Electronic Supplementary Information

Glycan-decorated HPMA copolymers as high-affinity lectin ligands

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A set of thirteen conjugates of *N*-(2-hydroxypropyl) methacrylamide (HPMA) copolymers tethered with chitooligosaccharidic epitopes of varying length were shown to be potent ligands of a model lectin, wheat germ agglutinin. The azide-functionalized oligosaccharidic epitopes were prepared by the action of Tyr470Asn mutant β-*N*-acetylhexosaminidase from *Talaromyces flavus* in a single reaction step and conjugated to HPMA copolymer precursors in a defined pattern and density through Cu^{+}-catalyzed azide-alkyne cycloaddition. The soluble, biocompatible and structurally flexible synthetic glycopolymers were studied for binding to wheat germ agglutinin in competitive enzyme-linked lectin assay (ELLA) and the kinetics of interaction was analyzed by surface plasmon resonance (SPR). To our knowledge, this work presents the first HPMA copolymers derivatized with long oligosaccharides that feature a high affinity to a lectin target. The binding affinities in low nanomolar and high picomolar ranges place the prepared glycopolymers among the best ligands of wheat germ agglutinin reported up to date.

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1. Functionalized chitooligomers 3, 5-9 – structural characterization

1.1. NMR data and spectra

Table S1: ^{1}H and ^{13}C NMR data (600.23 MHz for ^{1}H, 150.93 MHz for ^{13}C, MeOD, 25 ^{o}C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**3**)

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	69.62	T	4.057	1	ddd	11.0, 5.4, 3.3
				3.690	1	ddd	11.0, 8.1, 3.1
	2'	52.13	T	3.458	1	ddd	13.4, 8.1, 3.3
				3.329	1	ddd	13.4, 5.4, 3.1
Glc^{A}	**1**	102.81	D	4.508	1	d	8.4
	2	57.57	D	3.691	1	m	10.5, 8.4
	3	76.46	D	3.476	1	dd	10.5, 8.2
	4	72.42	D	3.339	1	dd	9.7, 8.2
	5	78.40	D	3.303	1	ddd	9.7, 5.7, 2.2
	6	63.09	T	3.907	1	dd	11.9, 2.2
				3.705	1	dd	11.9, 5.7
	2-CO	174.19	S	-	0		
	2-Ac	23.39	Q	1.997	3	s	

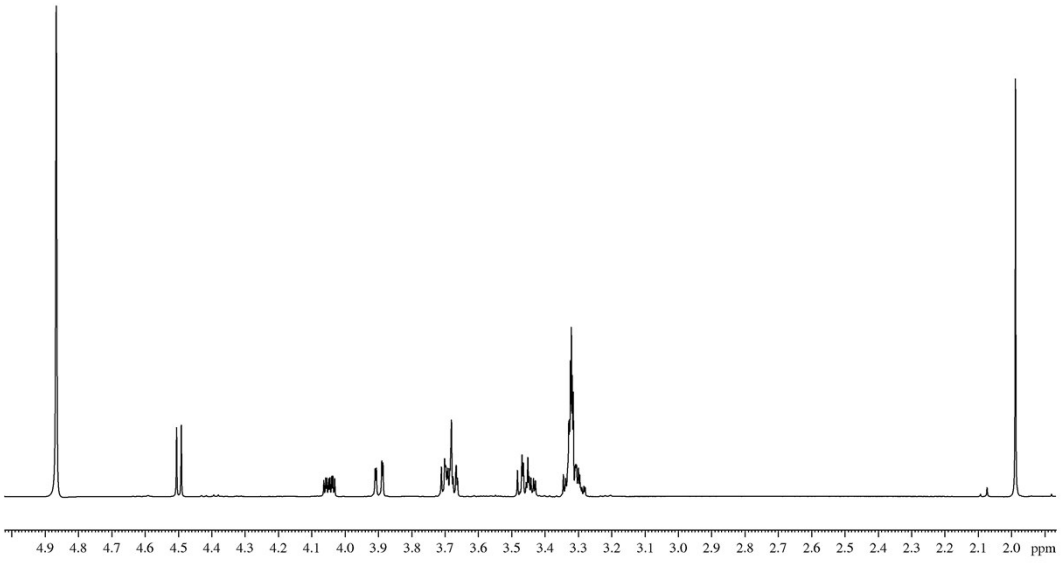

Fig. S1a. ^{1}H NMR spectrum of compound **3.**

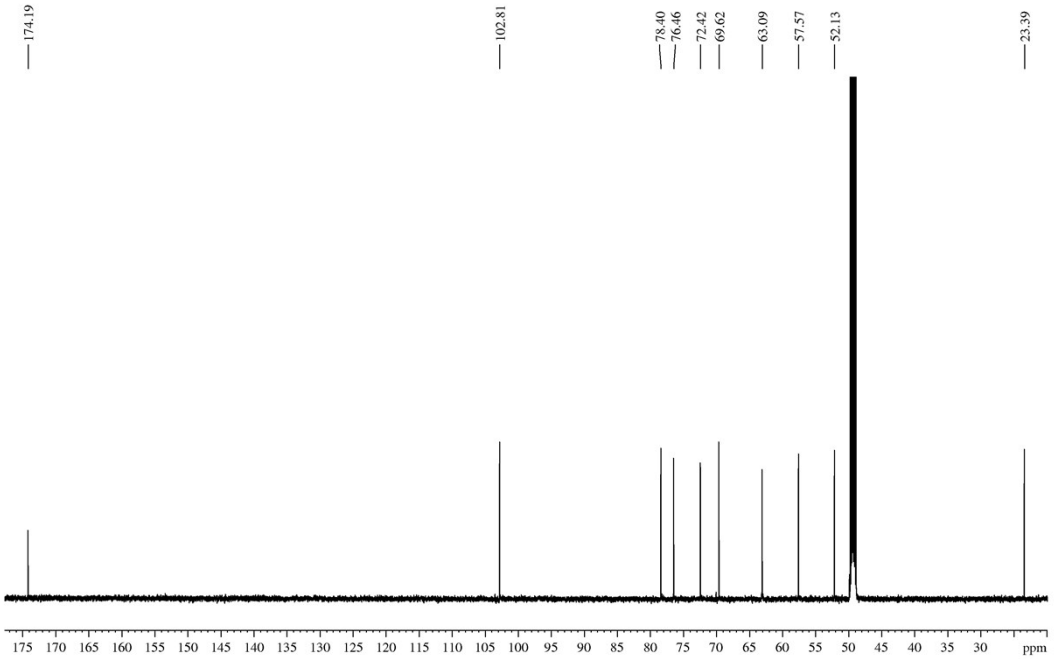

Fig. S1b. ^{13}C NMR spectrum of compound **3**.

Table S2: ^{1}H and ^{13}C NMR data (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C, D_2O, 25 °C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**5**)

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	68.97	T	3.776	1	ddd	11.4, 5.6, 3.0
				3.49[a]	1	m	
	2'	50.56	T	3.21[a]	1	m	
				3.152	1	ddd	13.8, 5.6, 3.0
Glc^A	**1**	101.14	D	4.313	1	d	8.3
	2	55.09	D	3.49[a]	1	m	
	3	72.74	D	3.433	1	dd	Σ*J* = 19.0
	4	79.65	D	3.355	1	dd	9.8, 8.3
	5	74.74	D	3.255	1	ddd	9.8, 5.5, 1.9
	6	60.32	T	3.594	1	dd	12.1, 1.9
				3.402	1	dd	12.1, 5.5
	2-CO	174.89	S	-	0		
	2-Ac	22.31	Q	1.774	3	s	
Glc^B	**1**	101.69	D	4.323	1	d	8.4
	2	55.78	D	3.49[a]	1	m	
	3	73.65	D	3.302	1	dd	10.2, 8.6
	4	69.89	D	3.22[a]	1		
	5	76.10	D	3.23[a]	1		
	6	60.72	T	3.655	1	dd	12.3, 1.8
				3.49[a]	1	m	
	2-CO	174.82	S	-	0		
	2-Ac	22.45	Q	1.806	3	s	

[a] ... HSQC readout

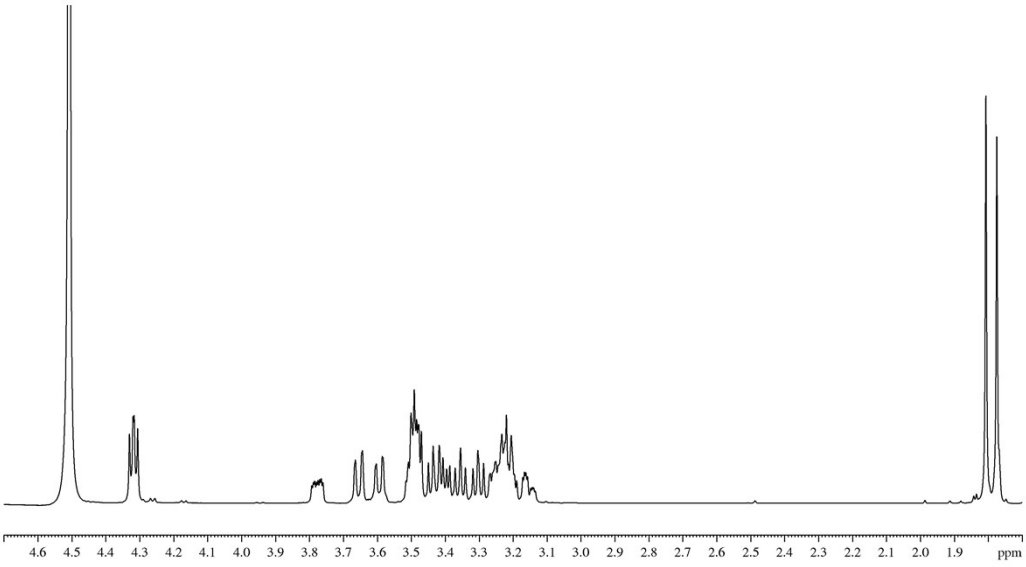

Fig. S2a. ^{1}H NMR spectrum of compound **5.**

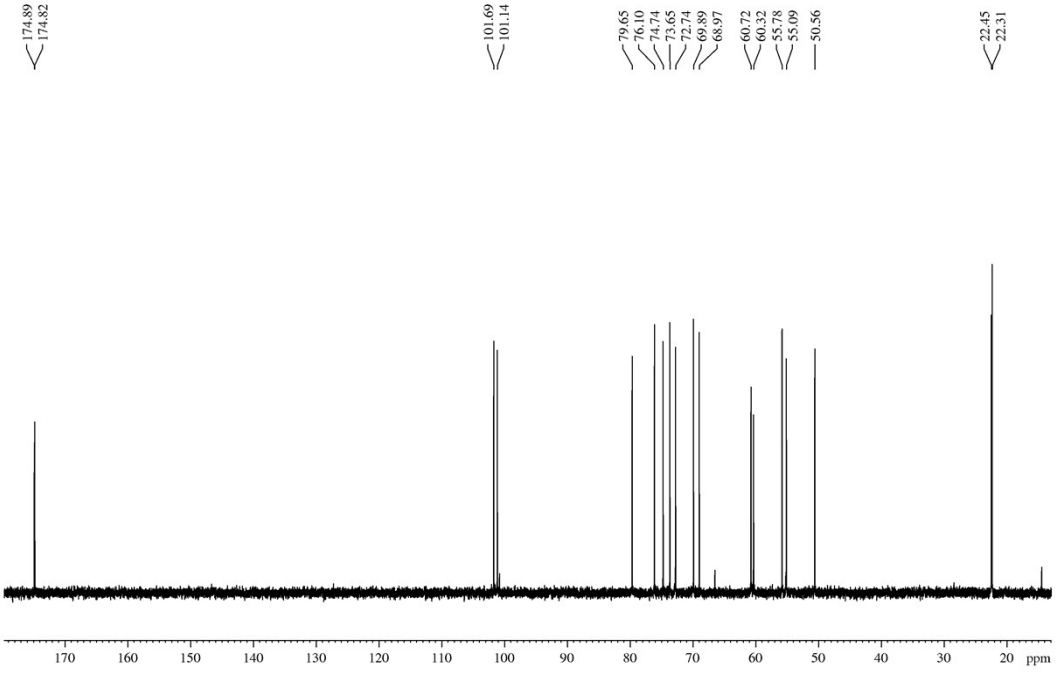

Fig. S2b. ^{13}C NMR spectrum of compound **5.**

Table S3: ^{1}H and ^{13}C NMR data (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C, D_2O, 25 °C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**6**)

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	68.97	T	3.774	1	ddd	11.4, 5.6, 3.0
				3.49[a]	1	m	
	2'	50.56	T	3.21[a]	1	m	
				3.150	1	ddd	13.8, 5.6, 3.0
Glc^A	**1**	101.13	D	4.308	1	d	8.3
	2	55.13	D	3.496	1	dd	10.3, 8.3
	3	72.67	D	3.424	1	dd	10.3, 8.4
	4	79.40	D	3.353	1	dd	9.7, 8.4
	5	74.77	D	3.245	1	ddd	9.7, 5.5, 20.
	6	60.27	T	3.589	1	m	
				3.397	1	m	
	2-CO	174.88	S	-			
	2-Ac	22.45	Q	1.773	3	s	
Glc^B	**1**	101.47	D	4.316	1	d	8.3
	2	55.21	D	3.513	1	dd	10.4, 8.3
	3	72.33	D	3.452	1	dd	10.4, 8.4
	4	79.30	D	3.383	1	dd	ΣJ = 17.7
	5	74.70	D	3.288	1	m	
	6	60.15	T	3.587	1	m	
				3.397	1	m	
	2-CO	174.82[b]	S	-			
	2-Ac	22.30	Q	1.797	3	s	
Glc^C	**1**	101.65	D	4.319	1	d	8.4
	2	55.78	D	3.487	1	dd	10.4, 8.3
	3	73.63	D	3.300	1	dd	10.4, 8.3
	4	69.89	D	3.201	1	dd	9.8, 8.3
	5	76.10	D	3.235	1	m	
	6	60.73	T	3.654	1	dd	12.4, 2.0
				3.49[a]	1	m	
	2-CO	174.80[b]	S	-	0		
	2-Ac	22.30	Q	1.800	3	s	

[a] ... HSQC readout

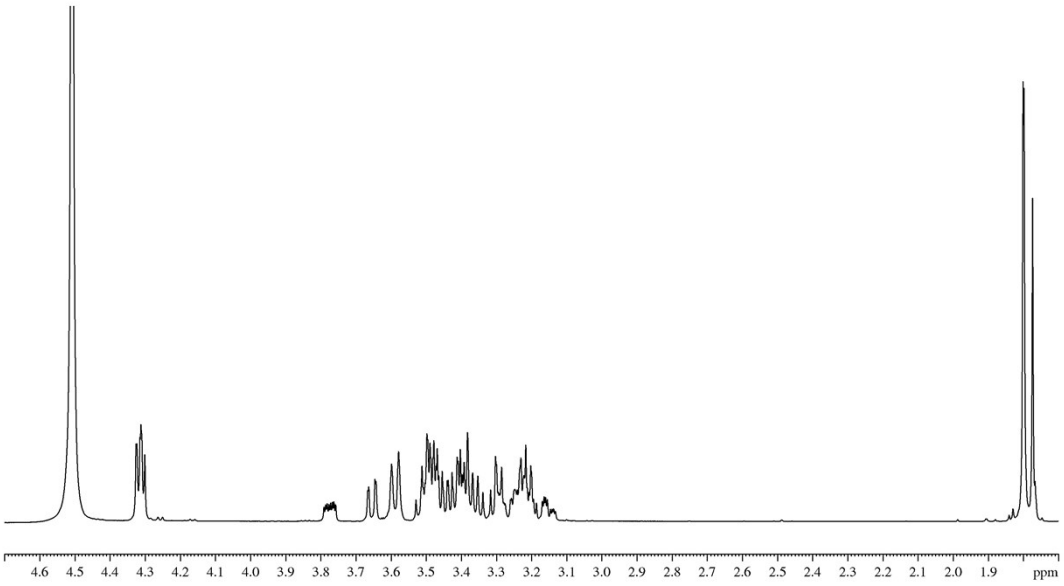

Fig. S3a. ^{1}H NMR spectrum of compound **6**.

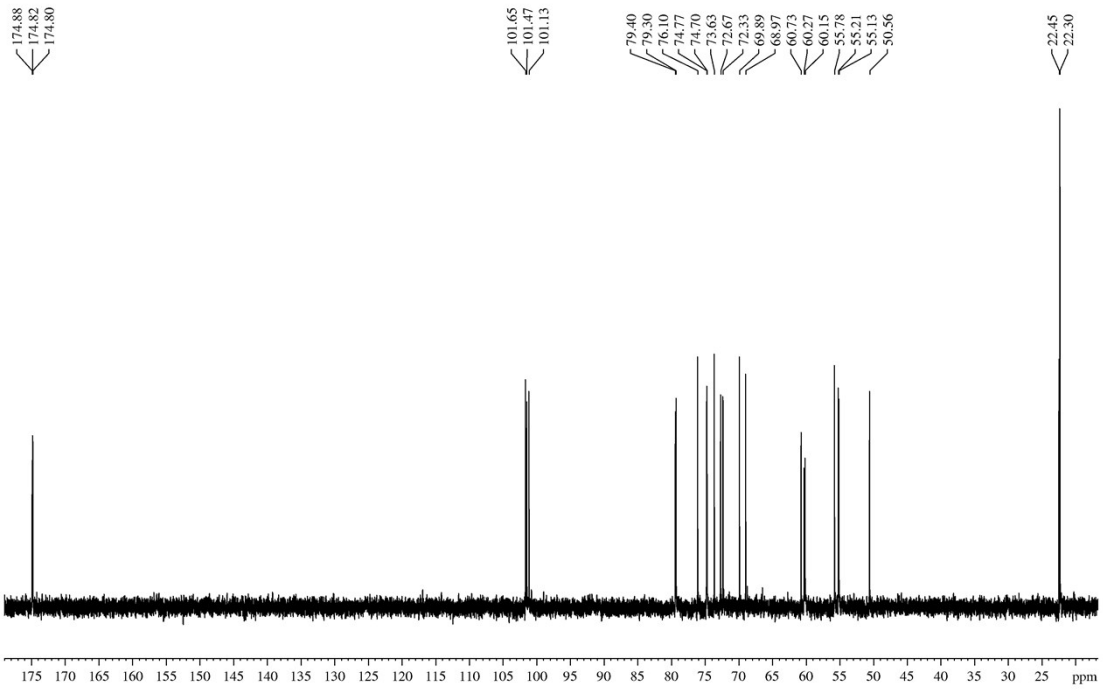

Fig. S3b. ^{13}C NMR spectrum of compound **6**.

Table S4: ^{1}H and ^{13}C NMR data (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C, D_2O, 25 °C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**7**)

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	68.97	T	3.772	1	ddd	11.4, 5.6, 3.0
				3.49[a]	1	m	
	2'	50.56	T	3.21[a]	1	m	
				3.149	1	ddd	13.8, 5.6, 3.0
Glc^A	**1**	101.13	D	4.306	1	d	8.3
	2	55.12	D	3.485	1	dd	10.4, 8.3
	3	72.67	D	3.422	1	dd	10.4, 8.4
	4	79.42	D	3.348	1	dd	9.7, 8.4
	5	74.77	D	3.25[a]	1	m	
	6	60.28	T	3.585	1	dd	
				3.39[a]	1	m	
	2-CO	174.88	S	-			
	2-Ac	22.45	Q	1.772	3	s	
Glc^B	**1**	101.47	D	4.311	1	d	8.3
	2	55.21	D	3.508[c]	1	dd	
	3	72.32	D	3.450	1	dd	10.4, 8.4
	4	79.34	D	3.38[a]	1	m	
	5	74.70	D	3.29[a]	1	m	
	6	60.17	T	3.585	1	dd	
				3.39[a]	1	m	
	2-CO	174.82[b]	S	-			
	2-Ac	22.31	Q	1.791	3	s	
Glc^C	**1**	101.43	D	4.311	1	d	8.3
	2	55.25	D	3.507[c]	1	dd	
	3	72.26	D	3.443	1	dd	10.4, 8.4
	4	79.07	D	3.38[a]	1	m	
	5	74.73	D	3.29[a]	1	m	
	6	60.12	T	3.585	1	dd	
				3.39[a]	1	m	
	2-CO	174.82[b]	S	-			
	2-Ac	22.31	Q	1.796	3	s	
Glc^D	**1**	101.66	D	4.317	1	d	8.4
	2	55.78	D	3.478	1	dd	10.4, 8.4
	3	73.63	D	3.299	1	dd	10.4, 8.4
	4	69.90	D	3.199	1	dd	9.8, 8.4
	5	76.10	D	3.23[a]	1	m	
	6	60.73	T	3.653	1	dd	12.4, 2.0
				3.48[a]	1	m	
	2-CO	174.79[b]	S	-	0		
	2-Ac	22.31	Q	1.799	3	s	

[a] ... HSQC readout; [b,c] ... might be interchanged

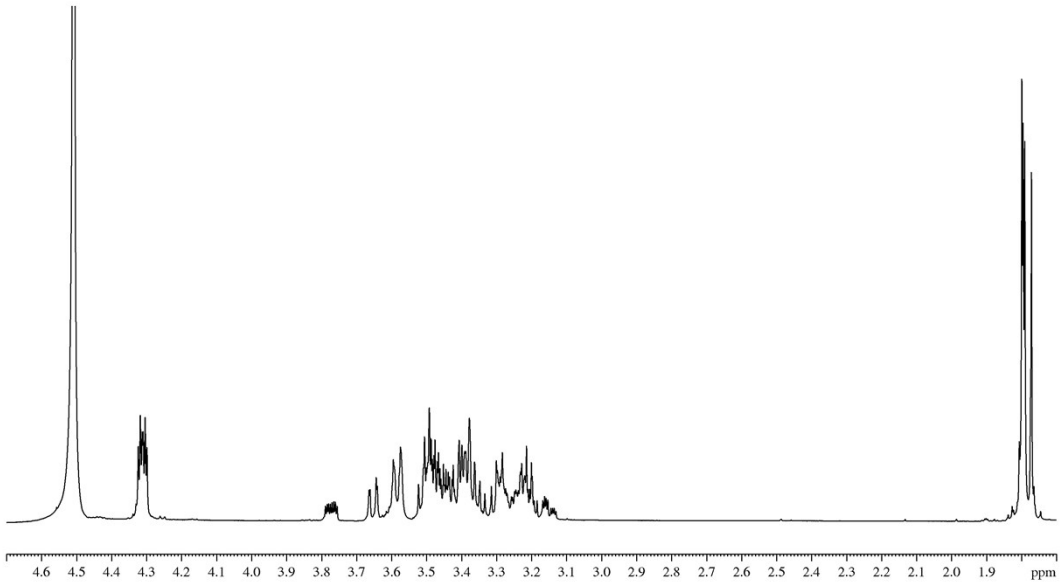

Fig. S4a. ^{1}H NMR spectrum of compound **7**.

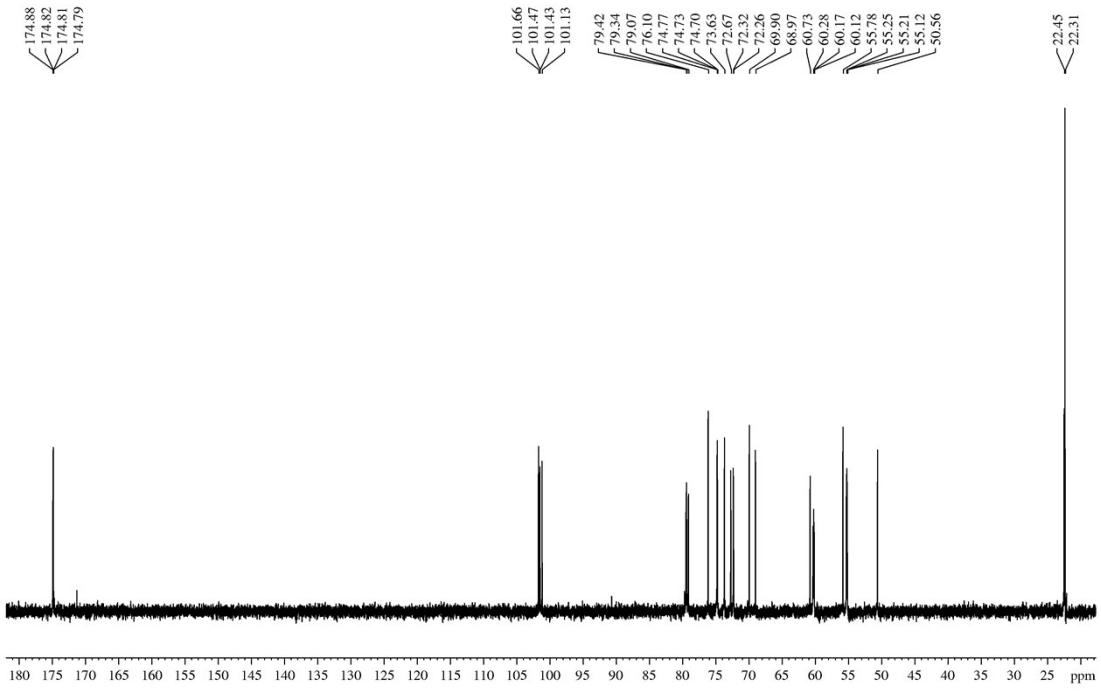

Fig. S4b. ^{13}C NMR spectrum of compound **7**.

Table S5: ^{1}H and ^{13}C NMR data (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C, D_2O, 25 °C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**8**).

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	68.97	T	3.758	1	ddd	11.4, 5.6, 3.0
				3.48[a]	1	m	
	2'	50.55	T	3.20[a]	1	m	
				3.135	1	ddd	13.8, 5.6, 3.0
Glc^A	**1**	101.12	D	4.292	1	d	8.3
	2	55.11	D	3.47[a]	1	m	
	3	72.65	D	3.42[a]	1	m	
	4	79.38	D	3.33[a]	1	m	
	5	74.75	D	3.23[a]	1	m	
	6	60.25	T	3.57[a]	1	m	
				3.38[a]	1	m	
	2-CO	174.88	S	-			
	2-Ac	22.45	Q	1.757	3	s	
Glc^B	**1**	101.44	D	4.294[e]	1	d	8.3
	2	55.21	D	3.49[a]	1	m	
	3	72.30	D	3.44[a]	1	m	
	4	79.32	D	3.36[a]	1	m	
	5	74.69[b]	D	3.27[a]	1	m	
	6	60.16	T	3.57[a]	1	m	
				3.38[a]	1	m	
	2-CO	174.83[c]	S	-			
	2-Ac	22.31	Q	1.776[f]	3	s	
Glc^C	**1**	101.42	D	4.297[e]	1	d	8.3
	2	55.24	D	3.49[a]	1	m	
	3	72.23	D	3.44[a]	1	m	
	4	79.10[d]	D	3.36[a]	1	m	
	5	74.72[b]	D	3.27[a]	1	m	
	6	60.11	T	3.57[a]	1	m	
				3.38[a]	1	m	
	2-CO	174.80[c]	S	-			
	2-Ac	22.31	Q	1.776[f]	3	s	
Glc^D	**1**	101.42	D	4.297[e]	1	d	8.3
	2	55.24	D	3.49[a]	1	m	
	3	72.23	D	3.44[a]	1	m	
	4	79.08[d]	D	3.36[a]	1	m	
	5	74.72[b]	D	3.27[a]	1	m	
	6	60.11	T	3.57[a]	1	m	
				3.38[a]	1	m	
	2-CO	174.80[c]	S	-			
	2-Ac	22.31	Q	1.780[f]	3	s	
Glc^E	**1**	101.64	D	4.304	1	d	8.4
	2	55.77	D	3.46[a]	1	m	
	3	73.60	D	3.290	1	dd	10.4, 8.4
	4	69.88	D	3.184	1	dd	9.8, 8.4
	5	76.09	D	3.22[a]	1	m	
	6	60.72	T	3.638	1	dd	12.4, 1.9
				3.47[a]	1	m	
	2-CO	174.80[c]	S	-	0		
	2-Ac	22.31	Q	1.785	3	s	

[a] ... HSQC readout; [b,c,d,e,f] ... might be interchanged

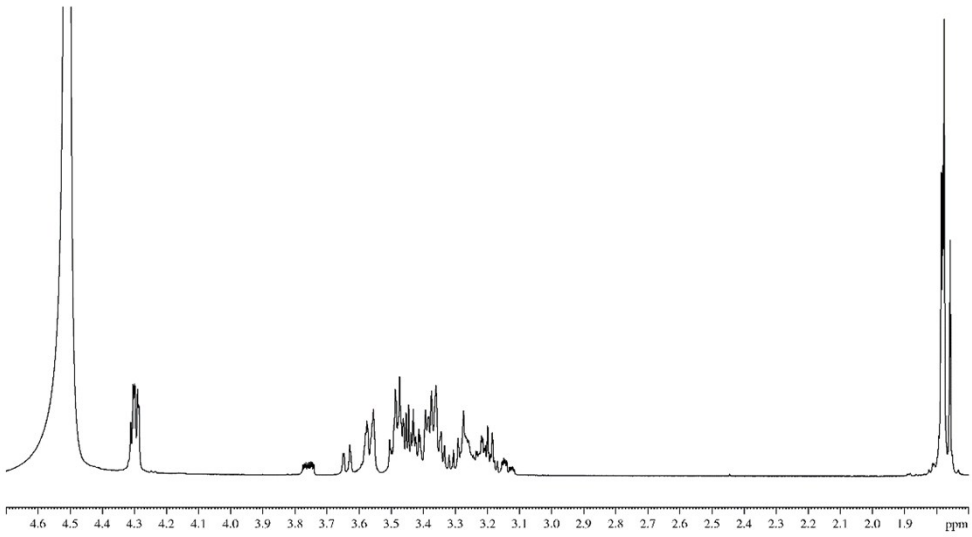

Fig. S5a. ^{1}H NMR spectrum of compound **8**

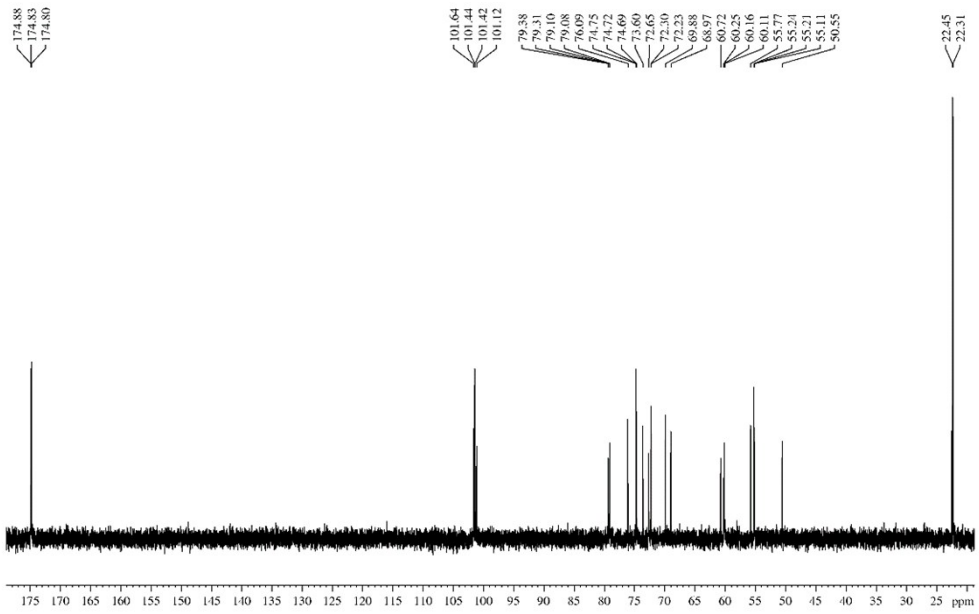

Fig. S5b. ^{13}C NMR spectrum of compound **8**.

Table S6: ^{1}H and ^{13}C NMR data (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C, D_2O, 25 °C) for 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)- 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**9**)

	Atom	δ_C	m.	δ_H	n_H	m.	*J*[Hz]
spacer	**1'**	68.98	T	3.774	1	ddd	11.4, 5.6, 3.0
				3.49[a]	1	m	
	2'	50.56	T	3.21[a]	1	m	
				3.153	1	ddd	13.8, 5.6, 3.0
Glc^{A}	**1**	101.13	D	4.309	1	d	8.3
	2	55.13	D	3.47[a]	1	m	
	3	72.67	D	3.42[a]	1	m	
	4	79.40	D	3.35[a]	1	m	
	5	74.76	D	3.25[a]	1	m	
	6	60.28	T	3.59[a]	1	m	
				3.38[a]	1	m	
	2-CO	174.90	S	-			
	2-Ac	22.46	Q	1.772	3	s	
Glc^{B} *	**1**	101.43	D	4.309, 4.314	4	d	8.3
	2	55.23, 55.25	D	3.48[a]	4	m	
Glc^{C} *	**3**	72.25, 72.31	D	3.45[a], 3.46[a]	4	m	
	4	79.12, 79.33	D	3.38[a] ,3.38[a]	4	m	
Glc^{D} *	**5**	74.73	D	3.29[a]	4	m	
	6	60.14, 60.19	T	3.58[a]	4	m	
Glc^{E} *				3.38[a]	4	m	
	2-CO	174.81, 174.84	S	-			
	2-Ac	22.32	Q	1.792, 1.797	12	s	
Glc^{F}	**1**	101.65	D	4.322	1	d	8.3
	2	55.78	D	3.47[a]	1	m	
	3	73.62	D	3.308	1	dd	10.4, 8.4
	4	69.90	D	3.200	1	dd	9.8, 8.4
	5	76.10	D	3.22[a]	1	m	
	6	60.73	T	3.654	1	dd	12.4, 2.0
				3.47[a]	1	m	
	2-CO	174.80	S	-	0		
	2-Ac	22.32	Q	1.801	3	s	

[a] ... HSQC readout

* ... data of individual GlcNAc units cannot be distinguished due to the strong signal overlap and the poor quality of ^{13}C NMR spectrum

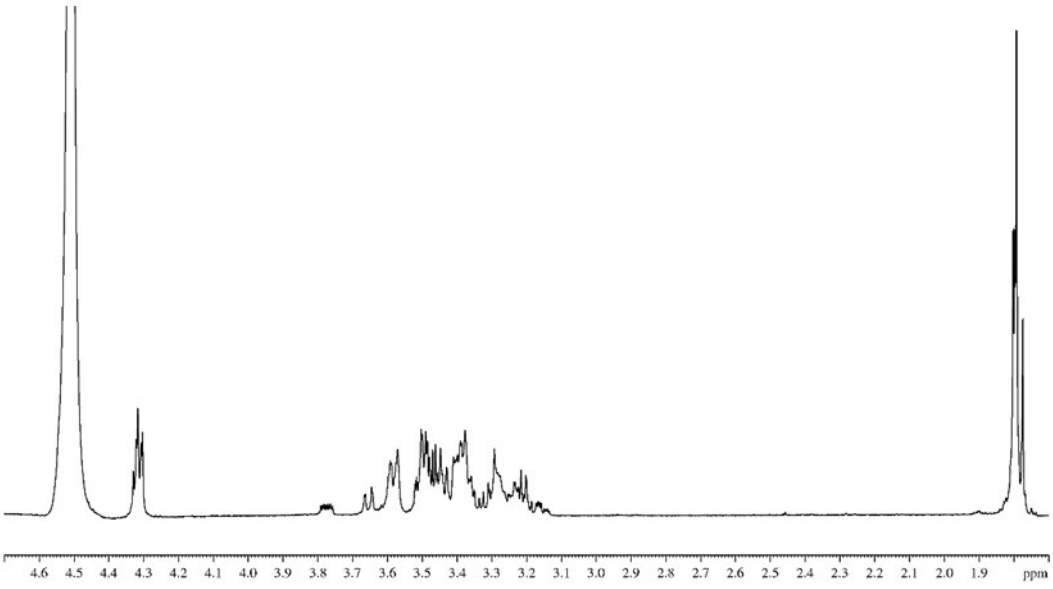

Fig. S6a. ^{1}H NMR spectrum of compound **9**.

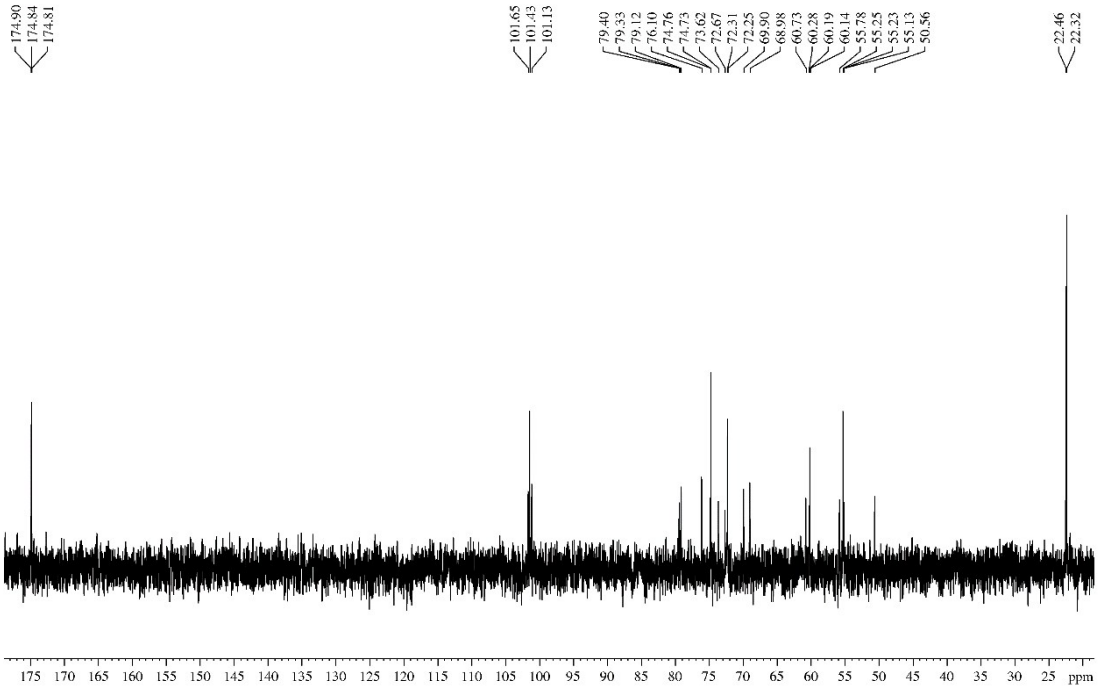

Fig. S6b. ^{13}C NMR spectrum of compound **9**.

1.2. MS spectra

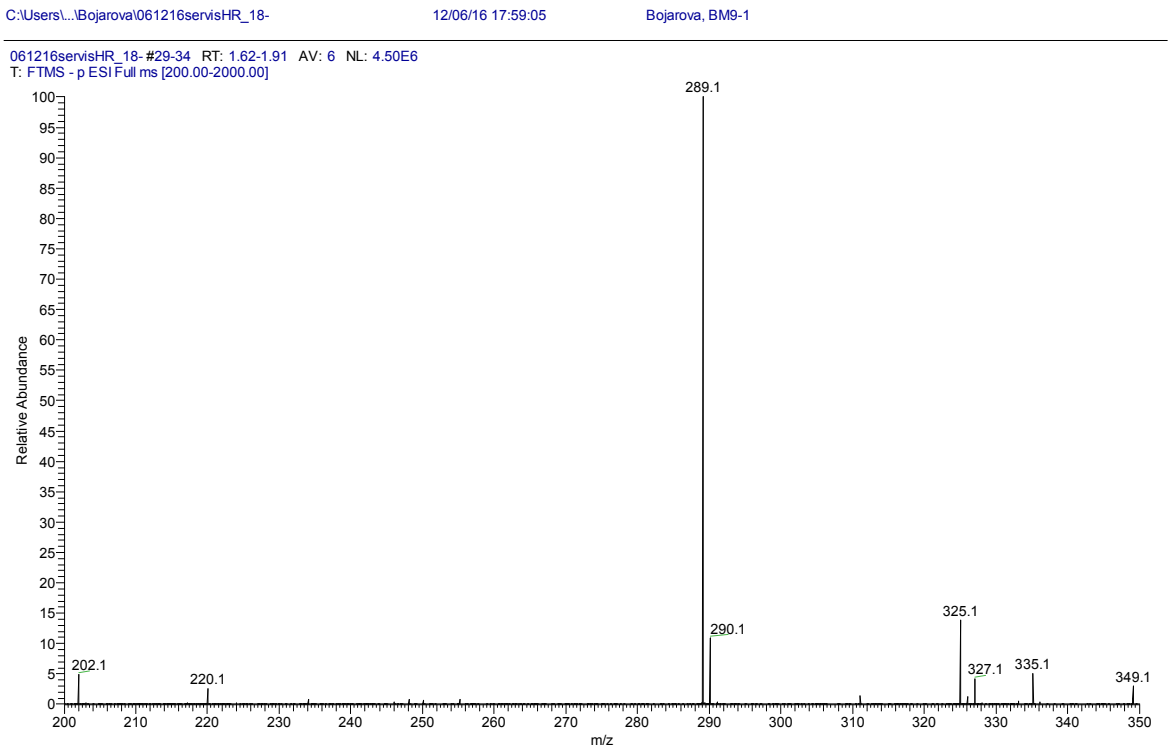

Fig. S7. MS spectrum (ESI-) of compound **3** ([M - H]$^-$, *m/z* 289.1; [M + Cl]$^-$, *m/z* 325.1; [M + HCOO]$^-$, *m/z* 335.1; [M + CH_3COO]$^-$, *m/z* 349.1).

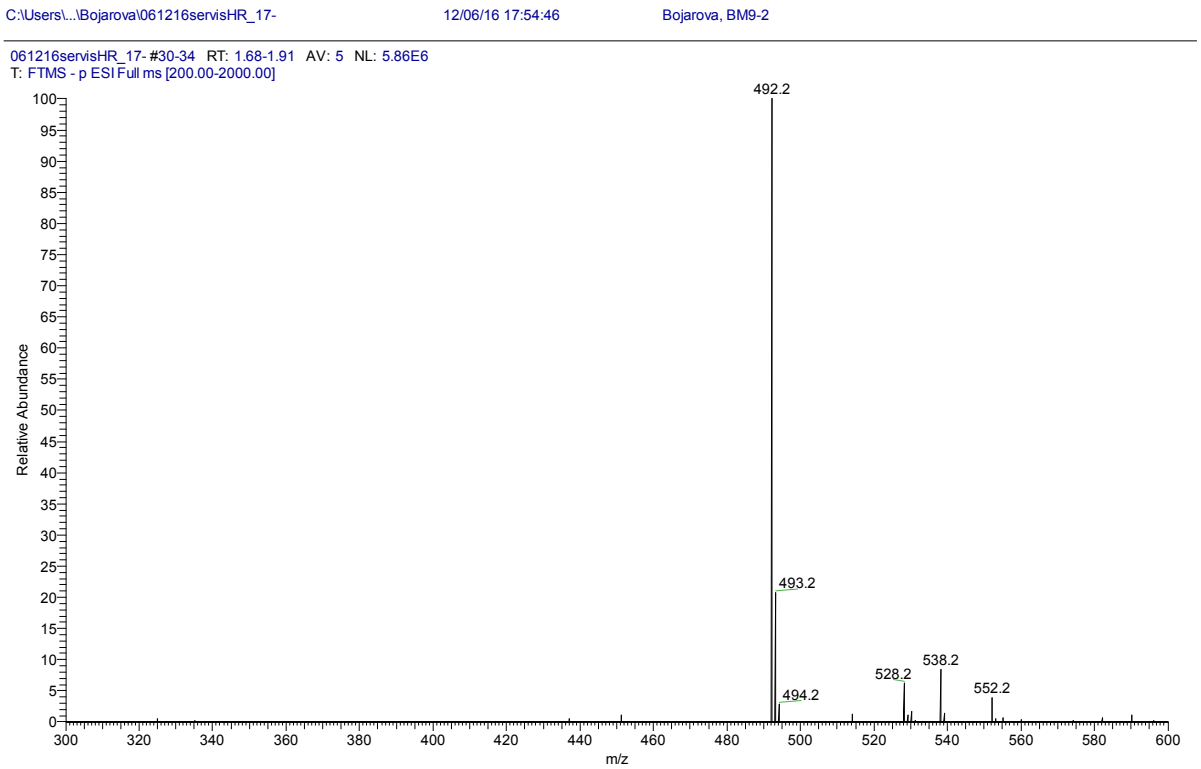

Fig. S8. MS spectrum (ESI-) of compound **5** ([M - H]$^-$, *m/z* 492.2; [M + Cl]$^-$, *m/z* 528.2; [M + HCOO]$^-$, *m/z* 538.2; [M + CH_3COO]$^-$, *m/z* 552.2).

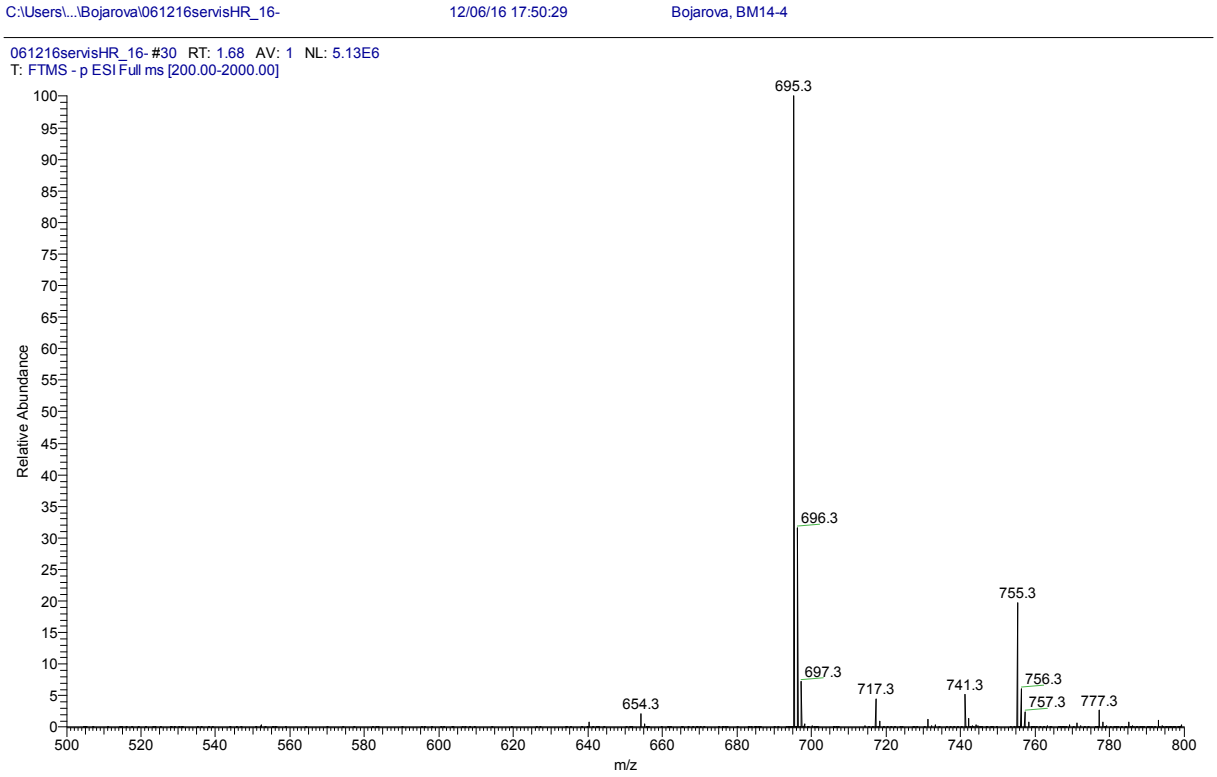

Fig. S9. MS spectrum (ESI-) of compound **6** ([M - H]$^-$, *m/z* 695.3; [M + Na - 2H]$^-$, *m/z* 717.3; [M + HCOO]$^-$, *m/z* 741.3; [M + CH_3COO]$^-$, *m/z* 755.3).

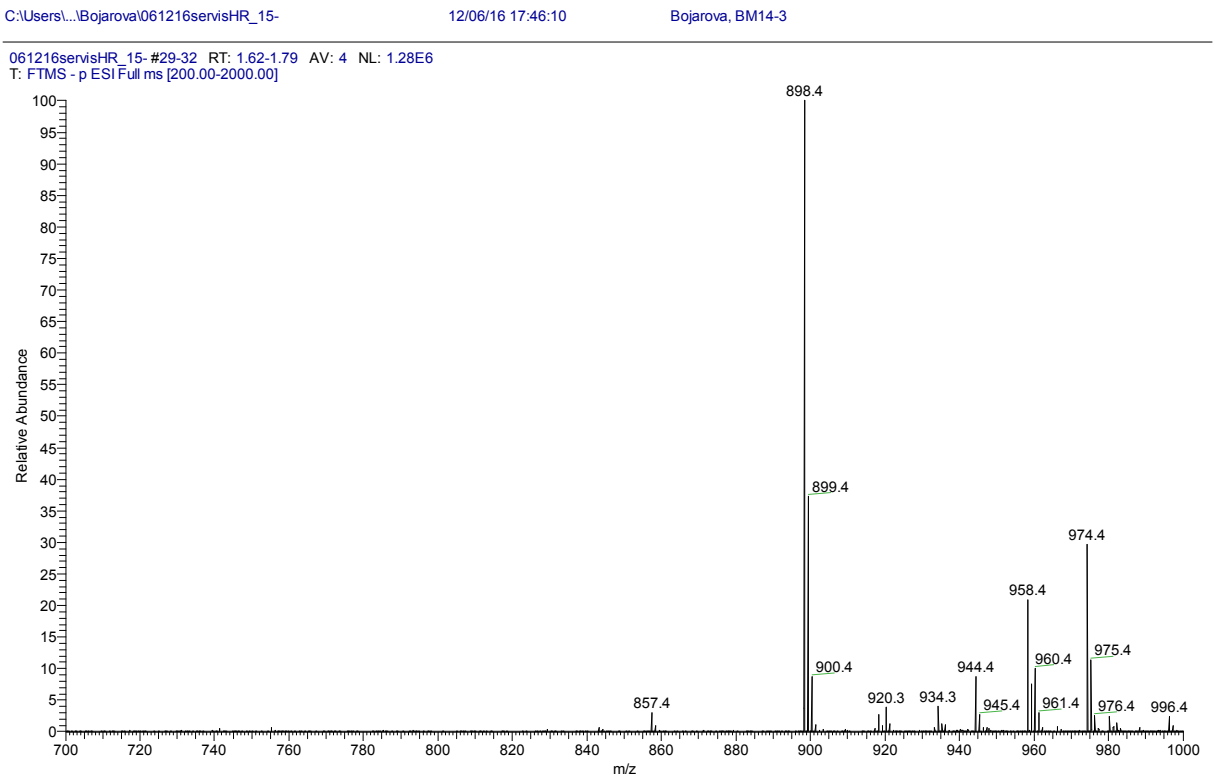

Fig. S10. MS spectrum (ESI-) of compound **7** ([M - H]$^-$, *m/z* 898.4; [M + Na - 2H]$^-$, *m/z* 920.3; [M + Cl]$^-$, *m/z* 934.3; [M + HCOO]$^-$, *m/z* 944.4; [M + CH_3COO]$^-$, *m/z* 958.4; [M + $C_2H_3O_3$]$^-$, *m/z* 958.4).

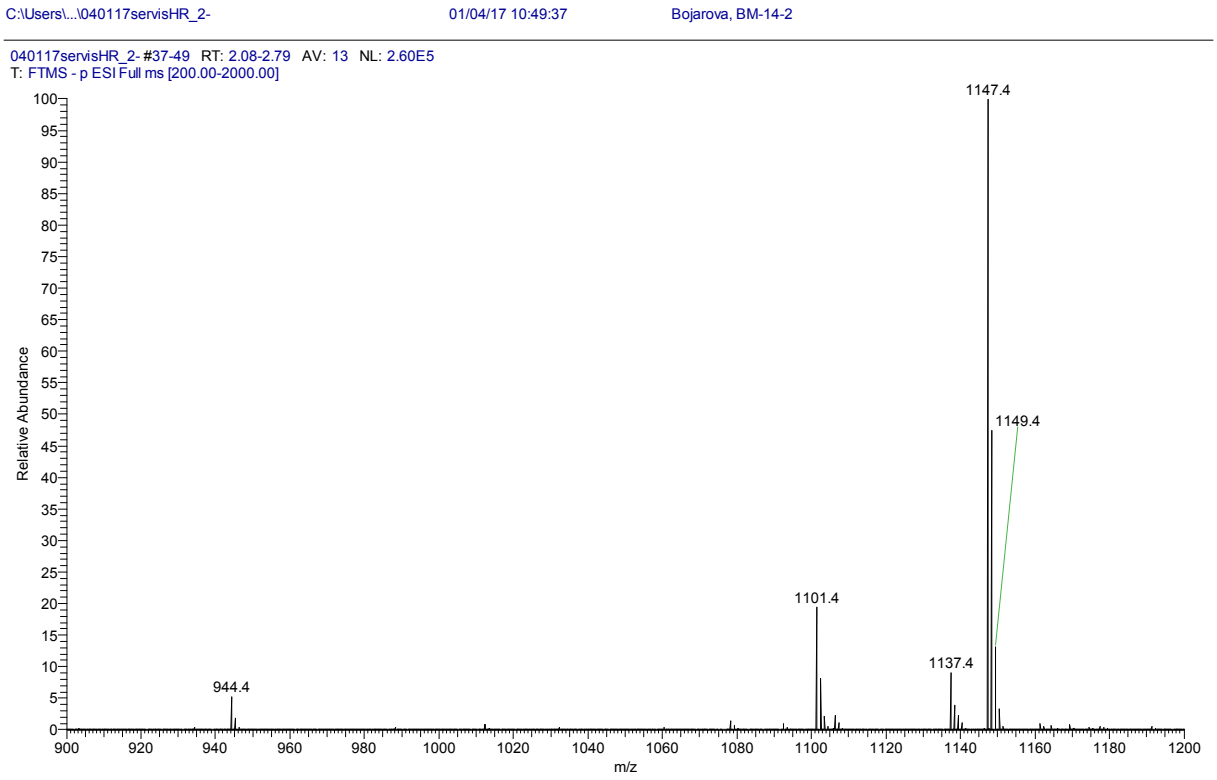

Fig. S11. MS spectrum (ESI-) of compound **8** ([M-H]$^-$, *m/z* 1101.4; [M + Cl]$^-$, *m/z* 1137.4; [M + HCOO]$^-$, *m/z* 1147.4).

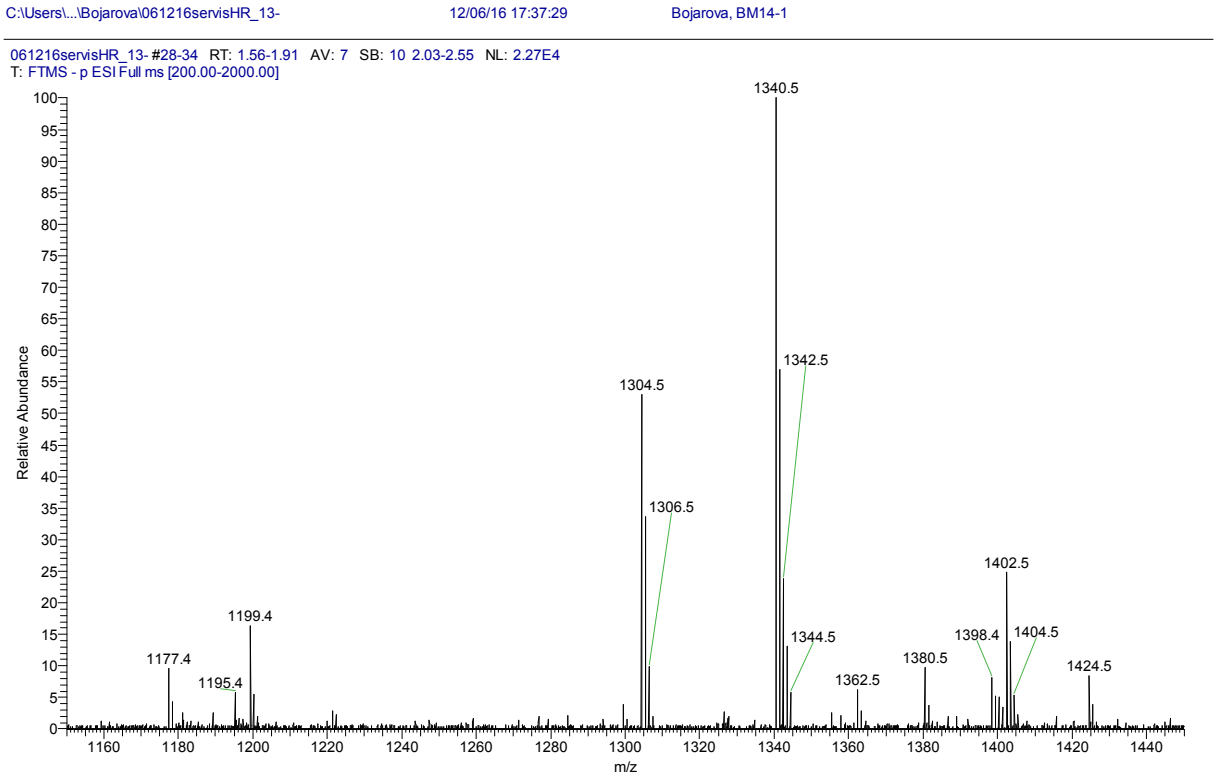

Fig. S12. MS spectrum (ESI-) of compound **9** ([M - H]$^-$, *m/z* 1304.5; [M + Cl]$^-$, *m/z* 1340.5; [M – H + Na + Cl]$^-$, *m/z* 1362.5; [M + $C_2H_3O_3$]$^-$, *m/z* 1380.5; [M + H_2PO_4]$^-$, *m/z* 1402.5; [M + $NaHPO_4$]$^-$, *m/z* 1424.5).

1.3. HPLC chromatograms

The analytical HPLC chromatograms were recorded from analyses on TSKgel Amide-80, 5 µm HILIC column (250 × 4.6 mm, Tosoh Bioscience, DE). Binary gradient elution was used: mobile phase A = 100 % acetonitrile; mobile phase B = water; gradient: 22 % B for 0–7 min, 22–35 % B for 7–20 min; 35 % B for 20–25 min, 35–22 % B for 25–26 min at a flow rate of 1 mL/min at 27 °C; samples were detected at 200 nm.

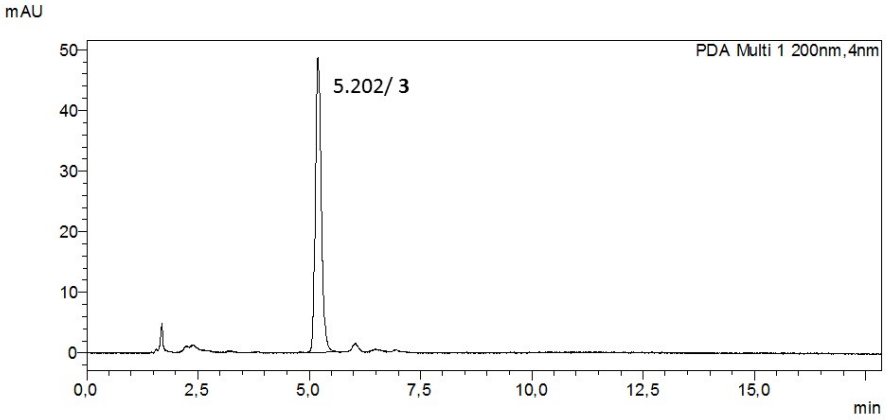

Fig. S13. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**3**); retention time 5.202 min.

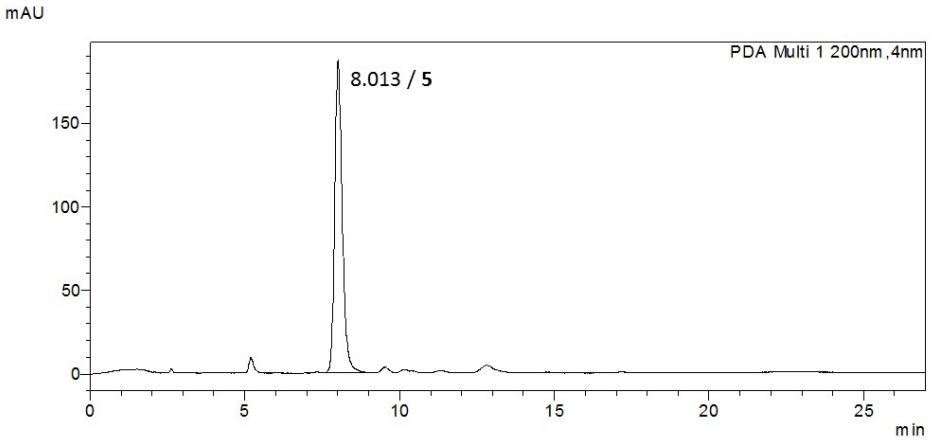

Fig. S14. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**5**); retention time 8.013 min.

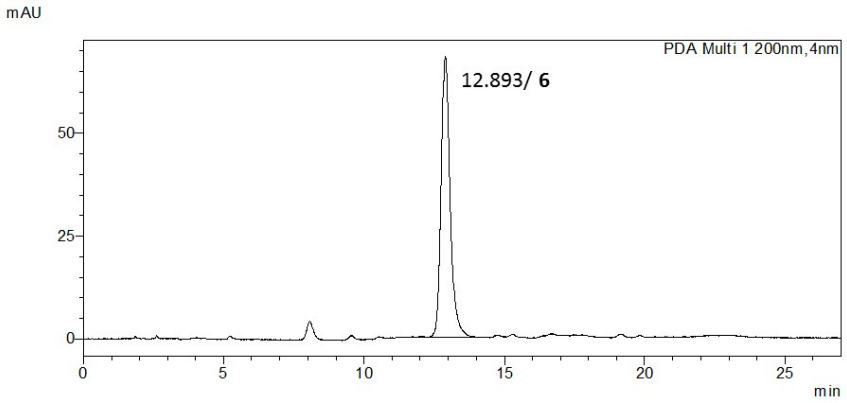

Fig. S15. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**6**); retention time 12.893 min.

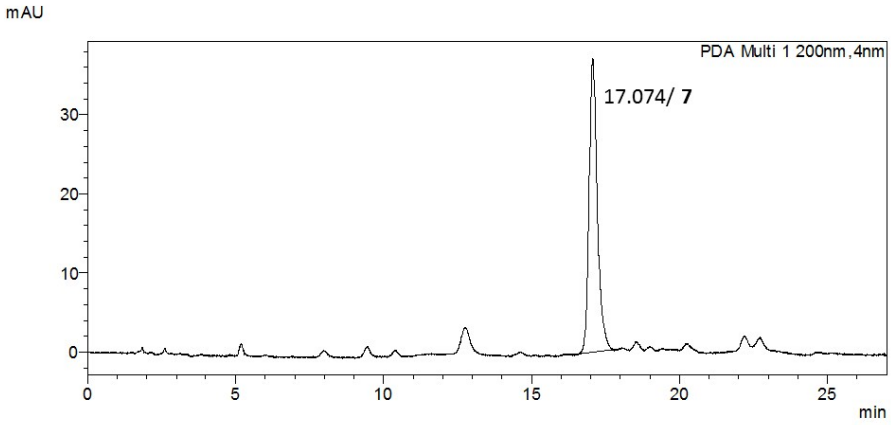

Fig. S16. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**7**); retention time 17.074 min.

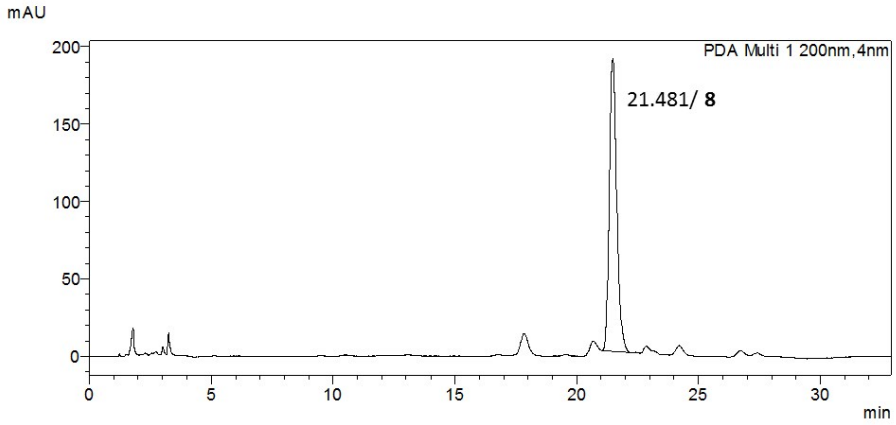

Fig. S17. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**8**); retention time 21.481 min.

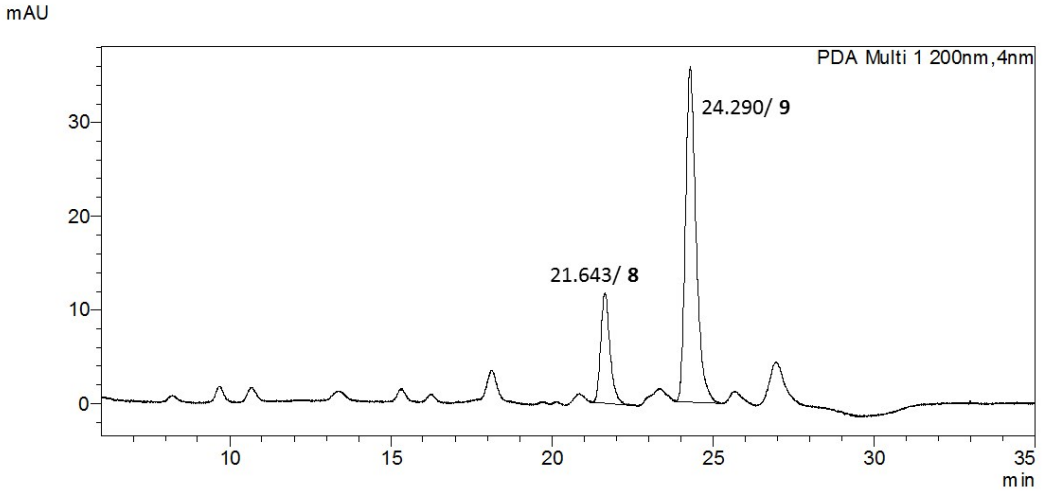

Fig. S18. HPLC chromatogram of 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**9**), containing a small impurity of pentamer **8** (15% related to peak area); retention time 24.290 min.

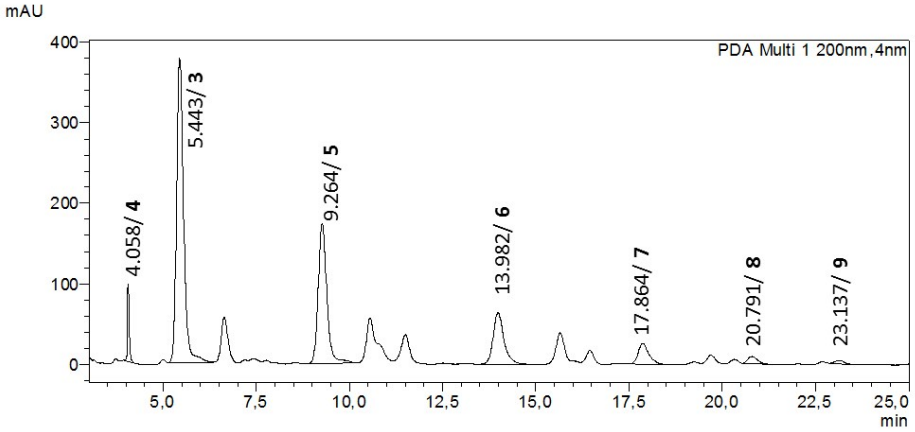

Fig. S19. A sample HPLC chromatogram of a reaction of *p*-nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside donor (**4**) and 2-azidoethyl 2-acetamido-2-deoxy-β-D-glucopyranoside acceptor (**3**) under the catalysis by Tyr70Asn mutant of the β-*N*-acetylhexosaminidase from *T. flavus*, in 50 mM citrate-phosphate buffer pH 5.0 at 35 °C, after 3 h. Functionalized chitooligomer products are detectable in the reaction mixture: dimer **5**, trimer **6**, tetramer **7**, pentamer **8**, and hexamer **9**.

2. Chitooligomer standards 26-29 – structural characterization

NMR data of chitooligomer standards *N*,*N*´-diacetylchitobiose (**26**) to *N*,*N*´,*N*´´,*N*´´´,*N*´´´´- pentaacetylchitopentaose (**29**) were compared with the previously reported data: ref.[1] for compounds **26**-**28**, ref.[2] for compound **29**; a very good agreement was observed for carbon chemical shifts. Due to the strong overlap of proton signals, ^{1}H NMR data are not suitable for unambiguous compound identification; therefore, we quote ^{13}C NMR only. The data for compounds **26**-**29** were measured on a Bruker AVANCE III 700 MHz spectrometer (700.13 MHz for ^{1}H, 176.05 MHz for ^{13}C) in D_2O (100 atom% D, Sigma-Aldrich, Steinheim, Germany) at 298 K.

***N,N´*-diacetylchitobiose (26)**. ^{13}C NMR (176.05 MHz, D_2O, 25 °C): 22.03 (Ac^A α), 22.27 (Ac^B), 22.33 (Ac^A β), 53.78 (C-2^A α), 55.74 (C-2^B β), 55.76 (C-2^B α), 56.23 (C-2^A β), 60.20 (C-6^A α), 60.33 (C-6^A β), 60.68 (C-6^B),69.45 (C-3^A α), 69.85 (C-4^B β), 69.87 (C-4^B α), 70.12 (C-5^A α), 72.70 (C-3^A β), 73.62 (C-3^B β), 73.63 (C-3^B α), 74.73 (C-5^A β), 76.05 (C-5^B α), 76.06 (C-5^B β), 79.56 (C-4^A β), 80.01 (C-4^A α), 90.59 (C-1^A α), 94.98 (C-1^A β), 101.64 (C-1^B β), 101.65 (C-1^B α), 174.63 (CO^A α), 174.76 (CO^B α), 174.78 (CO^B β), 174.90 (CO^A β).

***N,N´,N´´*- triacetylchitotriose (27)**. ^{13}C NMR (176.05 MHz, D_2O, 25 °C): 22.04 (Ac^A α), 22.27 (Ac^B, Ac^C), 22.33 (Ac^A β), 53.80 (C-2^A α), 55.18 (C-2^B β), 55.20 (C-2^B α), 55.74 (C-2^C), 56.27 (C-2^A β), 60.13 (C-6^B), 60.16 (C-6^A α), 60.28 (C-6^A β), 60.69 (C-6^C),69.40 (C-3^A α), 69.86 (C-4^C), 70.17 (C-5^A α), 72.30 (C-3^B β), 72.32 (C-3^B α), 72.63 (C-3^A β), 73.62 (C-3^C), 74.65 (C-5^B α), 74.67 (C-5^B β), 74.77 (C-5^A β), 76.07 (C-5^C), 79.27 (C-4^A β), 79.31 (C-4^B), 79.78 (C-4^A α), 90.60 (C-1^A α), 94.98 (C-1^A β), 101.42 (C-1^B β), 101.44 (C-1^B α), 101.62 (C-1^C), 174.63 (CO^A α), 174.75 (CO^B α), 174.76 (CO^B β), 174.79 (CO^C), 174.89 (CO^A β).

***N,N´,N´´,N´´´*- tetraacetylchitotetraose (28)**. ^{13}C NMR (176.05 MHz, D_2O, 25 °C): 22.04 (Ac^A α), 22.27 (Ac^B, Ac^C, Ac^D), 22.33 (Ac^A β), 53.80 (C-2^A α), 55.17 (C-2^C), 55.21 (C-2^B β), 55.23 (C-2^B α), 55.74 (C-2^D), 56.27 (C-2^A β), 60.09 (C-6^B), 60.13 (C-6^C), 60.16 (C-6^A α), 60.28 (C-6^A β), 60.69 (C-6^D),69.40 (C-3^A α), 69.86 (C-4^D), 70.16 (C-5^A α), 72.23 (C-3^B β), 72.24 (C-3^B α), 72.29 (C-3^C), 72.63 (C-3^A β), 73.60 (C-3^D), 74.67 (C-5^C), 74.68 (C-5^B α), 74.70 (C-5^B β), 74.76 (C-5^A β), 76.07 (C-5^D), 79.04 (C-4^B β), 79.07 (C-4^B α), 79.29 (C-4^C), 79.33 (C-4^A β), 79.78 (C-4^A α), 90.60 (C-1^A α), 94.98 (C-1^A β), 101.40 (C-1^C), 101.42 (C-1^B β), 101.44 (C-1^B α), 101.62 (C-1^D), 174.63 (CO^A α), 174.74 (CO^B α), 174.75 (CO^B β), 174.77 (CO^C), 174.79 (CO^D), 174.89 (CO^A β).

***N,N´,N´´,N´´´,N´´´´*- pentaacetylchitopentaose (29)**. ^{13}C NMR (176.05 MHz, D_2O, 25 °C): 22.03 (Ac^A α), 22.27 (Ac^B, Ac^C, Ac^D, Ac^E), 22.33 (Ac^A β), 53.80 (C-2^A α), 55.17 (C-2^D), 55.20 (C-2^B β, C-2^C), 55.23 (C-2^B α), 55.74 (C-2^E), 56.27 (C-2^A β), 60.09 (C-6^B, C-6^C), 60.13 (C-6^D), 60.16 (C-6^A α), 60.28 (C-6^A β), 60.69 (C-6^E),69.40 (C-3^A α), 69.85 (C-4^E), 70.16 (C-5^A α), 72.21 (C-3^C), 72.22 (C-3^B β), 72.24 (C-3^B α), 72.28 (C-3^D), 72.63 (C-3^A β), 73.59 (C-3^E), 74.66, 74.67 (C-5^C, C-5^D), 74.69, 74.70 (C-5^B α, C-5^B β), 74.75 (C-5^A β), 76.06 (C-5^E), 79.05 (C-4^B β, C-4^C), 79.08 (C-4^B α), 79.29 (C-4^D), 79.32 (C-4^A β), 79.78 (C-4^A α), 90.61 (C-1^A α), 94.99 (C-1^A β), 101.40 (C-1^C, C-1^D), 101.42 (C-1^B β), 101.44 (C-1^B α), 101.62 (C-1^E), 174.62 (CO^A α), 174.74 (CO^B α), 174.75 (CO^B β), 174.76, 174.77 (CO^C, CO^D), 174.78 (CO^E), 174.89 (CO^A β).

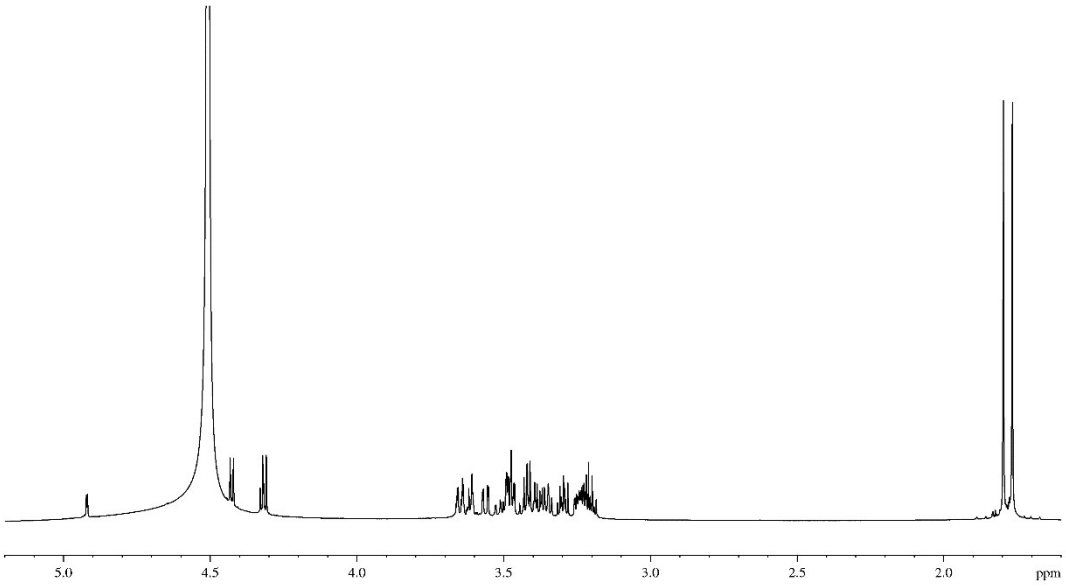

Fig. S20a. ^{1}H NMR spectrum of compound **26.**

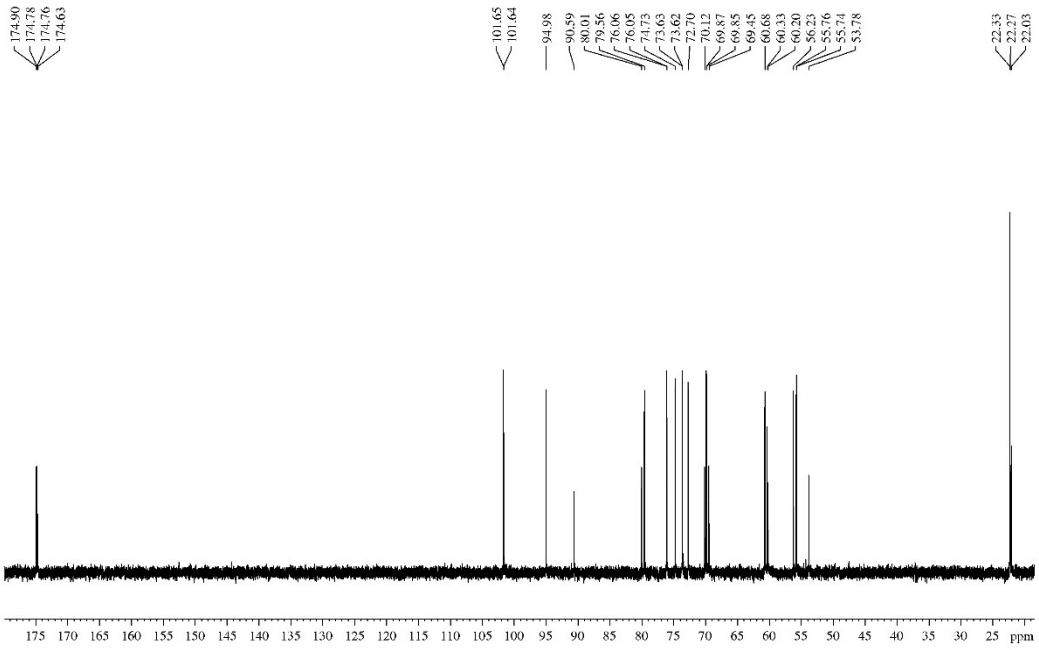

Fig. S20b. ^{13}C NMR spectrum of compound **26**.

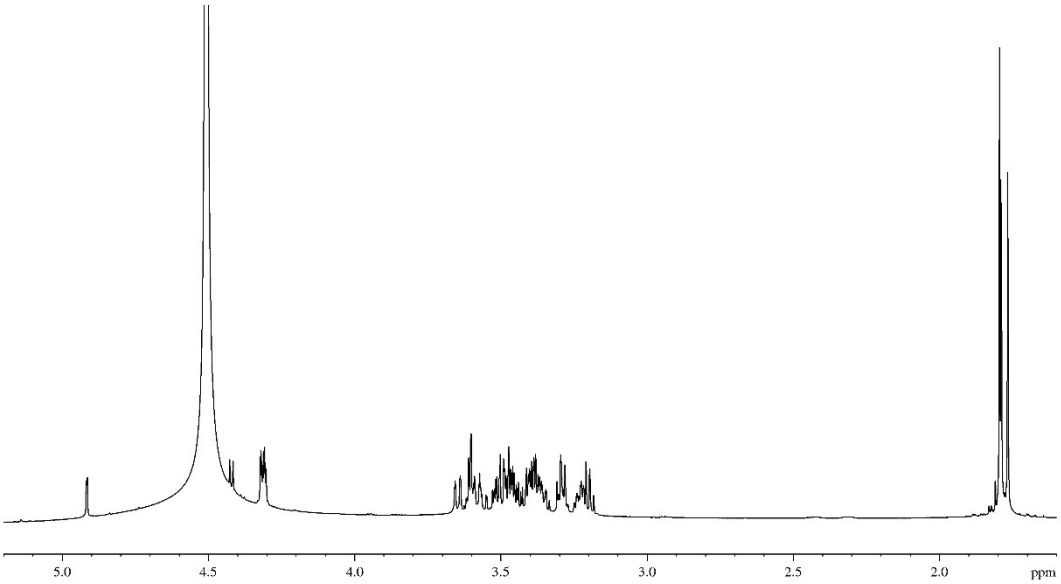

Fig. S21a. ^{1}H NMR spectrum of compound **27**.

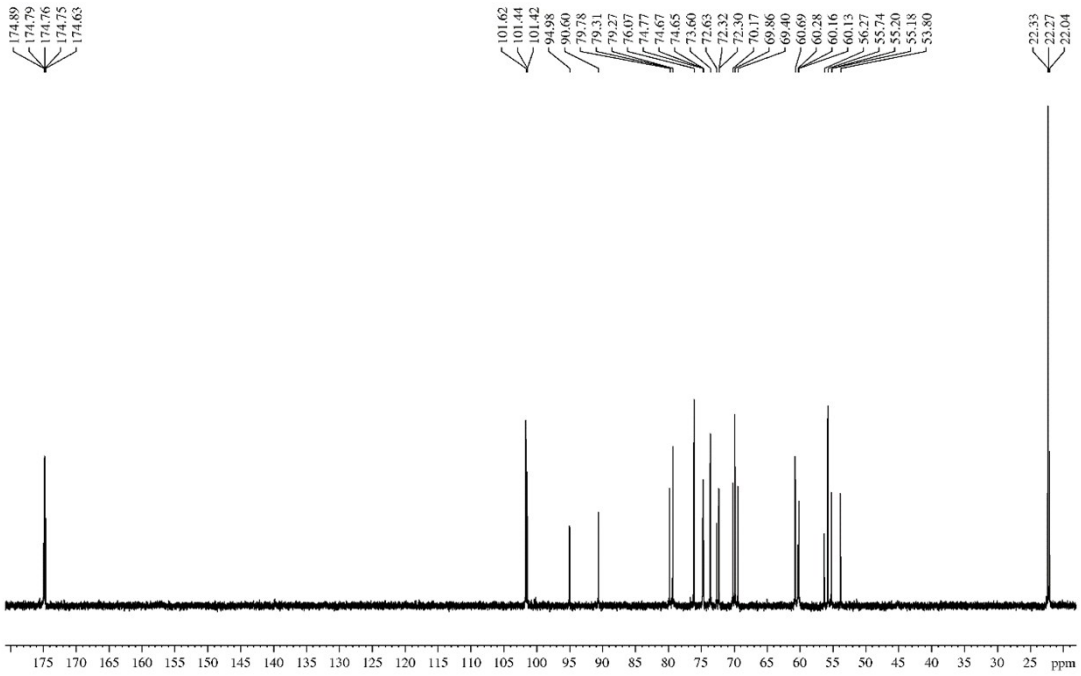

Fig. S21b. ^{13}C NMR spectrum of compound **27**.

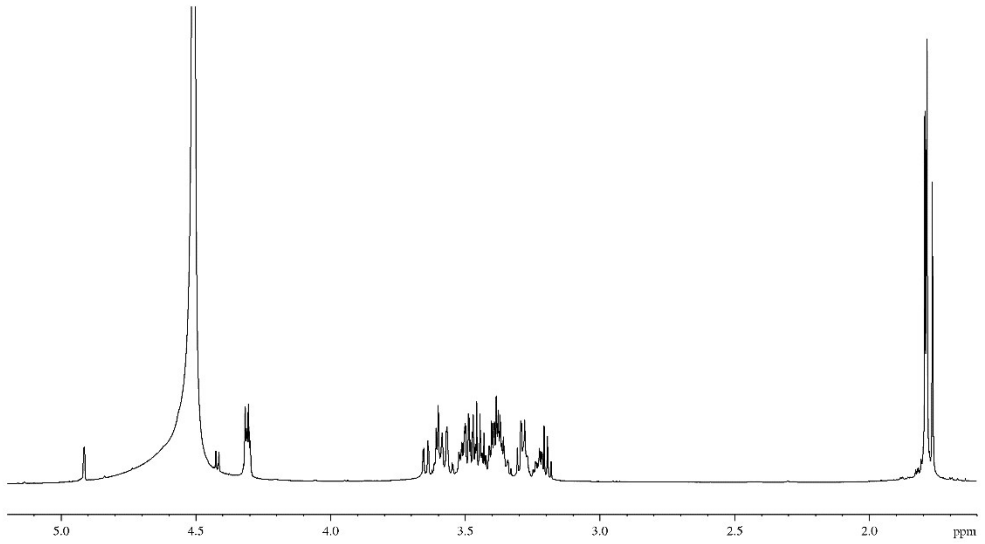

Fig. S22a. ^{1}H NMR spectrum of compound **28**.

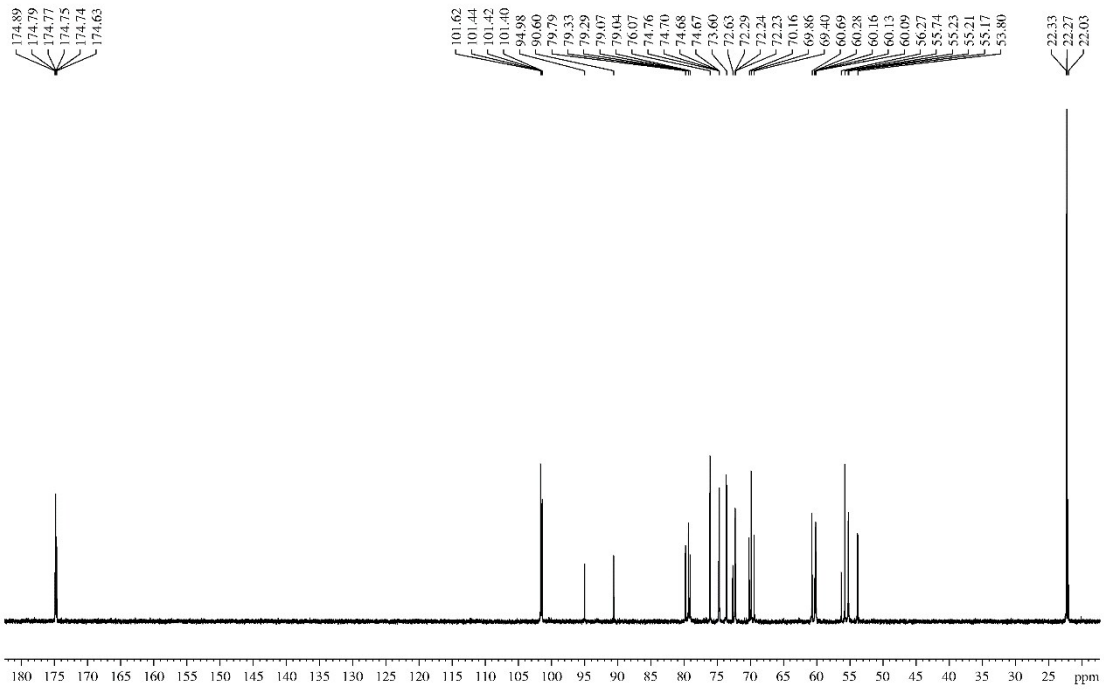

Fig. S22b. ^{13}C NMR spectrum of compound **28**.

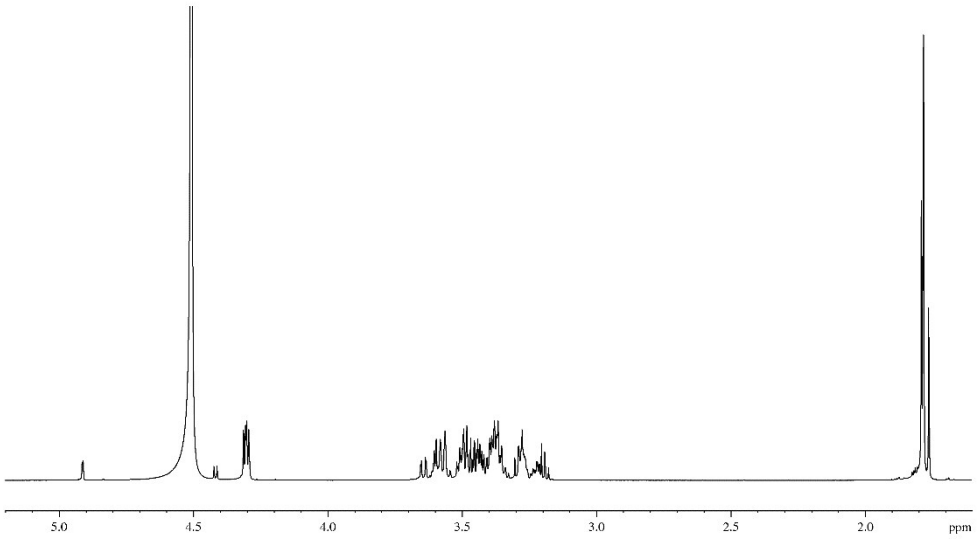

Fig. S23a. ^{1}H NMR spectrum of compound **29**.

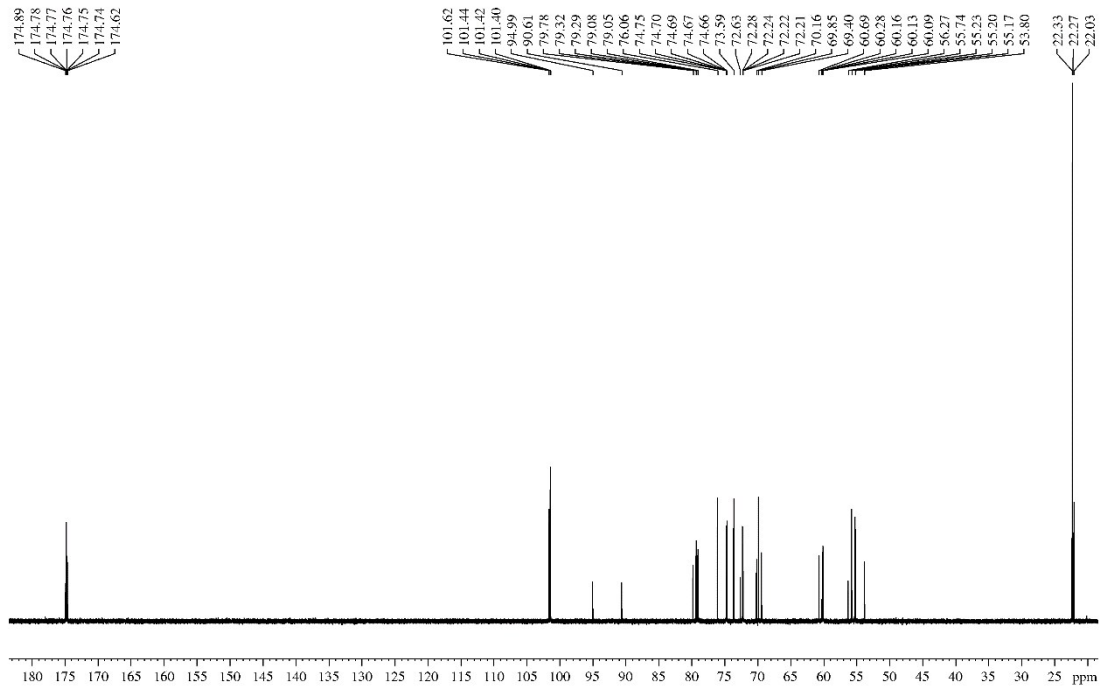

Fig. S23b. ^{13}C NMR spectrum of compound **29**.

3. Glycopolymers 13-25

3.1. Synthesis of polymer precursors 12a, 12b

Polymer precursor 12a. HPMA (**10**, 800 mg, 5.59 mmol) was dissolved in of *tert*-butyl alcohol (5.52 mL) and mixed with a solution of MA-AP-TT (**11**, 160 mg, 0.621 mmol), AIBN (4.97 mg, 17.7 µmol), and 2-cyanopropan-2-yl dithioate (7.84 mg, 35.5 µmol) in DMSO (1.38 mL, corresponds to 0.9 M solution of monomers). The reaction mixture was poured into a glass ampoule, bubbled with argon and sealed. After 16 h in a thermostat controlled water bath at 70°C, the ampoule was cooled, and the reaction mixture was poured into an excess of acetone (150 mL). The precipitate was filtered off and purified by re-precipitation from methanol (6 mL) into the mixture of acetone and diethyl ether (3:1; 120 mL). The copolymer intermediate (730 mg, 76 %; M_w = 22,900 g/mol, M_n = 20,600 g/mol, $Đ$ = 1.11) was filtered off and dried under vacuum.

For the removal of the dithiobenzoate end group, the copolymer intermediate (700 mg) and AIBN (70 mg) were dissolved in DMSO (5 mL), poured into a glass ampoule, bubbled with argon and sealed. After 2 h in a thermostat controlled water bath at 80 °C, the ampoule was cooled, and the copolymer was isolated by precipitation into acetone (150 mL). The precipitate was filtered off and purified by re-precipitation from methanol (6 mL) into the mixture of acetone and diethyl ether (3:1; 120 mL). The copolymer without terminal groups (621 mg) was filtered off and dried under vacuum.

For aminolysis, propargylamine (41 µL, 0.662 mmol) and DIPEA (111 µL, 0.662 mmol) were added to the stirred solution of the copolymer without terminal end-groups (616 mg) in dimethylformamide (6.2 mL). The reaction was carried out at 24 °C for 16 h. The polymer was purified by gel filtration on a column packed with Sephadex LH-20 (2.5×30 cm; GE Healthcare) in methanol mobile phase using UV detection. The polymer-containing fraction was concentrated *in vacuo* to 6 mL, and the polymer precursor **12a** was isolated by precipitation into an excess of acetone (120 mL), followed by filtration and drying under vacuum. Yield: 578 mg; M_w = 21,800 g/mol, M_n = 20,200 g/mol, $Đ$ = 1.08.

Polymer precursor 12b. HPMA (**10**, 300 mg, 2.10 mmol) was dissolved in of *tert*-butyl alcohol (2.33 mL) and mixed with a solution of MA-AP-TT (135 mg, 0.524 mmol), AIBN (2.10 mg, 7.48 µmol), and 2-cyanopropan-2-yl dithioate (3.31 mg, 15 µmol) in DMSO (0.58 mL, corresponds to 0.9 M solution of monomers). The reaction mixture was poured into a glass ampoule, bubbled with argon and sealed. After 16 h in a thermostat controlled water bath at 70°C, the ampoule was cooled, and the reaction mixture was poured into an excess of acetone (70 mL). The precipitate was filtered off and purified by re-precipitation from methanol (3 mL) into the mixture of acetone and diethyl ether (3:1; 60 mL). The copolymer intermediate (309 mg, 71 %; M_w = 24,700 g/mol, M_n = 21,900 g/mol, $Đ$ = 1.13) was filtered off and dried under vacuum.

For the removal of the dithiobenzoate end group, the copolymer intermediate (300 mg) and AIBN (30 mg) were dissolved in DMSO (2.1 mL), poured into a glass ampoule, bubbled with argon and sealed. After 2 h in a thermostat controlled water bath at 80 °C, the ampoule was cooled, and the copolymer was isolated by precipitation into acetone (60 mL). The precipitate was filtered off and purified by re-precipitation from methanol (2.5 mL) into the mixture of acetone and diethyl ether (3:1; 60 mL). The copolymer without terminal groups (243 mg) was filtered off and dried under vacuum.

For aminolysis, propargylamine (29 µL, 0.447 mmol) and DIPEA (78 µL, 0.447 mmol) were added to the stirred solution of the copolymer without terminal end-groups (238 mg) in dimethylformamide (2.4 mL). The reaction was carried out at 24 °C for 16 h. The polymer was purified by gel filtration on a column packed with Sephadex LH-20 (1.5×30 cm, GE Healthcare) in methanol mobile phase using UV detection. The polymer-containing fraction was concentrated *in vacuo* to 2.5 mL, and the polymer precursor **12b** was isolated by precipitation into an excess of acetone (50 mL), followed by filtration and drying under vacuum. Yield: 207 mg; M_w = 22,800 g/mol, M_n = 21,000 g/mol, $Đ$ = 1.09.

3.2. NMR spectra of glycopolymers and their polymer precursors

Glycopolymers and their polymer precursors were measured with Bruker Avance III 600 spectrometer operating at 600.2 MHz with DMSO-d_6 or D_2O as a solvent. The width of 90° pulse was 10 µs with relaxation delay 10 s. The acquisition time was 3.63 s with 200 scans.

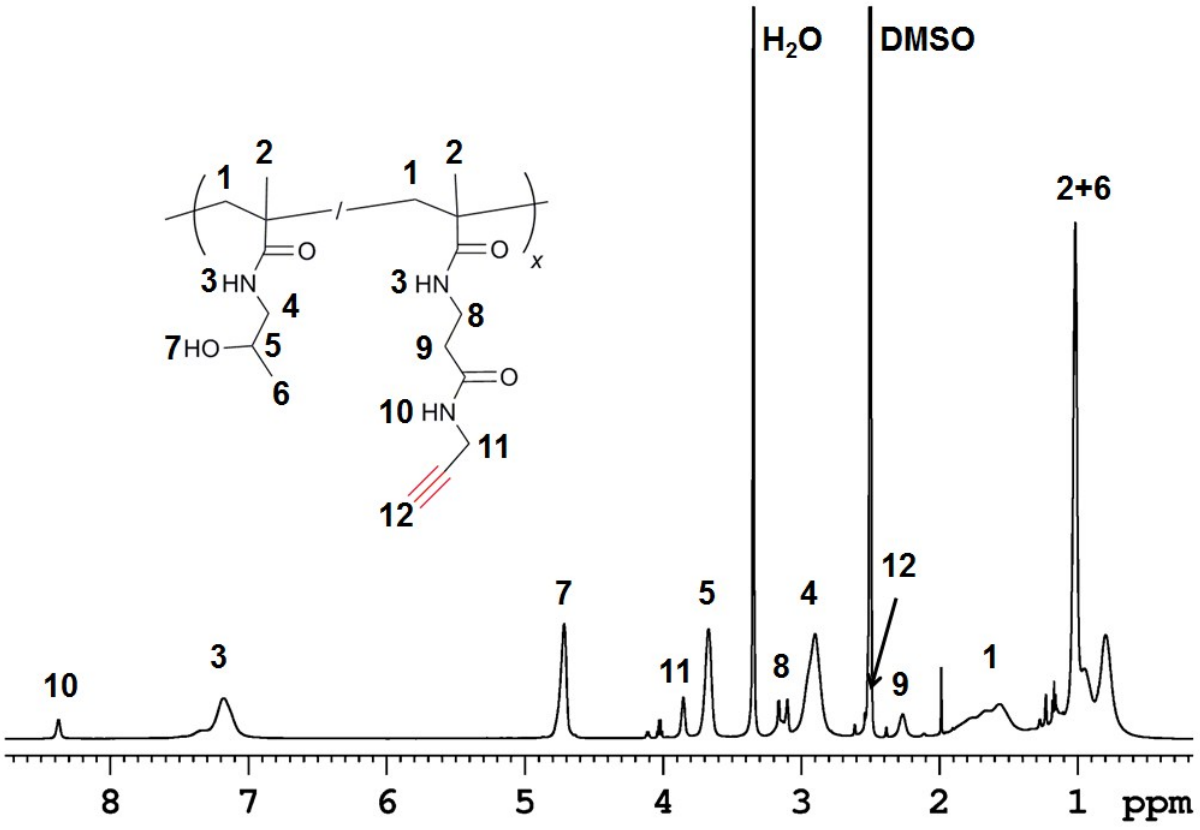

Fig. S24. ^{1}H NMR spectrum of polymer precursor **12a** in DMSO-d_6.

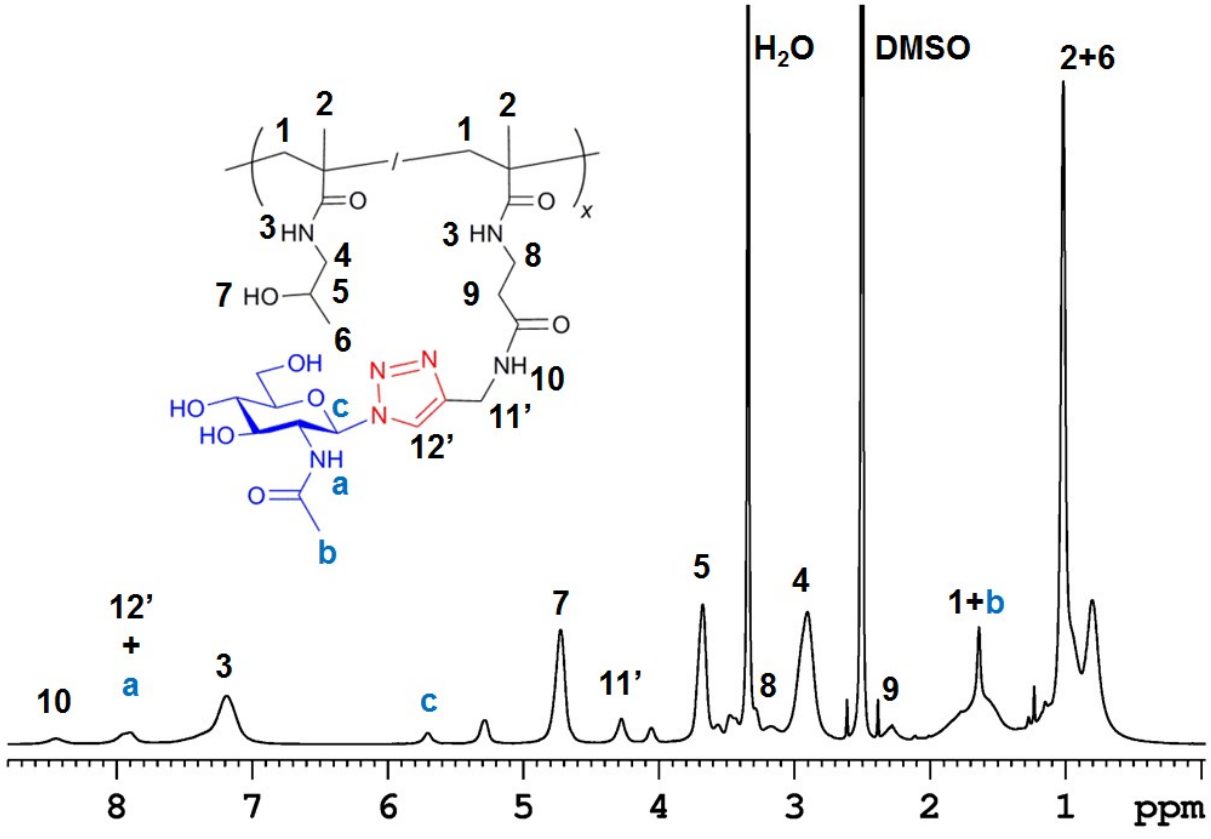

Fig. S25. ^{1}H NMR spectrum of glycopolymer **14** in DMSO-d_6.

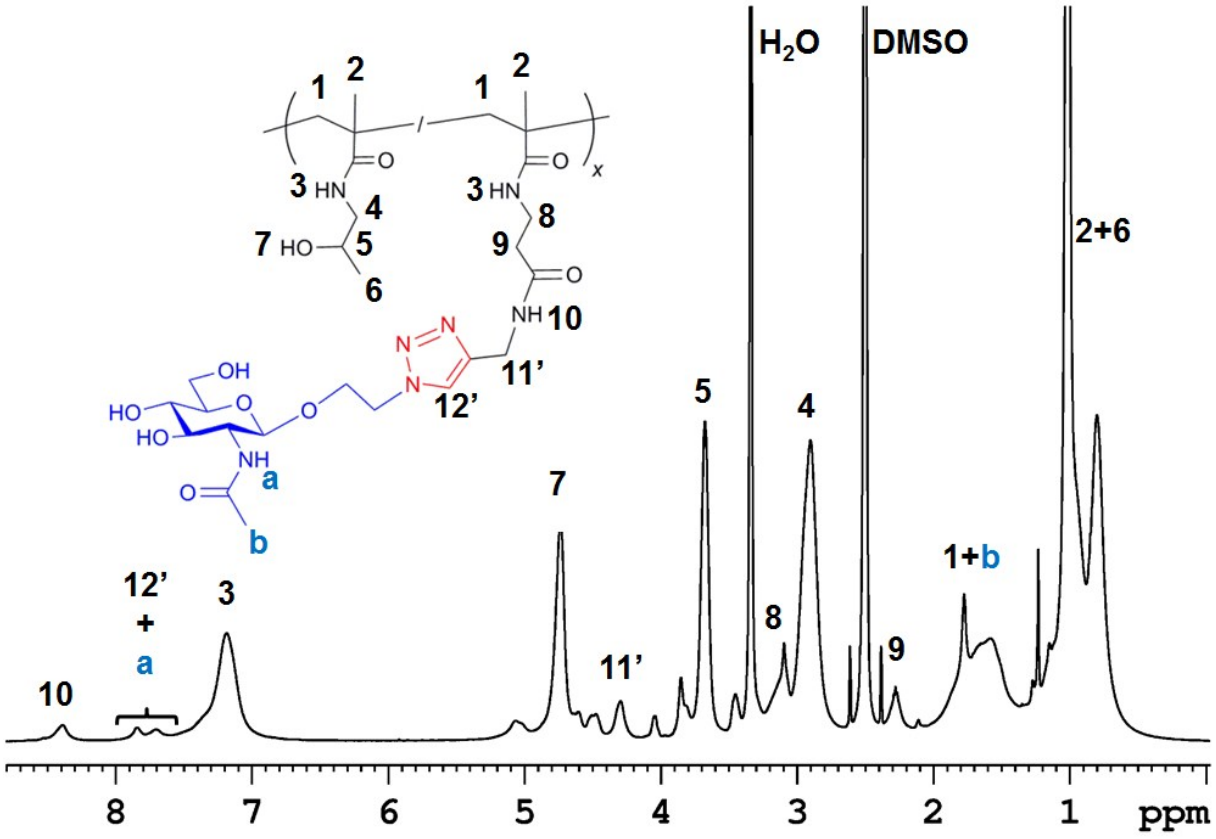

Fig. S26. ^{1}H NMR spectrum of glycopolymer **16** in DMSO-d_6.

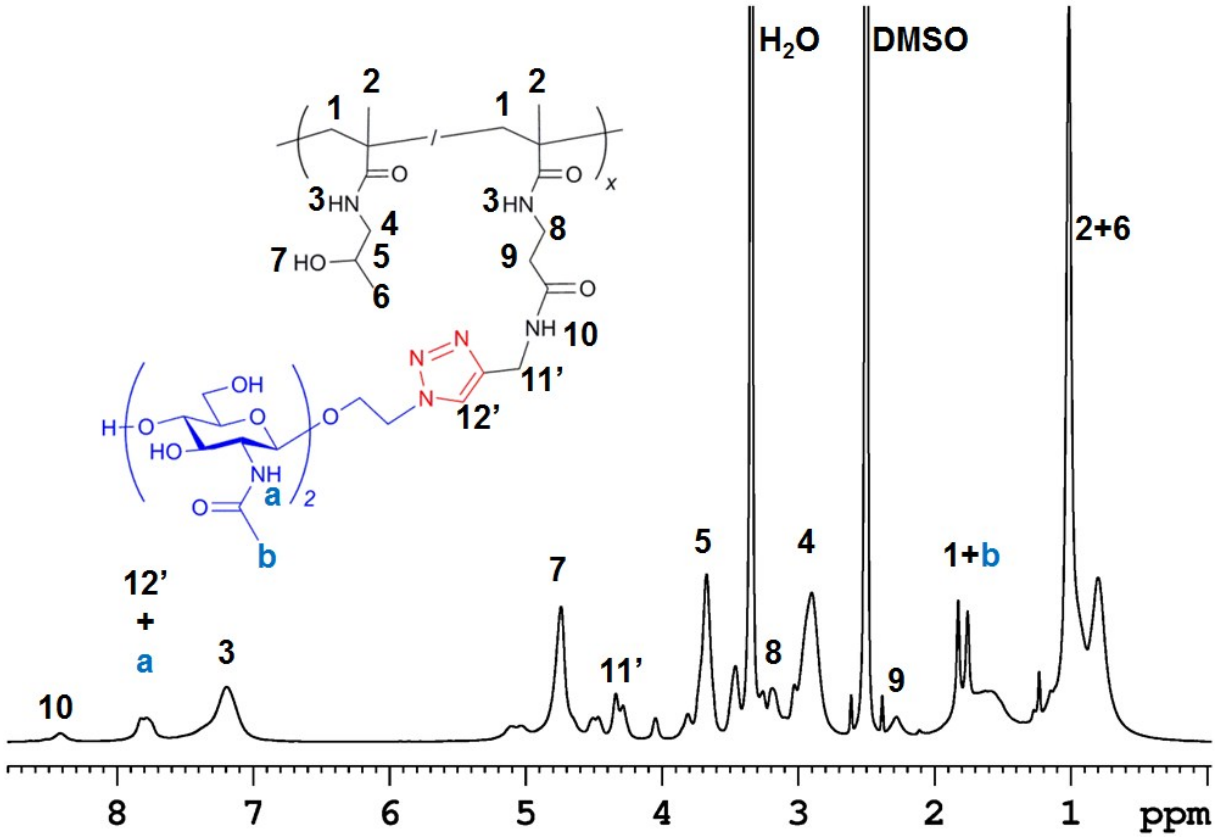

Fig. S27. ^{1}H NMR spectrum of glycopolymer **20** in DMSO-d_6.

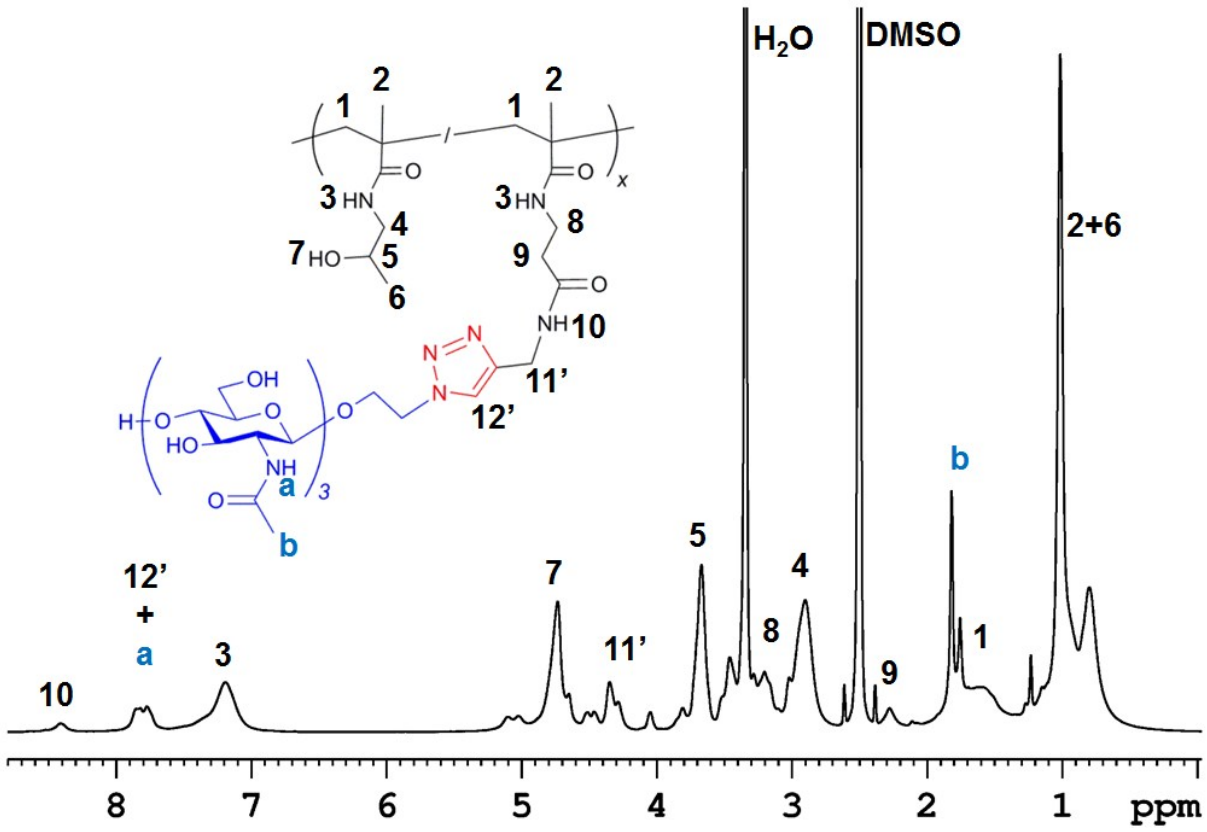

Fig. S28. ^{1}H NMR spectrum of glycopolymer **22** in DMSO-d_6.

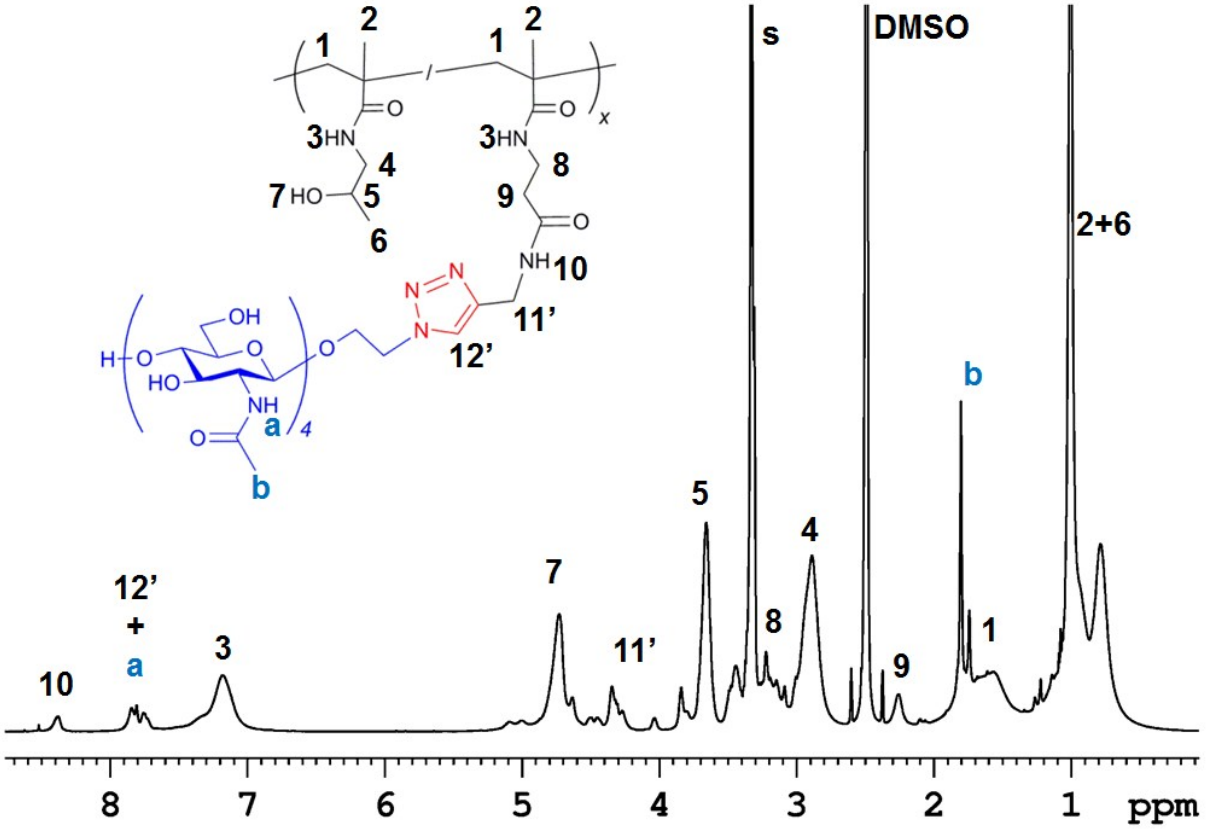

Fig. S29a. ^{1}H NMR spectrum of glycopolymer **24** in DMSO-d_6.

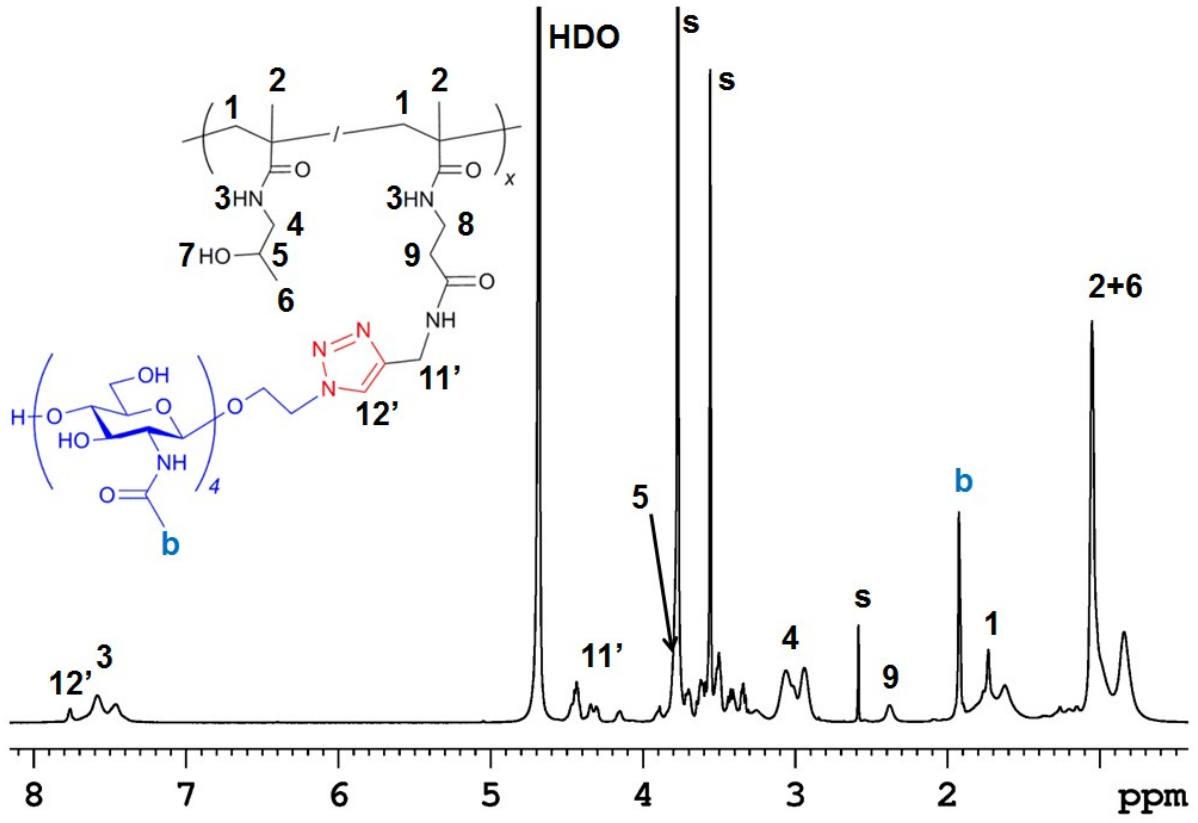

Fig. S29b. ^{1}H NMR spectrum of glycopolymer **24** in D_2O.

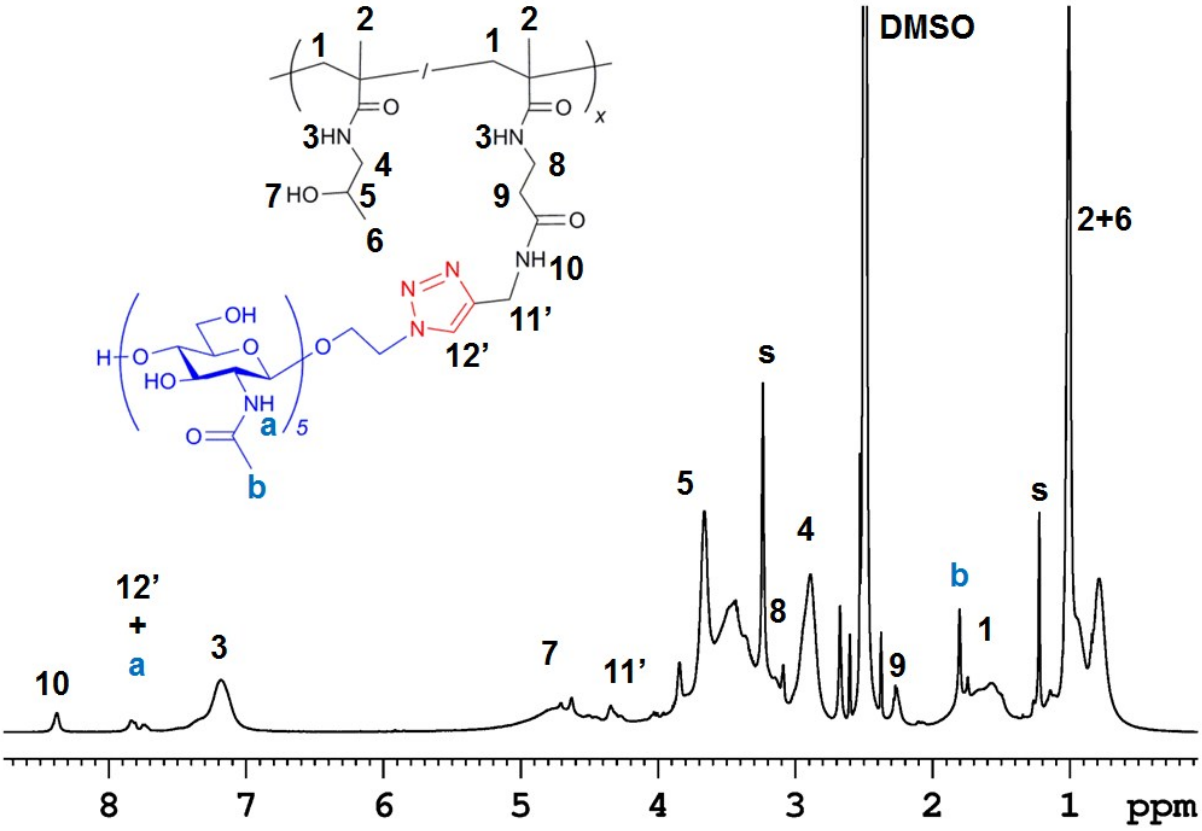

Fig. S30a. ^{1}H NMR spectrum of glycopolymer **25** in DMSO-d_6.

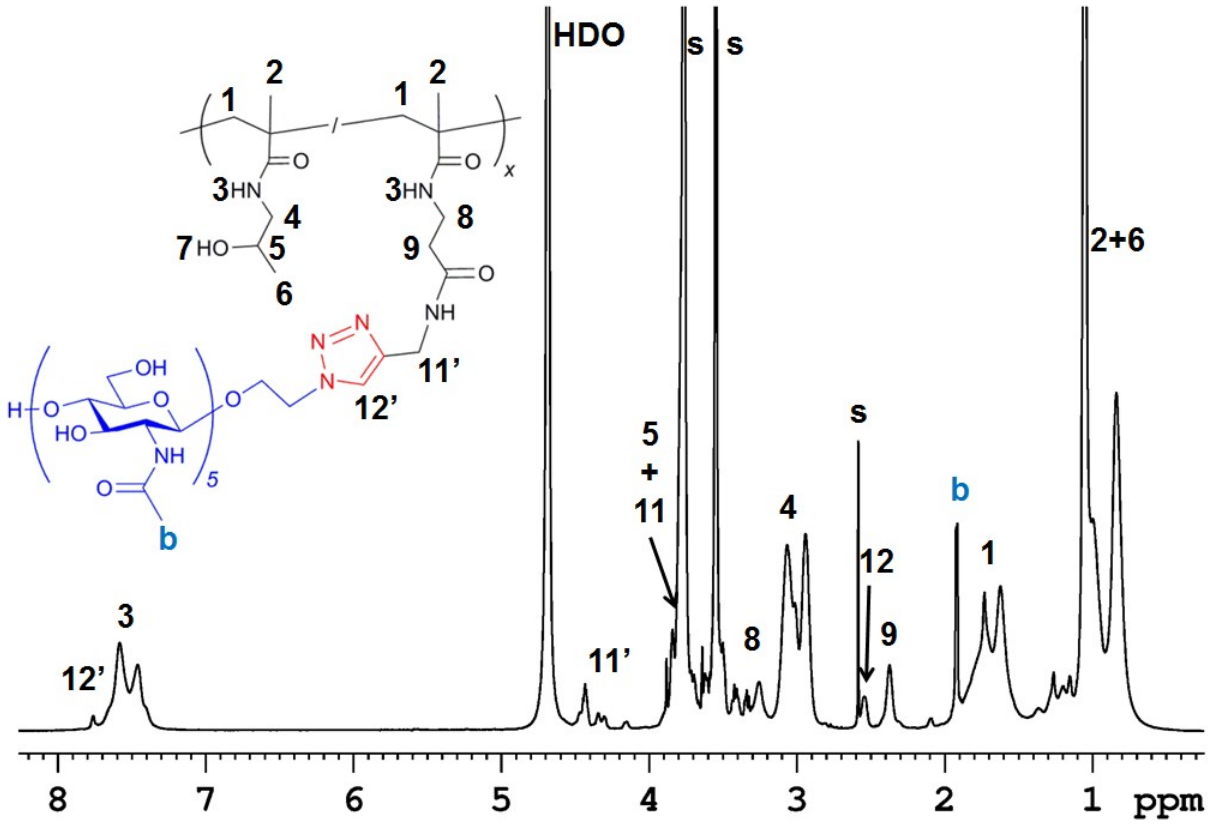

Fig. S30b. ^{1}H NMR spectrum of glycopolymer **25** in D_2O.

References

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