Synthesis of *O*-sulfated human syndecan-1 like glyco-polypeptides by incorporating peptide ligation and *O*-sulfated glycopeptide cassette strategies

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Compound Characterization Table

1. Materials and Methods

All commercial materials (Sigma, Acros, Alfa Aesar) used were reagent grade as supplied except where noted. Amino acids, resins and coupling reagents (Chem-Impex) were used without further purification. Anhydrous dichloromethane (DCM) was obtained from a solvent purification system. Anhydrous dimethylformamide (DMF) was obtained from a Sure/Seal™ container. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 glass plates. Compound spots were visualized by UV light (254 nm) and by staining with ninhydrin in EtOH or a yellow solution containing $Ce(NH_4)_2(NO_3)_6$ (0.5 g) and $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (24.0 g) in 6% H_2SO_4 (500 mL). Glycosylation reactions were performed in the presence of molecular sieves, which were flame-dried right before the reaction under high vacuum. Glycosylation solvents were dried using a solvent purification system and used directly without further drying. Flash column chromatography was performed on silica gel 60 (230-400 Mesh). NMR spectra were recorded on Agilent DDR2 500 MHz NMR spectrometers at 298 K and referenced using residual $CHCl_3$ for ^{1}H-NMR (δ 7.26 ppm), and $CDCl_3$ for ^{13}C-NMR (δ 77.0 ppm). High resolution mass spectra were recorded on a Waters Xevo G2-XS QTof quadropole mass spectrometer. Deconvolution spectra were obtained using the MaxEnt software implemented by Waters. The NMR spectra of the final product **1** were recorded on Bruker Avance III HD 900 MHz in D_2O at 298K.

Reverse phase HPLC was performed on Shimadzu workstation equipped with SCL-10Avp system controller, DGU-14A degasser, LC-8A solvent delivery pump and SPD-10A UV/vis detector. The analysis of the chromatograms was conducted using LabSolutions software. For peptide analysis, Agilent Zorbax 300SB-C18 (3.5 µm, 4.6 × 150 mm) column was used at a flow rate of 1.0 mL/min. For peptide purification, Vydac 218TP C18 (10 µm, 22 × 250 mm) column was used at a flow rate of 8 mL/min. Separation of non-sulfated peptide fragments involved a mobile phase of 0.1% TFA in water (Solvent A) and CH_3CN (Solvent B) using the stated linear gradient. Separation of sulfated peptide fragments involved a mobile phase of 25mM NH_4OAc (Solvent C) and CH_3CN (Solvent B). The UV absorption at 220 nm and 254 nm were monitored.

2. General Procedures

2.1 Resin loading

All the peptides were prepared on 2-chlorotrityl chloride PS resin (100-200 mesh size). The resin was pre-swollen in anhydrous DCM and manually loaded in the presence of the respective amino acid building block (1 equiv)/ *i*Pr_2NEt (2.5 equiv), with additional capping with MeOH. The loading level was estimated based on the concentration of the dibenzofulvene-piperidine adduct *N*-terminal Fmoc deprotection solution. Namely, a sample of this solution (2 × 3 mL) was transferred to two matched 1 cm quartz glass cuvettes and the UV/vis absorbance at λ = 301 nm was measured using the solution of piperidine/DMF (1:4 v/v) as a reference. An average of the two absorbance values were used to calculate the resin loading using ε = 7800 M^{-1} cm^{-1}. In general, a loading level at 0.4-0.5 mmol/g resin is preferred.

2.2 Microwave-assisted SPPS

Microwave-assisted SPPS was achieved on 0.1 mmol scale either with CEM Discover Bio system using Fmoc-Xaa-OH (5 equiv. with respect to resin loading)/ HATU (5 equiv.)/ *i*Pr_2NEt (6 equiv.), or with CEM Liberty Blue automatic system using Fmoc-Xaa-OH (0.2 M) under DIC (0.5 M)/ Oxyma (1 M, with 0.1 M *i*Pr_2NEt) activation protocol and the default programmed methods suggested by the vendor.

Deprotection

Temperature (°C)	Hold time (s)	Power (W)	Delta T (°C)
60	240	25	2

Coupling

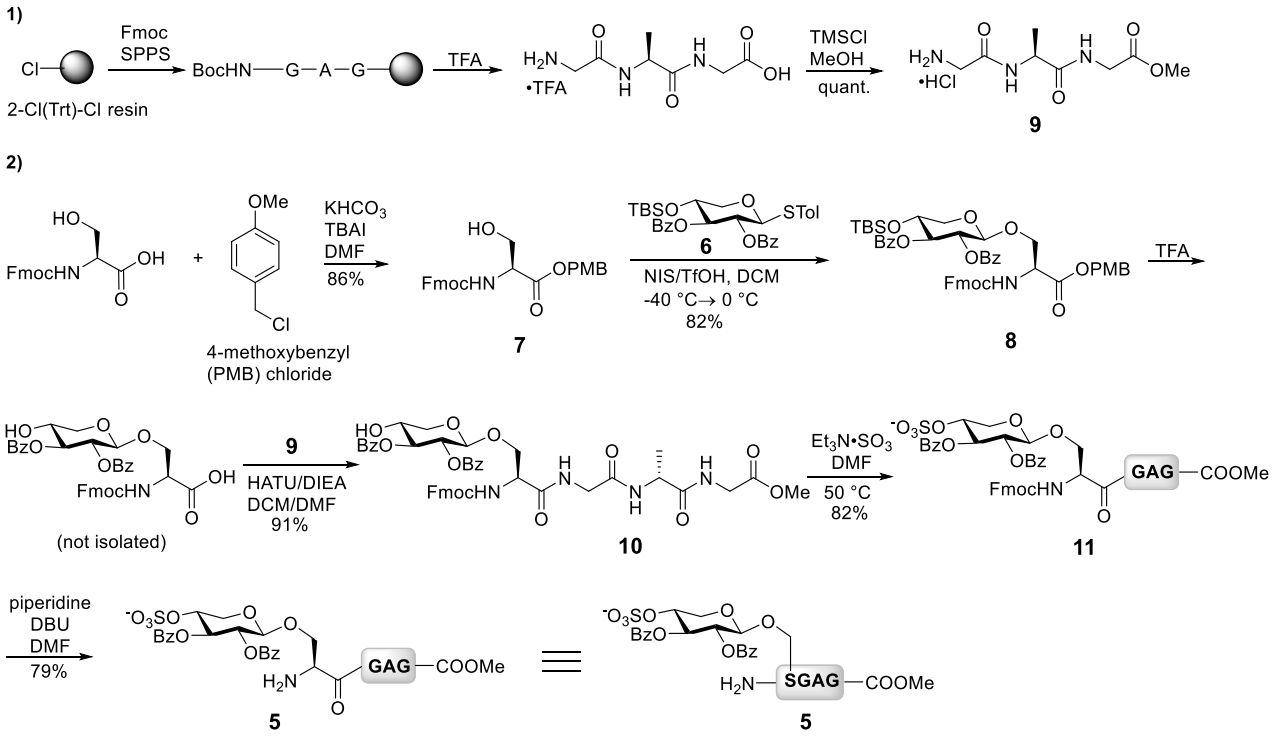
	Temperature (°C)	Hold time (s)	Power (W)	Delta T (°C)
Stage 1	25	120	0	2
Stage 2	50	480	20	1

2.3 Microwave-based Ag(I) ligation

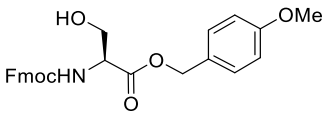
The reactions were performed using a CEM-Discover Bio synthesizer in sealed reaction vessels (7 mL). The stirring parameter in the microwave synthesizer was set to "Hi-speed". The reaction mixture was ramped to 50 ºC using the following power-temperature steps: 25 W, 20 minutes hold time. The reaction vessel was simultaneously cooled using nitrogen (250 psi) to maintain the set temperature.

3. Preparations and Characterizations

Preparation of Cassette Peptide 5



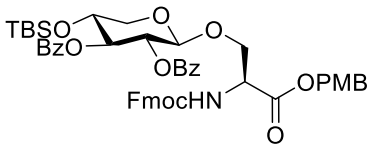
FmocNH-Ser-CO_2PMB **7**



Fmoc-Ser-OH (0.384 g, 1.18 mmol) was mixed with PMB chloride (0.24 mL, 1.77 mmol), $KHCO_3$ (0.200 g, 2 mmol) and tetrabutylammonium iodide (0.040 g, 0.108 mmol) in anhydrous DMF (5 mL). The reaction was kept at room temperature overnight until completion. It was extracted with EtOAc (50 mL × 3). The combined organic solution was washed with a saturated solution of NH_4Cl and brine sequentially. After drying over Na_2SO_4, the solution was concentrated and purified by silica gel column (hexane/DCM 1:1 → hexane/EtOAc 1:1) to give light yellow oil, which was further triturated with hexane to give the product **7** as white solid (0.45 g, 86%).

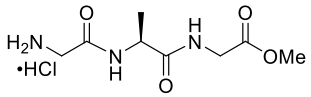
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.59 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.41 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.35 – 7.28 (m, 4H, Ar*H*), 6.90 – 6.84 (m, 2H, Ar*H)*, 5.70 (d, *J* = 7.6 Hz, 1H, FmocN*H*), 5.18 (d, *J* = 12.0 Hz, 1H, CH_3OPhCH_2O (×1)), 5.15 (d, *J* = 12.0 Hz, 1H, CH_3OPhCH_2O (×1)), 4.49 – 4.36 (m, 3H, Fmoc-CH_2 (×2), Ser-αH), 4.21 (t, *J* = 7.0 Hz, 1H, Fmoc-C*H*), 4.04 – 3.97 (m, 1H, Ser-βH (×1)), 3.96 – 3.89 (m, 1H, Ser-βH (×1), 3.79 (s, 3H, CH_3OPhCH_2O), 2.03 (t, *J* = 6.5 Hz, 1H, Ser-CH_2OH). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.3, 159.8, 143.6, 141.3, 141.3, 130.2, 127.7, 127.1, 127.1 (2C), 120.0 (2C), 114.0, 67.5, 67.2, 63.4, 56.1, 55.3, 47.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{26}NO_6$ 448.1755, found: 448.1767; $[M+NH_4]^+$ Calcd for $C_{26}H_{29}N_2O_6$ 465.2020, found: 465.2035

FmocNH-Ser(Xyl)-CO_2PMB **8**



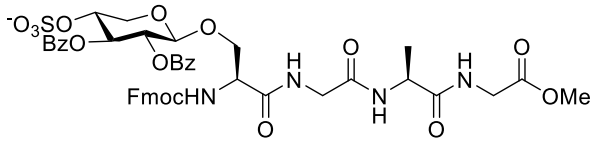
Xyloside donor **6** was prepared as previously reported.[1] **6** (1.057 g, 1.826 mmol) and glycosyl acceptor **7** (1.103 g, 2.465 mmol) were dissolved in anhydrous DCM (10 mL) followed by the addition of freshly activated 4 Å molecular sieves (800 mg). The mixture was stirred at room temperature for 1 h then cooled to -40 °C. NIS (0.616 g, 2.740 mmol) was added followed by the addition of TfOH (18.1 μL, 182 μmol). The reaction was stirred for 2 h from -40 °C to 0 °C. After the reaction was completed, the mixture was quenched with a saturated solution of $NaHCO_3$, diluted with DCM, filtered through Celite, washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4, concentrated and purified with silica gel column chromatography (hexane/EtOAc 4:1 → 3:1) to give the desired product **8** as foamy solid (1.344 g, 82%).^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.96 − 7.92 (m, 4H, Ar*H*), 7.78 (t, *J* = 7.0 Hz, 2H, Ar*H*), 7.57 – 7.49 (m, 3H, Ar*H*), 7.42 – 7.37 (m, 5H, Ar*H*), 7.33 – 7.24 (m, 6H, Ar*H*), 6.87 – 6.82 (m, 2H, Ar*H*), 5.56 (d, *J* = 8.4 Hz, 1H, FmocN*H*), 5.49 (t, *J* = 8.9 Hz, 1H, 3-H), 5.25 (dd, *J* = 9.3, 7.2 Hz, 1H, 2-H), 5.11 (d, *J* = 12.0 Hz, 1H, CH_3OPhCH_2O (×1)), 5.06 (d, *J* = 12.0 Hz, 1H, CH_3OPhCH_2O (×1)), 4.58 (d, *J* = 7.2 Hz, 1H, 1-H), 4.48 (dt, *J* = 8.6, 3.2 Hz, 1H, Ser-αH), 4.38 – 4.27 (m, 2H, Ser-βH (×1), Fmoc-CH_2 (×1)), 4.19 (dd, *J* = 10.5, 7.4 Hz, 1H, Fmoc-CH_2 (×1)), 4.12 (t, *J* = 7.2 Hz, 1H, Fmoc-C*H*), 3.97 (td, *J* = 8.8, 5.2 Hz, 1H, 4-H), 3.91 (dd, *J* = 11.7, 5.2 Hz, 1H, 5-H), 3.83 (dd, *J* = 10.3, 3.5 Hz, 1H, Ser-βH (×1)), 3.78 (s, 3H, CH_3OPhCH_2O), 3.36 (dd, *J* = 11.7, 9.4 Hz, 1H, 5-H), 0.77 (s, 9H, $C(CH_3)_3$), 0.04 (s, 3H, $Si(CH_3)_2$), -0.11 (s, 3H, $Si(CH_3)_2$). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.5, 165.5, 165.4, 159.7, 155.9, 143.9, 143.7, 141.3, 141.2, 133.2, 133.1, 130.1, 129.8, 129.7, 129.6, 129.2, 128.4, 128.3, 127.7 (2C), 127.3, 127.1, 125.2, 120.0, 113.9, 101.7, 74.7, 71.5, 69.2, 69.0, 67.3, 67.1, 65.9, 55.2, 54.3, 47.1, 25.4, 17.8, -4.8, -5.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{51}H_{56}NO_{12}Si$ 902.3566, found 902.3556; $[M+NH_4]^+$ Calcd for $C_{51}H_{59}N_2O_{12}Si$ 919.3832, found 919.3846

Tripeptide **9**



Tripeptide **9** was prepared on 0.5 mmol scale using CEM Discover Bio system following the general procedure of Microwave-assisted SPPS. After cleavage with TFA/H_2O (95/5, v/v), the crude peptide was concentrated under vacuo and dried overnight, which was subjected to trimethylsilyl chloride (2.5 mmol, 0.32 ml) in MeOH (1.5 mL).[2] The reaction was stirred at room temperature for 2 h and was concentrated under vacuo and washed with anhydrous Et_2O (20 ml × 3) to yield the product **9** as white solid without further purification. ^{1}H NMR (500 MHz, Methanol-d_4) δ 4.46 (q, J = 7.1 Hz, 1H, Ala-αH), 3.98 (d, J = 17.6 Hz, 1H, Gly-αH), 3.91 (d, J = 17.6 Hz, 1H, Gly-αH), 3.72 (s, 3H, COOCH_3), 3.71 – 3.67 (m, 2H, Gly-αH (×2)), 1.40 (d, J = 7.2 Hz, 3H, Ala-βH). ^{13}C NMR (126 MHz, Methanol-d_4) δ 173.8, 170.1, 165.6, 51.2, 48.9, 40.3, 40.0, 16.8. HRMS (ESI) m/z: $[M-HCl+H]^+$ Calcd for $C_8H_{16}N_3O_4$ 218.1135, found: 218.1149; $[M-HCl+Na]^+$ Calcd for $C_8H_{15}N_3O_4Na$ 240.0955, found: 240.0967

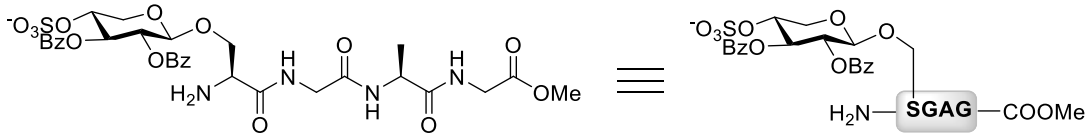
Tetrapeptide FmocNH-S(sulfo-Xyl)GAG-CO_2Me **11**



Compound **8** (0.1611 g, 0.179 mmol) was treated with TFA/H_2O (95/5, v/v, 0.5 mL) for 1 h and then concentrated under vacuo. The resulting residue was mixed with tripeptide **9** (60.0 mg, 0.276 mmol), HATU (81.7 mg, 0.215 mmol) and iPr$_2$NEt (93.5 μL, 0.537 mmol) in anhydrous DCM/DMF (1.5 mL/0.5 mL). The reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with DCM (150 mL), washed with 1N HCl (50 mL × 3) and brine (50 mL × 3). The organic phase was dried over Na_2SO_4, concentrated under *vacuo* and purified by flash column chromatography on silica gel (DCM/MeOH, 10:1) to give light oil, which was further triturated with hexane/DCM (1/1, v/v) to give compound **10** (0.141 g, 91 %) as white solid. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{45}H_{47}N_4O_{14}$ 867.3083, obsv: 867.3099.

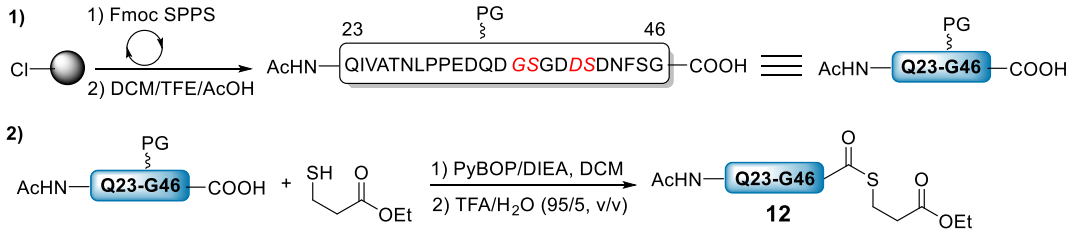
Compound **10** (64.2 mg, 0.074 mmol) was dissolved in anhydrous DMF (0.6 mL), followed by the addition of $NEt_3 \cdot SO_3$ (80.6 mg, 0.445 mmol). The resulting mixture was stirred at 50 °C overnight. After cooling down to room temperature, it was diluted with DCM and purified by flash column chromatography on silica gel (EtOAc/MeOH, 8:1 → 5:1) to give the desired product **11** as a white solid (57.1 mg, 82%). ^{1}H NMR (500 MHz, Methanol-d_4) δ 7.93 − 7.90 (m, 4H, ArH), 7.76 (d, J = 7.5 Hz, 2H, ArH), 7.58 – 7.56 (m, 2H, ArH), 7.53 – 7.42 (m, 2H, ArH), 7.39 – 7.25 (m, 8H, ArH), 5.63 (t, J = 8.8 Hz, 1H, 3-H), 5.29 (dd, J = 9.0, 7.0 Hz, 1H, 2-H), 4.88 (d, J = 7.0 Hz, 1H, 1-H), 4.68 (td, J = 8.9, 5.2 Hz, 1H, 4-H), 4.46 (dd, J = 12.0, 5.2 Hz, 1H, 5-H), 4.35 (q, J = 7.2 Hz, 1H, Ala-αH), 4.30 (t, J = 6.0 Hz, 1H, Ser-αH), 4.20 (m, 2H, Gly-αH(×2)), 4.10 – 4.02 (m, 2H, Ser-βH(×1)), 3.94 – 3.82 (m, 4H, FmocCH_2 (×1), Gly-αH(×2), Ser-βH(×1)), 3.74 – 3.67 (m, 3H, 5-H, FmocCH, FmocCH_2 (×1)), 3.64 (s, 3H, COOCH_3), 1.32 (d, J = 7.2 Hz, 3H, Ala-βH(×3)). ^{13}C NMR (126 MHz, Methanol-d_4) δ 174.1, 171.5, 170.4, 169.9, 165.9, 165.5, 157.1, 143.7 (2C), 141.1 (2C), 133.1, 132.9, 129.5, 129.4, 129.0, 128.2, 128.0, 127.4, 126.8, 124.9 (2C), 119.6, 100.4, 72.7, 72.3, 71.7, 68.0, 66.8, 63.2, 55.2, 51.3, 51.3, 49.1, 42.3, 40.5, 16.5. HRMS (ESI) m/z: $[M-H]^-$ Calcd for $C_{45}H_{45}N_4O_{17}S$ 945.2506, found: 945.2520

Tetrapeptide H_2N-S(sulfo-Xyl)GAG-CO_2Me **5**



Compound **11** (69.7 mg, 0.074 mmol) was treated with a mixture of DMF/DBU/piperidine (95/2.5/2.5, v/v/v, 1 mL) for 2 h until completion. The reaction mixture was diluted with DCM and purified by flash column chromatography on silica gel (EtOAc/MeOH, 10:1 → 5:1 then EtOAc/MeOH/H_2O 5:1.2:1). Upon concentration and lyophilization, the product **5** was obtained as white powder (42.2 mg, 79%). ^{1}H NMR (500 MHz, Methanol-d_4) δ 7.96 – 7.92 (m, 4H, Ar*H*), 7.60 – 7.55 (m, 1H, Ar*H*), 7.54 – 7.49 (m, 1H, Ar*H*), 7.45 – 7.40 (m, 2H, Ar*H*), 7.38 (t, *J* = 7.9 Hz, 2H, Ar*H*), 5.62 (t, *J* = 9.0 Hz, 1H, 3-H), 5.30 (dd, *J* = 9.2, 7.2 Hz, 1H, 2-H), 4.87 (d, *J* = 7.0 Hz, 1H, 1-H), 4.66 (td, *J* = 9.2, 5.3 Hz, 1H, 4-H), 4.46 (dd, *J* = 11.9, 5.3 Hz, 1H, 5-H), 4.40 (q, *J* = 7.2 Hz, 1H, Ala-αH), 4.04 (dd, *J* = 10.4, 6.4 Hz, 1H, Ser-βH(×1)), 3.94 (s, 2H, Gly-αH(×2)), 3.91 – 3.84 (m, 2H, Ser-βH(×1), Gly-αH(×1)), 3.81 – 3.73 (m, 2H, Ser- αH, Gly-αH(×1)), 3.72 – 3.66 (m, 4H, COOC*H*$_3$, 5-H), 1.37 (d, *J* = 7.2 Hz, 3H, Ala-βH(×3)). ^{13}C NMR (126 MHz, Methanol-d_4) δ 174.0, 170.2, 169.5, 165.8, 165.4, 133.2, 132.8, 129.5, 129.4 (2C), 129.1, 128.2, 127.9, 100.6, 72.6, 72.4, 71.9, 69.5, 63.4, 54.0, 51.2, 48.8, 42.1, 40.4, 16.6. HRMS (ESI) m/z: $[M-H]^-$ Calcd for $C_{30}H_{35}N_4O_{15}S$ 723.1825, found: 723.1829

Preparation of Peptide Thioester 12



The peptide was prepared on 0.1 mmol scale with CEM Liberty Blue automatic system following the general procedure for microwave assisted SPPS. Specifically, pseudoproline dipeptides FmocHN-Gly-Ser($\Psi^{Me,Me}$Pro)-COOH and FmocHN-Asp(O*t*Bu)-Ser($\Psi^{Me,Me}$Pro)-COOH were used as dipeptide building blocks (denoted in red). The removal of Fmoc group was executed using a deblock solution of piperidine/formic acid/DMF (19/1/80, v/v/v) at room temperature for 20 min. N-terminal acetylation was achieved with Ac_2O/*i*Pr_2NEt/DMF (1/1/8, v/v/v, 2ml) for 30 min. The peptidyl resin was subjected to mild acidic cleavage cocktail (DCM/TFE/AcOH 8/1/1, v/v/v, 15 ml ×2, 1 h for each round). Following filtration, the resulting cleavage solutions were combined and concentrated to give crude protected peptide (0.266 g, 66.0%).

The crude peptide (26.7 mg, 6.591 μmol) was treated with PyBOP (17.2 mg, 0.033 mmol), *i*Pr_2NEt (11.5 μL, 8.5 mg, 0.066 mmol), and ethyl 3-mercaptopropionate (25 μL, 26.5 mg, 0.198 mmol) in anhydrous DCM (1.3 mL) for 1 h. The reaction mixture was then concentrated; a solution of TFA/H_2O (95/5, v/v, 1 mL) was added and stirred at room temperature for 1 h. The resulting peptide was concentrated under a stream of condensed air and triturated with cold diethyl ether to give a white suspension, which was centrifuged and the ether subsequently decanted. Preparative HPLC purification (20% isocratic CH_3CN/H_2O containing 0.1% TFA for initial 10 min then 20-40% linear gradient CH_3CN/H_2O containing

0.1% TFA over 30 min) followed by concentration at reduced pressure and lyophilization afforded the titled peptide thioester **12** as a white powder (7.8 mg, 45% yield). HRMS (ESI) m/z: $[M+2H]^{2+}$ Calcd for $C_{103}H_{156}N_{28}O_{46}^{2+}$ 1319.0523, found: 1319.0624; $[M+3H]^{3+}$ Calcd for $C_{103}H_{157}N_{28}O_{46}^{3+}$ 879.7040, found: 879.7120

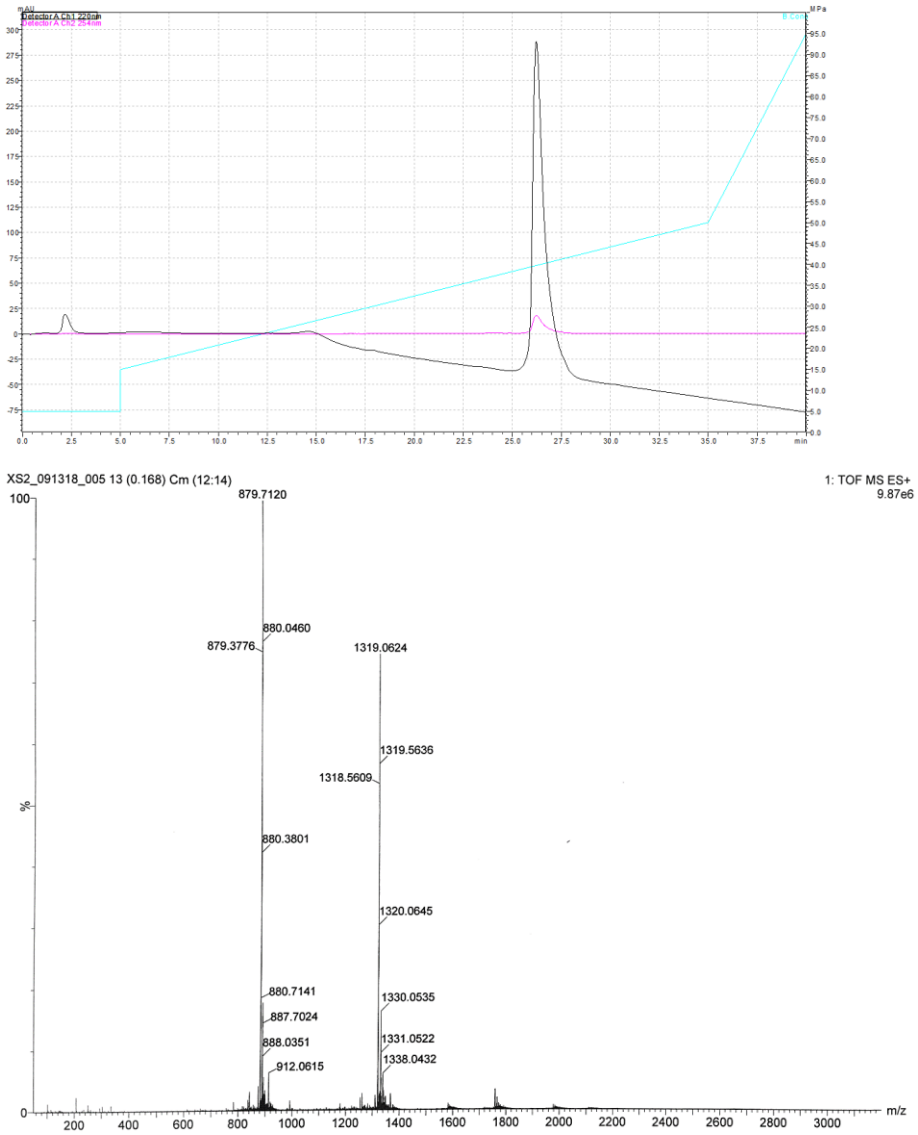
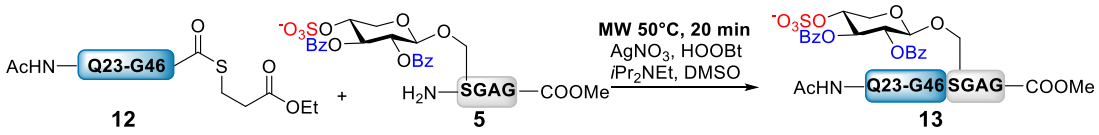
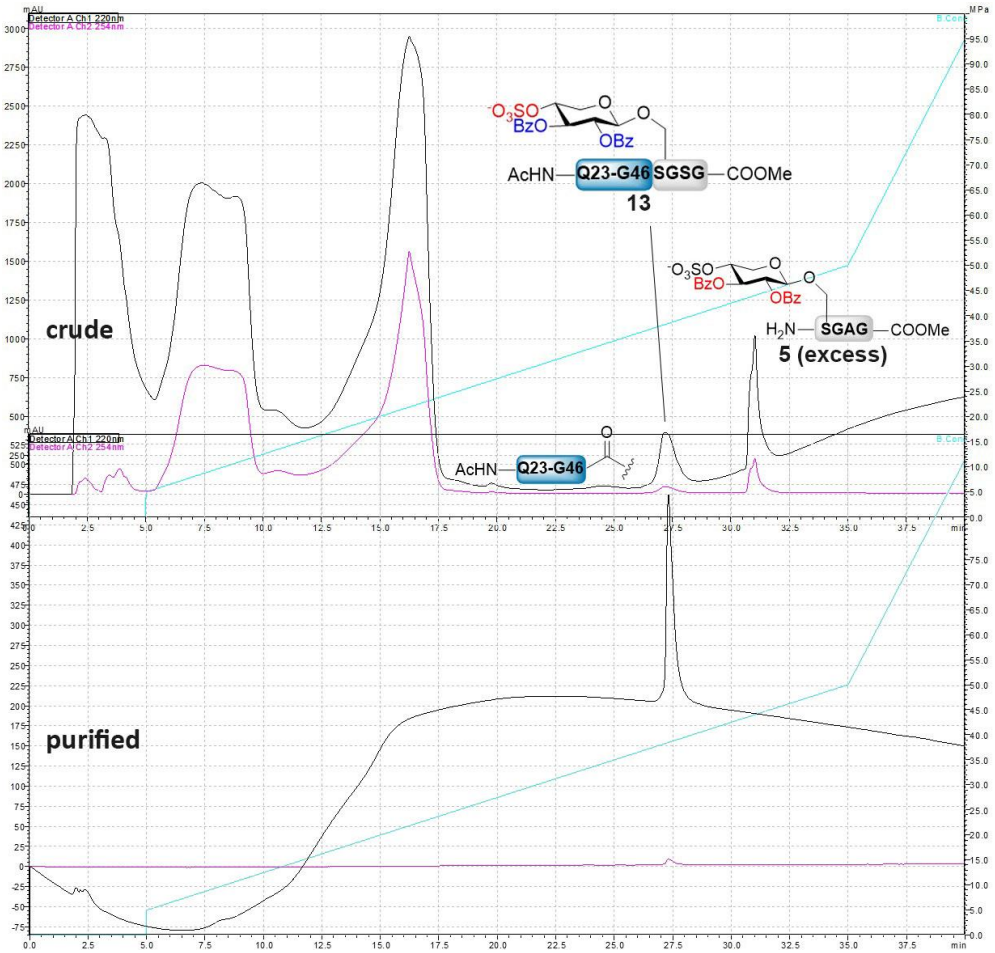


Figure S1. Analytical HPLC and ESI-MS characterization of purified product **12**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 15-50% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Ag(I) Ligation under Microwave Condition



The peptide *C*-terminal thioester **12** (3.8 mg, 1.442 µmol) was mixed with (sulfo-Xyl)SGAG tetrapeptide **5** (3.1 mg, 4.282 µmol), HOOBt (7.4 mg, 0.045 mmol) and $AgNO_3$ (2.6 mg, 0.015 mmol) in anhydrous DMSO (0.45 ml). The resulting mixture was treated with *i*Pr_2NEt (5.0 µL, 3.7 mg, 0.0288 mmol) and subjected to microwave irradiation (50 °C, 25 W, 20 min). The reaction was kept under stirring for additional 2 h at room temperature. Preparative HPLC purification (0% isocratic CH_3CN/25 mM NH_4OAc for initial 8 min then 5-50% linear gradient CH_3CN/25 mM NH_4OAc over 30 min) followed by concentration at reduced pressure and lyophilization till constant weight afforded the titled peptide **13** as a white powder (2.8 mg, 60% yield). (Recovery of peptide **5** 1.2 mg) HRMS (ESI) m/z: $[M-2H]^{2-}$ Calcd for $C_{133}H_{186}N_{32}O_{60}S^{2-}$ 1612.1126, found: 1612.1034; $[M-3H]^{3-}$ Calcd for $C_{133}H_{185}N_{32}O_{60}S^{3-}$ 1074.4060, found: 1074.4060; $[M-4H]^{4-}$ Calcd for $C_{133}H_{184}N_{32}O_{60}S^{4-}$ 805.5527, found: 805.5549



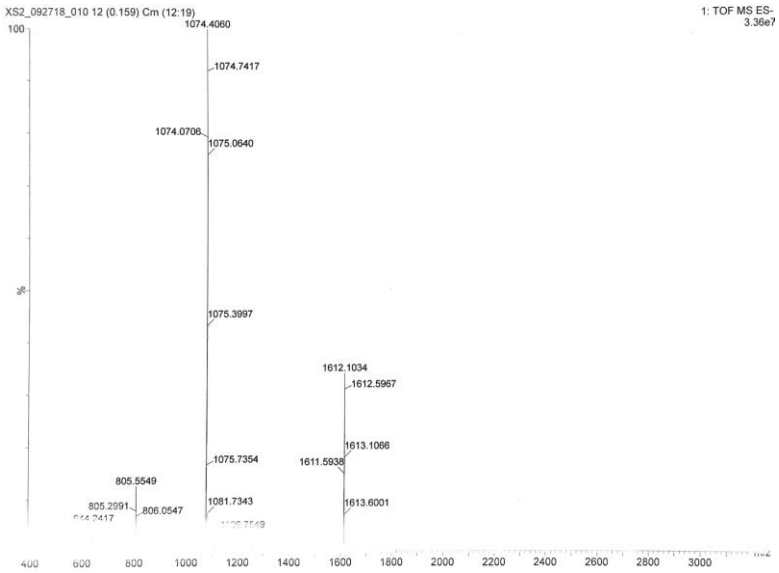
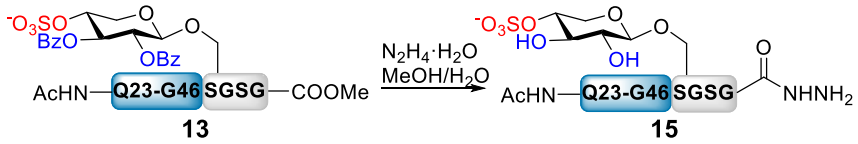


Figure S2. Analytical HPLC and ESI-MS characterization of purified product **13**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 15-50% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for crude reaction mixture and purified product).

Hydrazinolysis of Peptide 13



The peptide **13** (3.9 mg, 0.651 mmol) was treated with a mixture of $N_2H_4 \cdot H_2O$/MeOH/H_2O (20/80/1, v/v/v, 64 µL) under vigorous stirring at room temperature for 1 h. Preparative HPLC purification (0% isocratic CH_3CN/25 mM NH_4OAc for initial 8 min then 5-50% linear gradient CH_3CN/25 mM NH_4OAc over 30 min) followed by concentration at reduced pressure and lyophilization till constant weight afforded the titled peptide **15** as a white powder (3.0 mg, 77% yield). HRMS (ESI) m/z: $[M-2H]^{2-}$ Calcd for $C_{119}H_{178}N_{32}O_{58}S^{2-}$ 1508.0864, found: 1508.0867; $[M-3H]^{3-}$Calcd for $C_{119}H_{177}N_{32}O_{58}S^{3-}$ 1005.0552, found: 1005.0561; $[M-4H]^{4-}$ Calcd for $C_{119}H_{176}N_{32}O_{58}S^{4-}$ 753.5396, found: 753.5411

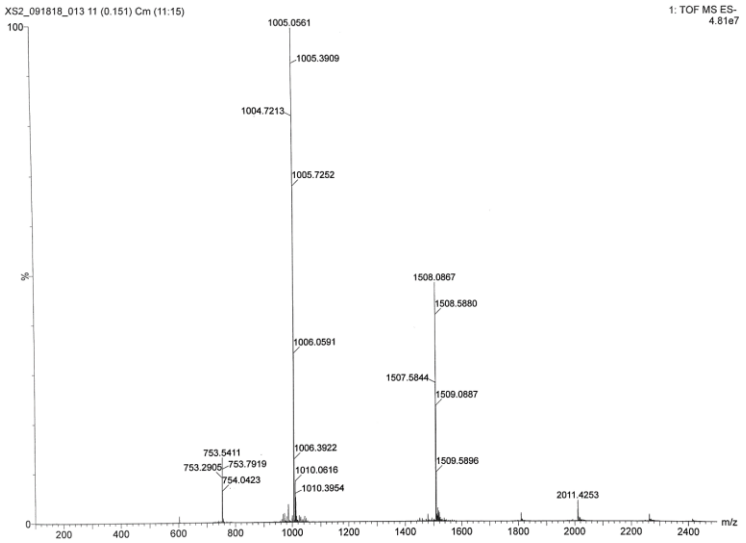
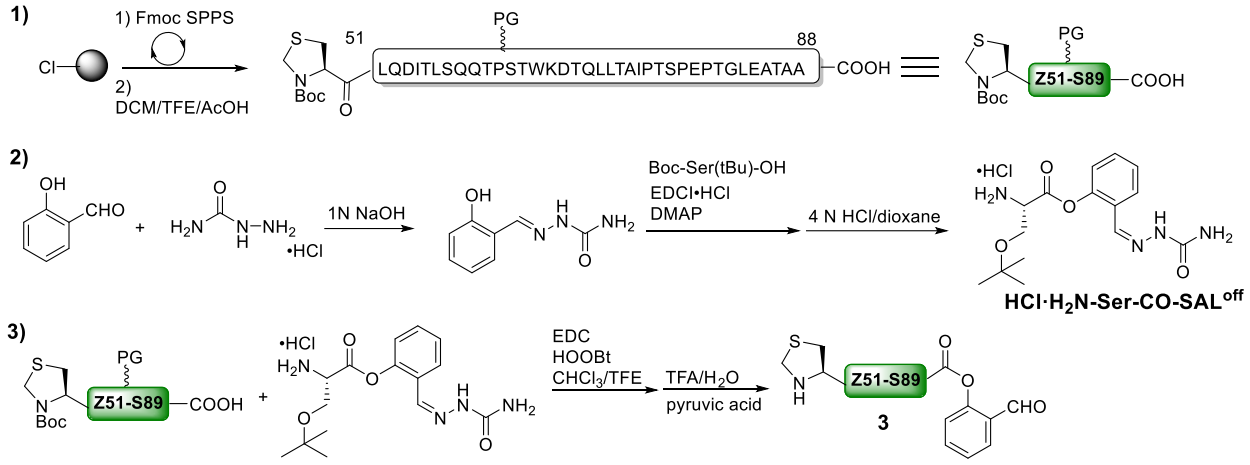


Figure S3. Analytical HPLC and ESI-MS characterization of purified product **15**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-95% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Preparation of peptide 3 salicylaldehyde (SAL) ester by *n+1* strategy

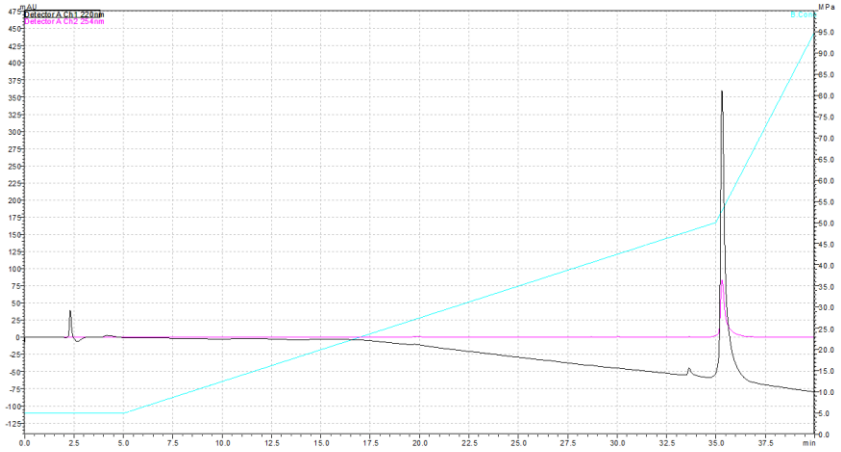


1) The peptide was prepared on 2-Cl-(Trt)-Cl resin on 0.1 mmol scale with CEM Discover Bio system as described in the general procedure and subjected to mild acidic cleavage cocktail (DCM/TFE/AcOH 8/1/1, v/v/v, 15 ml ×2, 1 h for each round). Following filtration, the resulting cleavage solutions were combined and concentrated to give crude protected peptide (0.477 g, 80.8%).

2) HCl·*H*$_2$*N*-Ser-*CO*-SAL^{off} was prepared as reported.[3]

3) The crude peptide (40.1 mg, 6.520 μmol) was dissolved in $CHCl_3$/trifluoroethanol (0.4 mL) and reacted with HCl·*H*$_2$*N*-Ser-*CO*-SAL^{off} (7.0 mg, 19.6 μmol) in the presence of EDC free base (3.0 mg, 3.5 μL, 19.6 μmol) and HOOBt (3.2 mg, 19.6 μmol). After stirring for 1 h, the reaction mixture was concentrated and subjected to 1.0 mL of TFA/H_2O (95/5, *v*/*v*) and pyruvic acid (93.2 μL, 1.30 mmol) for 2 h. The resulting

peptide SAL^{on} ester was concentrated under a stream of condensed air and triturated with cold diethyl ether to give a white suspension, which was centrifuged and the ether subsequently decanted. The crude peptide was dissolved in CH_3CN/H_2O with 0.1% TFA for 1 h to allow for fully deprotection of Trp side chain. Preparative HPLC purification (30% isocratic CH_3CN/H_2O containing 0.1% TFA for initial 10 min then 30-50% linear gradient CH_3CN/H_2O containing 0.1% TFA over 30 min) followed by concentration at reduced pressure and lyophilization afforded the titled peptide SAL^{on} ester **3** as a white powder (10.9 mg, 40% yield). HRMS (ESI) m/z: $[M+2H]^{2+}$ Calcd for $C_{186}H_{295}N_{45}O_{65}S^{2+}$ 2116.5469, found: 2116.5276; $[M+H+Na]^{2+}$ Calcd for $C_{186}H_{294}N_{45}O_{65}SNa^{2+}$ 2127.5379, found: 2127.5188; $[M+3H]^{3+}$ Calcd for $C_{186}H_{296}N_{45}O_{65}S^{3+}$ 1411.3670, found: 1411.3644; $[M+2H+Na]^{3+}$ Calcd for $C_{186}H_{295}N_{45}O_{65}SNa^{3+}$ 1418.6944, found: 1419.0227; $[M+H+2Na]^{3+}$ Calcd for $C_{186}H_{294}N_{45}O_{65}SNa_2^{3+}$ 1426.0217, found: 1426.3506; $[M+4H]^{4+}$ Calcd for $C_{186}H_{297}N_{45}O_{65}S^{4+}$ 1058.7771, found: 1058.7778; $[M+3H+Na]^{4+}$ Calcd for $C_{186}H_{296}N_{45}O_{65}SNa^{4+}$ 1064.2726, found: 1064.5197; $[M+2H+2Na]^{4+}$ Calcd for $C_{186}H_{295}N_{45}O_{65}SNa_2^{4+}$ 1069.7681, found: 1070.0155; $[M+4H+Na]^{5+}$ Calcd for $C_{186}H_{297}N_{45}O_{65}SNa^{4+}$ 851.6195, found: 852.0180.



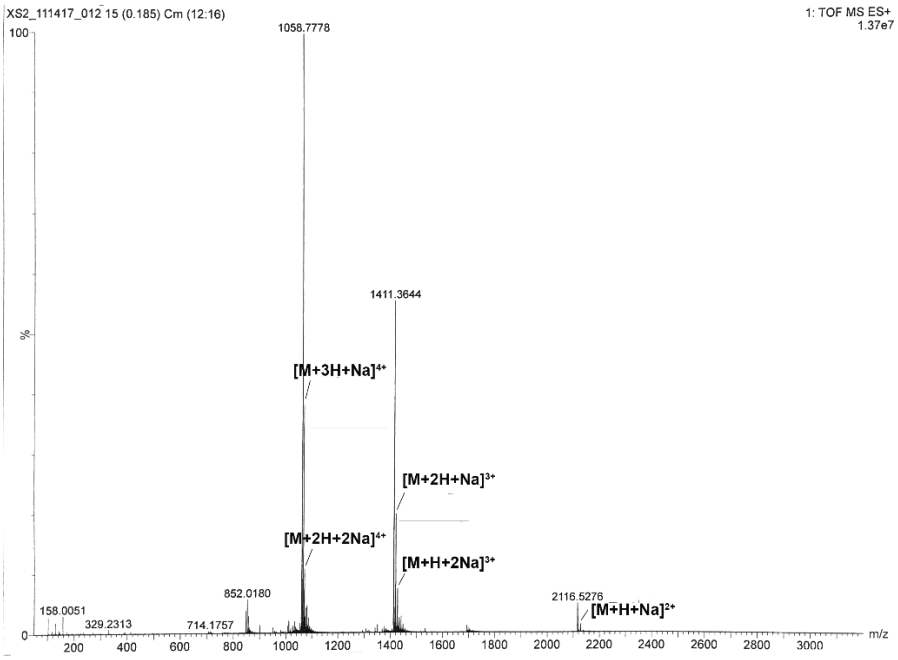
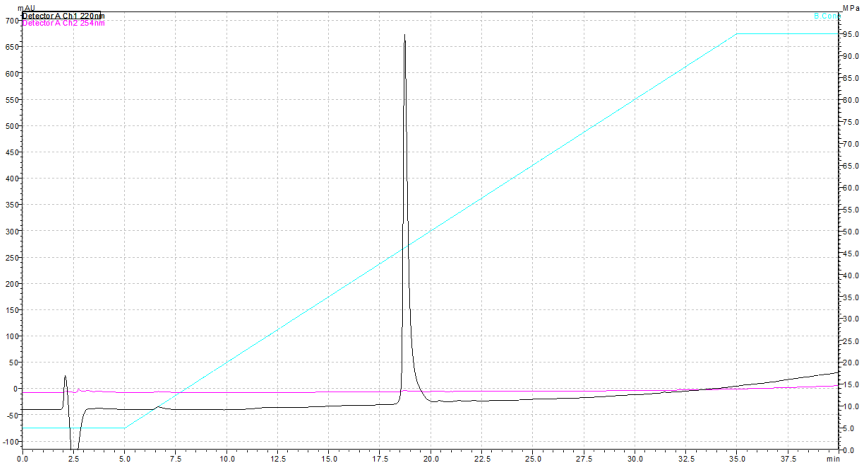


Figure S4. Analytical HPLC and ESI-MS characterization of purified product **3**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-50% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Preparation of peptide 4

The peptide was prepared on 0.1 mmol scale with CEM Discover Bio system following the general procedure for microwave assisted SPPS and subjected to mild acidic cleavage cocktail (DCM/TFE/AcOH 8/1/1, v/v/v, 15 ml × 2, 1 h for each round). Following filtration, the resulting cleavage solutions were combined and concentrated to give crude protected peptide (356.6 mg, 82.0%).

The crude peptide (67.1 mg, 15.4 μmol) was treated with TFA/H_2O/TIPS (95/2.5/2.5, v/v/v, 2 ml) for 2 h. The resulting peptide was concentrated under a stream of condensed air and triturated with cold diethyl ether to give a white suspension, which was centrifuged and the ether subsequently decanted. Preparative HPLC purification (15-50% linear gradient CH_3CN/H_2O containing 0.1% TFA over 30 min) followed by lyophilization yielded the peptide fragment **4** as white powder (32.1 mg, 65% yield). HRMS (ESI) m/z: $[M+2H]^{2+}$ Calcd for $C_{137}H_{226}N_{36}O_{51}^{2+}$ 1596.3110, found: 1596.2856; $[M+3H]^{3+}$ Calcd for $C_{137}H_{227}N_{36}O_{51}^{3+}$ 1064.5431, obsv:1064.5364; $[M+4H]^{4+}$ Calcd for $C_{137}H_{228}N_{36}O_{51}^{4+}$ 798.6591, found: 798.6584.



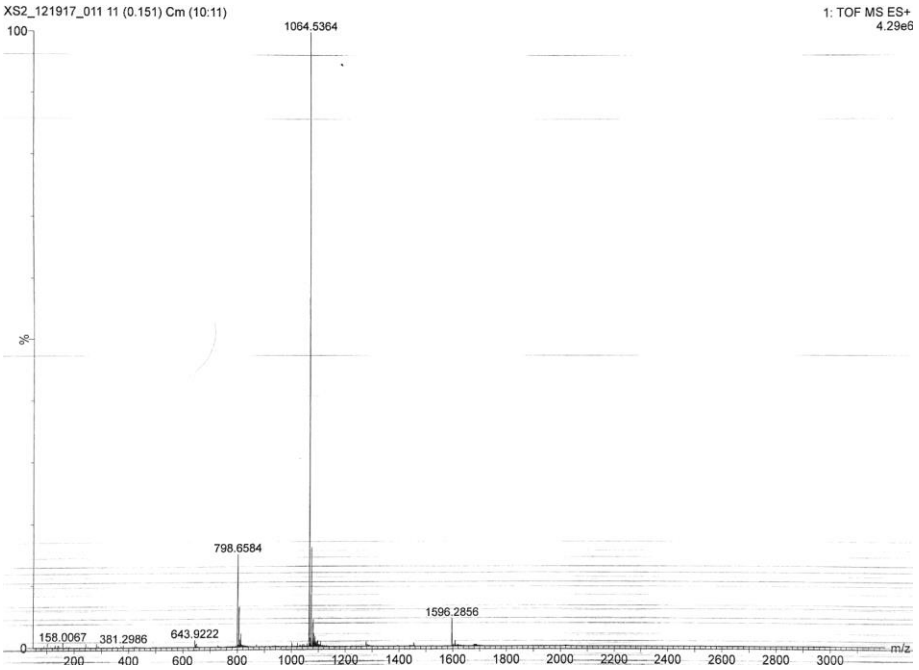
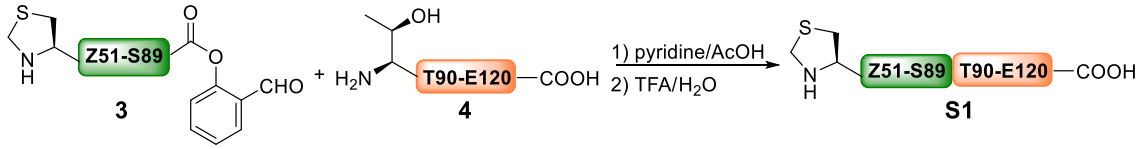
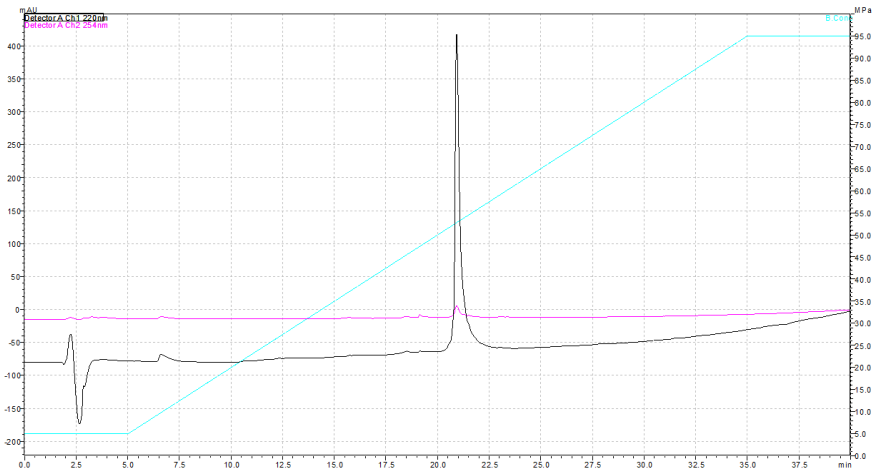


Figure S5. Analytical HPLC and ESI-MS characterization of purified product **4**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-95% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Preparation of peptide S1 via STL



The peptide SAL^{on} ester peptide **3** (10.5 mg, 1.6 equiv.) and peptide **4** (4.7 mg, 1.0 equiv, 17.5 mM) were incubated in pyridine/acetic acid (85 µL, 1/12 mole/mole) at room temperature. The reaction progress was monitored HPLC and ESI-MS. After the completion of the reaction, the solvent was blown off under a stream of condensed air. The residue was then treated with TFA/H_2O (95/5, v/v). Preparative HPLC purification (20–40% CH3CN/H2O containing 0.1% TFA over 30 min) followed by concentration at reduced pressure and lyophilization afforded of the titled peptide **S1** as a white powder (5.1 mg, 47% yield). (Recovery of peptide **3** 0.6 mg, 6%; recovery of peptide **4** 0.7 mg, 15%). HRMS (ESI) m/z: $[M+3H]^{3+}$ Calcd for $C_{316}H_{514}N_{81}O_{114}S^{3+}$ 2434.2239, found: 2434.5088; $[M+4H]^{4+}$ Calcd for $C_{316}H_{515}N_{81}O_{114}S^{4+}$ 1825.9198, found: 1826.1616; $[M+5H]^{5+}$ Calcd for $C_{316}H_{516}N_{81}O_{114}S^{5+}$ 1460.9373, found: 1461.1317; $[M+6H]^{6+}$ Calcd for $C_{316}H_{517}N_{81}O_{114}S^{6+}$ 1217.6156, found: 1217.7769; $[M+7H]^{7+}$ Calcd for $C_{316}H_{518}N_{81}O_{114}S^{7+}$ 1043.8144, found: 1043.9550; $[M+8H]^{8+}$ Calcd for $C_{316}H_{519}N_{81}O_{114}S^{8+}$ 913.4635, found: 913.5978; $[M+9H]^{9+}$ Calcd for $C_{316}H_{520}N_{81}O_{114}S^{9+}$ 812.0795, found: 812.1904; $[M+10H]^{10+}$ Calcd for $C_{316}H_{521}N_{81}O_{114}S^{10+}$ 730.9723, found: 731.0743.



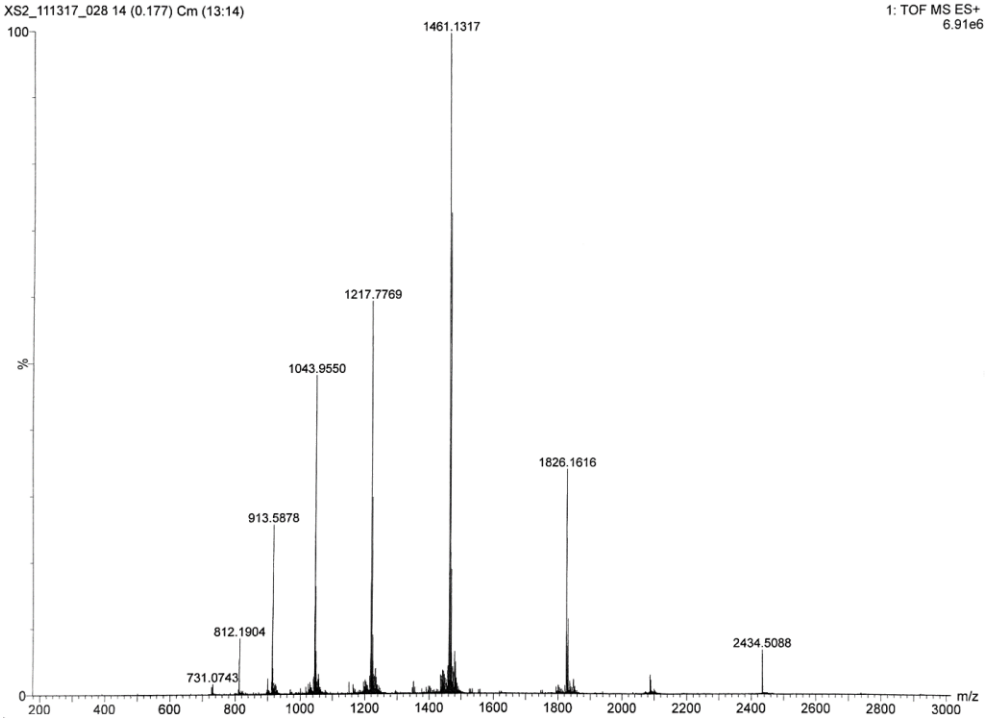
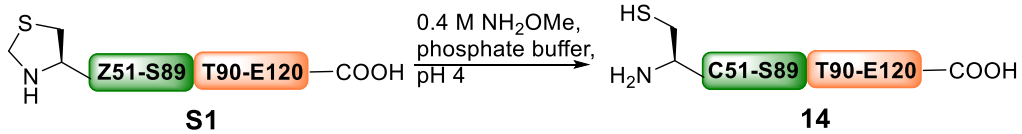


Figure S6. Analytical HPLC and ESI-MS characterization of purified product **S1**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 30-40% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for crude reaction mixture); isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-95% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Preparation of peptide 14



S1 **14**

The peptide **S1** (8.6 mg, 1.178 mmol) was dissolved in degassed NCL buffer (6 M Guanidine·HCl, 0.2 M NaH_2PO_4, 0.7 mL) containing $MeONH_2$·HCl (0.4 M) at pH 4.[4] The resulting solution was stirred at room

temperature and the reaction progress was monitored by HPLC and ESI-MS. After completion of the reaction, the mixture was treated with TCEP·HCl for 5 min to regenerate the Cys in the reduced form. Preparative HPLC purification (20–40% CH_3CN/H_2O containing 0.1% TFA over 30 min) followed by concentration at reduced pressure and lyophilization afforded of the titled peptide **14** as a white powder (7.1 mg, 83% yield). HRMS (ESI) m/z: $[M+3H]^{3+}$ Calcd for $C_{315}H_{514}N_{81}O_{114}S^{3+}$ 2430.2239, found: 2430.4751; $[M+4H]^{4+}$ Calcd for $C_{315}H_{515}N_{81}O_{114}S^{4+}$ 1822.9198, found: 1823.1573; $[M+5H]^{5+}$ Calcd for $C_{315}H_{516}N_{81}O_{114}S^{5+}$ 1458.5373, found: 1458.7302; $[M+6H]^{6+}$ Calcd for $C_{315}H_{517}N_{81}O_{114}S^{6+}$ 1215.6156, found: 1215.7750; $[M+7H]^{7+}$ Calcd for $C_{315}H_{518}N_{81}O_{114}S^{7+}$ 1042.1001, found: 1042.2388; $[M+8H]^{8+}$ Calcd for $C_{315}H_{519}N_{81}O_{114}S^{8+}$ 911.9635, found: 912.0859; $[M+9H]^{9+}$ Calcd for $C_{315}H_{520}N_{81}O_{114}S^{9+}$ 810.7462, found: 810.8551; $[M+10H]^{10+}$ Calcd for $C_{315}H_{521}N_{81}O_{114}S^{10+}$ 729.7723, found: 729.8714; $[M+11H]^{11+}$ Calcd for $C_{315}H_{522}N_{81}O_{114}S^{11+}$ 663.5209, found: 663.6113.

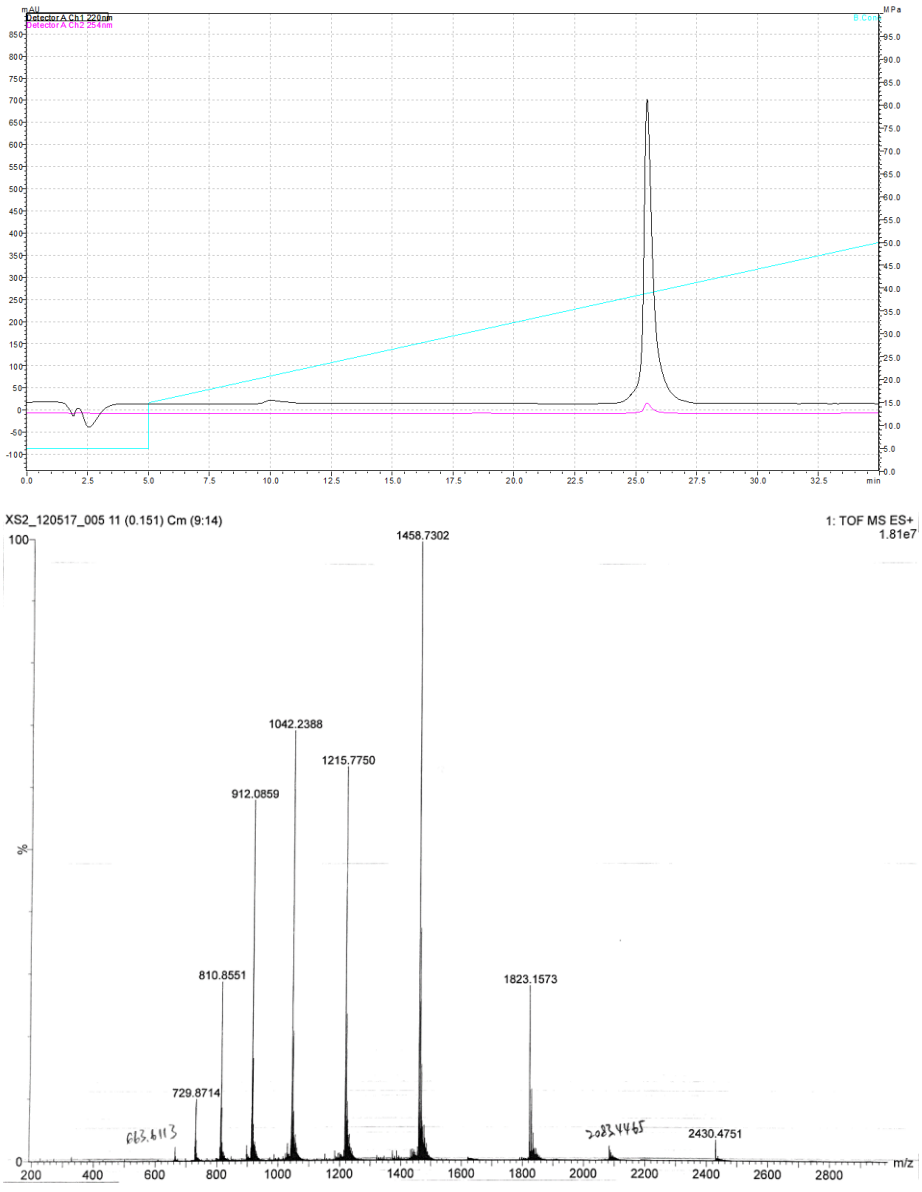
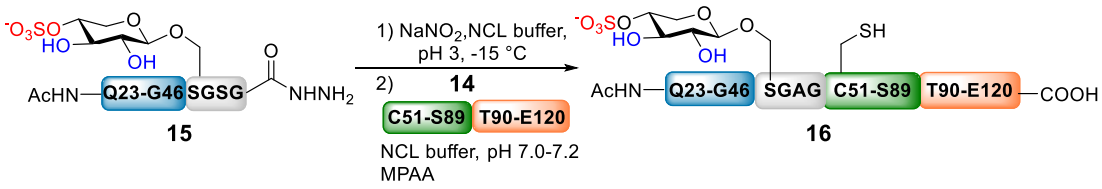
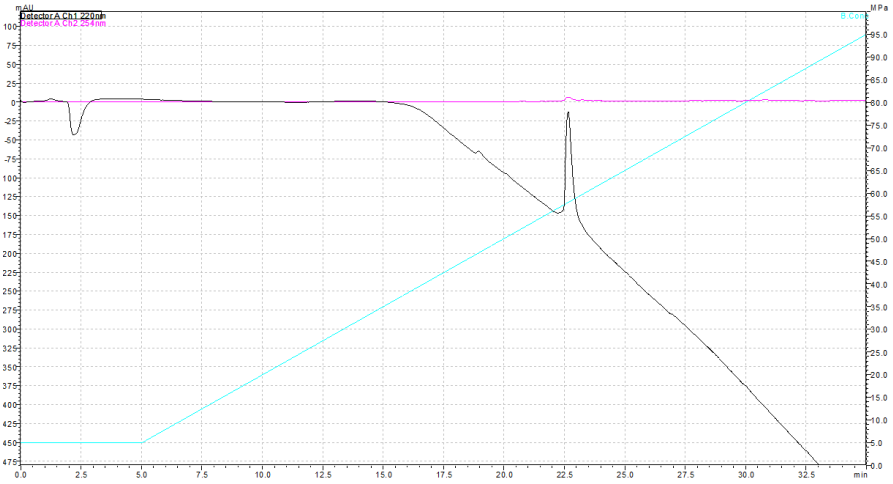


Figure S7. Analytical HPLC and ESI-MS characterization of purified product **14**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 20-40% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for crude reaction mixture); isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 15-50% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

Hydrazide Activation & NCL (one-pot)



The peptide hydrazide **15** (0.9 mg, 0.3 µmol) was dissolved in 70 µL NCL buffer (6 M guanidine-HCl, 0.2 M NaH_2PO_4, pH 3) at −15 °C. It was treated with $NaNO_2$ (7.5 µL, 0.2 M freshly dissolved in H_2O) and stirred for 15 min at −15 °C. The pH value of the solution was adjusted to 6.5 and the reaction vial was removed from the cold bath. A solution of MPAA (8 µL, 0.2 M freshly prepared in 6 M guanidine-HCl, 0.2 M NaH_2PO_4, pH 7) was added. Peptide **14** (1.6 mg, 0.22 µmol) was added. The final pH was maintained at 7.0 – 7.2. After 16 h, the ligation was completed. The reaction mixture was treated with TCEP·HCl for 5 min and the aqueous solution was washed with diethyl ether (3 x 1 mL). The product was purified by preparative HPLC (0% isocratic CH_3CN/25 mM NH_4OAc for initial 8 min then a linear gradient of 5-50% CH_3CN/25 mM NH_4OAc over 30 min) followed by concentration at reduced pressure and lyophilization till constant weight afforded of the titled peptide **16** as a white powder (0.8 mg, 36% yield). HRMS (ESI) m/z: $[M-4H]^{4-}$ Calcd for $C_{433}H_{683}N_{113}O_{171}S_2^{4-}$ 2567.6963, found: 2567.7449; $[M-5H]^{5-}$ Calcd for $C_{433}H_{682}N_{113}O_{171}S_2^{5-}$ 2053.9556, found: 2053.9233; $[M-6H]^{6-}$ Calcd for $C_{433}H_{681}N_{113}O_{171}S_2^{6-}$ 1711.4618, found: 1711.6259; $[M-7H]^{7-}$ Calcd for $C_{433}H_{680}N_{113}O_{171}S_2^{7-}$ 1466.8234, found: 1466.9808; $[M-8H]^{8-}$ Calcd for $C_{433}H_{679}N_{113}O_{171}S_2^{8-}$ 1283.3445, found: 1283.4744; $[M-9H]^{9-}$ Calcd for $C_{433}H_{678}N_{113}O_{171}S_2^{9-}$ 1140.6388, found: 1140.7588; $[M-10H]^{10-}$ Calcd for $C_{433}H_{677}N_{113}O_{171}S_2^{10-}$ 1026.4742, found: 1026.4807; $[M-11H]^{11-}$ Calcd for $C_{433}H_{676}N_{113}O_{171}S_2^{11-}$ 933.0668, found: 933.0719; $[M-12H]^{12-}$ Calcd for $C_{433}H_{675}N_{113}O_{171}S_2^{12-}$ 855.2273, found: 855.3157; $[M-13H]^{13-}$ Calcd for $C_{433}H_{674}N_{113}O_{171}S_2^{13-}$ 789.3631, found: 789.4450; $[M-14H]^{14-}$ Calcd for $C_{433}H_{673}N_{113}O_{171}S_2^{14-}$ 732.9080, found: 732.9832; $[M-15H]^{15-}$ Calcd for $C_{433}H_{672}N_{113}O_{171}S_2^{15-}$ 683.9804, found: 683.9821; $[M-16H]^{16-}$ Calcd for $C_{433}H_{671}N_{113}O_{171}S_2^{16-}$ 641.1686, found: 641.2412. $C_{433}H_{687}N_{113}O_{171}S_2$ Mol. Wt. calc: 10275.9990, (deconvoluted) found: 10276.0000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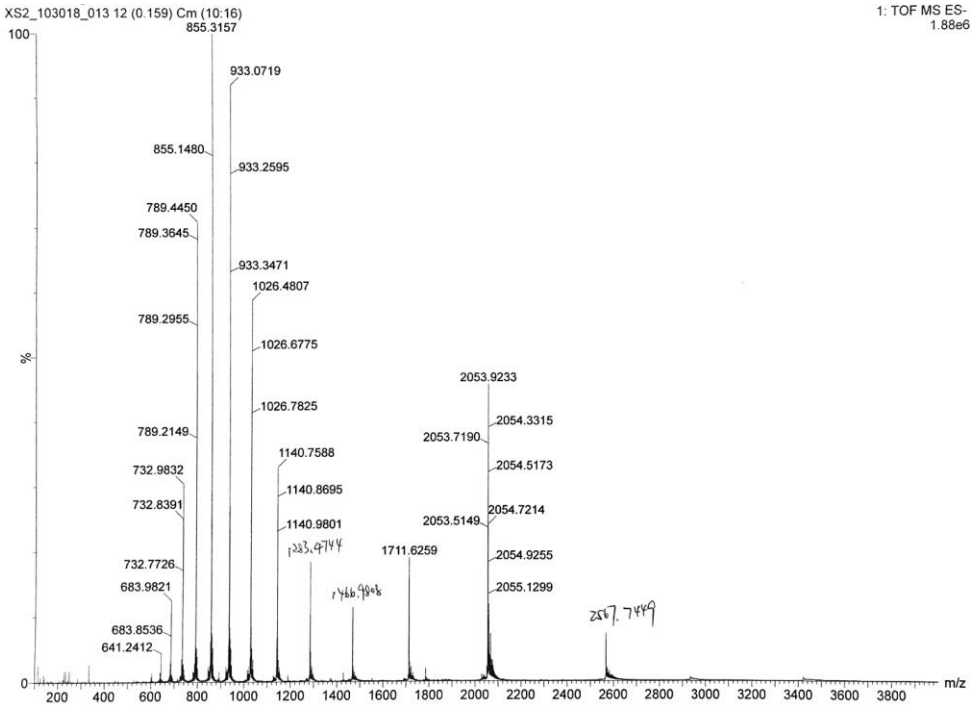
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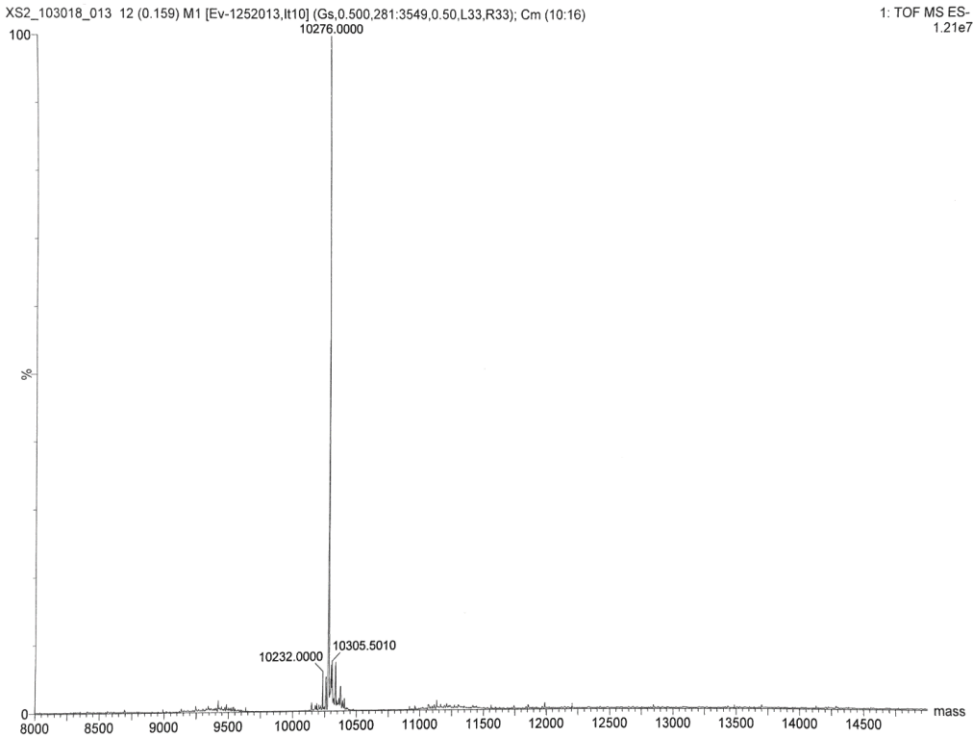
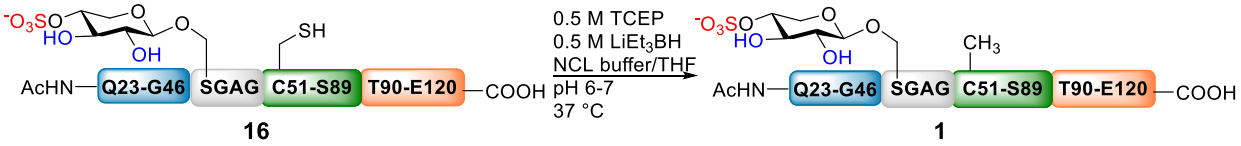


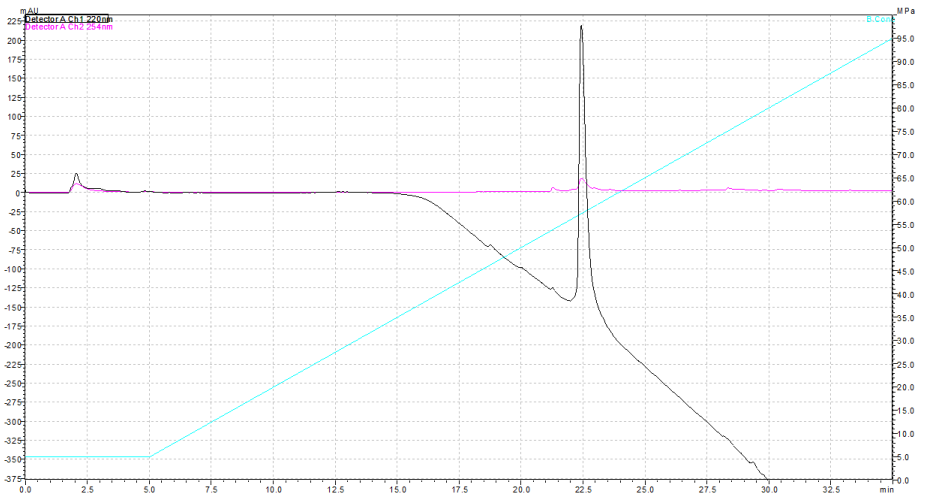
Figure S8. Analytical HPLC and ESI-MS characterization of purified product **16**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-95% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes.

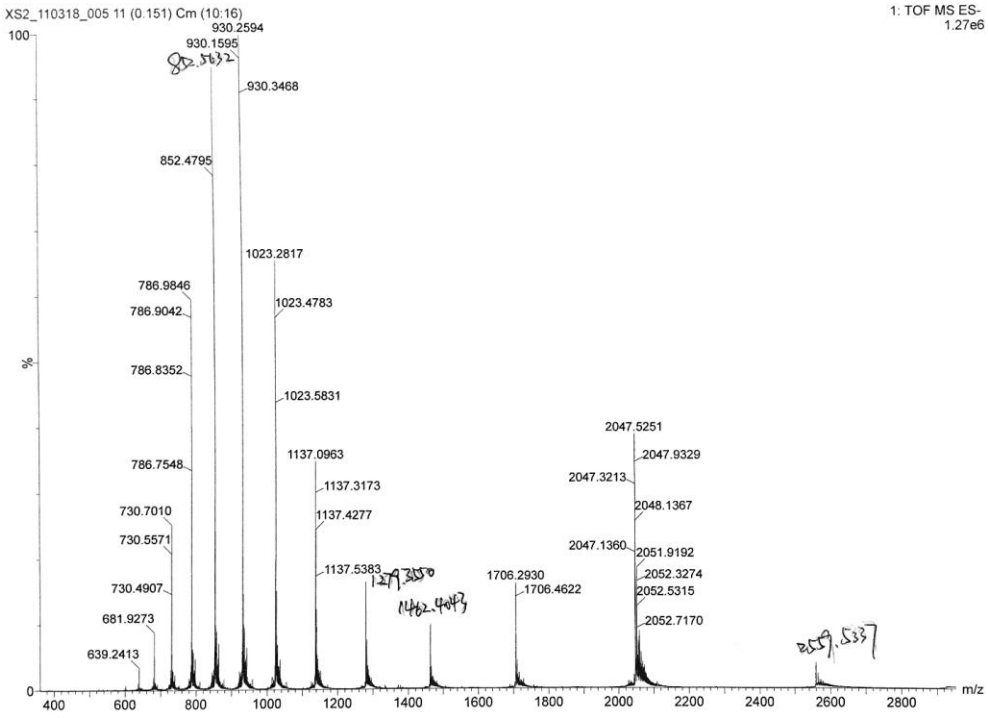
Desulfurization to afford Product 1



A solution of $LiEt_3BH$ (1 M in THF) was added slowly into an equal volume of TCEP·HCl (1 M in 6 M guanidine-HCl, 0.2 M NaH_2PO_4, pH 6). The pH of the mixture was adjusted to 6 – 7. The peptide **16** (2.3 mg, 0.22 μmol) was ported into a glass vial and treated with the above $LiEt_3BH$/TCEP premixed solution (0.24 mL). The reaction mixture was maintained at 37 °C, pH 6 – 7 for 15 h and purified by preparative HPLC (0% isocratic CH_3CN/25 mM NH_4OAc for initial 8 min then 5-50% linear gradient CH_3CN/25 mM NH_4OAc over 30 min) followed by concentration at reduced pressure and lyophilization till constant weight afforded of the titled product **1** as a white powder (1.4 mg, 61% yield). HRMS (ESI) m/z: $[M-4H]^{4-}$ Calcd for $C_{433}H_{683}N_{113}O_{171}S^{4-}$ 2559.7033, found: 2559.5337; $[M-5H]^{5-}$ Calcd for $C_{433}H_{682}N_{113}O_{171}S^{5-}$ 2047.5612, found: 2047.5251; $[M-6H]^{6-}$ Calcd for $C_{433}H_{681}N_{113}O_{171}S^{6-}$ 1706.1331, found: 1706.2930; $[M-7H]^{7-}$ Calcd for $C_{433}H_{680}N_{113}O_{171}S^{7-}$ 1462.2559, found: 1462.4043; $[M-8H]^{8-}$ Calcd for $C_{433}H_{679}N_{113}O_{171}S^{8-}$ 1279.3480, found: 1279.3550; $[M-9H]^{9-}$ Calcd for $C_{433}H_{678}N_{113}O_{171}S^{9-}$ 1137.0863, found: 1137.0963; $[M-10H]^{10-}$ Calcd for $C_{433}H_{677}N_{113}O_{171}S^{10-}$ 1023.2770, found: 1023.2817; $[M-11H]^{11-}$ Calcd for $C_{433}H_{676}N_{113}O_{171}S^{11-}$ 930.1602, found: 930.2594; $[M-12H]^{12-}$ Calcd for $C_{433}H_{675}N_{113}O_{171}S^{12-}$ 852.5629, found: 852.5632;

$[M-13H]^{13-}$ Calcd for $C_{433}H_{674}N_{113}O_{171}S^{13-}$ 786.9037, found: 786.9846; $[M-14H]^{14-}$ Calcd for $C_{433}H_{673}N_{113}O_{171}S^{14-}$ 730.6243, found: 730.7010; $[M-15H]^{15-}$ Calcd for $C_{433}H_{672}N_{113}O_{171}S^{15-}$ 681.8489, found: 681.9273; $[M-16H]^{16-}$ Calcd for $C_{433}H_{671}N_{113}O_{171}S^{16-}$: 639.1704, found: 639.2413. $C_{433}H_{687}N_{113}O_{171}S$ Mol. Wt. calc: 10243.9390, (deconvoluted) found: 10244.0000





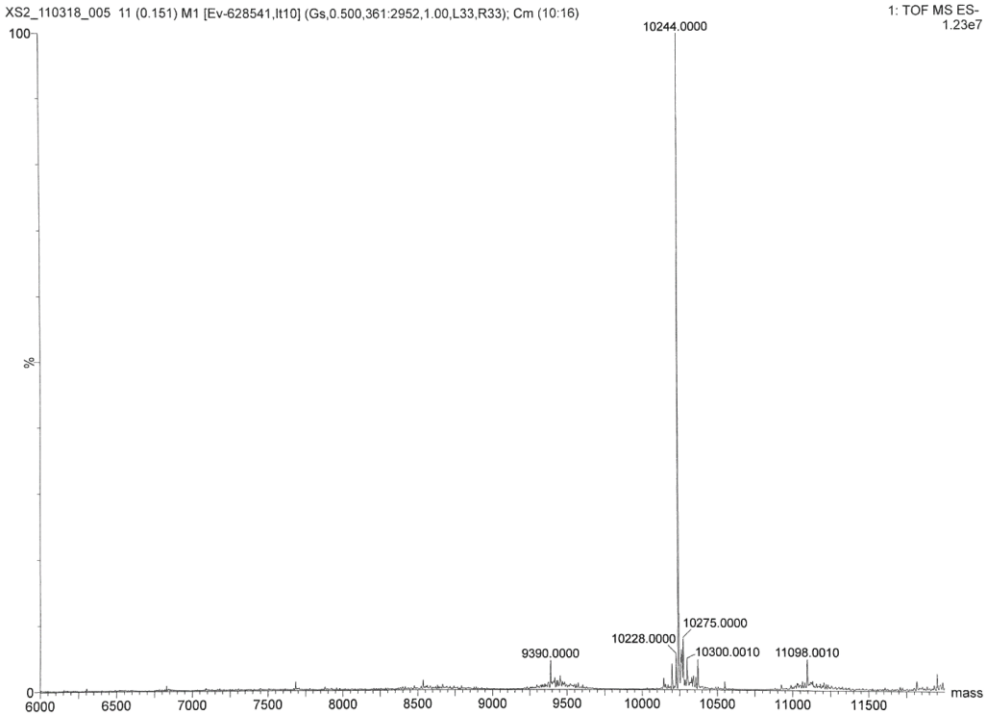


Figure S9. Analytical HPLC and ESI-MS characterization of purified product **1**. Dual wavelength UV detector (220 nm in black and 254 nm in purple). Gradient (in turquoise): isocratic 5% CH_3CN/H_2O with 0.1% TFA for initial 5 minutes, then 5-95% CH_3CN/H_2O with 0.1% TFA linear gradient over 30 minutes (for purified product).

^{1}H and ^{13}C NMR Chemical Shifts of Xyloside of **1**

Carbon	^{13}C δ (ppm)	Proton	^{1}H δ (ppm)
C-1	102.7	1-H	4.35
C-2	72.5	2-H	3.29, dd, *J* = 9.6, 7.8 Hz
C-3	73.1	3-H	3.54
C-4	76.0	4-H	4.12
C-5	63.2	5-H	3.37
		5-H’	4.13

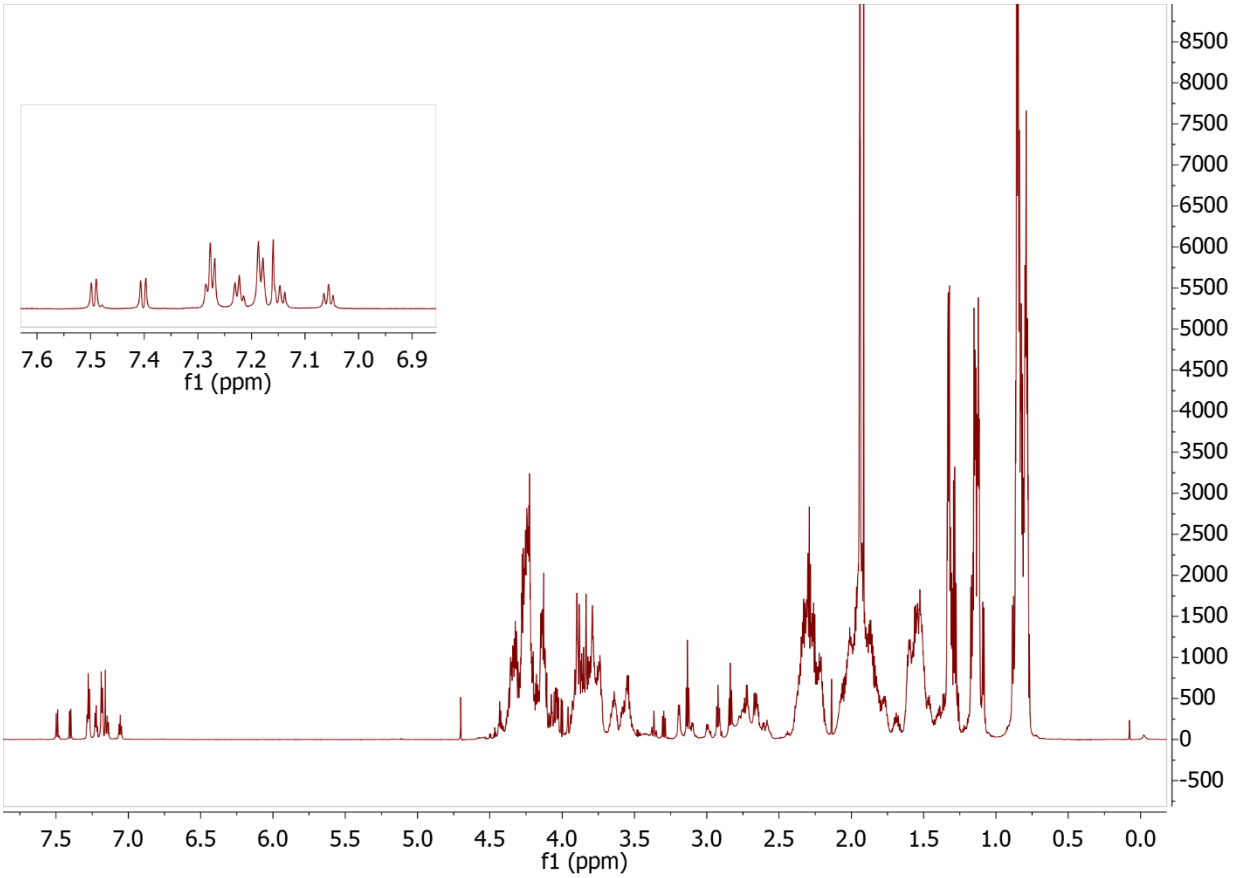


Figure S10. ^{1}H NMR of syndecan-1 like glyco-polypeptide **1**.

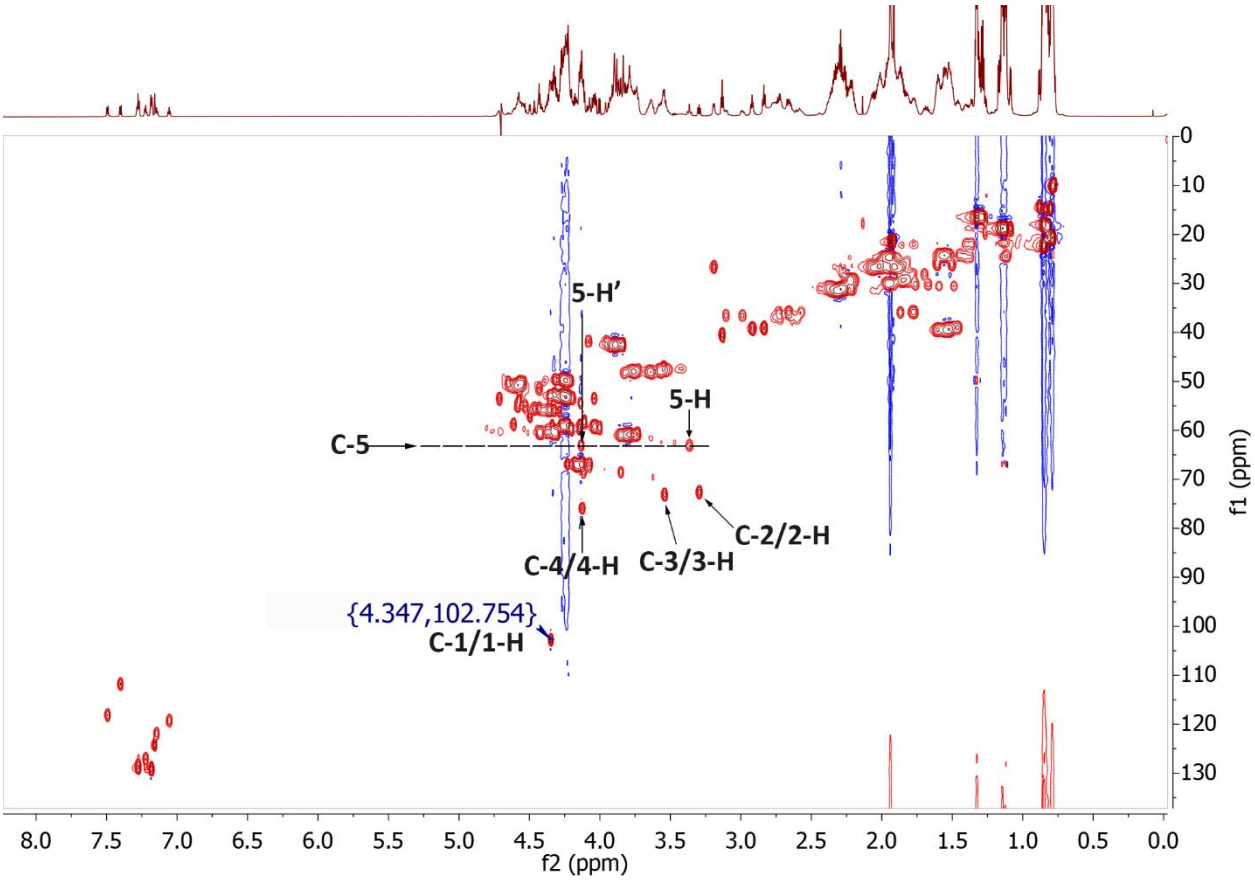


Figure S11. HSQC of syndecan-1 like glyco-polypeptide **1**. Characteristic cross peaks concerning the presence of xyloside were mapped.

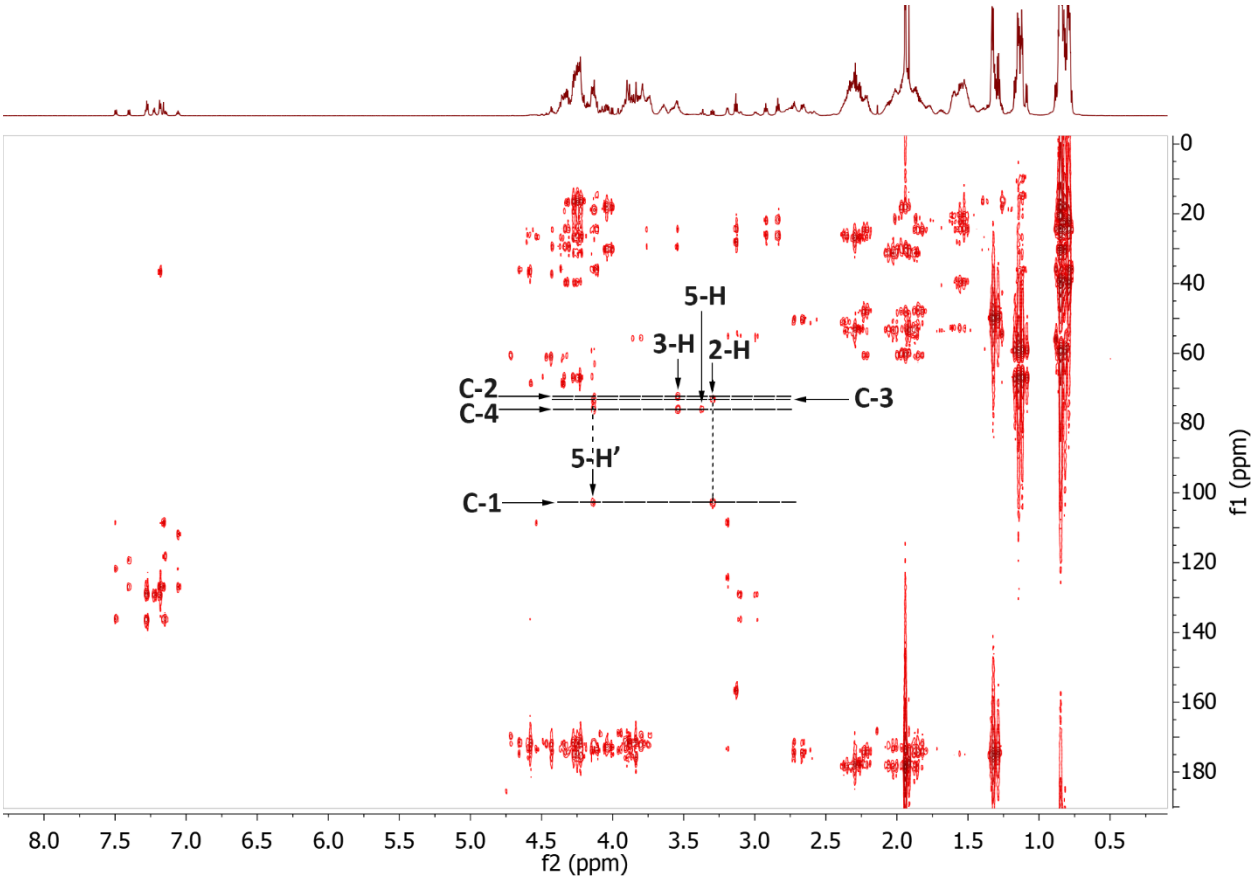


Figure S12. HMBC of syndecan-1 like glyco-polypeptide **1**. Characteristic cross peaks concerning the presence of xyloside were mapped.

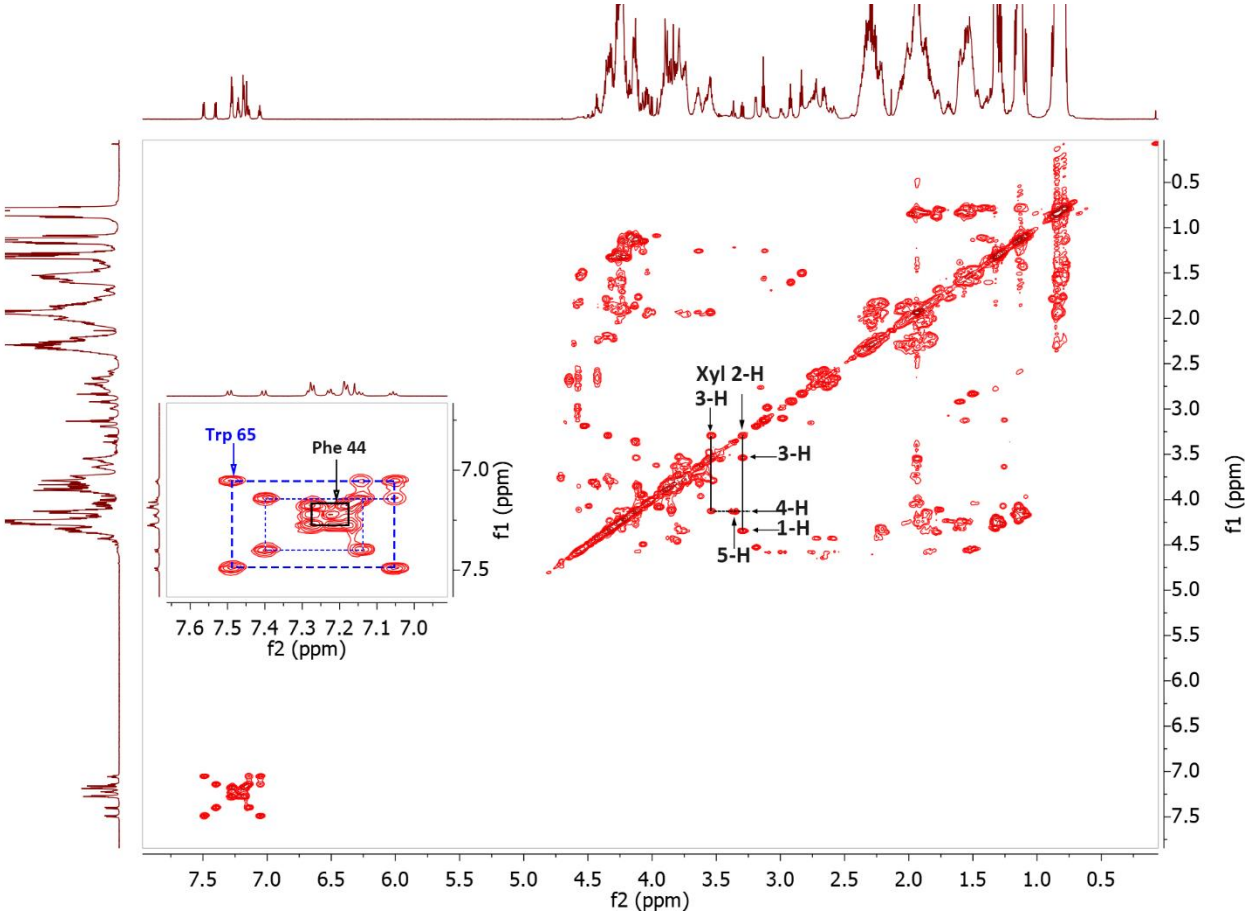


Figure S13. COSY of syndecan-1 like glyco-polypeptide **1**. Characteristic cross peaks concerning the presence of Trp 65, Phe 44 and xyloside were mapped.

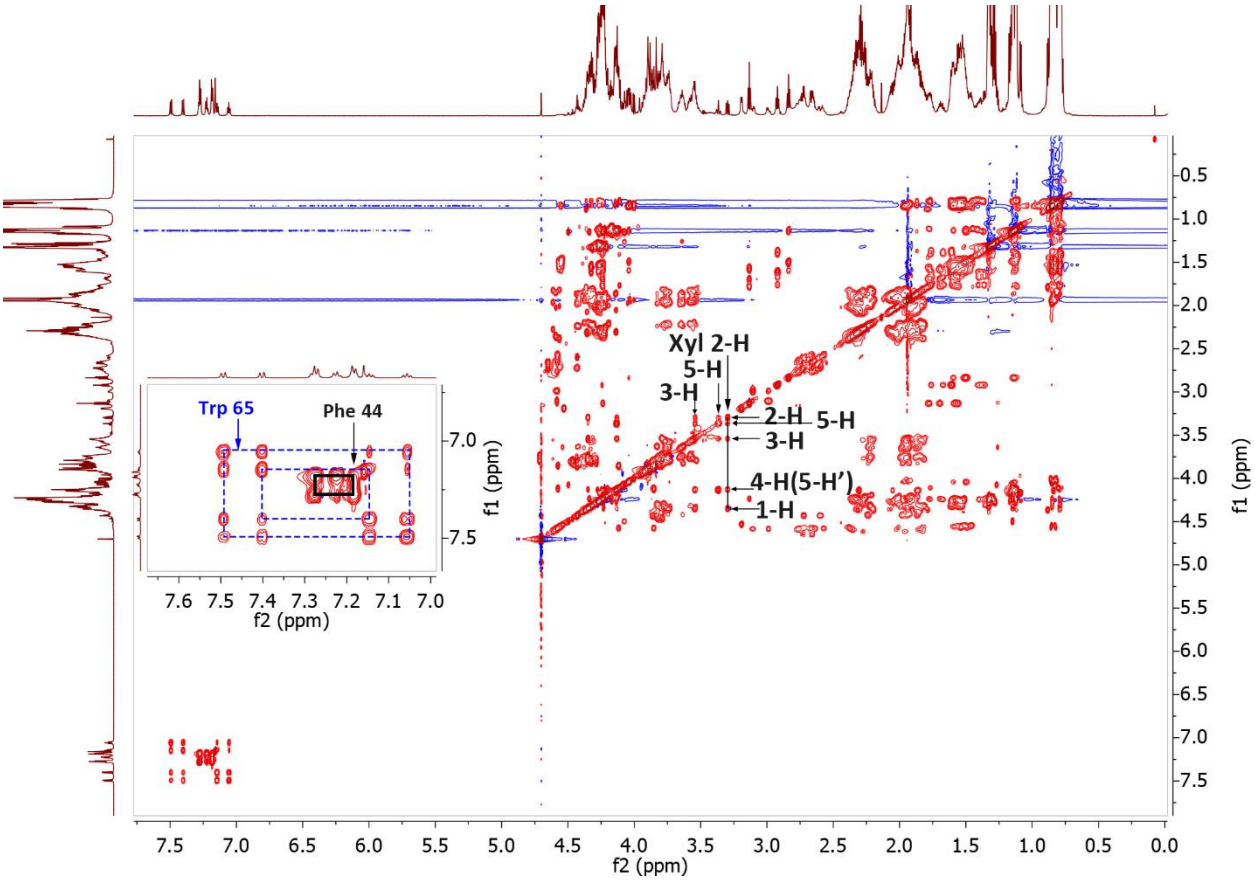
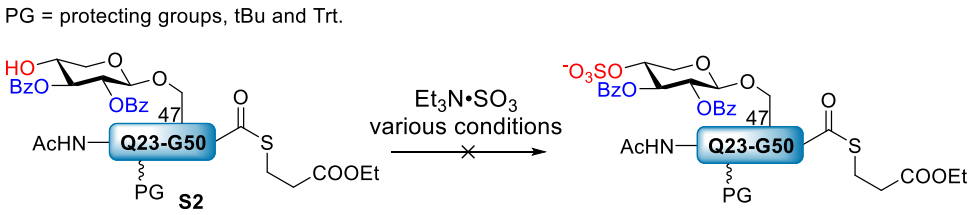


Figure S14. TOCSY of syndecan-1 like glyco-polypeptide **1**. Characteristic cross peaks concerning the presence of Trp 65, Phe 44 and xyloside were mapped.

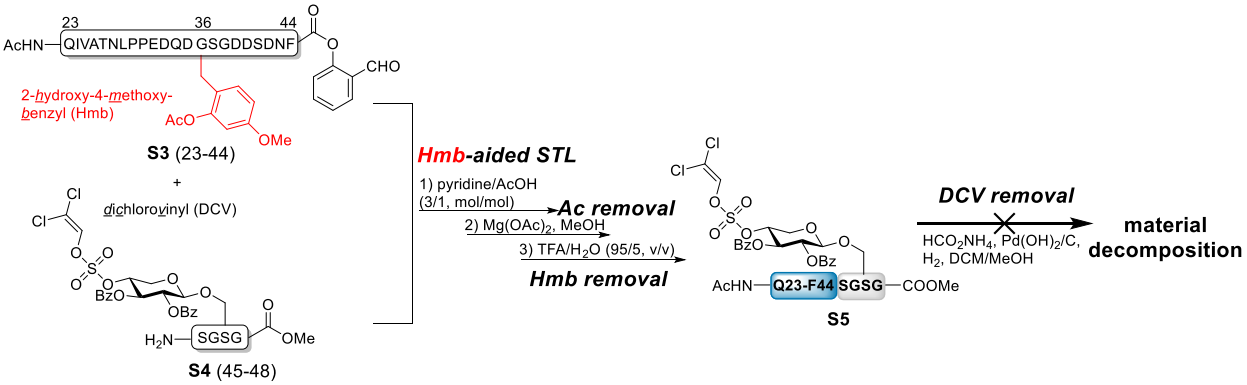
Late-stage sulfation was attempted on glycopeptide fragment **S2**. No desired product was observed (Table S1). Entry 1: conventional sulfation condition; Entry 2, sulfation under microwave;[5] Entry 3, acid-catalyzed sulfation at low temperatures.[6]

Table S1. Attempts of direct sulfation on orthogonally protected fragment Q23−G50



entry	solvent (conc.)	$Et_3N{\cdot}SO_3$ equiv	temperature and duration	results
1	DMF (30 mM)	5	55-60 °C, oil bath, 10.5 h	No desired product
2	Et_3N/pyridine/DMF (1/10/5, v/v/v, 0.4 mM)	25	MW 50 °C, 20 min → MW 80 °C, 20 min → MW 100 °C, 20 min	No desired product
3[a]	TfOH in DMF (20 mM)	5	-50 °C, 1 h → -10 °C → 10 °C	No desired product

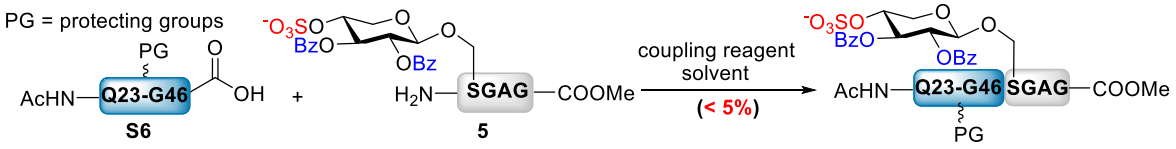
[a]Procedure: peptide and $Et_3N{\cdot}SO_3$ at -50 °C, TfOH (1 equiv) was added; the reaction was maintained at -50 °C for 1h, which was gradually warmed to -10 °C over 1h, and TfOH (1 equiv.) was added again at -10 °C. The reaction was then gradually warmed to 10 °C.



Scheme S1. Attempts with DCV-protected sulfate building blocks. DCV protected glycosyl amino acid was prepared, which was applied to SPPS for peptide chain elongation leading to DCV protected glycopeptide **S4**. While STL between peptides **S3** and **S4** yielded the intermediate peptide **S5**, unfortunately, no desired glycopeptide was obtained due to material decomposition during DCV removal.

With the tetrapeptide cassette **5**, the direct coupling approach was tested (**Table S2**). With a variety of peptide coupling conditions (concentration, stoichiometry, coupling reagents, solvents), <5% of the desired product was detected within the initial 2 h. No further progress was observed with reaction time extended to 2 days.

Table S2. Direct coupling between peptide **S6** and cassette **5**[a]



[a]Reactions were monitored by ESI-MS for up to 55 h.

entry	coupling reagents	molar ratio of **S6**/**5**	concentration of **5**	solvent (v/v)	product
1	HATU/*i*Pr$_2$NEt	2/1	1 mM	CHCl3/TFE (3/1)	< 5%
2	HATU/*i*Pr$_2$NEt	1/5	0.1 M	DCM/DMF (1/1)	< 5%
3	EDC/HOOBt	1/5	0.1 M	DCM/DMF (1/1)	< 5%

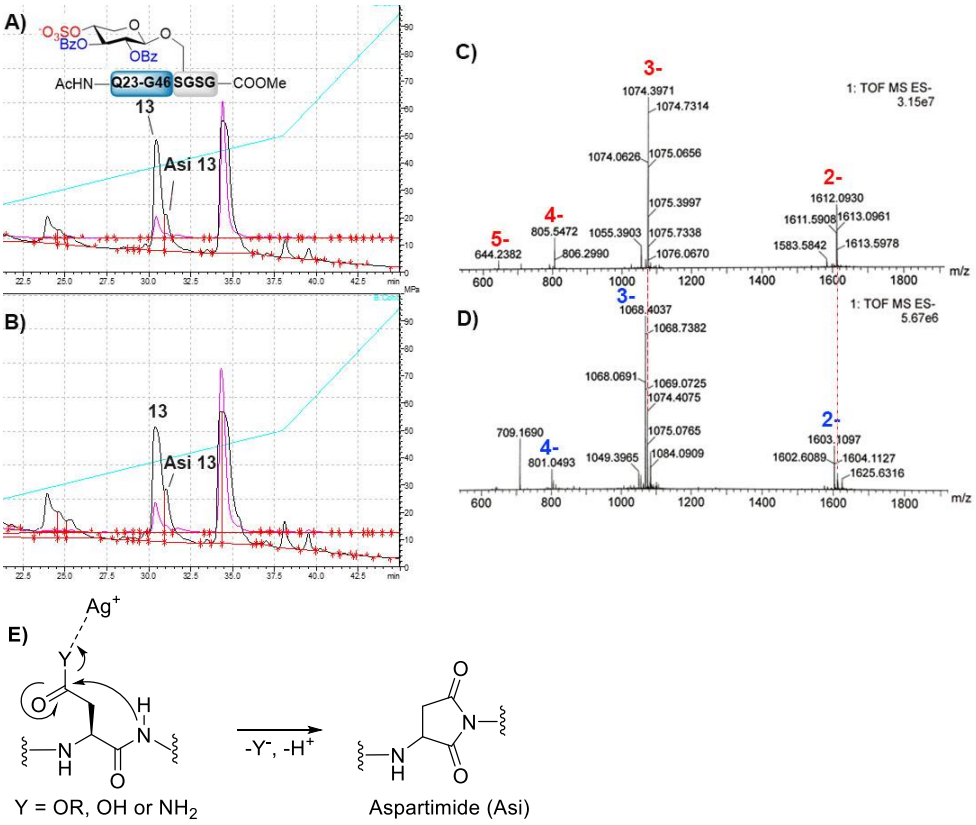
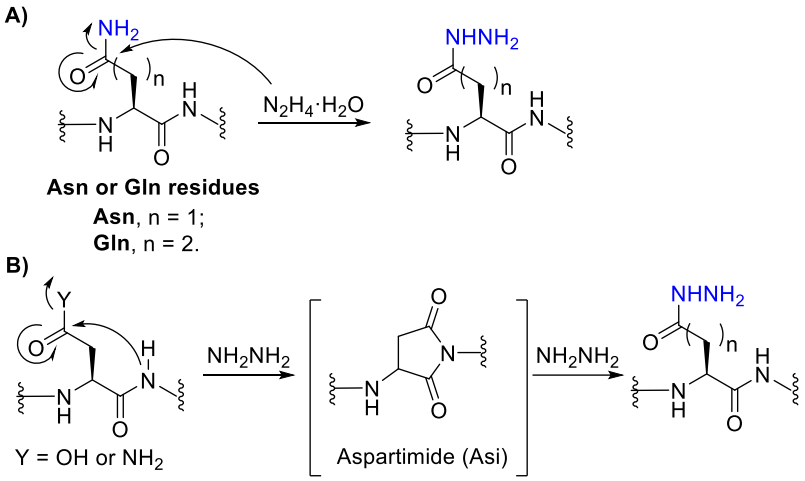


Figure S15. Increased aspartimide (Asi) formation during Ag(I)-ligation with prolonged reaction time. A) Reaction at 60 °C (oil bath) for 30 min. B) Reaction at 60 °C (oil bath) for 1.5 h. Calculated percentage of Asi product based on UV (220 nm) integration: 20.5% as in A, 25.0% as in B. C) ESI-MS of desired product (from major HPLC elution peak). D) ESI-MS of mixture of Asi product and desired product (from HPLC shoulder peak). E) A plausible pathway for the formation of Asi product.



Scheme S2. Plausible pathways for the formation of acyl hydrazide on the peptide side chain amide.

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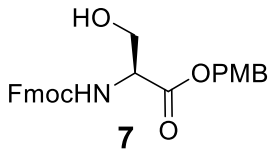
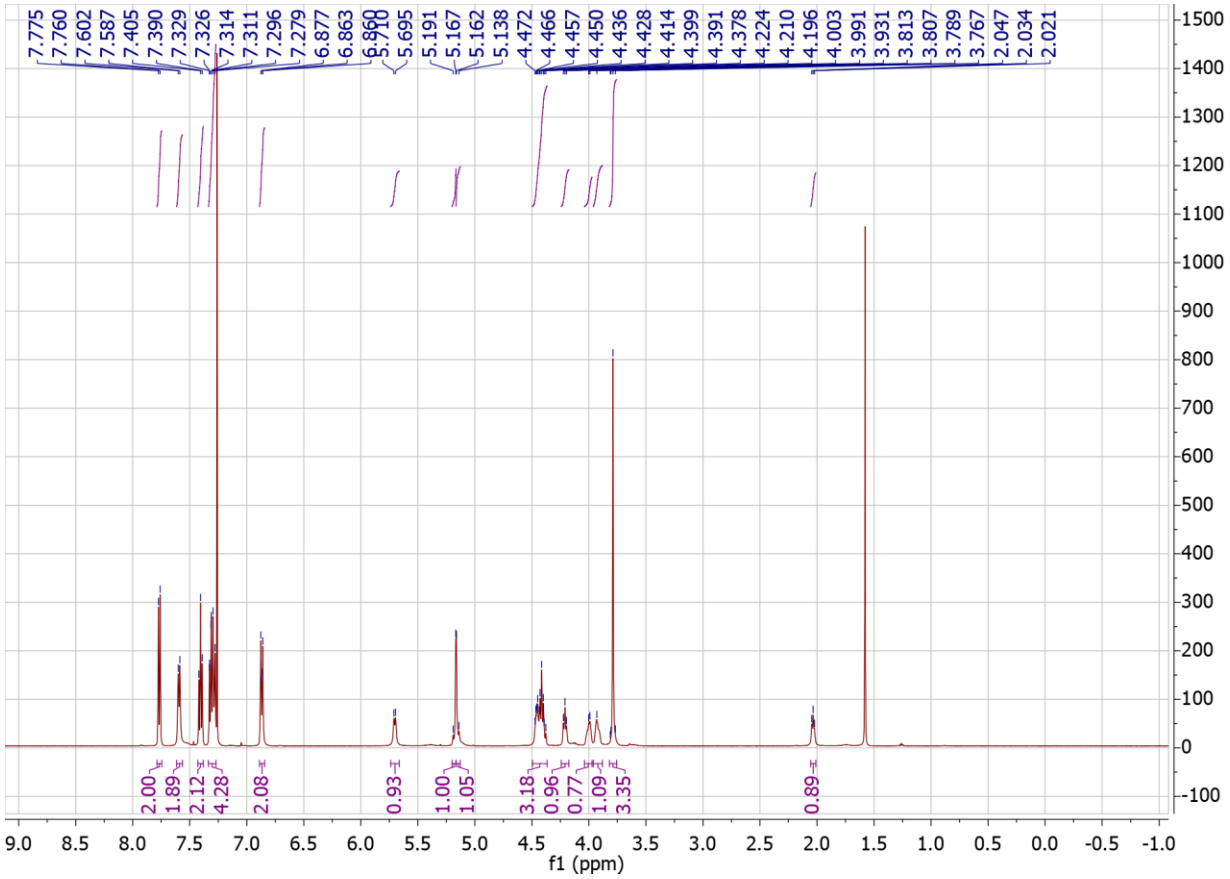
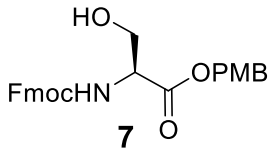


7

^{1}H NMR ($CDCl_3$, 500 MHz) of **7**





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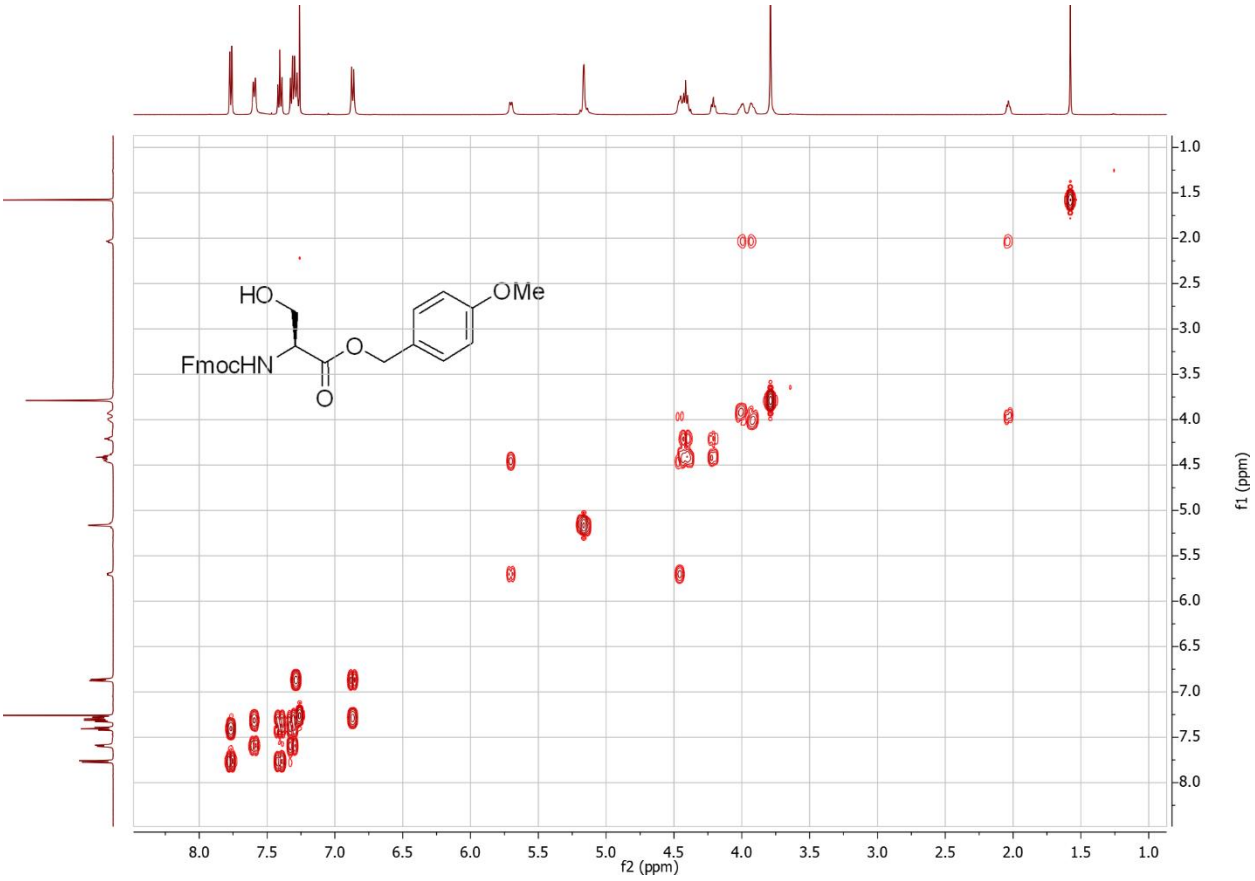
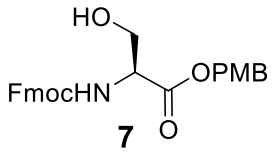
gCOSY ($CDCl_3$, 500 MHz) of **7**





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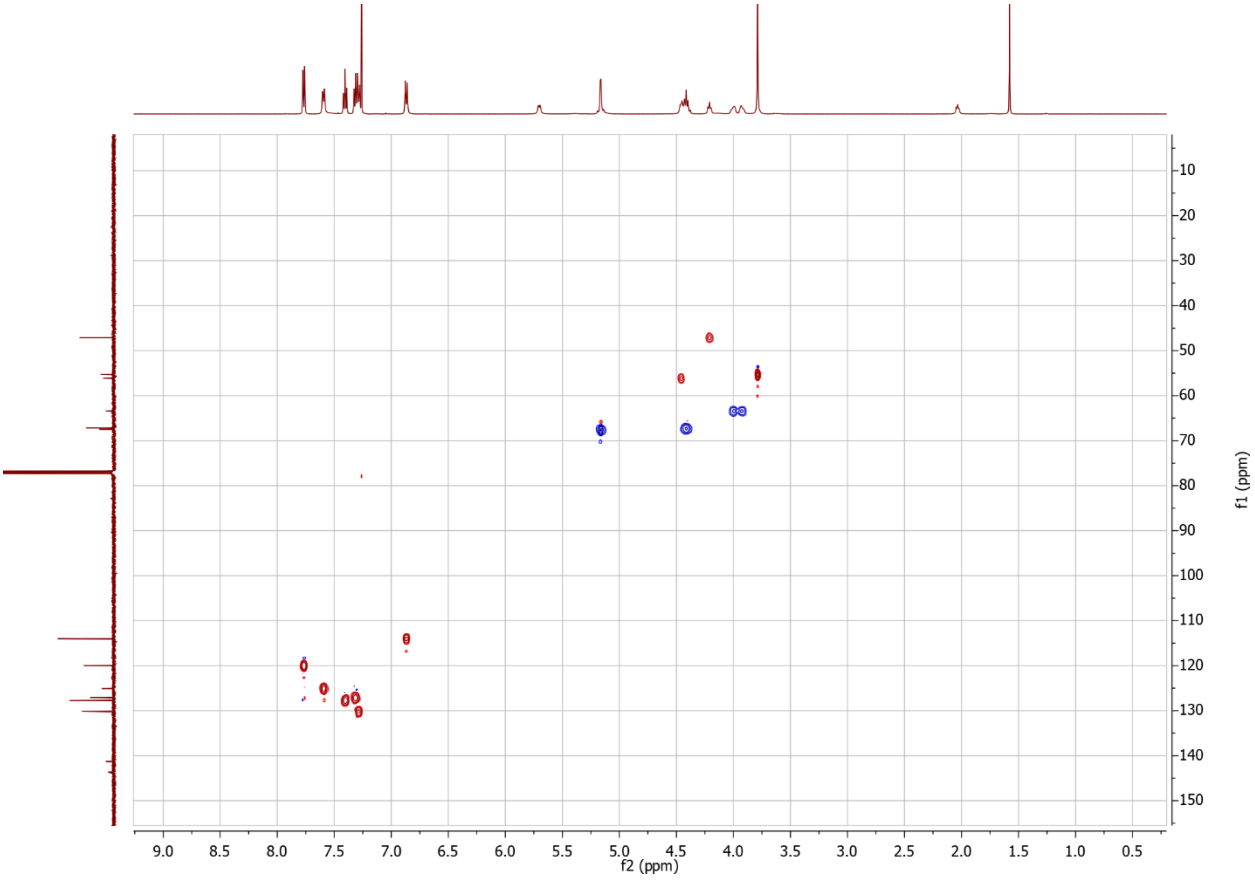
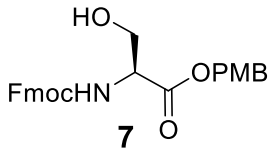
gHSQC ($CDCl_3$, 500 MHz) of **7**





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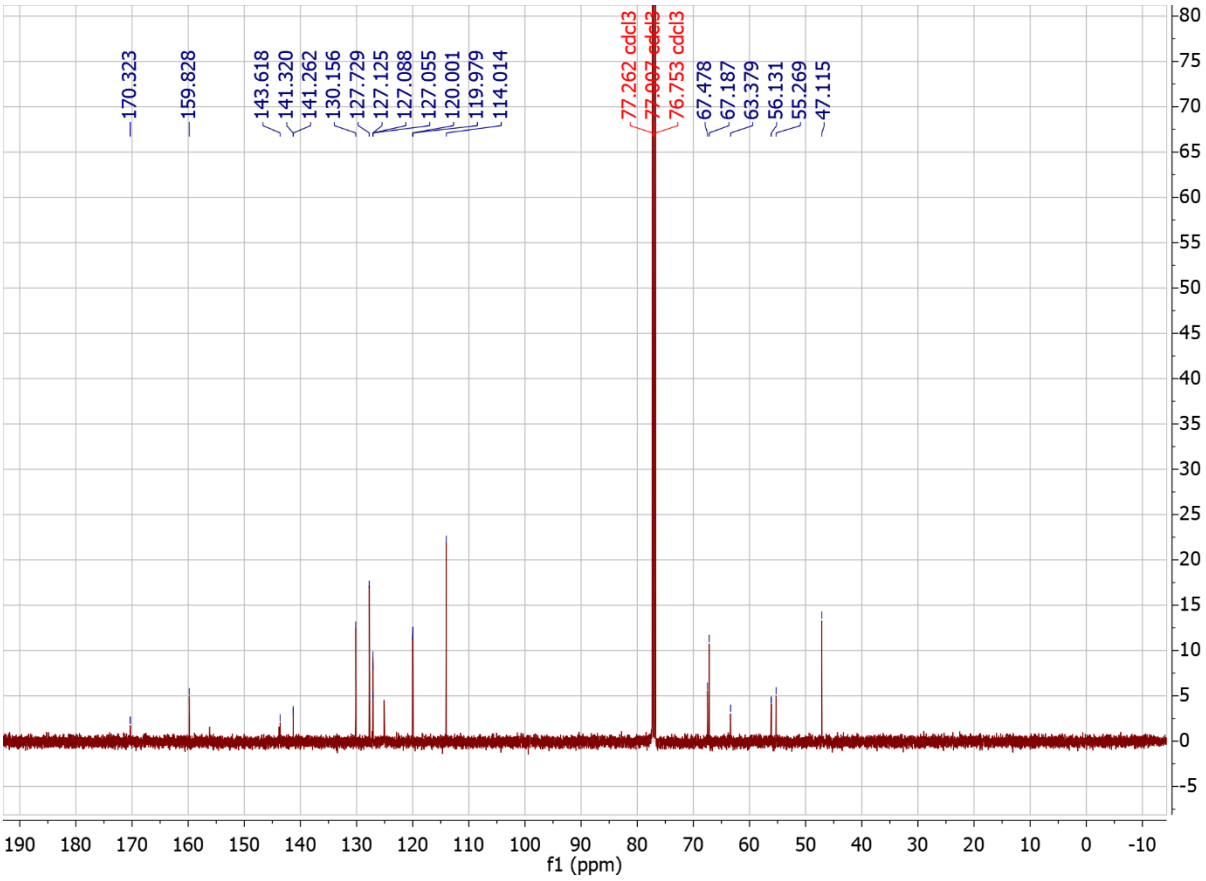
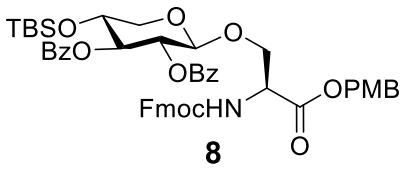
^{13}C NMR ($CDCl_3$, 126 MHz) of **7**





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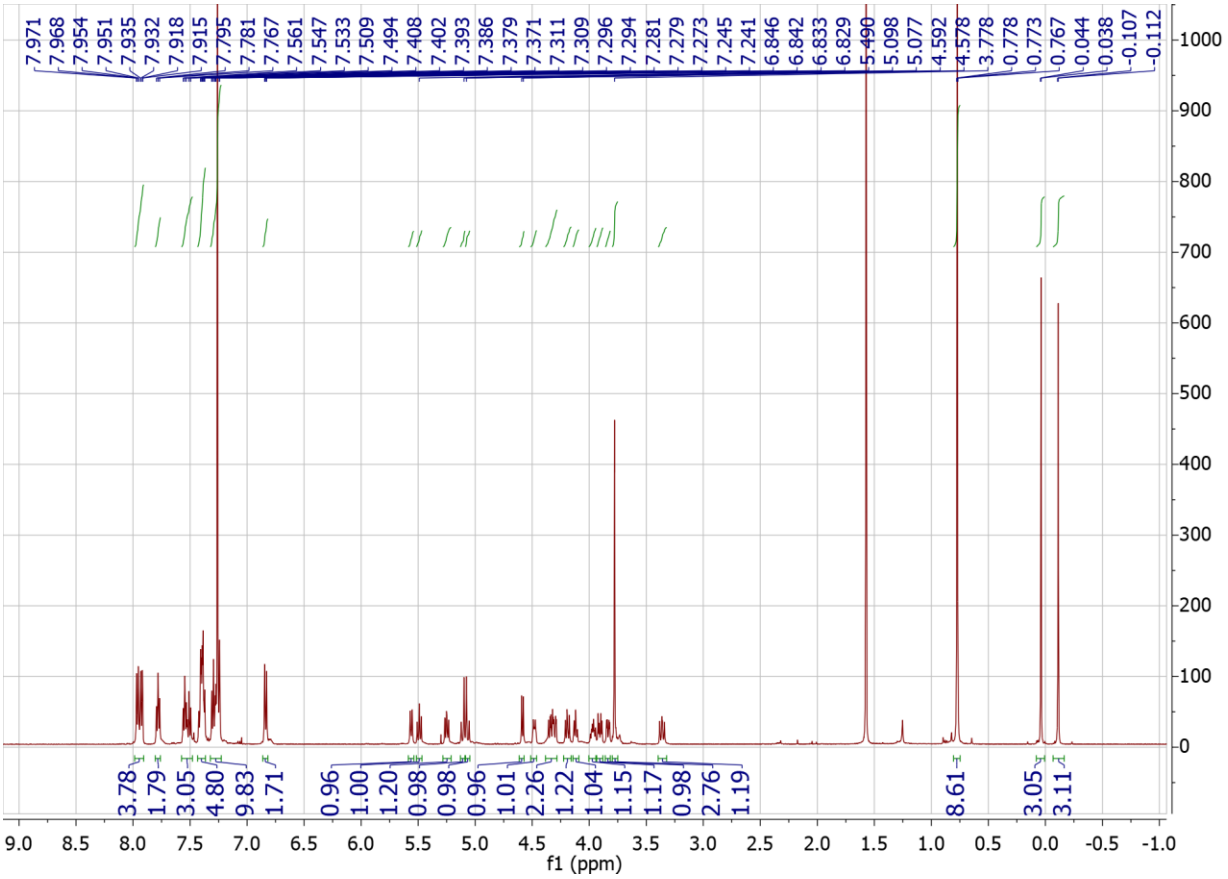
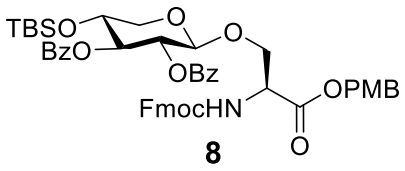
^{1}H NMR ($CDCl_3$, 500 MHz) of **8**





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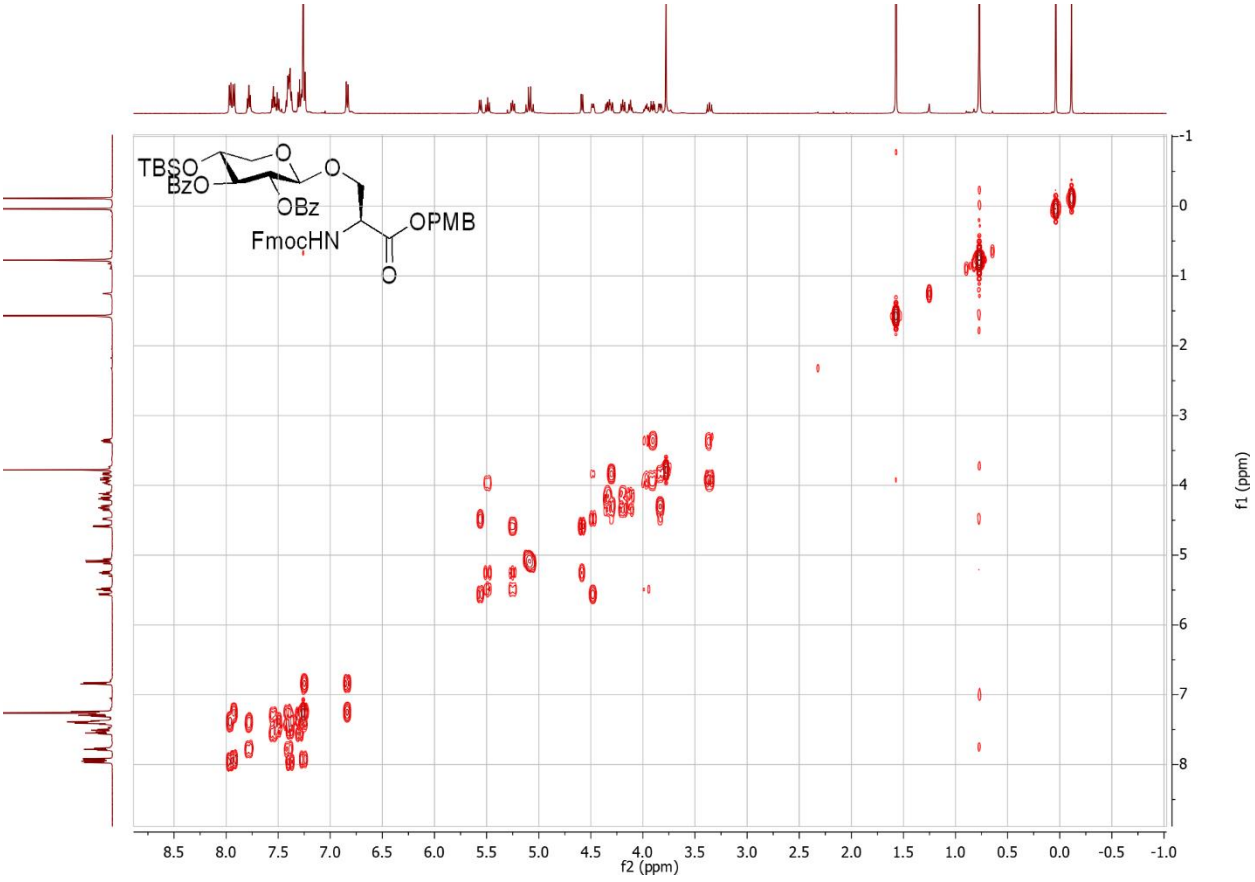

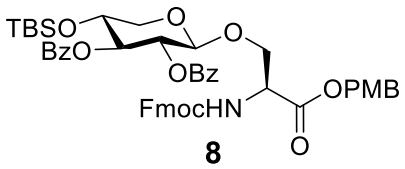

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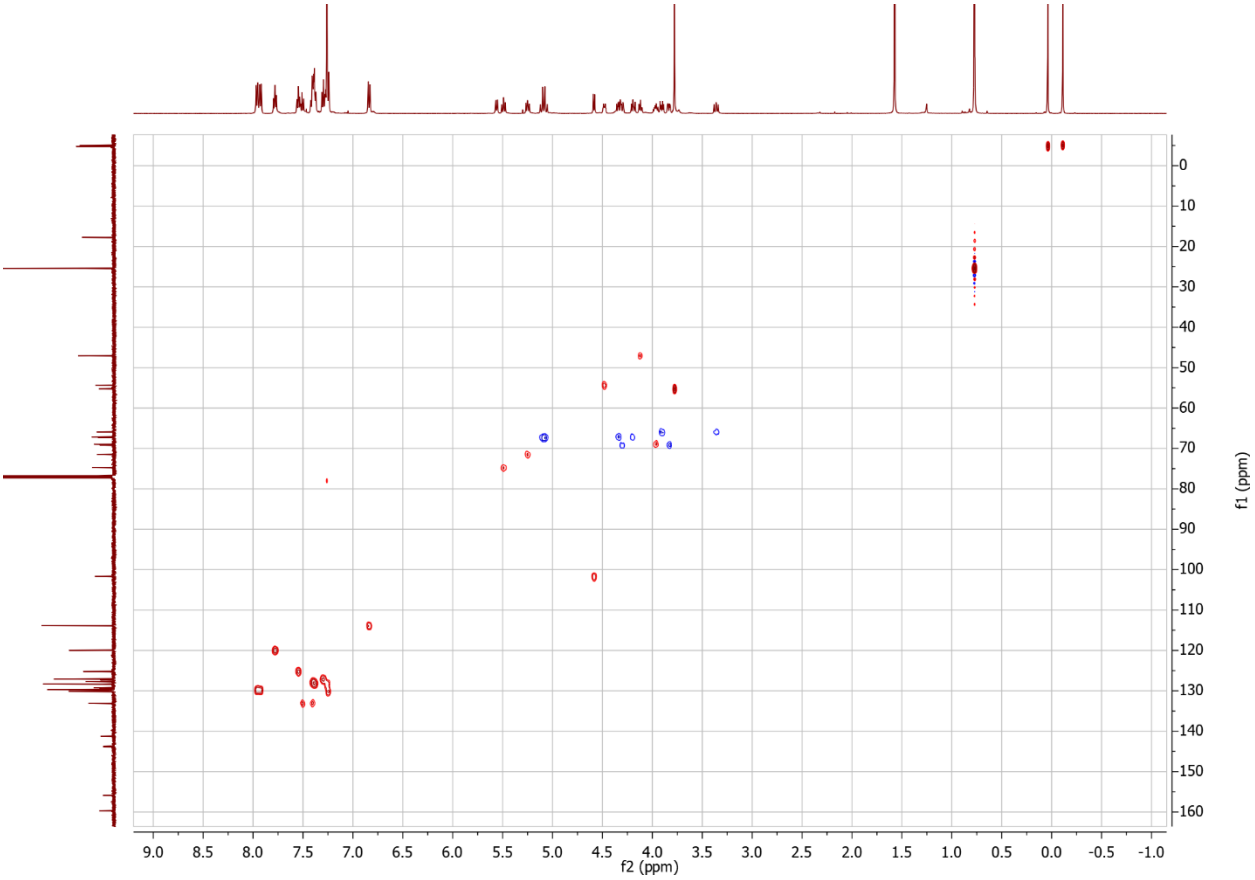

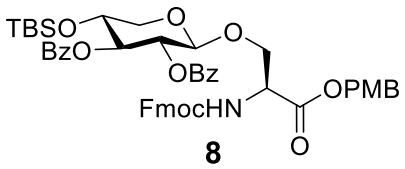

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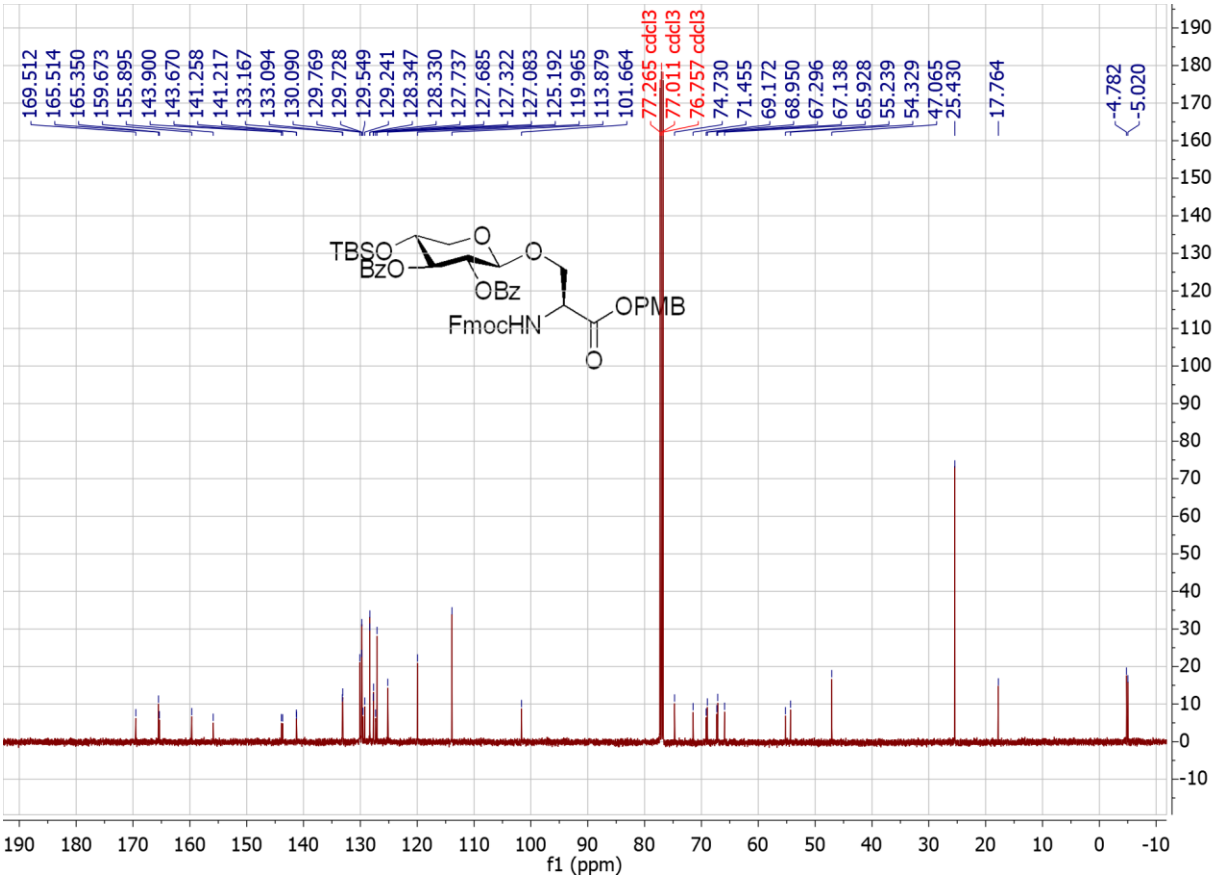
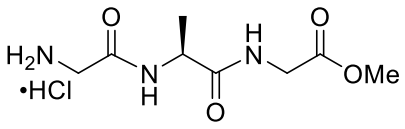
^{13}C NMR ($CDCl_3$, 126 MHz) of **8**





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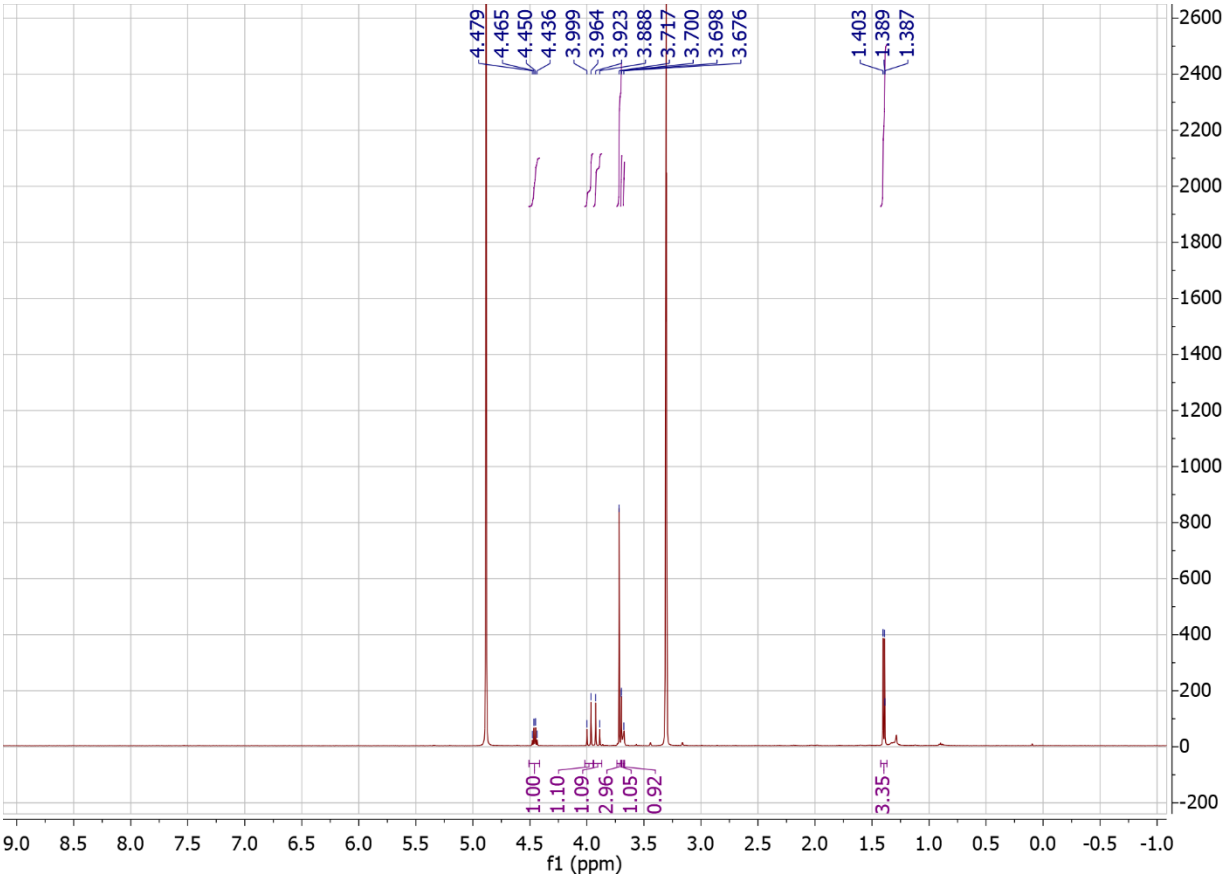
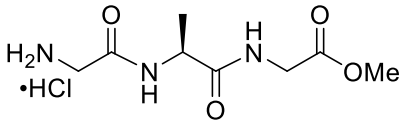
^{1}H NMR (CD_3OD, 500 MHz) of **9**





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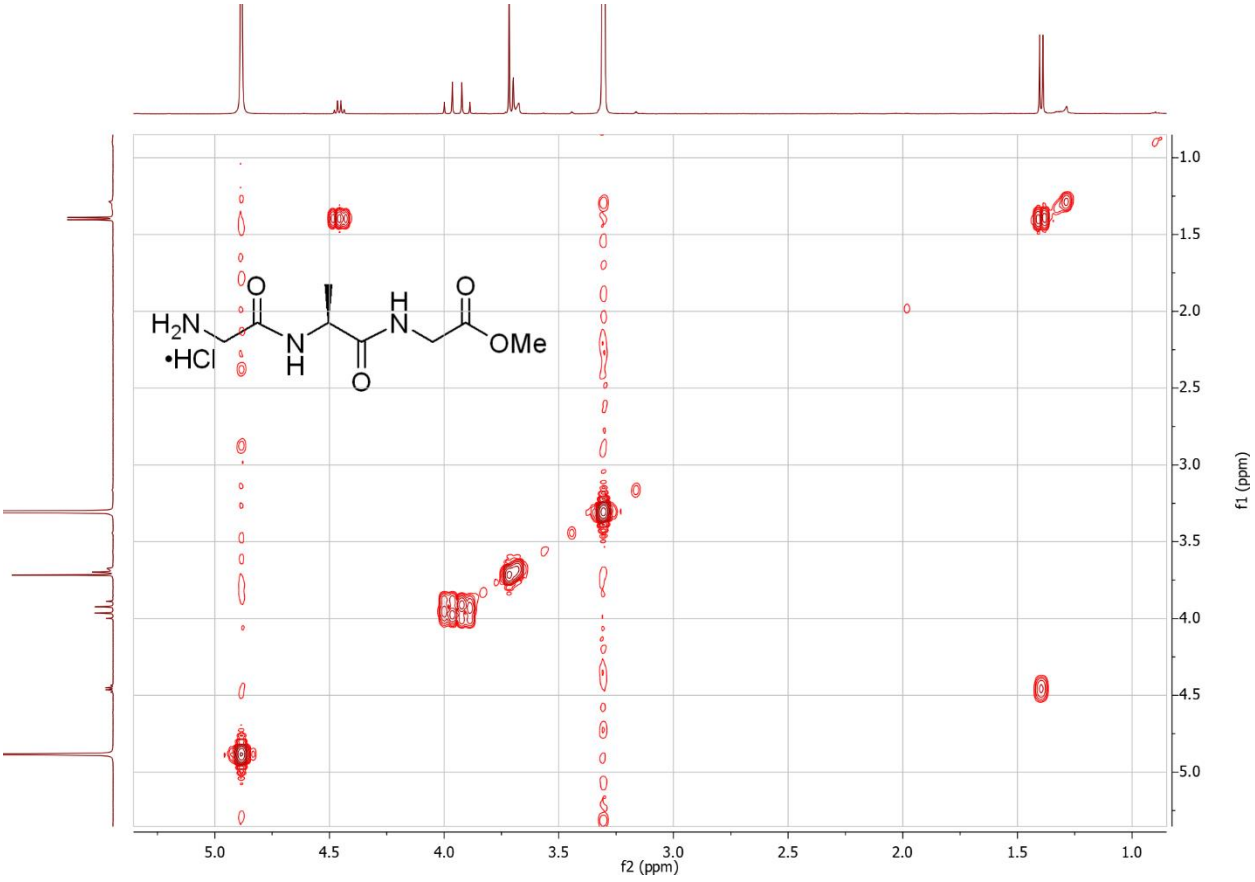
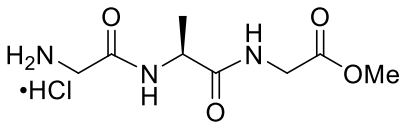
gCOSY (CD_3OD, 500 MHz) of **9**





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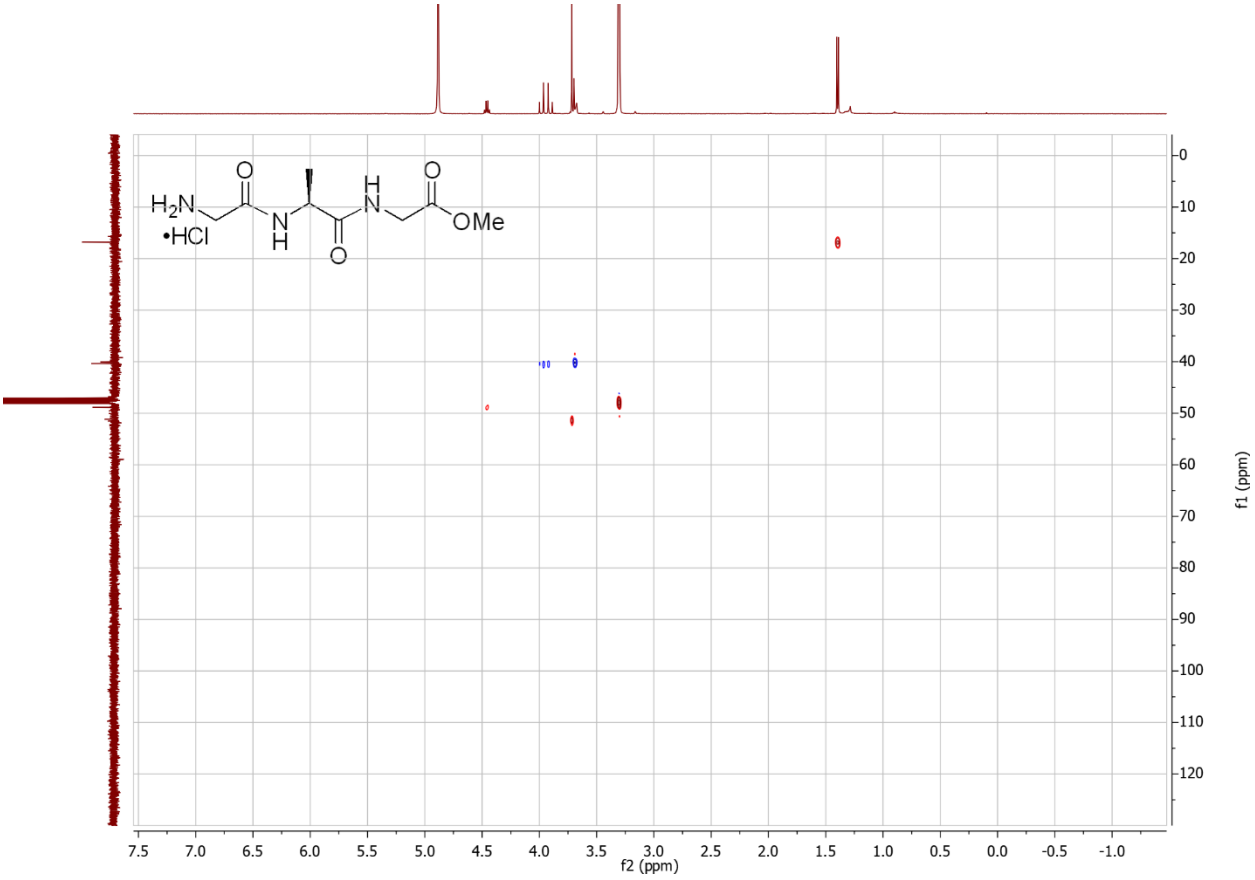
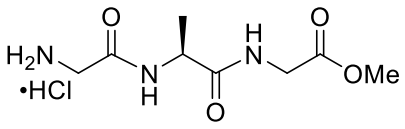
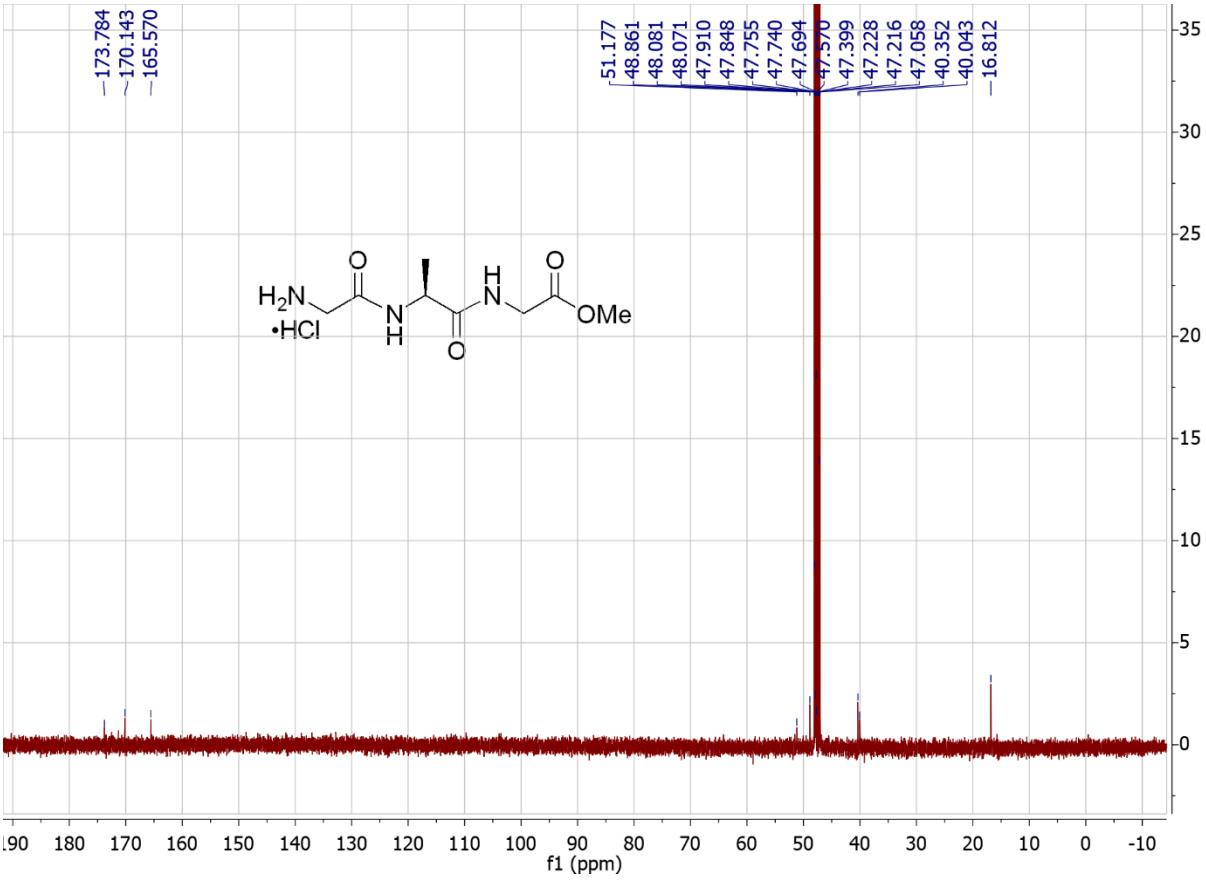
gHSQC (CD_3OD, 500 MHz) of **9**

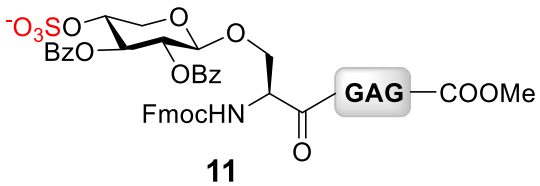




9

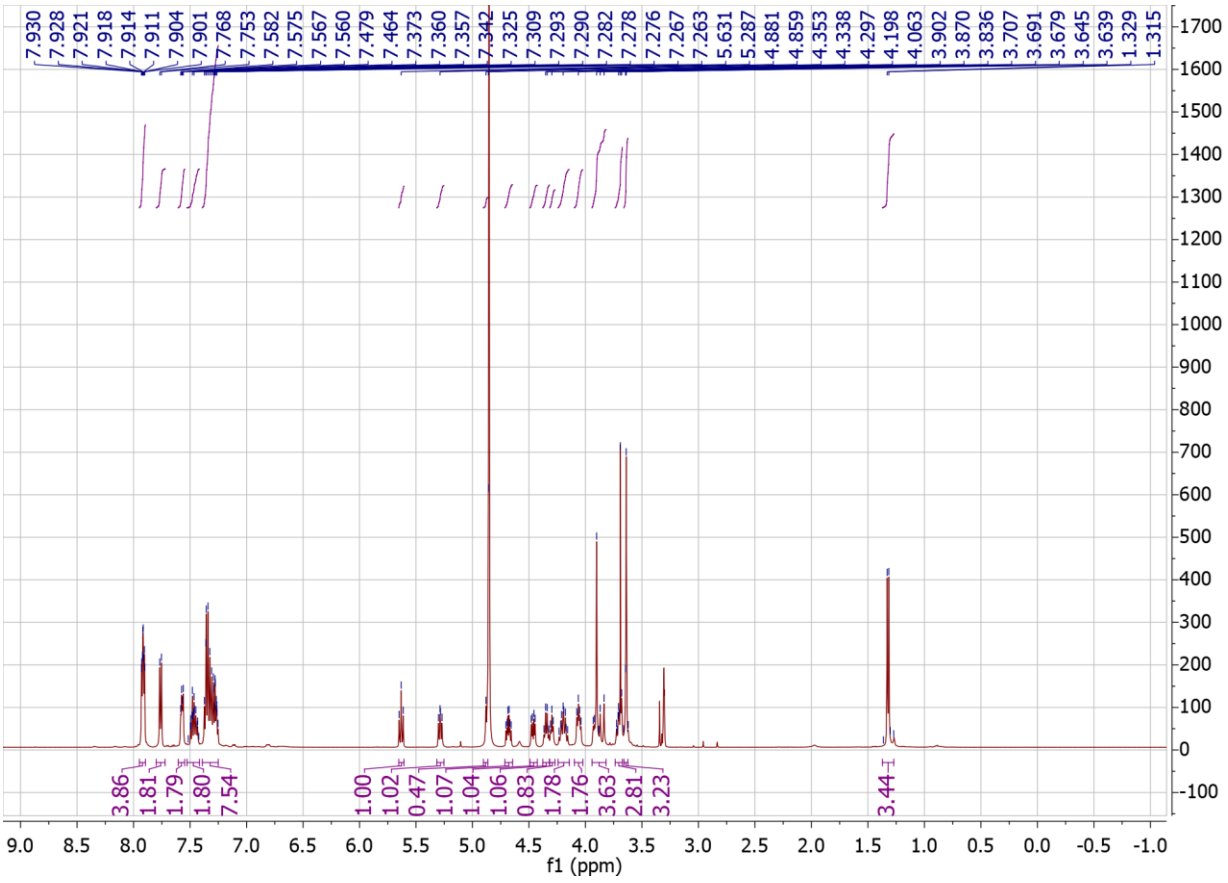
^{13}C NMR (CD_3OD, 126 MHz) of **9**

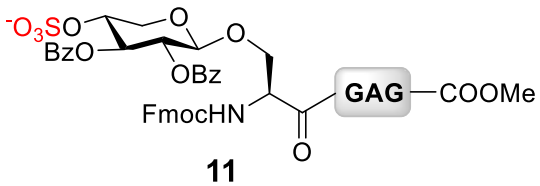




11

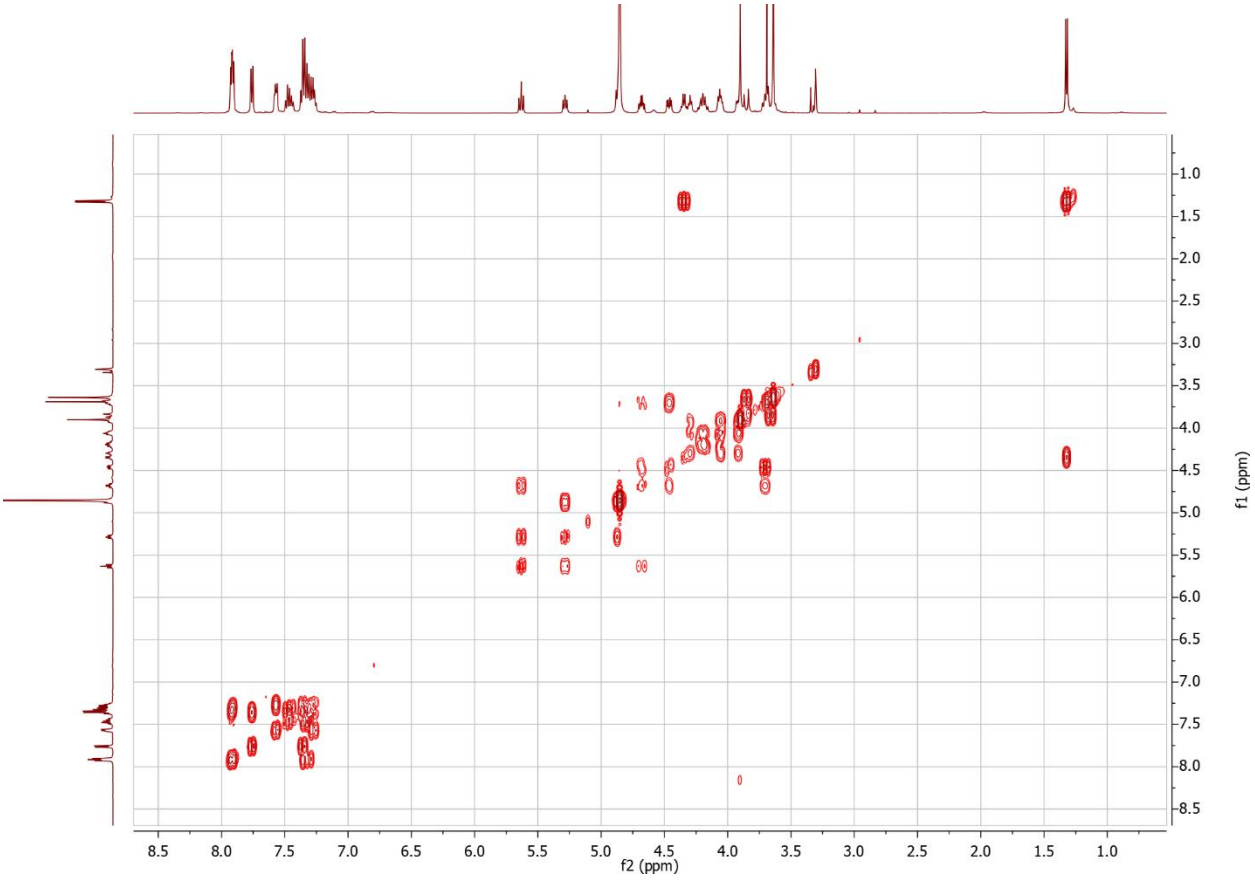
^{1}H NMR (CD_3OD, 500 MHz) of **11**

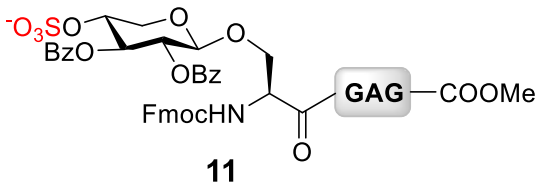




11

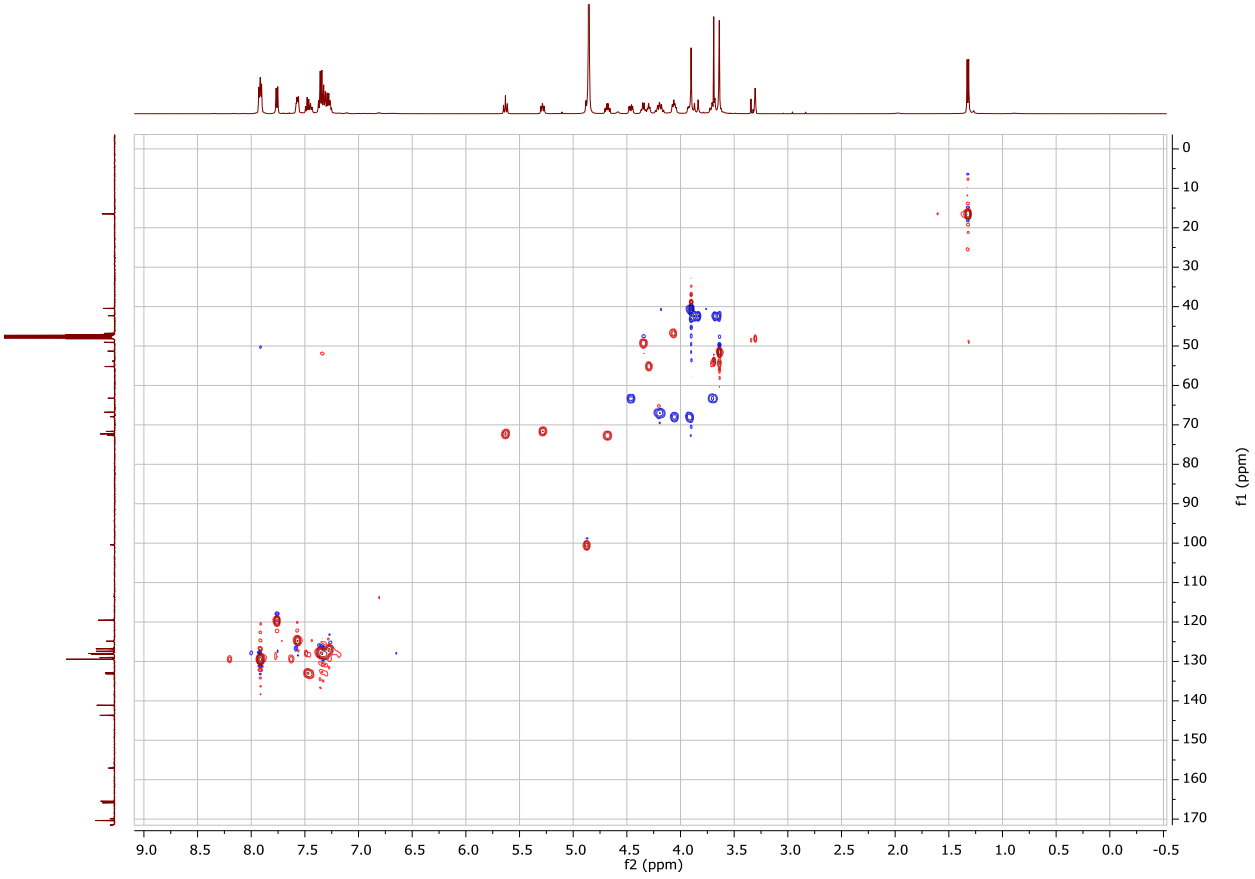
gCOSY (CD_3OD, 500 MHz) of **11**

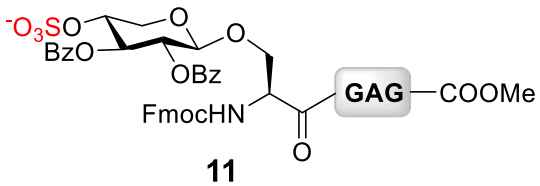




11

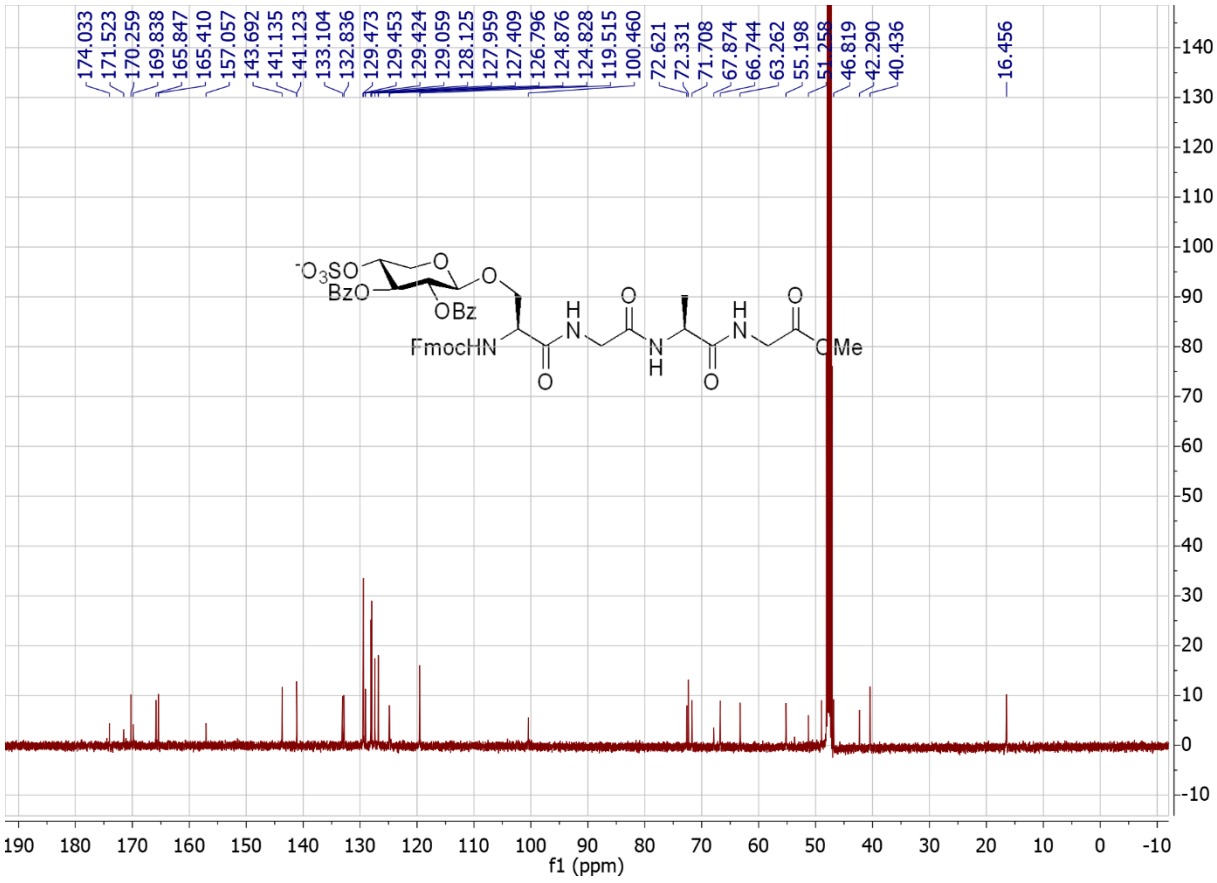
gHSQC (CD_3OD, 500 MHz) of **11**

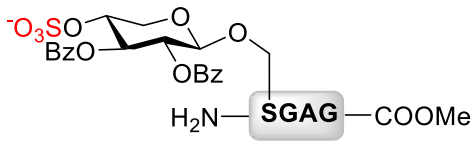




11

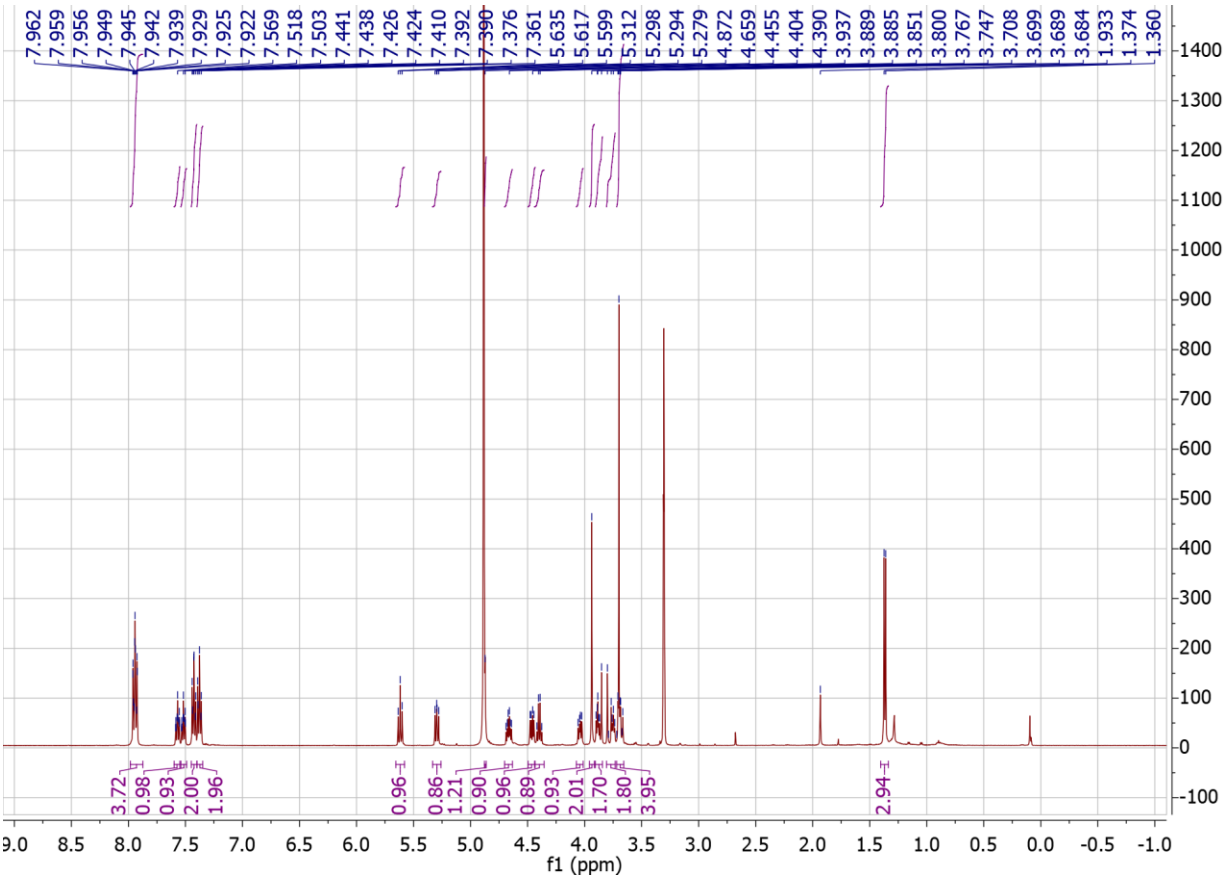
^{13}C NMR (CD_3OD, 126 MHz) of **11**

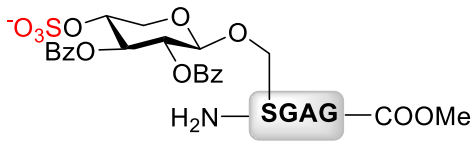




5

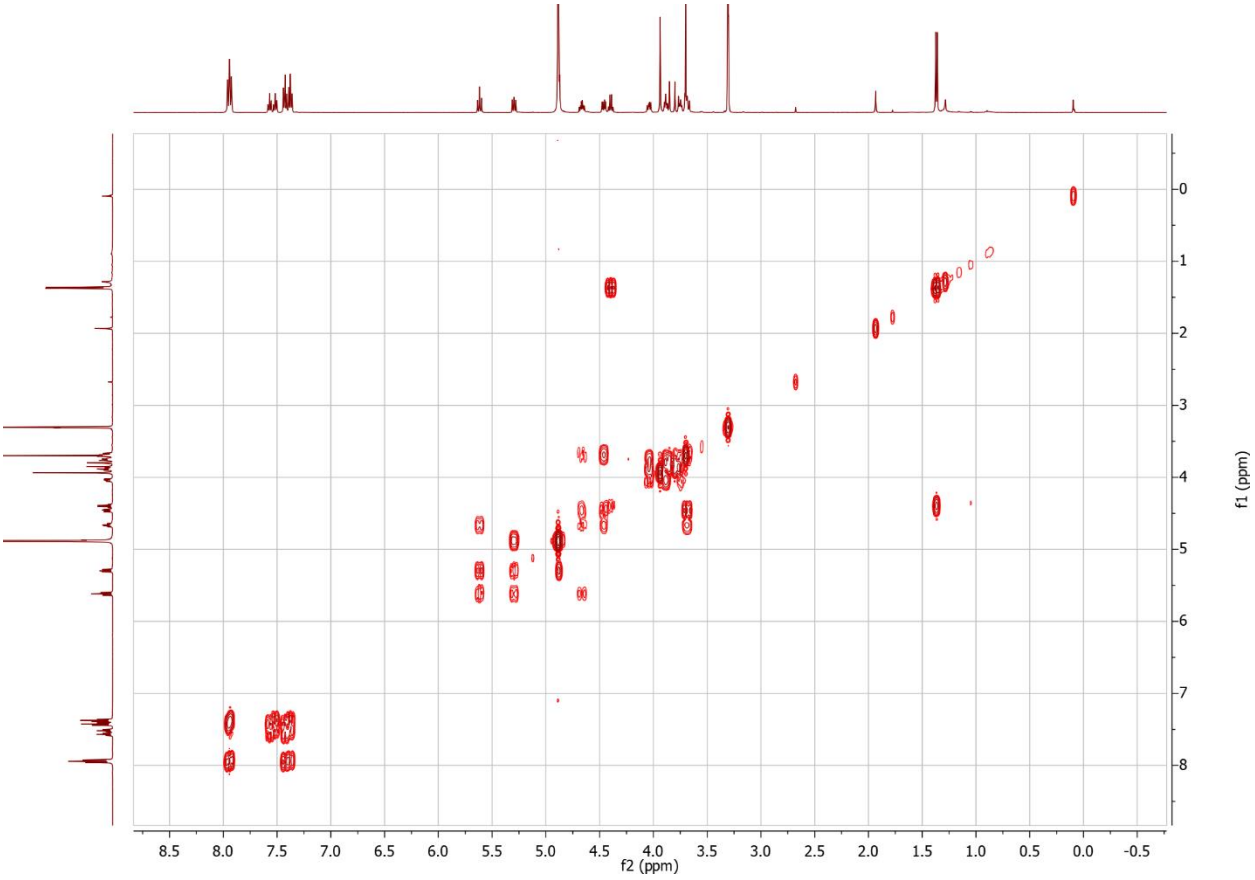
^{1}H NMR (CD_3OD, 500 MHz) of **5**

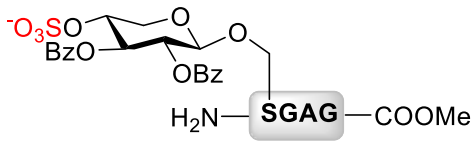




5

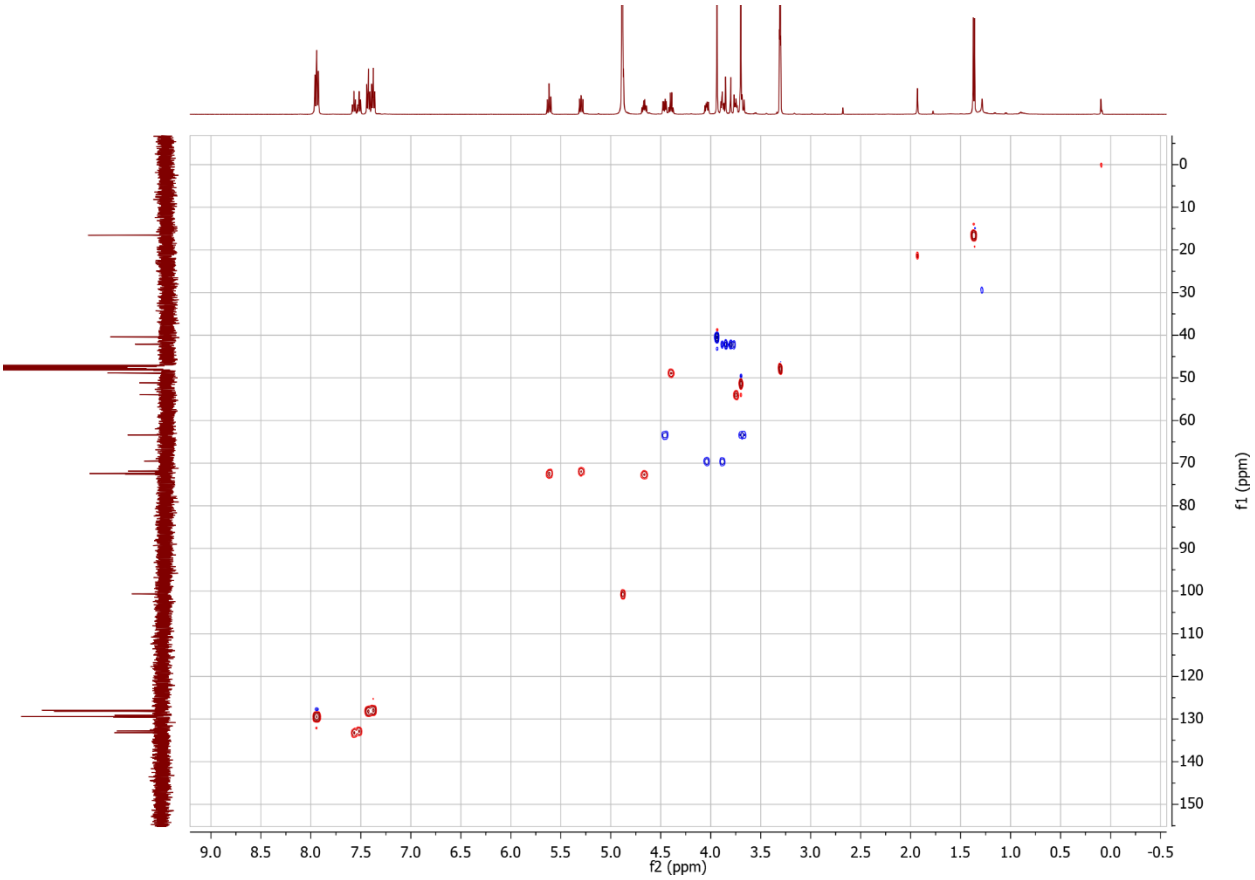
gCOSY (CD_3OD, 500 MHz) of **5**

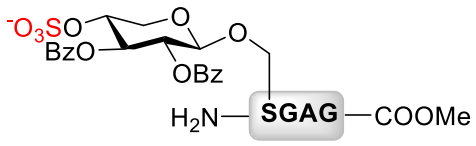




5

gHSQC (CD_3OD, 500 MHz) of **5**





5

^{13}C NMR (CD_3OD, 126 MHz) of **5**