NMR (400 MHz, CDCl3) δ [ppm] = 5.38 (d, 1H, $J_{1\text{-}2}$= 1.6 Hz, **H-1**,); 5.31-5.23 (m, 2H, **H-2**, **H-3**); 5.13 (m, 1H, **H-4**); 4.33-4.28 (dd,1H, J_{gem}= 12 Hz, $J_{6a\text{-}5}$= 5.6 Hz, **H-6a**); 4.18-4.12 (m, 2H, **H-6b, H-5**); 2. 17 (s, 3H, -**OAc**); 2.11 (s, 3H, -**OAc**); 2.06 (s, 3H, -**OAc**); 1.99 (s, 3H, -**OAc**).

^{13}C NMR (400 MHz, $CDCl_3$) δ [ppm] = 100.7 (-**C**OCH_3), 100.5 (-**C**OCH_3), 100.5 (-**C**OCH_3), 100.49 (-**C**OCH_3), 79.83 (**C-1**), 75.6 (**C2**), 75.2 (**C3** or **C4**), 74.9 (**C5**), 74.3 (**C3** or **C4**), 73.46 (**C6**), 63.07 (CO**C**H_3), 60.04 (CO**C**H_3), 63.03 (CO**C**H_3), 63.01 (CO**C**H_3).

ESI MS (+): theoretical mass [M+ Na+]: 396.3 m/z, experimental mass [M+Na$^+$]: 396.35 m/z.

TLC: R_f = 0.52 (EtOAc:Hex:Tol= 3:3:1).

Synthesis of 1-azido-α-D-mannopyranose (M1).[1]



Compound **4.2** (1.4 g, 3.75 mmol) was dissolved in MeOH (0.1 M) and NaOMe (81 mg, 1.50 mmol) was added stepwise. The reaction was left stirring at r.t. for 30 min until TLC (DCM: MeOH-7:3) showed the consumption of the starting material. Amberlite IR120 (H^+ from) was added and left reacting until neutral pH was reached. The resin was filtered off and over cotton and the solvent was removed under reduced pressure. The product **M1** was obtained as a colourless oil (yield: 95%,0.73 g).

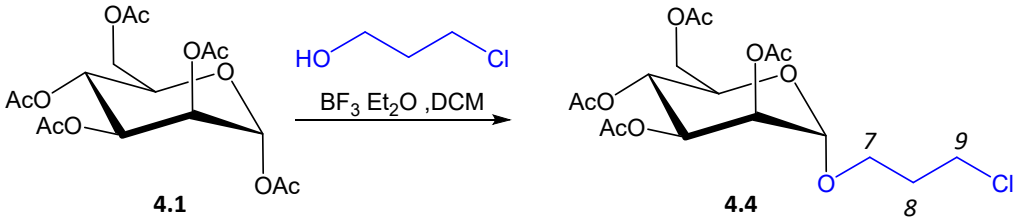
^{1}H NMR (400 MHz, D_2O) δ [ppm] = 5.49 (d, $J_{1\text{-}2}$= 1.8 Hz, 1H, H-1), 3.94 (1H- H-6a), 3.90 (dd, $J_{1\text{-}2}$= 1.8 , J2-3= 3.2 Hz, 1H, H-2), 3.89-3.75 (m, 3H, H-6b, H-3, H-5), 3.71-3.65 (t, 1H, H-4).

^{13}C NMR (400 MHz, D_2O) δ [ppm] = 89.76 (C-1), 74.75 (C-2), 69.84 (C-5 or C-3), 69.78 (C-5 or C-3), 66.4 (C-4), 60.85 (C-6).

FT-IR: peak at 2114 cm^{-1} corresponding to R-N=N=N stretching.

TOF MS ESI(+): theoretical mass [M+Na$^+$]: 228.15 m/z, experimental mass [M+Na$^+$]: 228,0593 m/z

Synthesis of 3-chloropropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.4).[2]



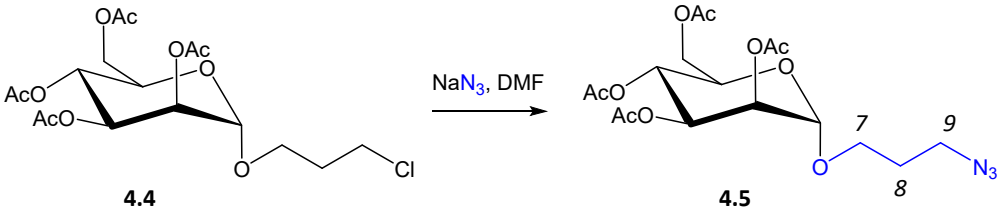
To an ice cooled solution of 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose (**4.1**) (3,0 g, 7.67 mmol) in dry DCM (0.2 M), 3-chloro-1-propanol (1.92 ml, 23 mmol) and BF_3Et_2O (2.84 ml, 23 mmol) were added dropwise. The reaction was than warmed up to room temperature and left reacting for 72 h. The reaction was monitored by TLC (Hex:EOAc-7:3). It was than quenched with until neutral pH and extracted with DCM. The organic layer was washed with a saturated solution of $NaHCO_3$ and brine and dried over Na_2SO_4. The solvent was removed under reduce pressure and the crude product was obtained as an oil. It was purified by column chromatography (Hex:EtOAc 1:9 → 7:3). The pure product (**4.4**) was obtained as a colourless oil (yield: 49%, 1,56 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 – 5.26 (m, 3H, **H2**,**H-3** and **H-4**), 4.79 (d, J = 1.8 Hz, 1H, **H-1**), 4.24 (dd, J_{gem} = 12.3, $J_{6\text{-}5}$ = 5.4 Hz, 1H, **H-6'**), 4.09 (dd, J_{gem} = 12.3, $J_{6\text{-}5}$ = 2.5 Hz, 1H, **H-6''**), 3.97 (ddd, $J_{5\text{-}4}$ = 8.4, $J_{5\text{-}6a}$ = 5.4, $J_{5\text{-}6b}$ = 2.5 Hz, 1H, **H-5**), 3.86 (dd, J_{gem}= 9.7, $J_{7\text{-}8}$ = 5.6 Hz, 1H, **H-7a**), 3.55 (dt, J_{gem} = 9.7, $J_{7\text{-}8}$ = 5.6 Hz, 1H, **H-7b**), 3.49 (td, J = 6.2, 1.6 Hz, 2H, **H-9**), 2.19 – 2.07 (m, 2H, **H-8**), 2.11 (s, 3H**, -OAc**), 2.06 (s, 3H**, -OAc**), 2.01 (s, 3H, **-OAc**), 1.95 (s, 3H, **-OAc**).

^{13}C NMR (101 MHz, $CDCl_3$) δ 97.64 (**C-1**), 69.47 (**C-3** or **C-4**), 69.06 (**C-5**), 68.68 (**C-3** or **C-4**), 65.54 (**C-7**), 62.44 (**C-6**), 32.02 (**C-8**), 30.05 (**C-9**), 20.78 (**-OAc**), 20.69 (**-OAc**), 20.59 (2 x **-OAc**).

ESI MS (+): theoretical mass [M+ Na^+]: 396.3 m/z, experimental mass [M+Na^+]: 396.35 m/z.
TLC: R_f = 0.52 (Hex:EtOAc= 7:3).

Synthesis of 3-Azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.5).[2]



4.4 **4.5**

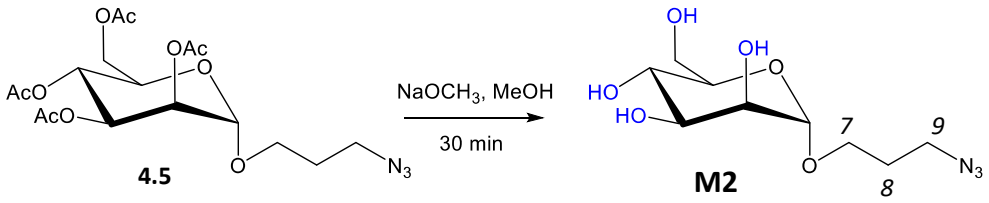
Sodium azide (0.75 g, 11.3 mmol) was added portion wise to a stirred solution of 3-chloropropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (**4.4**) (1.56 g, 3.8 mmol) in DMF (0.2 M). The reaction was refluxed at 70 °C and left reacting overnight, until TLC (Hex:EOAc-7:3) showed the disappearance of the starting material. It was then diluted in water and extracted with Et_2O (3 x 30 ml). The organic layers were combined and washed with saturated solution of $NaHCO_3$ (2 x 30 ml) and brine (2 x 30 ml) and dried over Na_2SO_4. After having filtered off the solids, the solvent was removed with rotary evaporator and the pure product (**4.5**) was obtained as a white powder (yield: 95%, 1.5 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 5.35 – 5.22 (m, 3H, **H-2** and **H-3** and **H-4**), 4.82 (d, $J_{1\text{-}2}$ = 1.5 Hz, 1H, **H-1**), 4.28 (dd, J_{gem} = 12.2, $J_{6a\text{-}5}$ = 5.4 Hz, 1H, **H-6'**), 4.12 (dd, J_{gem} = 12.2, $J_{6b\text{-}5}$ = 2.4 Hz, 1H, **H-6''**), 3.97 (ddd, $J_{5\text{-}4}$ = 8.0, $J_{5\text{-}6a}$ = 5.4, $J_{5\text{-}6b}$ = 2.4 Hz, 1H, **H-5**), 3.87 – 3.75 (m, 1H, **H-7'**), 3.53 (dt, J_{gem}= 10.0, $J_{7''\text{-}8}$ = 5.9 Hz, 1H, **H-7''**), 3.43 (t, $J_{9\text{-}8}$ = 6.5 Hz, 2H, **H-9**), 2.16 (s, 3H, **-OAc**), 2.11 (s, 3H, **-OAc**), 2.05 (s, 3H, **-OAc**), 2.00 (s, 3H, **-OAc**) 1.95 – 1.82 (m, 2H, **H-8**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 97.65 (**C-1**), 1, 69.51 (**C-2**), 69.04 (**C-5**), 68.67 (**C-3 or C-4**), 66.15 (**C-4 or C-3**),64.87 (**C-7**), 62.51 (**C-6**), 48.10 **C-9**), 28.65 (**C-8**), 20.70 (**-OAc**).

FT-IR: peak at 2097 cm^{-1} corresponding to R-N=N=N stretching.

Synthesis of 3-azidopropyl α-D-mannopyranoside (M2).[2]



4.5 **M2**

Compound **4.5** (1,56 g, 3.61 mmol) was dissolved in MeOH (0.1 M) and NaOMe (78 mg, 1.45 mmol) was added stepwise. The reaction was left stirring at r.t. for 30 min until TLC (DCM: MeOH-7:3) showed the consumption of the starting material. Amberlite IR120 (H^+ from) was added and left reacting until neutral pH was reached. The resin was filtered off and over cotton and the solvent was removed under reduced pressure. The product **M2** was obtained as a colourless oil (yield: 91%, 0.86 g).

^{1}H NMR (400 MHz, D_2O) δ [ppm] =4.8 (d, 1H, $J_{1\text{-}2}$= 1.6 Hz, **H-1**), 3.97 (dd, $J_{1\text{-}2}$= 1.6 Hz,$J_{2\text{-}3}$= 3.4 Hz, 1H, **H-2**), 3.91 (dd, J_{gem}= 12.5 Hz, $J_{6a\text{-}5}$=1.9, 1H, **H-6a**), 3.88-3.81 (m, 2H, **H-3**, **H-7a**), 3.86-3.83 (m, 2H,**H-7a**,),

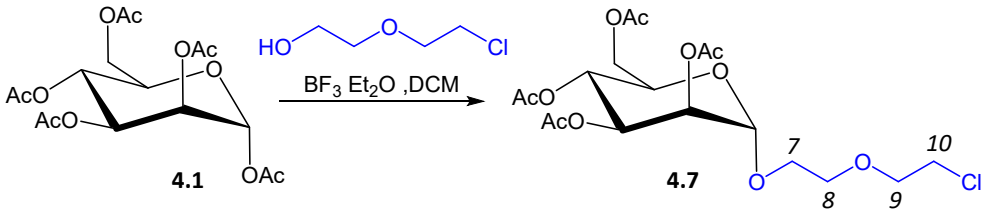
3.78 (dd, J_{gem}=2.5 Hz, J_{6b-5}=5.6 Hz, 1H, **H-6b**) 3.70-3.66 (m, 3H, **H-4**, **H-5** and **H-7a**), 3.62 (dd, 1H, J_{gem} = 5.9 Hz, J_{7-8}= Hz, **H-7b**), 3.48 (td, J_{gem}, J_{9-8}=, 2H, **H-9a**, **H-9b**), 1.97-1.89 (m, 2H, **H-8**)

^{13}C NMR (101 MHz, D_2O) δ [ppm] = 99.78 (**C-1**); 72.3 (**C-2**), 70.59 (**C-3** or **C-4**), 70.05 (**C-3** or **C-4**), 66.74 (**C-5**), 64.80 (**C-6**), 60.91 (**C-7**), 48.22 (**C-9**), 27.85 (**C-8**).

FT-IR: peak at 2094 cm^{-1} corresponding to R-N=N=N stretching.

TOF MS ESI(+): theoretical mass [M+ Na^+]: 286.23 w/z, experimental mass [M+ Na^+] 286.1016 w/z

Synthesis of 2-(2-chloroethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.7).[3]



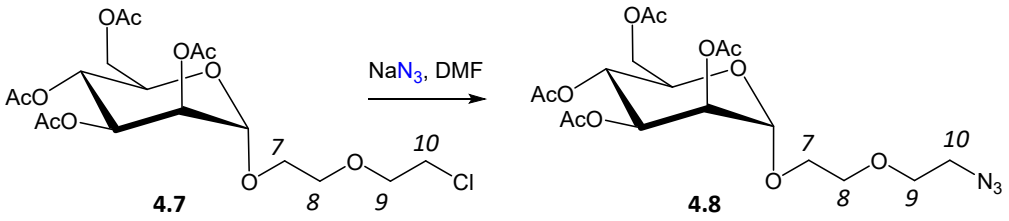
To an ice cooled solution of 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose (**4.1**) (3 g, 7.69 mmol) in dry DCM (0.2 M), ethylene glycol mono-2-chloroethyl ether (2.47 ml, 23 mol) and BF_3Et_2O (3.8 ml, 30.7 mmol.) were added dropwise. The reaction was than warmed up to room temperature and left reacting at r.t. and monitored *via* TLC (Hex:EtOAc= 2:8). After 72 hr, the reaction mixture was quenched with $NaHCO_3$ (2 x 30 ml) until neutral pH and extracted with DCM. The organic layer was washed with a saturated solution of brine and dried over Na_2SO_4. After having filtered off the solids, the solvent was removed with a rotary evaporator and the crude product was obtained as an oil. It was purified by column chromatography (Hex:EtOAc 1:9 → 2:8). The eluent was removed under vacuum to yield the target compound (**4.7**) as a colourless oil (yield: 41%, 1.39 g).

^{1}H NMR (400 MHz, D_2O) δ [ppm] = 5,37 (dd, 1H, J_{1-2}=3.4 Hz, J_{2-3}= 10 Hz, **H-2**), 5.37-5.27 (m, 2H, **H-3**, **H-4**), 4.89 (d, J_{1-2}= 1.5 Hz, 1H, **H-1**), 4,29 (dd, 1H, J= 5.5 Hz, J_{gem}= 12.8 Hz, **H-6a**) 4.20-4.10 (m, 2H, **H-5**, **H-6b**), 3.87-3.80 (m, 1H, **H-7a**), 3.77-3.74(m, 2H, **H7b**, **H-10a**), 3.70-3.67 (m,3H, **H-10b**, **H-8**), 3.64-3.62 (m, 2H, **H-9**), 2.16 (s, 3H**, -OCH$_3$**), 2.10(s, 3H**, -OCH$_3$**), 2.04 (s, 3H**, -OCH$_3$**), 2.04 (s, 3H**, -OCH$_3$**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170,8 (-**C**OCH_3), 170.2 (-**C**OCH_3), 170.0 (-**C**OCH_3), 169.9(-**C**OCH_3), 97.8 (**C1**), 71.5 (**C8** or **C9**), 70.2 (**C8** or **C9**), 69.7 (**C2**), 69.2 (**C3** or **C4**), 68.5 (**C5**), 67.3 (**C7**), 66.3 (**C3** or **C4**), 62.6 (**C6**), 43.0 (**C10**), 21.0 9 (-CO**C**H_3), 20.9 (-CO**C**H_3), 20.8 (2 × -CO**C**H_3).

ESI MS (+): theoretical mass [M+ Na^+]: 477.83 m/z, experimental mass [M+ Na^+]: 477.44 m/z.
TLC: R_f = 0.59 (Hex:EtOAc= 3:7).

Synthesis of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.8).[4]



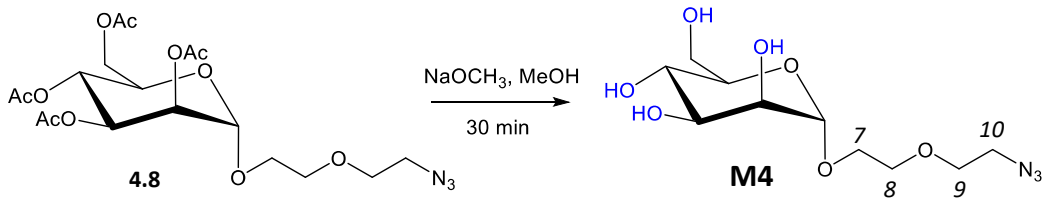
Sodium azide (1.39 g, 20 mmol) was added portion wise to a stirred solution of compound **4.7** (3.18 g, 7 mmol) in DMF(0.2 M). The reaction was refluxed at 70 °C and left reacting overnight, until TLC

(Hex:EtOAc= 2:8) showed the disappearance of the starting material. It was then diluted in water and extracted with Et_2O (3 x 30 ml). The organic layers were combined and washed with saturated solution of $NaHCO_3$ (2 x 30 ml) and brine (2 x 30 ml) and dried over Na_2SO_4. After having filtered off the solids, the solvent was removed with rotary evaporator and the pure product **4.8** was obtained as a white powder (yield: 85%, 2.66 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 5.37 (dd, 1H, J_{2-3}=10 Hz, J1-=3.4 Hz, **H-2**), 5.31-5.26 (m, 2H, **H-3**, **H-4**), 4.88 (d, 1H, J_{1-2}= 1.4 Hz, **H-1**), 4,28 (dd,1H, J_{gem}= 5.2, J_{5-6}=12.4, **H-6a**), 4.12-4.06 (m, 2H, **H-6b**, **H-5**), 3.87-3.81 (m,1H, **H-7a**), 3.77 (m, 1H, **H-7b**), 3.71-3.60 (m, 4H, **H-8**, **H-9**), 3.39 (t, 2H, **H-10**) 2.15 (s, 3H**, -OCH$_3$**), 2.10 (s, 3H**, -OCH$_3$**), 2.03 (s, 3H**, -OCH$_3$**), 1.99 (s, 3H**, -OCH$_3$**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170,8 (-**C**OCH$_3$), 170.2 (-**C**OCH$_3$), 170.0 (-**C**OCH$_3$), 169.9(-**C**OCH$_3$), 97.8 (**C1**), 70.3 (**C8** or **C9**), 70.2 (**C8** or **C9**), 69.7 (**C2**), 69.2 (**C3** or **C4**), 68.5 (**C5**), 67.3 (**C7**), 66.3 (**C3** or **C4**), 62.6 (**C6**), 50.9 (**C10**), 21.0 (-CO**C**H$_3$), 20.9 (-CO**C**H$_3$), 20.8 (2 × -CO**C**H$_3$).

<u>Synthesis of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (M4).</u>[4]



Compound **4.8** (2.66 g, 5.94 mmol) was dissolved in MeOH (0.1 M) and NaOMe (128 mg, 2.3 mmol) was added stepwise. The reaction was left stirring at r.t. for 30 min until TLC (DCM: MeOH-7:3) showed the consumption of the starting material. Amberlite IR120 (H^+ from) was added and left reacting until neutral pH was reached. The resin was filtered off and over cotton and the solvent was removed under reduced pressure. The product **M4** was obtained as a colourless oil (yield =93%, 1.58 g).

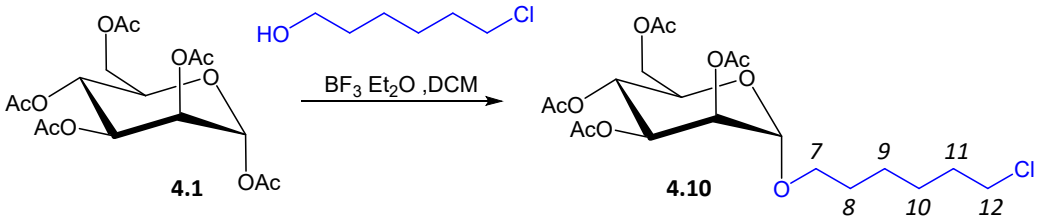
^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 4.92 (d, 1H, J_{1-2}=1.2 Hz, H-1), 4.00 (dd, 1H, J_{1-2}= 1.2 Hz, J_{2-3}= 3.1 Hz, H-2), 3.93-3.9 (m, 3H, H-4, H-6a, H-7a), 3.88-3.85 (m, 1H, H-3), 3.80-3.77 (m, 5H, H-9, H-8, H-7b), 3.69-3.65 (m, 2H, H-5, H-6b), 3.54-3.51 (m, 2H, H-10)

^{13}C NMR (101 MHz, D_2O) δ [ppm] = 99.9 (C-1), 72.7 (C-45), 70.4 (C-2), 69.98 (C-3), 69.41 (C8 or C9), 69.31 (C8 or C9), 66.7 (C-4), 66.3 (C-6), 60.9 (C-7),50.14 (C-10) 69.3 (C-3), 69.4 (C-8 or C-9), 69.3 (C-8 or C-9).

FT-IR: peak at 2111 cm^{-1} corresponding to R-N=N=N stretching.

TOF MS ESI(+): theoretical mass [M+ Na$^+$]:, experimental mass [M+ Na$^+$] 316.1127.

Synthesis of 6-chlorohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.10).[5]



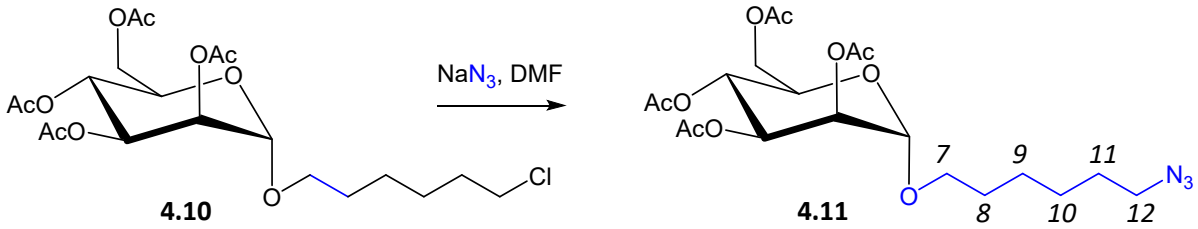
To an ice cooled solution of 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose (**4.1**) (3 g, 7.68 mmol) in dry DCM (0.2 M),6-chlorohexanol (3,07 ml, 23.02 mmol) and BF_3Et_2O (2.84 ml, 4 eq.) were added dropwise. The reaction was than warmed up to room temperature and left reacting at r.t. and monitored *via* TLC (Hex:EtOAc= 3:7). After 72 hr, the reaction mixture was quenched with $NaHCO_3$ (2 × 30 ml) until neutral pH and extracted with DCM (2 × 30 ml). The organic layers ware collected and washed with brine (2 × 30 ml), dried over Na_2SO_4. Filtered and the excess of solvent was removed with a rotary evaporator. The crude product was purified by column chromatography (Hex:EtOAc 1:9→ 3:7). The eluent was removed under vacuum to yield the target compound **4.10** as a colourless oil (yield 80%, 2.87g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 5.35 (dd, 1H, $J_{2,3}$= 10Hz, $J_{1,2}$= 3.4 Hz, 1H, **H-2**); 5.31-5.24 (m, 2H, **H-3**, **H-4**), 4.8 (dd,1H, $J_{1,2}$= 1.2 Hz, **H-1**), 4,28 (dd, 1H, J= 5.3 Hz, J_{gem}= 12.2, **H-6a**) 4.14-4. 09 (m, 2H, **H-5**, **H-6a**,), 3.72-3.64 (m,1H, **H-7a**), 3.56-3.52 (m, 2H, **H-7b**, **H-12a**) 3.48-3.32 (m,1H, **H-12b**), 2.15 (s, 3H**, -OCH$_3$**), 2.10 (s, 3H**, -OCH$_3$**), 2.04 (s, 3H, **-OCH$_3$**), 1.99 (s, 3H, **-OCH$_3$**), 1.83-1.76 (m, 2H, **H-8**), 1.66-1.1.57 (m, 2H, **H-11**), 1.52-1.37 (m, 4H, **H-9**, **H-10**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170 8 (-**C**OCH_3), 170.3 (-**C**OCH_3), 170.1 (-**C**OCH_3), 169.9 (-**C**OCH_3), 97.8 (**C1**), 69.8 (**C2**), 69.3 (**C3** or **C4**),68.6 (**C5**), 68.4 (**C3** or **C4**), 66.4 (**C7**), 62.7 (**C6**), 45.1 (**C12**), 32.6 (**C8**), 29.2 (**C9** or **C10** or **C11**), 26.7 (**C9** or **C10** or **C11**), 25.6 (**C9** or **C10** or **C11**), 21.0 (-CO**C**H_3), 20.9 (-CO**C**H_3), 20.8 (2 × -CO**C**H_3).

TLC: R_f = 0.6 (Hex:EtOAc= 3:7).
ESI MS (+): theoretical mass [M+ N^+]: 489.89m/z, experimental mass [M+ Na^+]: 489.5m/z.

Synthesis of 6-Azidohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.11).[5]



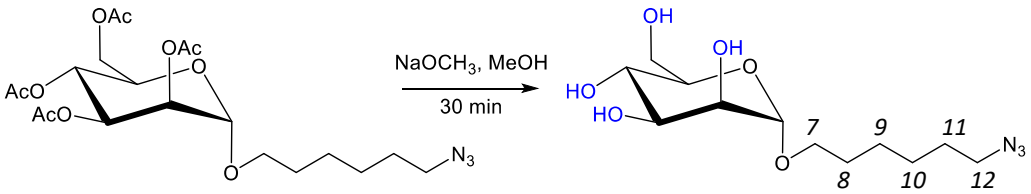
Sodium azide (1.3 g, 20 mmol) was added portion wise to a stirred solution of compound **4.10** (2.87 g, 6.33 mmol) in DMF (0.2 M). The reaction was refluxed at 70 °C and left reacting overnight, until TLC (Hex:EtOAc= 3:7) showed the disappearance of the starting material. It was then diluted in water and extracted with Et_2O (3 x 30 ml). The organic layers were combined and washed with saturated solution of $NaHCO_3$ (2 x 30 ml) and brine (2 x 30 ml) and dried over Na_2SO_4. After having filtered off the solids,

the solvent was removed with rotary evaporator and the pure product was obtained as a white powder (yield: 81%, 2.35 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 5.28 (dd, 1H, J_{1-2}= 3,4 Hz, J_{2-3}= 10 Hz, **H-2**); 5.28-5.16 (m, 2H, **H-3**, **H-4**), 4.73 (d, 1H, J_{1-2}= 1.3, **H-1**), 4.21 (dd, 1H, J_{gem}=12.2, J= 5.3 Hz, **H-6a**) 4.10 (dd,1H, J_{gem}=12.2, J=5.3, **H-6b**), 3.99-3.96 (m, 1H, **H-5**), 3.68 (ddd, J_{gem}=19.0, J=9.6, J=6.4 Hz, **H-7a**), 3.45 (dt, 1H, J 9.6Hz, J=6.4 Hz, **H-7b**,) 3.28 (m,2H, **H-12a**, **H-12b**), 2.15 (s, 3H**, -OCH$_3$**), 2.10 (s, 3H**, -OCH$_3$**), 2.04 (s, 3H**, -OCH$_3$**), 1.99 (s, 3H**, -OCH$_3$**), 1.83-1.76 (m, 2H, **H-8**), 1.66-1.39 (m, 8H, **H-9**, **H-10**, **H-11**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170 8 (-**C**OCH_3), 170.3 (-**C**OCH_3), 170.1 (-**C**OCH_3), 169.9 (-**C**OCH_3), 97.8 (**C1**), 69.8 (**C2**), 69.3 (**C3** or **C4**),68.6 (**C5**), 68.4 (**C3** or **C4**), 66.4 (**C7**), 62.7 (**C6**), 51.5 (**C12**), 32.6 (**C8**), 29.2 (**C9** or **C10** or **C11**), 26.7 (**C9** or **C10** or **C11**), 25.6 (**C9** or **C10** or **C11**), 21.0 (-CO**C**H_3), 20.9 (-CO**C**H_3), 20.8 (2 × -CO**C**H_3).

Synthesis of 6-azidohexyl α-D-mannopyranoside (M3).[5]



4.11 **M3**

Compound **4.11**(2.35, 5.12 mmol) was dissolved in MeOH (0.1 M) and NaOMe (0.832 mg, 12.8 mmol) was added stepwise. The reaction was left stirring at r.t. for 30 min until TLC (DCM: MeOH-7:3) showed the consumption of the starting material. Amberlite IR120 (H^+ from) was added and left reacting until neutral pH was reached. The resin was filtered off and over cotton and the solvent was removed under reduced pressure. The product **4.12** was obtained as a colourless oil (yield= 98%, 1.47 g).

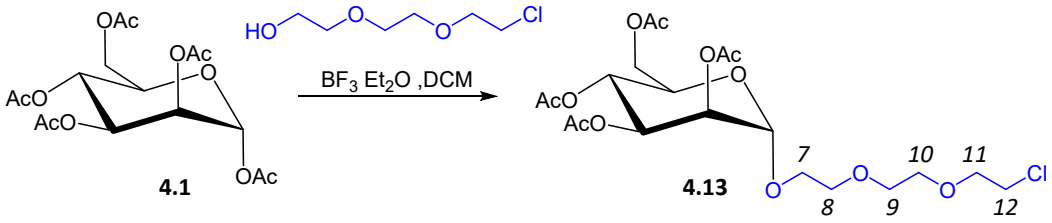
^{1}H NMR (400 MHz, D_2O) δ [ppm] = 4.88 (d, J_{1-2}=1.5 Hz, 1H, **H-1**) 3.95 (dd, J_{1-2}= 1.5 Hz, J_{2-3}= 3.4 Hz, 1H, **H-2**), 3.90 (dd, J_{gem}= 1.5 Hz, J_{5-6}= 12.5 Hz, 1H, **H-6a**), 3.82-3.73 (m, 3H, **H-3, H-4, H-7a**), 3.69-3.63(m, 2H, , **H-6b, H-7b**), 3.58 (m, 1H, **H-5**), 3.35 (t, 2H, J= 6.6 Hz, **H-12**), 1.66-1.60 (m, 4H, **H-10**, **H-11**), 1.46-1.39 (m, 4H, **H-8**, **H-9**).

^{13}C NMR (101 MHz, D_2O) δ [ppm] = 99.66 (**C-1**), 72.72 (**C-5**), 70.64 (**C-2**), 70.09 (**C-3**), 67.77 (**C-3**), 67.77(**C-6**), 66.77 (C-4), 60.92 (C-7), 51.15 (**C-12**), 28.34 (C10 or C11), 27.89 (C10 or C11), 25.7 (C8 or C9), 24.96 (C8 or C9).

FT-IR: peak at 2097 cm^{-1} corresponding to R-N=N=N stretching.

TOF MS ESI(+): theoretical mass [M+ Na^+] 328.31 :, experimental mass [M+ Na^+] 328.1490 w/z.

Synthesis of 2-[2-(2-chloroethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.13).[6]



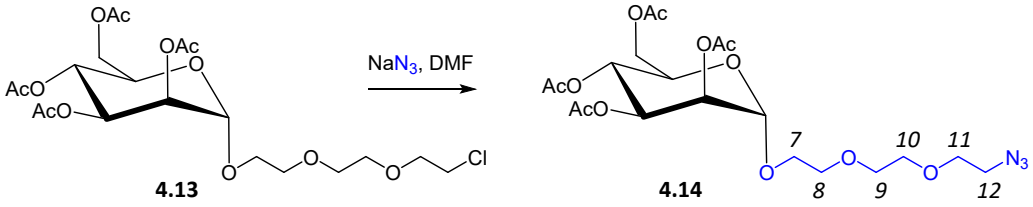
To an ice-cooled solution of 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose (**4.1)** (3 g, 7.69 mmol) and 2-2-[2-(2-chloroethoxy)ethoxy]ethanol (3.35 ml, 23 mmol) in dry DCM (0.2 M), BF_3Et_2O (2.83 ml, 23 mmol) was added dropwise. The reaction was left reacting at r.t. for 72 hr and monitored *via* TLC (EtOAc: Hex= 8:2). The reactive solution was quenched at 0 °C with K_2CO_3 until neutral pH and extracted with DCM (2 × 30 ml). The organic phase was washed with saturated solution of $NaHCO_3$ (2 × 30 ml) and brine (2 × 30 ml). After having dried the organic layer over Na_2SO_4, the solvent was evaporated under reduce pressure. The crude product was purified by column chromatography (Hex:EtOAc 1:9→ 2:8) and the eluent was removed under vacuum to obtained the target **4.13** compound as a syrup (yield=54%, 2.22 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] = 5.36 (dd, 1H, $J_{2\text{-}3}$= 10 Hz, $J_{1\text{-}2}$=3.4 Hz, **H-2**), 5,31-5.26 (m, 2H, **H-3**, **H-4**), 4.87 (d, 1H, $J_{1\text{-}2}$=1.4 Hz, **H-1**), 4.29 (dd, 1H, J_{gem}=12.3 Hz, J=5.4 Hz, **H-6a**), 4.14-4.04 (m, 2H, **H-5**, **H-6b**), 3.84-3.80 (m, 1H, H-7a), 3.78-3.75 (m, 2H, **H-7b**, **H-12a**), 3.70-3.62 (m, 9H, **H-8**, **H-9**, **H-10**, **H-11**, **H-12b**), 2.16 (s, 3H**, -OCH$_3$**), 2.10 (s, 3H**, -OCH$_3$**), 2.04 (s, 3H**, -OCH$_3$**), 1.99 (s, 3H**, -OCH$_3$**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170.8 (-**C**OCH$_3$), 170.2 (-**C**OCH$_3$), 170.1 (-**C**OCH$_3$), 169.8 (-**C**OCH$_3$), 97.8 (**C1**), 71.5 (**C8** or **C9** or **C10** or **C11**), 70.9 (**C8** or **C9** or **C10** or **C11**), 70.8 (**C8** or **C9** or **C10** or **C11**), 70.2 (**C8** or **C9** or **C10** or **C11**), 69.7 (**C2**), 69.3 (**C3** or **C4**), 68.6 (**C5**), 67.6 (**C7**), 66.3(**C3** or **C4**), 62.6 (**C6**), 42.9 (**C12**), 21.5 (-CO**C**H$_3$), 20.8 (2 × -CO**C**H$_3$), 20.6 (-CO**C**H$_3$).

ESI MS (+): theoretical mass [M+ Na$^+$]: 521.89 m/z, experimental mass [M+Na$^+$]: 521.66 m/z.
TLC: R_f = 0.43 (Hex:EtOAc= 2:8).

Synthesis of 2-[2-(2-azidoethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (4.14).[6]

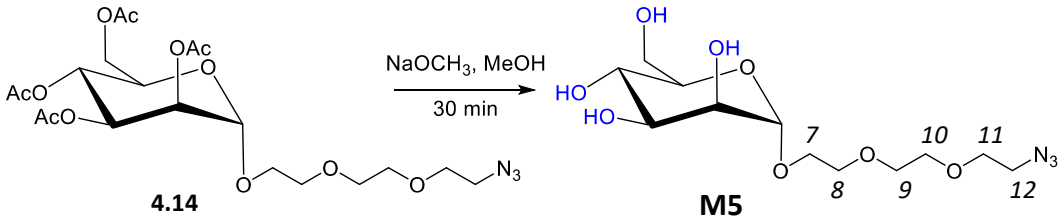


Sodium azide (867 mg, 13.35 mmol) was added portion wise to a stirred solution of compound **4.13** (2.22 g, 4.45 mmol) in DMF (0.2 M). The reaction was refluxed at 70 °C and left reacting overnight, until TLC (Hex:EtOAc= 2:8) showed the disappearance of the starting material. It was then diluted in water and extracted with Et_2O (3 x 30 ml). The organic layers were combined and washed with saturated solution of $NaHCO_3$ (2 x 30 ml) and brine (2 x 30 ml) and dried over Na_2SO_4. After having filtered off the solids, the solvent was removed with rotary evaporator and the pure product (**4.14**) was obtained as a white powder (yield: 81%, 1,8 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ [ppm] =5.36 (dd, 1H, J_{1-2}=3.4 Hz, J_{2-3}=10 Hz, **H-2**), 5.31-5.26 (m, 2H, **H-3**, **H-4**), 4.86 (d, 1H, J_{1-2}=1.1 Hz, **H-1**), 4.28 (dd, 1H, J_{gem}=12.2 Hz, J= 5.0 Hz, **H-6a**), 4.12-4.04 (m, 2H, **H-5**, **H-6b**), 3.85-3.74 (m, 1H, **H-7a**), 3.70-3.62 (m, 9H, **H-7b**, **H-8**, **H-9**, **H-10**, **H-11**), 3.39 9t, 2H, **H-12**), 2.17 (s, 3H**, -OCH$_3$**), 2.10 (s, 3H**, -OCH$_3$**), 2.04 (s, 3H**, -OCH$_3$**), 1.99 (s, 3H**, -OCH$_3$**).

^{13}C NMR (101 MHz, $CDCl_3$) δ [ppm] = 170.8 (-**C**OCH_3), 170.2 (-**C**OCH_3), 170.1 (-**C**OCH_3), 169.8 (-**C**OCH_3), 97.8 (**C1**), 70.9 (**C8** or **C9** or **C10** or **C11**), 70.8 (**C8** or **C9** or **C10** or **C11**), 70.2 (**C8** or **C9** or **C10** or **C11**), 70.1 (**C8** or **C9** or **C10** or **C11**), 69.7 (**C2**), 69.3 (**C3** or **C4**), 68.6 (**C5**), 67.6 (**C7**), 66.3(**C3** or **C4**), 62.6 (**C6**), 42.9 (**C12**), 21.0 (-CO**C**H_3), 20.9 (-CO**C**H_3) 20.8 (2 × -CO**C**H_3).

<u>Synthesis of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (M5).</u>6



Compound **4.14** (1.8 g, 3.58 mmol) was dissolved in MeOH (0.1 M) and NaOMe (65 mg, 1.43 mmol) was added stepwise. The reaction was left stirring at r.t. for 30 min until TLC (DCM: MeOH-7:3) showed the consumption of the starting material. Amberlite IR120 (H^+ from) was added and left reacting until neutral pH was reached. The resin was filtered off and over cotton and the solvent was removed under reduced pressure. The product **M5** was obtained as a colourless oil (yield =95%, 1.14 g).

FT-IR: peak at 2104 cm^{-1} corresponding to R-N=N=N stretching.

TOF MS ESI(+): theoretical mass [M+ Na^+] 360.31 :, experimental mass [M+ Na^+] 360.1383 w/z.

^{1}H NMR (400 MHz, D_2O) δ [ppm] = 4.91 (d, J_{1-2}= 1.6 Hz, 1H, **H-1**), 3.98 (dd, J_{1-2}= 1.6 Hz, J_{2-3}=3.4 Hz, 1H, **H-2**), 3.92-3.87 (m, 3H,H-4, **H-6a, H-7a**),3.84 (m, 1H, H-3), 3.79-3.71 (m, 10H, **H-7b**, **H-8**, **H-9**, **H-10**, **H-11**), 3,70-3,66 (m, 2H, H-5, H-6b), 3.52 (t, 2H, **H-12a**, **H-12b**).

^{13}C NMR (101 MHz, D_2O) δ [ppm] = 99.9 (**C-1**), 72.7 (**C-5**),70.5 (**C-2**), 69.9 (C-3), 69.6 (**C8** or **C9** or **C10** or **C-11**),69.56 (**C8**, or **C9** or **C10** or **C-11**), 69.51 (**C8**, or **C9** or **C10** or **C-11**), 69.2 (**C8**, or **C9** or **C10** or **C-11**), 66.7 (C-4)66.4 (**C-6**), 60.9 (C-7), 50.1 (**C-12**).

2.2 Spectra of mannosides

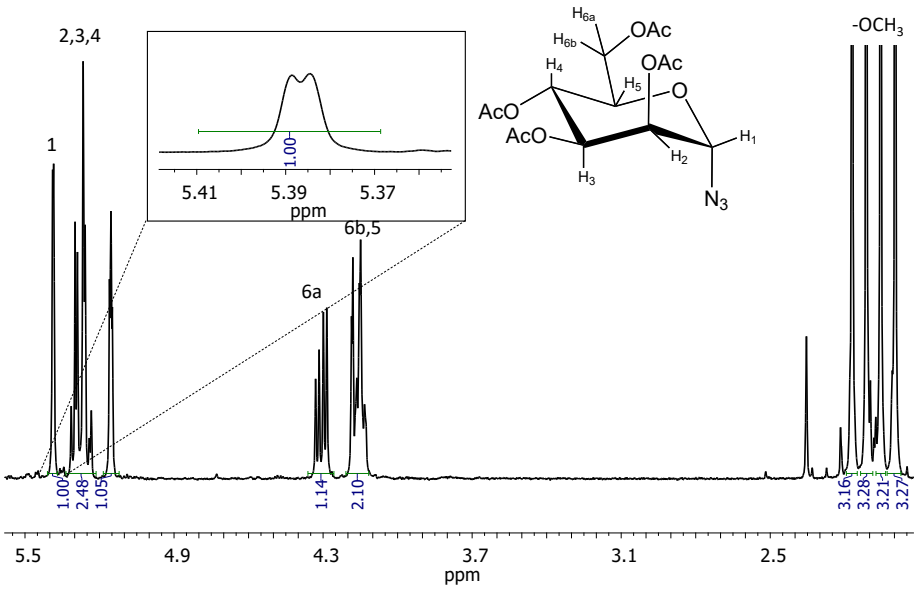


Figure S16. ^{1}H-NMR spectrum of penta-O-acetyl-α-D-azido-mannopyranose ($CDCl_3$, 400 MHz).

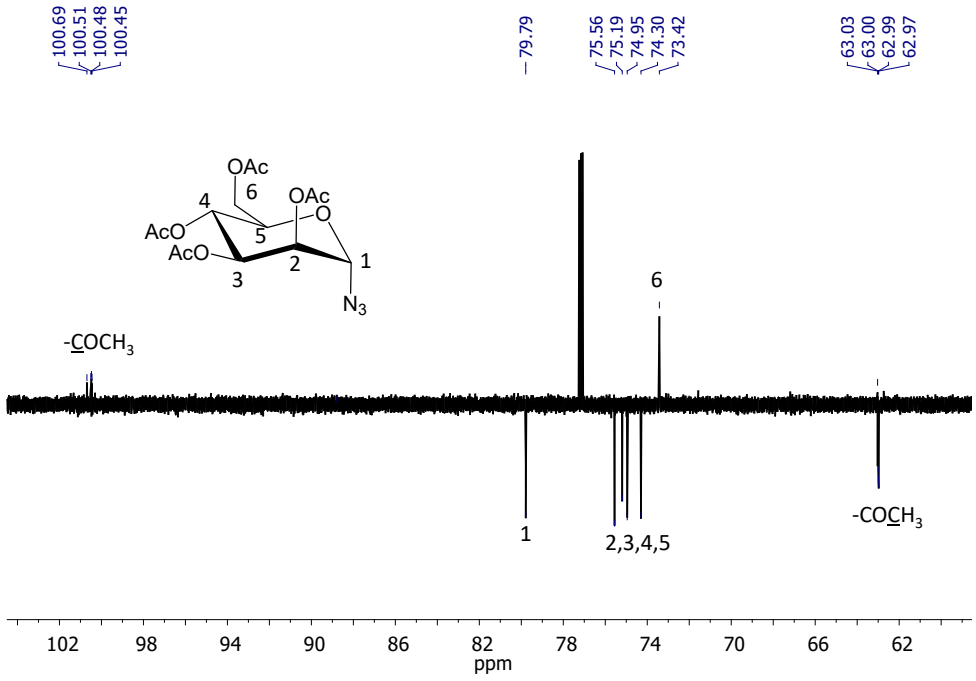


Figure S17. ^{13}C-NMR spectrum of penta-O-acetyl-α-D-azido-mannopyranose ($CDCl_3$, 400 MHz).

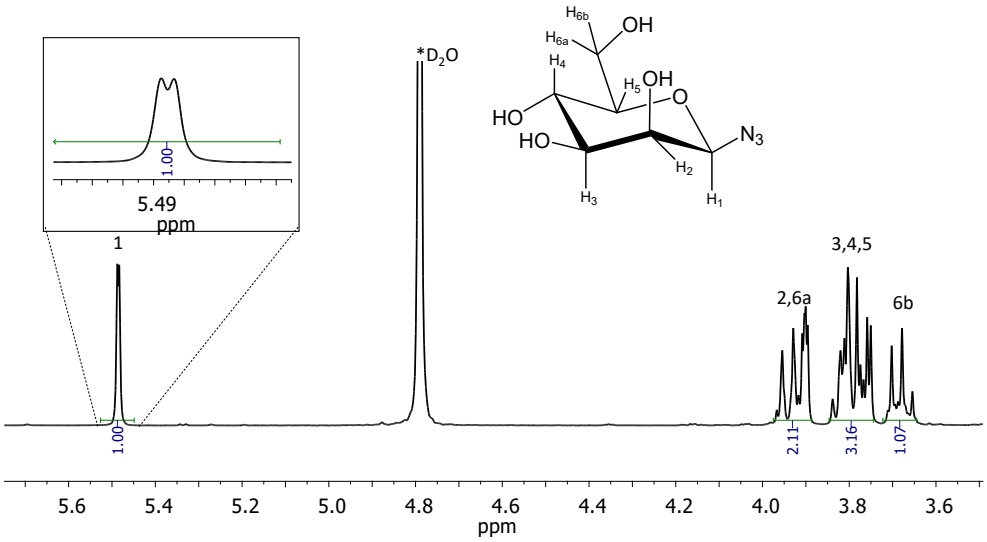


Figure S18. ^{1}H-NMR spectrum of α-D-azido-mannopyranose (D_2O, 400 MHz).

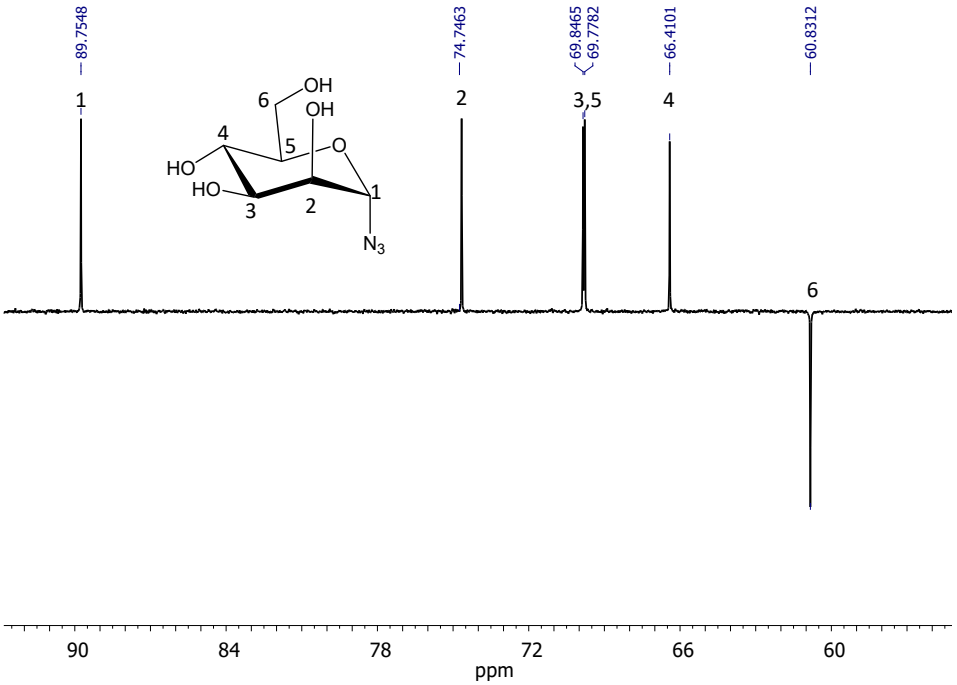


Figure S19. ^{13}C-NMR spectrum of α-D-azido-mannopyranose (D_2O, 400 MHz).

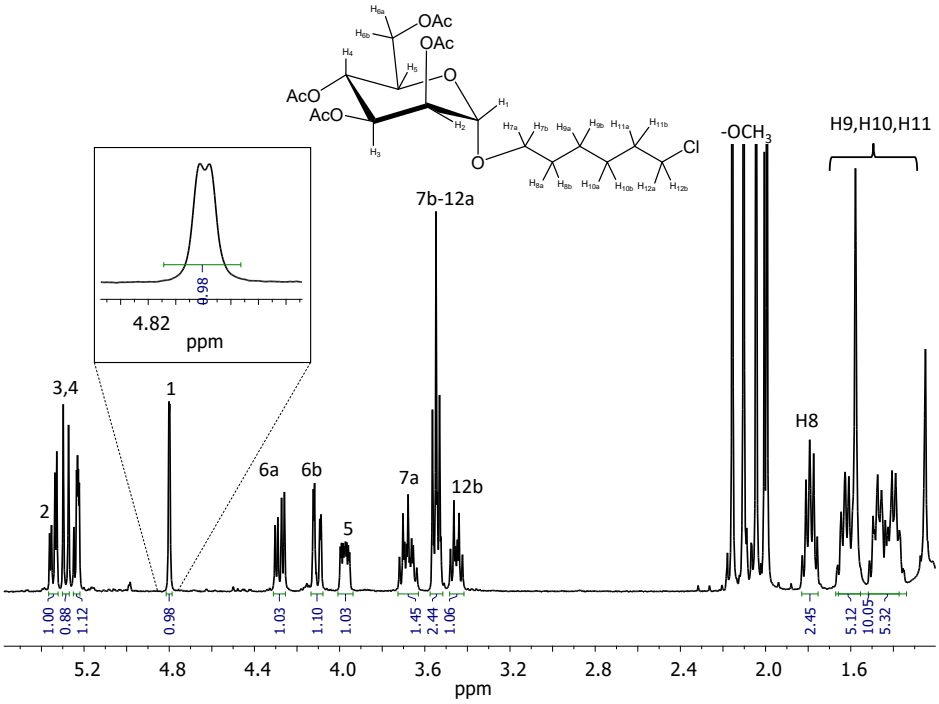


Figure S20. ^{1}H-NMR spectrum of 6-chlorohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

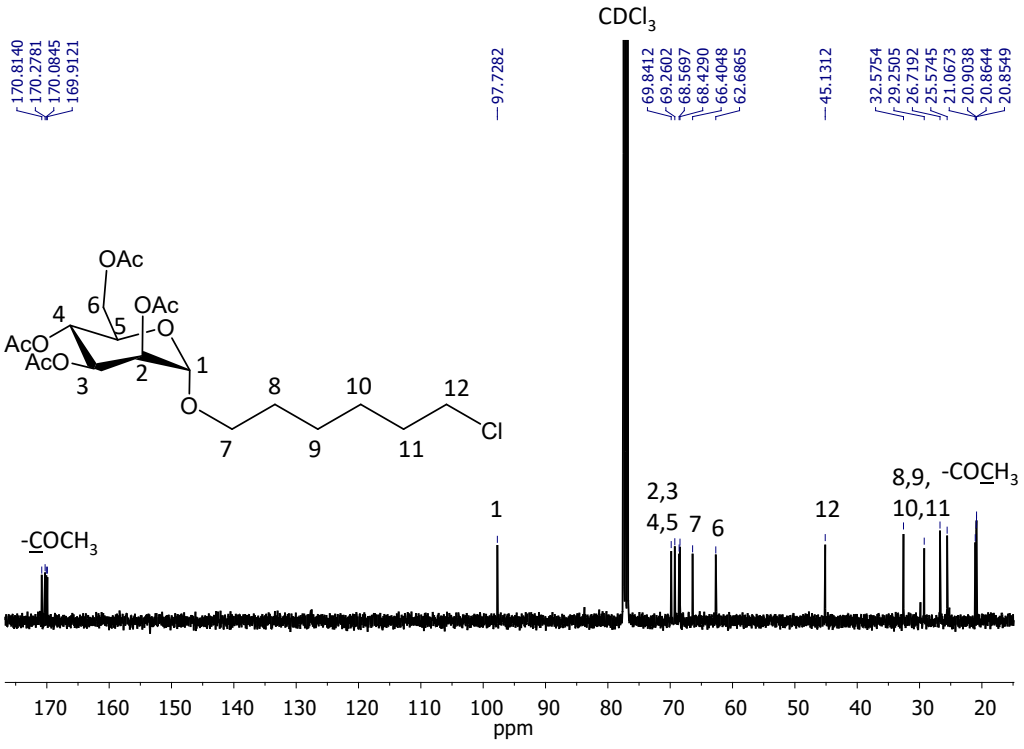


Figure S21. ^{13}C-NMR spectrum of 6-chlorohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

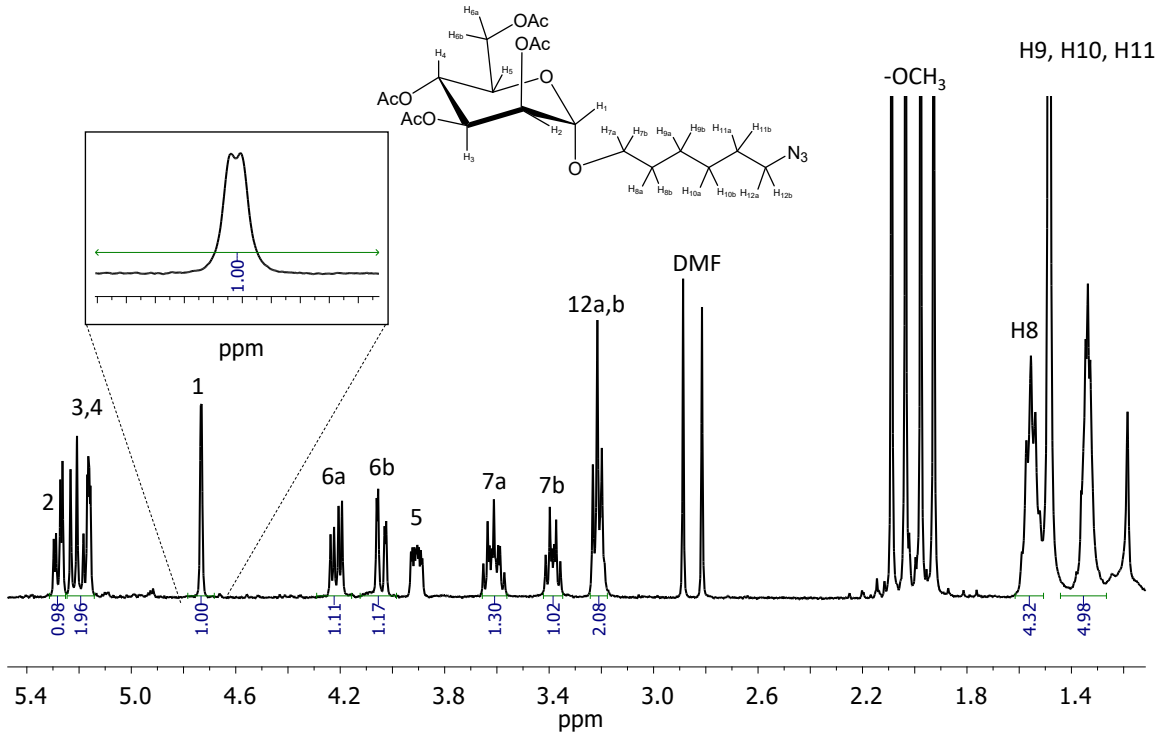


Figure S22. ^{1}H-NMR spectrum of 6-azidohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

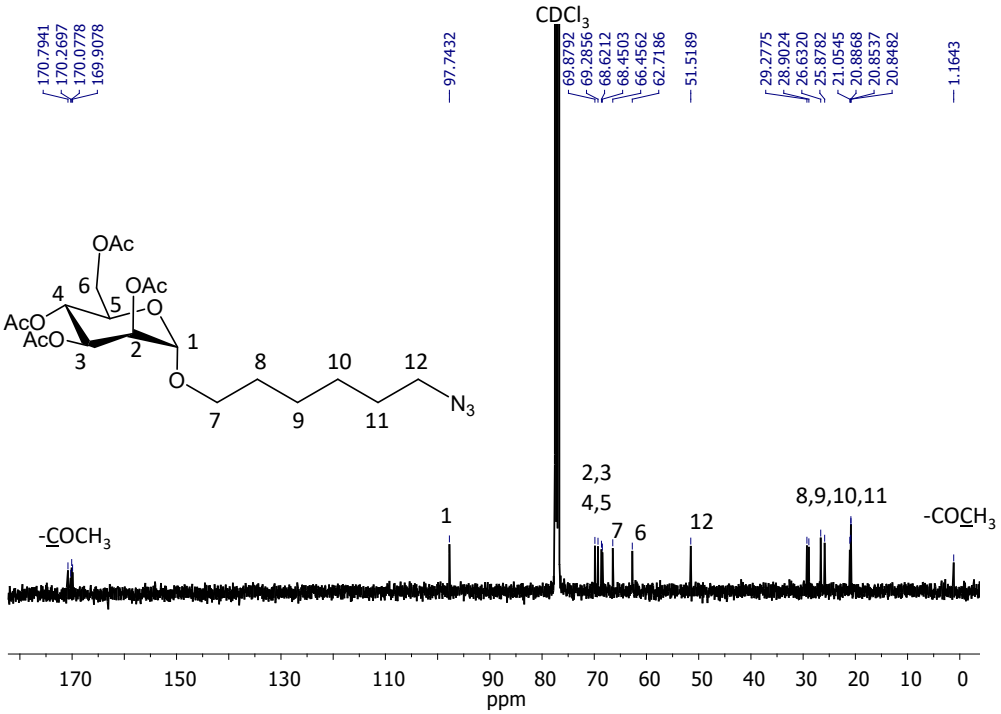


Figure S23. ^{13}C-NMR spectrum of 6-azidohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

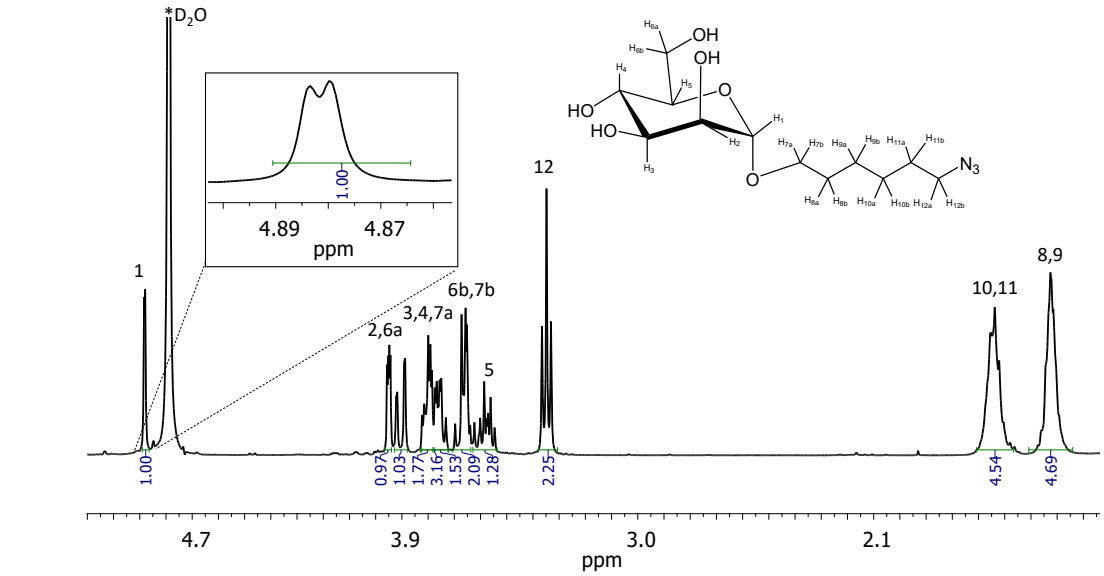


Figure S24. ^{1}H-NMR spectrum of 6-azidohexyl α-D-mannopyranoside (D_2O, 400 MHz).

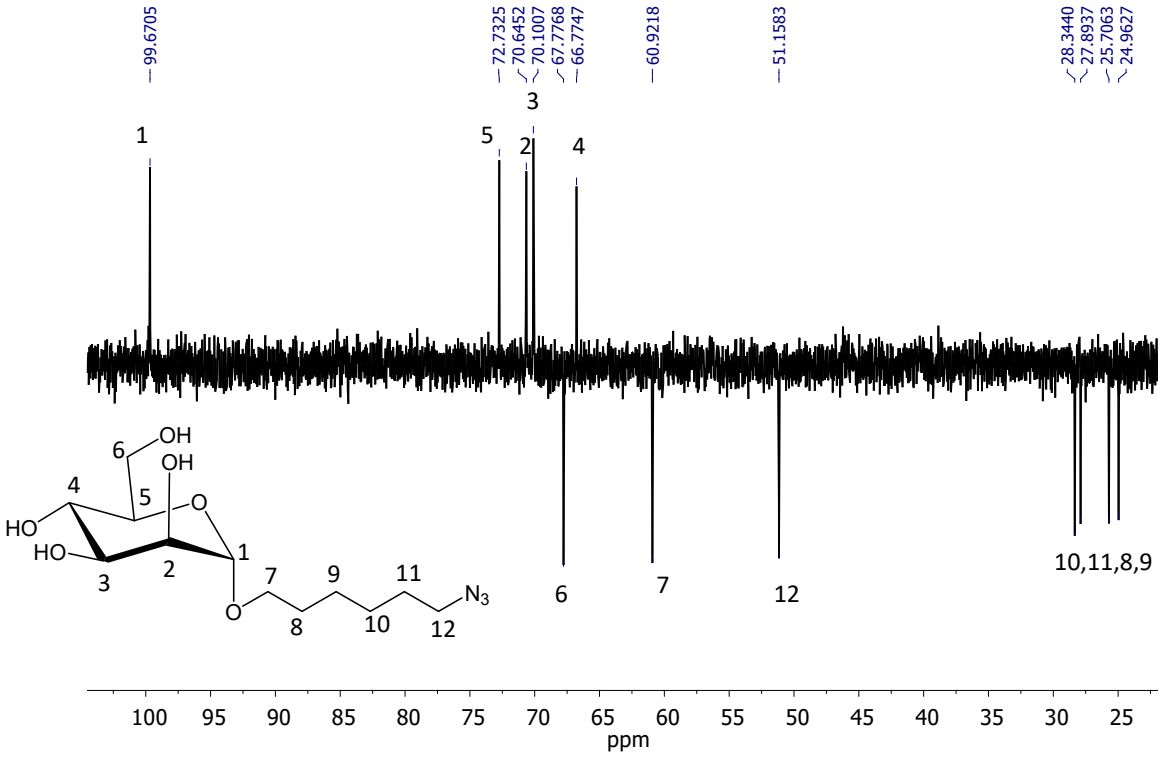


Figure S25. ^{13}C-NMR spectrum of 6-azidohexyl α-D-mannopyranoside (D2O, 400 MHz).

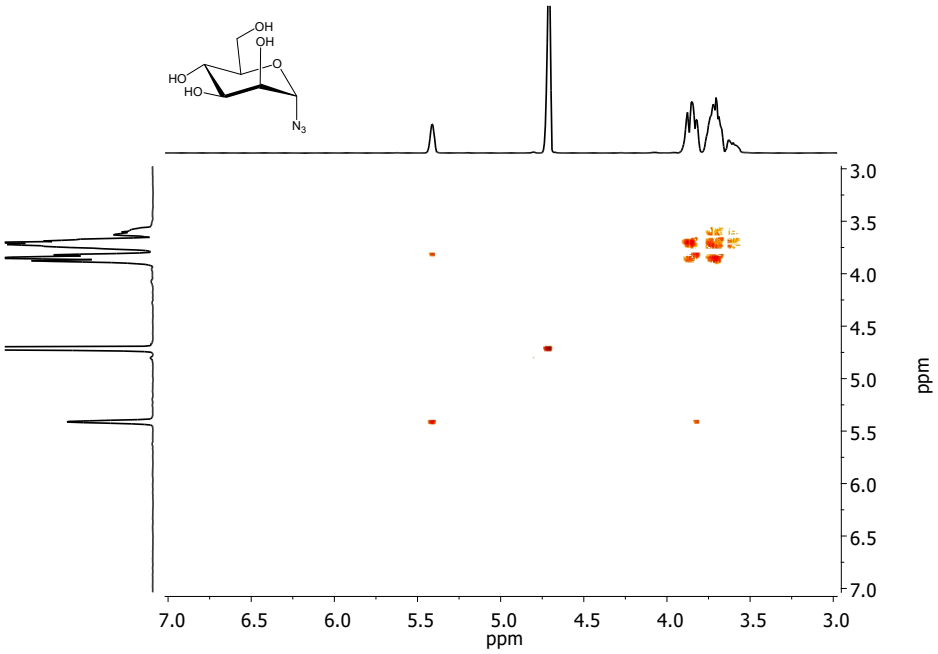


Figure S26. COSY spectrum of 1-azido-α-D-mannopyranose (D_2O, 400 MHz).

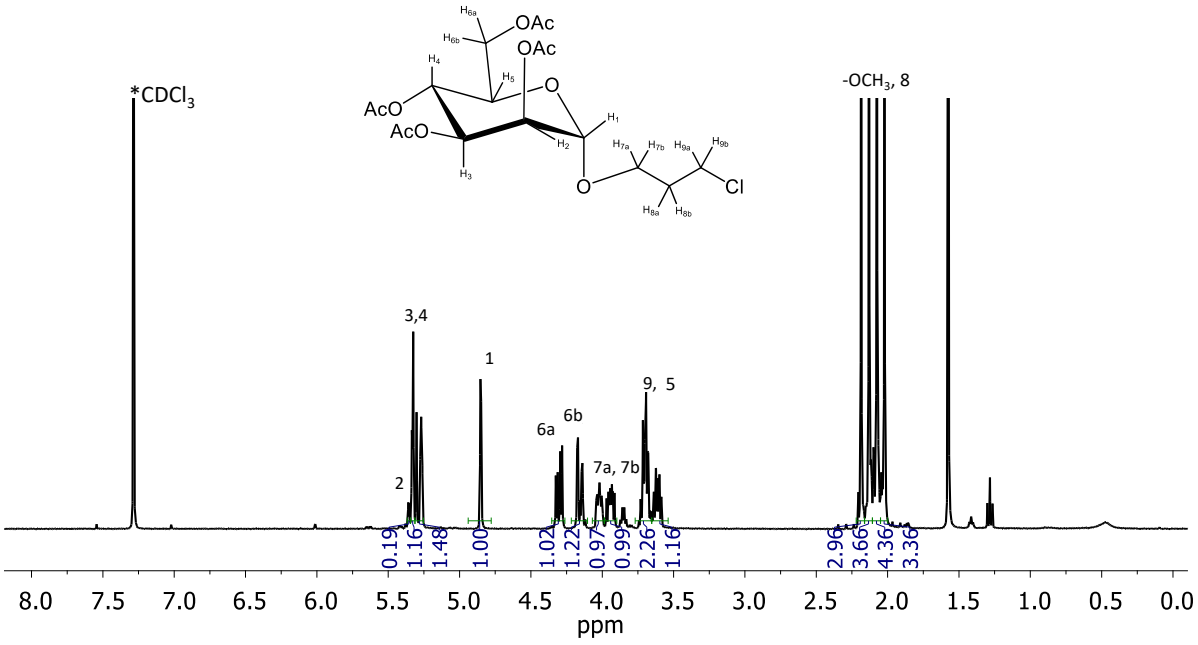


Figure S27. ^{1}H-NMR spectrum of 3-chloropropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

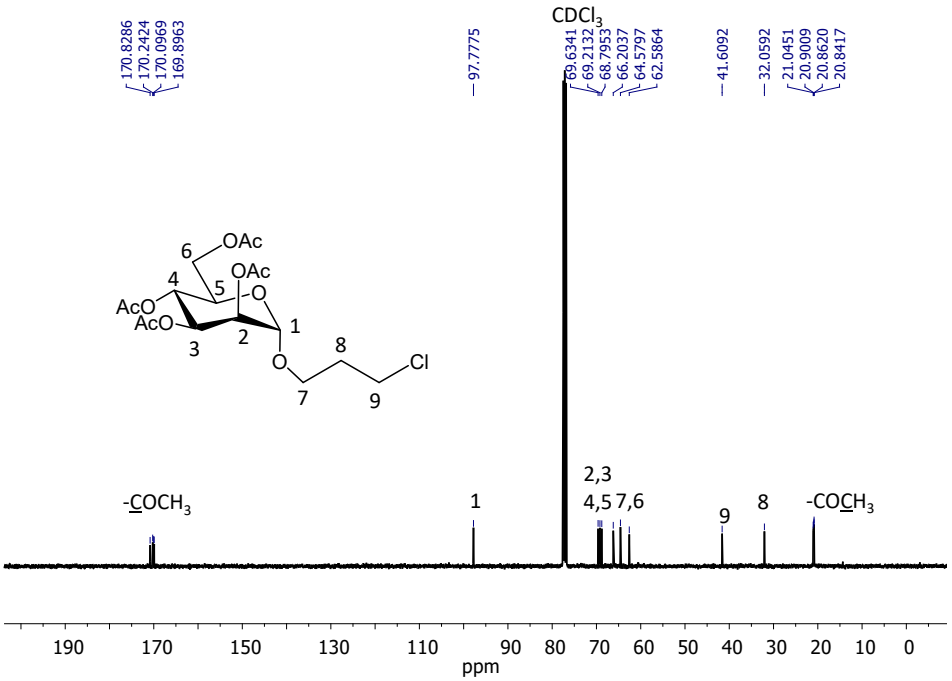


Figure S28. ^{13}C-NMR spectrum of 3-chloropropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

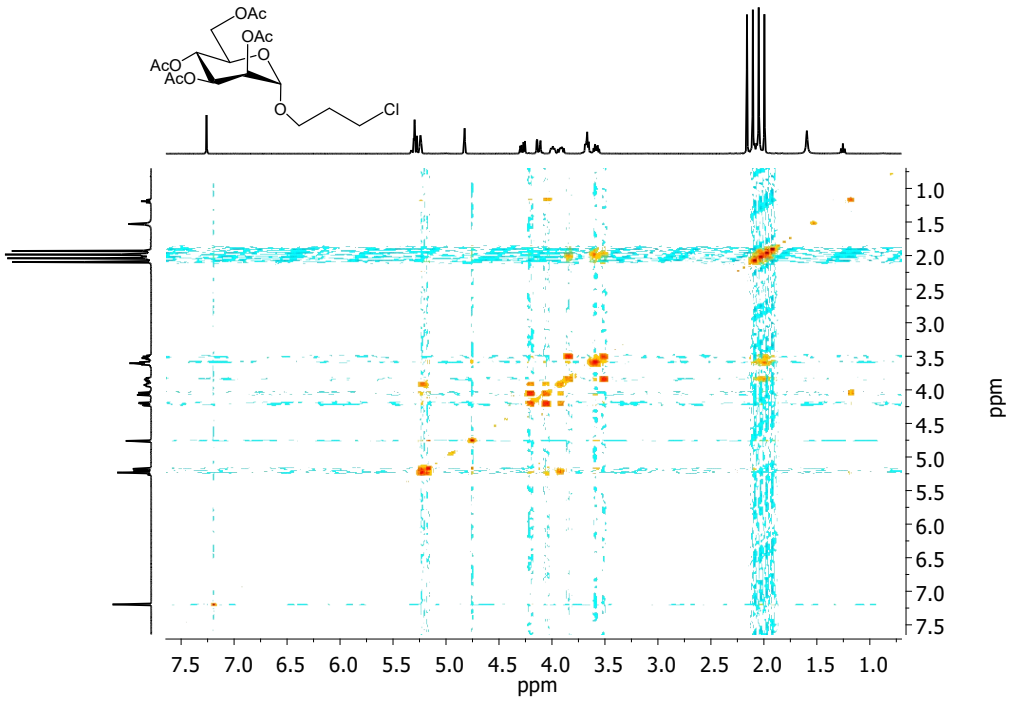


Figure S29. COSY spectrum of 3-chloropropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

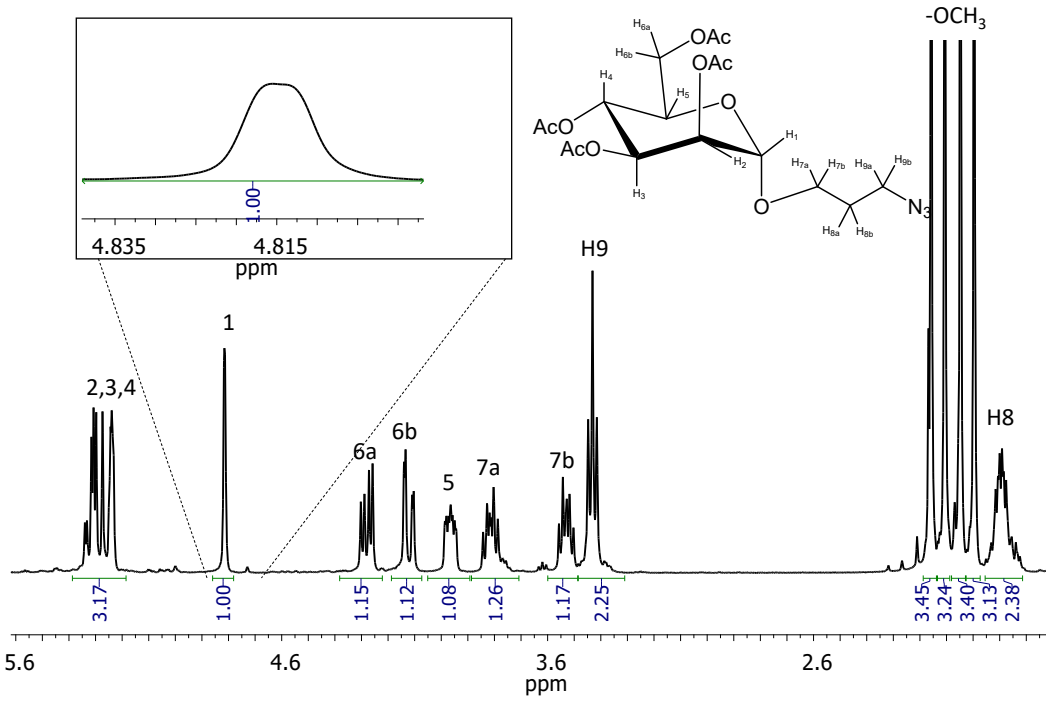


Figure S30. ^{1}H-NMR spectrum of 3-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

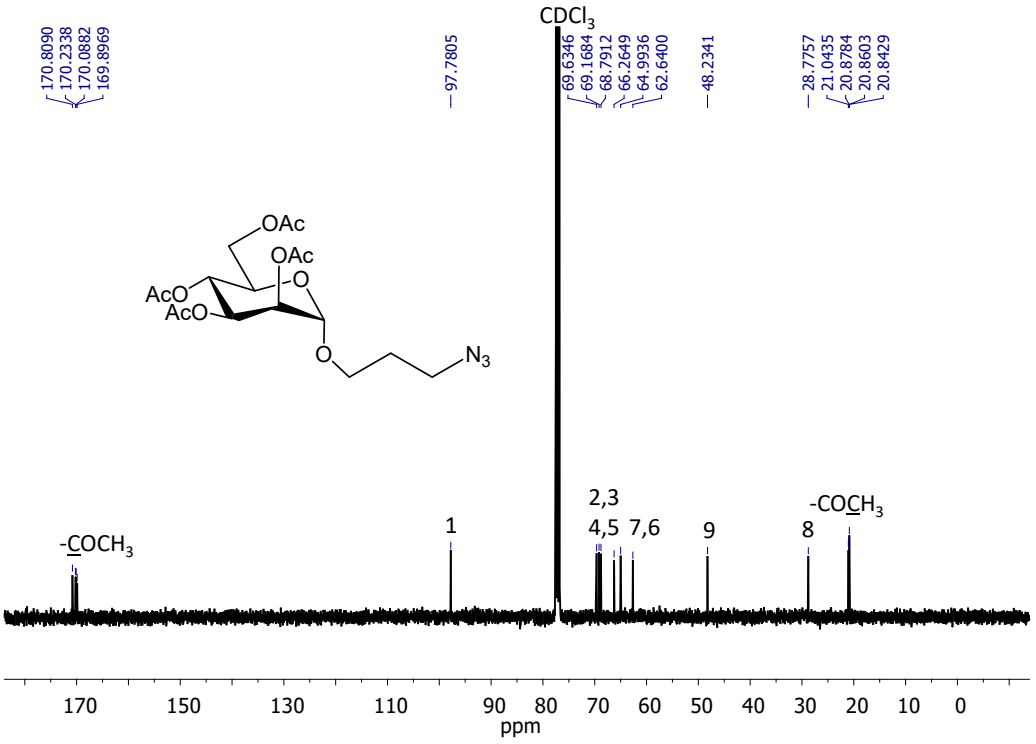


Figure S31. ^{13}C-NMR spectrum of 3-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

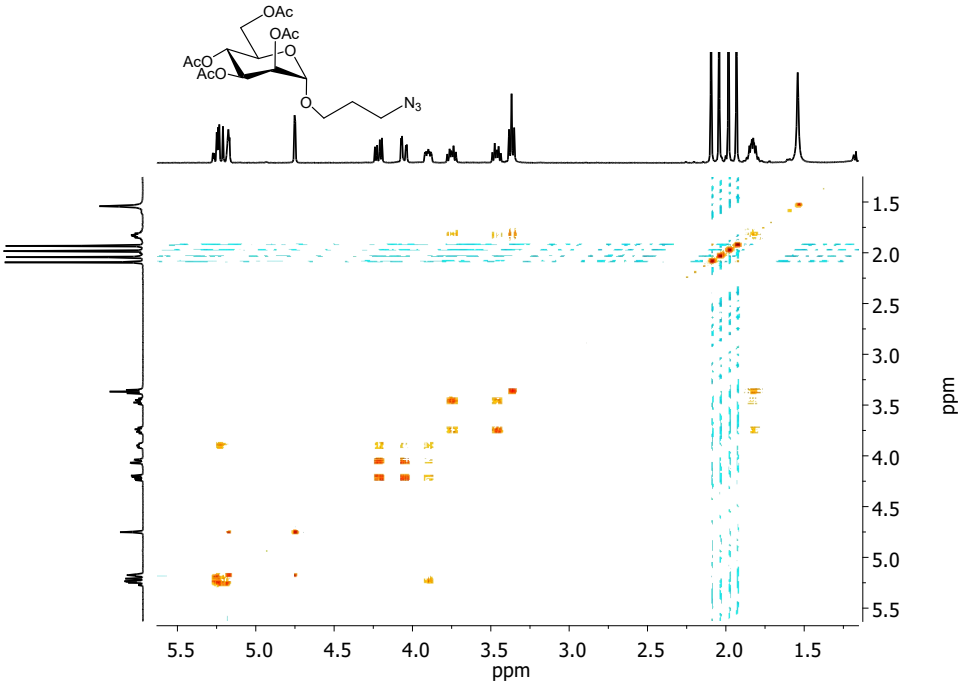


Figure S32. COSY spectrum of 3-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

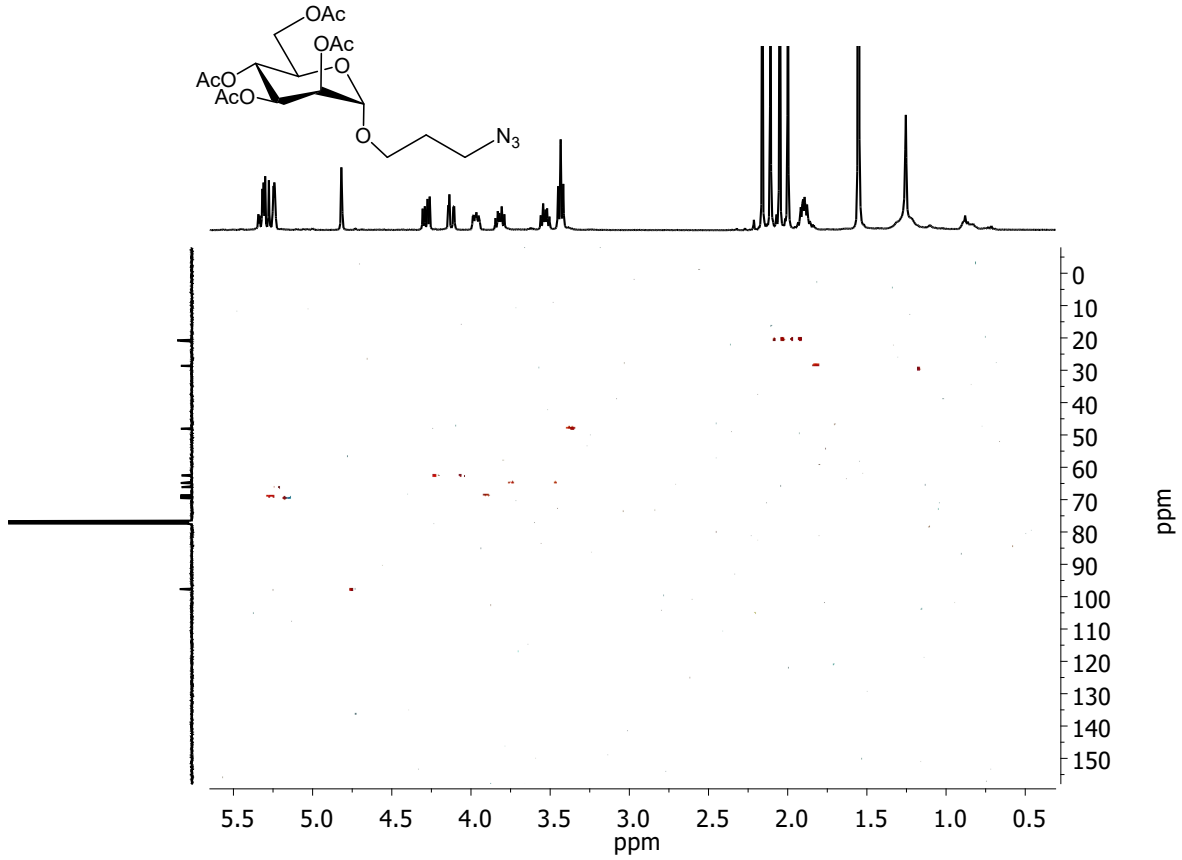


Figure S33. HSQC-NMR spectrum of 3-azidopropyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

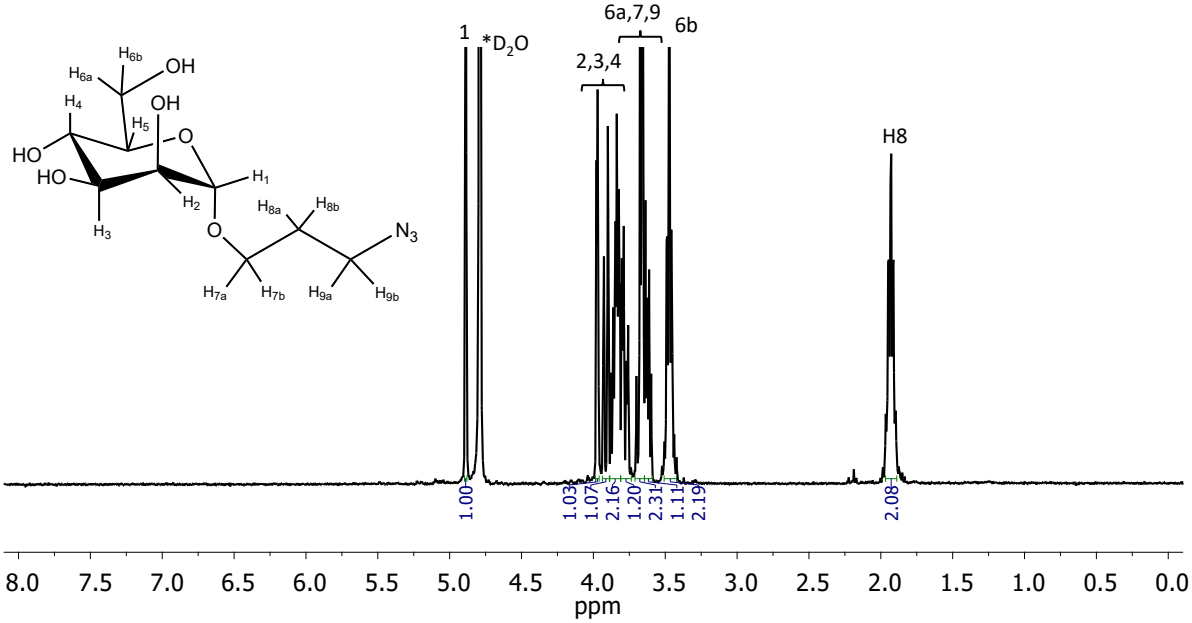


Figure S34. Full ^{1}H-NMR spectrum of 3-azidopropyl α-D-mannopyranoside (D_2O, 400 MHz).

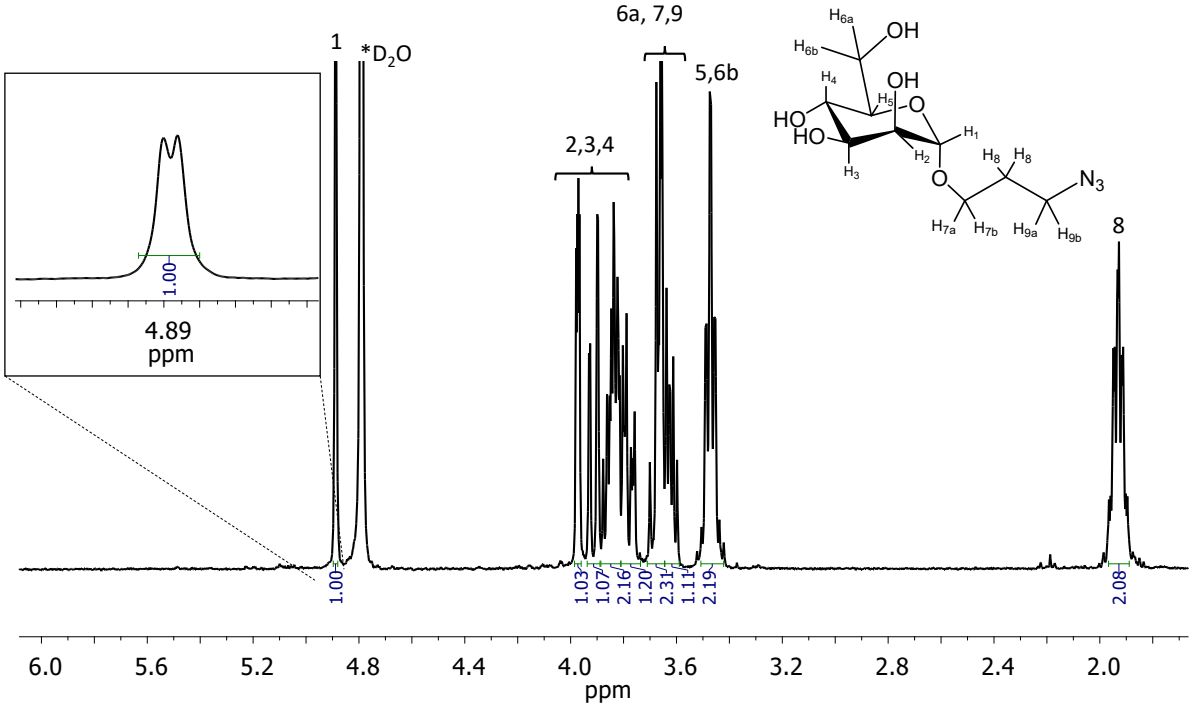


Figure S35. ^{1}H-NMR spectrum of 3-azidopropyl α-D-mannopyranoside (D_2O, 400 MHz).

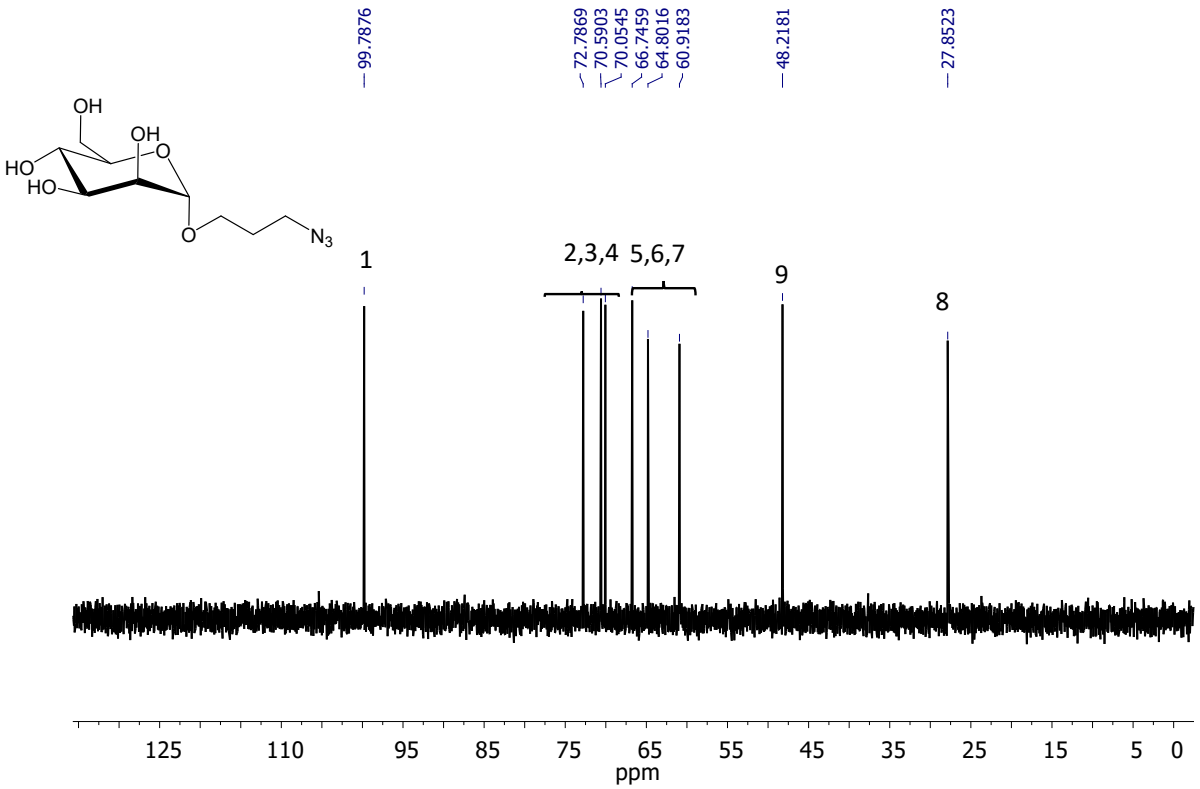


Figure S36. ^{13}C-NMR spectrum of 3-azidopropyl α-D-mannopyranoside (D_2O, 400 MHz).

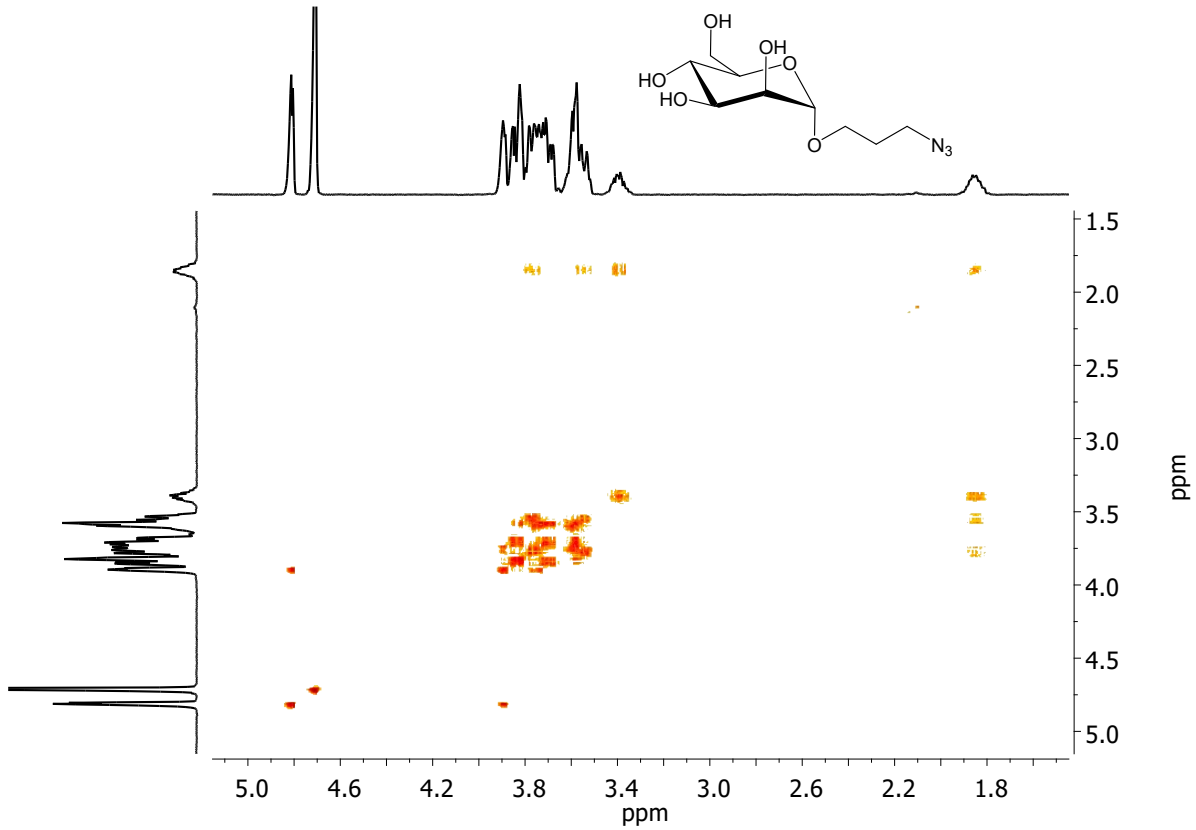


Figure S37. COSY spectrum of 3-azidopropyl α-D-mannopyranoside (D_2O, 400 MHz).

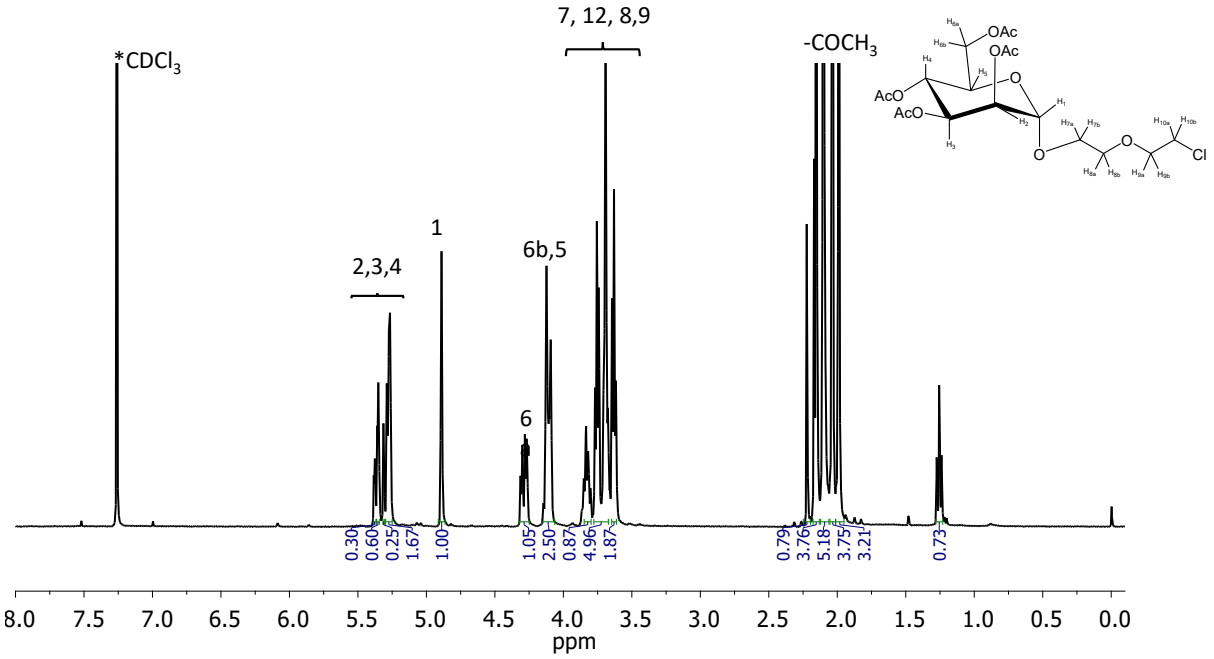


Figure S38. Figure S.4.17. Full ^{1}H-NMR spectrum of 2-(2-chloroethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

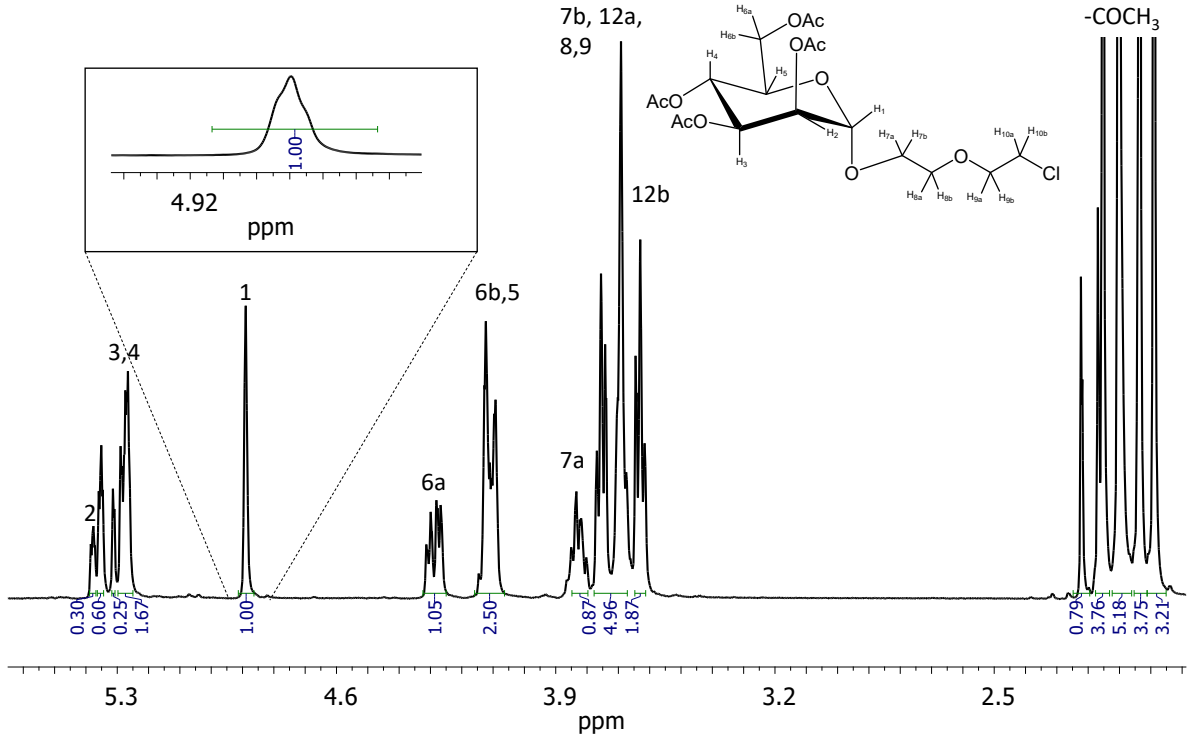


Figure S39. Figure S.4.18. ^{1}H-NMR spectrum of 2-(2-chloroethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

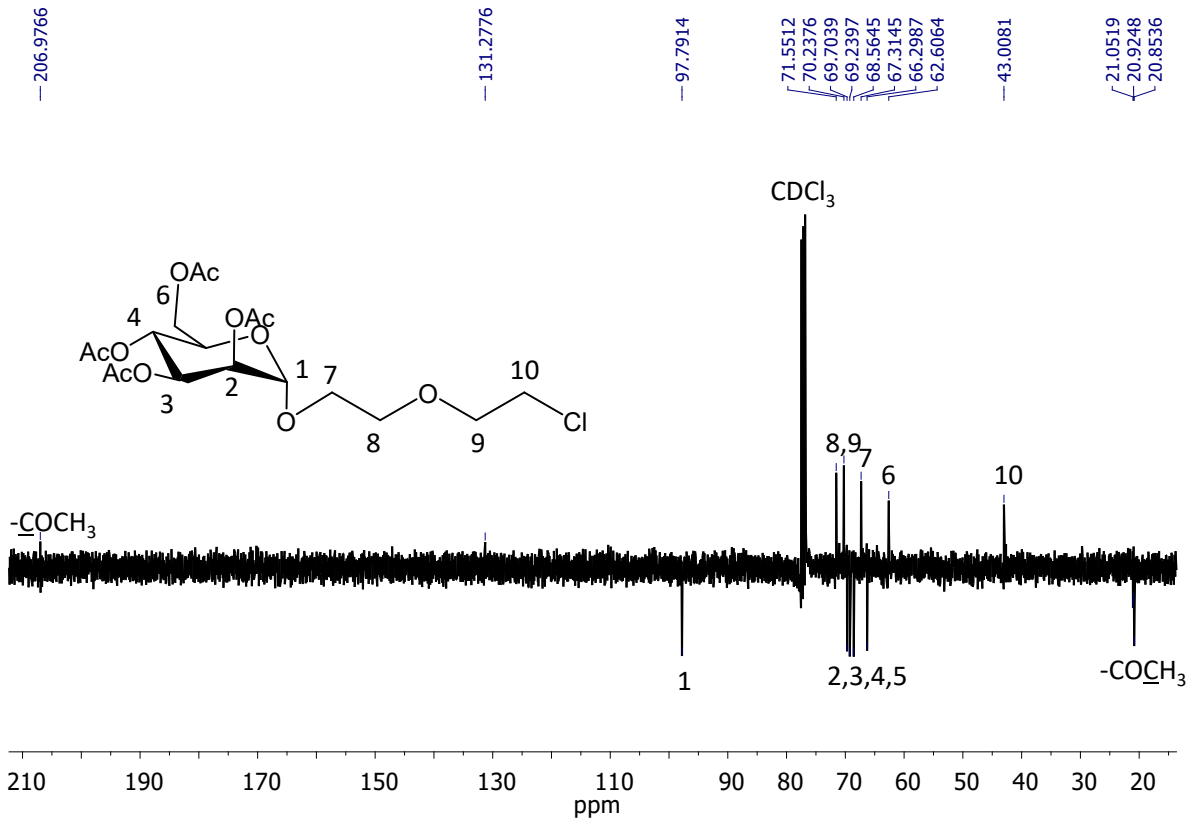


Figure S40. ^{13}C-NMR spectrum of 2-(2-chloroethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

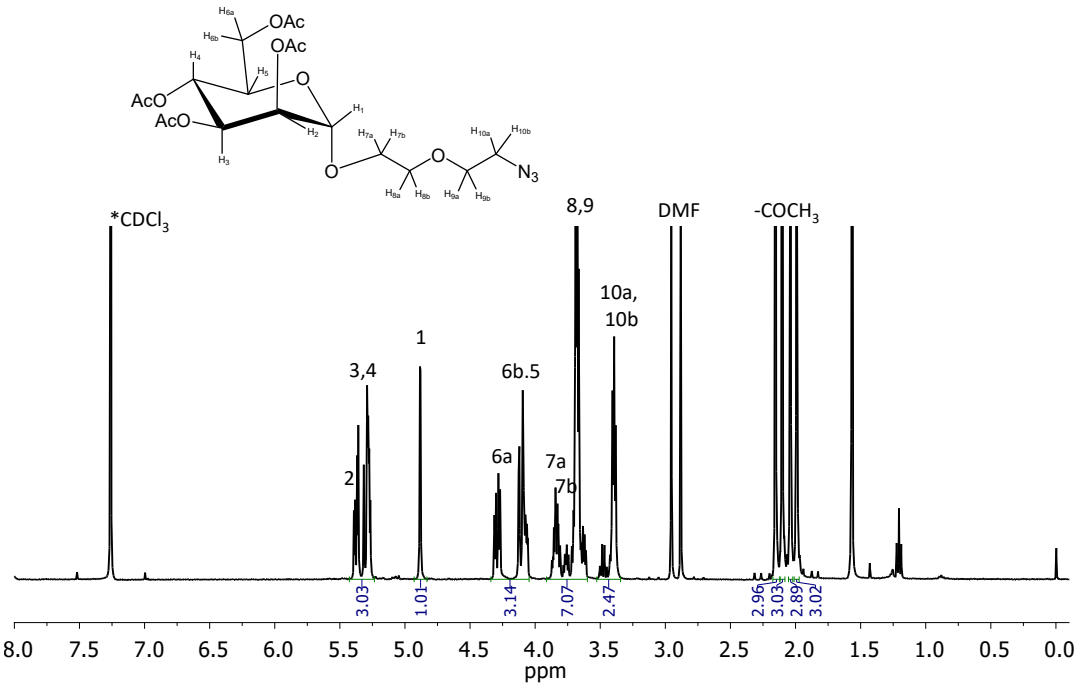


Figure S41. Full ^{1}H-NMR spectrum of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

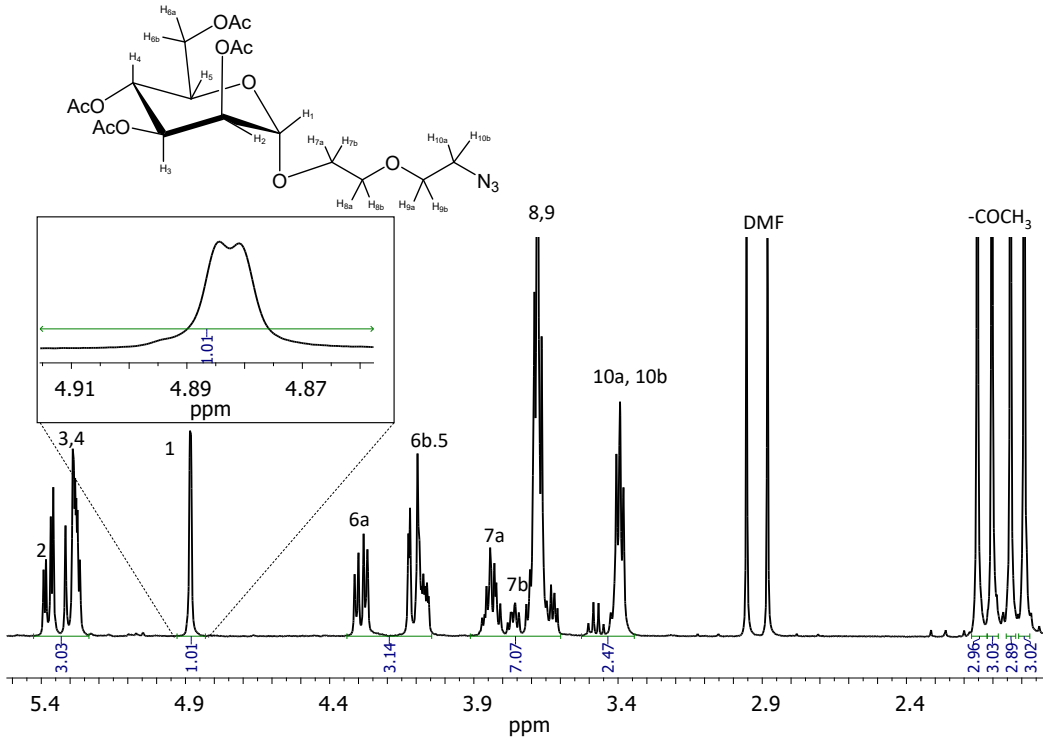


Figure S42. Figure S4.21. ^{1}H-NMR spectrum of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

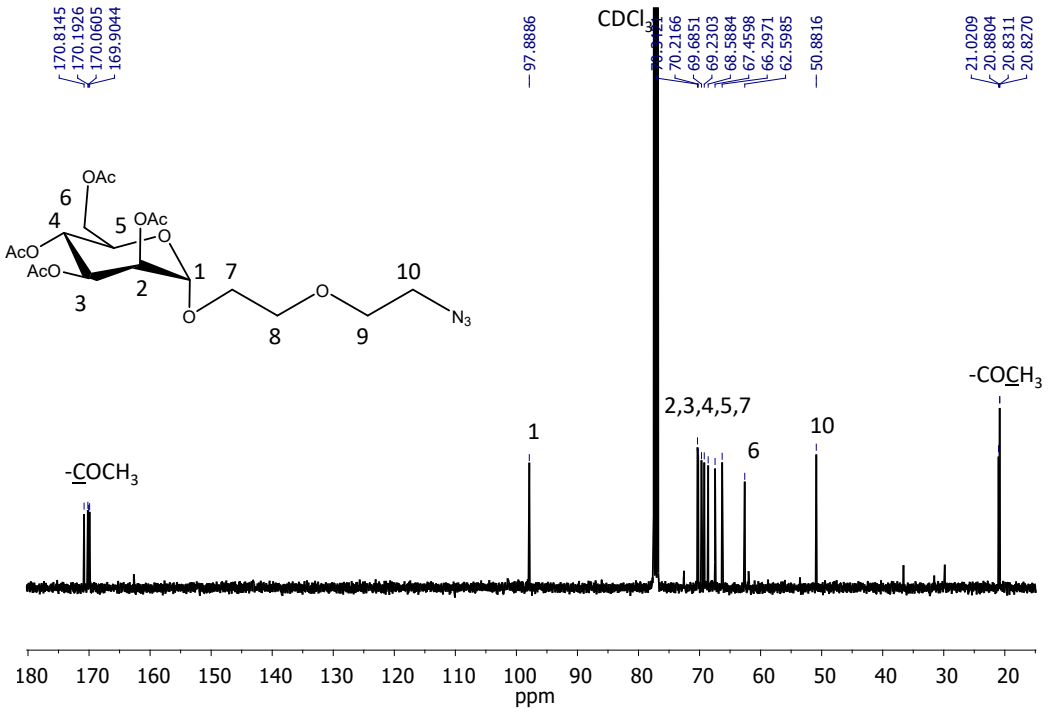


Figure S43. ^{13}C-NMR spectrum of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

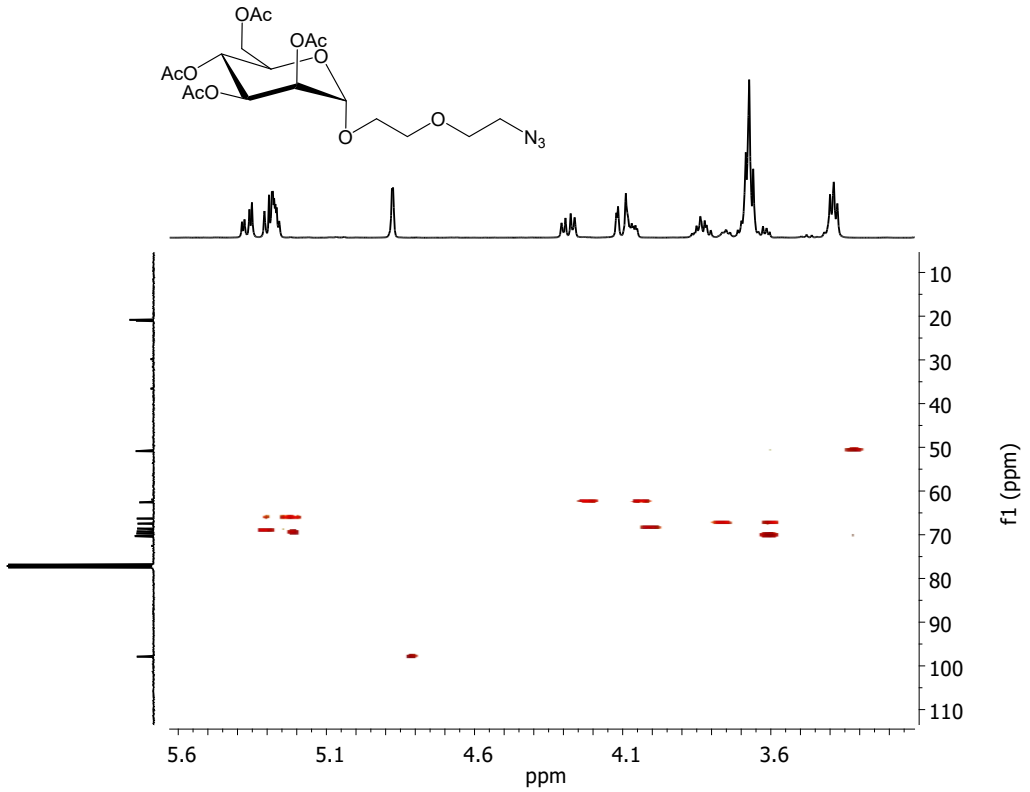


Figure S44. HSQC spectrum of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

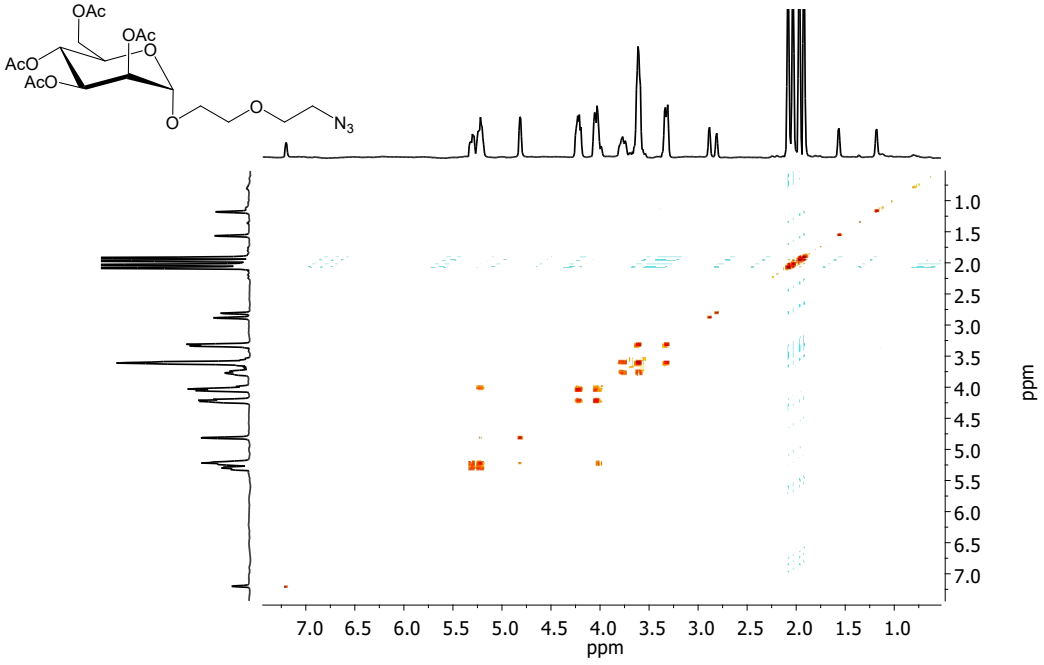


Figure S45. COSY spectrum of 2-(2-azidoethoxy)ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

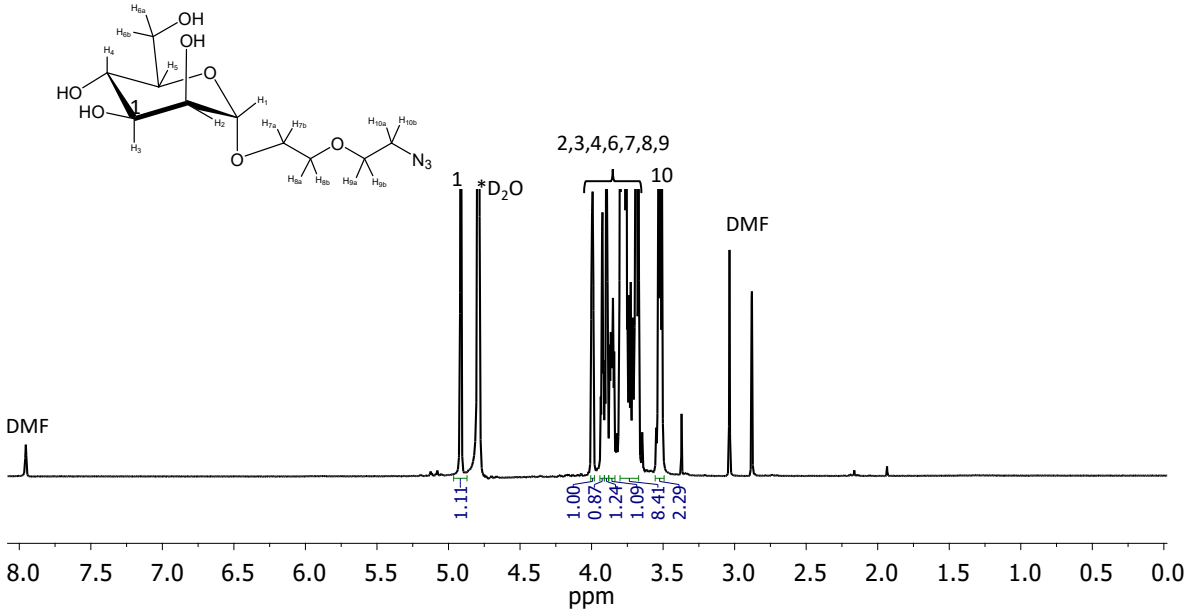


Figure S46. Full ^{1}H-NMR spectrum of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (D_2O, 400 MHz).

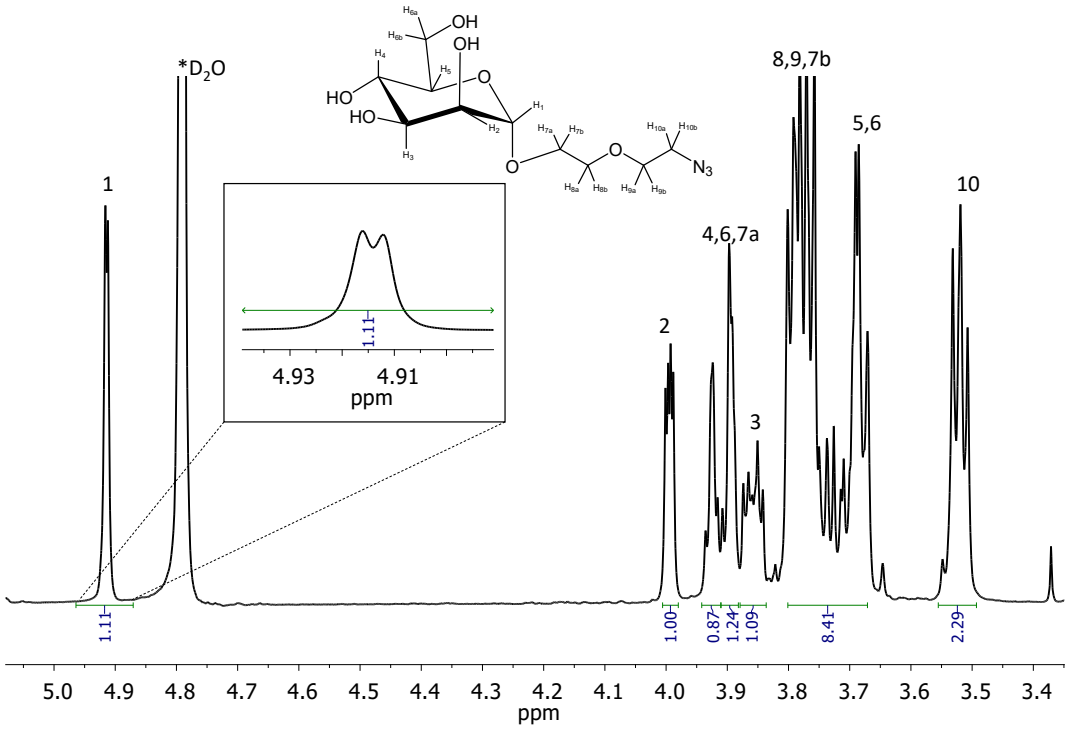


Figure S47. ^{1}H-NMR spectrum of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (D_2O, 400 MHz).

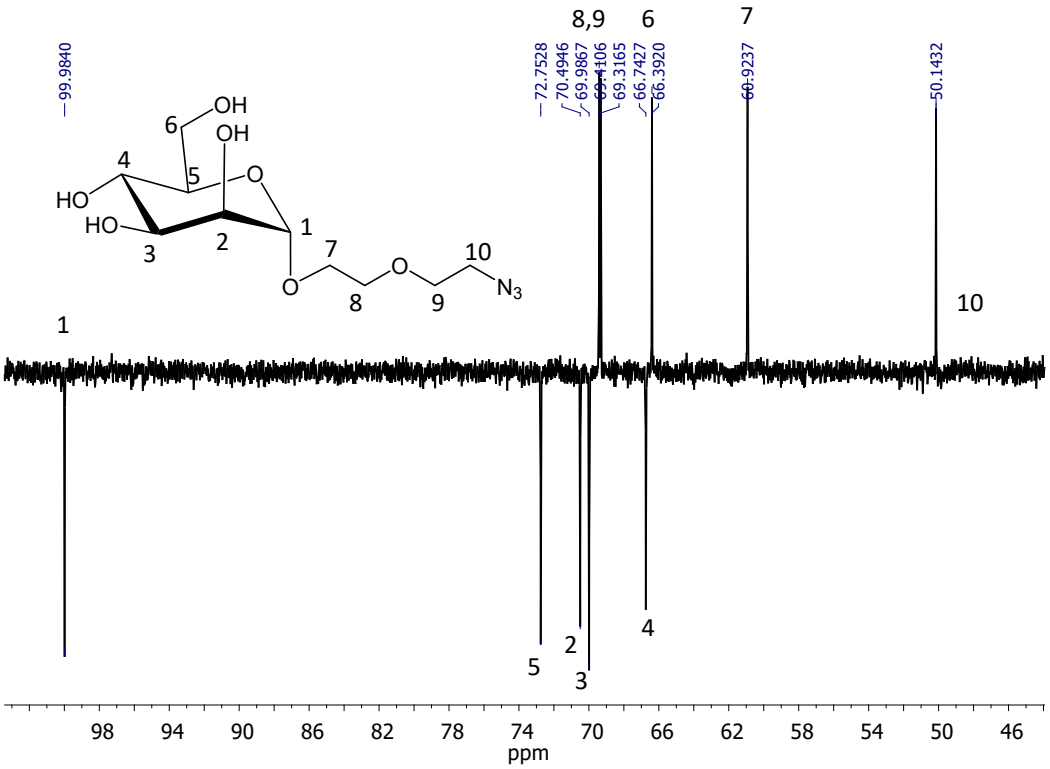


Figure S48. ^{13}C-NMR spectrum of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (D_2O, 400 MHz).

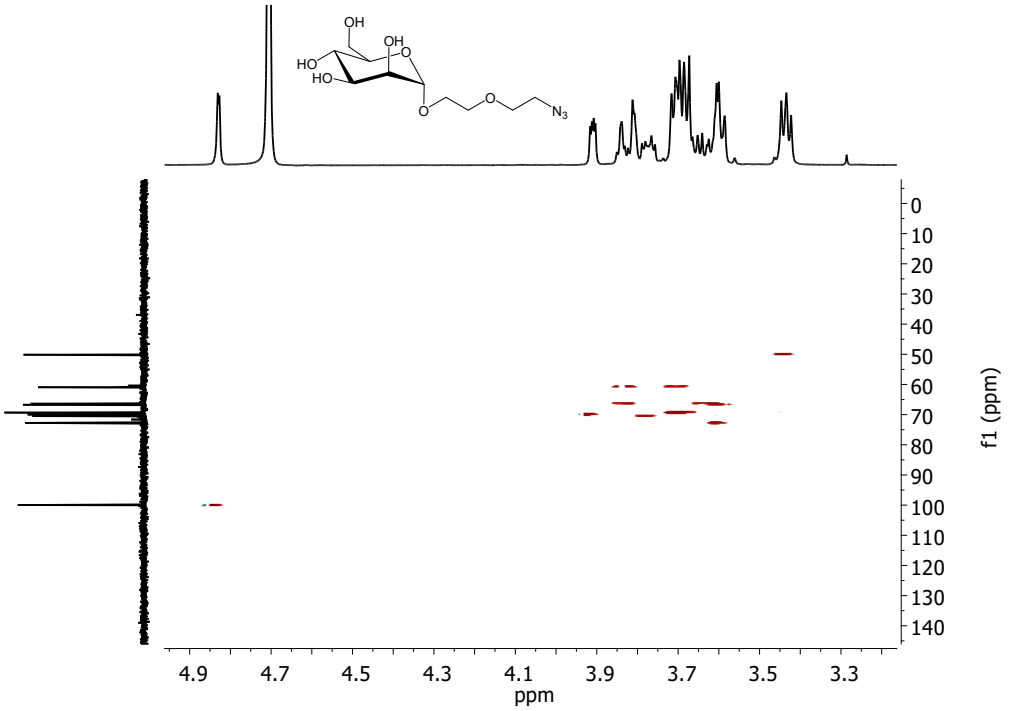


Figure S49. HSQC-NMR spectrum of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (D_2O, 400 MHz).

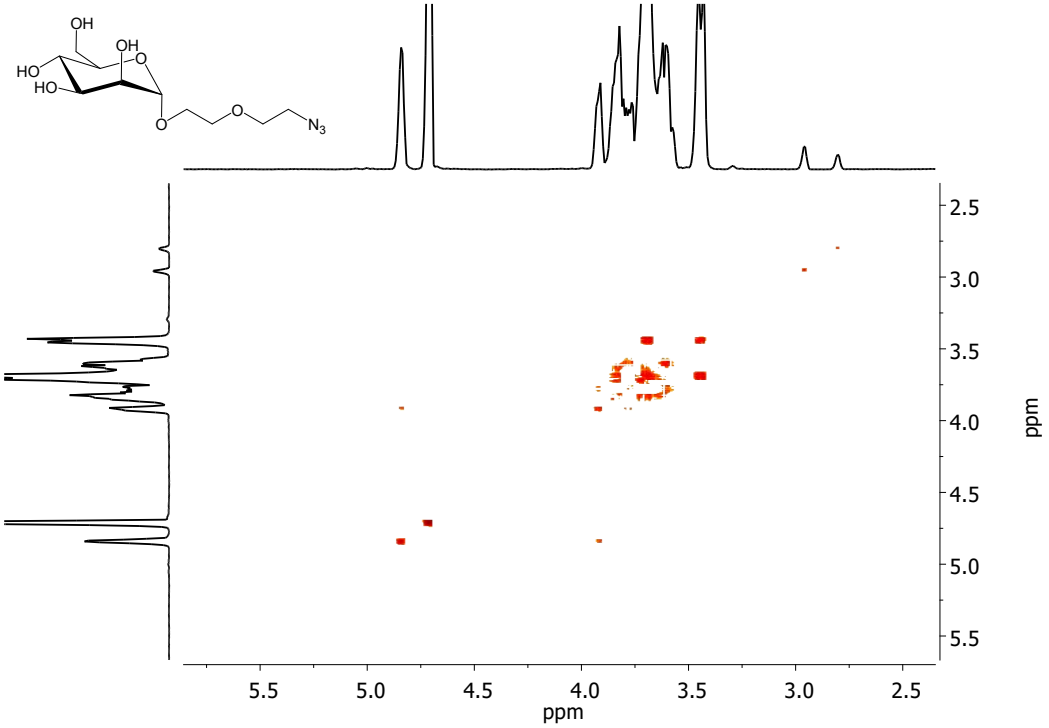


Figure S50. COSY spectrum of 2-(2-azidoethoxy)ethyl α-D-mannopyranoside (D_2O, 400 MHz).

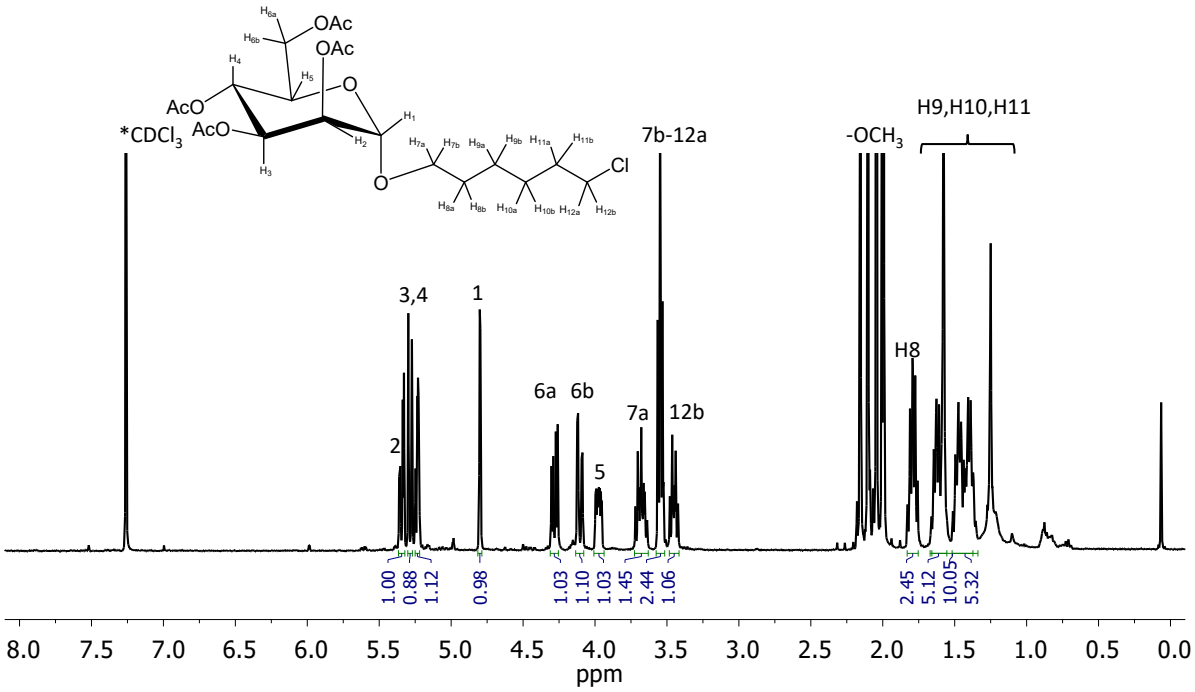


Figure S51. Full ^{1}H-NMR spectrum of 6-chlorohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

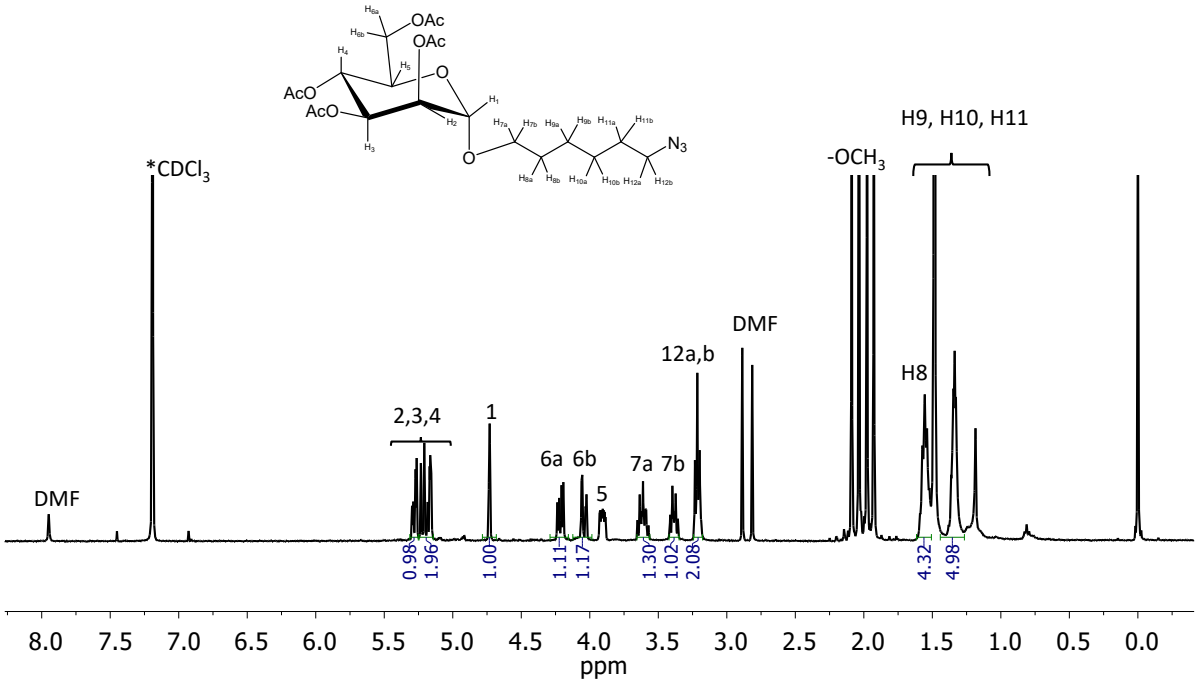


Figure S52. Full ^{1}H-NMR spectrum of 6-azidohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

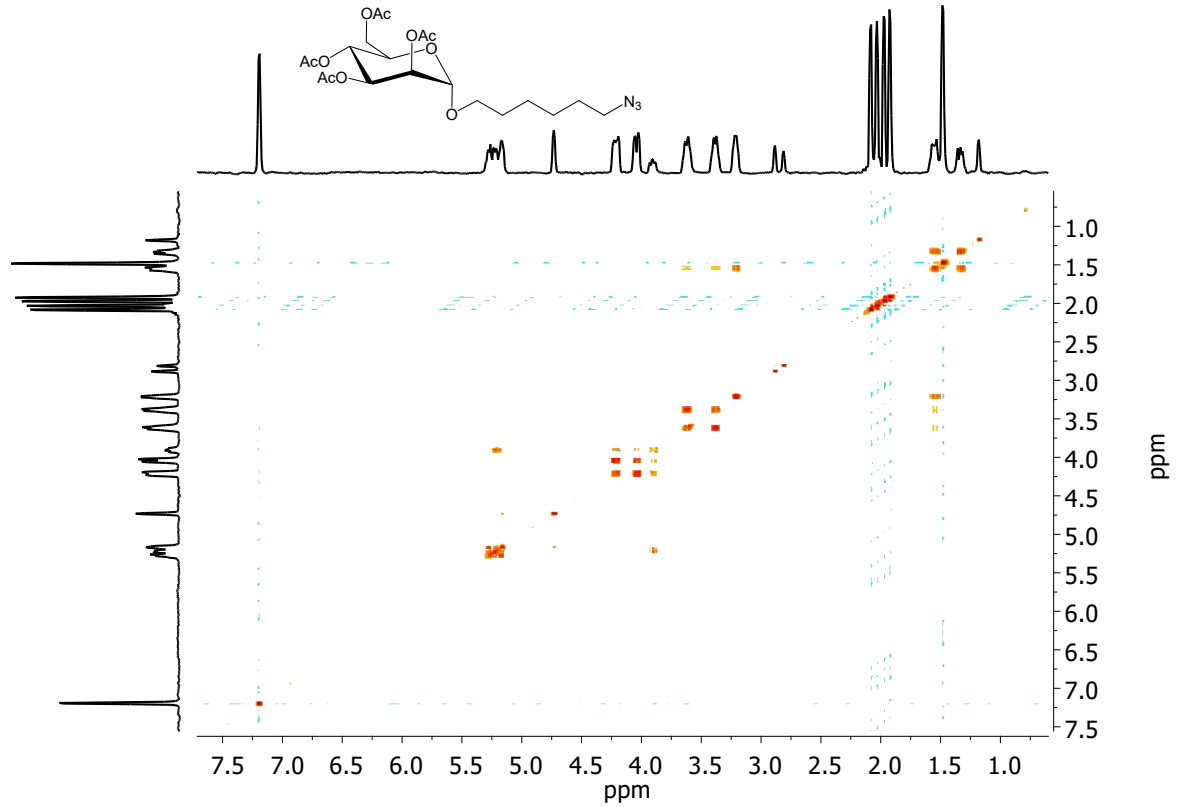


Figure S53. COSY NMR spectrum of 6-azidohexyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

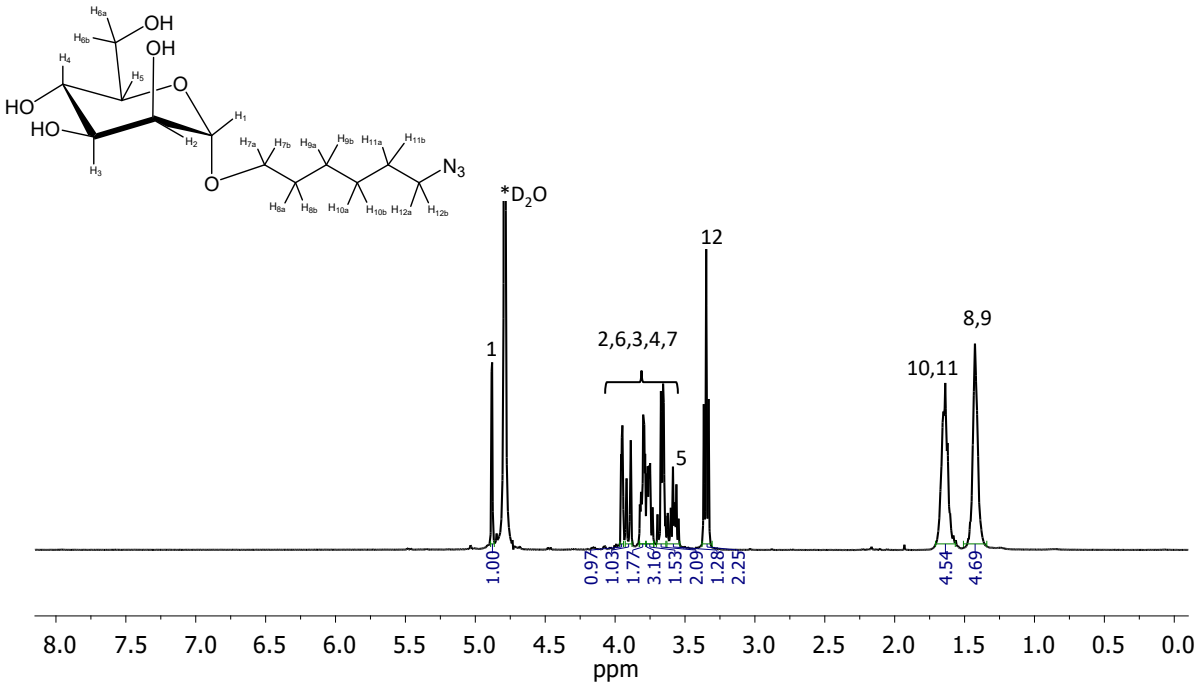


Figure S54. Full ^{1}H-NMR spectrum of 6-azidohexyl α-D-mannopyranoside (D_2O, 400 MHz).

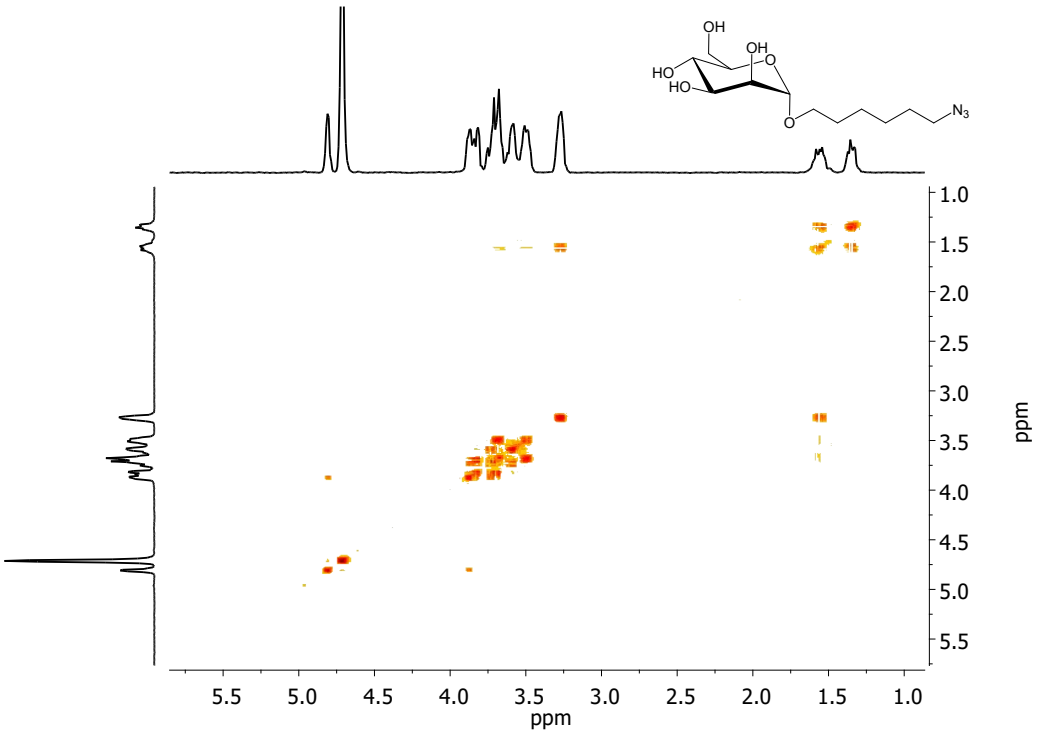


Figure S55. COSY NMR spectrum of 6-azidohexyl α-D-mannopyranoside (D_2O, 400 MHz).

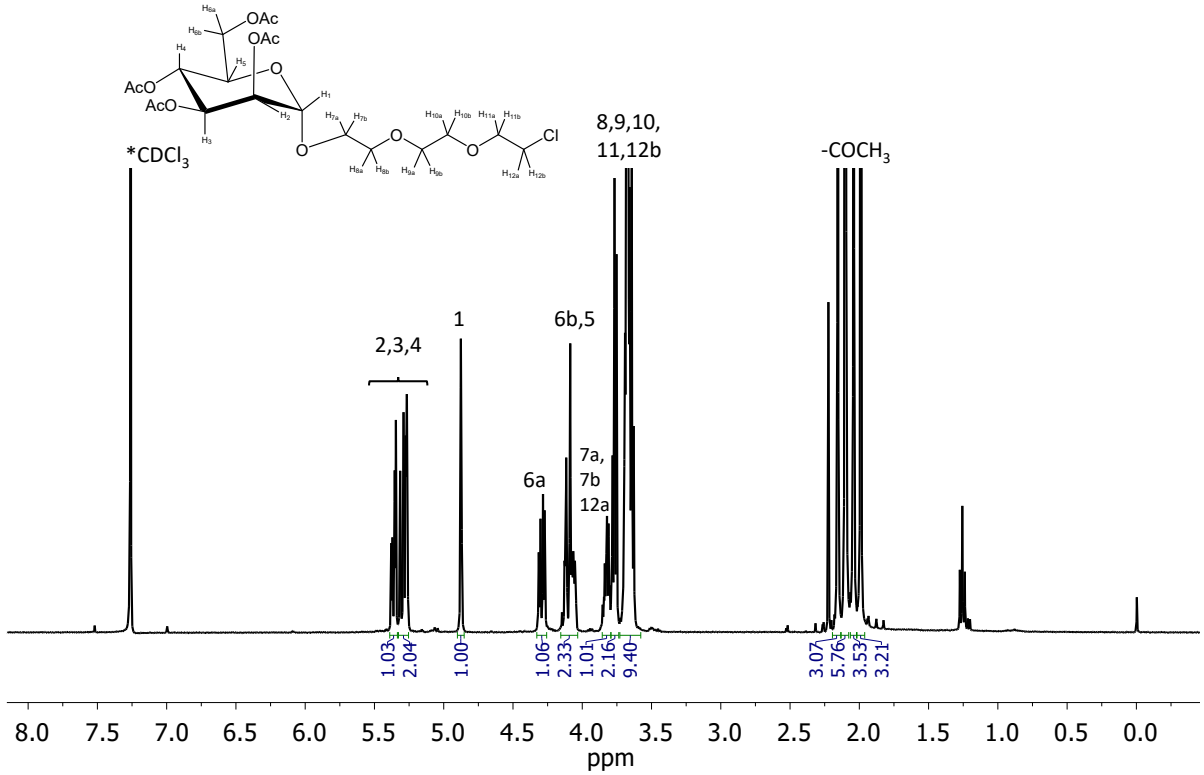


Figure S56. Full ^{1}H-NMR spectrum of 2-[2-(2-chloroethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

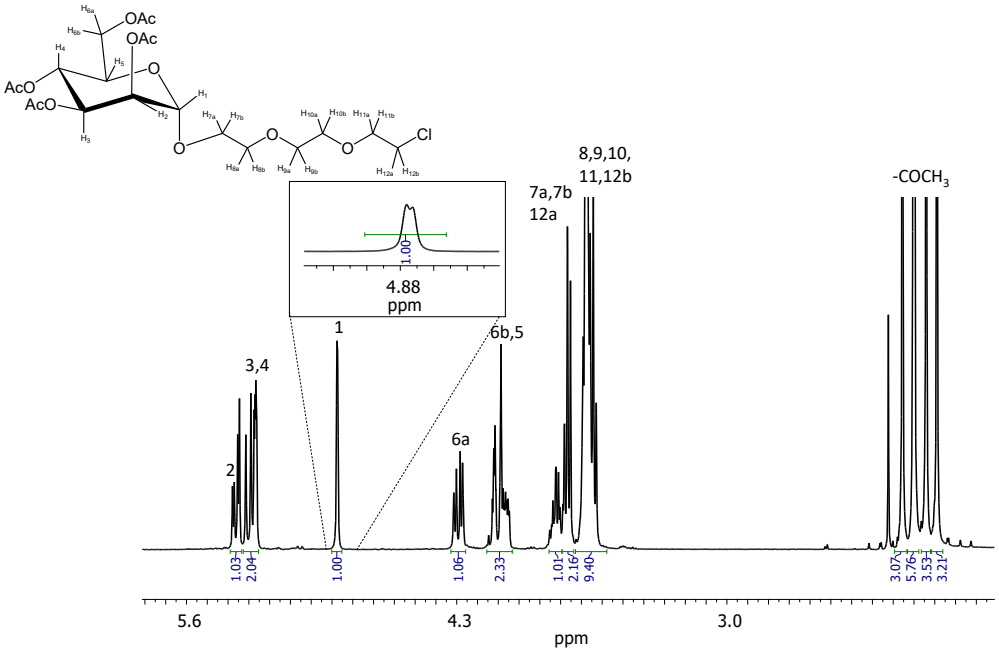


Figure S57. ^{1}H-NMR spectrum of 2-[2-(2-chloroethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

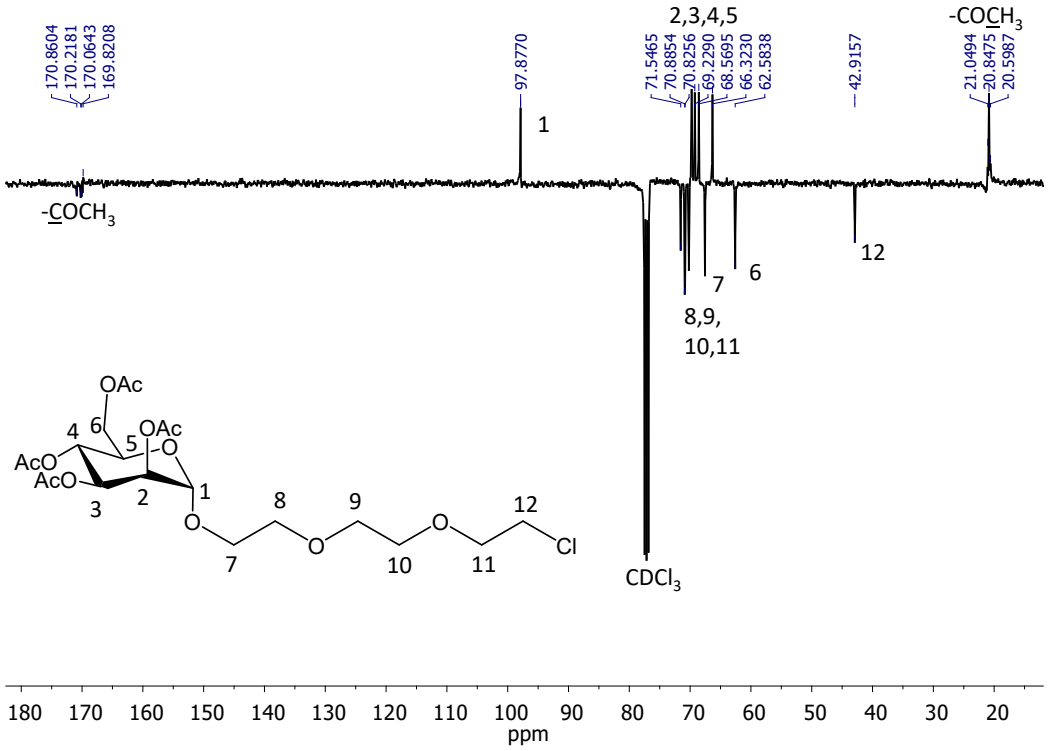


Figure S58. ^{13}C-NMR spectrum of 2-[2-(2-chloroethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

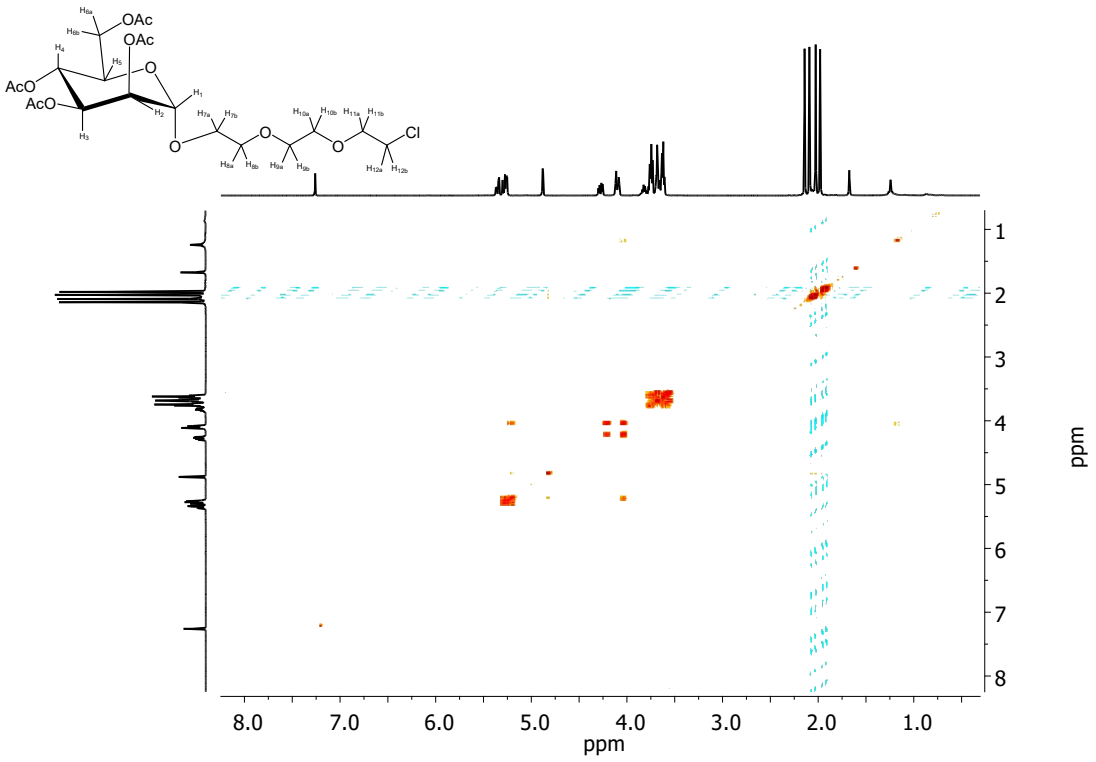


Figure S59. COSY NMR spectrum of 2-[2-(2-chloroethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

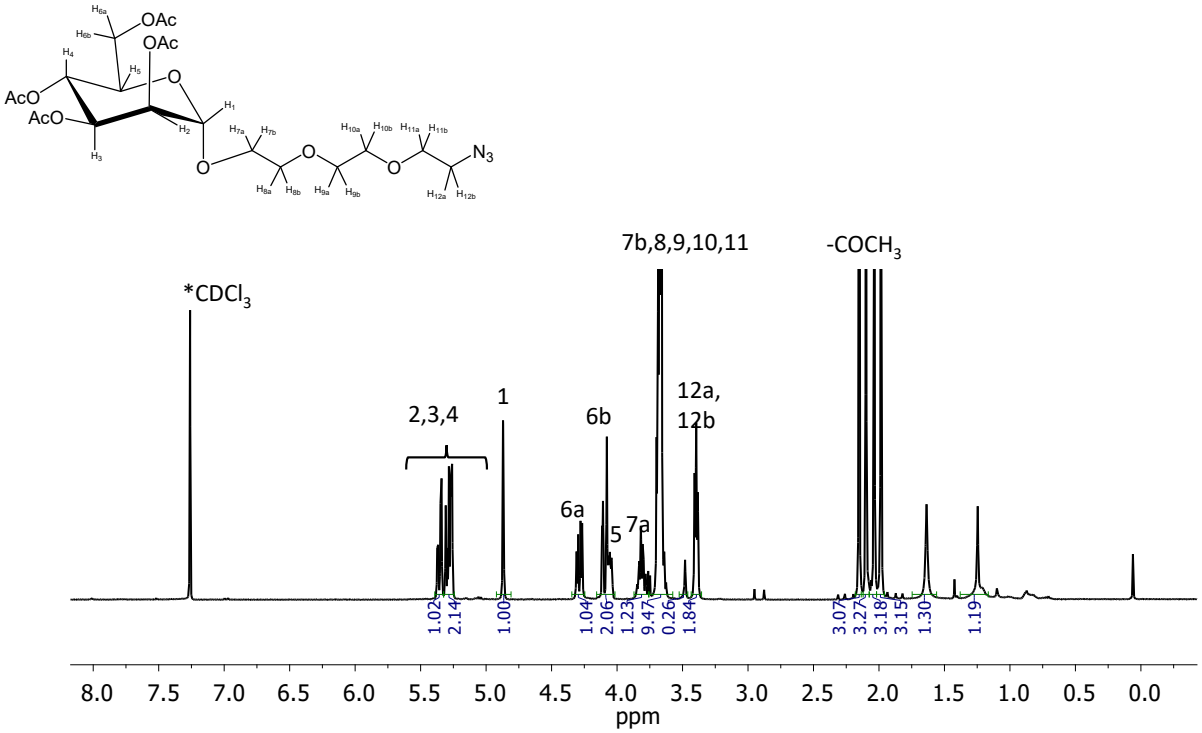


Figure S60. Full ^{1}H-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

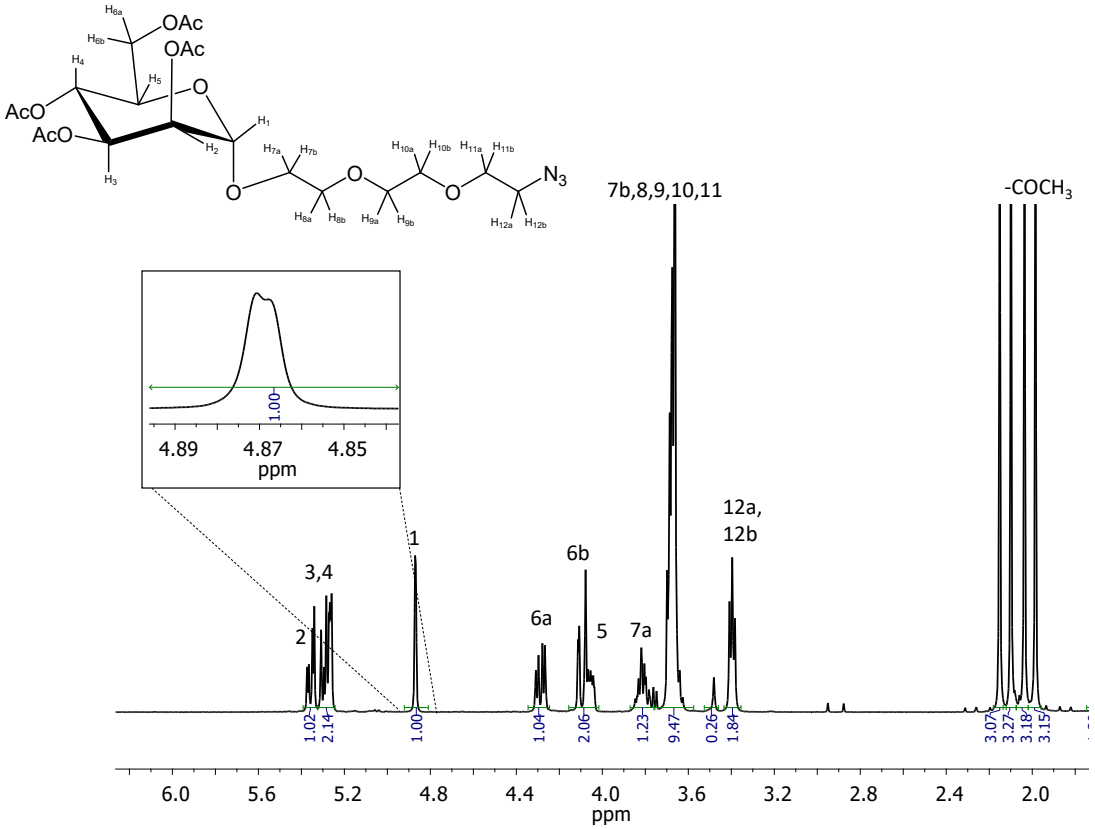


Figure S61. Full ^{1}H-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

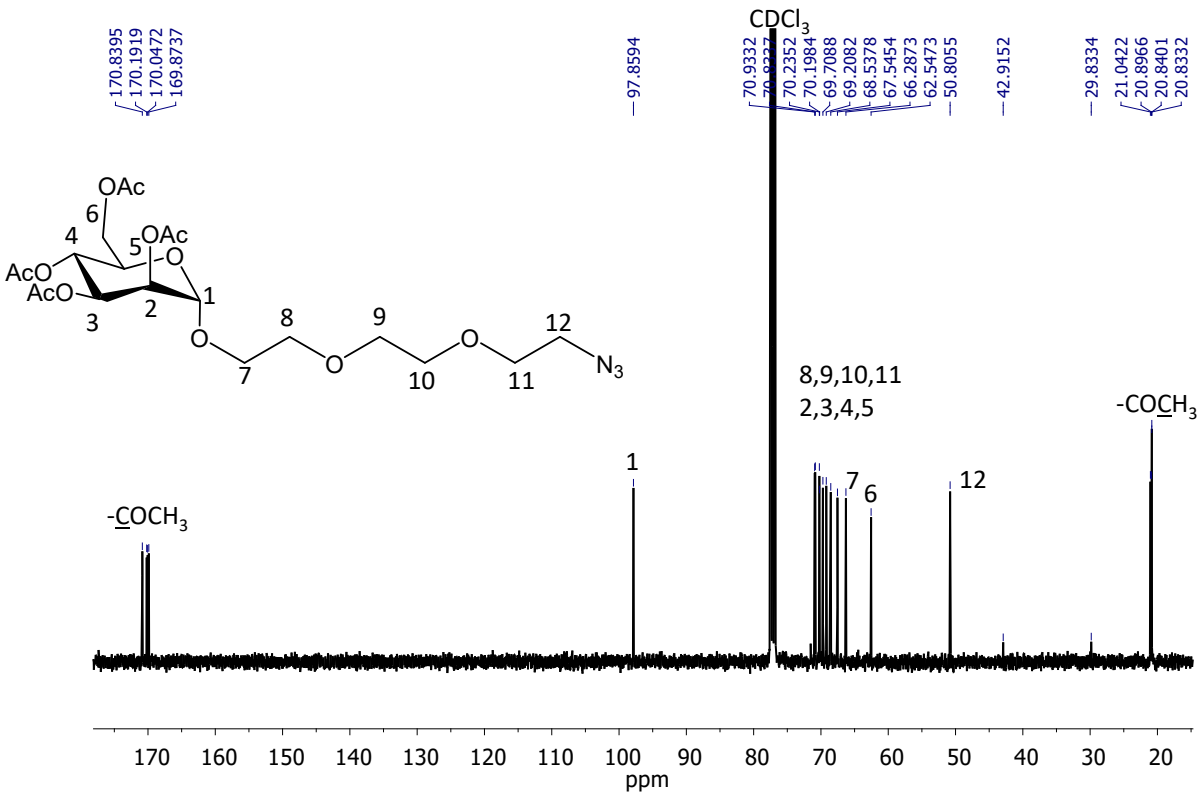


Figure S62. ^{13}C-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

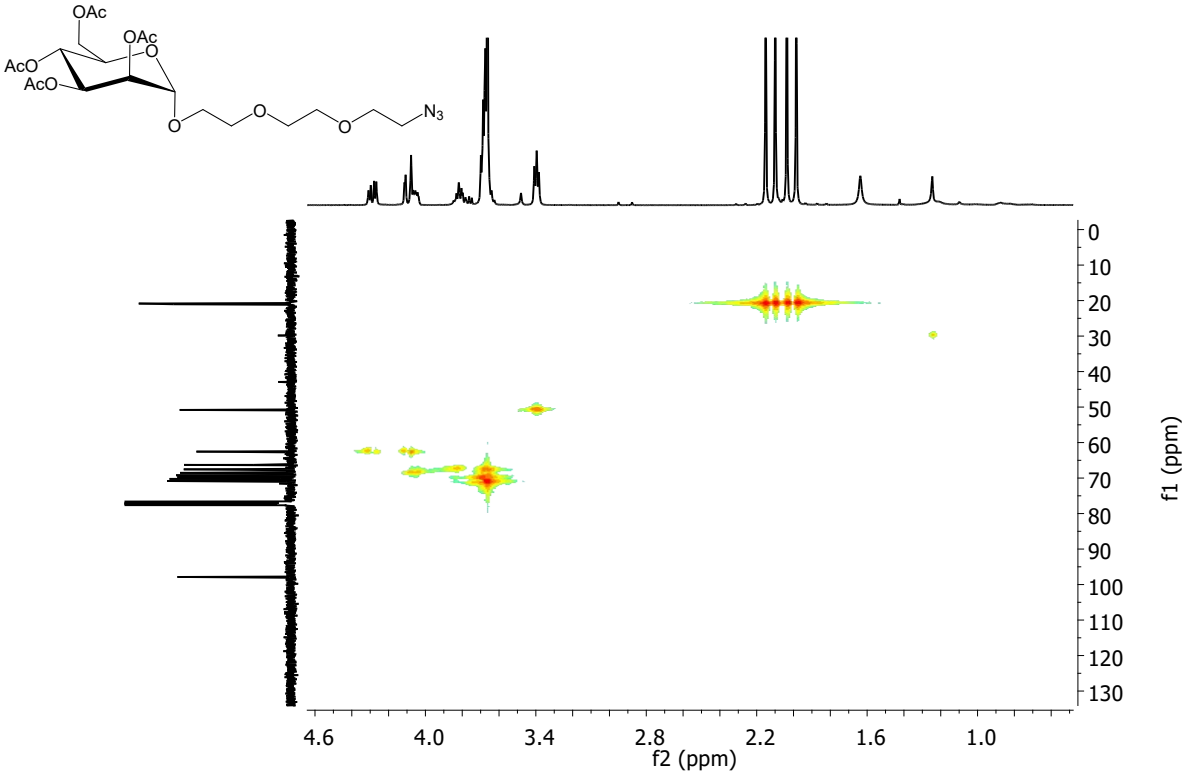


Figure S63. HSQC spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside ($CDCl_3$, 400 MHz).

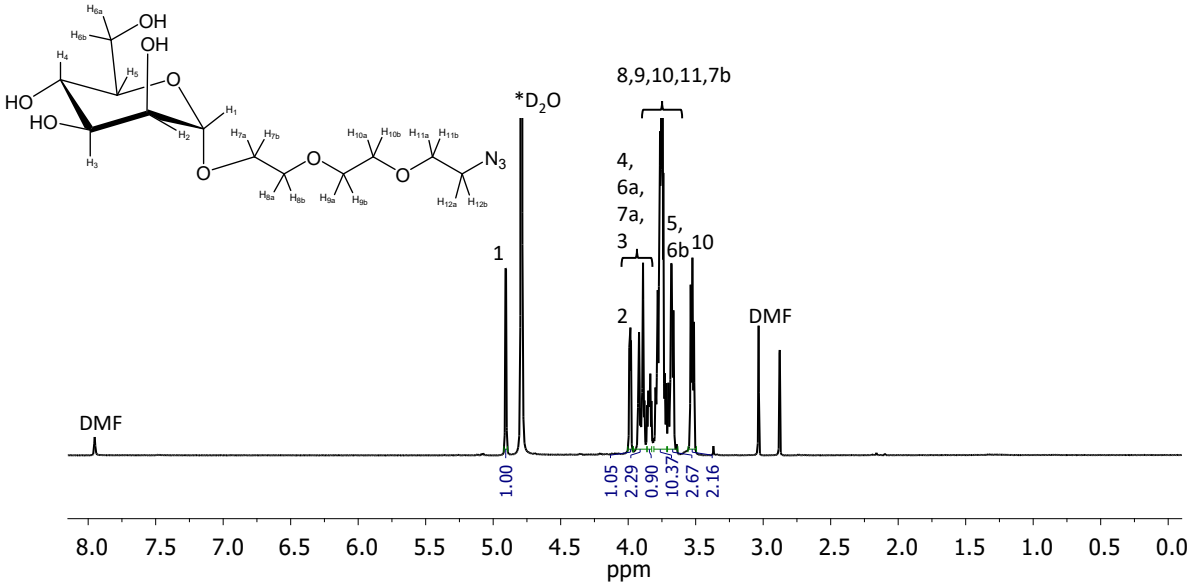


Figure S64. Full ^{1}H-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (D_2O, 400 MHz).

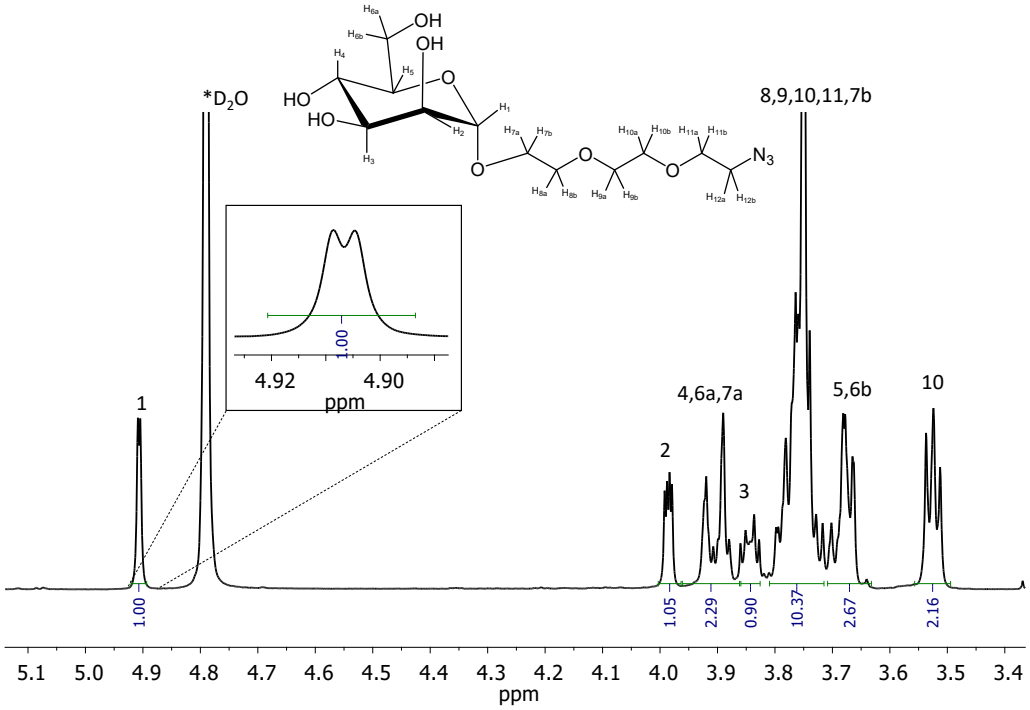


Figure S65. ^{1}H-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (D_2O, 400 MHz).

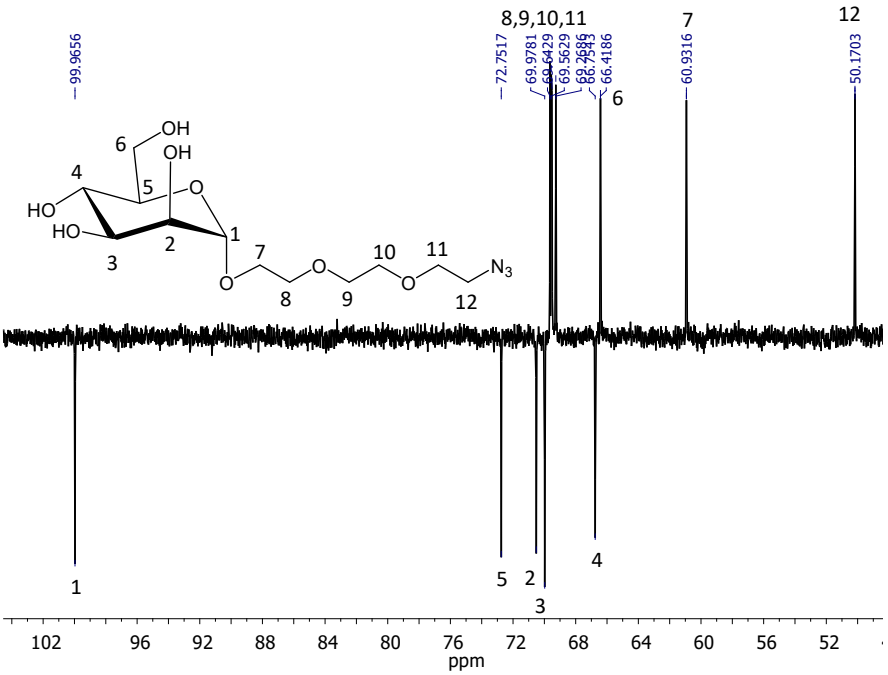


Figure S66. ^{13}C-NMR spectrum of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (D_2O, 400 MHz).

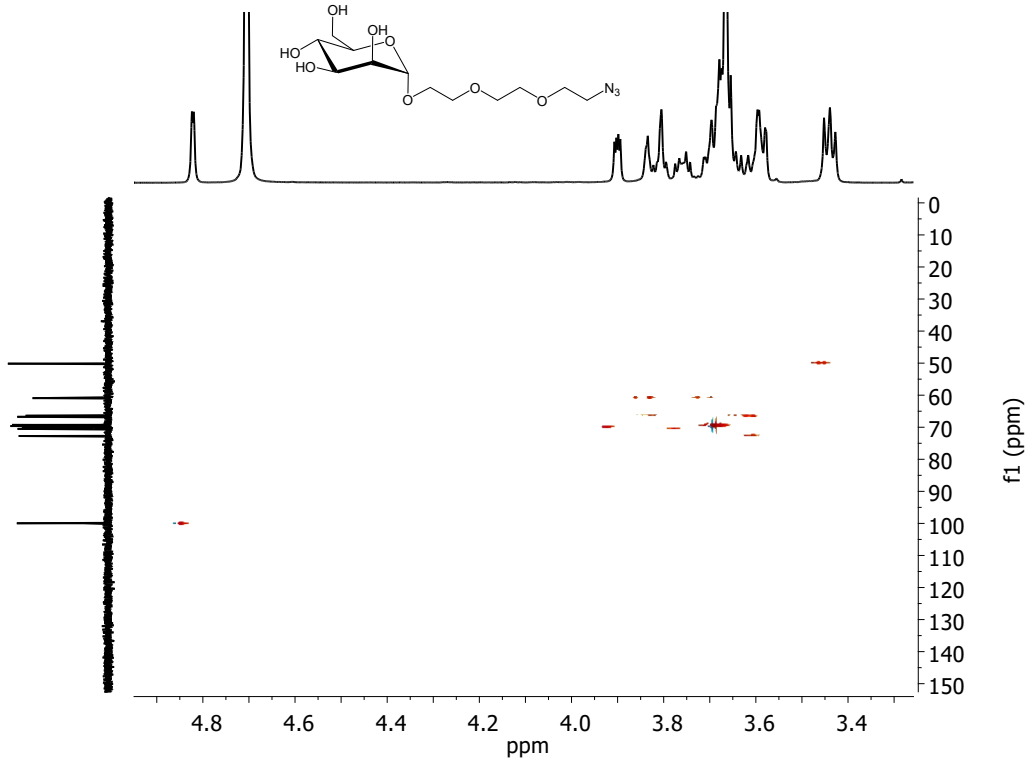


Figure S67. HSQC of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (D_2O, 400 MHz).

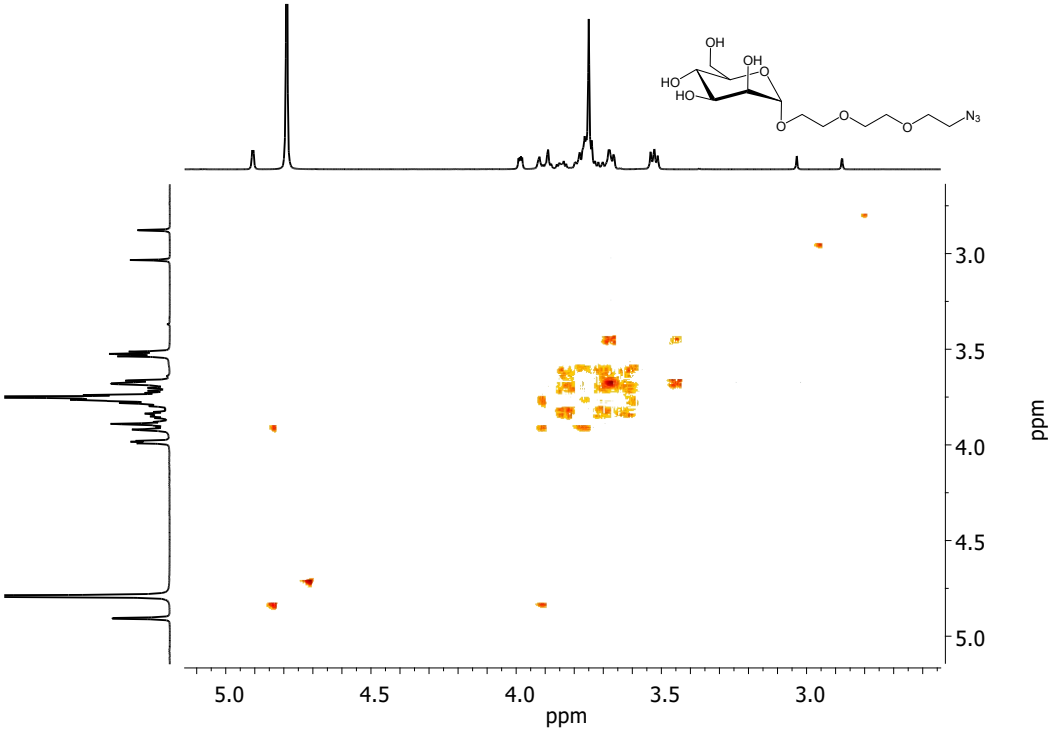


Figure S68. COSY of 2-[2-(2-azidoethoxy)ethoxy]ethyl α-D-mannopyranoside (D_2O, 400 MHz).

3 Functional nanoparticles

Table S2. Feeds ratio for the fabrication of fluorescein labelled-mannosylated NPs.

Man.	Man-N_3	Fluorescein azide	NP (DP_{HPMA} = 300)	Na Asc	$CuSO_4$
M1	0.5 mg (0.002 mmol)	0.8 mg (0.75 mmol)	20.4 mg (0.0008 mmol)	3 mg (0.01 mmol)	0.8 mg (0.005 mmol)
M2	0.63 (0.002 mmol)	0.8 mg (0.75 mmol)	20.4 mg (0.0008 mmol)	3 mg (0.01 mmol)	0.8 mg (0.005 mmol)
M4	0.67 mg (0.002 mmol)	0.8 mg (0.75 mmol)	20.4 mg (0.0008 mmol)	3 mg (0.01 mmol)	0.8 mg (0.005 mmol)
M3	0.7 mg (0.002 mmol)	0.8 mg (0.75 mmol)	20.4 mg (0.0008 mmol)	3 mg (0.01 mmol)	0.8 mg (0.005 mmol)
M5	0.37 mg (0.002 ml)	0.8 mg (0.75 mmol)	10.2 mg (0.0008 mmol)	3 mg (0.01 mmol)	0.8 mg (0.005 mmol)

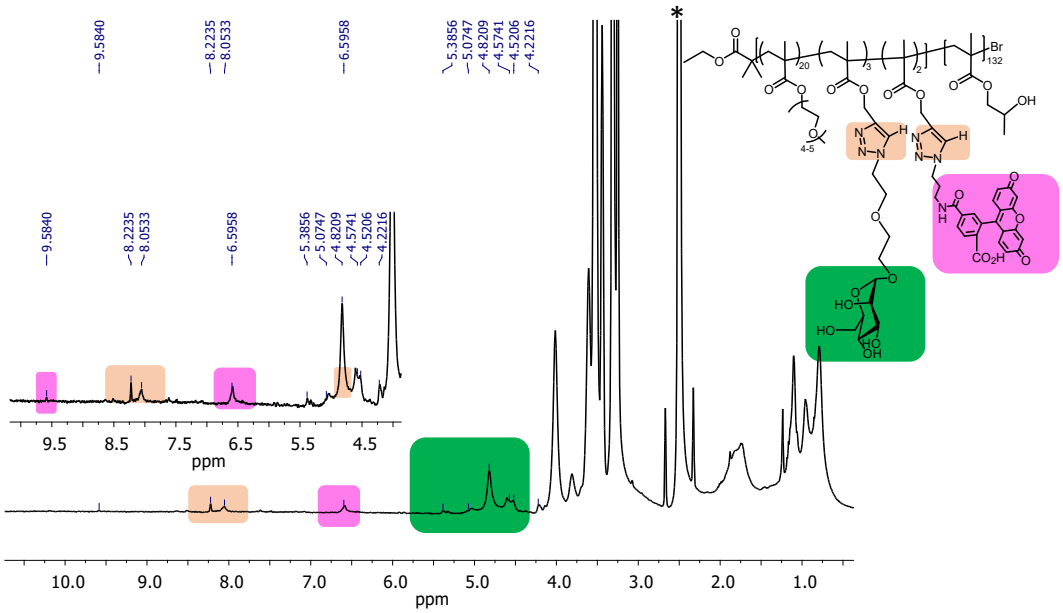


Figure S69. ^{1}H-NMR spectrum of (Fluor)-(M4)-NPs (400 MHz, DMSO-d_6, 303 K).

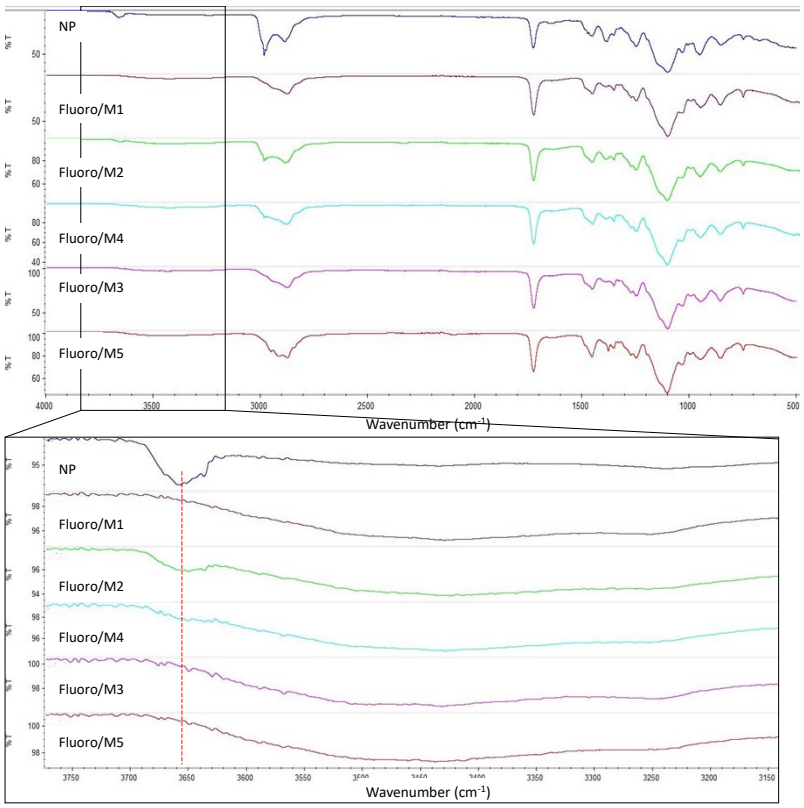


Figure S70. FT-IR spectra of NPs before and after co-clicking for shell functionalisation.

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