Supporting Information

Precipitation-Free High-Affinity Multivalent Binding by Inline Lectin Ligands

Philipp Rohse,[a] Sabrina Weickert,[a] Malte Drescher[a] and Valentin Wittmann*[a]

[a] *University of Konstanz, Department of Chemistry and Konstanz Research School Chemical Biology (KoRS-CB), Universitätsstraße 10, 78457 Konstanz, Germany. E-mail: mail@valentin-wittmann.de*

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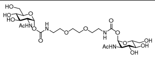
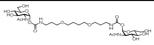
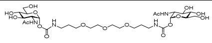
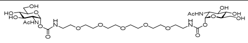
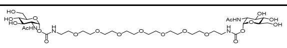
Supporting Table and Figure

Table S1 Thermodynamic binding parameters for divalent ligands **1**–**5** binding to WGA at pH 7.0 and 298 K determined by ITC

Compound	K_d (μM)	n^a L:P	ΔH (kcal mol^{-1})	$-T\Delta S$ (kcal mol^{-1})	ΔG (kcal mol^{-1})	$\beta_{Kd}{}^c$
GlcNAc	1830 ± 81	4^b	−7.1 ± 0.5	4.4 ± 0.8	−2.6 ± 0.2	1
 **1**	1.92 ± 0.06	1.90 ± 0.04	−13.8±0.1	6.0 ± 0.1	−7.8 ± 0.03	950
 **2**	0.128 ± 0.006	1.51 ± 0.01	−18.2 ± 0.1	8.8 ± 0.1	−9.40 ± 0.02	14,300
 **3**	0.102 ± 0.011	1.79 ± 0.08	−19.3 ± 0.1	9.7 ± 0.03	−9.55 ± 0.05	17,940
 **4**	0.208 ± 0.018	1.55 ± 0.06	−17.2 ± 0.5	8.1 ± 0.5	−9.12 ± 0.04	8,800
 **5**	0.730 ± 0.011	1.70 ± 0.01	−17.6 ± 0.6	9.2 ± 0.6	−8.39 ± 0.01	2,510

[a] Binding stoichiometry, L = ligand, P = protein (dimeric WGA). [b] Fixed during fit.[1] [c] Relative binding affinity.

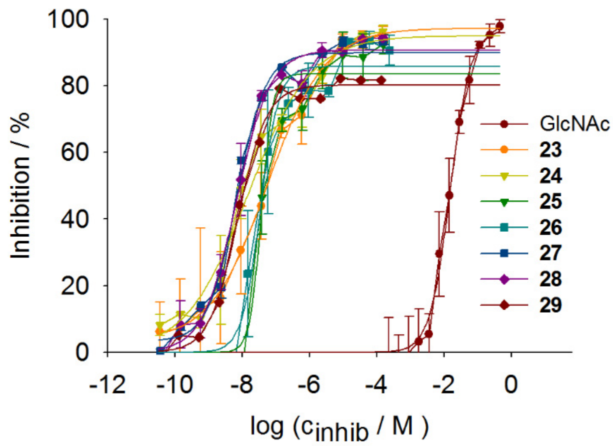


Fig. S1 Dose-response curves for inhibition of the binding of HRP-labeled WGA to GlcNAc-coated microtiter plates by tetravalent glycopeptides **23**–**29**.

General Methods

Wheat germ agglutinin (lectin from *Triticum vulgaris*) was purchased from *Sigma Aldrich*. All reactions were monitored by TLC on silica gel 60 F254 (*Merck*) on aluminum sheets with detection by UV light (λ = 254 nm). Additionally, acidic ethanolic *p*-anisaldehyde solution followed by gentle heating was used for visualization. Preparative flash column chromatography (FC) was performed manually of with an MPLC-*Reveleris* system from *Büchi* on silica (*Macherey-Nagel* Kieselgel 60 M, 0.04–0.064 mm). NMR spectra were recorded at room temperature on Avance III 400 and Avance III 600 instruments from *Bruker*. Chemical shifts are reported relative to solvent signals ($CDCl_3$: $\delta_H = 7.26$, $\delta_C = 77.16$; DMSO-d_6: $\delta_H = 2.50$, $\delta_C = 39.52$). Signals were assigned by first-order analysis and, when feasible, assignments were supported by two-dimensional $^1H,^1H$ and $^1H,^{13}C$ correlation spectroscopy (COSY, HMBC and HSQC). High-resolution mass spectra (HRMS-ESI) were recorded on a *Thermo* LTQ Orbitrap Discovery with electrospray ionization. Semi-preparative high performance liquid chromatography (HPLC) was conducted on a LC-20A prominence system (pumps LC-20AT, auto sampler SIL-20A, column oven CTO-20AC, diode array detector SPD-M20A, ELSD-LT II detector, controller CBM-20A and software LC-solution) from *Shimadzu*. A binary gradient of acetonitrile (with 0.1 % formic acid or trifluoroacetic acid) (B) in water (with 0.1 % formic acid or trifluoroacetic acid) (A) was used. For analytical HPLC a Nucleodur 100-5 C18 ec column (250 x 4 mm, flow 0.9 mL min^{-1}) and a Nucleodur 100-3 C18ec column column (125 x 4 mm, flow 0.4 mL min^{-1}) from *Macherey-Nagel* were used.

For analytical HPLC a Nucleodur 100-3 C18 ec column (125 x 4 mm, flow 0.4 mL min^{-1}, column 1) from *Macherey-Nagel* was used. For semi-preparative HPLC a Kinetex C18 column from *Phenomenex* (250 x 21.2 mm, flow 9 mL min^{-1}, column 2) was used.

For semi-preparative HPLC a Eurosphere 100 C18 column from *Knauer* (16 × 250 mm, flow 8 mL min^{-1}) and a Kinetex C18 column from *Phenomenex* (250 x 21.2 mm, flow 9 mL min^{-1}) were used. UV-Vis Absorption was measured using a Cary 50 instrument from *Varian*. Microtiter plates were read out with a FLUOstar OPTIMA plate reader from *BMG Labtech*.

Synthesis

General procedure for the preparation of oligoethylene glycol active carbonates, GP1

Oligoethylene glycol was dissolved in dry CH_2Cl_2. Then a solution of 4-nitrophenyl chloroformate **14** (2.2 eq) in dry CH_2Cl_2 was added dropwise to the first solution at 0°C. Then DMAP (0.05 eq.) was added upon which the solution turned deep yellow. The solution was stirred for 18 h at r.t. Then CH_2Cl_2 was added, the solution was washed 3x with water, the aqueous phase was extracted with CH_2Cl_2 and the combined organic phases were dried over Na_2SO_4. The solvent was evaporated and the solution was purified by flash column chromatography (petroleum ether/EtOAc 3:1 to 0:1 in 20 min, GRACE Reveleris system).

General procedure for the preparation of inline lectin ligands, GP2

Compound **25**[2] (2 eq) was dissolved in dry DMF. Active carbonate of oligoethylene glycol (1.2 eq.) was dissolved in dry DMF and added to the first solution. Then EtN*i*-Pr_2 (2 eq.) was added and the solution was stirred at r.t. for 4 h. Then the solvent was removed under reduced pressure and crude product was purified by preparative HPLC.

1,8-Bis(2-acetamido-2-deoxy-α-D-glucopyranosyl)carboxamido-3,6-dioxaoctan 1. Active carbonate **6** (5.72 mmol, 2.93 g) was placed in a Schlenk flask and dissolved in dry CH_2Cl_2 (20 mL). A solution of 1,8.diamino-3,6-dioxaoctane (2.6 mmol, 385 mg) and EtN*i*-Pr_2 (5.2 mmol, 672 mg, 884 µL) in CH_2Cl_2 (20 mL) was added whereby the solution turned yellow. The mixture was stirred for 45 min at r.t. and the solvent was evaporated. The crude product was purified by manual FC (CH_2Cl_2/MeOH 30:1 to 15:1). The obtained compound (124 mg, 0.14 mmol) was dissolved in $EtNMe_2$/MeOH 1:5 and stirred for 12 h at room temperature. The solvent was evaporated under reduced pressure and **1** was obtained as white amorphous solid (55 mg, 17 %). R_f = 0.11 ($MeCN/H_2O$ 4:1); ^1H NMR (400 MHz, D_2O): δ = 5.99 (2H, d, J = 3.5 Hz, H-1), 4.09 (2H, dd, J = 10.8, 3.5 Hz, H-2), 3.89-3.76 (8H, m, H-3, H-4, H-6), 3.73 (4H, s, CH_2), 3.67 (4H, t, J = 5.3 Hz, CH_2CH_2N), 3.61 (2H, t, J = 9.4 Hz, H-5), 3.40 (4H, t, J = 5.3 Hz, CH_2N), ^{13}C NMR (100 MHz, D_2O): δ = 174.6 (C=O), 156.4 (O(C=O)N), 91.6 (C-1), 73.8 (C-4), 70.7 (C-3), 69.4 , 69.4 , 69.1 (C-5, CH_2, CH_2CH_2N), 60.2 (C-6), 52.6 (C-2), 40.0 (CH_2N), 21.8 (CH_3); HRMS: calcd for $C_{24}H_{42}N_4O_{16}$ 643.2669 $[M+H]^+$, found 643.2608.

1,17-Bis(2-acetamido-2-deoxy-α-D-glucopyranosyl)carboxamido-3,6,9,12,15-pentaoxaheptadecan 4. Active carbonate **6** (0.975 mmol, 0.5 g) was put into a Schlenk flask and was dissolved in dry CH_2Cl_2 (10 mL). Then 3,6,9,12,15-pentaoxaheptadecane-1,17-diamine (0.39 mmol, 109 mg) and EtN*i*-Pr_2 (0.39 mmol, 101 mg, 133 µL) were added and the solution was stirred at r.t. for 2 d. The solvent was evaporated and the crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 20:1 to 15:1). The obtained compound was dissolved in dry MeOH (6.5 mL) and a 0.5 N solution of sodium methoxide in methanol (400 µL) was added. The solution was stirred at r.t. for 19 h. Then water was added and the solution was neutralized with Amberlite IRC-120. The ion exchange resin was washed with water and the solvent was evaporated. The crude product was purified by manual FC ($MeCN/H_2O$ 4:1). The product **4** was obtained as a white amorphous solid (317 mg, 42 %) R_f = 0.19 ($MeCN/H_2O$ 4:1); ^1H NMR (400 MHz, D_2O): δ = 5.98 (2H, d, J = 3.6 Hz, H-1), 4.09 (2H, dd, J = 10.7 Hz, 3.6 Hz, H-2), 3.87-3.76 (8H, m, H-3, H-4, H-6), 3.74 (16H, m, CH_2CH_2), 3.67 (4H, t, J = 5.3 Hz, OCH_2), 3.61 (2H, m, H-5), 3.39 (4H, t, CH_2N), 2.06 ppm (6H, s, OAc). ^{13}C NMR (101 MHz, D_2O): δ = 163.6 (NHAc), 156.4 (O(CO)N), 91.6 (C-1), 73.8 (C-3), 70.7, 69.6, 69.4, 69.4, 69.1 (OCH_2), 60.2 (C-6), 52.6 (C-2), 40.0 (CH_2N), 21.8 ppm (CH_3). HRMS: calcd for $C_{30}H_{53}N_4O_{19}$ 774.3377 $[M+H]^+$, found 774.3324.

1,23-Bis(2-acetamido-2-deoxy-α-D-glucopyranosyl)carboxamido-3,6,9,12,15,18,21-heptaoxatricosan 5. 3,6,9,12,15,18,21-heptaoxatricosane-1,23-diamine (1.0 mmol, 0.37 g) was dissolved in dry CH_2Cl_2 (30 mL). Then EtN*i*-Pr_2 (2.0 mmol, 0.26g, 340 µL) and active carbonate **6** (2.2 mmol, 1.13 g) were added and the solution was stirred for 30 min. at r.t. The solvent was evaporated and the crude product was purified by manual FC (CH_2Cl_2/MeOH 20:1 – 10:1). The intermediate was obtained as a white amorphous solid (814 mg, 73 %). R_f (CH_2Cl_2/MeOH 10:1) = 0.37; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.13 (2H, d, J = 9.5 Hz, N*H*Ac), 6.04 (2H, d, J = 3.6 Hz, H-1), 5.98 (2H, t, J = 5.6 Hz, N*H*CH_2), 5.24-5.17 (4H, m, H-3, H-4), 4.52 (2H, ddd, J = 9.9, 9.9, 3.6 Hz, H-2), 4.25 (2H, dd, J = 12.5, 3.7 Hz, H-6a), 4.08-4.01 (4H, m, H6-b, H-5), 3.74-3.65 (24H, m, OCH_2CH_2O), 3.60 (4H, m, NCH_2CH_2O), 3.40 (4H, m, NCH_2CH_2O), 2.07 (6H, s, OAc), 2.02 (12H, s, OAc), 1.94 ppm (6H, s, OAc). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.4, 170.9, 170.4, 169.2 (8x*C*(O)CH_3), 154.2 (O*C*(O)N), 91.9 (C-1), 71.3, 70.7, 70.6, 70.5, 70.5 (3xOCH_2CH_2O, 2xNCH_2CH_2O), 69.8, 69.5, 67.9 (C-3, C-4, C-5), 61.7 (H-6), 50.9 (C-2), 41.3 (NCH_2CH_2O), 23.1, 20.8, 20.7 ppm (8xC(O)CH_3). HRMS: m/z calcd for $C_{46}H_{75}N_4O_{27}^+$ 1115.4613 $[M+H]^+$, found 1115.4568. A part of the intermediate (626 mg, 0.6 mmol) was dissolved in a mixture of MeOH/$EtNMe_2$ (5 mL) and stirred at r.t. until LC-MS analysis (column 1, 1–30 % MeCN in H_2O + 0.1 % formic acid in 20 min) showed full conversion. The solvent was evaporated and the crude was purified by semi-preparative HPLC (column 2, 1–30 % MeCN in H_2O + 0.1 % formic acid in 20 min). The product **5** was obtained as white amorphous solid (207 mg, 40 %, 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.98 (2H, d, J = 3.5 Hz, H-1), 4.08 (2H, dd, J = 10.7, 3.6 Hz, H-2), 3.88-3.77 (8H, m, H-3, H-5, H-6), 3.74 (24H, m, OCH_2CH_2O), 3.67 (4H, m, $NHCH_2CH_2O$), 3.60 (2H, m, H-4), 3.40 (4H, m, $NHCH_2CH_2O$), 2.05 ppm (6H, s, OAc); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.6 (OAc), 156.4 (O(CO)NH), 91.6 (C-1), 73.8, 70.7, 69.6, 69.6, 69.4, 69.4, 69.1, 60.2 C-6), 52.6 (C-2), 40.0 ($NHCH_2CH_2O$), 21.8 ppm (OAc); HRMS: calcd. for $C_{34}H_{62}N_4O_{21}$: 863.3979 $[M+H]^+$, found 863.3979.

3,6,9,12,15,18-Hexaoxaicosane-1,20-diyl bis(4-nitrophenyl) bis(carbonate) 16. Compound **16** was synthesized according to GP1 using heptaethylene glycol **8** (0.491 g, 1.35 mmol). The product **16** was obtained as a yellow oil (0.24 g, 28 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (4H, d, J = 9.2 Hz, H-3_{Ar}), 7.38 (4H, d, J = 9.2 Hz, H-2_{Ar}), 4.47–4.43 (4H, m, 4H, (CO)OCH_2), 3.85–3.80 (4H, m, (CO)OCH_2CH_2) 3.72–3.60 ppm (20H, m, $(OCH_2CH_2O)_5$); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.5, 152.5, 145.4 (C-a, $C_{Carbonyl}$, C-1_{Ar}), 125.4 (C-3_{Ar}), 121.9 (C-2_{Ar}) 70.8 ($(OCH_2CH_2O)_5$), 68.8 ((CO)OCH_2), 68.4 ppm ((CO)OCH_2CH_2); HRMS (ESI): calcd. for $C_{28}H_{36}N_2O_{16}$: 657.2138 $[M+H]^+$, found 657.2185.

Bis(4-nitrophenyl) (3,6,9,12,15,18,21-heptaoxatricosane-1,23-diyl) bis(carbonate) 17. Compound **17** was synthesized according to GP1 using octaethylene glycol **9** (0.5 g, 1.35 mmol). The product **17** was obtained as a yellow oil (0.48 g, 49 %); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.27$ (4H, d, $J = 9.2$ Hz, H-3_{Ar}), 7.39 (4H, d, $J = 9.1$ Hz, H-2_{Ar}), 4.45–4.41 (4H, m, (CO)CH_2), 3.83–3.79 (4H, m, (CO)CH_2CH_2) 3.72–3.60 ppm (24H, m, $(OCH_2CH_2O)_6$); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 155.5$, 152.5, 145.4 (C-4_{Ar}, $C_{Carbonyl}$, C-1_{Ar}), 125.4 (C-3_{Ar}), 121.8 (C-2_{Ar}) 70.7 ($(OCH_2CH_2O)_6$), 68.8 ((CO)CH_2), 68.5 ppm ((CO)CH_2CH_2); HRMS (ESI): calcd. for $C_{30}H_{40}N_2O_{17}$: 701.2400 $[M+H]^+$, found 701.2402.

3,6,9,12,15,18,21,24-Octaoxahexacosane-1,26-diyl bis(4-nitrophenyl) bis(carbonate) 18. Compound **18** was synthesized according to GP1 using nonaethylene glycol **10** (0.5 g, 1.21 mmol). The product **18** was obtained as a yellow oil (0.26 g, 30 %). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.28$ (4H, d, $J = 9.2$ Hz, H-3_{Ar}), 7.39 (4H, d, $J = 9.2$ Hz, H-2_{Ar}), 4.45–4.41 (4H, m, (CO)CH_2), 3.82–3.78 (4H, m, (CO)CH_2CH_2), 3.78–3.53 ppm (28H, m, $(OCH_2CH_2O)_7$); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 155.7$, 145.6 (C-4_{Ar}, $C_{Carbonyl}$, C-1_{Ar}), 125.4 (C-3_{Ar}), 121.9 (C-2_{Ar}), 70.7 ($(OCH_2CH_2O)_7$), 68.6 ((CO)CH_2), 68.3 ppm ((CO)CH_2CH_2). HRMS (ESI): calcd. for $C_{32}H_{44}N_2O_{18}$: 745.2662 $[M+H]^+$, found 745.2664.

Bis(4-nitrophenyl) (3,6,9,12,15,18,21,24,27-nonaoxanonacosane-1,29-diyl) bis(carbonate) 19. Compound 98 was synthesized according to GP1 using decaethylene glycol **11** (0.5 g, 1.09 mmol). The product **19** was obtained as a yellow oil (0.25 g, 30 %). $R_f = 0.69$ (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.28$ (4H, d, J = 9.2 Hz, H-3_{Ar}), 7.39 (d, J = 9.2 Hz, 4H; H-2_{Ar}), 4.46–4.42 (4H, m, (CO)CH_2), 3.83–3.79 (4H, m, (CO)CH_2CH_2), 3.78–3.53 ppm (32H, m, $(OCH_2CH_2O)_8$); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 161.1$, 155.6, 145.5 (C-4_{Ar}, $C_{Carbonyl}$, C-1_{Ar}), 125.4 (C-3_{Ar}), 121.9 (C-2_{Ar}), 70.8 ($(OCH_2CH_2O)_8$), 68.7 ((CO)CH_2), 68.4 ppm (($COCH_2CH_2$); HRMS (ESI): calcd. for $C_{34}H_{48}N_2O_{19}$ 789.2924 $[M+H]^+$, found 789.2925.

3,6,9,12,15,18,21,24,27,30-Decaoxadotriacontane-1,32-diyl-bis(4-nitrophenyl)bis(carbonate) 20. Compound **20** was synthesized according to GP1 using undecaethylene glycol **12** (0.603 g, 1.2 mmol). The product **20** was obtained as a yellow oil (0.83 g, 8 %). $R_f = 0.45$ (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 8.25 (4H, d, $J = 9.1$ Hz, H-3_{Ar}), 7.37 (4H, d, $J = 9.1$ Hz, H-2_{Ar}), 4.44–4.39 (4H, m, (CO)CH_2), 3.81–3.77 (4H, m, (CO)CH_2CH_2), 3.71–3.54 ppm (36H, m, $(OCH_2CH_2O)_9$); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 155.6$, 152.3, 145.5 (C-4_{Ar}, $C_{Carbonyl}$, C-1_{Ar}), 125.7 (C-3_{Ar}), 121.6 (C-2_{Ar}) 70.6 ($(OCH_2CH_2O)_9$), 68.6 ((CO)CH_2), 68.3 ppm ((CO)CH_2CH_2); HRMS (ESI): calcd. for $C_{36}H_{52}N_2O_{20}$: 833.3186 $[M+H]^+$, found 833.3198.

Bis(4-nitrophenyl)(3,6,9,12,15,18,21,24,27,30,33-undecaoxapentatriacontane-1,35-diyl) bis(carbonate) 21. Compound **21** was synthesized according to GP1 using dodecaethylene glycol **13** (0.66 g, 1.20 mmol). The product 100 was obtained as a yellow oil (0.25 g, 24 %). $R_f = 0.41$ (EtOAc); ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 8.28 (4H, d, J = 9.1 Hz, H-3_{Ar}), 7.39 (4H, d, J = 9.1 Hz, H-2_{Ar}), 4.46–4.42 (4H, m, (CO)CH_2), 3.83–3.79 (4H, m, 4H; (CO)CH_2CH_2) 3.72–3.36 ppm (40H, m, $(OCH_2CH_2O)_{10}$); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.5, 152.5, 145.4 (C-4_{Ar}, $C_{Carbonyl}$, C-1_{Ar}), 125.3 (C-3_{Ar}), 121.8 (C-2_{Ar}) 70.4 ($(OCH_2CH_2O)_{10}$), 68.7 ((CO)CH_2), 68.4 ppm (C-b); HRMS (ESI): calcd. for $C_{38}H_{56}N_2O_{21}$: 877.3448 $[M+H]^+$, found 877.3444.

iLec 23. Compound **23** was synthesized according to GP2. Hexaethylene glycol carbonate **15** (35 mg, 0.057 mmol) was reacted with compound **22** (67 mg, 0.094 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **23** was obtained as a white solid (17 mg, 21 %); ^{1}H NMR (400 MHz, D_2O): δ = 5.97 (2H, d, J = 3.7 Hz, H-1), 5.93 (2H, d, J = 3.5 Hz, H-1‘), 4.32–4.18 (4H, m, H-d), 4.09–4.08 (2H, d, H-2‘), 4.06–4.05 (2H, m, H-2), 3.86–3.66 (48H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 8xCH_2CH_2), 3.64–54 (12H, m, H-c, H-c’, H-4, H-6’a), 3.50–3.45 (2H, m, H-4‘), 3.43–3.36 (2H, m, H-6’b), 3.29–3.22 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.05 (6H; s, OAc), 1.87–1.77 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, D_2O): δ = 174.5 ((C=O)Ac, (C=O)Ac‘), 157.7 (N(C=O)OCH_2)), 156.3 (O(C=O)NCH_2), 156.2 (O(C=O)NCH_2), 91.5 (C-1), 91.4 (C-1‘), 73.8 (C-5), 72.1 (C-5‘), 70.8 (C-4‘), 70.7 (C-3), 70.5 (C-3‘), 69.7 (C-4), 69.6, 69.6 (9 x CH_2CH_2), 68.9 (C-e), 68.2 (C-c, C-c’), 64.3 (C-d), 60.3 (C-6), 52.7 (C-2‘), 52.6 (C-2), 41.1 (C-6‘) 37.4 (C-a, C-a’), 28.6 (C-b, C-b’), 21.8 ppm (CH_3); HRMS: calcd. for $C_{70}H_{124}N_{10}O_{41}$: 1761.7998, found 1761.7961.

iLec 24. Compound **24** was synthesized according to GP10. Heptaethylene glycol carbonate **16** (180 mg, 0.186 mmol) was reacted with compound **22** (200 mg, 0.281 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **24** was obtained as a white solid (82 mg, 32 %). ^{1}H-NMR (400 MHz, D_2O): δ = 5.97 (2H, d, J = 3.6 Hz, H-1), 5.94 (2H, d, J = 3.6 Hz, H-1‘), 4.31–4.19 (4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.07–4.06 (2H, m, H-2), 3.88–3.68 (52H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 9xCH_2CH_2), 3.64–3.55 (12H, m, H-c, H-c’, H-4, H-6’a), 3.50–3.46 (2H, m, H-4‘), 3.43–3.37 (2H, m, H-6’b), 3.28–3.22 (8H, m, H-a, H-a’), 2.06 (6H, s, OAc), 2.05 (6H, s, OAc), 1.86–1.79 ppm (8H, m, H-b, H-b’); ^{13}C-NMR (101 MHz, D_2O): δ = 174.5 ((C=O)Ac), 174.5 ((C=O)Ac’), 158.4 (N(C=O)OCH_2)), 156.3 (O(C=O)NCH_2), 156.2 (O(C=O)NCH_2), 91.5 (C-1), 91.4 (C-1‘), 73.8 (C-5), 72.3 (C-5‘), 70.8 (C-4‘), 70.7 (C-3), 70.5 (C-3‘), 69.6 (C-4), 69.0 (C-e), 69.9 (9 x CH_2CH_2), 68.1 (C-c, C-c’), 64.3 (C-e), 60.3 (C-6), 52.7 (C-2‘), 52.6 (C-2), 41.0 (C-6‘) 37.4 (C-a, C-a’), 28.7 (C-b, C-b’), 21.8 ppm (CH_3); HRMS (ESI): calcd. for $C_{72}H_{128}N_{10}O_{42}$: 1843.7819 $[M+K]^+$, found 1843.7480.

iLec 25. Compound **25** was synthesized according to GP10. Octaethylene glycol carbonate **17** (38 mg, 0.054 mmol) was reacted with compound **22** (64 mg, 0.09 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **25** was obtained as a white solid (67 mg, 80 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.97 (2H, d, J = 3.5 Hz, H-1), 5.93 (2H, d, J = 3.6 Hz, H-1‘), 4.31–4.17

(4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.06–4.05 (2H, m, H-2), 3.88–3.66 (56 H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 10xCH_2CH_2), 3.63–3.53 (12H, m, H-c, H-c’, H-4, H-6’a), 3.51–3.44 (2H, m, H-4‘), 3.43–3.36 (2H, m, H-6’b), 3.28–3.22 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.04 (6H, s, OAc), 1.87–1.78 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.0 ((*C*=O)Ac, (*C*=O)Ac‘), 159.4 (N(*C*=O)OCH_2)), 157.7 (O(*C*=O)NCH_2), 156.6 (O(*C*=O)NCH_2), 92.9 (C-1), 92.8 (C-1‘), 75.2 (C-5), 73.8 (C-5‘), 72.2 (C-4‘), 72.1 (C-3), 72.0 (C-3‘), 71.1 (C-4), 71.0 (10 x CH_2CH_2), 70.4 (N(C=O)$OCH_2\mathit{C}H_2O$), 70.0 (O(C=O)$NCH_2CH_2\mathit{C}H_2$), 65.8 (N(C=O)$O\mathit{C}H_2CH_2O$), 61.7 (C-6), 54.1 (C-2‘), 54.1 (C-2), 42.5 (C-6‘) 38.8 (O(C=O)$N\mathit{C}H_2CH_2CH_2$), 30.1 (O(C=O)$NCH_2\mathit{C}H_2CH_2$), 23.2 ppm (CH_3); HRMS: calcd. for $C_{74}H_{132}N_{10}O_{43}$: 955.3987 $[M+Na+K]^{2+}$, found 955.3918.

iLec 26. Compound **26** was synthesized according to GP10. Nonaethylene glycol carbonate **18** (40 mg, 0.054 mmol) was reacted with compound **22** (64 mg, 0.09 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **26** was obtained as a white solid (38 mg, 45 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.96 (2H, d, J = 3.8 Hz, H-1), 5.93 (2H, d, J = 3.6 Hz, H-1‘), 4.31–4.17 (4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.06–4.05 (2H, m, H-2), 3.88–3.67 (60H, m, H-6, H-3, H-5‘, 4H, H-e, H-3‘, H-5, 11xCH_2CH_2), 3.64–3.53 (12H, m, H-c, H-c’, H-4, H-6’a), 3.51–3.44 (2H, m, H-4‘), 3.43–3.36 (2H, m, H-6’b), 3.28–3.22 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.04 (6H, s, OAc), 1.87–1.77 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.0 ((*C*=O)Ac, (*C*=O)Ac‘), 159.8 (N(*C*=O)OCH_2)), 157.7 (O(*C*=O)NCH_2), 157.6 (O(*C*=O)NCH_2), 92.9 (C-1), 92.8 (C-1‘), 75.2 (C-5), 73.7 (C-5‘), 72.2 (C-4‘), 72.0 (C-3), 71.9 (C-3‘), 71.1 (C-4), 71.0 (11 x CH_2CH_2), 70.8 (C-e), 69.5 (C-c, C-c’), 65.7 (C-d), 61.7 (C-6), 54.1 (C-2‘), 54.0 (C-2), 42.4 (C-6‘) 38.8 (C-a, C-a’), 30.0 (C-b, C-b’), 23.2 ppm (CH_3); HRMS: calcd. for $C_{76}H_{136}N_{10}O_{44}$: 977.4017 $[M+Na+K]^{2+}$, found 977.4017.

iLec 27. Compound **27** was synthesized according to GP10. Decaethylene glycol carbonate **19** (43 mg, 0.054 mmol) was reacted with compound **22** (64 mg, 0.09 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **115** was obtained as a white solid (39 mg, 45 %); ^1H NMR (400 MHz, $CDCl_3$): δ = 5.97 (2H, d, J = 3.6 Hz, H-1), 5.93 (2H, d, J = 3.6 Hz, H-1‘), 4.32–4.19 (4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.06–4.05 (2H, m, H-2), 3.88–3.66 (64H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 12xCH_2CH_2), 3.64–3.53 (12H, m, H-c, H-c’, H-4, H-6’a), 3.51–3.44 (2H, m, H-4‘), 3.44–3.36 (2H, m, H-6’b), 3.29–3.22 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.05 (6H, s, OAc), 1.87–1.78 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.0 ((*C*=O)Ac, (*C*=O)Ac‘), 159.8 (N(*C*=O)OCH_2)), 157.7 (O(*C*=O)NCH_2), 157.6 (O(*C*=O)NCH_2), 92.9 (C-1), 92.8 (C-1‘), 75.2 (C-5), 73.8 (C-5‘), 72.2 (C-4‘), 72.1 (C-3), 72.0 (C-3‘), 71.1 (12 x CH_2CH_2), 70.8 (C-4), 70.4 (C-e), 69.6 (C-c, C-c’), 65.8 (C-d), 61.7 (C-6), 54.1 (C-2‘, C-2), 42.4 (C-6‘) 38.8 (C-a, C-a’), 30.1 (C-b, C-b’), 23.2 ppm(CH_3); HRMS: calcd. for $C_{78}H_{140}N_{10}O_{45}$: 999.4249 $[M+Na+K]^{2+}$, found 999.4138.

iLec 28. Compound **28** was synthesized according to GP10. Undecaethylene glycol carbonate **20** (71 mg, 0.086 mmol) was reacted with compound **22** (102 mg, 0.14 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **28** was obtained as a white solid (43 mg, 31 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.97 (2H, d, J = 3.6 Hz, H-1), 5.93 (2H, d, J = 3.6 Hz, H-1‘), 4.31–4.18 (4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.06–4.05 (2H, m, H-2), 3.88–3.66 (68H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 13xCH_2CH_2), 3.65–3.53 (12H, m, H-c, H-c’, H-4, H-6’a), 3.50–3.44 (2H, m, H-4‘), 3.43–3.36 (2H, m, H-6’b), 3.29–3.21 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.05 (6H, s, OAc), 1.87–1.77 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 175.9, 175.9 ((*C*=O)Ac, (*C*=O)Ac‘), 159.9 (N(*C*=O)OCH_2)), 157.7 (O(*C*=O)NCH_2), 157.6 (O(*C*=O)NCH_2), 92.9 (C-1), 92.8 (C-1‘), 75.2 (C-5), 73.8 (C-5‘), 72.2 (C-4‘), 72.1 (C-3), 72.0 (C-3‘), 71.0 (13 x CH_2CH_2), 70.8 (C-4), 70.4 (C-e), 69.6 (C-c, C-c’), 65.9 (C-d), 61.7 (C-6), 54.1, 54.1 (C-2‘, C-2), 42.5 (C-6‘) 38.8 (C-a, C-a’), 30.1 (C-b, C-b’), 23.2 ppm (CH_3).; HRMS: calcd. for $C_{80}H_{144}N_{10}O_{46}$: 1021.4380 $[M+Na+K]^{2+}$, found 1021.4244.

iLec 29. Compound **29** was synthesized according to GP10. Dodecaethylene glycol carbonate **21** (53 mg, 0.06 mmol) was reacted with compound **22** (71 mg, 0.1 mmol). Purification by semi-preparative HPLC (column 2, 1–30 % (B) in (A) + 0.1 % FA in 20 min). The product **29** was obtained as a white solid (64 mg, 63 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.97 (2H, d, J = 3.6 Hz, H-1), 5.93 (2H, d, J = 3.6 Hz, H-1‘), 4.33–4.18 (4H, m, H-d), 4.09–4.08 (2H, m, H-2‘), 4.06–4.05 (2H, m, H-2), 3.88–3.66 (72H, m, H-6, H-3, H-5‘, H-e, H-3‘, H-5, 14xCH_2CH_2), 3.64–3.53 (12H, m, H-c, H-c’, H-4, H-6’a), 3.51–3.44 (2H, m, H-4‘), 3.43–3.36 (2H, m, H-6’b), 3.30–3.21 (8H, m, H-a, H-a’), 2.05 (6H, s, OAc), 2.04 (6H, s, OAc), 1.88–1.77 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 175.9, 175.9 ((*C*=O)Ac, (*C*=O)Ac‘), 159.9 (N(*C*=O)OCH_2)), 157.7 (O(*C*=O)NCH_2), 157.6 (O(*C*=O)NCH_2), 92.9 (C-1), 92.8 (C-1‘), 75.2 (C-5), 73.8 (C-5‘), 72.2 (C-4‘), 72.1 (C-3), 72.0 (C-3‘), 71.0 (14 x CH_2CH_2), 70.8 (C-4), 70.4 (C-e), 69.6 (C-c, C-c’), 65.7 (C-d), 61.7 (C-6), 54.1, 54.1 (C-2‘, C-2), 42.5 (C-6‘) 38.8 (C-a, C-a’), 30.1 (C-b, C-b’), 23.2 ppm (CH_3); HRMS: calcd. for $C_{82}H_{148}N_{10}O_{47}$: 1043.4511 $[M+N+K]^{2+}$, found 1043.4368.

1-(2-Acetamido-6-azido-3,4-bis-O-acetyl-2,6-dideoxy-α-D-glucopyranosyloxycarbonylamino)-13-tert-butylcarboxamido-4,7,10-trioxatridecan 33. Compound **31** (222 mg, 0.69 mmol) was placed in a Schlenk flask and dissolved in dry CH_2Cl_2 (8 mL). Then EtN*i*-Pr_2 (179 mg, 1.39 mmol) was added and carbonate **32** (412 mg, 0.83 mmol) was added as a solid. The solution was stirred for 50 min. Then the solution was diluted with CH_2Cl_2 and washed 6 x with a saturated solution of $NaHCO_3$. The organic layer was dried with $MgSO_4$ and the solvent was evaporated. The crude product was purified by manual FC (CH_2Cl_2/MeOH, 25:1). The product **33** was obtained as a colorless syrup (343 mg, 73%). R_f = 0.42 (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.03 (d, J = 3.7 Hz, 1H; H-1), 6.03–5.94 (m, 1H; NH), 5.82–5.73 (1H, m, NH), 5.19–5.12 (1H, m, H-3), 5.12–5.05 (1H, m, H-4), 5.02–4.91 (1H, m, N-H), 4.46 (1H, ddd, J = 10.6, 9.5, 3.7 Hz, H-2), 3.98–3.93 (1H, m, H-5), 3.67–3.44 (12H, m, 6xCH_2), 3.38–3.21 (4H, m, H-6, H-a), 3.21–3.09 (2H, m, H-a'), 2.00 (3H, s, OAc-4), 1.99 (3H, s, OAc-3), 1.90 (3H, s, NHAc), 1.84–1.75 (2H, m, H-b), 1.74–1.66 (2H, m, H-b'), 1.04 ppm (9H, s, Boc); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.4 (O*C*(O)CH_3-3), 170.2 (NH*C*(O)CH_3), 169.2 (O*C*(O)CH_3-4), 156.1 (NH*C*(O)OC$(CH_3)_3$, 153.9 (NH*C*(O)O), 91.3 (C-1), 79.1 (*C*$(CH_3)_3$), 70.9 (C-3), 70.5 (C-5, CH_2), 69.5 (NHCH_2CH_2*C*H_2O), 69.4 (O*C*$H_2CH_2CH_2$NHBoc), 69.1 (C-4), 50.8 (C-2, C-6), 39.5 (NH*C*$H_2CH_2CH_2$O), 38.5 (OCH_2CH_2*C*H_2NHBoc), 29.8 (OCH_2*C*H_2CH_2NHBoc), 29.1 (NHCH_2*C*H_2CH_2O), 28.5 (C(*C*$H_3)_3$), 23.0 (NHC(O)*C*H_3), 20.7 (OC(O)*C*H_3-4), 20.6 ppm (OC(O)*C*H_3-3); HRMS: calcd. for $C_{28}H_{48}N_6O_{13}$: 699.3172 $[M+Na]^+$, found 699.3077.

1-(2-acetamido-6-azido-2,6-dideoxy-α-D-glucopyranosyloxycarbonylamino)-13-tert-butylcarboxamido-4,7,10-trioxatridecan 34. Compound **33** (23 mg, 29 µmol) was dissolved in methanol (1 mL) and potassium carbonate (2 mg, 15 µmol) was added. The mixture was stirred at RT for 40 min. Then Amberlite IRC-120 ion exchange resin was added until pH = 7 was reached. The resin was filtered and the solvent was evaporated. The product **34** was obtained as a colorless syrup (19 mg, quant.). R_f = 0.27 (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (400 MHz, MeOD): δ = 6.02 (1H, d, J = 3.6 Hz, H-1), 4.05 (1H, dd, J = 10.8, 3.6 Hz, H-2), 3.87–3.81 (1H, m, H-5), 3.74–3.52 (14H, m, H-3, CH_2, H-6a), 3.48–3.40 (2H, m, H-6b, H-4), 3.28–3.22 (2H, m, H-a), 3.15 (2H, t, J = 6.7 Hz, H-a'), 2.00 (3H, s, OAc), 1.85–1.78 (2H, m, H-b), 1.78–1.71 (2H, m, H-b'), 1.46 (9H, s, Boc); ^{13}C NMR (101 MHz, MeOD): δ = 173.8 (C(O)CH_3), 170.3 (C(O)), 156.8 (C(O)), 92.7 (C-1), 74.5 (C-5), 72.6 (C-3), 72.2 (C-4), 71.5 (CH_2), 71.2 (CH_2), 54.4 (C-2), 52.4 (C-6), 39.1 (CH_2), 30.8 (CH_2), 28.8 (Boc), 22.5 ppm (OAc); HRMS: calcd. for $C_{24}H_{44}N_6O_{11}$: 593.3141 $[M+H]^+$, found 593.3091.

1-(2-Acetamido-6-amino-2,6-dideoxy-α-D-glucopyranosyloxycarbonylamino)-13-tert-butylcarboxamido-4,7,10-trioxatridecan 35. Compound **34** (426 mg, 0.72 mmol) was dissolved in methanol (11 mL) and palladium 5 % on charcoal (74 mg) was added. The suspension was vigorously stirred under an atmosphere of hydrogen until TLC showed completion. The suspension was filtered through a bed of celite and the solvent was evaporated. The product **35** was obtained as a colorless oil (361 mg, 74 %); ^{1}H NMR (400 MHz, MeOD): δ = 5.99 (1H, d, J = 3.6 Hz, H-1), 4.11 (1H, dd, J = 3.6, 10.8 Hz, H-2), 4.00–3.93 (1H, m, H-5), 3.84–3.77 (1H, m, H-3), 3.75–3.65 (8H, m, OCH_2CH_2O), 3.63–3.59 (4H, m, H-c, H-c'), 3.55–3.44 (2H, m, H-4, H-6a), 3.29–3.13 (5H, m, H-6b, H-a, H-a'), 2.05 (3H, s, OAc), 1.89-1.75 (4H, m, H-b, H-b'), 1.46 ppm (9H, s, Boc); ^{13}C NMR (101 MHz, MeOD): δ = 174.6 (CH_3(*C*O)NH, 158.2 (NH(*C*O)O), 156.2 (NH(*C*O)O), 91.2 (C-1), 71.2 (C-4), 70.2 (C-3), 69.6 (O*C*H_2*C*H_2O), 69.3 (C-5), 68.4, 68.2 (C-c, C-c'), 52.4 (C-2), 40.3 (C-6), 37.5 (C-a, C-a'), 28.8, 28.6 (C-b, C-b'), 27.7 (Boc), 21.8 ppm (OAc); HRMS: calcd. for $C_{24}H_{46}N_4O_{11}$: 567.3236 $[M+H]^+$, found 567.3218.

Compound 36. Compound **35** (272 mg, 0.48 mmol) was dissolved in dry DMF (3 mL) and NEt*i*Pr_2 (81 µL, 0.48 mmol) was added. Hexaethylene glycol active carbonate **15** (98 mg, 0.16 mmol) was dissolved in dry DMF (3 mL) and added to the first solution. The solution was stirred for 2 h at room temperature. Then pyridine (400 µL, 3.73 mmol) and acetic anhydride (400 µL, 3.73 mmol) were added and the solution was stirred for 21 h at room temperature. Then the solvent was evaporated and the residue was purified by manual FC (CH_2Cl_2/MeOH, 20:1 to 10:1). Compound **36** was obtained as a colorless amorphous solid (205 mg, 78 % yield). R_f = 0.31 (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.09–6.00 (2H, m, NHAc), 5.98 (2H, d, J = 3.6 Hz, H-1), 5.87–5.78 (2H, m, OC(O)N*H*), 5.35–5.28 (2H, m, OC(O)NH-6), 5.15 (2H, dd, J = 10.9, 9.6 Hz, H-3), 4.99–4.92 (2H, m, H-4), 4.42 (2H, ddd, J = 10.9, 9.3, 3.7 Hz, H-2), 4.20–4.10 (4H, m, H-d), 3.92–3.84 (2H, m, H-5), 3.66–3.46 (44H, m, OC*H*$_2$C*H*$_2$O, C-e, H-c’, H-c), 3.41–3.33 (2H, m, H-6a), 3.32–3.23 (6H, m, H-6b, H-a, 3.22–3.13 (4H, m, H-a’), 2.01 (6H, s, OAc-4), 1.98 (6H, s, OAc-3), 1.89 (6H, s, OAc-2), 1.82–1.74 (4H, m, H-b), 1.74–1.68 (4H, m, H-b’), 1.40 pp, (18H, s, Boc); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.5 (*C*(O)CH_3-3), 170.2 (*C*(O)CH_3-2), 169.4 (*C*(O)CH_3-4), 156.5 (O(CO)O), 156.2 ((CO)O*t*-Bu), 154.1 ((CO)NH-1), 91.4 (C-1), 71.0 (C-3), 70.6, 70.5, 70.4 (C-5, O*C*H$_2$*C*H$_2$O), 70.2 C-c’, 70.1 (C-c), 68.7 (C-4), 64.3 (C-d), 51.0 (C-2), 41.1 (C-6), 39.4 (C-a’), 38.4 (C-a), 29.7 (C-b), 29.1 (C-b’), 28.5 (CH_3-Boc), 22.9 (Ac-2), 20.7 (Ac-3), 20.6 ppm (Ac-4); HRMS: calcd. for $C_{70}H_{122}N_8O_{25}$: 1635.8085 $[M+H]^+$, found 1635.7939.

Compound 38. Compound **36** (205 mg, 0.12 mmol) was dissolved in CH_2Cl_2/TFA 2:1 (4.5 mL) and stirred for 2 min. The solvent was blown off and the residue was dried under reduced pressure and co-evaporated with toluene (2x). The residue was dissolved in dry CH_2Cl_2 (3mL) and EtN*i*Pr_2 (320 µL, 1.9 mmol) was added. Compound **32** (208 mg, 0.42 mmol, 3.4 eq) was dissolved in dry CH_2Cl_2 (3 mL) and added. The solution was stirred at room temperature for 30 min. The solution was washed with water (1x) and the aqueous phase was re-extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The crude was purified by manual FC (CH_2Cl_2/MeOH, 10:1 to 7:1). The product **38** was obtained as a colorless amorphous solid (225 mg, 83 %); R_f = 0.27 (CH_2Cl_2/MeOH ,10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.13 (2H, d, J = 3.6 Hz, 2H; H-1), 6.09 (2H, d, J = 3.6 Hz, H-1’), 5.45–5.34 (4H, m, H-3, H-3’), 5.20–5.13 (2H, m, H-4), 5.10–5.03 (2H, m, H-4’), 4.55–4.47 (4H, m, H-2, H-2’), 4.32–4.18 (6H, m, H-5, H-d), 4.14–4.08 (2H, m, H-5), 3.81–3.61 (44H, m, H-e, OC*H*$_2$C*H*$_2$O, H-c, H-c’), 3.57–3.51 (2H, m, H6a), 3.50–3.39 (6H, m, H-6b, H-6a’, H-6b’), 3.37–3.31 (8H, m, H-a, H-a’), 2.13 (12H, m, OAc-4, OAc-4’), 2.10 (6H, s, OAc-3), 2.09 (6H, s, OAc-3’), 2.04 (6H, s, OAc-2), 2.03 (6H, s, OAc-2’), 1.96–1.84 ppm (8H, m, H-b, H-b’); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5 (C(O)CH_3-2), 173.5 (C(O)CH_3-2’), 172.0 (C(O)CH_3-3), 172.0 (C(O)CH_3-3’), 171.3 (C(O)CH_3-4), 171.1 (C(O)CH_3-4’), 158.7 (O(*C*O)O), 156.3 (O(CO)NH), 156.1 (O(CO)NH’), 92.4 (C-1’), 92.2 (C-1), 71.9 (C-3), 71.8 (C-5), 71.6, 71.5, 71.2 (OCH_2CH_2O), 70.8 (C-4), 70.7 (C-4’), 70.4 (OCH_2CH_2O), 69.6, 69.6 (C-c, C-c’), 65.3 (C-d), 52.1 (C-2), 51.2 (C-2'), 51.8 8 (C-6), 42.1 (C-6'), 39.3 (C-a, C-a'), 30.7 (C-b, C-b'), 22.4 (OAc-2), 20.8 (OAc-3), 20.7 ppm (OAc-4) HRMS: calcd. for $C_{86}H_{138}N_{16}O_{47}$: 2147.8973 $[M+H]^+$, found 2147.8846.

Compound 40. Compound **39** (205 mg, 0.1 mmol) was dissolved in MeOH (3 mL) and water (2 mL) and potassium carbonate was added (26 mg, 0.19 mmol). The mixture was stirred at RT for 3 h and was neutralized with Amberlite IRC-120 ion exchange resin. The solution was filtered and the solvent was evaporated. The product **40** was obtained as a white amorphous solid (161 mg, 93 %). ^{1}H NMR (400 MHz, MeOD): δ = 6.05 (2H, d, J = 3.5 Hz, H-1), 6.01 (2H, d, J = 3.5 Hz, H-1'), 4.29–4.15 (4H, m, H-d), 4.06 (4H, dd, H-2, H-2'), 3.91–3.84 (2H, m, H-5), 3.79–3.54 (56H, m, H-3, H-3', H-5', H-e, OCH_2CH_2O, H-6a, H-6a', H-c, H-c'), 3.53–3.43 (4H, m, H-4, H-6b), 3.41–3.31 (4H, m, H-4', H-6b'), 3.31–3.22 (8H, m, H-a, H-a'), 2.06–2.00 (12H, m, OAc), 1.87–1.77 ppm (8H, m, H-b, H-b'); ^{13}C NMR (101 MHz, MeOD): δ = 173.8 (OAc-2), 159.2 (NH(*C*O)O), 156.9 (O(*C*O)$NHCH_2$-1), 156.7 (O(*C*O)$NHCH_2$-1'), 92.7 (C-1), 92.6 (C-1'), 74.4 (C-5), 74.1 (C-5'), 73.0 (C-4), 72.5 (C-4'), 72.1 (C-3), 71.9 (C-3'), 71.5 (OCH_2CH_2O), 71.2 (OCH_2CH_2O), 70.5 (OCH_2CH_2O), 69.6 ($NHCH_2CH_2CH_2O$-1), 69.6 ($NHCH_2CH_2CH_2O$-1'), 65.3 (O(CO)OCH_2), 54.5 (C-2), 54.4 (C-2'), 52.3 (C-6), 42.8 (C-6'), 39.2 ($NHCH_2CH_2CH_2O$-1), 39.1 ($NHCH_2CH_2CH_2O$-1'), 30.7 ($NHCH_2CH_2CH_2O$), 22.6 ppm (OAc). HRMS: calcd. for $C_{70}H_{122}N_{16}O_{39}$: 1811.8128 $[M+H]^+$, found 1811.7861.

Compound 37. Compound **35** (19 mg, 0.4 mmol) was dissolved in dry DMF (1.5 mL) and NEt*i*-Pr_2 (6 µL, 0.04 mmol) was added. Carbonate **21** (10 mg, 0.1 mmol) was dissolved in dry DMF (1.5 mL) and added. The solution was stirred at RT for 3 h. Then pyridine (100 µL) and acetic anhydride (100 µL) were added and the solution was stirred for 1 d. The solvent was evaporated and the crude was purified by flash column chromatography (CH_2Cl_2/MeOH, 10:1). The product **37** was obtained as a colorless oil (17 mg, 78 %). R_f= 0.37 (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (2H, d, J = 3.6 Hz, H-1), 5.99–5.93 (2H, m, NH-2), 5.82–5.73 (2H, m, H-a'), 5.28–5.22 (2H, m, NH-6), 5.21–5.14 (2H, m, H-3), 5.04–4.94 (4H, m, NHBoc, H-4), 4.44 (2H, ddd, J = 3.7, 9.5, 11.0 Hz, H-2), 4.25–4.10 (4H, m, H-d), 3.93–3.86 (2H, m, H-5), 3.72–3.49 (60H, m, OCH_2CH_2O, H-e, H-c, H-c'), 3.45–3.37 (2H, m, H-6a), 3.36–3.26 (6H, m, H-6b, H-a'), 3.26–3.14 (4H, m, H-a), 2.04 (6H, s, OAc-4), 2.01 (6H, s, OAc-3), 1.92 (6H, s, OAc-2), 1.88–1.78 (4H, m, H-b'), 1.78–1.70 (4H, m, H-b), 1.43 ppm (18H, s, Boc); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.6 (*C*OCH_3-3), 170.3 (*C*OCH_3-2), 169.5 (*C*OCH_3-4), 156.5 ((*C*O)OCH_2CH_2O), 156.3 ((*C*O)OC$(CH_3)_3$), 154.1 ((*C*O)$NHCH_2CH_2CH_2$), 91.5 (C-1), 71.1 (C-3), 70.6 (CH_2CH_2, C-5), 70.3, 69.6, 68.9 (C-4) 64.4 (C-d), 51.1 (C-2), 41.2 (C-6), 39.6 (C-a'), 38.6 (C-a) 29.8 (C-b'), 29.1 (C-b), 28.6 (Boc), 23.1 (COCH_3-4), 20.9 (COCH_3-3), 20.8 ppm (COCH_3-2); HRMS: calcd. for $C_{82}H_{146}N_8O_{41}$: 1899.9658 $[M+H]^+$, found 1899.9425.

Compound 39. Compound **37** (222 mg, 0.12 mmol) was dissolved in CH_2Cl_2/TFA 2:1 (6 mL) and stirred for 10 min. The solvent was evaporated and the crude was co-evaporated with toluene two times. The residue was dissolved in dry CH_2Cl_2 (3 mL) and NEt*i*-Pr_2 (240 μL, 1.4 mmol) was added so that the solution was basic. Compound **32** (173 mg, 0.35 mmol) was dissolved in dry CH_2Cl_2 (3 mL) and added. The solution was stirred at RT for 30 min. Washed with water (1x) and re-extracted with CH_2Cl_2. The combined organic phases were dried with Na_2SO_4 and the solvent was evaporated. The crude was purified by manual FC (CH_2Cl_2/MeOH, 15:1–5:1). The product **39** was obtained as a colorless oil (254 mg, 90 %). R_f = 0.60 (CH_2Cl_2/MeOH, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.20 (2H, d, J = 3.5 Hz, H-1), 6.16 (2H, d, J = 3.5 Hz, H-1'), 5.51–5.41 (4H, m, H-3, H-3'), 5.27–5.20 (2H, m, H-4), 5.17–5.09 (2H, m, H-4'), 4.64–4.53 (4H, m, H-2, H-2'), 4.39–4.25 (6H, m, H-d, H-5), 4.21–4.15 (2H, m, H-5'), 3.91–3.67 (68H, m, H-e, OCH_2CH_2O), H-c, H-c'), 3.66-3.47 (8H, m, H-6, H-6'), 3.46–3.37 (8H, m, H-a, H-a'), 2.24–2.18 (12H, m, Ac-4, Ac-4'), 2.17 (6H, s, Ac-3), 2.16 (6H, s, Ac-3'), 2.11 (6H, s, Ac-2), 2.10 (6H, s, Ac-2'), 2.02–1.91 ppm (8H, m, H-b, H-b'); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4 ((*C*O)CH_3-2), 171.9 ((*C*O)CH_3-3), 171.2 ((*C*O)CH_3-4), 171.1 ((*C*O)CH_3-4'), 158.6 (NH(*C*O)OCH_2CH_2O), 156.2 (O(*C*O)NH$CH_2CH_2CH_2$-1), 156.0 (O(*C*O)NH$CH_2CH_2CH_2$-1'), 92.3 (C-1), 92.2 (C-1'), 71.9, 71.7, 71.4, 71.4, 71.4, 71.4, 71.2, 70.7, 70.6, 70.4 (C-3, C-3', C-4, C-4', C-5, C-5', OCH_2CH_2O) 69.6 (C-c), 69.5 (C-c'), 65.2 (C-d), 52.0 (C-2), 51.9 (C-2'), 51.7 (C-6), 42.0 (C-6'), 39.3 (C-a), 39.2 (C-a'), 30.7 (C-b, C-b'), 22.4 (OAc-2), 20.8 (OAc), 20.7 (OAc), 20.7 ppm (OAc); HRMS: calcd. for $C_{98}H_{162}N_{16}O_{53}$: 2434.0365 $[M+Na]^+$, found 2434.0322.

Compound 41. Compound **39** (254 mg, 0.11 mmol) was dissolved in MeOH (3mL) and Water (2mL) and K_2CO_3 (33 mg, 0.21 mmol) was added. The solution was stirred for 22 h, neutralized with ion exchange resin Amberlite IRC-120 and the solvent was evaporated. The product **41** was obtained as a colorless amorphous solid (195 mg, 89 %). R_f = 0.16 (CH_2Cl_2/MeOH, 5:1); ^{1}H NMR (400 MHz, MeOD): δ = 6.06 (2H, d, J = 3.5 Hz, H-1), 6.02 (2H, d, J = 3.5 Hz, H-1'), 4.30–4.16 (4H, m, H-d), 4.12–4.01 (4H, m, H-2, H-2'), 3.92–3.84 (2H, m, H-5), 3.80–3.54 (76H, m, H-3, H-5', OCH_2CH_2O, H-e, H-c, H-c', H6a, H6a'), 3.53–3.44 (4H, m, H6b, H4), 3.43–3.33 (4H, m, H6b', H4'), 3.32–3.21 (8H, m, H-a, H-a'), 2.05 (6H, s, OAc), 2.04 (6H, s, OAc), 1.92–1.74 ppm (8H, m, H-b, H-b'); ^{13}C NMR (101 MHz, MeOD): δ = 173.8 (NH(*C*O)CH_3), 159.1 ((*C*O)OCH_2CH_2), 156.9 (O(*C*O)NH$CH_2CH_2CH_2$O-1'), 156.7 (O(*C*O)NH$CH_2CH_2CH_2$O-1), 92.7 (C-1'), 92.5 (C-1), 74.4 (C-5), 74.1 (C-5'), 72.9 (C-4), 72.5 (C-4'), 72.1 (C-3), 71.8 C-3'), 71.4 (OCH_2CH_2), 71.2, 70.4, 69.6 (C-c, C-c'), 65.2 (C-d), 54.5 (C-2), 54.4 (C-2'), 52.3 (C-6), 42.8 (C-6'), 39.2, 39.1 (C-a, C-a'), 30.7 (C-b, C-b'), 22.5 ppm (OAc); HRMS: calcd. for $C_{82}H_{146}N_{16}O_{45}$: 2075.9701 $[M+H]^+$, found 2075.9433.

Compound 43. Compound **40** (123 mg, 0.068 mmol) was dissolved in MeOH (5 mL) and 5 % Pd/C (30 mg) was added. The solution was stirred under hydrogen atmosphere for 2 h. The solution was filtered through celite and the solvent was evaporated. The crude was dissolved together with compound **42**[3] (76 mg, 0.27 mmol) in dry MeOH (5 mL) The solution was stirred for 2 d. The solvent was evaporated and the crude was purified by semi-preparative HPLC (column 2, 20-38 % (B) in (A) + 0.1 % formic acid in 12 min). The product **43** was obtained as a white solid (18 mg, 14 %). Analytical HPLC: t_R = 9.5 min (column 1, 10-50% (B) in (A) + 0.1 % formic acid in 10 min); HRMS: calcd. for $C_{88}H_{150}N_{14}O_{43}$ $[M+2H]^{2+}$ 1046.5064; found 1046.5077.

Compound 44. Compound **41** (185 mg, 0.09 mg) was dissolved in MeOH (5 mL) and Pd (5 % on charcoal) (30 mg) was added. The solution was stirred under hydrogen atmosphere for 22 h. It was filtered through celite and the solvent was evaporated. The crude was dissolved together with compound **42** (68 mg, 0.24 mmol) in dry MeOH (5 mL) and stirred for 3 d. The solvent was evaporated and the crude was purified by semi-preparative HPLC (column 2, 20-50 % (B) in (A) + 0.1 % formic acid in 20 min). The product **44** was obtained as a white solid (74 mg, 39 %). Analytical HPLC: t_R = 9.8 min (column 1, 10-50% (B) in (A) + 0.1 % formic acid in 10 min); HRMS: calcd. for $C_{100}H_{174}N_{14}O_{49}$ $[M+2H]^{2+}$ 1178.5850; found 1178.5865.

Isothermal Titration Calorimetry

Isothermal titration calorimetry was performed on a GE Microcal iTC$_{200}$ system. Wheat germ agglutinin was dissolved in buffer (50 mM sodium phosphate/50 mM KCl, pH 7.0), allowed to dissolve for 15 min, and centrifuged for 5 min at 10,000 rpm. The protein concentration of the supernatant was determined by measuring the absorption at 280 nm using a molar extinction coefficient E_{280} = 59200 L mol^{-1} cm^{-1} (ExPASy ProtParam tool[4]). The protein solution was diluted to a concentration of 20 µM for divalent ligands and 4 µM for tetravalent ligands. The ligands were dissolved in the same buffer solution and the concentration was adjusted to 20-fold of the protein concentration for divalent ligands and 10 fold for tetravalent ligands. The titrations were performed at 298 K, 1000 rpm stirring speed, a reference power of 6 µcal s^{-1} and an initial delay of 600 s for equilibration. Usually, 19 injections of 2 µL and a duration of 4 s each were performed. Spacing between injections was 120 s. Prior to the first titration an injection of 0.4 µL was performed. The data were processed and analyzed using Origin 7 with the iTC Data analysis plugin by Microcal. Baseline correction and integration were carried out manually, and for data fitting the “one set of sites” model was used.

Dynamic Light Scattering

Dynamic light scattering was performed on a Viscotek 802 DLS System. WGA was dissolved in buffer (50 mM sodium phosphate/50 mM KCl, pH 7.0) and the protein concentration was determined as described above. Ligand concentrations were equal to the protein concentration for tetravalent ligands and twice the protein concentration for divalent ligands (see below). The solutions were filtered through a 100 nm cutoff filter (*Whatman*, Anotop 10, 0.1 μm, 10 mm) prior to measurement. The measurement was performed at 293 K in a 12 μL sample cell, laser wavelength 830 nm, scattering angle 90°. Each sample was measured in duplicate with 10 scans over 5 s for each run. Evaluation of data was performed with OmniSIZE Version 3 by *Viscotek*.

Enzyme Linked Lectin Assay

Assays were carried out as previously described[5] using a different linker for coating of the microtiter plates. Briefly, microtiter plates with covalently immobilized reference ligand 11-amino-3,6,9-trioxaundecyl 2-acetamido-2-deoxy-*β*-D-glucopyranoside[6] were incubated with mixtures of horseradish peroxidase (HRP)-labeled WGA (1 μg mL^{-1}) and the respective WGA ligand in varying concentrations. After incubation, the plates were washed and remaining labeled WGA bound to the reference ligand was quantified by an HRP-catalyzed color reaction using 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) as substrate. From dose-response curves for inhibition of the binding of HRP-labeled WGA to the immobilized reference ligand, the concentrations that reduce the binding of labeled WGA by 50 % (IC_{50} values) were determined as a measure of potency of the synthesized inhibitors.

Precipitation Assay

WGA was dissolved in ITC buffer at a concentration of 15–30 μM and centrifuged for 5 min at 10 000 rpm. The solution was partitioned to 9 aliquots of 100 or 200 μL. Then buffer and ligand solutions were added so that the total volume of each sample was 150 or 300 μL. The volume of ligand was calculated so that the first sample contained no ligand and the last sample contained the ligand in a concentration of 3–4 fold of the protein concentration. The samples were shaken for 1 h at RT. Then the samples were centrifuged at 10 000 rpm for 15 min. 50 μL of the supernatant were diluted to 200 μL and the UV absorption at 280 nm was measured. The concentration of the sample containing no ligand was used as blank value (0 % precipitation). Using the protein concentration of the samples containing ligand, the proportion of precipitated protein was calculated.

EPR Sample Preparation

For EPR experiments in the absence of WGA, spin-labeled iLecs were dissolved in MilliQ water and adjusted to a concentration of 150 μM. Samples of 10 μL volume were prepared and lyophilized in order to dispose of the deuterated solvent. Subsequently, the EPR samples were dissolved in 10 μL D_2O.

For EPR experiments in the presence of WGA, the lectin was purchased as lyophilized powder (SigmaAldrich), and dissolved in MilliQ water. The lectin concentration was determined spectrophotometrically with a molar extinction coefficient E_{280} = 59200 L mol^{-1} cm^{-1}. Samples were prepared such that they contained 200 μM WGA and 150 μM of the respective iLec in a final sample volume of 10 μL. The EPR samples were lyophilized and afterwards dissolved in 10 μL D_2O.

For the EPR measurements, 2.5 μL glycerol-d_8 (20 % v/v) was added to all iLec samples with or without WGA. The samples were transferred into Q-band quartz sample tubes with an inner diameter of 1 mm and shock frozen in liquid nitrogen before the measurement.

EPR Measurements

Q-band EPR experiments were performed with a commercial ELEXSYS E580 spectrometer equipped with an EN5107D2 Q-band probehead and a 10 W solid state amplifier (all Bruker Biospin). A CF935 cryostat was used for temperature control with a helium gas flow system (Oxford Instruments). The experiments were performed at $T = 50\ K$.

In the four-pulse DEER experiment the frequency of the pump pulse was set to the resonance frequency of the microwave resonator and the pump pulse was positioned on the maximum of the nitroxide spectrum at this frequency. The frequency offset of the observer pulses was chosen as $\Delta\nu$ = 44 MHz. The pump pulse length was adjusted to deliver a flip angle π, resulting in pulse lengths between 20 and 26 ns. The refocused echo observer pulse sequence was adjusted to deliver flip angles $\frac{\pi}{2}$ and π, resulting in π pulse lengths between 40 and 52 ns. The pulse separation time τ_1 was 400 ns and dipolar evolution times were 6000 ns. In one case, the dipolar oscillations in the DEER time trace persisted after this evolution time and the measurement was thus repeated with a dipolar evolution time of 12,000 ns. Nuclear modulation artifacts of the deuterated solvents were suppressed by variation of the interpulse delay τ_1 by averaging 8 traces with $\Delta\tau_1$ = 16 ns. An eight-step phase cycle was employed.

DEER Data Analysis

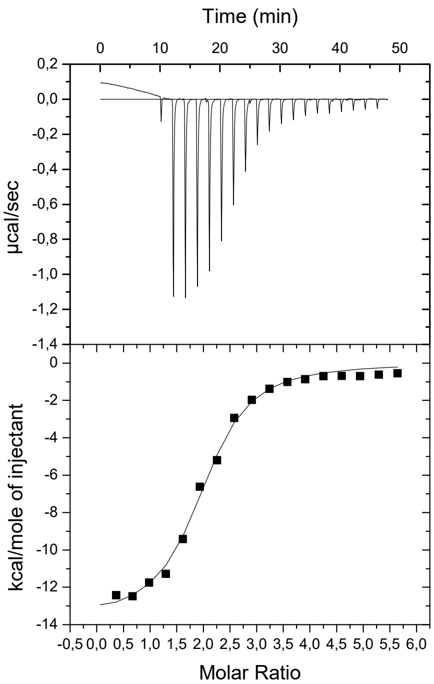
DEER data were analyzed using the DeerAnalysis 2016 software package for MATLAB.[7] Extraction of the dipolar evolutions function was achieved by background-correction with a three-dimensional homogeneous background function. Background-corrected data were subjected to model-free analysis by Tikhonov regularization in order to obtain the distance distributions. Distance distributions were validated using the validation tool of DEERAnalysis 2016. For this purpose, 100 regularizations were calculated for each data set, gradually changing the background start and the white noise level, in order to create an error estimate and an appropriate background start for the Tikhonov regularization.

The number of spins per cluster in the samples of iLecs in the presence of WGA was determined as described by Bode *et al*.[8] The number n of spins per cluster was calculated as

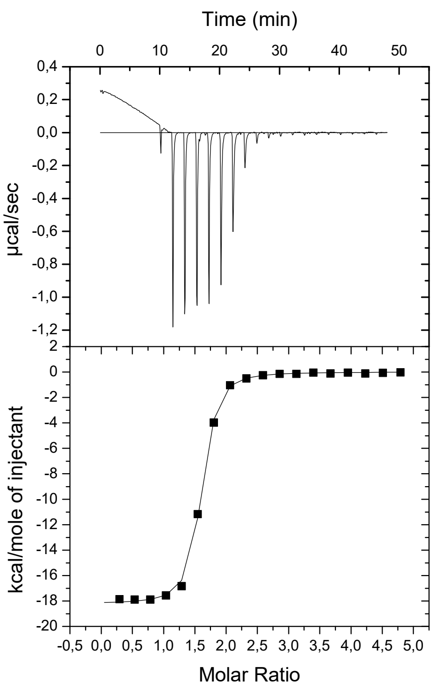
$$n = \frac{\ln(V_\lambda)}{\ln(1-\lambda_B)} + 1,$$

where V_λ is the echo intensity of the background-corrected DEER time trace at the end of the dipolar evolution time, and λ_B is the modulation depth of a sample that contains 100% biradical. For the determination of λ_B, the samples containing pure iLecs were used. Small deviations in the pump pulse lengths of different measurements were corrected by re-calculating the excitation bandwidths of all measurements to a pump pulse length of 24 ns.

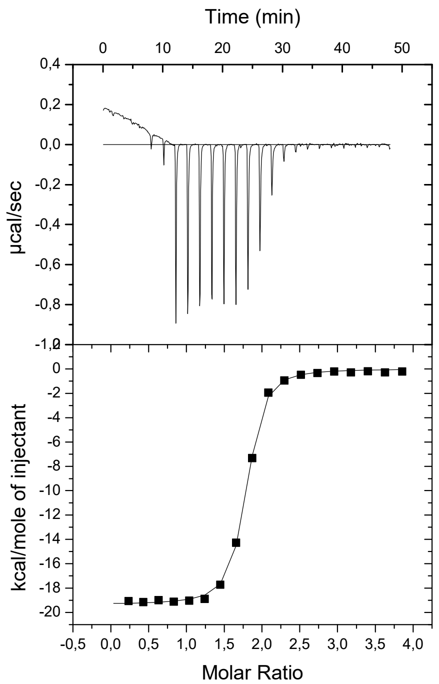
ITC Data of Divalent Ligands 1–5



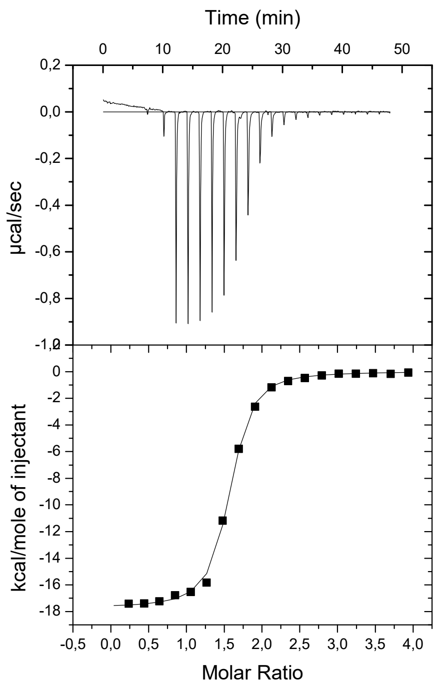
ITC binding profile of **1** ([WGA] = 19 μM, [**1**] = 561 μM)



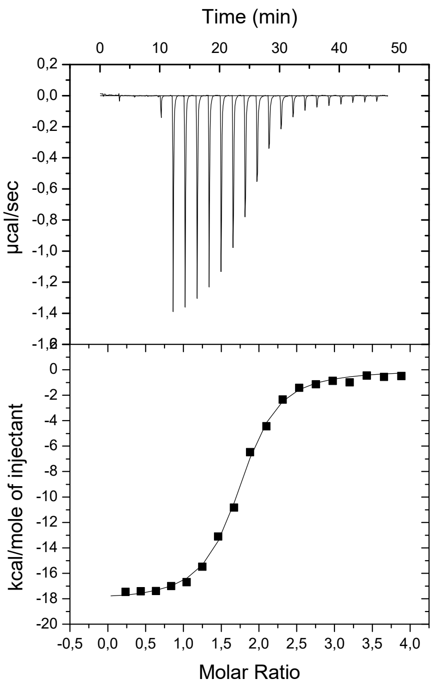
ITC binding profile of **2** ([WGA] = 16 μM, [**2**] = 389 μM)



ITC binding profile of **3** ([WGA] = 13 μM, [**3**] = 265 μM)

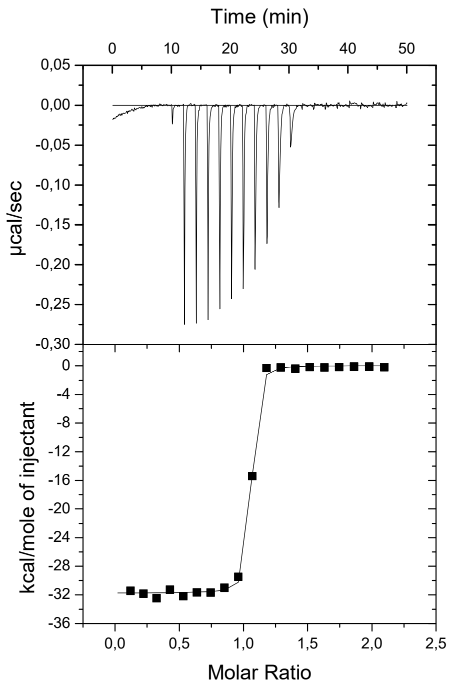


ITC binding profile of **4** ([WGA] = 14 μM, [**4**] = 280 μM)

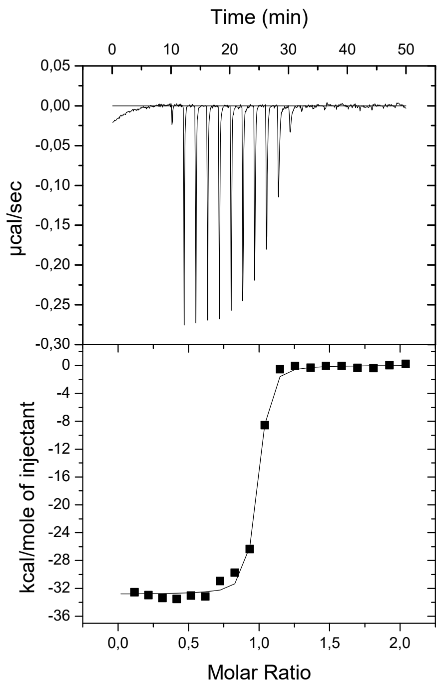


ITC binding profile of **5** ([WGA] = 20 μM, [**5**] = 398 μM)

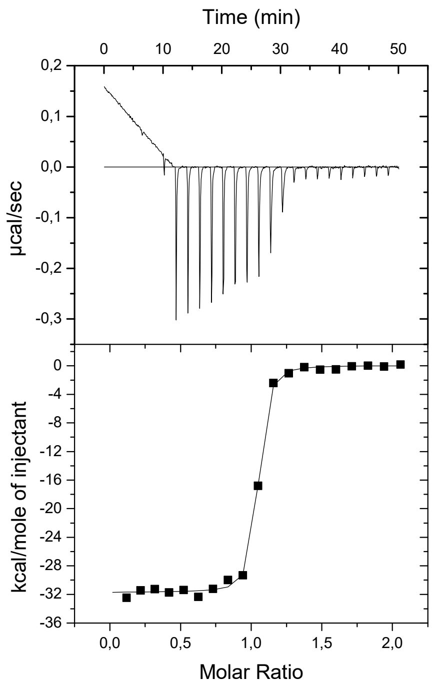
ITC Data of Inline Lectin Ligands 23–29, 43, 44



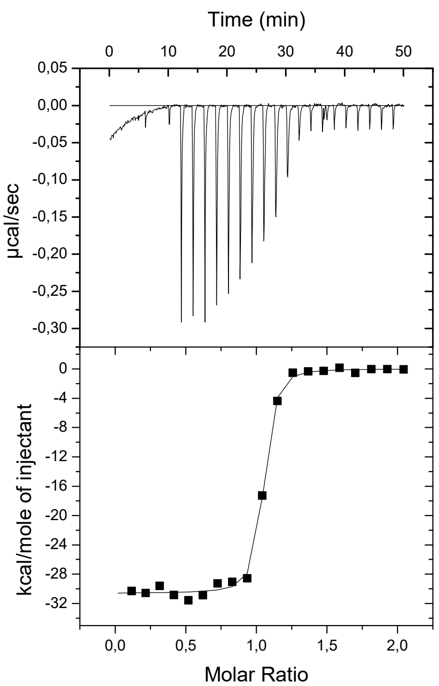
ITC binding profile of **23** ([WGA] = 5 μM, [**23**] = 47 μM)



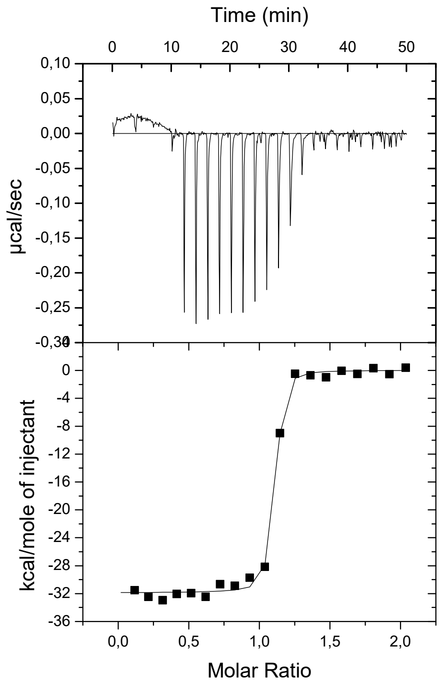
ITC binding profile of **24** ([WGA] = 5 μM, [**24**] = 45 μM)



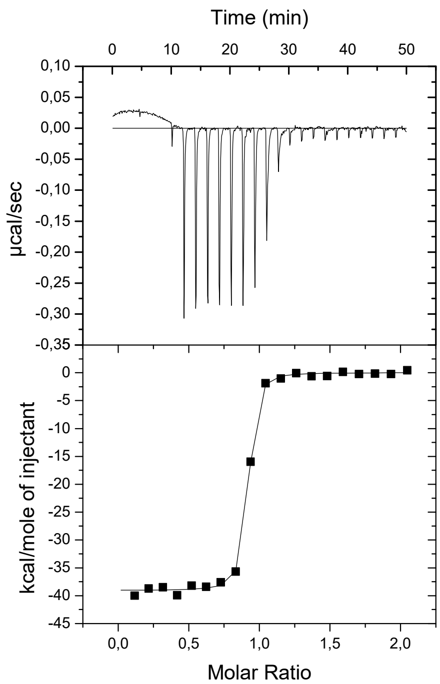
ITC binding profile of **25** ([WGA] = 5 μM, [**25**] = 47 μM)



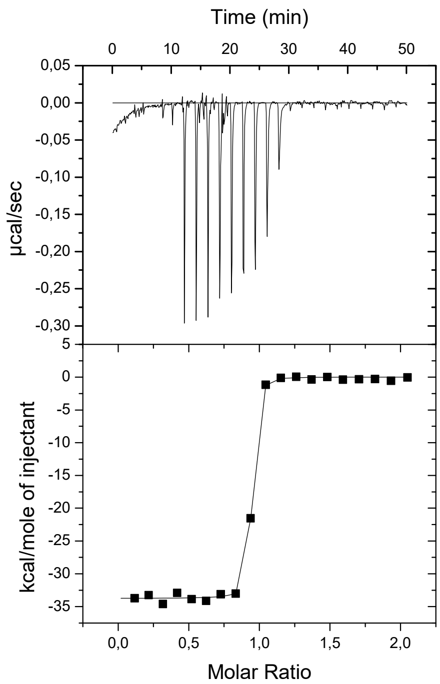
ITC binding profile of **26** ([WGA] = 5 μM, [**26**] = 48 μM)



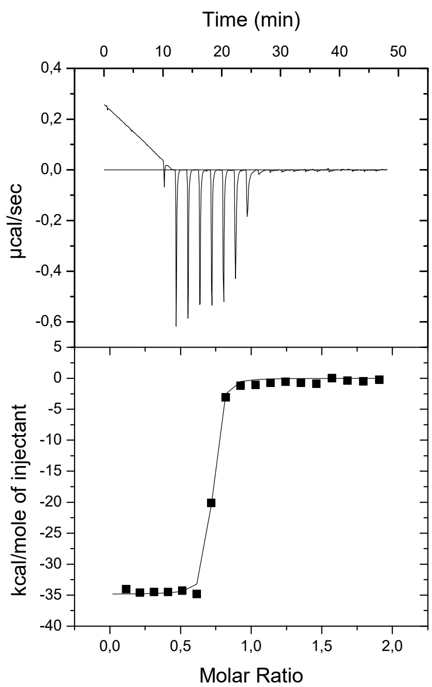
ITC binding profile of **27** ([WGA] = 4 μM, [**27**] = 44 μM)



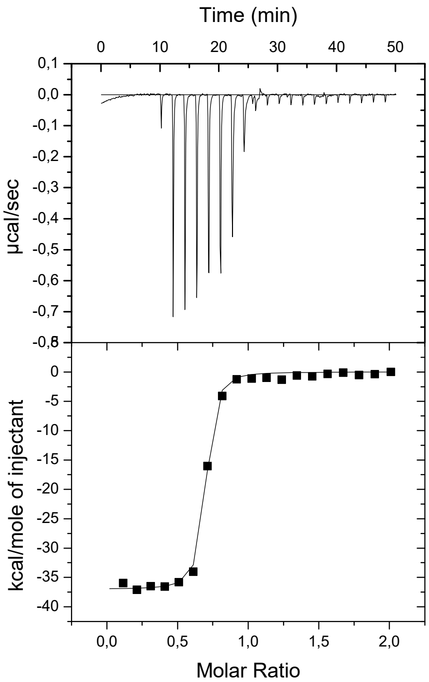
ITC binding profile of **28** ([WGA] = 4.7 μM, [**28**] = 47 μM)



ITC binding profile of **29** ([WGA] = 5 μM, [**29**] = 45 μM)

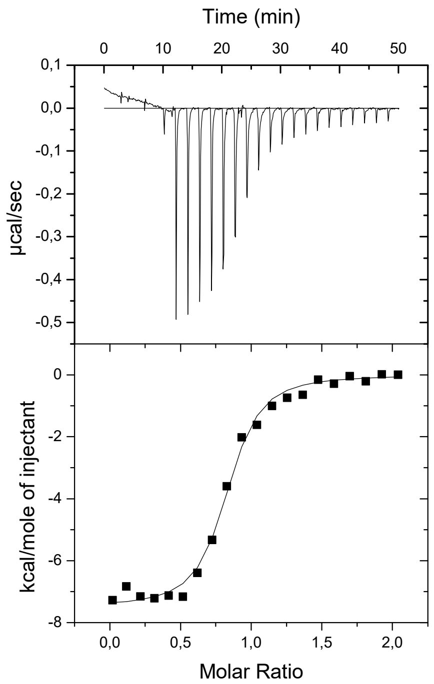


ITC binding profile of **43** ([WGA] = 11 μM, [**43**] = 108 μM)

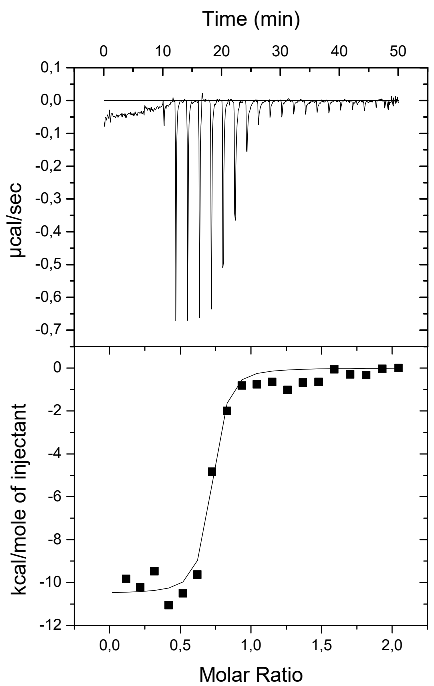


ITC binding profile of **44** ([WGA] = 11 μM, [**44**] = 107 μM)

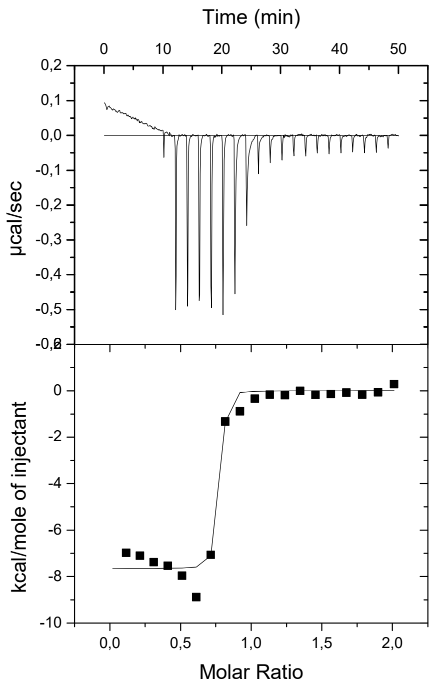
ITC Data of Competitive Experiments



ITC binding profile of **30** ([WGA] = 36 μM, [**30**] = 362 μM, [GlcNAc] = 10 mM)

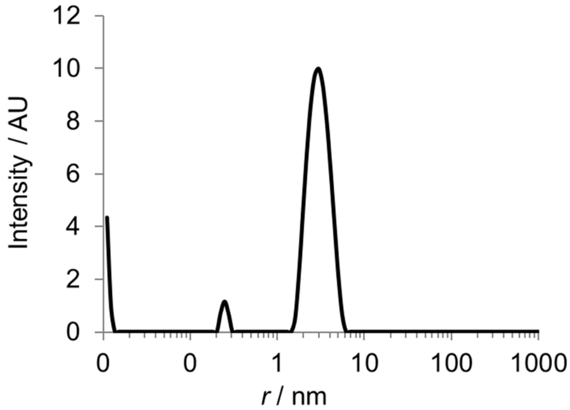


ITC binding profile of **23** ([WGA] = 36 μM, [**23**] = 363 μM, [GlcNAc] = 10 mM)

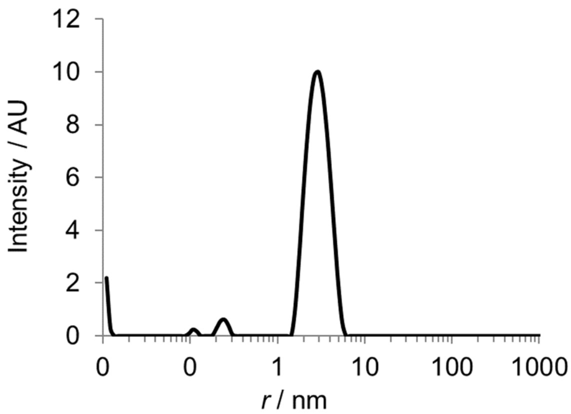


ITC binding profile of **29** ([WGA] = 36 μM, [**29**] = 357 μM, [GlcNAc] = 10 mM)

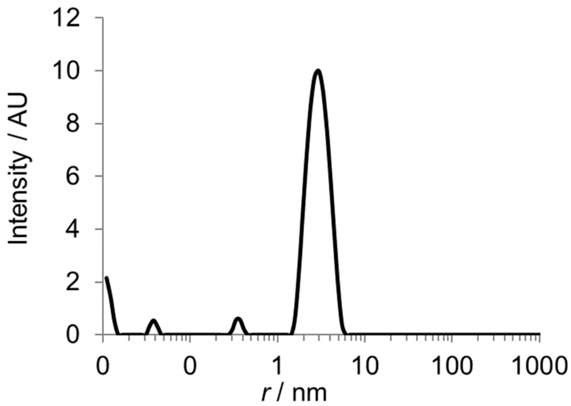
DLS Data of Ligands 1–5, 23–29, 43, 44



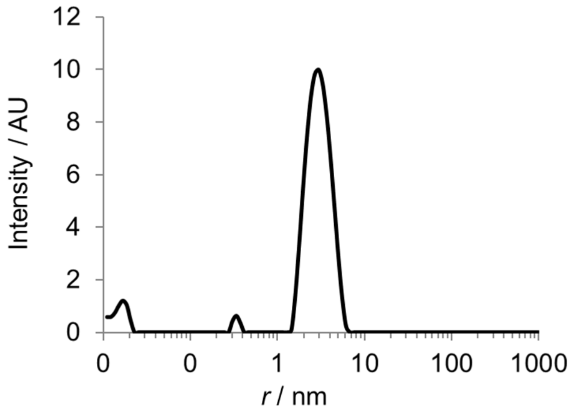
DLS profile of **1** incubated with WGA ([WGA] = 33 μM, [**1**] = 17 μM)



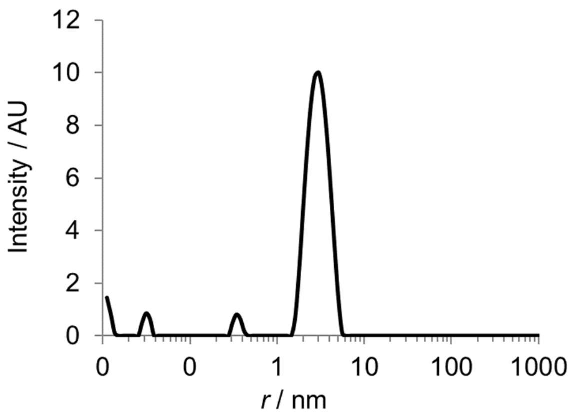
DLS profile of **2** incubated with WGA ([WGA] = 43 μM, [**2**] = 21 μM)



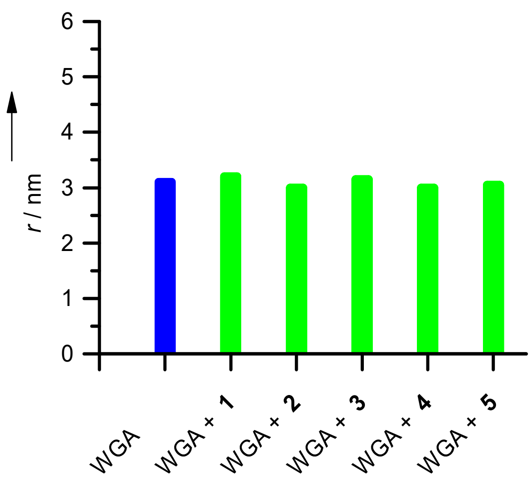
DLS profile of **3** incubated with WGA ([WGA] = 32 μM, [**3**] = 16 μM)



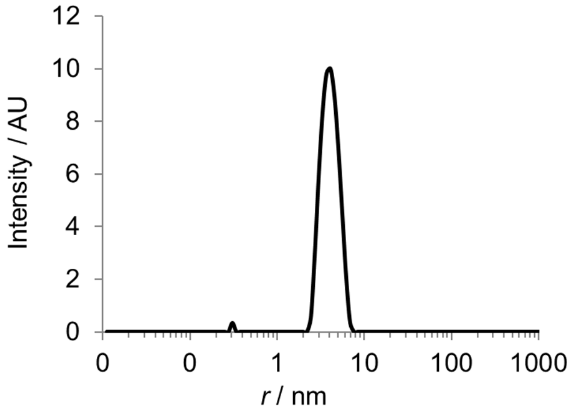
DLS profile of **4** incubated with WGA ([WGA] = 42 μM, [**4**] = 21 μM)



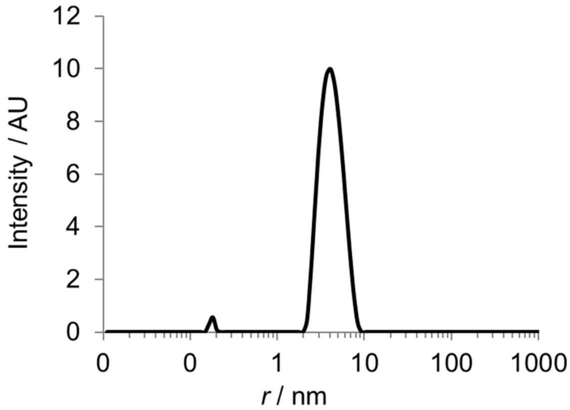
DLS profile of **5** incubated with WGA ([WGA] = 42 μM, [**5**] = 21 μM)



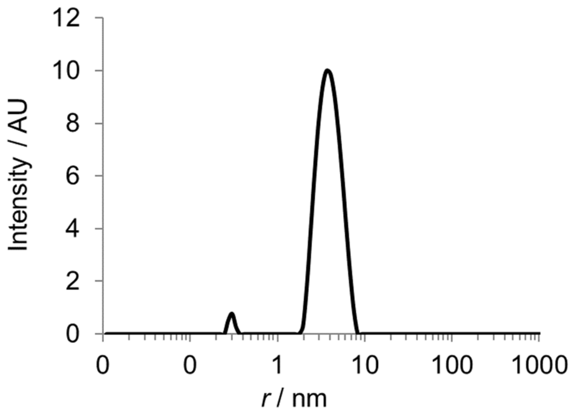
Hydrodynamic radii of WGA (blue) and WGA incubated with compounds **1–5** (green)



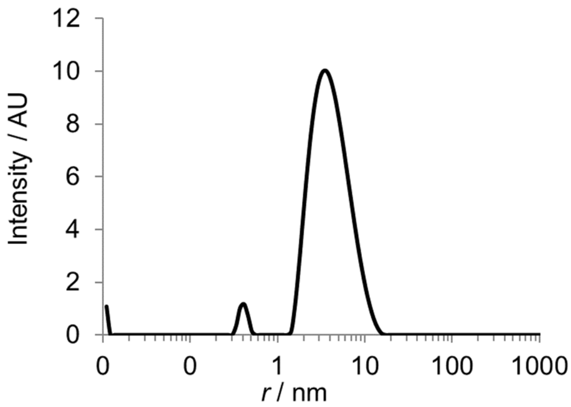
DLS profile of **23** incubated with WGA ([WGA] = 30 μM, [**23**] = 30 μM)



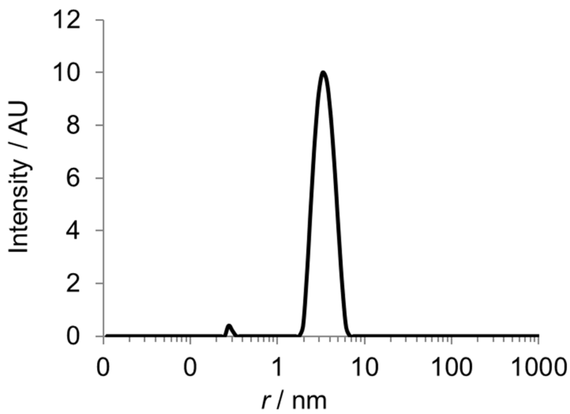
DLS profile of **24** incubated with WGA ([WGA] = 30 μM, [**24**] = 30 μM)



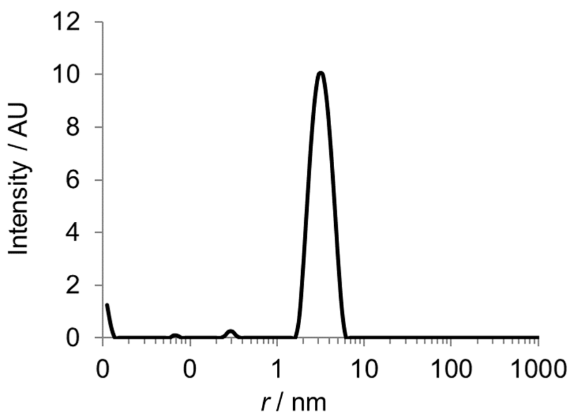
DLS profile of **25** incubated with WGA ([WGA] = 30 μM, [**25**] = 30 μM)



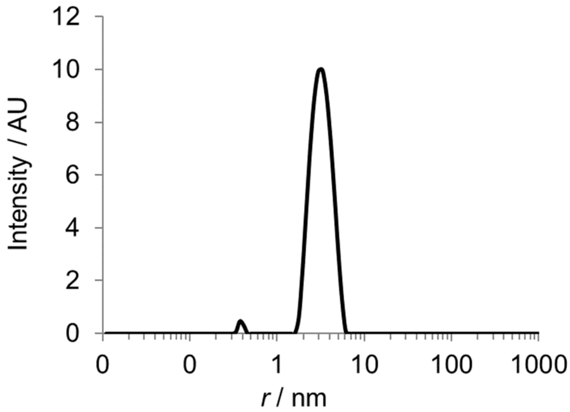
DLS profile of **26** incubated with WGA ([WGA] = 30 μM, [**26**] = 30 μM)



DLS profile of **27** incubated with WGA ([WGA] = 40 μM, [**27**] = 40 μM)

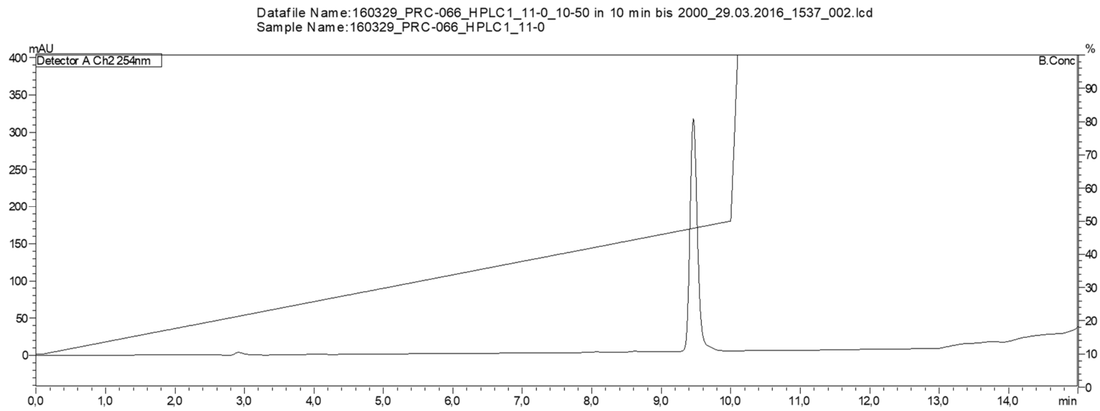


DLS profile of **28** incubated with WGA ([WGA] = 40 μM, [**28**] = 40 μM)

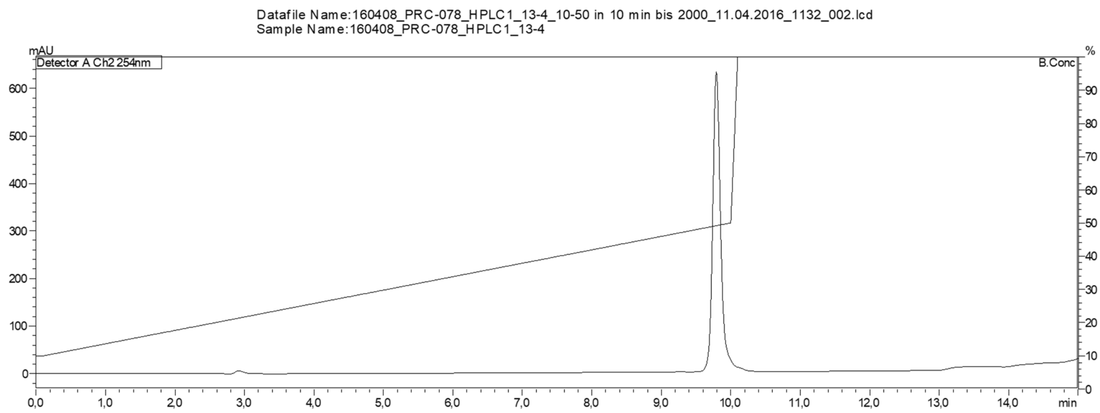


DLS profile of **29** incubated with WGA ([WGA] = 40 μM, [**29**] = 40 μM)

HPLC Profiles of Spin-Labeled iLecs 43 and 44

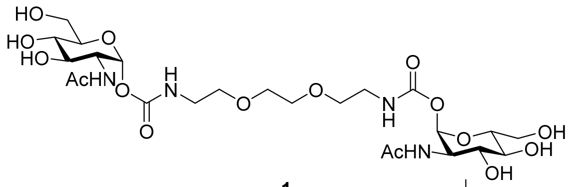


HPLC profile of **43** (10-50% MeCN in H_2O + 0.1% formic acid in 10 min, Macherey Nagel Nucleodur 100-3 C18ec column)

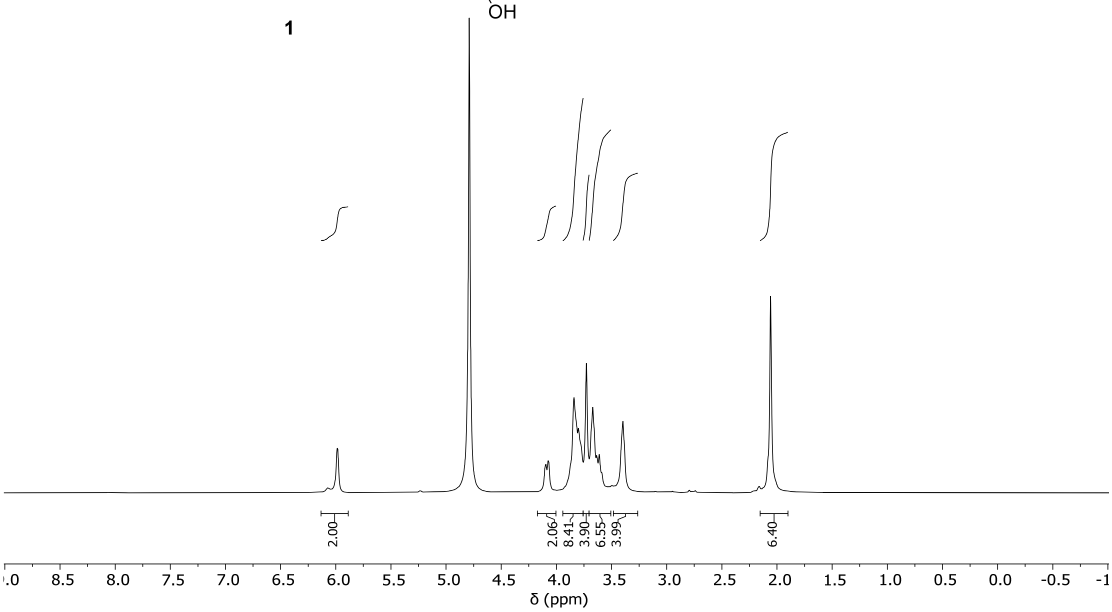


HPLC profile of **44** (10-50% MeCN in H_2O + 0.1% formic acid in 10 min, Macherey Nagel Nucleodur 100-3 C18ec column)

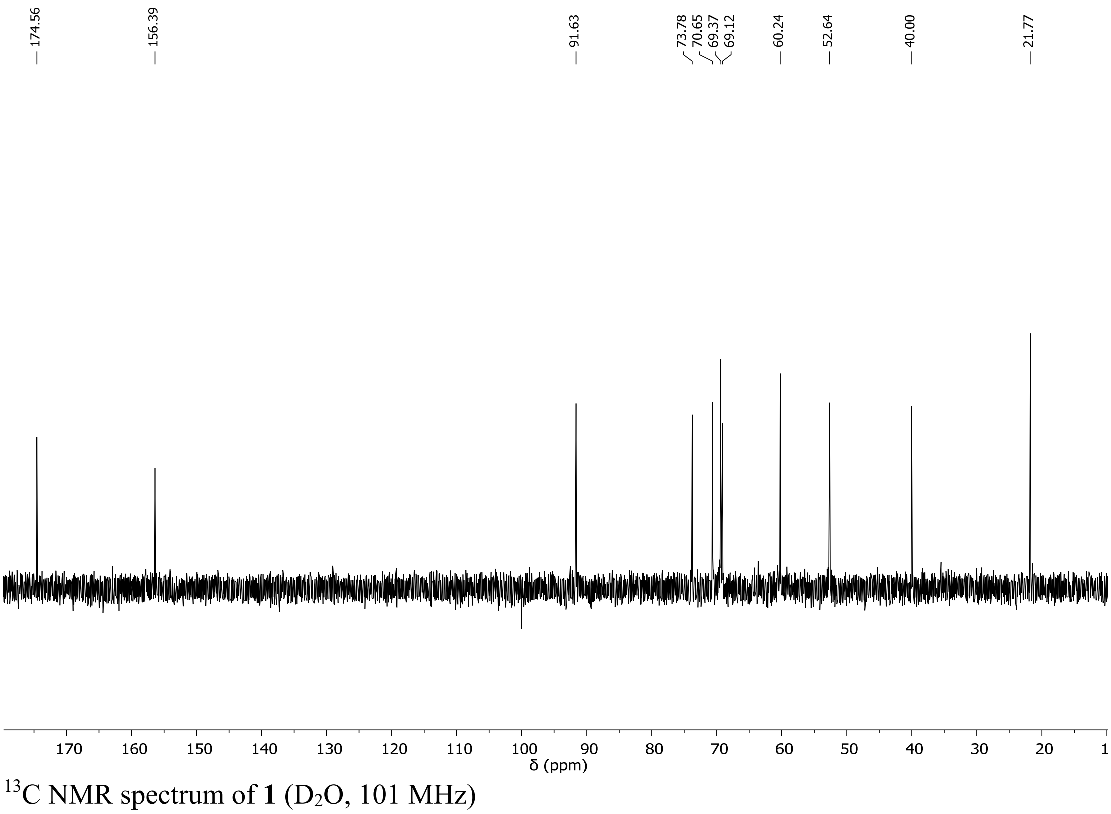
NMR Spectra



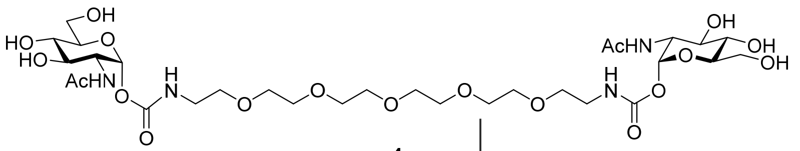
1



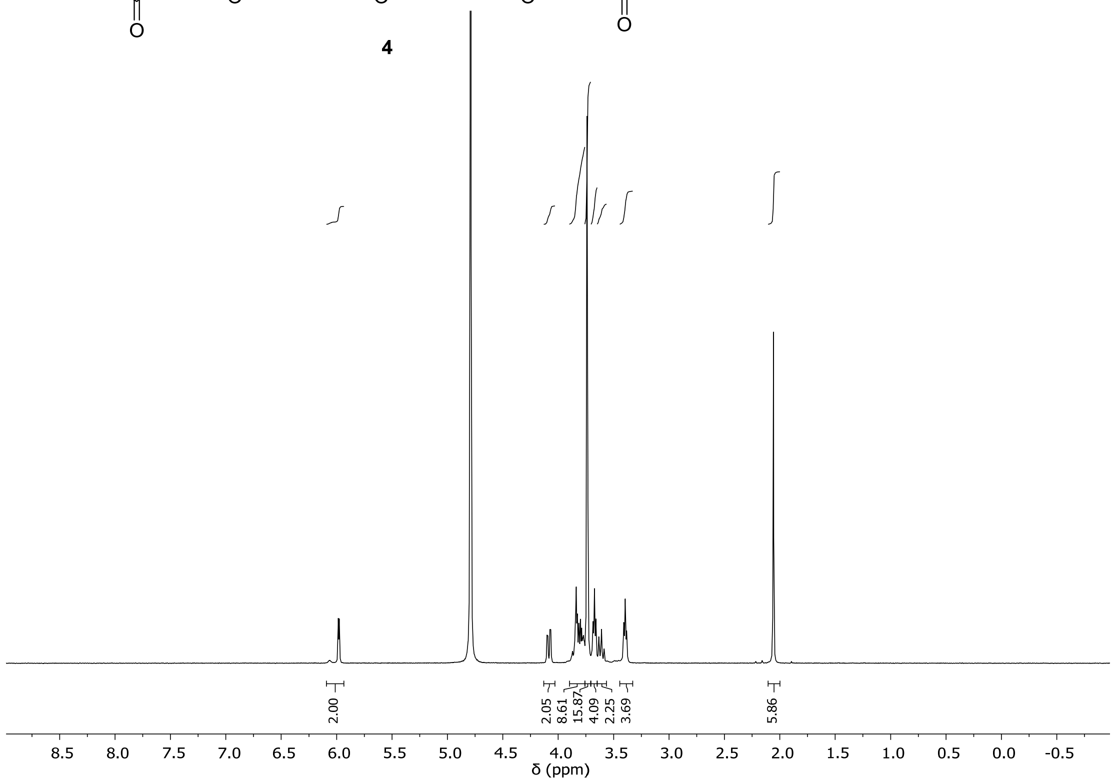
[1]H NMR spectrum of **1** (D_2O, 400 MHz)



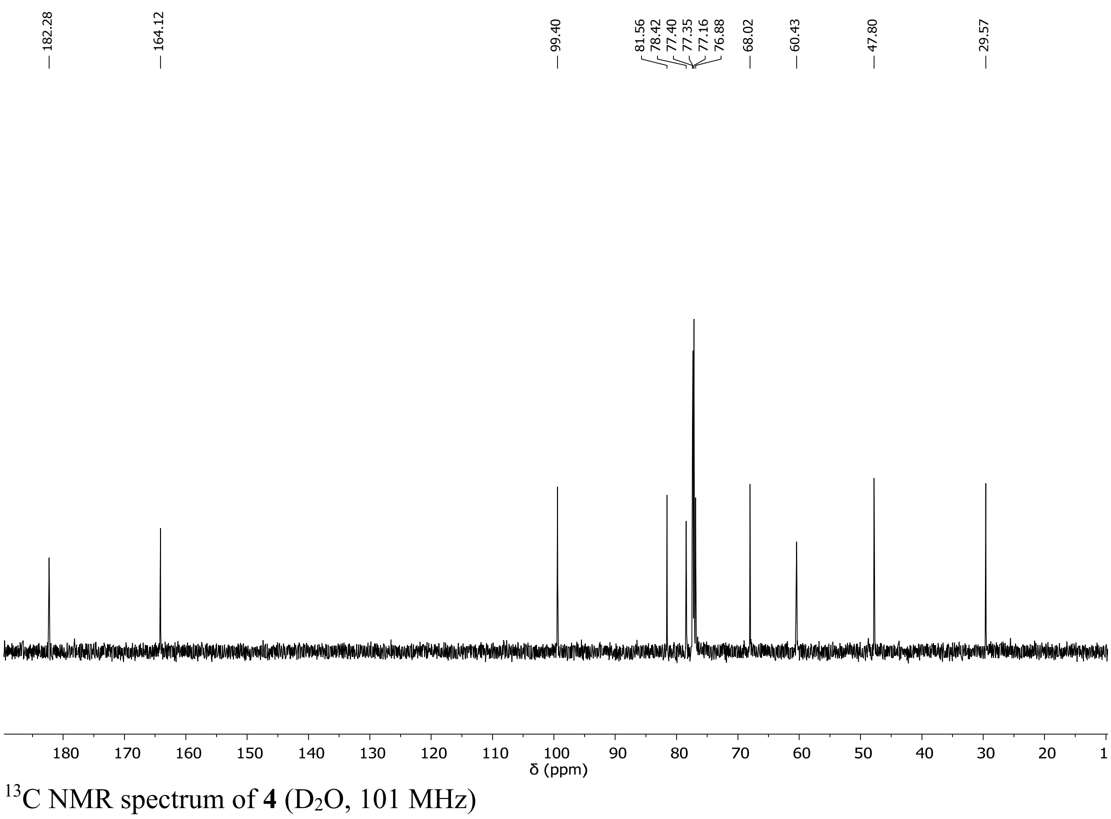
[13]C NMR spectrum of **1** (D_2O, 101 MHz)



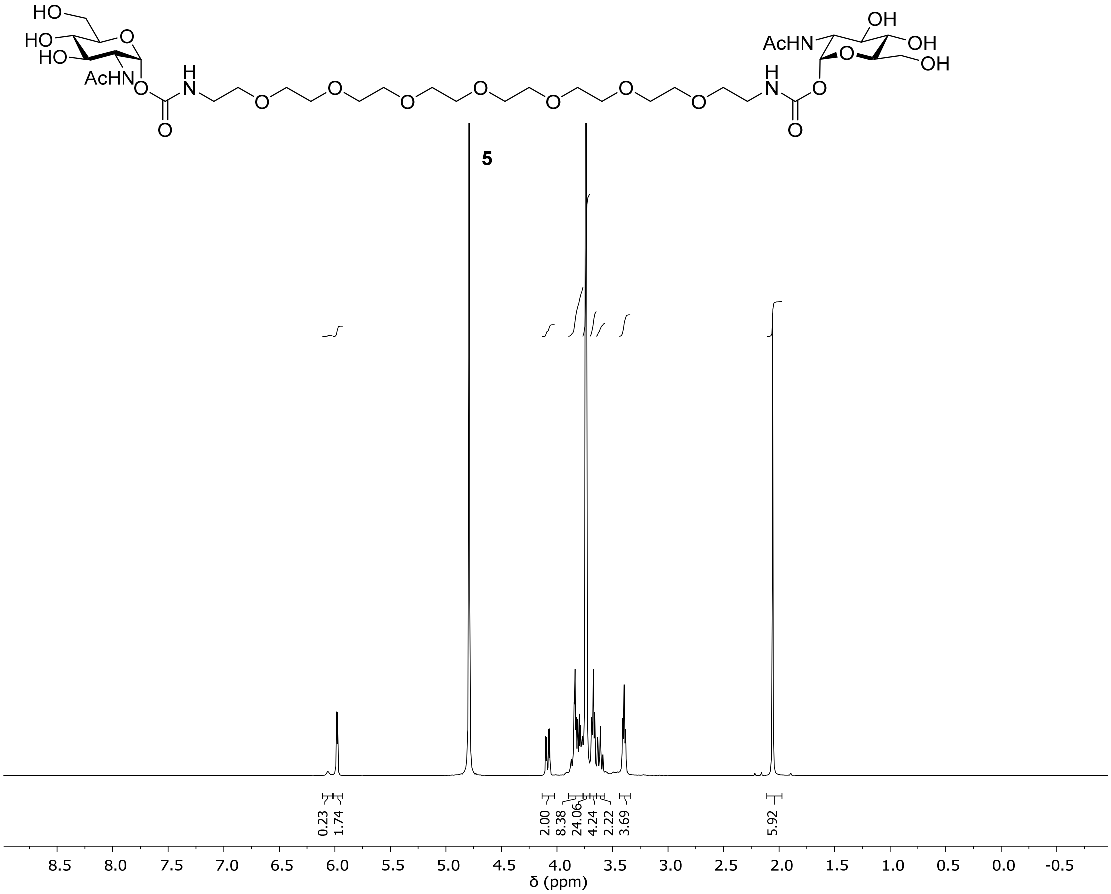
4



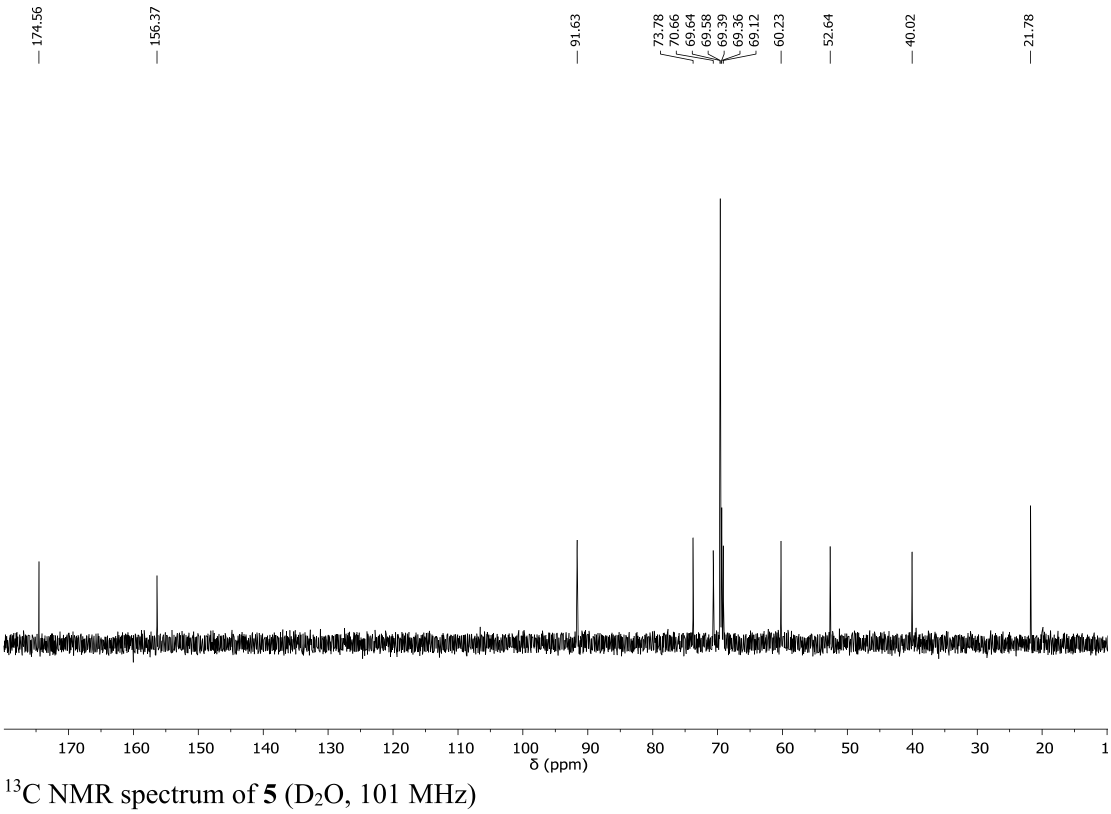
^{1}H NMR spectrum of **4** (D_2O, 400 MHz)



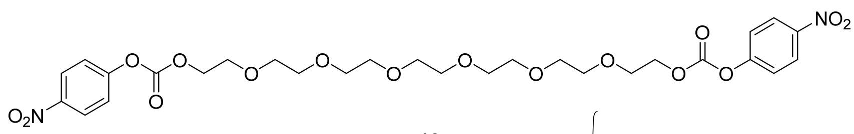
^{13}C NMR spectrum of **4** (D_2O, 101 MHz)



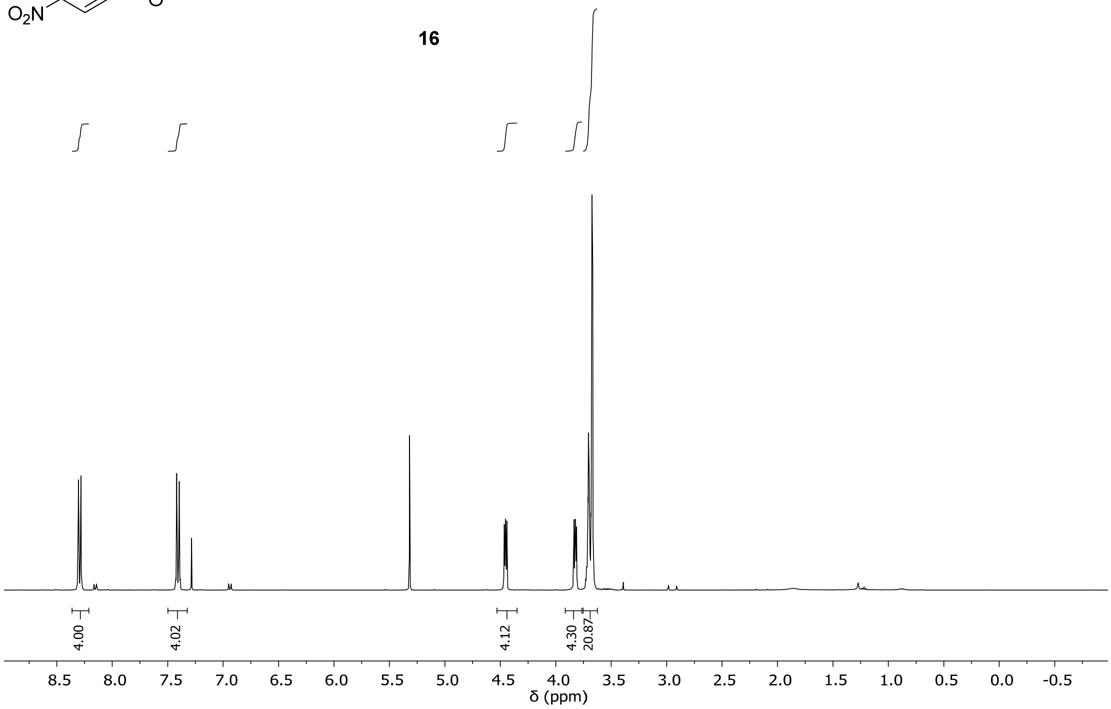
[1]H NMR spectrum of **5** (D_2O, 400 MHz)



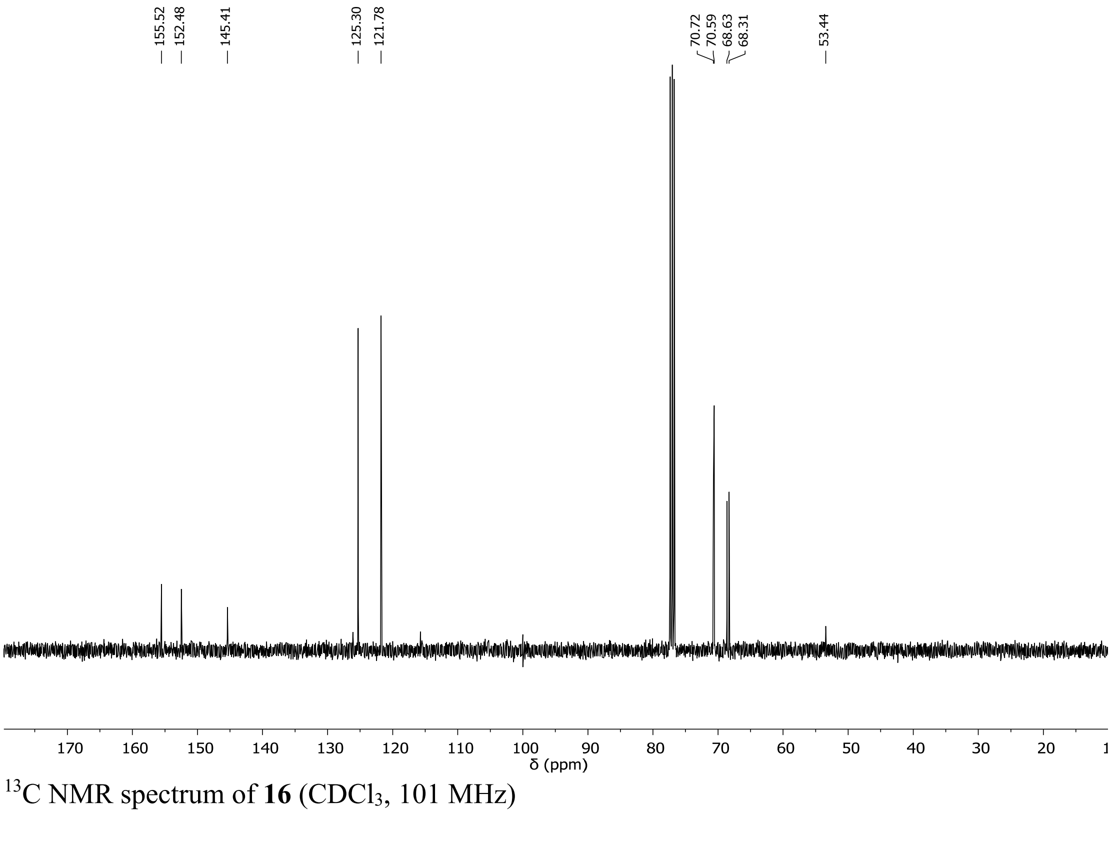
[13]C NMR spectrum of **5** (D_2O, 101 MHz)



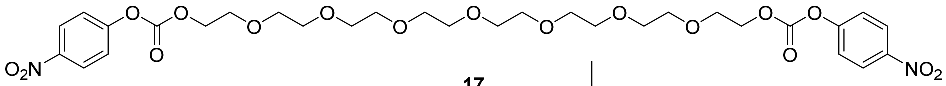
16



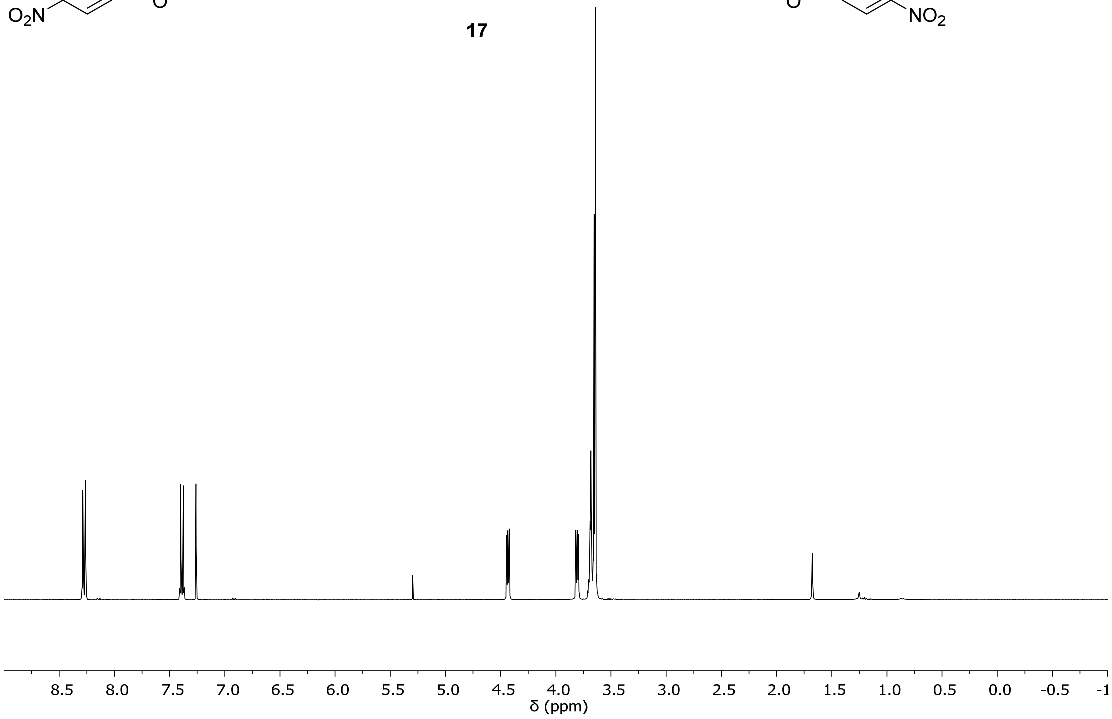
[1]H NMR spectrum of **16** ($CDCl_3$, 400 MHz)



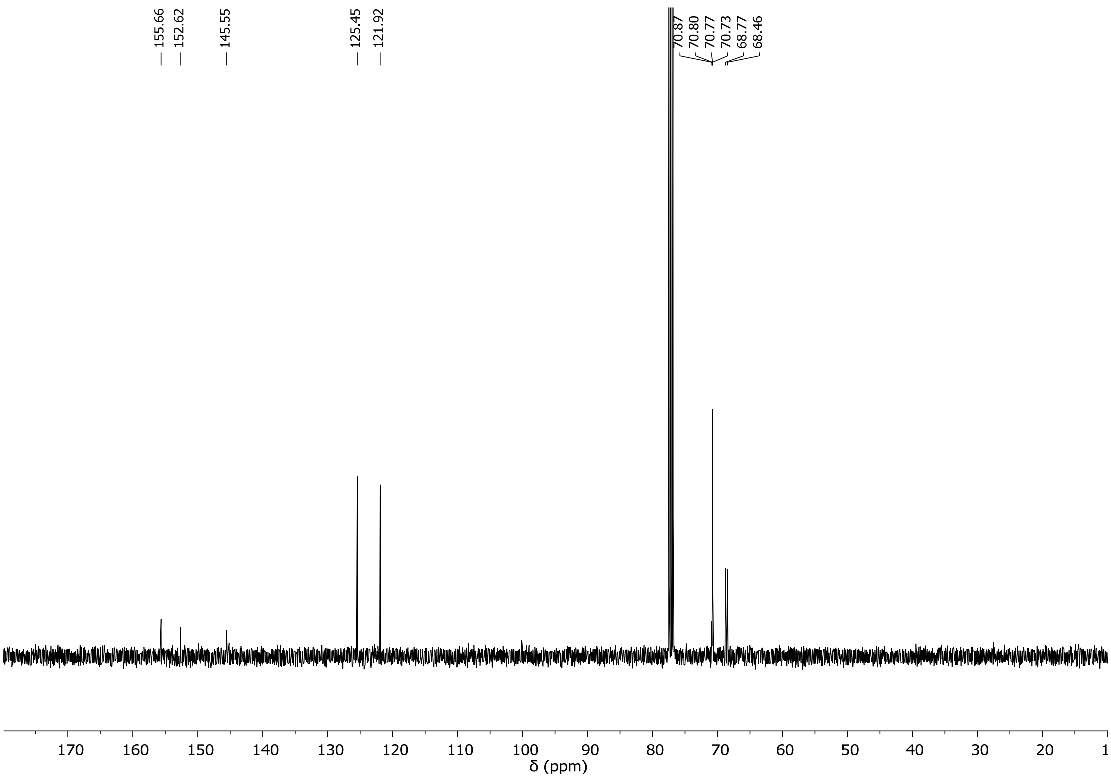
[13]C NMR spectrum of **16** ($CDCl_3$, 101 MHz)



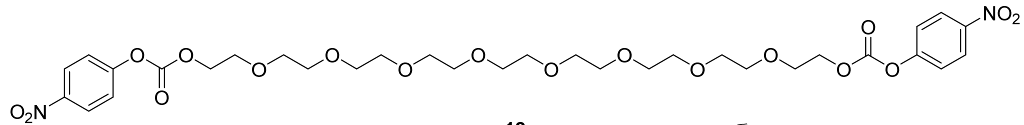
17



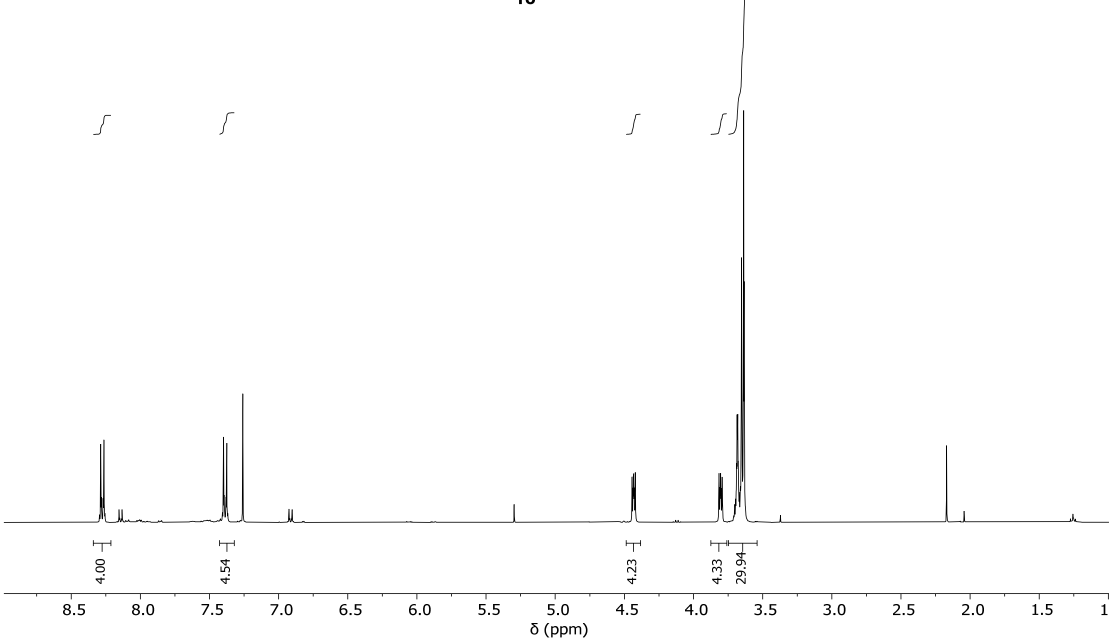
^{1}H NMR spectrum of **17** ($CDCl_3$, 400 MHz)



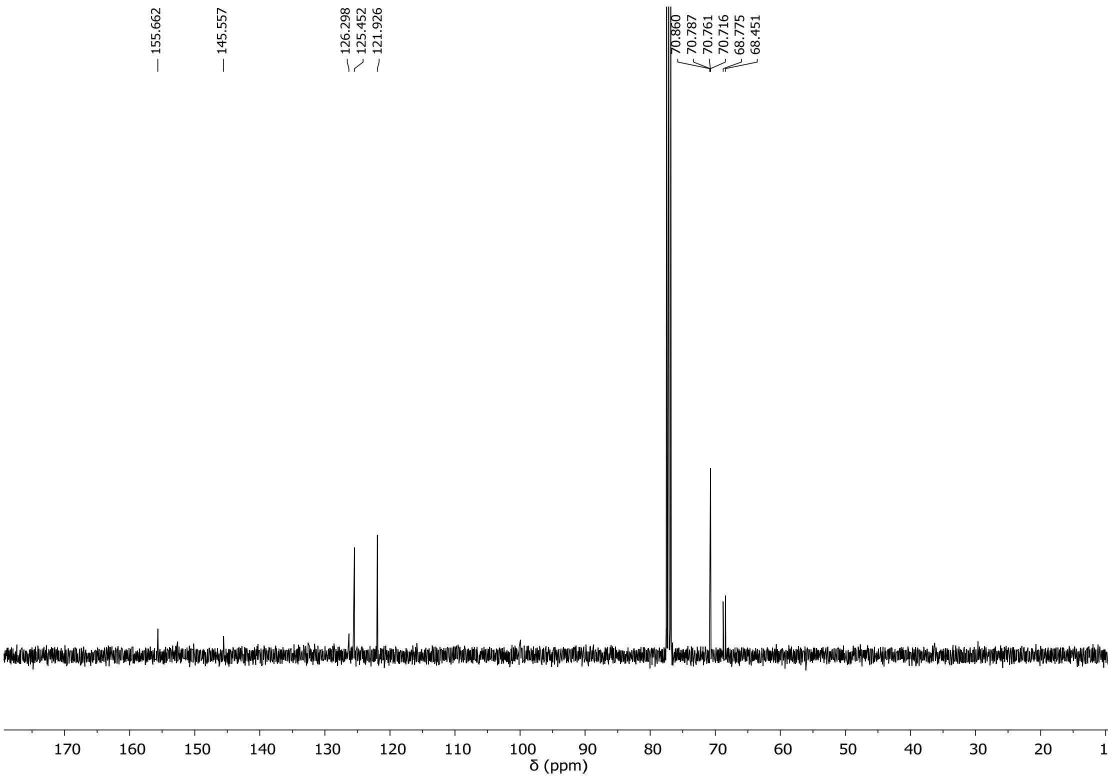
^{13}C NMR spectrum of **17** ($CDCl_3$, 101 MHz)



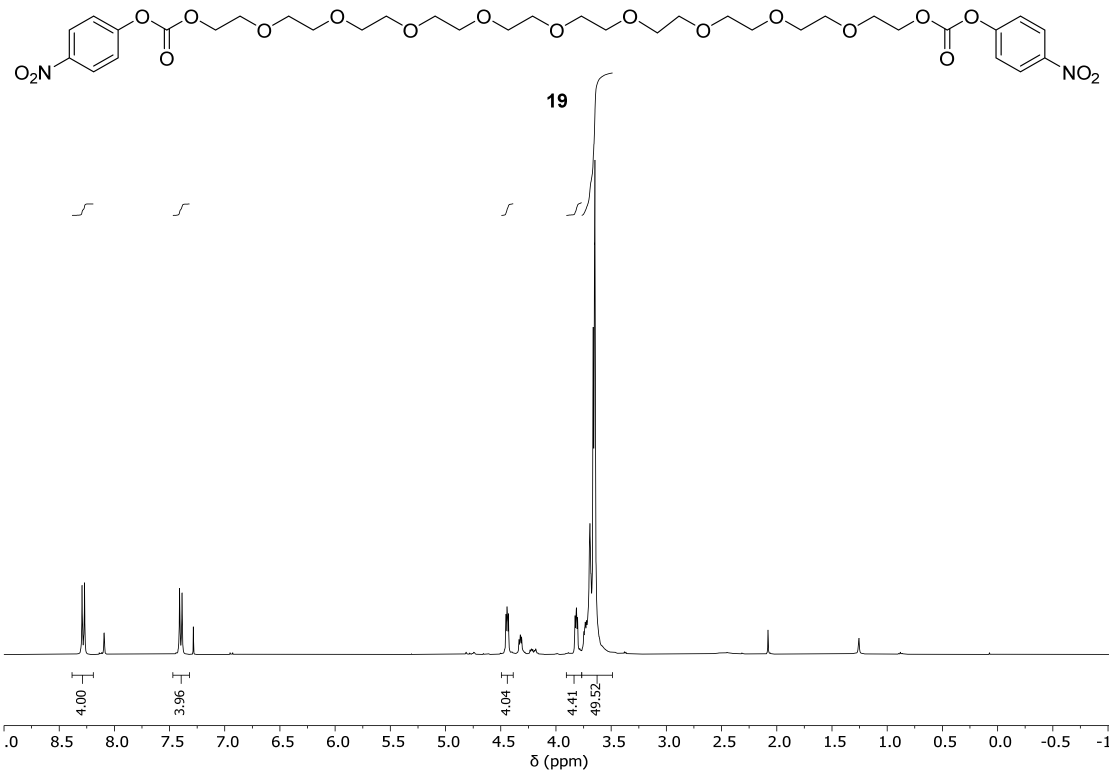
18



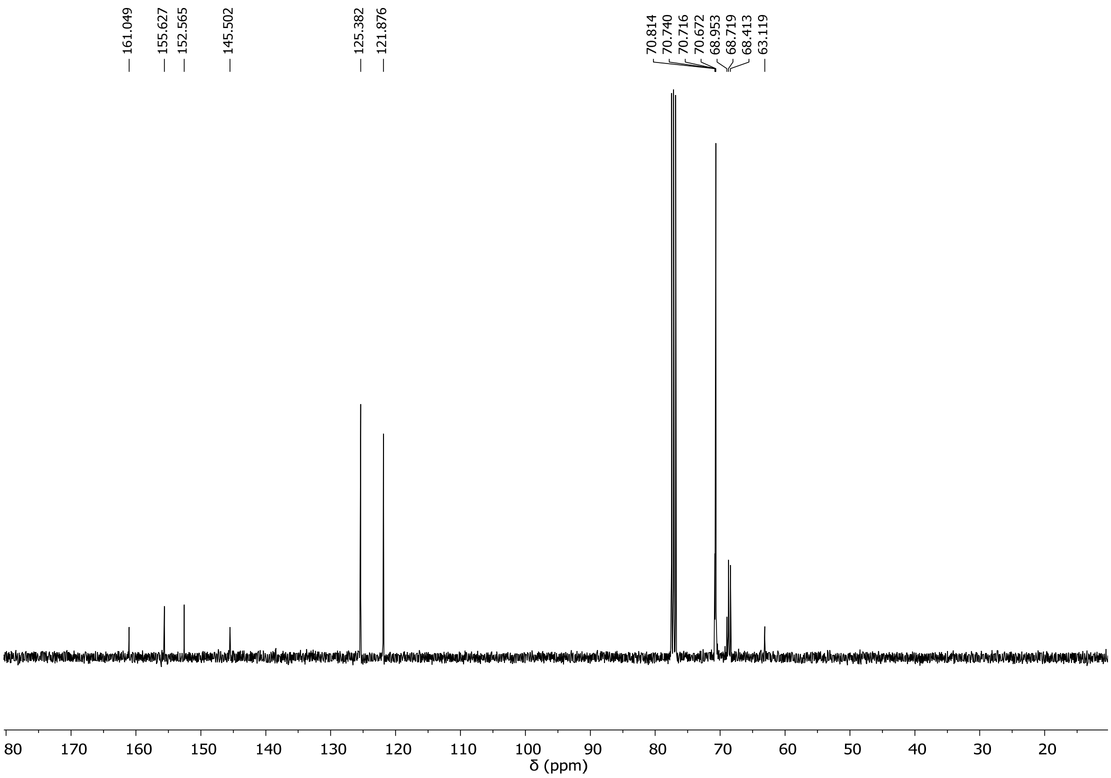
^{1}H NMR spectrum of **18** ($CDCl_3$, 400 MHz)



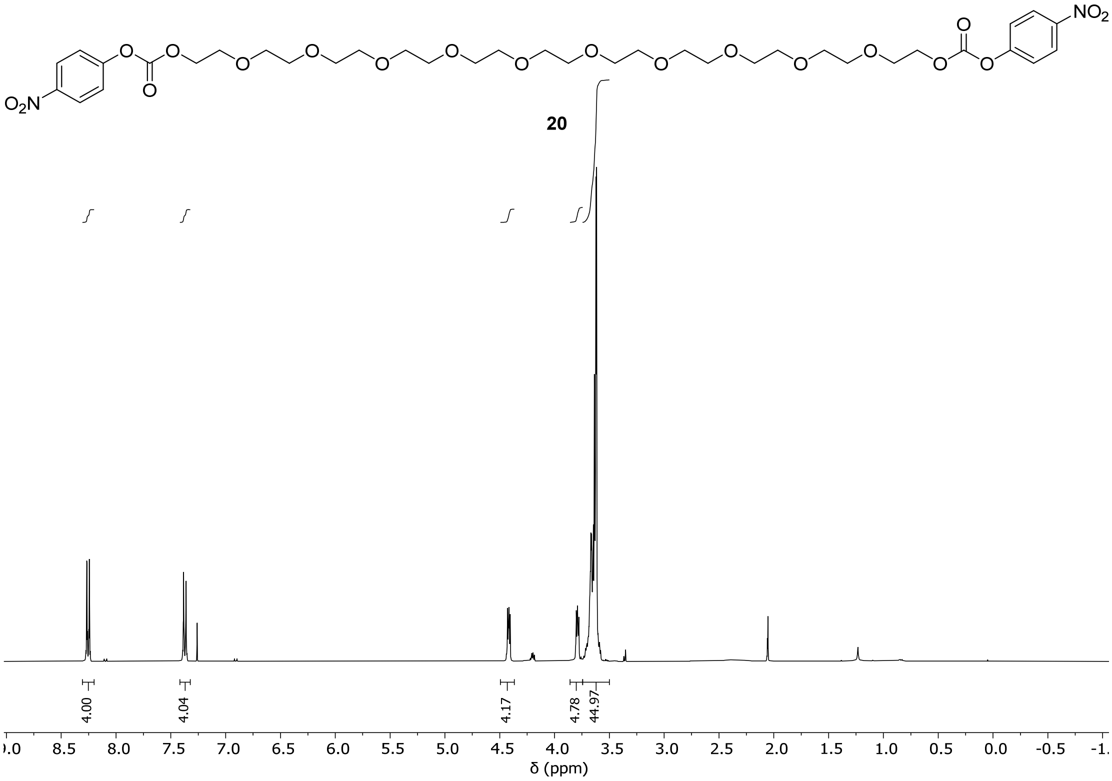
^{13}C NMR spectrum of **18** ($CDCl_3$, 101 MHz)



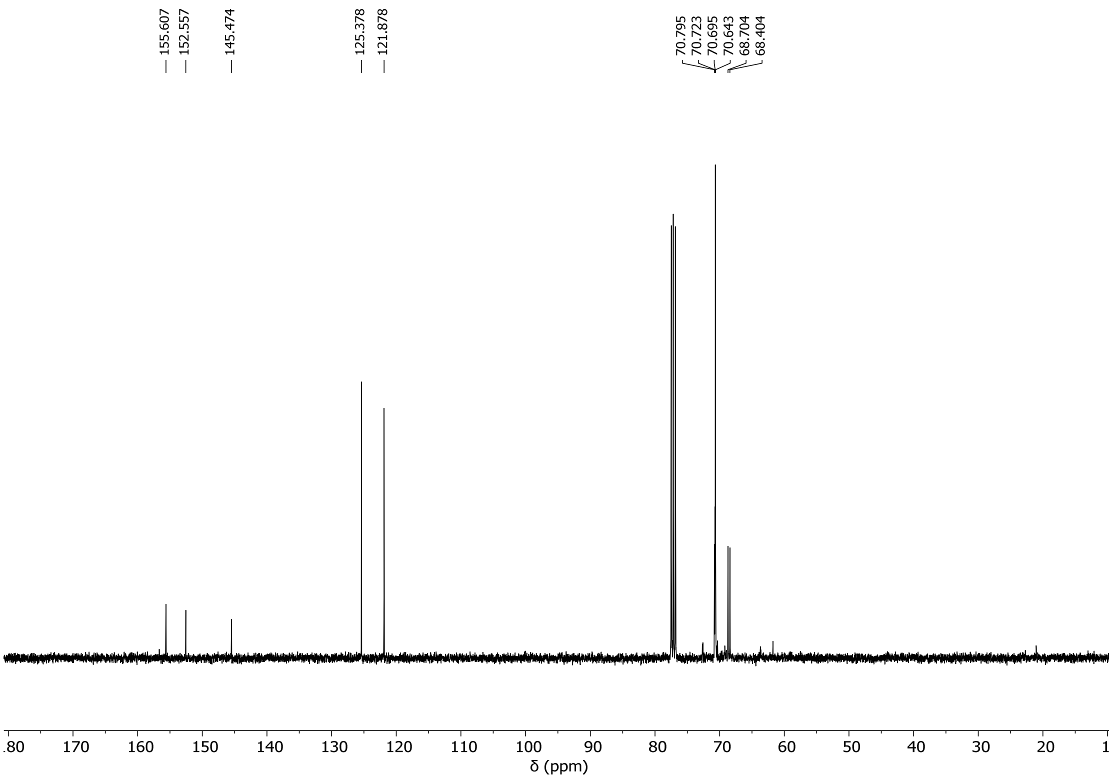
[1]H NMR spectrum of **19** ($CDCl_3$, 400 MHz)



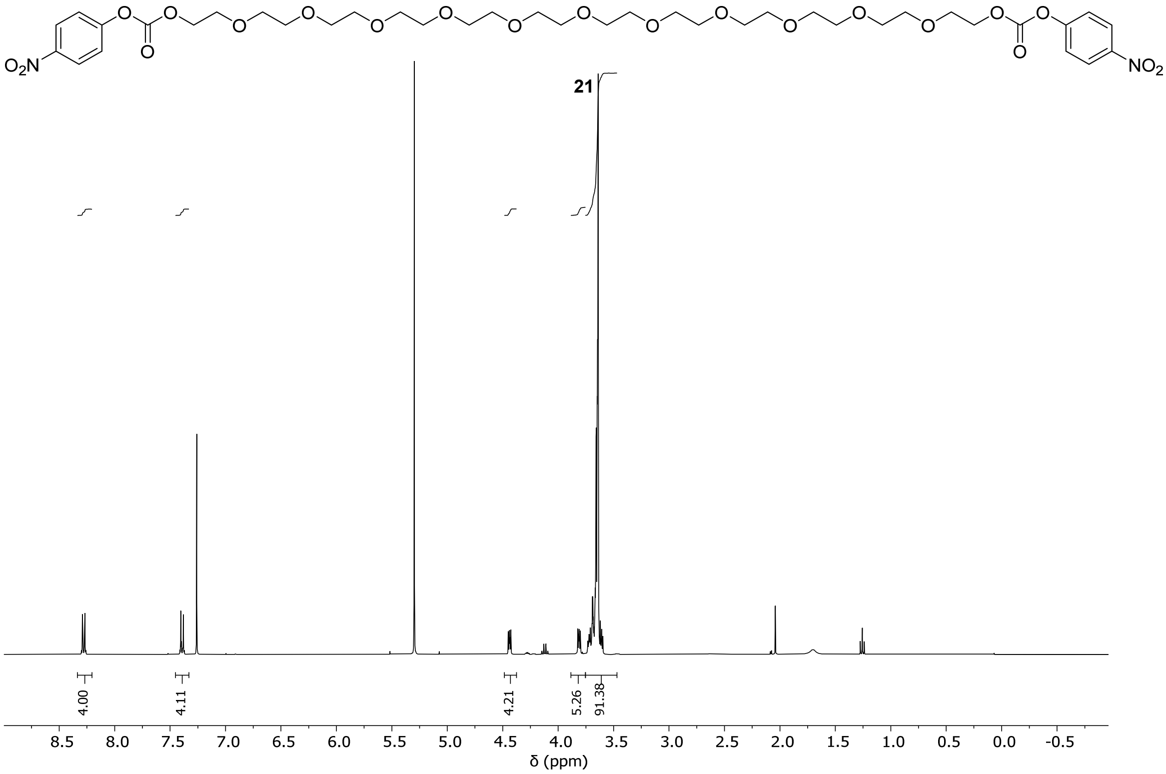
[13]C NMR spectrum of **19** ($CDCl_3$, 101 MHz)



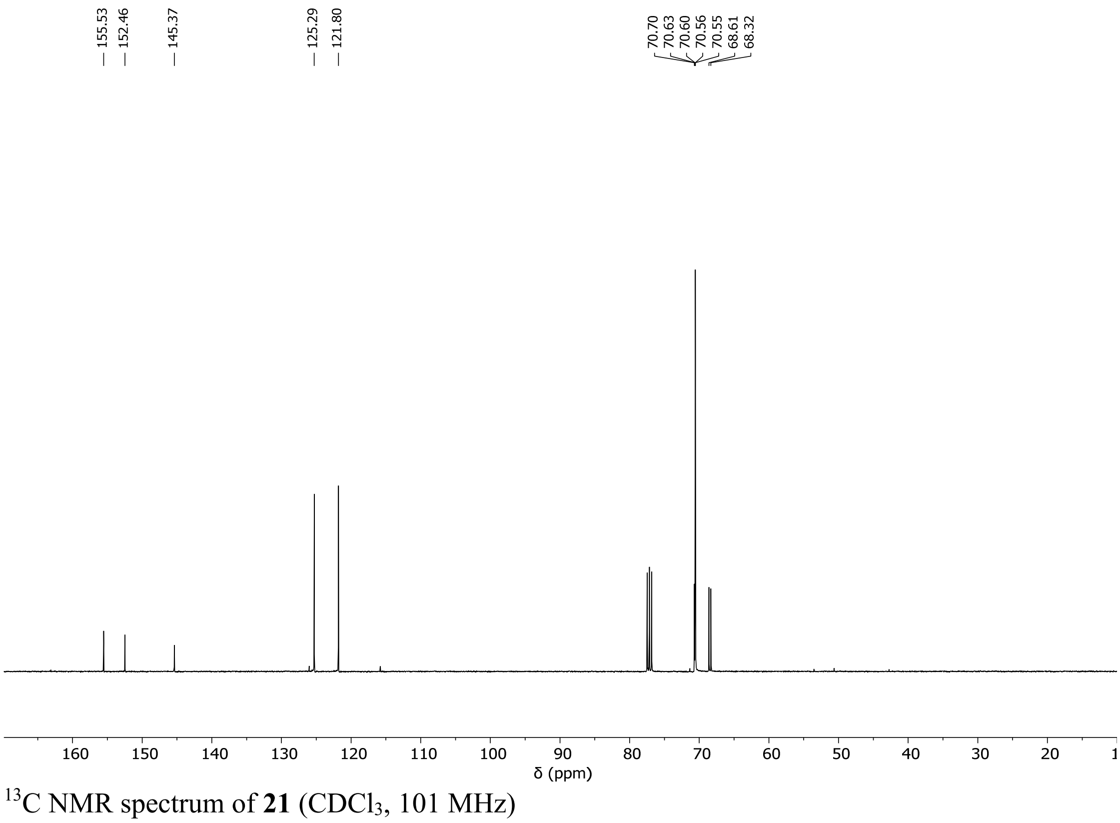
^{1}H NMR spectrum of **20** ($CDCl_3$, 400 MHz)



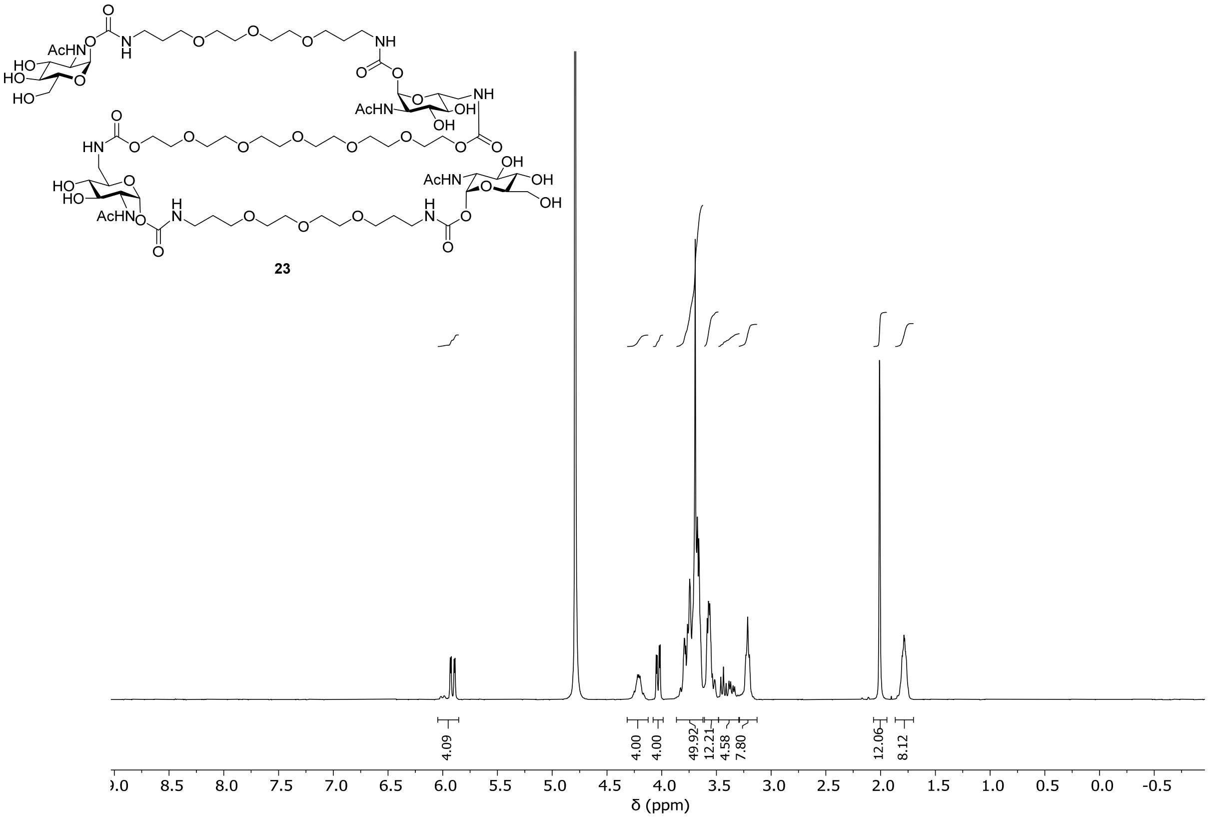
^{13}C NMR spectrum of **20** ($CDCl_3$, 101 MHz)



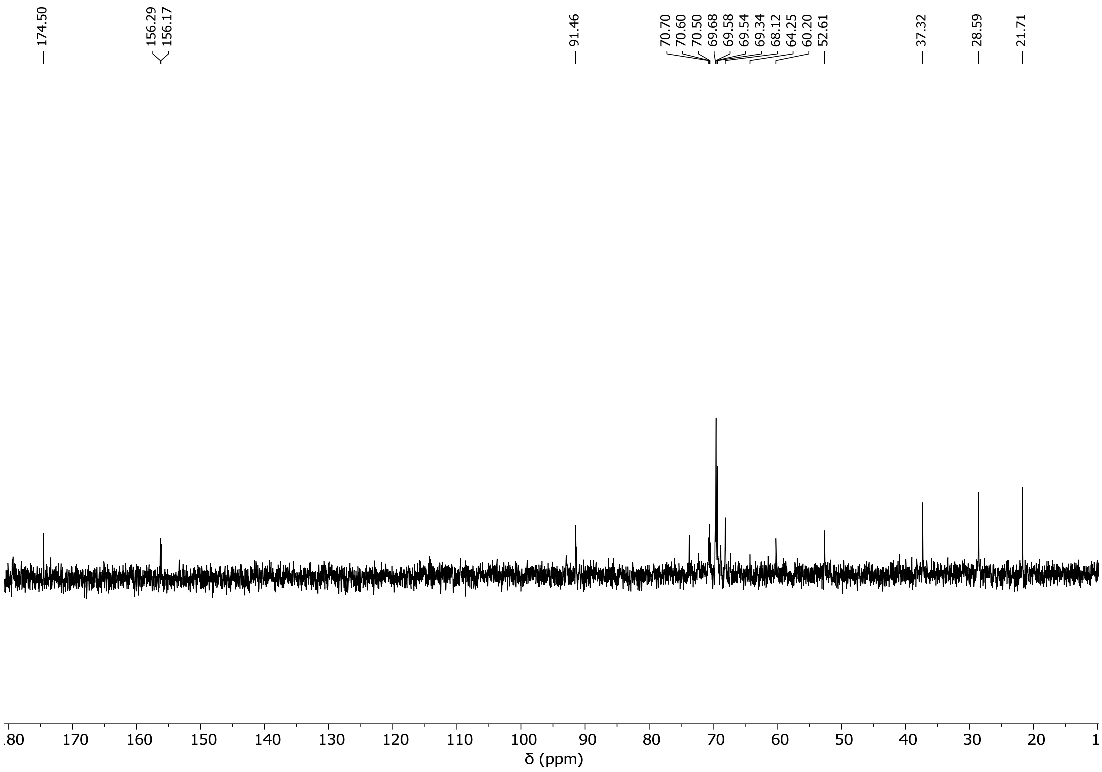
[1]H NMR spectrum of **21** ($CDCl_3$, 400 MHz)



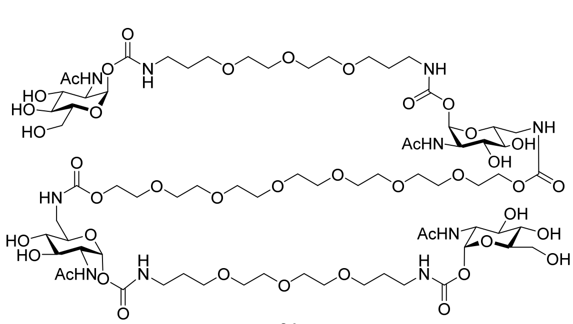
[13]C NMR spectrum of **21** ($CDCl_3$, 101 MHz)



[1]H NMR spectrum of **23** (D_2O, 400 MHz)



[13]C NMR spectrum of **23** (D_2O, 101 MHz)



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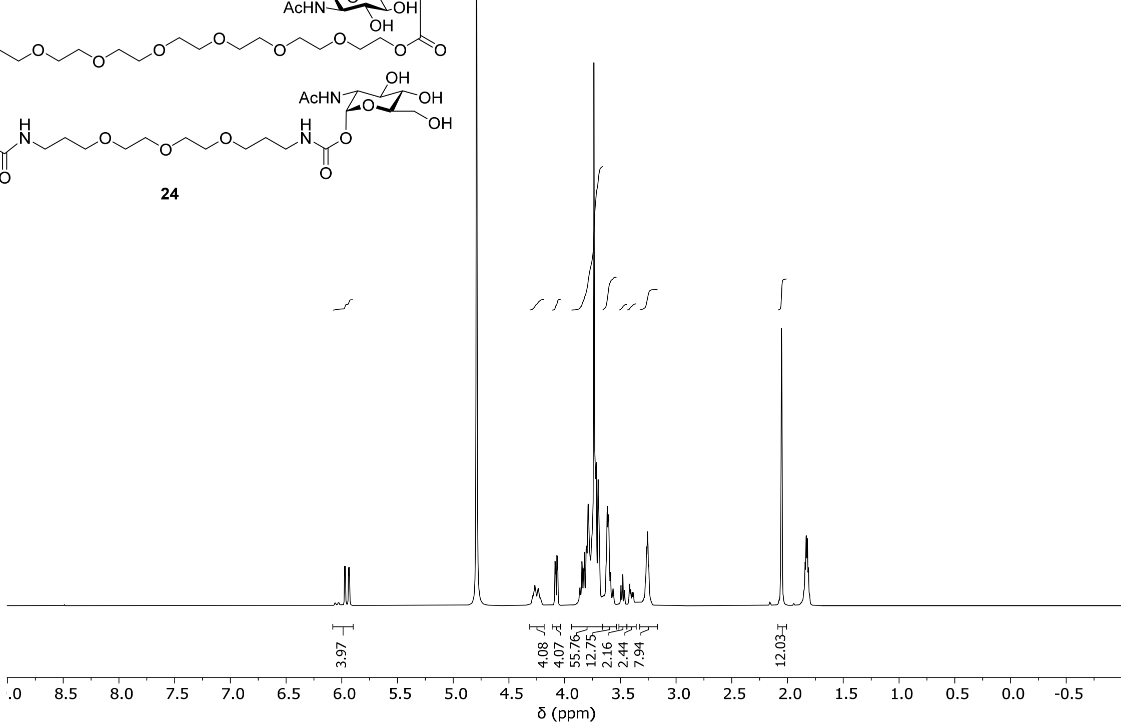
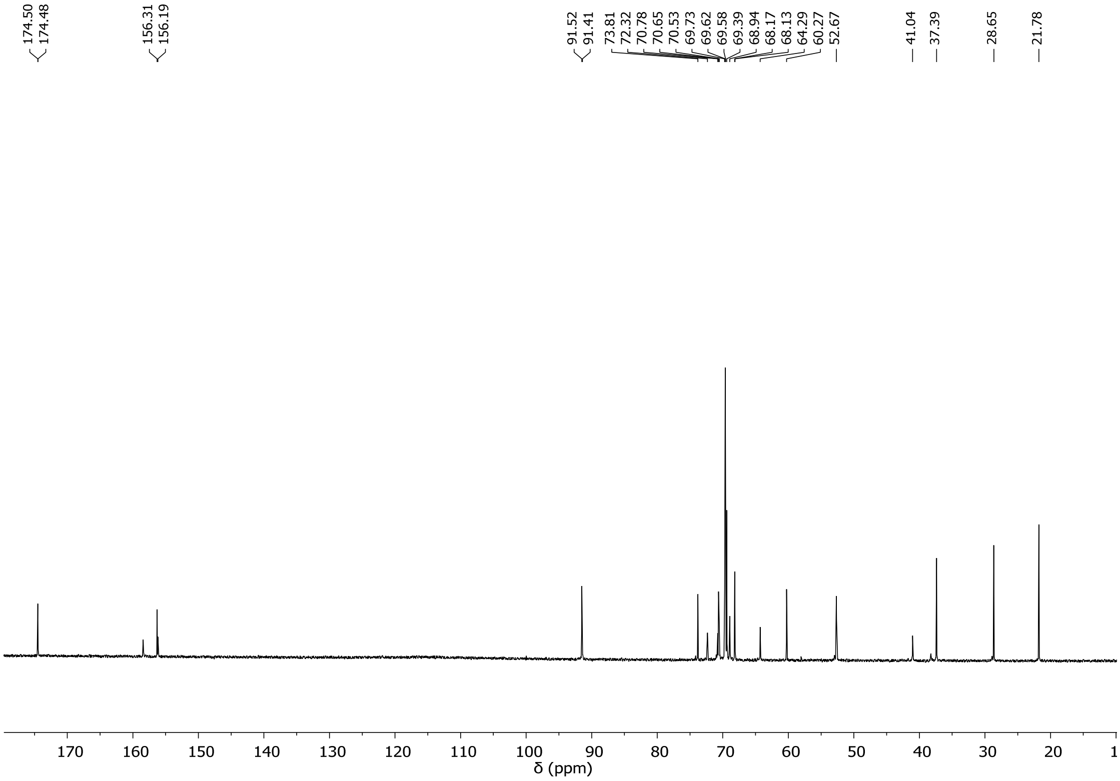
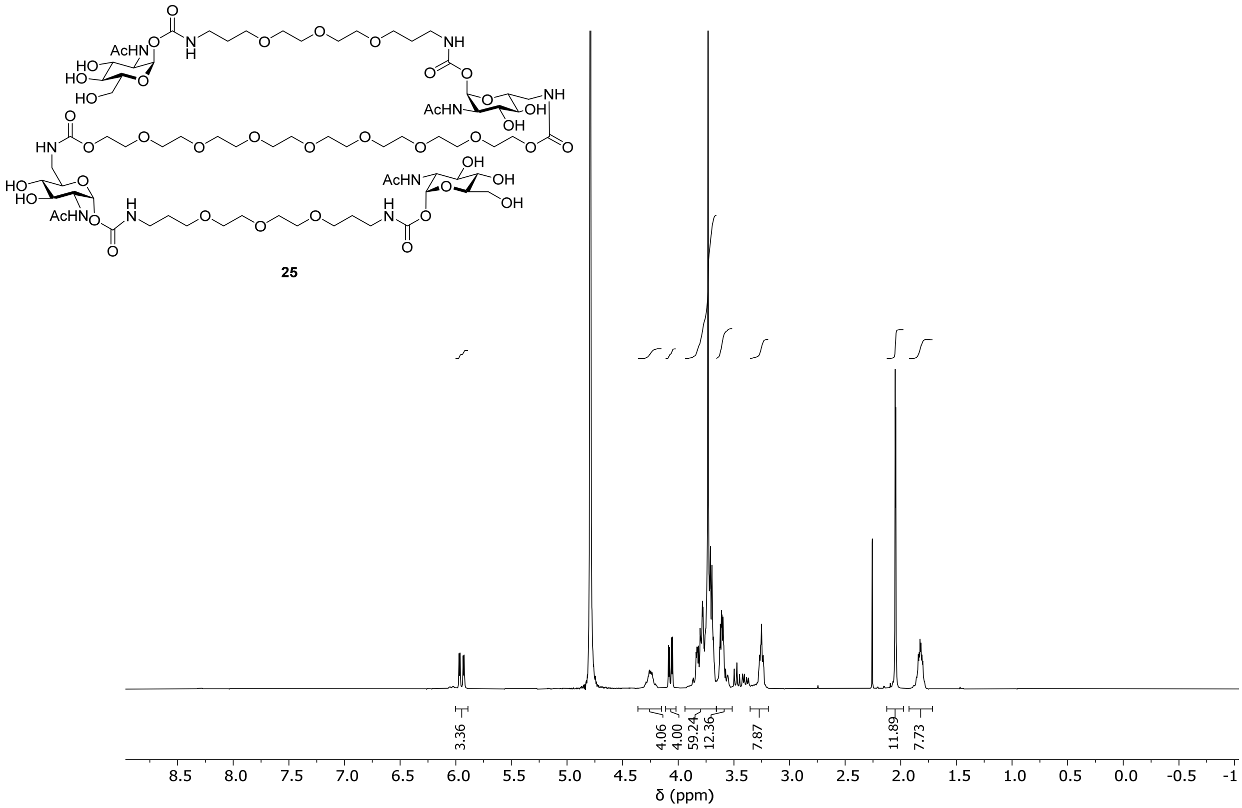


^{1}H NMR spectrum of **24** (D_2O, 400 MHz)



^{13}C NMR spectrum of **24** (D_2O, 101 MHz)



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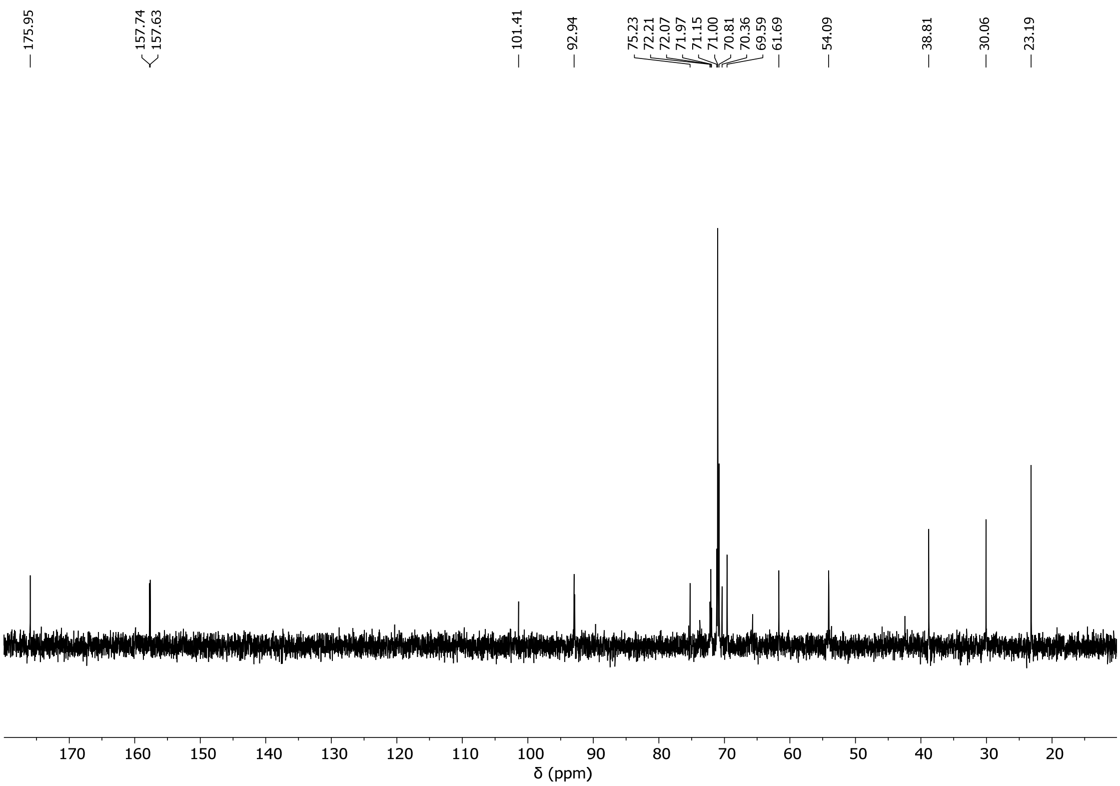
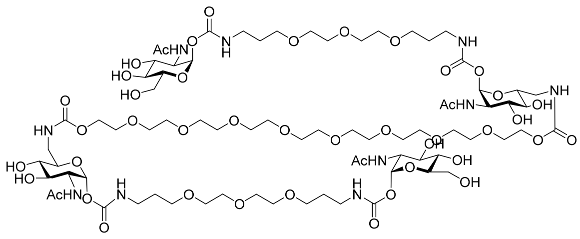
^{1}H NMR spectrum of **25** (D_2O, 400 MHz)



^{13}C NMR spectrum of **25** (D_2O, 101 MHz)



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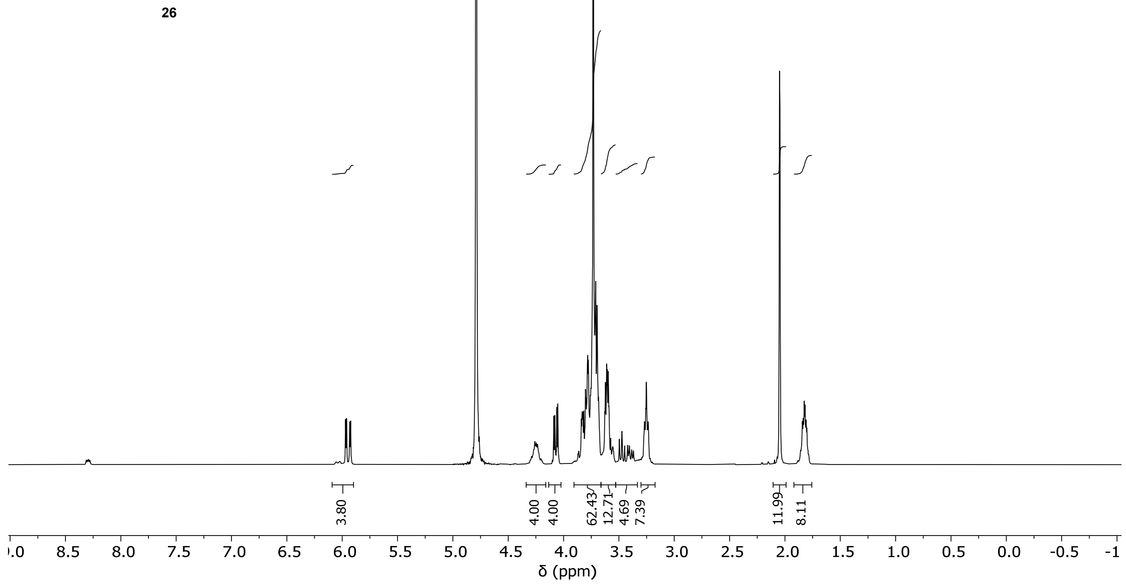
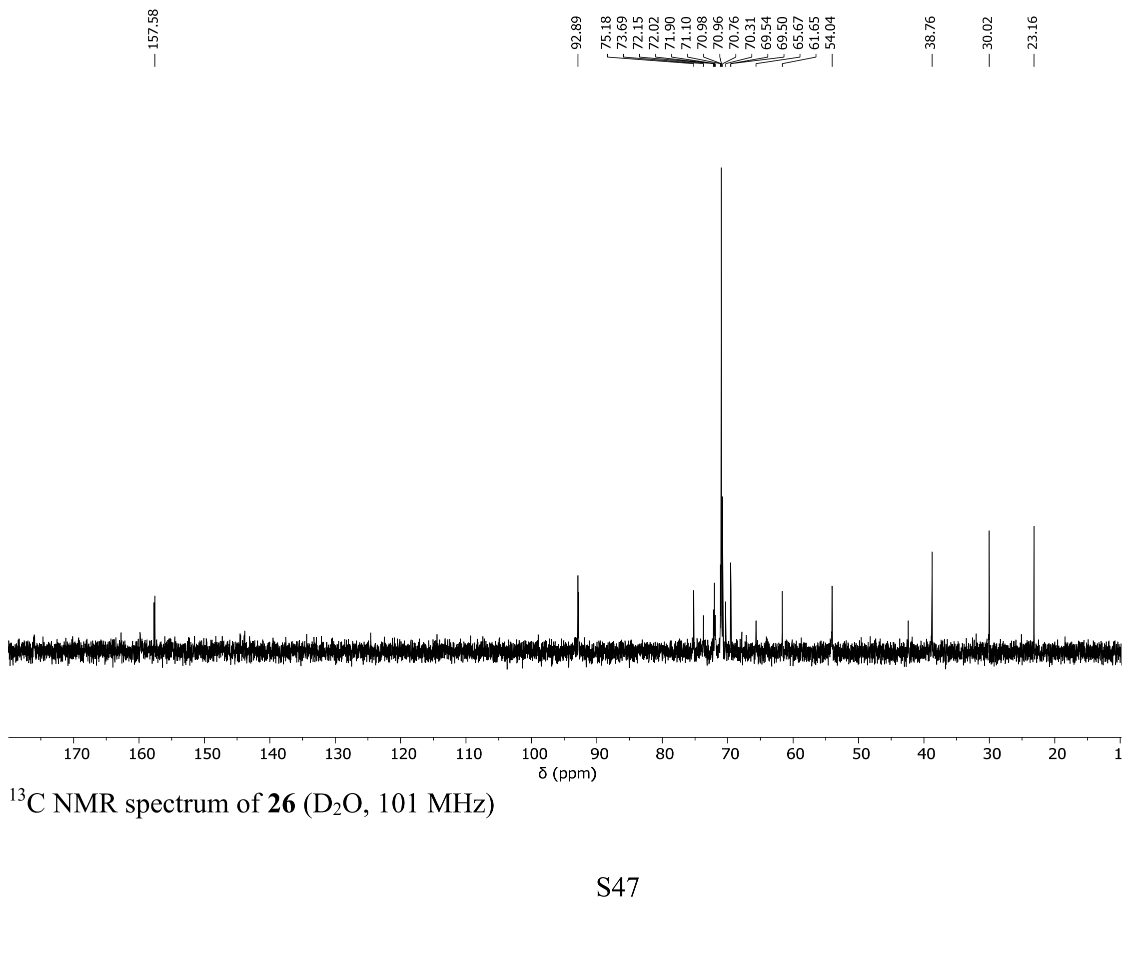
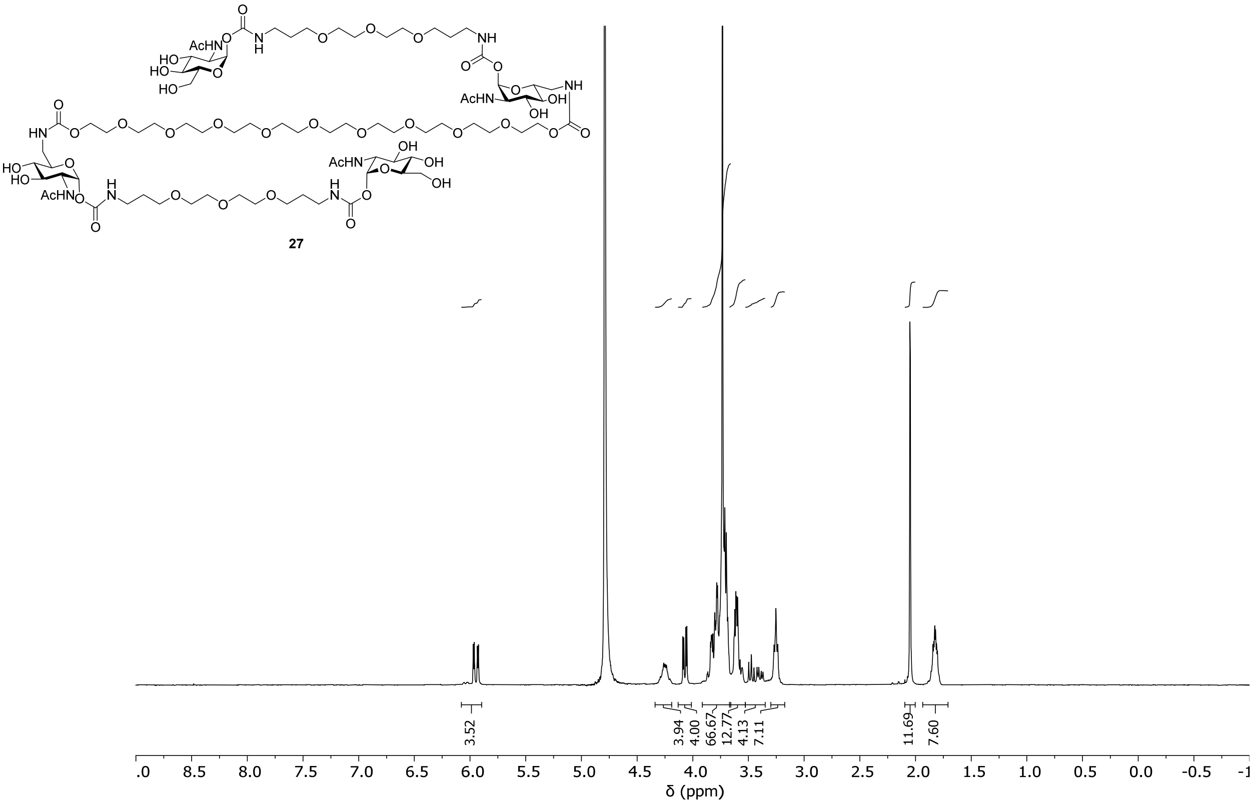


[1]H NMR spectrum of **26** (D_2O, 400 MHz)



[13]C NMR spectrum of **26** (D_2O, 101 MHz)



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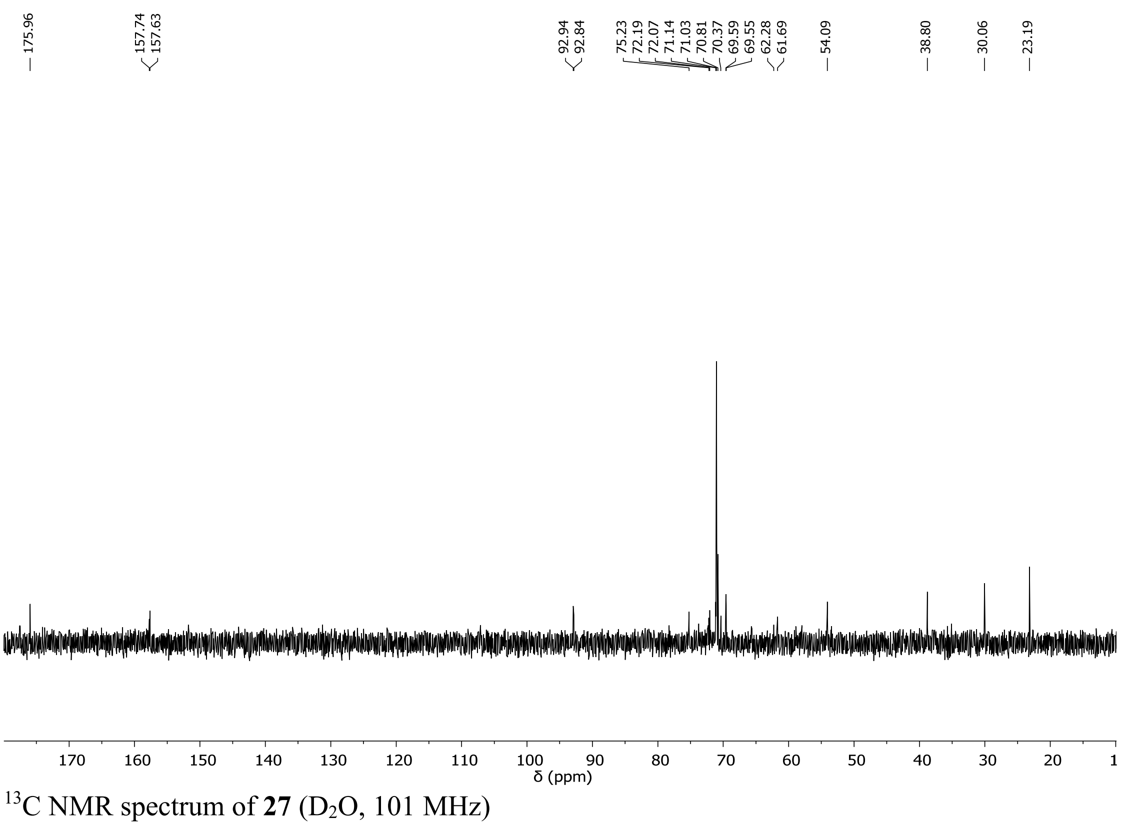
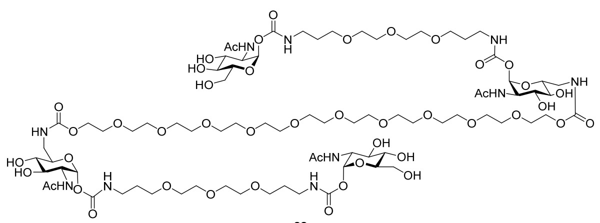
[1]H NMR spectrum of **27** (D_2O, 400 MHz)



[13]C NMR spectrum of **27** (D_2O, 101 MHz)



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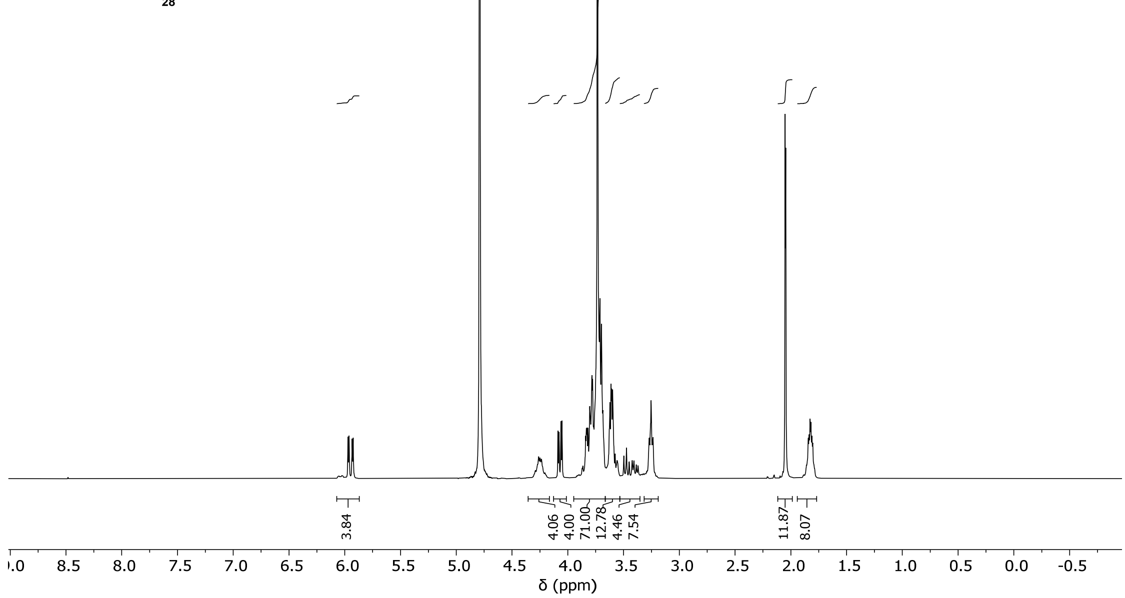
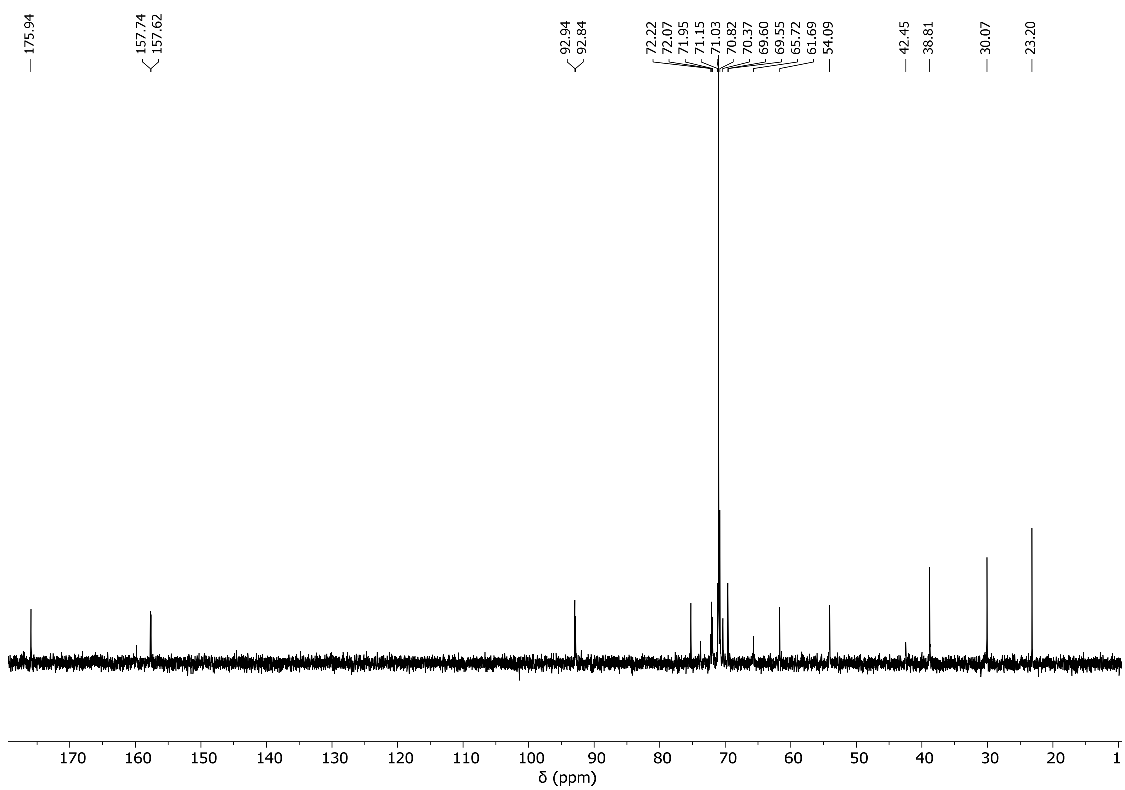
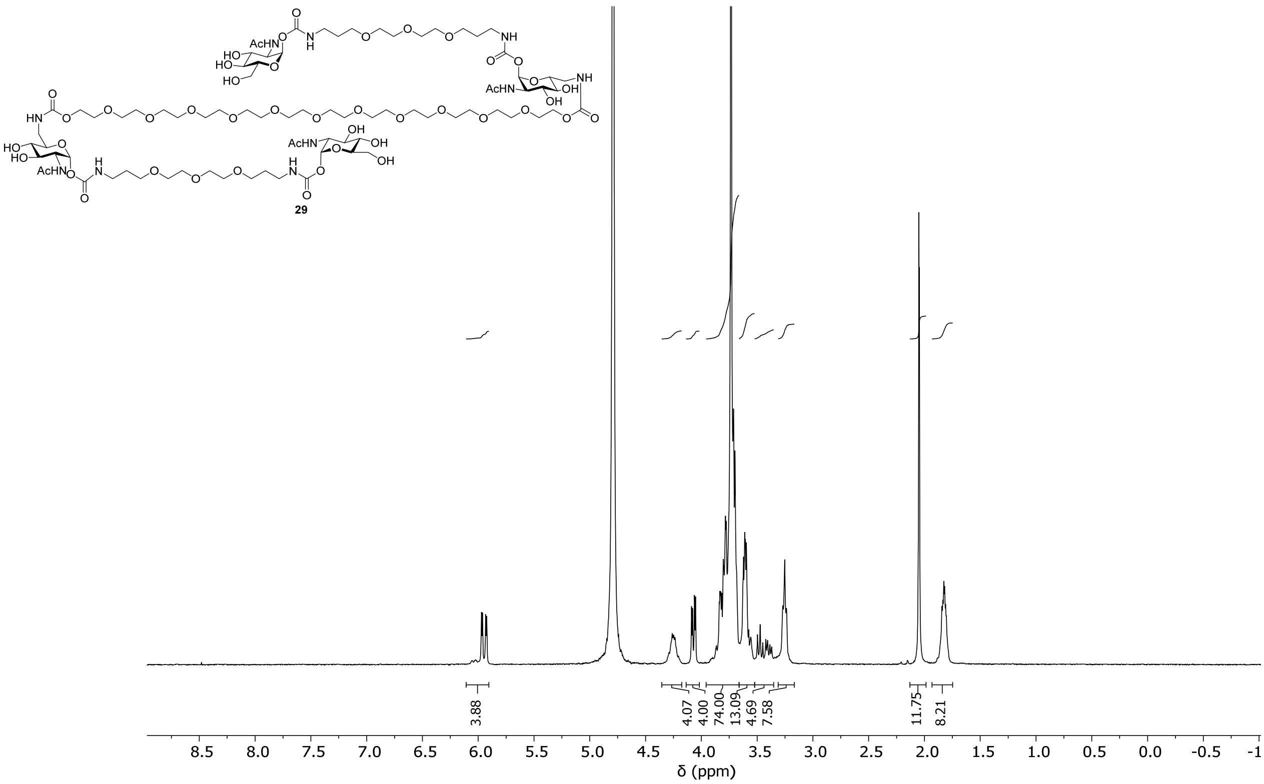


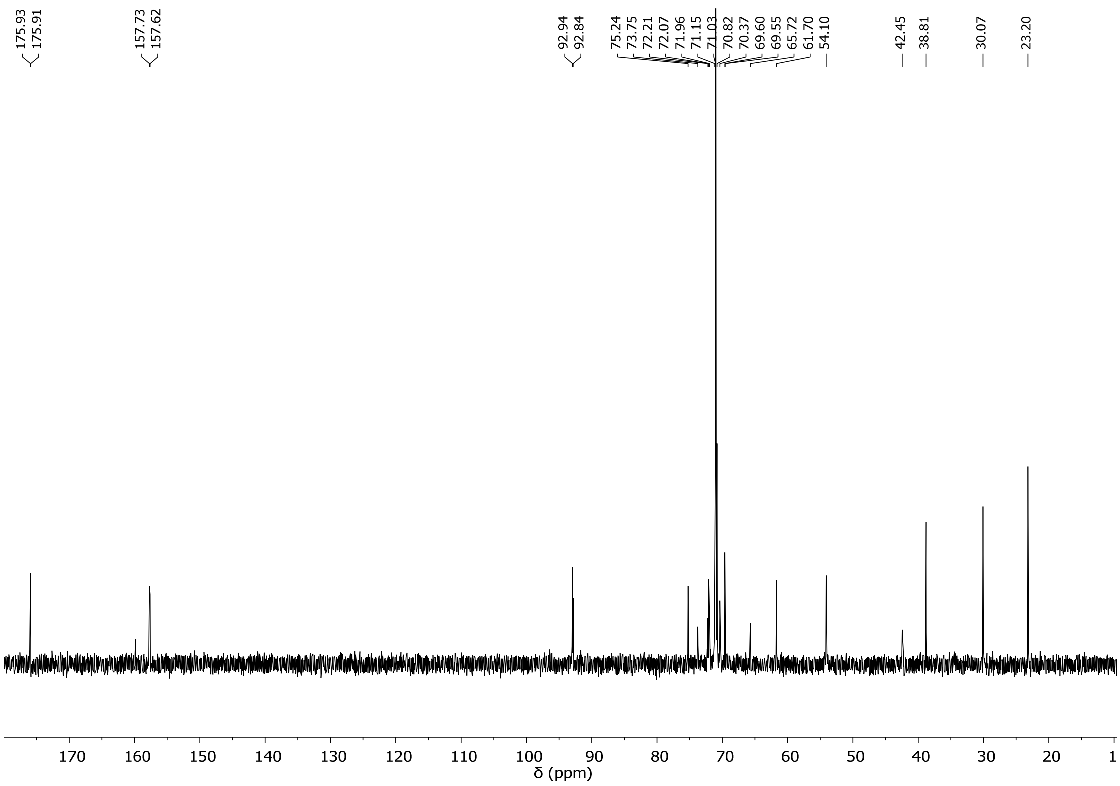
[1]H NMR spectrum of **28** (D_2O, 400 MHz)



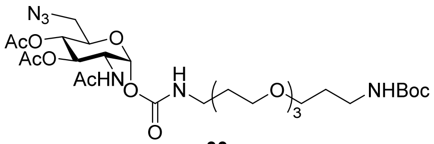
[13]C NMR spectrum of **28** (D_2O, 101 MHz)



[1]H NMR spectrum of **29** (D_2O, 400 MHz)



[13]C NMR spectrum of **29** (D_2O, 101 MHz)



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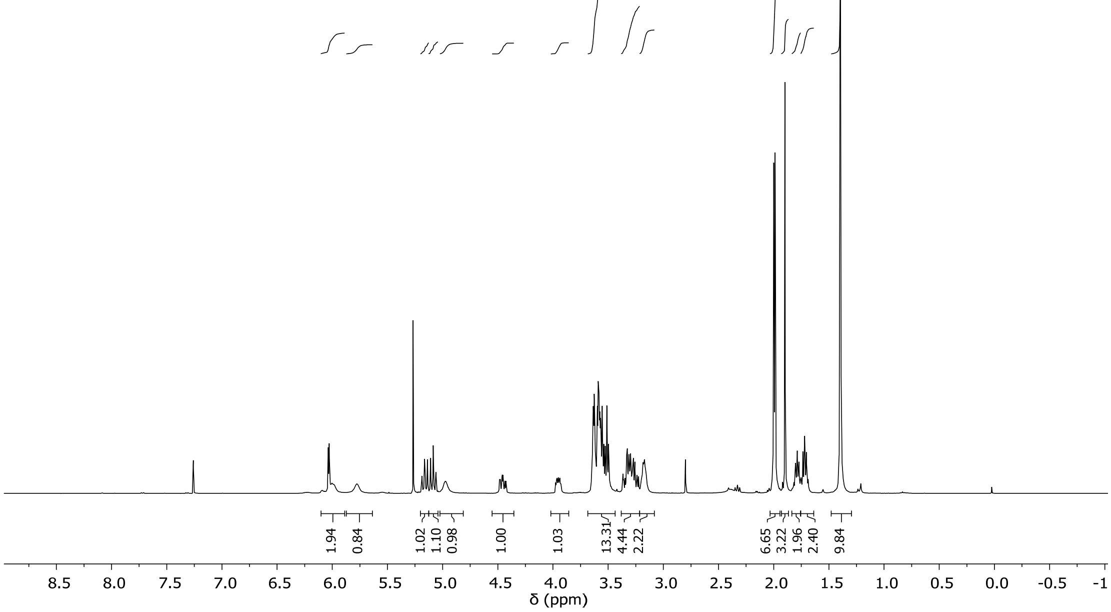
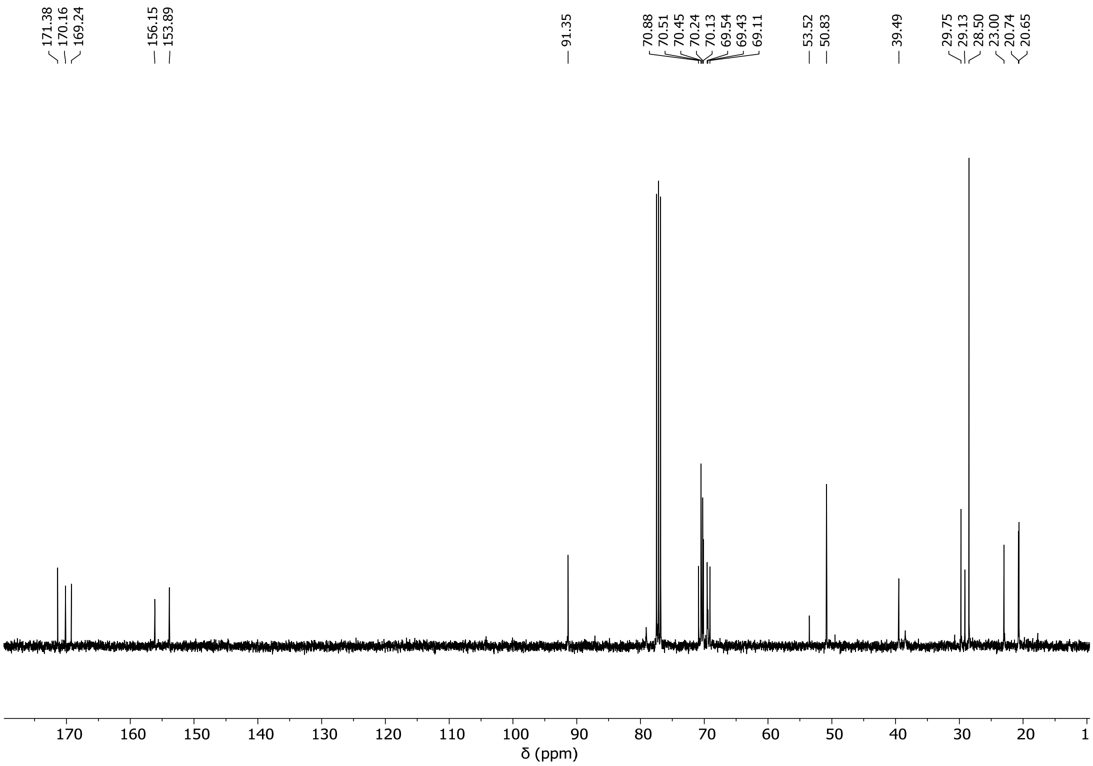
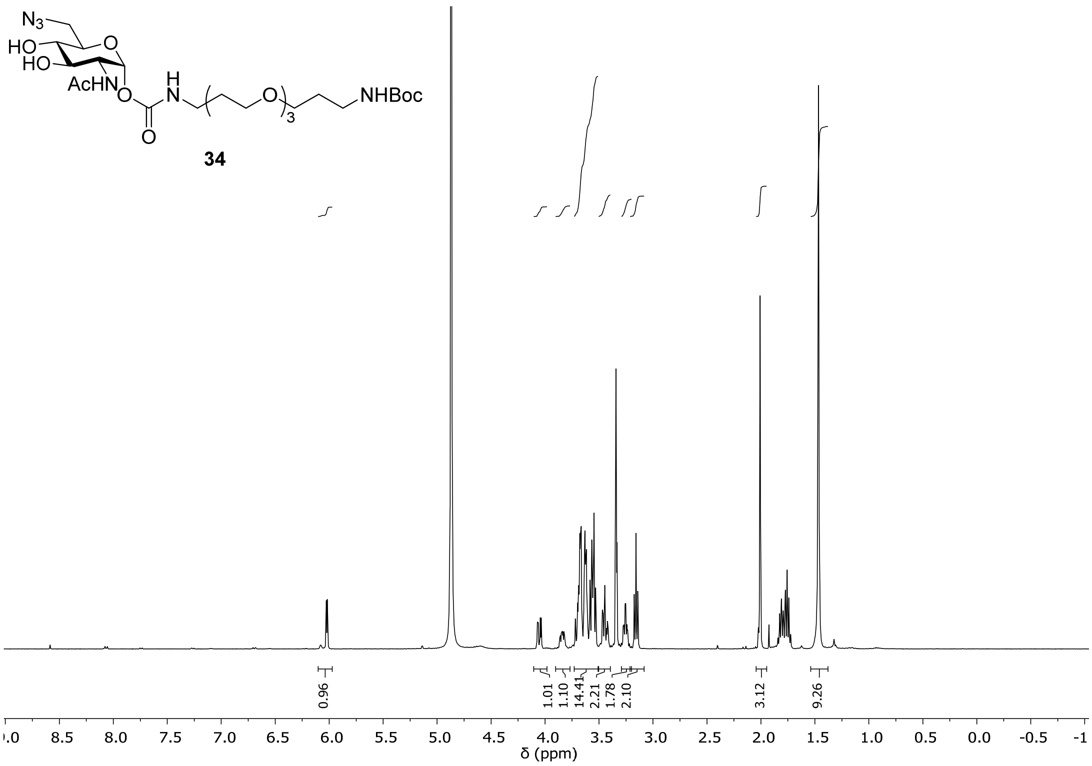


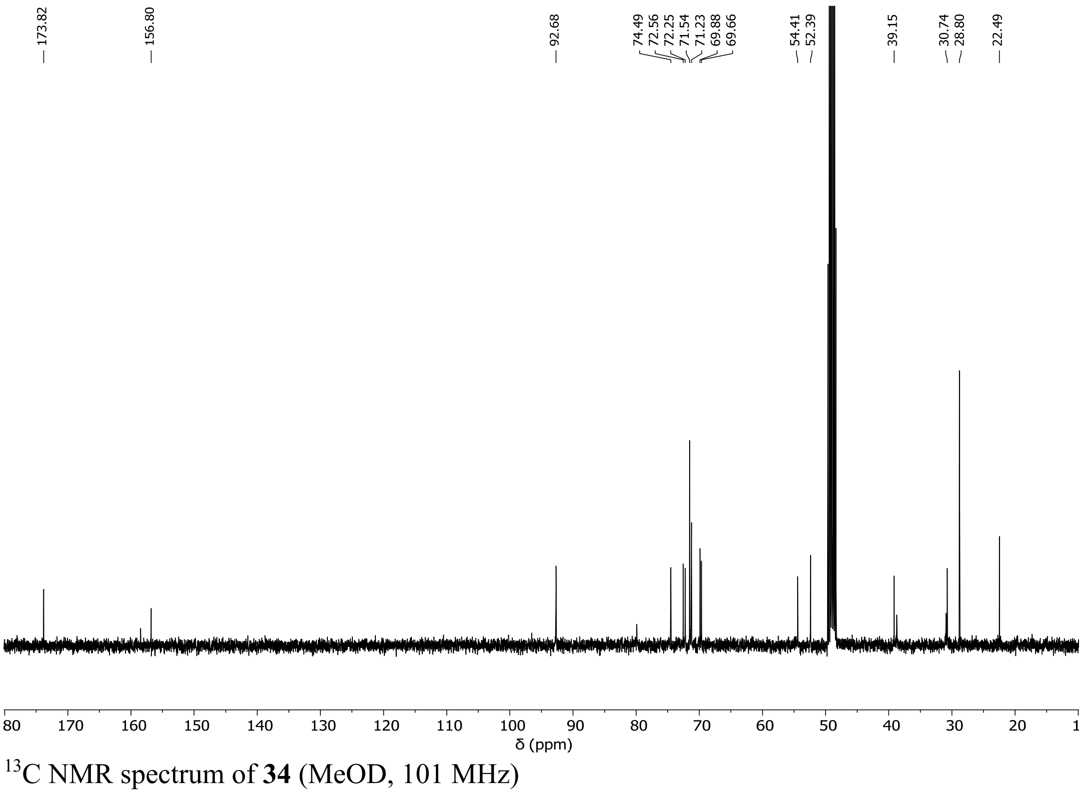
[1]H NMR spectrum of **33** ($CDCl_3$, 400 MHz)



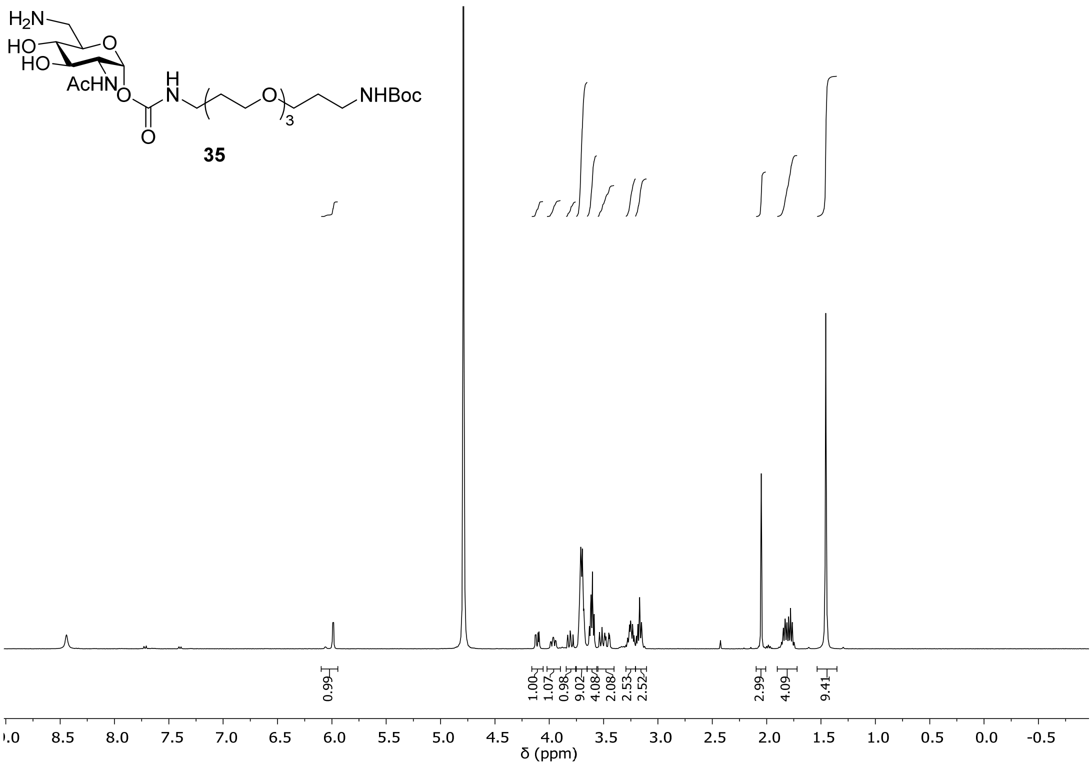
[13]C NMR spectrum of **33** ($CDCl_3$, 101 MHz)



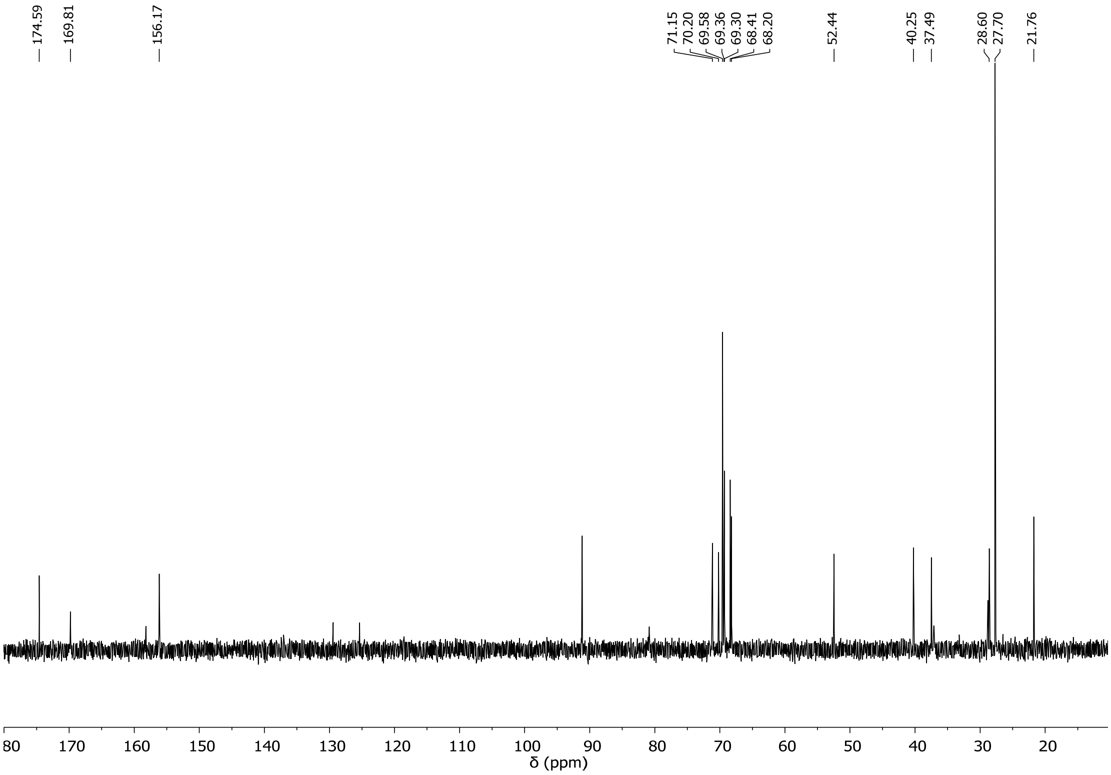
¹H NMR spectrum of **34** (MeOD, 400 MHz)



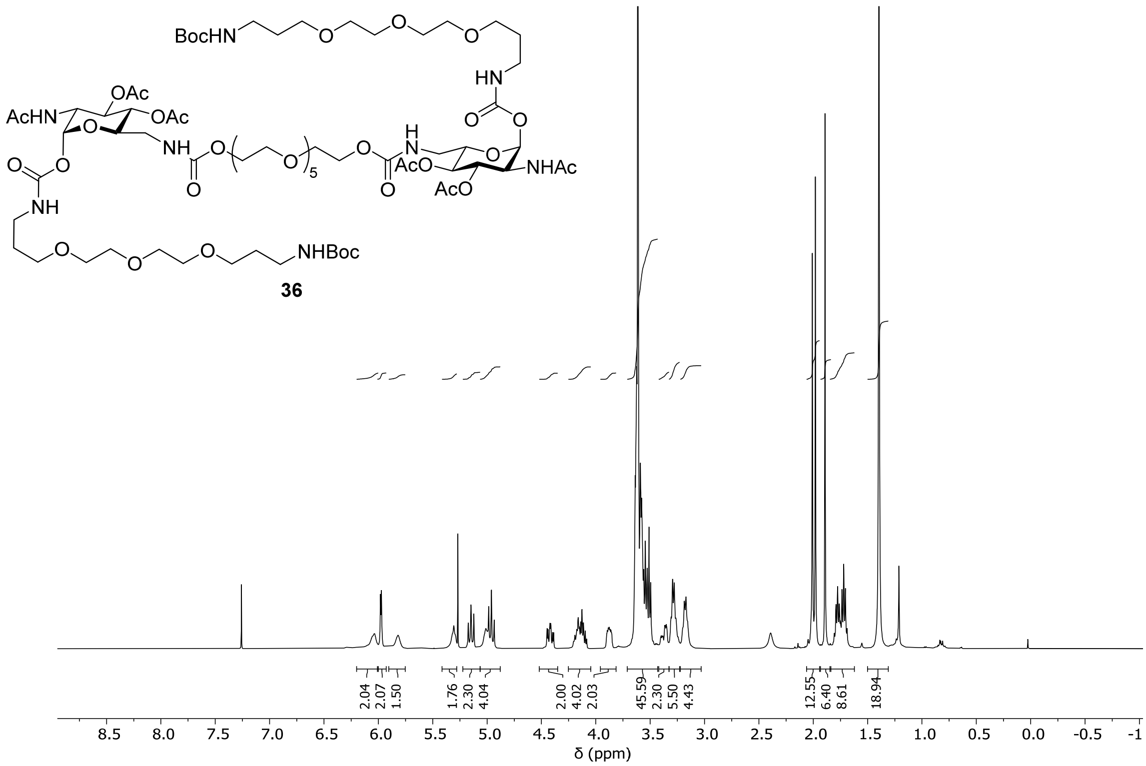
¹³C NMR spectrum of **34** (MeOD, 101 MHz)



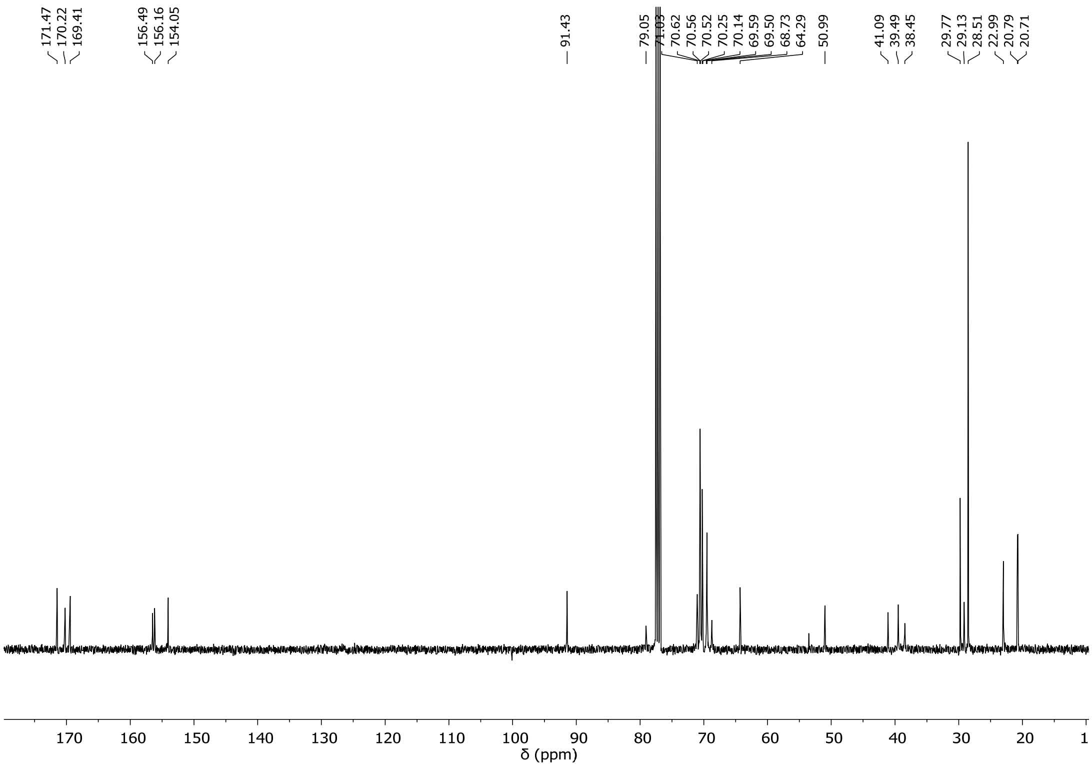
^{1}H NMR spectrum of **35** (MeOD, 400 MHz)



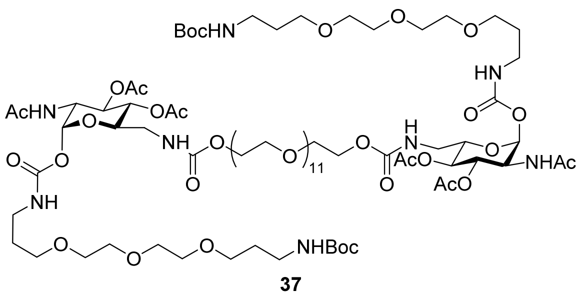
^{13}C NMR spectrum of **35** (MeOD, 101 MHz)

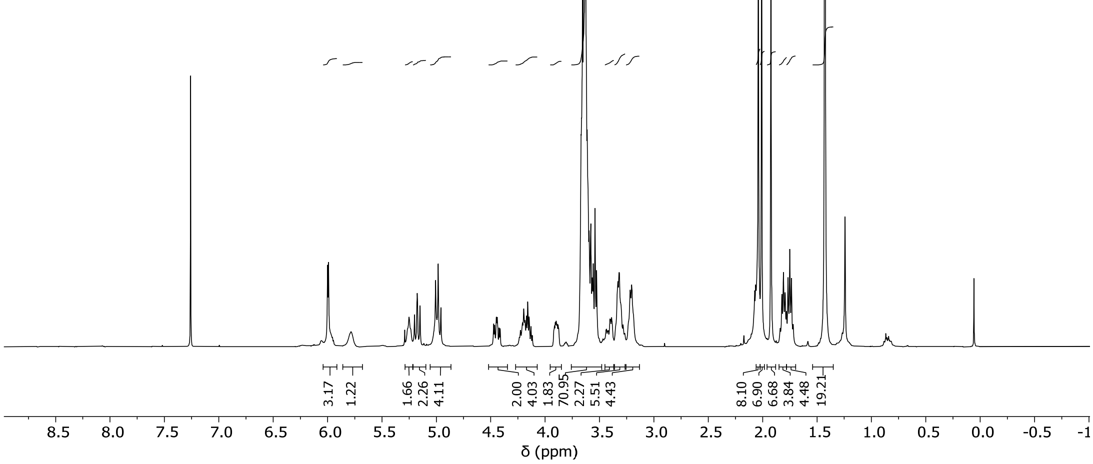


^{1}H NMR spectrum of **36** ($CDCl_3$, 400 MHz)

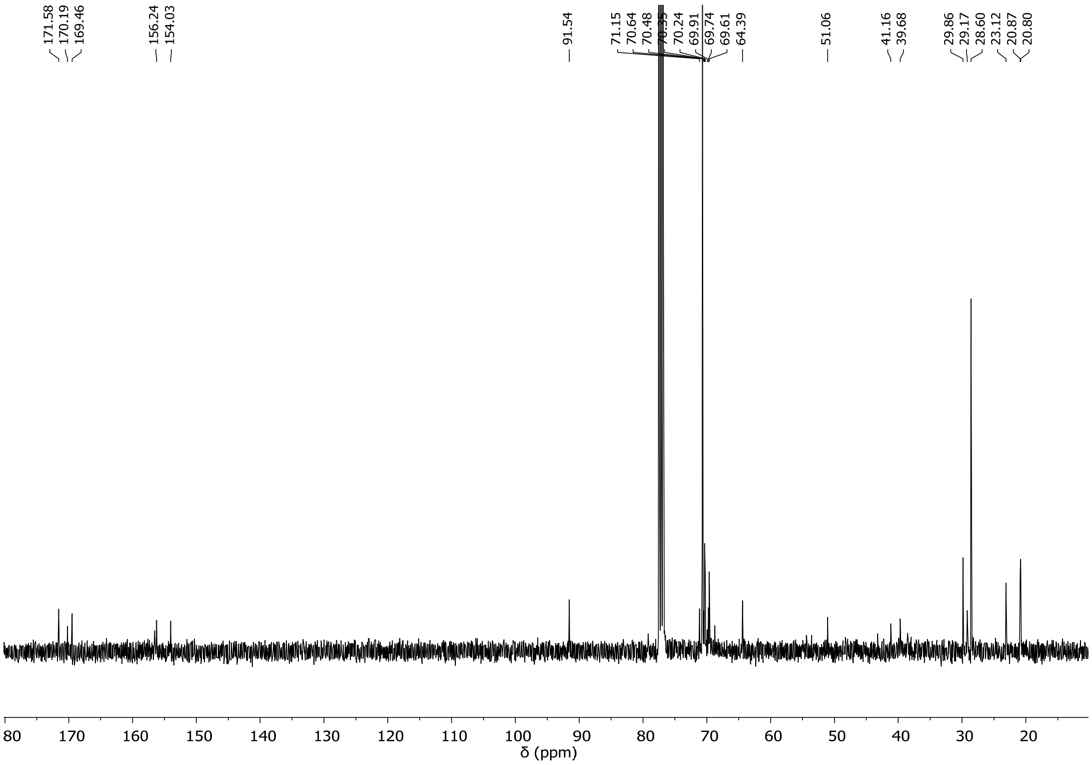


^{13}C NMR spectrum of **36** ($CDCl_3$, 101 MHz)

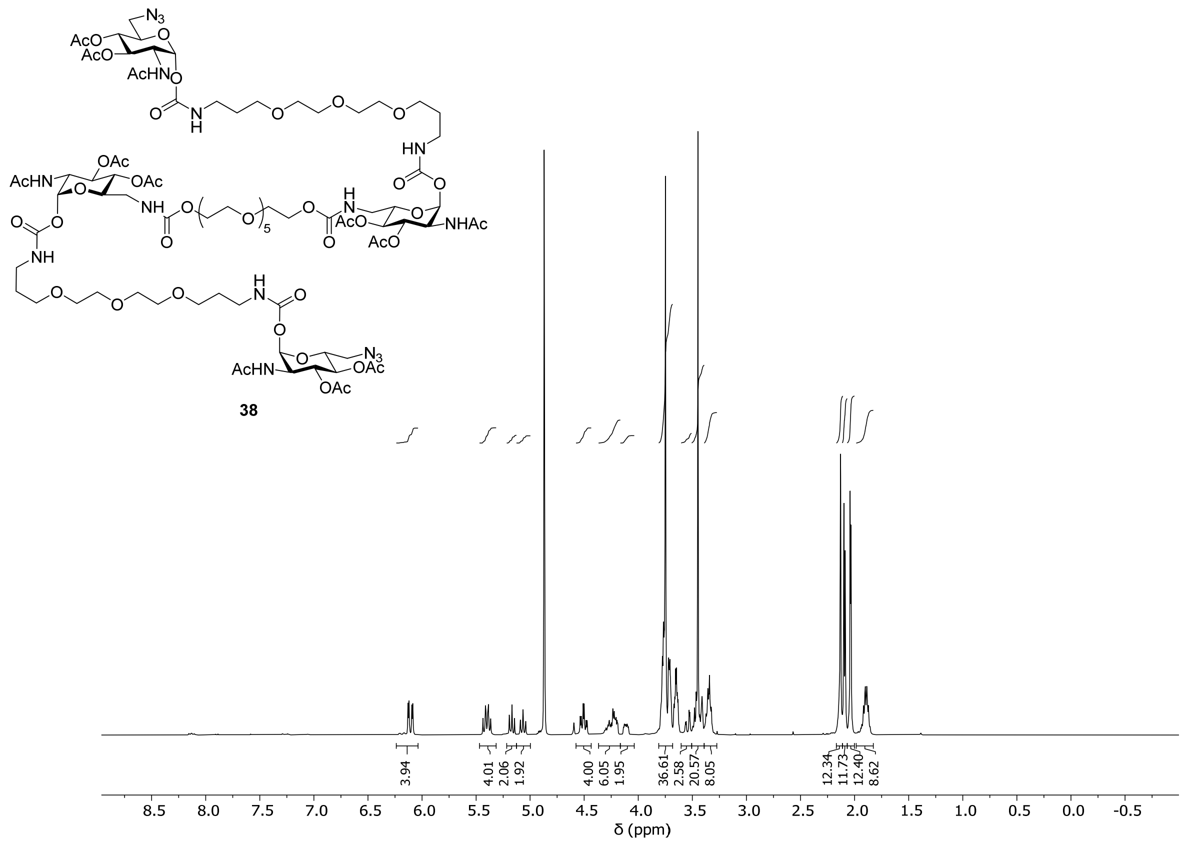




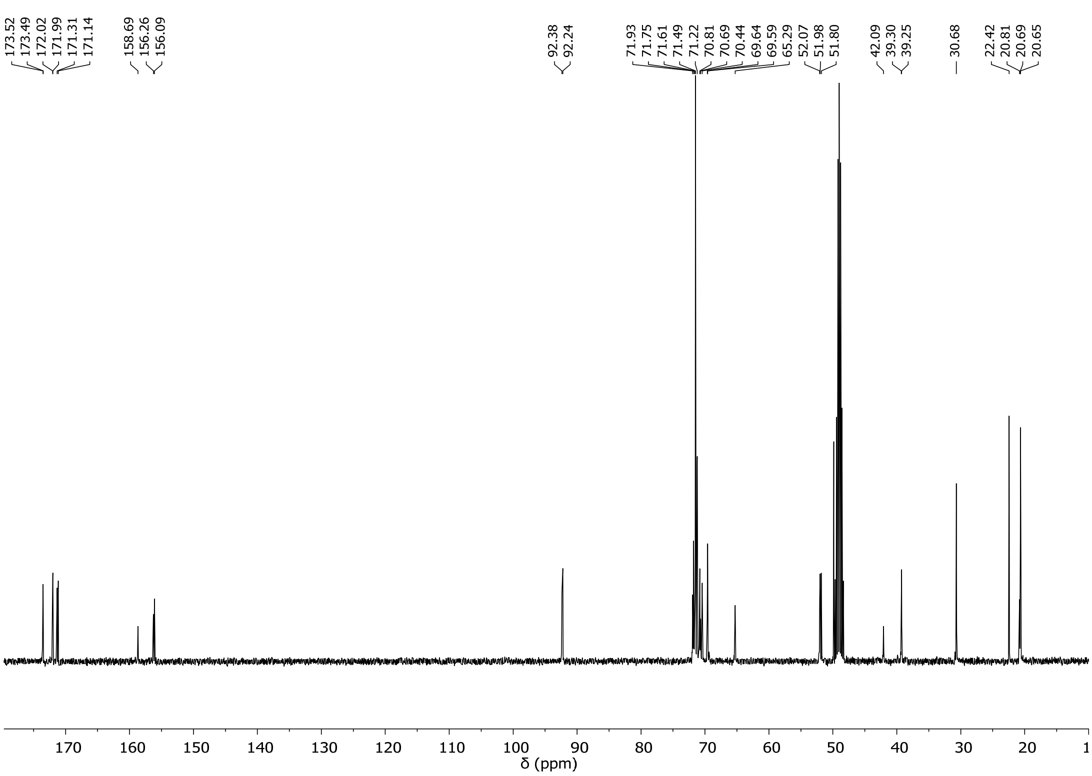
^{1}H NMR spectrum of **37** ($CDCl_3$, 400 MHz)



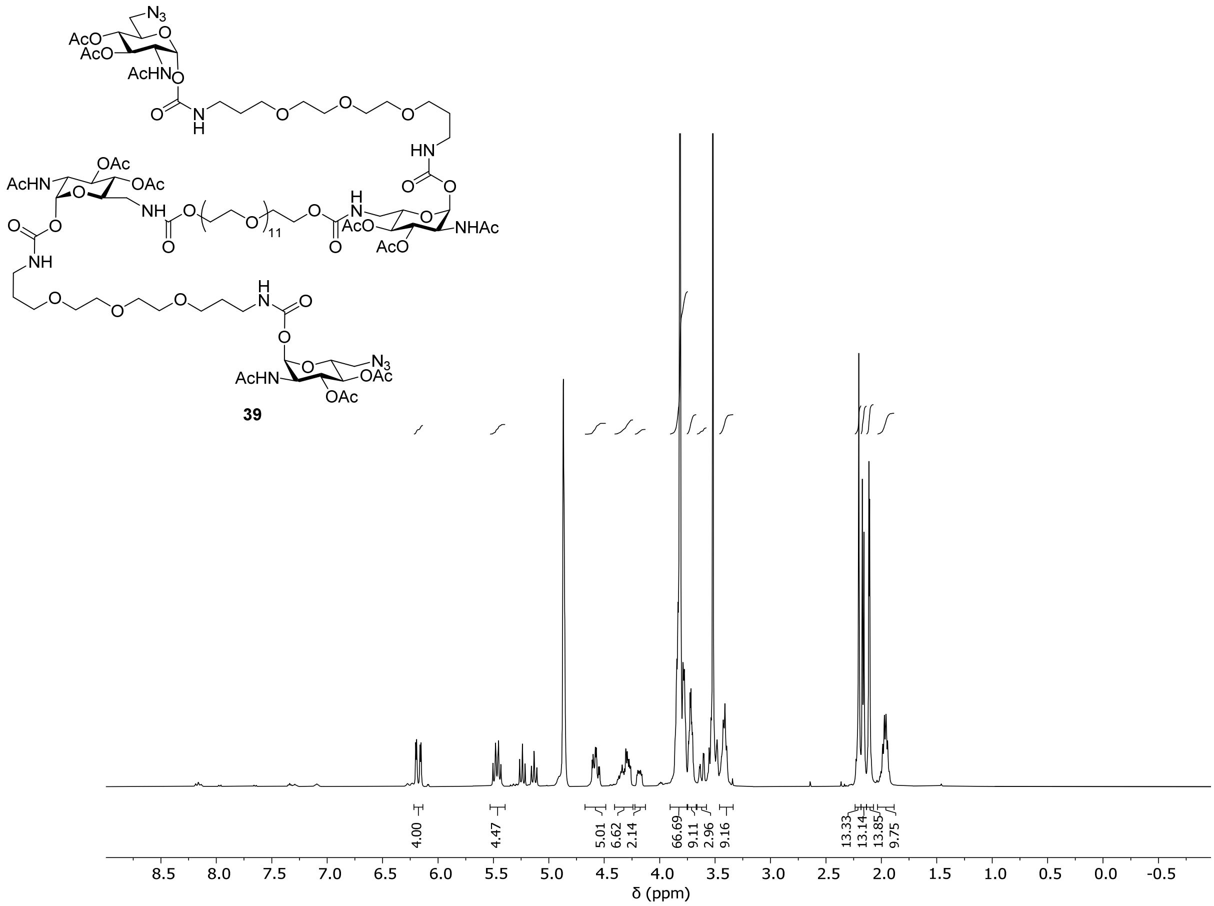
^{13}C NMR spectrum of **37** ($CDCl_3$, 101 MHz)



[1]H NMR spectrum of **38** (MeOD, 400 MHz)



[13]C NMR spectrum of **38** (MeOD, 101 MHz)



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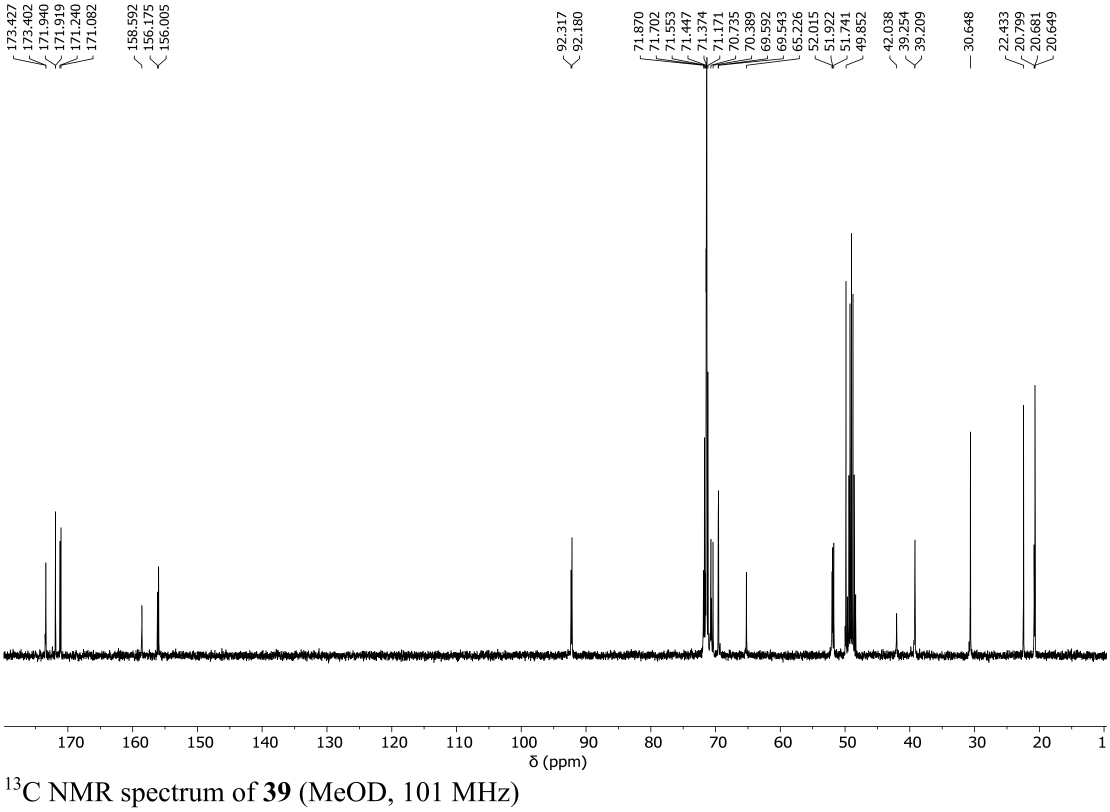
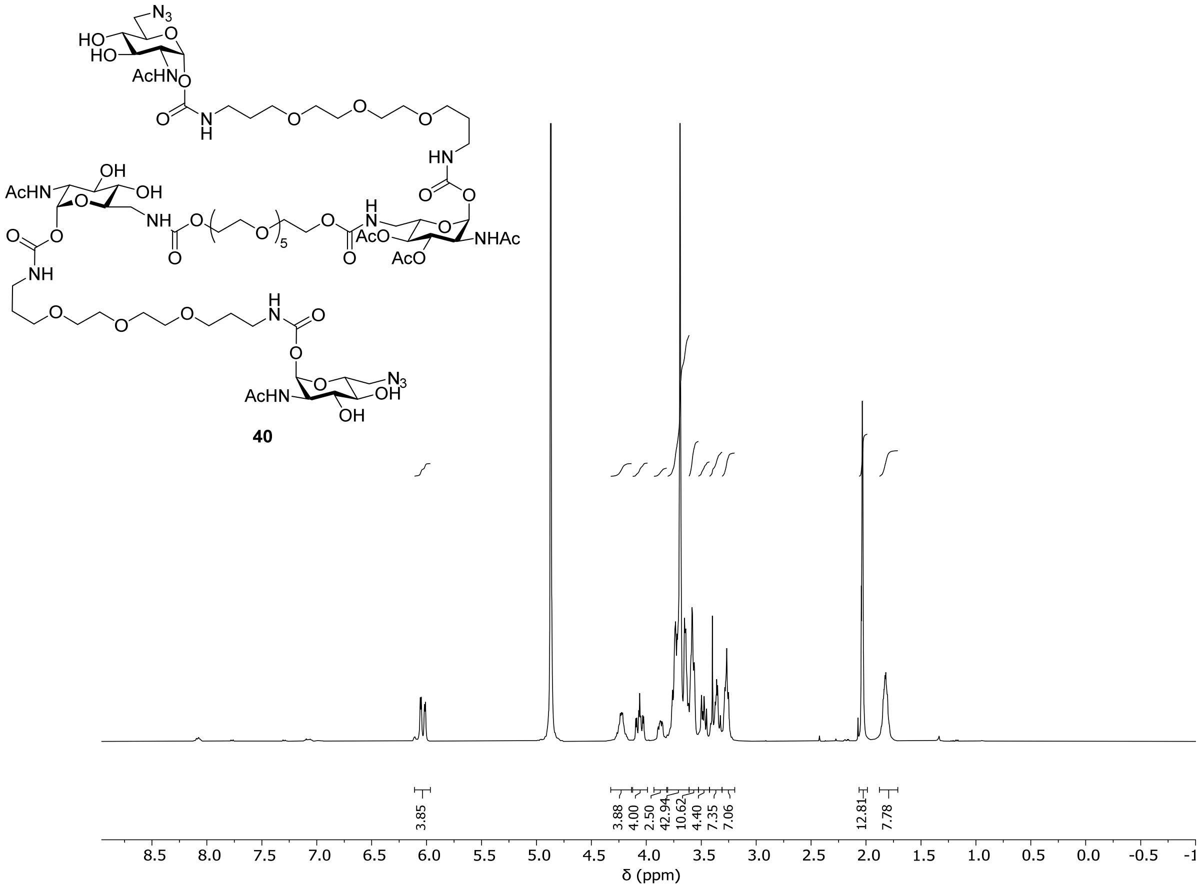
[1]H NMR spectrum of **39** (MeOD, 400 MHz)

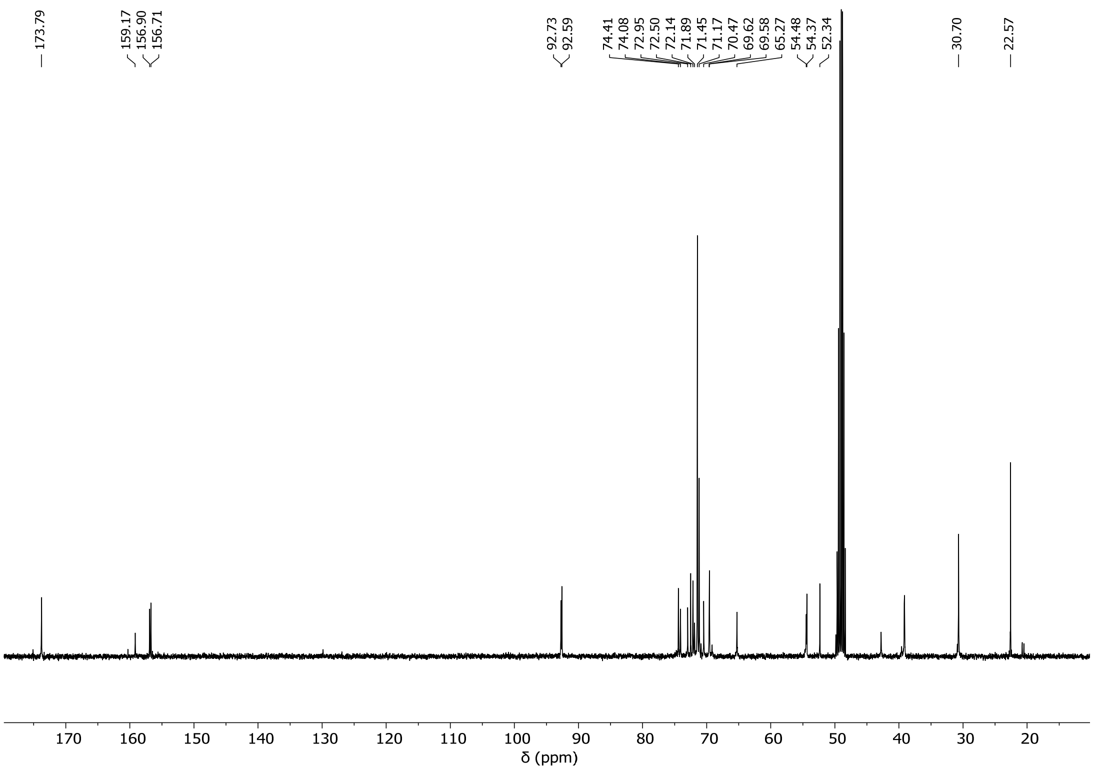


[13]C NMR spectrum of **39** (MeOD, 101 MHz)

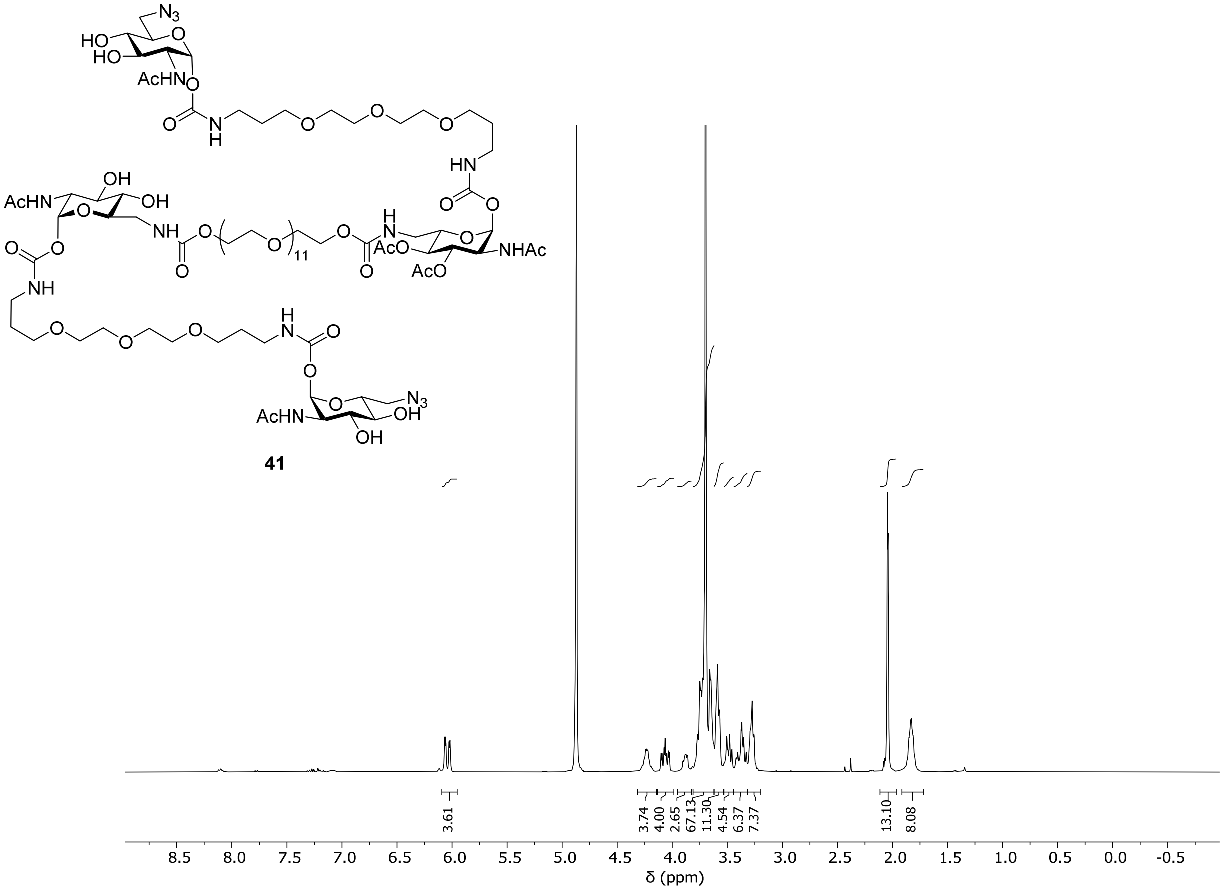


40

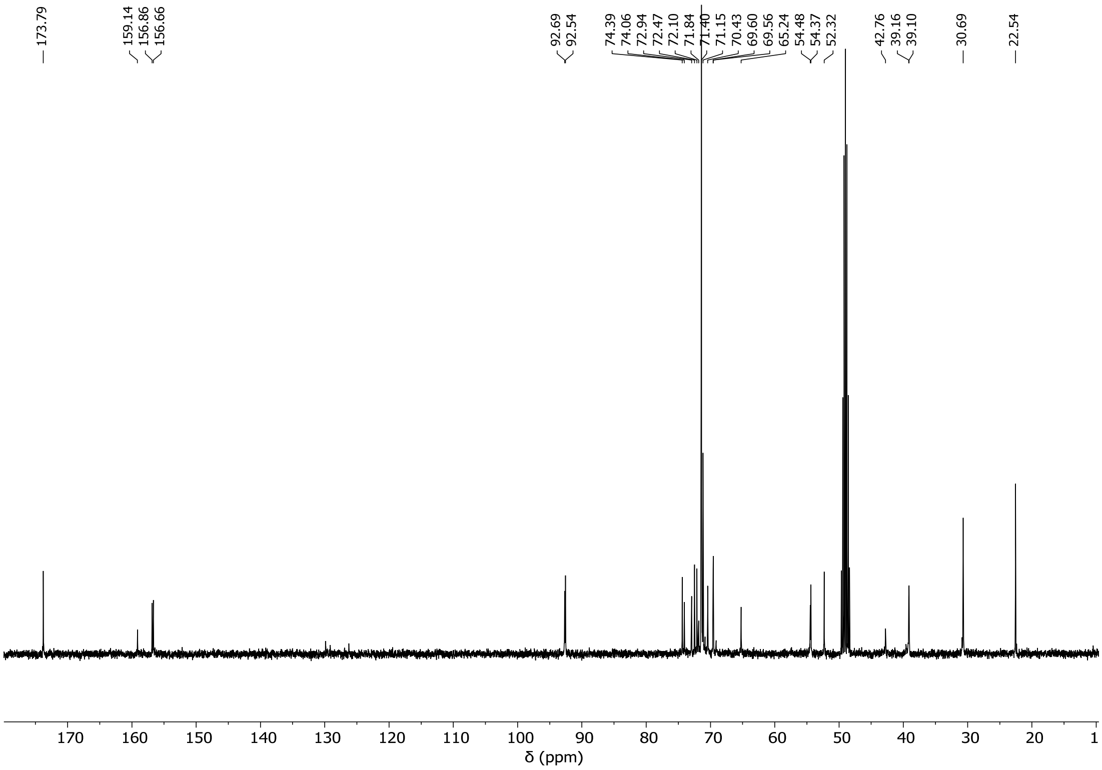
^{1}H NMR spectrum of **40** (MeOD, 400 MHz)



^{13}C NMR spectrum of **40** (MeOD, 101 MHz)



[1]H NMR spectrum of **41** (MeOD, 400 MHz)



[13]C NMR spectrum of **41** (MeOD, 101 MHz)

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