Supporting Information to

Facilitated Synthesis of Heterofunctional Glycopolypeptides

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Materials.

Amino acids, DL- and L-allylglycine (>98%), were received from BoaoPharma, triphosgene from Merck, 1-thio-β-D-glucose-2,3,4,6-tetraacetate (**2**, 97%), 3-mercaptopropionic acid (**4**, 99%+), *N*-acetylcysteamine (**5**, 95%), thioacetic acid (**6**, 96%), 1-hexylamine (>99.5%), and *N*,*N*-dimethylformamide (DMF; ≥99.8%, extra dry) from Sigma-Aldrich. α-Pinene came from Alfa Aesar, tetrahydrofuran (THF; 99.5%, extra dry), and dichloromethane (DCM; ≥99.8%, extra dry) from Acros Organics, and n-heptane from Roth (99%). All chemicals were used as received unless otherwise noted.

Amino acid *N*-carboxyanhydrides (NCAs)

NCAs of DL- and L-allylglycine (AGly-NCA) were synthesized as described earlier (K.-S. Krannig, H. Schlaad, *J. Am. Chem. Soc.* **2012**, *134*, 18542-18545). Yield: 50-60%. ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 6.59 (s, 1H, N*H*), 5.74 (m, 1H, H_2C=C*H*), 5.28 (m, 2H, H_2C=CH), 4.40 (dd, ^{3}J = 7.0 Hz, ^{4}J = 4.3 Hz, 1H, H_2C-C*H*-NH), 2.53 (td, ^{3}J = 14.6 Hz, ^{3}J = 7.4 Hz, 1H diast., H_2C-CH-NH), 2.10 (td, ^{3}J = 14.6 Hz, ^{3}J = 7.4 Hz, 1H diast., H_2C-CH-NH). ^{13}C-NMR (100.1 MHz, $CDCl_3$): δ (ppm) = 168.8 (-N-*C*(=O)-O-), 152.5 (-CH-*C*(=O)-O-), 129.9 (H_2C=CH-), 121.5 (H_2C=CH), 57.2 (*C*(=O)-C*H*-NH-), 35.8 (HC-*C*H_2-CH). Mp: DL-AGly NCA 88-90 °C (rep. 89-91 °C), L-AGly NCA 49-51 °C (rep. 48-50 °C) (J. Sun, H. Schlaad, *Macromolecules* **2010**, *43*, 4445-4448).

One-pot glycosylation/polymerization

AGly-NCA **1** (1.0 eq), benzophenone (0.2 eq), and the respective amount of AcGlcSH **2** (0.5-0.8 eq) were dissolved in dry THF (0.15 M) under an argon atmosphere, and the reaction mixture was irradiated with UV light from two energy saving lamps (Exo Terra ReptiGlo 5.0 26W) for ~45 min. Then, dry DMF (overall concentration 5 wt%) and desired amount of a 0.1 M solution of freshly distilled 1-hexylamine in dry DMF were added and the reaction mixture was stirred for 7 days under reduced pressure (ca. 0.5 mbar) at room temperature. The polymerization was quenched by precipitation into a ten-fold volume of

isopropanol. The product was collected by centrifugation and dried at 65 °C in high vacuum. ^{1}H-NMR (400.1 MHz, TFA-d): δ (ppm) = 5.6-5.8 (-*H*C=C-), 5.6-5.4 (S-C*H*-O), 5.4-5.3 (Glc), 5.3-5.2 (-HC=CH_2, Glc), 4.3-4.8 (C(=O)-C*H*-NH), 3.8-4.0 (Glc), 3.4 (CH_2-CH_2--NH_2), 2.9-2.4 (S-CH_2), 2.3-1.6 (S-CH_2-CH_2-CH_2, O*Ac*), 1.3-1.2 (CH_3-CH_2-CH_2-CH_2-CH_2-), 0.8 (CH_3).

Post-polymerization functionalization

Glycopolypeptide **P1**, benzophenone (0.1 eq with respect to double bonds), and thiol **4**-**6** (1.5 eq) were dissolved in THF (ca. 1.0 wt% with respect to AGly units) and put under an inert argon atmosphere. The vessel was sealed and placed in the UV chamber (ExoTerra ReptiGlo 5.0 UVB lamp, 26 W) for 16 h. The reaction mixture was diluted and extensively dialyzed (RC 1000) against THF. Removal of THF and freeze-drying from 1,4-dioxane yielded the final products as fluffy solids.

Analytical instrumentation and methods

NMR measurements were conducted at room temperature using a Bruker DPX-400 spectrometer operating at 400.1 MHz (^{1}H) and 100.1 MHz (^{13}C). Deuterated chloroform, THF and trifluoroacetic acid (TFA) were used as solvents (Sigma-Aldrich); ^{1}H NMR signals were referenced to the signals of $CDCl_3$ δ 7.26 ppm, THF-d_8 δ 1.72/3.58 ppm (^{13}C 25.5/67.7 ppm), and TFA-d δ 11.52 ppm, respectively. Melting points were determined using a MEL-TEMP® apparatus from Lab Devices INC, USA with a Fluke 51 thermometer. FT-IR Spectra were recorded on a Varian 1000 spectrometer. Polymers were measured as dry powders on a single reflection diamond ATR. NCA conversions were followed by casting a thin film of the reaction solutions on $CaCl_2$ plates and measurements in transition mode. Data analysis was conducted with Varian Resolutions FTS 1000 software. Size exclusion chromatography (SEC) with simultaneous UV and RI detection was performed with *N*-methyl-2-pyrrolidone (NMP + 5 wt% LiBr) as the eluent, flow rate: 0.8 ml/min, at +70 °C using a set of two 300×8 mm^2 PSS-GRAM columns with average particle sizes of 7 µm and porosities of 100 and 1000 Å. Calibration was done using poly(methyl methacrylate) (PMMA) standards (PSS, Mainz).

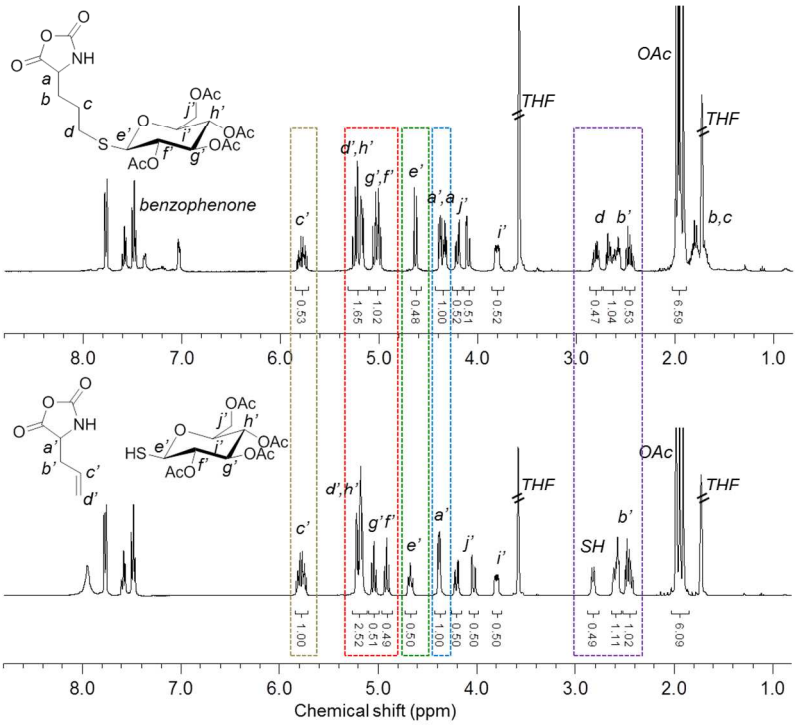

Figure S1. ^{1}H-NMR spectra (400.1 MHz, THF-d_8) of a mixture of AGly NCA **1**(L) (1 eq)/AcGlcSH **2** (0.5 eq) (+ benzophenone) (bottom) and the crude product mixture **1**(L)/**3**(L) (glyco-NCA) after UV irradiation for 45 min (top) (reaction **A**).

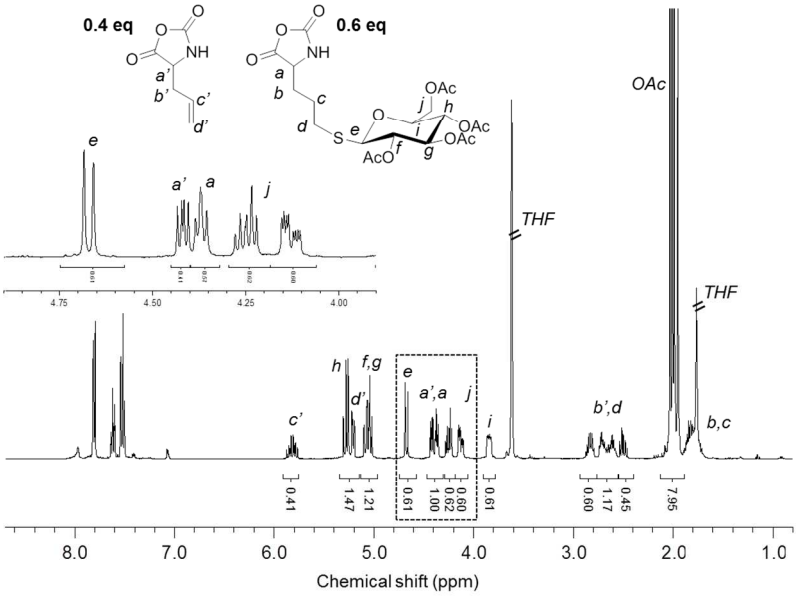

Figure S2. ^{1}H-NMR spectrum (400.1 MHz, THF-d_8) of the crude product mixture **1**(DL)/**3**(DL) obtained from a mixture of AGly NCA **1**(DL) (1 eq)/AcGlcSH **2** (0.6 eq) (+ benzophenone) after UV irradiation for 45 min (reaction **B**).

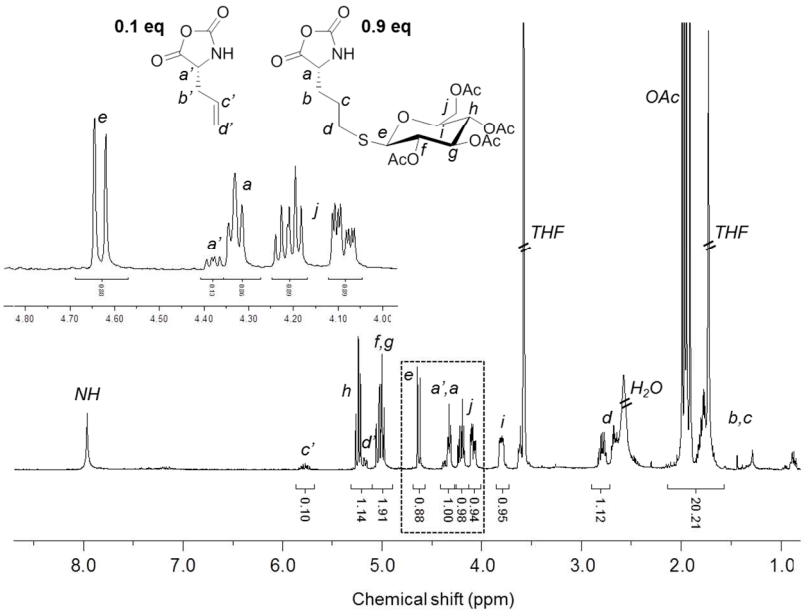

Figure S3. ^{1}H-NMR spectra (400.1 MHz, THF-d_8) of the isolated product mixture **1**(L)/**3**(L) obtained from a mixture of AGly NCA **1**(L) (1 eq)/AcGlcSH **2** (0.9 eq) (+ benzophenone) after UV irradiation for 45 min (reaction **C**).

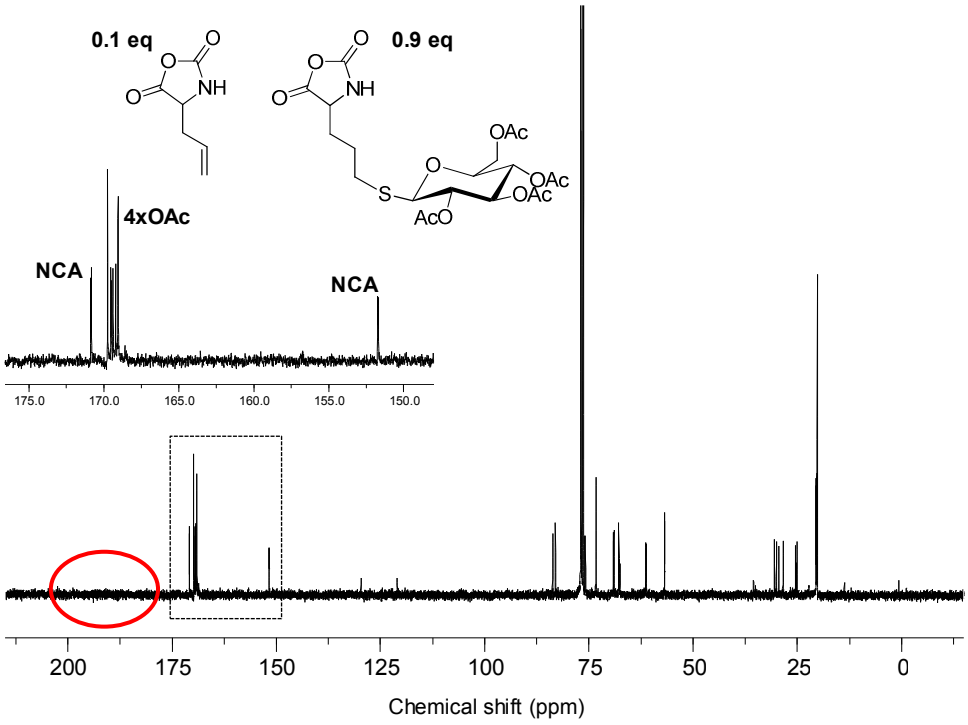

Figure S4. ^{13}C-NMR spectra (100.1 MHz, THF-d_8) of the isolated product mixture **1** (L)/**3** (L) obtained from a mixture of AGly NCA **1**(L) (1 eq)/AcGlcSH **2** (0.9 eq) (+ benzophenone) after UV irradiation for 45 min (reaction **C**).

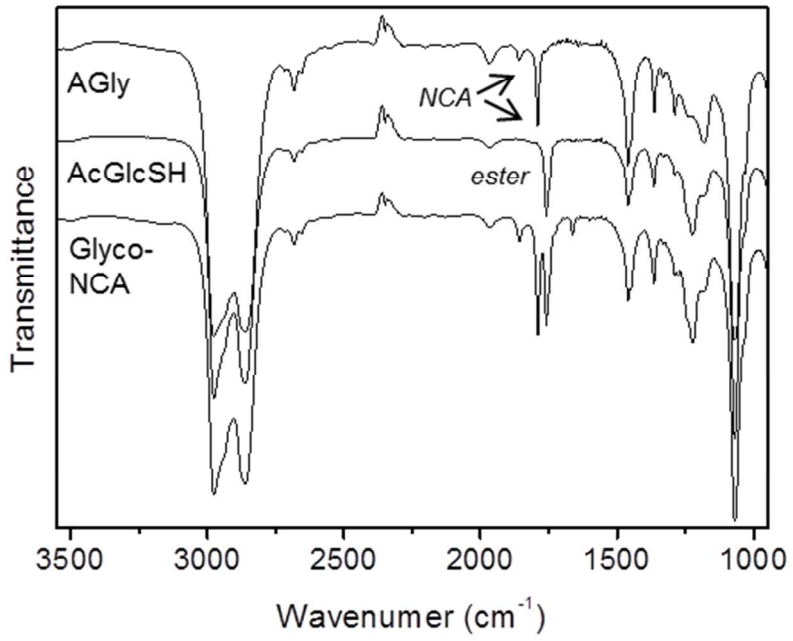

Figure S5. FT-IR spectra of AGly NCA **1** (L) (top), AcGlcSH **2** (middle), and the crude product mixture **1**(L)/**3**(L) after UV irradiation (bottom) (reaction **A**).

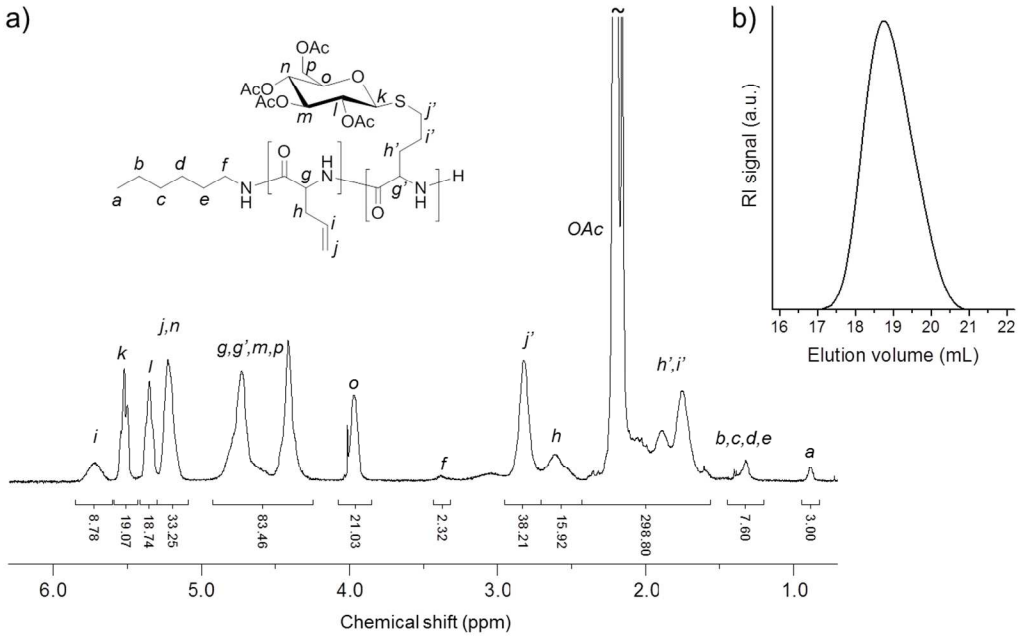

Figure S6. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the isolated glycopolypeptide **P1** ([**1**(DL)]$_0$/[**2**]$_0$ = 1.0/0.8, [NCA]$_0$/[NH$_2$]$_0$ = 30).

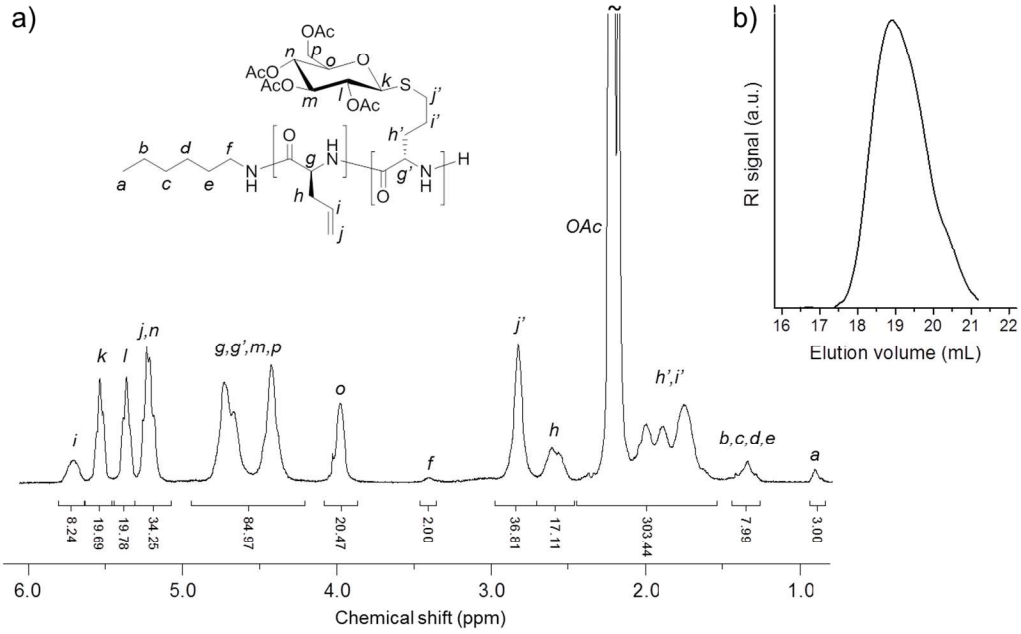

Figure S7. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the isolated glycopolypeptide **P2** ([**1**(L)]$_0$/[**2**]$_0$ = 1.0/0.8, [NCA]$_0$/[NH$_2$]$_0$ = 30).

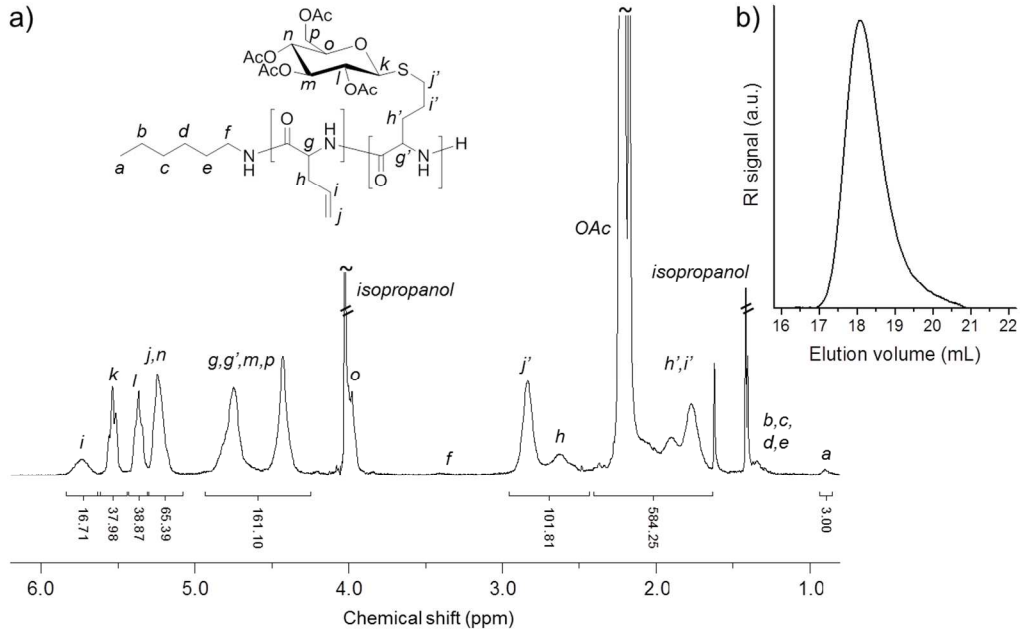

Figure S8. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the isolated glycopolypeptide **P3** ([**1**(DL)]$_0$/[**2**]$_0$ = 1.0/0.8, [NCA]$_0$/[NH$_2$]$_0$ = 90).

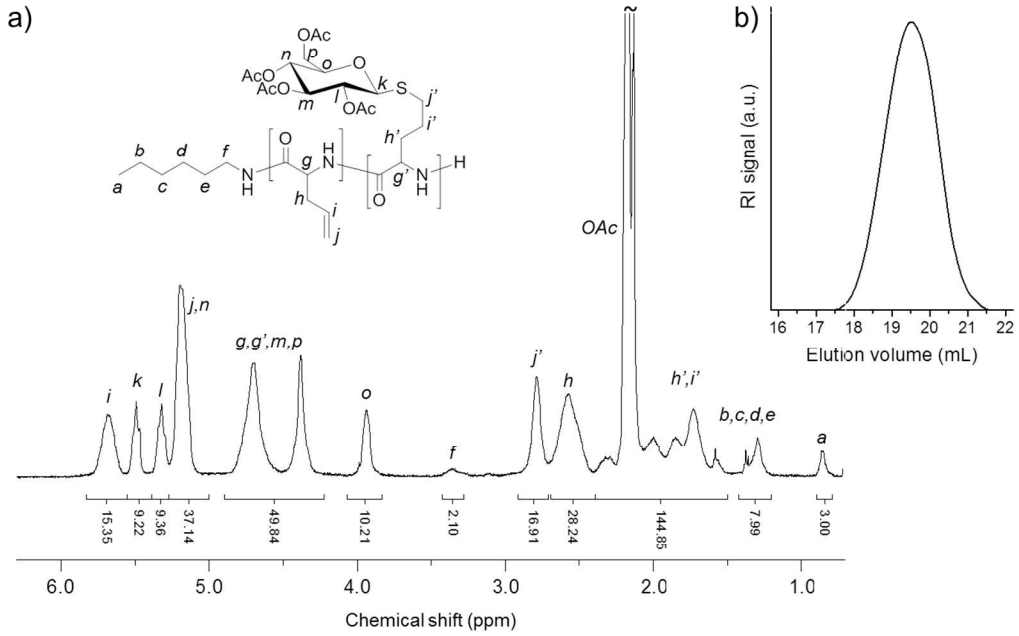

Figure S9. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the isolated glycopolypeptide **P4** ([**1**(DL)]$_0$/[**2**]$_0$ = 1.0/0.5, [NCA]$_0$/[NH$_2$]$_0$ = 30).

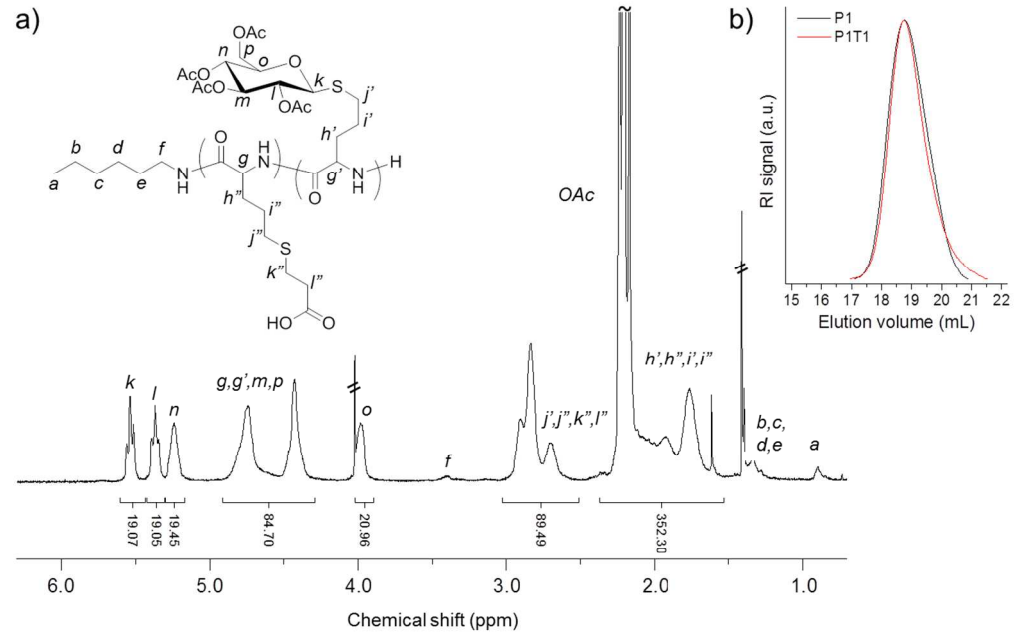

Figure S10. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the glycopolypeptide **P1T1** (**P1** modified with 3-mercapto-propionic acid **4**).

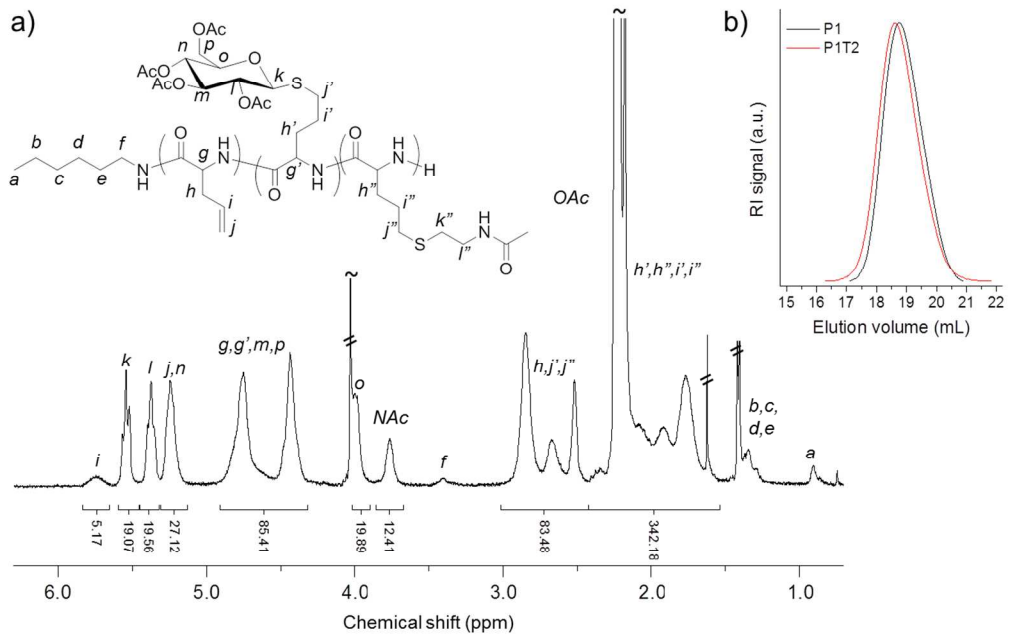

Figure S11. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the glycopolypeptide **P1T2** (**P1** modified with *N*-acetyl-cysteamine **5**).

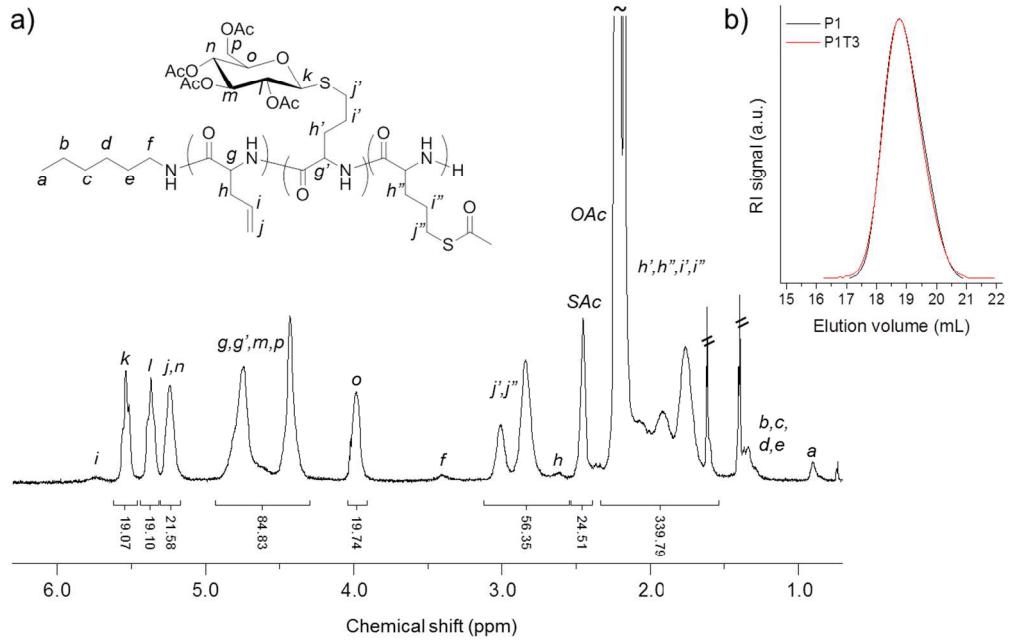

Figure S12. a) ^{1}H-NMR spectrum (400.1 MHz, TFA-d) and b) SEC trace (eluent: NMP + 0.5 wt% LiBr, 70 °C, stationary phase: PSS-GRAM) of the glycopolypeptide **P1T3** (**P1** modified with thioacetic acid **6**).