Supporting Information (SI)

Photoinitiated Thiol-ene Mediated Functionalization of 4,5-Enoses

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Supporting Information I

General methods, synthetic procedures and characterization

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1. General experimental details

All starting materials and reagents were commercial (Sigma-Aldrich, Merck, Fluorochem, Alfa-Aesar, Acros and Biosynth) and used without further purification unless otherwise stated. All UV reactions were carried out in a Luzchem photoreactor LZC-4 (120 V / 60 Hz) containing 14 UV-A lamps irradiating at 352 nm. Glycal synthesis reactions were conducted using anhydrous solvents under an atmosphere of N_2. Dry solvents were obtained using equipment based on Grubb's design and stored under N_2 in a Young's flask over 4Å molecular sieves, except for anhydrous DMF and pyridine (Acros). For air sensitive reactions, solvents were added *via* syringe through rubber septa. Analytical thin-layer chromatography (TLC) was performed using Merck 60 F254 silica gel aluminium plates (pre-coated, 0.2 mm tick, 4 x 6 cm from 20 x 20 plates), and visualised by UV light (254 nm), 10% H_2SO_4 in EtOH followed by heat or molybdenum staining [ammonium molybdate (5.0 g) and concentrated H_2SO_4 (5.3 mL) in 100 mL H_2O] followed by heat. Flash column chromatography was performed using silica gel (Merck or Davisil, 230-400 mesh, 63-40 μm), the used eluents are specified in each case, and the proportions indicate the volume:volume ratio. The isolated products appear in order of elution, supported by their retention factor values (R_f). NMR spectra were recorded at 20 ºC in a Bruker AV 400 spectrometer (400.13 MHz for ^{1}H and 100.6 MHz for ^{13}C) and a Bruker AV 600 spectrometer (600.13 MHz for ^{1}H and 150.9 MHz for ^{13}C), using $CDCl_3$, CD_3OD and D_2O (purchased from Apollo Scientific and Merck) as solvents. ^{1}H NMR and ^{13}C NMR chemical shifts (δ in ppm) are referenced to internal solvent $CDCl_3$ (δ = 7.260 and 77.16 ppm, respectively), CD_3OD (δ = 3.310 and 49.00 ppm, respectively) and D_2O (δ = 4.790 ppm). Multiplicities are reported as s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, td = triplet of doublets, tt = triplet of triplets, m = multiplet, and coupling constants as *J* (in Hz). DEPT 135 experiments were used to determine the type of carbon nucleus (C *vs* CH *vs* CH_2 *vs* CH_3). The assignment of the signals was confirmed by 2D spectra (COSY, HSQC, HMBC), and TOCSY was used to unequivocally discern between diastereomers. NMR data was processed using Mestrenova software. High-resolution mass spectrometry (HRMS) analysis was performed with a ThermoScientific LTQ Orbitrap XL and Q-Tof Premier Waters MALDI-quadrupole time-of-flight (Q-Tof) mass spectrometer equipped with a Z-spray electrospray ionization (ESI), electron ionization (EI), atmospheric-pressure chemical ionization (APCI), and matrix assisted laser desorption ionization (MALDI) sources, using DCTB (*trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]-malononitrile) as the MALDI matrix.

3,4,6-Tri-*O*-acetyl-1,2-dideoxy-D-*arabino*-hex-1-enopyranose (**S1**), 2,3,4,6-tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (**S2**) and D-mannose (**S8**) were purchased from Biosynth. Methyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-*α*-L-idopyranosyl)uronate-(1→4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-*α*-D-glucopyranoside (**23**) was purchased from Heparin Building Blocks.

2. Synthesis and characterization

2.1. General synthetic procedures

2.1.1. Photoinitiated thiol-ene reaction

The appropriate 4,5-glycal or 1,2-glycal (1 equiv), 2,2-dimethoxy-2-phenylacetophenone (DPAP, 0.1 equiv) and 4-methoxyacetophenone (MAP, 0.1 equiv) were dissolved in the appropriate thiol (3 equiv). The reaction mixture was stirred and irradiated in the UV oven at room temperature for 1-6 h. The reaction progress was monitored by TLC. Once the reaction was completed, the mixture was purified by silica gel flash column chromatography.

2.1.2. Uronic acid esterification

According to an analogous previously described method,[1] the appropriate uronic acid (1 equiv), K_2CO_3 (3 equiv) and CH_3I (3 equiv) were dissolved in DMF. The reaction mixture was stirred at room temperature for 5-14 h. Then, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ solution and extracted with CH_2Cl_2. The aqueous layer was back extracted twice with CH_2Cl_2, and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography.

2.1.3. DBU-mediated β-elimination

According to a previously described method,[2] and applying slight modifications, to a solution of the appropriate saccharide (1 equiv) in CH_2Cl_2 at 0 ºC was added dropwise 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 2 equiv), and the reaction mixture was stirred at room temperature for 2-19 h. Then, the reaction was diluted with CH_2Cl_2 and washed with 1M aqueous HCl solution and saturated aqueous $NaHCO_3$ solution. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography.

2.1.4. DMP oxidation and Et_3N-mediated β-elimination

To a solution of the appropriate saccharide (1 equiv) in CH_2Cl_2 was added Dess-Martin periodinane (DMP, 1.2 equiv), and the reaction mixture was stirred at room temperature for 6 h. Then, the reaction was diluted with CH_2Cl_2, washed with saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ solutions, and H_2O. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude was dissolved in CH_2Cl_2, and Et_3N (1.2 equiv) was added dropwise, and the reaction mixture was stirred at room temperature for 1-2 h. After that, the reaction was diluted with CH_2Cl_2 and washed with 1M aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, H_2O and brine. The organic

layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography.

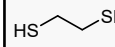
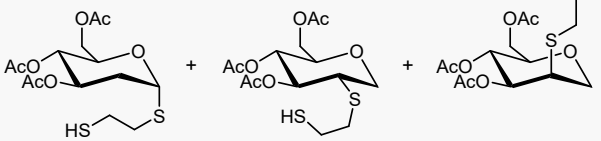
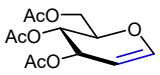
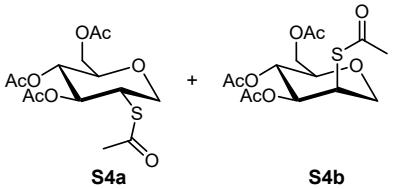
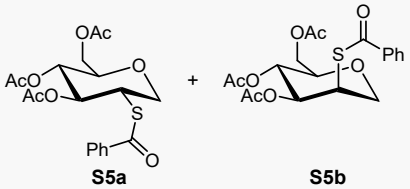
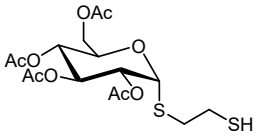
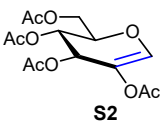
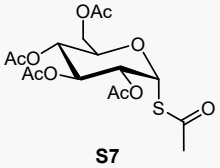
2.1.5. $NaBH_4$ reduction

To a solution of the appropriate 4,5-glycal (1 equiv) in THF at 0 ºC was added $NaBH_4$ (1.2 equiv), and the reaction mixture was stirred at room temperature for 1-2 h. Then, the reaction was quenched with saturated aqueous NH_4Cl solution, and the organic solvent was removed *in vacuo*. After that, the residue was dissolved in EtOAc, and washed with H_2O and brine. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography.

2.2. Synthesis and characterization of compounds

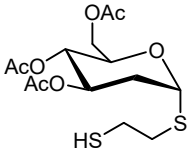
2.2.1. Thiol-ene reactions on 1,2-glycals

Table S1. Thiol-ene condition tests on commercially available 1,2-glycals.

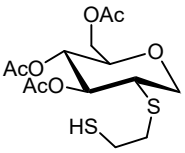
1,2-glycal	thiol	time (h)	product(s)	yield (%)	a:b(:c) ratio
		1	 **S3a** **S3b** **S3c**	99	10:54:36
 **S1**		1.5	 **S4a** **S4b**	93	20:80
		4	 **S5a** **S5b**	66	24:76
		1	 **S6**	77	-
 **S2**		2.5	 **S7**	45	-

3,4,6-tri-O-acetyl-2-deoxy-1-S-(2-mercaptoethyl)-1-thio-α-D-glucopyranose (S3a), 3,4,6-tri-O-acetyl-1-deoxy-2-S-(2-mercaptoethyl)-2-thio-D-glucopyranose (S3b) and 3,4,6-tri-O-acetyl-1-deoxy-2-S-(2-mercaptoethyl)-2-thio-D-mannopyranose (S3c)

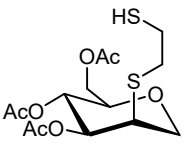
According to general procedure 2.1.1., commercial 3,4,6-tri-*O*-acetyl-1,2-dideoxy-D-*arabino*-hex-1-enopyranose (**S1**, 75 mg, 0.27 mmol), **4a** (0.07 mL, 0.83 mmol), DPAP (6.9 mg, 0.027 mmol) and MAP (4.1 mg, 0.027 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **S3a** (10.1 mg, 10%) as a colourless syrup, **S3b** (54.5 mg, 54%) as a colourless syrup and **S3c** (35.7 mg, 35%) as a colourless syrup. Combined isolated yield: 100.3 mg, 99%, **S3a/S3b/S3c** = 10:54:36. $\mathbf{R_f}$ (**S3a**/**S3b**/**S3c**) = 0.25 / 0.17 / 0.15 (hexane/acetone 80:20).



***S3a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.44 (d, J = 5.2 Hz, 1H, H-1), 5.22 (ddd, J = 11.6, 8.8, 5.6 Hz, 1H, H-3), 4.96 (td, J = 9.6, 3.6 Hz, 1H, H-4), 4.38 (ddd, J = 10.0, 5.2, 2.4 Hz, 1H, H-5), 4.31 (dd, J = 12.0, 5.2 Hz, 1H, H-6a), 4.06 (dd, J = 12.0, 2.4 Hz, 1H, H-6b), 2.98-2.73 (m, 4H, SCH_2 and $C\underline{H}_2SH$), 2.29 (ddd, J = 13.6, 5.2, 1.2 Hz, 1H, H-H-2ax), 2.18 (ddd, J = 11.2, 5.6, 2.4 Hz, 1H, H-2eq), 2.09 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.65 (d, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.8 (CO), 170.2 (CO), 170.0 (CO), 80.6 (C-1), 69.6 (C-4), 69.4 (C-3), 68.5 (C-5), 62.5 (C-6), 35.5 (SCH_2), 35.3 (C-2), 24.8 (CH_2SH), 21.0 (CH_3), 20.9 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{22}NaO_7S_2$ $[M+Na]^+$: 389.0705; found: 389.0700.



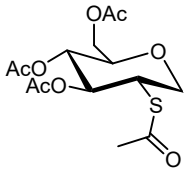
***S3b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.00-4.93 (m, 2H, H-3 and H-4), 4.23 (dd, J = 12.4, 4.8 Hz, 1H, H-6a), 4.13 (dd, J = 12.0, 5.2 Hz, 1H, H-1eq), 4.08 (dd, J = 12.4, 2.0 Hz, 1H, H-6b), 3.62-3.55 (m, 1H, H-5), 3.37 (t, J = 12.0 Hz, 1H, H-1ax), 2.91-2.84 (m, 1H, H-2), 2.80-2.74 (m, 2H, SCH_2), 2.70-2.60 (m, 2H, $C\underline{H}_2SH$), 2.082 (s, 3H, CH_3CO), 2.078 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.68 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.8 (CO), 170.4 (CO), 169.9 (CO), 76.7 (C-5), 74.1 (C-3), 70.4 (C-1), 69.6 (C-4), 62.4 (C-6), 45.8 (C-2), 35.7 (SCH_2), 25.1 (CH_2SH), 20.91 (CH_3), 20.90 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{22}NaO_7S_2$ $[M+Na]^+$: 389.0705; found: 389.0699.



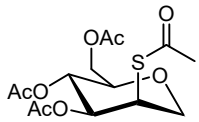
***S3c*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.27 (t, J = 9.2 Hz, 1H, H-4), 5.09 (dd, J = 8.2, 4.4 Hz, 1H, H-3), 4.18 (dd, J = 12.4, 5.2 Hz, 1H, H-6a), 4.13 (dd, J = 12.4, 2.8 Hz, 1H, H-6b), 4.10 (dd, J = 12.4, 2.8 Hz, 1H, H-1ax), 3.82 (dd, J = 12.4, 2.4 Hz, 1H, H-1eq), 3.58 (ddd, J = 9.0, 5.2, 2.8 Hz, 1H, H-5), 3.38 (dt, J = 4.4, 2.2 Hz, 1H, H-2), 2.85-2.78 (m, 2H, SCH_2), 2.72-2.65 (m, 2H, $C\underline{H}_2SH$), 2.10 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 1.72 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.9 (CO), 170.5 (CO), 169.6 (CO), 77.1 (C-5), 74.0 (C-3), 69.6 (C-1), 66.7 (C-4), 62.7 (C-6), 46.4 (C-2), 36.7 (SCH_2), 24.9 (CH_2SH), 21.0 (CH_3), 20.9 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{22}NaO_7S_2$ $[M+Na]^+$: 389.0705; found: 389.0701.

3,4,6-tri-O-acetyl-2-S-acetyl-1-deoxy-2-thio-D-glucopyranose (S4a) and 3,4,6-tri-O-acetyl-2-S-acetyl-1-deoxy-2-thio-D-mannopyranose (S4b)

According to general procedure 2.1.1., commercial **S1** (100 mg, 0.37 mmol), **4g** (0.08 mL, 1.10 mmol), DPAP (9.4 mg, 0.037 mmol) and MAP (5.5 mg, 0.037 mmol) were reacted for 1.5 h. Flash chromatography using hexane/acetone (90:10) afforded **S4a**[3] (24.7 mg, 19%) as an off-white solid and **S4b**[3] (94.7 mg, 74%) as an off-white solid. Combined isolated yield: 119.4 mg, 93%, **S4a**/**S4b** = 20:80. $\mathbf{R_f}$ (**S4a**/**S4b**) = 0.17 / 0.12 (hexane/acetone 80:20).



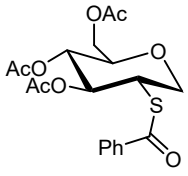
***S4a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.09 (dd, J = 11.2, 9.0 Hz, 1H, H-3), 5.02 (t, J = 9.2 Hz, 1H, H-4), 4.22 (dd, J = 12.4, 4.8 Hz, 1H, H-6a), 4.11 (dd, J = 12.0, 2.0 Hz, 1H, H-6b), 4.05 (dd, J = 11.6, 5.2 Hz, 1H, H-1eq), 3.76 (td, J = 11.2, 5.2 Hz, 1H, H-2), 3.60 (ddd, J = 9.6, 4.8, 2.4 Hz, 1H, H-5), 3.39 (t, J = 11.6 Hz, 1H, H-1ax), 2.32 (s, 3H, CH_3COS), 2.09 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 193.4 (COS), 170.8 (CO), 170.4 (CO), 169.7 (CO), 76.7 (C-5), 72.0 (C-3), 69.7 (C-4), 69.2 (C-1), 62.4 (C-6), 43.2 (C-2), 30.9 ($\underline{C}H_3COS$), 20.9 (CH_3), 20.7 ($2CH_3$) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{20}NaO_8S$ $[M+Na]^+$: 371.0777; found: 371.0780.



***S4b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.20 (dd, J = 9.6, 4.8 Hz, 1H, H-3), 5.06 (t, J = 9.6 Hz, 1H, H-4), 4.22 (dt, J = 4.0, 2.0 Hz, 1H, H-2), 4.16 (dd, J = 12.4, 5.2 Hz, 1H, H-6a), 4.11 (dd, J = 12.4, 2.4 Hz, 1H, H-6b), 4.02 (dd, J = 12.8, 2.0 Hz, 1H, H-1eq), 3.90 (dd, J = 12.4, 2.0 Hz, 1H, H-1ax), 3.58 (ddd, J = 9.6, 4.8, 2.4 Hz, 1H, H-5), 2.37 (s, 3H, CH_3COS), 2.10 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 194.2 (COS), 170.8 (CO), 170.2 (CO), 169.6 (CO), 77.3 (C-5), 72.0 (C-3), 69.9 (C-1), 66.9 (C-4), 62.7 (C-6), 45.0 (C-2), 30.7 ($\underline{C}H_3COS$), 20.9 (CH_3), 20.84 (CH_3), 20.80 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{20}NaO_8S$ $[M+Na]^+$: 371.0777; found: 371.0775.

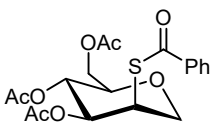
3,4,6-tri-O-acetyl-2-S-benzoyl-1-deoxy-2-thio-D-glucopyranose (S5a) and 3,4,6-tri-O-benzoyl-2-S-acetyl-1-deoxy-2-thio-D-mannopyranose (S5b)

According to general procedure 2.1.1., commercial **S1** (100 mg, 0.37 mmol), thiobenzoic acid (0.13 mL, 1.10 mmol), DPAP (9.4 mg, 0.037 mmol) and MAP (5.5 mg, 0.037 mmol) were reacted for 4 h. Flash chromatography using hexane/acetone (90:10) afforded **S5a** (24.3 mg, 16%) as a yellowish syrup and **S5b** (75.8 mg, 50%) as an off-white solid. Combined isolated yield: 100.1 mg, 66%, **S5a**/**S5b** = 24:76. $\mathbf{R_f}$ (**S5a**/**S5b**) = 0.18 / 0.14 (hexane/acetone 80:20).



***S5a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95-7.90 (m, 2H, 2CH), 7.62-7.57 (m, 1H, CH), 7.48-7.42 (m, 2H, 2CH), 5.23 (dd, J = 11.2, 9.2 Hz, 1H, H-3), 5.10 (t, J = 9.6 Hz, 1H, H-4), 4.26 (dd, J = 12.4, 4.8 Hz, 1H, H-6a), 4.17 (dd, J = 11.6, 5.2 Hz, 1H, H-1eq), 4.15 (dd, J = 12.4, 2.0 Hz, 1H, H-6b), 4.03 (td, J = 11.2, 5.6 Hz, 1H, H-2),

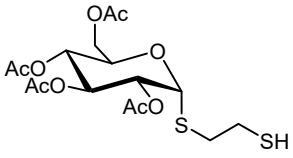
3.66 (ddd, *J* = 10.0, 4.8, 2.4 Hz, 1H, H-5), 3.49 (t, *J* = 11.6 Hz, 1H, H-1ax), 2.11 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 189.3 (COS), 170.9 (CO), 170.5 (CO), 169.7 (CO), 136.4 (C), 134.1 (CH), 128.9 (CH), 127.6 (CH), 76.8 (C-5), 72.2 (C-3), 69.9 (C-4), 69.5 (C-1), 62.5 (C-6), 43.1 (C-2), 20.9 (CH_3), 20.8 ($2CH_3$) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{19}H_{22}NaO_8S$ $[M+Na]^+$: 433.0933; found: 433.0919.



***S5b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 2H, 2CH), 7.63-7.58 (m, 1H, CH), 7.50-7.45 (m, 2H, 2CH), 5.30 (dd, *J* = 9.6, 4.8 Hz, 1H, H-3), 5.17 (t, *J* = 9.6 Hz, 1H, H-4), 4.50 (dt, *J* = 4.4, 2.2 Hz, 1H, H-2), 4.21 (dd, *J* = 12.4, 5.6 Hz, 1H, H-6a), 4.115 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6b), 4.14 (dd, *J* = 12.4, 2.0 Hz, 1H, H-1eq), 4.00 (dd, *J* = 12.8, 2.0 Hz, 1H, H-1ax), 3.64 (ddd, *J* = 9.6, 5.2, 2.4 Hz, 1H, H-5), 2.12 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 1. (s, 3H, CH_3CO) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 190.3 (COS), 170.9 (CO), 170.3 (CO), 169.7 (CO), 136.5 (C), 134.0 (CH), 128.9 (CH), 127.6 (CH), 77.4 (C-5), 72.1 (C-3), 70.2 (C-1), 67.1 (C-4), 62.8 (C-6), 44.9 (C-2), 20.93 (CH_3), 20.90 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{19}H_{22}NaO_8S$ $[M+Na]^+$: 433.0933; found: 433.0931.

2-mercaptoethyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-glucopyranoside (S6)

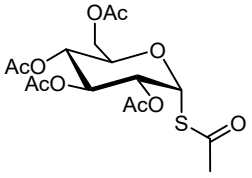
According to general procedure 2.1.1., commercial 2,3,4,6-tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (**S2**, 100 mg, 0.30 mmol), **4a** (0.08 mL, 0.91 mmol), DPAP (7.7 mg, 0.03 mmol) and MAP (4.5 mg, 0.03 mmol) were reacted for 1 h. Flash chromatography using CH_2Cl_2/EtOAc (95:5) afforded **S6**[4] (98.9 mg, 77%) as an off-white solid. $\mathbf{R_f}$ (**S6**) = 0.52 (CH_2Cl_2/EtOAc 95:5).



***S6*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.70 (d, *J* = 5.8 Hz, 1H, H-1), 5.35 (t, *J* = 9.8 Hz, 1H, H-3), 5.06-4.99 (m, 2H, H-2 and H-4), 4.43 (ddd, *J* = 10.4, 5.2, 2.0 Hz, 1H, H-5), 4.27 (dd, *J* = 12.4, 5.2 Hz, 1H, H-6a), 4.10 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6b), 2.86-2.72 (m, 4H, SCH_2 and $C\underline{H}_2SH$), 2.10 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.63 (d, *J* = 8.0 Hz, 1H, SH) ppm.

2,3,4,6-tetra-O-acetyl-1-S-acetyl-1-thio-α-D-glucopyranose (S7)

According to general procedure 2.1.1., commercial **S2** (100 mg, 0.30 mmol), **4g** (65 µL, 0.91 mmol), DPAP (7.7 mg, 0.03 mmol) and MAP (4.5 mg, 0.03 mmol) were reacted for 2.5 h. Flash chromatography using hexane/acetone (85:15) afforded **S7**[4,5] (55.4 mg, 45%) as an off-white solid. $\mathbf{R_f}$ (**S7**) = 0.23 (hexane/acetone 75:25).

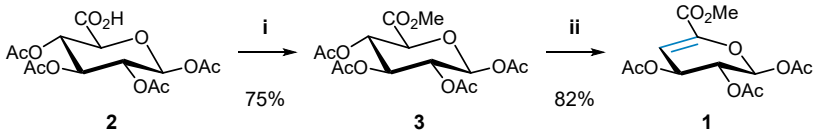


***S7*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.21 (d, *J* = 5.2 Hz, 1H, H-1), 5.24 (dd, *J* = 10.0, 5.2 Hz, 1H, H-2), 5.18 (t, *J* = 10.0 Hz, 1H, H-3), 5.09 (t, *J* = 10.0 Hz, 1H, H-4), 4.27 (dd, *J* = 12.4, 4.0 Hz, 1H, H-6a), 4.05 (dd, *J* = 12.4, 2.0 Hz, 1H, H-

6b), 3.96 (ddd, J = 10.0, 4.0, 2.0 Hz, 1H, H-5), 2.42 (s, 3H, CH_3COS), 2.08 (s, 3H, CH_3CO), 2.02 (s, 6H, $2CH_3CO$), 2.01 (s, 3H, CH_3CO) ppm.

2.2.2. Synthesis of 4,5-glycal 1

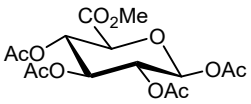
Synthesis of methyl 1,2,3-tri-O-acetyl-4-deoxy-β-D-gluco-hex-4-enopyranuronate (1)



Scheme S1. Synthesis of **1** from **2**. Reaction conditions: (i) CH_3I, K_2CO_3, DMF, rt, 5h; (ii) DBU, CH_2Cl_2, 0 ºC rt, 19h.

Methyl 1,2,3,4-tetra-O-acetyl-β-D-glucopyranuronate (3)

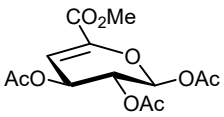
According to general procedure 2.1.2., 1,2,3,4-tetra-*O*-acetyl-*β*-D-glucopyranuronic acid[6] (**2**, 4 g, 11.04 mmol), K_2CO_3 (4.58 g, 33.12 mmol) and CH_3I (2.06 mL, 33.12 mmol) in DMF (36 mL) were reacted for 5 h. After the appropriate quenching and extraction, the residue was washed repeatedly with Et_2O affording **3**[7] (3.12 g, 75%) as an off-white solid that was used without further purification.



***3*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.77 (d, J = 7.8 Hz, 1H, H-1), 5.34-5.29 (m, 1H, H-3), 5.25 (t, J = 9.4 Hz, 1H, H-4), 5.15 (dd, J = 8.9, 7.7 Hz, 1H, H-2), 4.18 (d, J = 9.4 Hz, 1H, H-5), 3.75 (s, 3H, OCH_3), 2.12 (s, 3H, CH_3CO), 2.04 (s, 6H, $2CH_3CO$), 2.03 (s, 3H, CH_3CO) ppm.

Methyl 1,2,3-tri-O-acetyl-4-deoxy-β-D-gluco-hex-4-enopyranuronate (1)

According to general procedure 2.1.3., **3** (3.12 g, 8.29 mmol) and DBU (2.48 mL, 16.58 mmol) in CH_2Cl_2 (20 mL) were reacted for 19 h. Flash chromatography using CH_2Cl_2/Et_2O (90:10) afforded **1**[2] (2.15 g, 82%) as a white solid. $\mathbf{R_f}$ (**1**) = 0.70 (CH_2Cl_2/Et_2O 90:10).

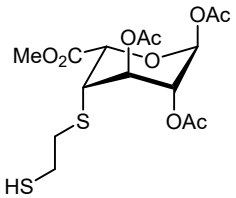


***1*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.39 (dd, J = 3.2, 1.2 Hz, 1H, H-1), 6.27 (dd, J = 4.8, 1.2 Hz, 1H, H-4), 5.23 (ddd, J = 4.8, 2.4, 1.2 Hz, 1H, H-3), 5.15 (ddd, J = 3.2, 2.4, 1.2 Hz, 1H, H-2), 3.83 (s, 3H, OCH_3), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.7 (CO), 169.2 (CO), 168.5 (CO), 161.8 (COO), 143.1 (C-5), 107.0 (C-4), 88.6 (C-1), 66.9 (C-2), 63.8 (C-3), 52.9 (OCH_3), 20.9 (CH_3), 20.78 (CH_3), 20.76 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{13}H_{20}NO_9$ $[M+NH_4]^+$: 334.1133; found: 334.1138.

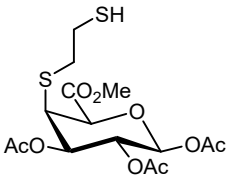
2.2.3. Thiol-ene reactions on 4,5-glycal 1

Methyl 1,2,3-tri-O-acetyl-4-S-(2-mercaptoethyl)-4-thio-α-L-idopyranuronate (5a) and methyl 1,2,3-tri-O-acetyl-4-S-(2-mercaptoethyl)-4-thio-β-D-galactopyranuronate (6a)

According to general procedure 2.1.1., methyl 1,2,3-tri-*O*-acetyl-4-deoxy-*β*-D-gluco-hex-4-enopyranuronate (**1**, 75 mg, 0.24 mmol), 1,2-ethanedithiol (**4a**, 0.06 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **5a** (24.3 mg, 25%) as a colourless syrup and **6a** (70.1 mg, 72%) as an off-white solid. Combined isolated yield: 94.4 mg, 97%, **5a**/**6a** = 26:74. $\mathbf{R_f}$ (**5a**/**6a**) = 0.32 / 0.25 (hexane/acetone 75:25).



***5a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.16 (dd, J = 2.4, 0.8 Hz, 1H, H-1), 5.26 (td, J = 3.6, 0.8 Hz, 1H, H-3), 4.96 (d, J = 3.6 Hz, 1H, H-5), 4.76 (ddd, J = 3.6, 2.4, 0.8 Hz, 1H, H-2), 3.85 (s, 3H, OCH_3), 3.12 (app t, J = 3.6 Hz, 1H, H-4), 2.83-2.76 (m, 2H, SCH_2), 2.76-2.69 (m, 2H, $C\underline{H}_2SH$), 2.14 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 1.66 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} RMN** (101 MHz, $CDCl_3$) δ 169.6 (CO), 169.5 (CO), 168.8 (COO), 168.3 (CO), 91.3 (C-1), 69.99 (C-5), 69.97 (C-3), 67.0 (C-2), 52.9 (OCH_3), 43.9 (C-4), 38.2 (SCH_2), 24.7 (CH_2SH), 21.1 (CH_3), 21.0 (CH_3), 20.9 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{15}H_{22}NaO_9S_2$ $[M+Na]^+$: 433.0603; found: 433.0595.

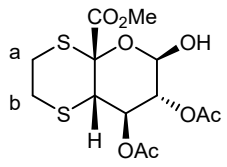


***6a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.64 (d, J = 8.4 Hz, 1H, H-1), 5.34 (dd, J = 10.0, 8.4 Hz, 1H, H-2), 5.17 (dd, J = 10.0, 4.4 Hz, 1H, H-3), 4.53 (d, J = 2.0 Hz, 1H, H-5), 3.84 (s, 3H, OCH_3), 3.67 (dd, J = 4.4, 2.0 Hz, 1H, H-4), 2.82-2.70 (m, 2H, SCH_2), 2.65-2.57 (m, 2H, $C\underline{H}_2SH$), 2.13 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 1.74 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.4 (CO), 169.3 (CO), 169.2 (CO), 166.7 (COO), 92.1 (C-1), 75.0 (C-5), 72.8 (C-3), 68.6 (C-2), 53.1 (OCH_3), 48.5 (C-4), 38.0 (SCH_2), 24.6 (CH_2SH), 21.0 ($2CH_3$), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{15}H_{22}NaO_9S_2$ $[M+Na]^+$: 433.0603; found: 433.0590.

*** 1 mmol scale synthesis of 5a and 6a:** According to general procedure 2.1.1., 4,5-glycal **1** (316.3 mg, 1 mmol), **4a** (0.25 mL, 3 mmol), DPAP (25.6 mg, 0.1 mmol) and MAP (15 mg, 0.1 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **5a** (57.5 mg, 14%) as a colourless syrup and **6a** (299.6 mg, 73%) as an off-white solid. Combined isolated yield: 357.1 mg, 87%, **5a**/**6a** = 16:84.

** **Condition tests:** Thiol-ene reaction was tested using other photoinitiators, light sources, low temperature, and thiol-Michael addition conditions. The tests were carried out on **1** (75 mg, 0.24 mmol) using **4a** (0.06 mL, 0.72 mmol), and following the parameters collected in Table 1.

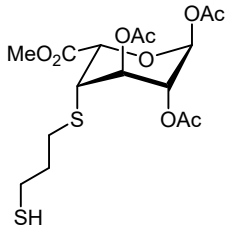
*** ***Methyl 4,5-(ethane-1,2-dithiyl)-4-deoxy-2,3-di-O-acetyl-β-D-glucopyranuronate (6a')*:** Compound **6a'** was obtained by spontaneous intramolecular cyclization during the concentration step by heating while attempting to recrystallize **6a** in ethanol. Compound **6a'** was isolated as colourless, plate-shaped crystals.



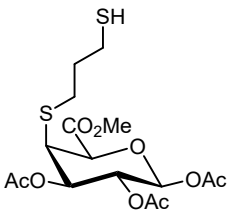
***6a'*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.94 (dd, J = 10.8, 9.6 Hz, 1H, H-3), 5.28 (t, J = 8.0 Hz, 1H, H-1), 4.98 (dd, J = 9.6, 8.0 Hz, 1H, H-2), 3.89 (s, 3H, OCH_3), 3.53 (ddd, J = 14.0, 12.8, 2.8 Hz, 1H, ½SCH_2-a), 3.37 (br d, J = 8.0 Hz, 1H, OH), 3.30 (d, J = 10.8 Hz, 1H, H-4), 3.09-2.98 (m, 2H, ½SCH_2-a and ½SCH_2-b), 2.35 (ddd, J = 14.8, 4.0, 2.8 Hz, 1H, ½SCH_2-b), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.9 (CO), 170.4 (CO), 167.2 (COO), 94.0 (C-1), 83.2 (C-5), 74.8 (C-2), 67.1 (C-3), 54.0 (OCH_3), 44.7 (C-4), 33.4 (SCH_2-a), 22.6 (SCH_2-b), 20.9 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{13}H_{18}NaO_8S_2$ $[M+Na]^+$: 389.0341; found: 389.0336.

Methyl 1,2,3-tri-O-acetyl-4-S-(3-mercaptopropyl)-4-thio-α-L-idopyranuronate (5b) and methyl 1,2,3-tri-O-acetyl-4-S-(3-mercaptopropyl)-4-thio-β-D-galactopyranuronate (6b)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), 1,3-propanedithiol (**4b**, 0.07 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **5b** (22.1 mg, 22%) as a colourless syrup and **6b** (71.4 mg, 71%) as an off-white solid. Combined isolated yield: 93.5 mg, 92%, **5b**/**6b** = 23:77. **R_f** (**5b**/**6b**) = 0.21 / 0.16 (hexane/acetone 75:25).



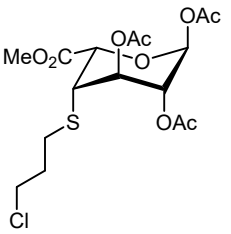
***5b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.16 (dd, J = 2.8, 0.8 Hz, 1H, H-1), 5.28 (td, J = 4.0, 0.8 Hz, 1H, H-3), 4.94 (d, J = 4.0 Hz, 1H, H-5), 4.76 (ddd, J = 4.0, 2.8, 0.8 Hz, 1H, H-2), 3.84 (s, 3H, OCH_3), 3.11 (app t, J = 4.0 Hz, 1H, H-4), 2.70 (td, J = 7.2, 0.8 Hz, 2H, SCH_2), 2.60 (dt, J = 8.0, 7.2 Hz, 2H, C$\underline{H_2}$SH), 2.13 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 1.87 (p, J = 7.2 Hz, 2H, CH_2), 1.35 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.6 (CO), 169.4 (CO), 168.8 (COO), 168.3 (CO), 91.3 (C-1), 70.2 (C-5), 69.8 (C-3), 67.2 (C-2), 52.8 (OCH_3), 43.9 (C-4), 33.3 (CH_2), 32.4 (SCH_2), 23.2 (CH_2SH), 21.0 (CH_3), 20.99 (CH_3), 20.92 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{24}NaO_9S_2$ $[M+Na]^+$: 447.0759; found: 447.0745.



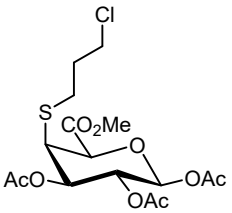
***6b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.63 (d, J = 8.0 Hz, 1H, H-1), 5.35 (dd, J = 10.0, 8.0 Hz, 1H, H-2), 5.17 (dd, J = 10.0, 4.4 Hz, 1H, H-3), 4.53 (d, J = 2.0 Hz, 1H, H-5), 3.82 (s, 3H, OCH_3), 3.66 (dd, J = 4.4, 2.0 Hz, 1H, H-4), 2.74-2.55 (m, 4H, SCH_2 and $C\underline{H}_2SH$), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 1.80 (p, J = 7.2 Hz, 2H, CH_2), 1.33 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.3 (CO), 169.3 (CO), 169.2 (CO), 167.0 (COO), 92.1 (C-1), 75.0 (C-5), 72.9 (C-3), 68.7 (C-2), 52.9 (OCH_3), 48.4 (C-4), 33.2 (CH_2), 32.3 (SCH_2), 23.1 (CH_2SH), 20.96 (CH_3), 20.95 (CH_3), 20.7 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{15}H_{22}NaO_9S_2$ $[M+Na]^+$: 447.0759; found: 447.0752.

Methyl 1,2,3-tri-O-acetyl-4-S-(3-chloropropyl)-4-thio-α-L-idopyranuronate (5c) and methyl 1,2,3-tri-O-acetyl-4-S-(3-chloropropyl)-4-thio-β-D-galactopyranuronate (6c)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), 3-chloropropanethiol (**4c**, 0.07 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **5c** (16.4 mg, 16%) as a colourless syrup and **6c** (72.7 mg, 71%) as an off-white solid. Combined isolated yield: 89.1 mg, 87%, **5c**/**6c** = 18:82. $\mathbf{R_f}$ (**5c**/**6c**) = 0.28 / 0.21 (hexane/acetone 75:25).



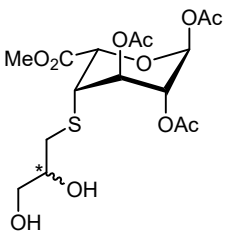
***5c*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.17 (d, J = 2.8 Hz, 1H, H-1), 5.27 (t, J = 3.6 Hz, 1H, H-3), 4.96 (d, J = 3.6 Hz, 1H, H-5), 4.76 (ddd, J = 3.6, 2.8, 0.8 Hz, 1H, H-2), 3.85 (s, 3H, OCH_3), 3.61 (t, J = 6.4 Hz, 2H, CH_2Cl), 3.12 (t, J = 3.6 Hz, 1H, H-4), 2.74 (t, J = 6.8 Hz, 2H, SCH_2), 2.13 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.04 (tt, J = 6.8, 6.4 Hz, 2H, CH_2) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.5 (CO), 169.4 (CO), 168.7 (COO), 168.2 (CO), 91.2 (C-1), 69.9 (C-5), 69.7 (C-3), 66.9 (C-2), 52.7 (OCH_3), 43.8 (C-4), 43.1 (CH_2Cl), 32.0 (CH_2), 31.1 (SCH_2), 21.0 (CH_3), 20.9 (CH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{23}ClNaO_9S$ $[M+Na]^+$: 449.0649; found: 449.0649.



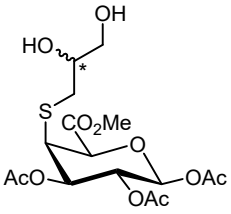
***6c*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.64 (d, J = 8.4 Hz, 1H, H-1), 5.36 (dd, J = 10.0, 8.4 Hz, 1H, H-2), 5.18 (dd, J = 10.0, 4.4 Hz, 1H, H-3), 4.54 (d, J = 2.0 Hz, 1H, H-5), 3.83 (s, 3H, OCH_3), 3.67 (dd, J = 4.4, 2.0 Hz, 1H, H-4), 3.60 (t, J = 6.4 Hz, 2H, CH_2Cl), 2.75 (dt, J = 12.8, 6.8 Hz, 1H, ½SCH_2), 2.66 (dt, J = 12.8, 6.8 Hz, 1H, ½SCH_2), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 1.96 (p, J = 6.8 Hz, 2H, CH_2) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.3 (CO), 169.2 (CO), 168.9 (CO), 166.9 (COO), 92.0 (C-1), 74.9 (C-5), 72.8 (C-3), 68.6 (C-2), 52.9 (OCH_3), 48.4 (C-4), 43.0 (CH_2Cl), 32.0 (CH_2), 30.9 (SCH_2), 20.9 (CH_3), 20.8 (CH_3), 20.6 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{23}ClNaO_9S$ $[M+Na]^+$: 449.0649; found: 449.0645.

Methyl 1,2,3-tri-O-acetyl-4-S-((R,S)-2,3-dihydroxypropyl)-4-thio-α-L-idopyranuronate (5d) and methyl 1,2,3-tri-O-acetyl-4-S-((R,S)-2,3-dihydroxypropyl)-4-thio-β-D-galactopyranuronate (6d)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), 3-mercapto-1,2-propanediol (**4d**, 0.07 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 3.5 h. Flash chromatography using hexane/acetone (55:45) afforded **5d** (10 mg, 10%) as a colourless syrup and **6d** (40.3 mg, 40%) as an off-white solid. Combined isolated yield: 50.3 mg, 50%, **5d**/**6d** = 20:80. $\mathbf{R_f}$ (**5d**/**6d**) = 0.17 / 0.12 (hexane/acetone 60:40).



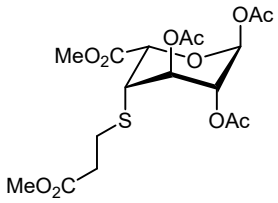
***5d*: ^{1}H NMR** (400 MHz, $CDCl_3$) *R*,*S* mixture δ 6.16 (t, *J* = 2.8 Hz, 1H, H-1), 5.32 (app q, *J* = 3.6 Hz, 1H, H-3), 4.98 (dd, *J* = 3.6, 2.0 Hz, 1H, H-5), 4.77 (tdd, *J* = 3.6, 2.8, 0.8 Hz, 1H, H-2), 3.86 (s, 3H, OCH_3), 3.82-3.79 (m, 1H, *C<u>H</u>OH), 3.70 (ddd, *J* = 11.2, 3.6, 2.0 Hz, 1H, ½C<u>H</u>$_2$OH), 3.55 (ddd, *J* = 11.2, 8.8, 6.0 Hz, 1H, ½C<u>H</u>$_2$OH), 3.31 (app t, *J* = 3.6 Hz, 1H, H-4), 2.76 (ddd, *J* = 14.0, 4.4, 2.8 Hz, 1H, ½SCH_2), 2.67 (ddd, *J* = 14.0, 8.0, 1.2 Hz, 1H, ½SCH_2), 2.41 (br s, 2H, 2 OH), 2.13 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) *R*,*S* mixture δ 169.6 (CO), 169.2 (CO), 169.1 (COO), 168.3 (CO), 91.30 (C-1), 91.26 (C-1'), 71.24 (*CHOH), 71.20 (*CHOH'), 70.2 (C-5), 70.0 (C-5'), 69.9 (C-3), 69.8 (C-3'), 67.1 (C-2), 67.0 (C-2'), 65.25 (CH_2OH), 65.21 (CH_2OH'), 52.94 (OCH_3), 52.90 (OCH_3'), 44.2 (C-4), 43.8 (C-4'), 37.4 (SCH_2), 37.1 (SCH_2'), 21.1 (CH_3), 21.0 (CH_3), 20.9 (CH_3) ppm. **HRMS** (ESI$^+$) *m/z* calcd. for $C_{16}H_{24}NaO_{11}S$ $[M+Na]^+$: 447.0937; found: 447.0931.



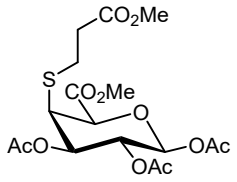
***6d*: ^{1}H NMR** (400 MHz, $CDCl_3$) *R*,*S* mixture δ 5.64 (d, *J* = 8.0 Hz, 1H, H-1), 5.37 (dd, *J* = 10.0, 8.0 Hz, ½H, H-2), 5.31 (dd, *J* = 10.0, 8.0 Hz, ½H, H-2'), 5.22 (dd, *J* = 7.2, 4.4 Hz, ½H, H-3), 5.20 (dd, *J* = 7.2, 4.4 Hz, ½H, H-3'), 4.56 (dd, *J* = 3.6, 2.0 Hz, 1H, H-5), 3.84 (s, 3H, OCH_3), 3.77 (td, *J* = 3.6, 2.0 Hz, 1H, H-4), 3.74-3.65 (m, 2H, *CHOH and ½C<u>H</u>$_2$OH), 3.54 (dd, *J* = 11.0, 5.2 Hz, ½H, ½C<u>H</u>$_2$OH), 3.50 (dd, *J* = 11.0, 5.2 Hz, ½H, ½C<u>H</u>$_2$OH'), 2.74-2.66 (m, 2H, SCH_2), 2.41 (br s, 2H, 2 OH), 2.13 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) *R*,*S* mixture δ 170.37 (CO), 170.33 (CO'), 169.40 (CO), 169.37 (CO'), 169.2 (CO), 167.61 (COO), 167.60 (COO'), 92.2 (C-1), 92.1 (C-1'), 75.1 (C-5), 75.0 (C-5'), 72.8 (C-3), 72.3 (C-3'), 70.9 (*CHOH), 70.0 (*CHOH), 68.73 (C-2), 68.66 (C-2'), 65.1 (CH_2OH), 53.2 (OCH_3), 48.8 (C-4), 48.4 (C-4'), 37.51 (SCH_2), 37.44 (SCH_2'), 20.9 (CH_3), 20.86 (CH_3), 20.81 (CH_3'), 20.7 (CH_3) ppm. **HRMS** (ESI$^+$) *m/z* calcd. for $C_{16}H_{24}NaO_{11}S$ $[M+Na]^+$: 447.0937; found: 447.0935.

Methyl 1,2,3-tri-O-acetyl-4-S-(3-methoxy-3-oxopropyl)-4-thio-α-L-idopyranuronate (5e) and methyl 1,2,3-tri-O-acetyl-4-S-(3-methoxy-3-oxopropyl)-4-thio-β-D-galactopyranuronate (6e)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), 3-mercaptopropionate (**4e**, 0.08 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (80:20) afforded **5e** (21 mg, 20%) as a colourless syrup and **6e** (82.7 mg, 79%) as an off-white solid. Combined isolated yield: 103.7 mg, 99%, **5e**/**6e** = 20:80. $\mathbf{R_f}$ (**5e**/**6e**) = 0.25 / 0.19 (hexane/acetone 70:30).



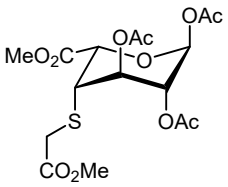
***5e*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.15 (d, J = 2.8 Hz, 1H, H-1), 5.28 (t, J = 3.6 Hz, 1H, H-3), 4.95 (d, J = 3.6 Hz, 1H, H-5), 4.76 (ddd, J = 3.6, 2.8, 0.8 Hz, 1H, H-2), 3.84 (s, 3H, OCH_3), 3.69 (S, 3H, OCH_3) 3.15 (t, J = 3.6 Hz, 1H, H-4), 2.86-2.82 (m, 2H, SCH_2), 2.64 (t, J = 7.0 Hz, 2H, CH_2CO), 2.13 (s, 3H, CH_3CO), 2.10 (s, 6H, $2CH_3CO$) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 172.1 (COO), 169.6 (CO), 169.5 (CO), 168.8 (COO), 168.3 (CO), 91.3 (C-1), 70.2 (C-5), 70.0 (C-3), 67.1 (C-2), 52.8 (OCH_3), 52.0 (OCH_3), 44.3 (C-4), 34.8 (CH_2), 29.4 (SCH_2), 21.0 (CH_3), 20.98 (CH_3), 20.94 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{17}H_{24}NaO_{11}S$ $[M+Na]^+$: 459.0931; found: 459.0934.



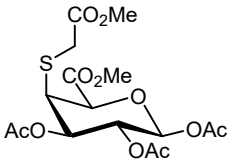
***6e*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.63 (d, J = 8.0 Hz, 1H, H-1), 5.33 (dd, J = 10.0, 8.0 Hz, 1H, H-2), 5.18 (dd, J = 10.0, 4.4 Hz, 1H, H-3), 4.52 (d, J = 2.0 Hz, 1H, H-5), 3.82 (s, 3H, OCH_3), 3.70-3.68 (m, 1H, H-4), 3.68 (s, 3H, OCH_3), 2.84 (dt, J = 13.2, 7.2 Hz, 1H, ½SCH_2), 2.76 (dt, J = 13.2, 7.2 Hz, 1H, ½SCH_2), 2.54 (t, J = 7.2 Hz, 2H, CH_2CO), 2.12 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.9 (COO), 170.4 (CO), 169.3 (CO), 169.2 (CO), 166.9 (COO), 92.2 (C-1), 74.9 (C-5), 72.8 (C-3), 68.7 (C-2), 52.9 (OCH_3), 52.0 (OCH_3), 48.7 (C-4), 34.7 (CH_2), 28.8 (SCH_2), 20.9 (CH_3), 20.8 (CH_3), 20.7 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{17}H_{24}NaO_{11}S$ $[M+Na]^+$: 459.0931; found: 459.0928.

Methyl 1,2,3-tri-O-acetyl-4-S-(2-methoxy-2-oxoethyl)-4-thio-α-L-idopyranuronate (5f) and methyl 1,2,3-tri-O-acetyl-4-S-(2-methoxy-2-oxoethyl)-4-thio-β-D-galactopyranuronate (6f)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), 2-mercaptoacetate (**4f**, 0.07 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 2.5 h. Flash chromatography using hexane/acetone (80:20) afforded **5f** (19.2 mg, 19%) as a colourless syrup and **6f** (42.6 mg, 42%) as an off-white solid. Combined isolated yield: 61.8 mg, 61%, **5f**/**6f** = 31:69. $\mathbf{R_f}$ (**5f**/**6f**) = 0.26 / 0.20 (hexane/acetone 70:30).



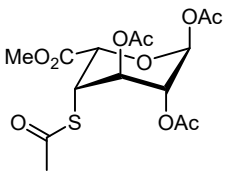
***5f*: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.14 (d, J = 3.6 Hz, 1H, H-1), 5.37 (t, J = 4.2 Hz, 1H, H-3), 4.99 (d, J = 3.6 Hz, 1H, H-5), 4.80 (t, J = 3.6 Hz, 1H, H-2), 3.85 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.39 (t, J = 4.2 Hz, 1H, H-4), 3.32 (d, J = 15.0 Hz, 1H, ½SCH_2), 3.26 (d, J = 15.0 Hz, 1H, ½SCH_2), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 170.4 (COO), 169.5 (CO), 169.1 (CO), 168.7 (COO), 168.3 (CO), 91.2 (C-1), 70.3 (C-5), 69.5 (C-3), 67.2 (C-2), 52.85 (OCH_3), 51.81 (OCH_3), 44.5 (C-4), 35.3 (SCH_2), 21.0 (CH_3), 20.96 (CH_3), 20.94 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{22}NaO_{11}S$ $[M+Na]^+$: 445.0781; found: 445.0776.



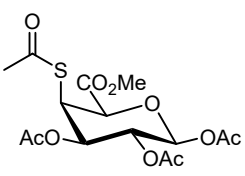
***6f*: ^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.65 (d, J = 7.8 Hz, 1H, H-1), 5.35 (dd, J = 10.2, 7.8 Hz, 1H, H-2), 5.25 (dd, J = 10.2, 4.2 Hz, 1H, H-3), 4.53 (d, J = 2.4 Hz, 1H, H-5), 3.89 (dd, J = 4.2, 2.4 Hz, 1H, H-4), 3.82 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.30 (d, J = 14.4 Hz, 1H, ½SCH_2), 3.24 (d, J = 14.4 Hz, 1H, ½SCH_2), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$) δ 170.2 (CO), 170.0 (COO), 169.3 (CO), 169.1 (CO), 166.7 (COO), 92.2 (C-1), 74.8 (C-5), 72.5 (C-3), 68.7 (C-2), 53.0 (OCH_3), 52.6 (OCH_3), 48.1 (C-4), 34.4 (SCH_2), 21.0 (CH_3), 20.9 (CH_3), 20.7 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{22}NaO_{11}S$ $[M+Na]^+$: 445.0781; found: 445.0780.

Methyl 1,2,3-tri-O-acetyl-4-S-acetyl-4-thio-α-L-idopyranuronate (5g) and methyl 1,2,3-tri-O-acetyl-4-S-acetyl-4-thio-β-D-galactopyranuronate (6g)

According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), thioacetic acid (**4g**, 0.05 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 6 h. Flash chromatography using hexane/acetone (85:15) afforded **5g** (8.5 mg, 9%) as a colourless syrup and **6g** (11.3 mg, 12%) as an off-white solid. Combined isolated yield: 19.8 mg, 21%, **5g**/**6g** = 43:57. $\mathbf{R_f}$ (**5g**/**6g**) = 0.27 / 0.22 (hexane/acetone 70:30).



***5g*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.13 (d, J = 3.6 Hz, 1H, H-1), 5.18 (dd, J = 4.0, 3.6 Hz, 1H, H-3), 5.00 (d, J = 3.6 Hz, 1H, H-5), 4.81 (t, J = 3.6 Hz, 1H, H-2), 4.21 (dd, J = 4.0, 3.6 Hz, 1H, H-4), 3.74 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3COS), 2.13 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 192.5 (COS), 169.0 (CO), 168.9 (2 CO), 168.2 (COO), 90.8 (C-1), 69.3 (C-5), 69.0 (C-3), 66.5 (C-2), 52.7 (OCH_3), 40.6 (C-4), 30.4 ($\underline{C}H_3COS$), 20.92 (CH_3), 20.88 ($2CH_3$) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{15}H_{20}NaO_{10}S$ $[M+Na]^+$: 415.0673; found: 415.0673.

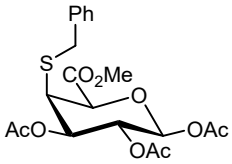


***6g*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.68 (d, J = 8.0 Hz, 1H, H-1), 5.32 (dd, J = 10.0, 4.0 Hz, 1H, H-3), 5.16 (dd, J = 10.0, 8.0 Hz, 1H, H-2), 4.62 (d, J = 2.4 Hz, 1H, H-5), 4.60 (dd, J = 4.0, 2.4 Hz, 1H, H-4), 3.74 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3COS), 2.11 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 1.97 (s, 3H,

CH_3CO) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 192.9 (COS), 169.9 (CO), 169.3 (CO), 169.0 (CO), 166.3 (COO), 92.2 (C-1), 73.8 (C-5), 70.7 (C-3), 68.7 (C-2), 53.0 (OCH_3), 46.1 (C-4), 30.8 ($\underline{C}H_3COS$), 20.9 (CH_3), 20.7 ($2CH_3$) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{15}H_{20}NaO_{10}S$ $[M+Na]^+$: 415.0675; found: 415.0671.

Methyl 1,2,3-tri-O-acetyl-4-S-benzyl-4-thio-β-D-galactopyranuronate (6h)

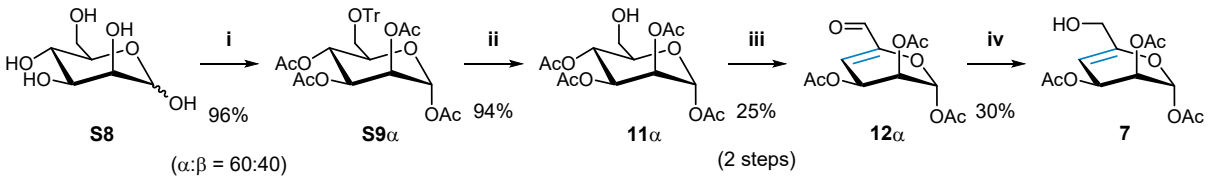
According to general procedure 2.1.1., 4,5-glycal **1** (75 mg, 0.24 mmol), benzyl mercaptan (**4h**, 0.08 mL, 0.72 mmol), DPAP (6.1 mg, 0.024 mmol) and MAP (3.6 mg, 0.024 mmol) were reacted for 2.5 h. Flash chromatography using hexane/acetone (80:20) afforded **6h** (27.2 mg, 26%) as a colourless syrup. **R_f** (**6h**) = 0.26 (hexane/acetone 70:30).



***6h*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 3H, 3CH), 7.23-7.19 (m, 2H, 2CH), 5.62 (d, *J* = 8.0 Hz, 1H, H-1), 5.34 (dd, *J* = 10.0, 8.0 Hz, 1H, H-2), 5.12 (dd, *J* = 10.0, 4.4 Hz, 1H, H-3), 4.46 (d, *J* = 1.6 Hz, 1H, H-5), 3.71 (d, *J* = 13.2 Hz, 1H, ½SCH_2), 3.65 (d, *J* = 13.2 Hz, 1H, ½SCH_2), 3.63 (s, 3H, OCH_3), 3.60 (dd, *J* = 4.4, 1.6 Hz, 1H, H-4), 2.10 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 170.1 (CO), 169.3 (CO), 169.2 (CO), 166.7 (COO), 137.7 (C), 129.3 (CH), 128.8 (CH), 127.5 (CH), 92.2 (C-1), 74.9 (C-5), 72.7 (C-3), 68.9 (C-2), 52.8 (OCH_3), 46.4 (C-4), 37.6 (SCH_2), 21.0 (CH_3), 20.8 (CH_3), 20.7 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{20}H_{24}NaO_9S$ $[M+Na]^+$: 463.1039; found: 463.1035.

2.2.4. Synthesis of 4,5-glycals 7-10

Synthesis of 1,2,3-tri-O-acetyl-4-deoxy-α-D-manno-hex-4-eno-1,5-pyranoside (7)

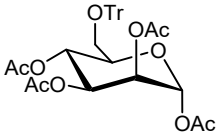


Scheme S2. Synthesis of **7** from **S8**. Reaction conditions: (i) a) TrCl, pyridine, 50 ºC, 3 h; b) Ac_2O, 0 ºC to rt, 18 h; (ii) NaI, TMSCl, CH_3CN, 0 ºC, 20 min; (iii) a) DMP, CH_2Cl_2, rt, 6 h; b) Et_3N, CH_2Cl_2, rt, 1 h; (iv) $NaBH_4$, THF, 0 ºC to rt, 1 h.

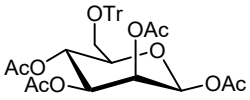
1,2,3,4-tetra-O-acetyl-6-O-triphenylmethyl-α/β-D-mannopyranose (S9α/β)

According to a previously described method,[8] a suspension of D-mannose (**S8**, 12 g, 66.6 mmol) and trityl chloride (TrCl, 18.57 g, 66.6 mmol) in pyridine (60 mL) was stirred under an inert atmosphere at 50 ºC for 3 h. Then, the reaction mixture was cooled to 0 ºC, and Ac_2O (35 mL) was added dropwise. After stirring for 18 h at room temperature, the mixture was poured into ice and stirred vigorously for

1.5 h to afford a white solid, which was collected by vacuum filtration and washed with ice-cold H_2O. The solid was dissolved in CH_2Cl_2 and washed with H_2O to remove remaining pyridine. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography using hexane/EtOAc (75:25), affording **S9***α*[9] (22.42 g, 57%) as an off-white solid and **S9***β*[9] (15.34 g, 39%) as an off-white solid. Combined isolated yield: 37.76 g, 96%, **S9***α*/**S9***β* = 60:40. $\mathbf{R_f}$ (**S9***α*/**S9***β*) = 0.38 / 0.33 (hexane/acetone 75:25).



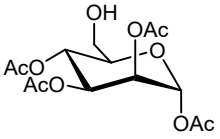
***S9α*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.2 Hz, 6H, CH), 7.29 (t, *J* = 7.2 Hz, 6H, CH), 7.22 (t, *J* = 7.2 Hz, 3H, CH), 6.17 (d, *J* = 2.0 Hz, 1H, H-1), 5.51 (t, *J* = 10.0 Hz, 1H, H-4), 5.30 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3), 5.26 (ddd, *J* = 3.2, 2.0, 0.8 Hz, 1H, H-2), 3.92 (ddd, *J* = 10.0, 4.2, 2.8 Hz, 1H, H-5), 3.31 (dd, *J* = 10.0, 2.8 Hz, 1H, H-6b), 3.08 (dd, *J* = 10.0, 4.2 Hz, 1H, H-6a), 2.23 (s, 3H, CH_3CO), 2.16 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.74 (s, 3H, CH_3CO) ppm.



***S9β*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.2 Hz, 6H, CH), 7.29 (t, *J* = 7.2 Hz, 6H, CH), 7.22 (t, *J* = 7.2 Hz, 3H, CH), 5.86 (s, 1H, H-1), 5.46 (d, *J* = 3.2 Hz, 1H, H-2), 5.37 (t, *J* = 10.0 Hz, 1H, H-4), 5.07 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3), 3.65 (ddd, *J* = 10.0, 4.4, 2.8 Hz, 1H, H-5), 3.34 (dd, *J* = 10.0, 2.8 Hz, 1H, H-6b), 3.17 (dd, *J* = 10.0, 4.4 Hz, 1H, H-6a), 2.24 (s, 3H, CH_3CO), 2.13 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.75 (s, 3H, CH_3CO) ppm.

1,2,3,4-tetra-O-acetyl-α-D-mannopyranoside (11α)

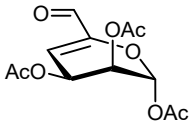
According to a previously described method,[9] **S9***α* (10.7 g, 18.1 mmol) and NaI (8.42 g, 56.1 mmol), previously dried under high vacuum, were suspended in CH_3CN (50 mL) and cooled to 0 ºC. Then, TMSCl (7.1 mL, 56.1 mmol) was added dropwise, and the mixture was stirred for 20 min. A solution of $Na_2S_2O_3 \cdot 5H_2O$ (9.89 g, 39.9 mmol) in H_2O (100 mL) was added and stirring continued for 20 min. After that, the solvent was removed *in vacuo*, and the residue was dissolved in CH_2Cl_2 and washed with brine. The aqueous layer was back extracted with CH_2Cl_2, and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography using hexane/EtOAc (60:40), affording **11***α*[8] (5.93 g, 94%) as an off-white solid. $\mathbf{R_f}$ (**11***α*) = 0.21 (hexane/acetone 50:50).



***11α*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.09 (d, *J* = 1.6 Hz, 1H, H-1), 5.40 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3), 5.30 (t, *J* = 10.0 Hz, 1H, H-4), 5.27 (dd, *J* = 3.2, 1.6 Hz, 1H, H-2), 3.85 (ddd, *J* = 10.0, 4.4, 2.4 Hz, 1H, H-5), 3.71 (dd, *J* = 12.7, 2.4 Hz, 1H, H-6b), 3.61 (dd, *J* = 12.7, 4.4 Hz, 1H, H-6a), 2.79 (br s, 1H, OH), 2.16 (s, 6H, $2CH_3CO$), 2.08 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO) ppm.

1,2,3-tri-O-acetyl-4-deoxy-α-D-manno-hex-4-enodialdo-1,5-pyranoside (12α)

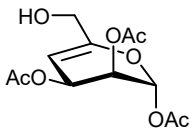
According to general procedure 2.1.4., **11***α* (2.9 g, 8.33 mmol) and DMP (4.24 g, 9.99 mmol) in CH_2Cl_2 (20 mL) were reacted for 6 h. After the appropriate quenching and extraction, the crude and Et_3N (1.39 mL, 9.99 mmol) in CH_2Cl_2 (60 mL) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **12***α* (595.8 mg, 25%) as an off-white solid. $\mathbf{R_f}$ (**12***α*) = 0.41 (hexane/acetone 70:30).



***12α*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.24 (s, 1H, CHO), 6.41 (d, J = 3.6 Hz, 1H, H-1), 5.87 (dd, J = 2.8, 1.6 Hz, 1H, H-4), 5.81 (dd, J = 4.4, 2.8 Hz, 1H, H-3), 5.33 (ddd, J = 4.4, 3.6, 1.6 Hz, 1H, H-2), 2.14 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 184.9 (CHO), 170.0 (CO), 169.7 (CO), 168.0 (CO), 149.6 (C-5), 115.7 (C-4), 89.2 (C-1), 63.8 (C-3), 62.8 (C-2), 20.9 (CH_3), 20.8 (CH_3), 20.7 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{12}H_{14}NaO_8$ $[M+Na]^+$: 309.0586; found: 309.0580.

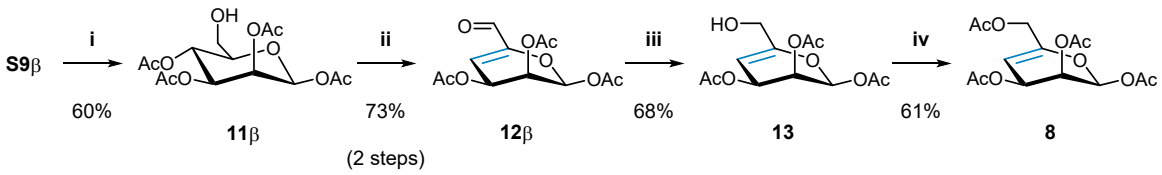
1,2,3-tri-O-acetyl-4-deoxy-α-D-manno-hex-4-eno-1,5-pyranoside (7)

According to general procedure 2.1.5., **12***α* (430 mg, 1.50 mmol) and $NaBH_4$ (68.2 mg, 1.80 mmol) in THF (20 mL) were reacted for 1 h. Flash chromatography using hexane/acetone (85:15) afforded **7** (130 mg, 30%) as a yellowish syrup. $\mathbf{R_f}$ (**7**) = 0.16 (hexane/acetone 70:30).



***7*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.25 (d, J = 5.6 Hz, 1H, H-1), 5.59 (tt, J = 4.0, 1.2 Hz, 1H, H-3), 5.22 (ddd, J = 5.6, 4.0, 0.8 Hz, 1H, H-2), 5.01 (dq, J = 4.0, 0.8 Hz, 1H, H-4), 4.05 (ap q, J = 1.2 Hz, 2H, H-6ab), 2.14 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.4 (CO), 169.8 (CO), 169.1 (CO), 153.8 (C-5), 95.1 (C-4), 89.0 (C-1), 65.5 (C-3), 63.2 (C-2), 61.8 (C-6), 21.0 ($2CH_3$), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{12}H_{16}NaO_8$ $[M+Na]^+$: 311.0743; found: 311.0744.

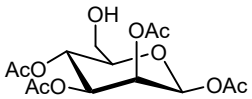
Synthesis of 1,2,3,6-tetra-O-acetyl-4-deoxy-β-D-manno-hex-4-eno-1,5-pyranoside (8)



Scheme S3. Synthesis of **8** from **S9***β*. Reaction conditions: (i) HBr/AcOH 33% w/w, AcOH, 15 ºC, 10 s; (ii) a) DMP, CH_2Cl_2, rt, 6 h; b) Et_3N, DCM, rt, 2 h; (iii) $NaBH_4$, THF, 0 ºC to rt, 2 h; (iv) Ac_2O, DMAP, pyridine, CH_2Cl_2, rt, 3 h.

1,2,3,4-tetra-O-acetyl-β-D-mannopyranose (11β)

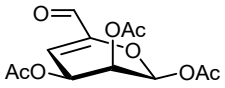
Similarly to a previously described method,[8] **S9***β* (10.2 g, 17.27 mmol) was dissolved in AcOH (120 mL) at 40 ºC. The solution was cooled to 15 ºC and HBr/AcOH (33% w/w in AcOH, 5 mL, 20.72 mmol) was added dropwise, and the mixture was stirred for 10 s. Then, the reaction mixture was filtered through Celite onto H_2O and the solid washed with AcOH. The solution was quenched with saturated aqueous $NaHCO_3$ solution, obtaining a white suspension which was extracted with $CHCl_3$. The organic layer was washed with saturated aqueous $NaHCO_3$ solution and H_2O. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in the minimum amount of hot $CHCl_3$ and induced to crystallise with Et_2O. The crystals were collected by filtration and dried, affording **11***β*[9] (3.6 g, 60%) as a white solid. $\mathbf{R_f}$ (**11***β*) = 0.33 (hexane/EtOAc 50:50).



***11β*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.88 (d, J = 1.2 Hz, 1H, H-1), 5.50 (dd, J = 3.2, 1.2 Hz, 1H, H-2), 5.27 (app t, J = 9.9 Hz, 1H, H-4), 5.18 (dd, J = 9.9, 3.2 Hz, 1H, H-3), 3.82-3.58 (m, 3H, H-5, H-6a,b), 2.22 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO) ppm.

1,2,3-tri-O-acetyl-4-deoxy-β-D-manno-hex-4-enodialdo-1,5-pyranoside (12β)

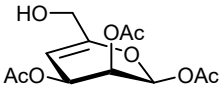
According to general procedure 2.1.4., **11***β* (1.5 g, 4.31 mmol) and DMP (2.19 g, 5.17 mmol) in CH_2Cl_2 (16 mL) were reacted for 6 h. After the appropriate quenching and extraction, the crude and Et_3N (0.72 mL, 5.17 mmol) in CH_2Cl_2 (30 mL) were reacted for 2 h. Flash chromatography using hexane/EtOAc (70:30) afforded **12***β* (520 mg, 63%) as a yellow syrup. $\mathbf{R_f}$ (**12***β*) = 0.45 (hexane/EtOAc 75:25).



***12β*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.24 (s, 1H, CHO), 6.44 (dd, J = 2.0, 1.2 Hz, 1H, H-1), 5.90 (d, J = 4.0 Hz, 1H, H-4), 5.74 (ddd, J = 4.8, 4.0, 1.2 Hz, 1H, H-3), 5.37 (dd, J = 4.8, 2.0 Hz, 1H, H-2), 2.10 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 185.0 (CHO), 170.0 (CO), 169.7 (CO), 168.6 (CO), 150.2 (C-5), 114.6 (C-4), 88.4 (C-1), 65.0 (C-3), 62.2 (C-2), 20.8 (CH_3), 20.6 (CH_3), 20.5 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{12}H_{18}NO_8$ $[M+NH_4]^+$: 304.1032; found: 304.1039.

1,2,3-tri-O-acetyl-4-deoxy-β-D-manno-hex-4-eno-1,5-pyranoside (13)

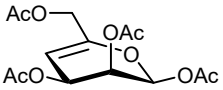
According to general procedure 2.1.5., **12***β* (1.3 g, 4.50 mmol) and $NaBH_4$ (2.04 g, 5.41 mmol) in THF (45 mL) were reacted for 2 h. Flash chromatography using hexane/EtOAc (70:30) afforded **13** (890 mg, 68%) as a colourless syrup. $\mathbf{R_f}$ (**13**) = 0.63 (hexane/acetone 75:25).



***13*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.32 (dd, J = 2.8, 1.2 Hz, 1H, H-1), 5.52 (tq, J = 4.8, 1.2 Hz, 1H, H-3), 5.30 (dd, J = 4.8, 2.8 Hz, 1H, H-2), 5.09 (dt, J = 4.8, 1.2 Hz, 1H, H-4), 4.03 (br s, 2H, H-6ab), 2.46 (br s, 1H, OH), 2.12 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.6 (CO), 169.9 (CO), 169.5 (CO), 154.2 (C-5), 95.0 (C-4), 87.9 (C-1), 65.9 (C-2), 61.7 (C-3), 61.6 (C-6), 20.92 (CH_3), 20.90 (CH_3), 20.6 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{12}H_{20}NO_8$ $[M+NH_4]^+$: 306.1189; found: 306.1197.

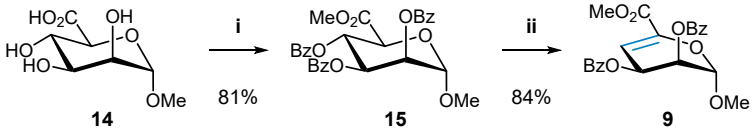
1,2,3,6-tetra-O-acetyl-4-deoxy-β-D-manno-hex-4-eno-1,5-pyranoside (8)

To a solution of **13** (90 mg, 0.31 mmol) in CH_2Cl_2 (3.1 mL) was added DMAP (19.1 mg, 0.16 mmol), pyridine (38 µL, 0.47 mmol), and Ac_2O (0.06 mL, 0.62 mmol), and the reaction mixture was stirred at room temperature for 3 h. Then, the reaction was diluted with CH_2Cl_2, washed with 1M aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, H_2O and brine. The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography using Pet. ether/EtOAc (75:25), affording **8** (62.9 mg, 61%) as a colourless syrup. $\mathbf{R_f}$ (**8**) = 0.61 (Pet. ether/EtOAc 50:50).



***8*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.27 (dd, J = 2.8, 1.2 Hz, 1H, H-1), 5.46 (tq, J = 4.8, 1.2 Hz, 1H, H-3), 5.24 (dd, J = 4.8, 2.8 Hz, 1H, H-2), 5.04 (dt, J = 4.8, 1.2 Hz, 1H, H-4), 4.42 (ap q, 2H, H-6ab), 2.06 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.3 (CO), 170.0 (CO), 169.6 (CO), 169.1 (CO), 149.9 (C-5), 97.5 (C-4), 87.7 (C-1), 65.5 (C-2), 62.0 (C-6), 61.3 (C-3), 20.71 (CH_3), 20.70 (CH_3), 20.6 (CH_3), 20.4 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{22}NO_9$ $[M+NH_4]^+$: 348.1289; found: 348.1299.

Synthesis of methyl (methyl 2,3-di-O-benzoyl-4-deoxy-α-L-threo-hex-4-enopyranosid) uronate (9)

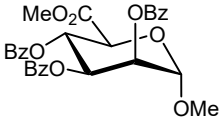


Scheme S4. Synthesis of **9** from **14**. Reaction conditions: (i) a) CH_3I, K_2CO_3, DMF, rt, 14h; b) BzCl, pyridine, 0 ºC to rt, 12h; (ii) DBU, CH_2Cl_2, 0 ºC to rt, 2h.

Methyl (methyl 2,3,4-tri-O-benzoyl-α-D-mannopyranosid)uronate (15)

According to general procedure 2.1.2., methyl α-D-mannopyranosiduronic acid[10] (**14**, 826 mg, 3.97 mmol), K_2CO_3 (1.65 g, 11.90 mmol) and CH_3I (0.74 mL, 11.90 mmol) in DMF (5 mL) were reacted

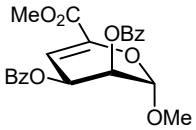
for 14 h. After the appropriate quenching and extraction, the residue was dissolved in pyridine (3 mL) and cooled to 0 ºC, and benzoyl chloride (BzCl, 1.43 mL, 12.3 mmol) was added dropwise. After stirring for 12 h at room temperature, the reaction was diluted with CH_2Cl_2 and washed with H_2O. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography using hexane/EtOAc (75:25), affording **15**[11] (1.72 g, 81%) as a white solid. $\mathbf{R_f}$ (**15**) = 0.50 (hexane/EtOAc 70:30).



***15*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 8.4, 1.4 Hz, 2H, 2CH), 7.98 (dd, J = 8.4, 1.4 Hz, 2H, 2CH), 7.85 (dd, J = 8.4, 1.4 Hz, 2H, 2CH), 7.64-7.58 (m, 1H, CH), 7.56-7.38 (m, 6H, 6CH), 7.32-7.27 (m, 2H, 2CH), 5.99-5.90 (m, 2H, H-3 and H-4), 5.67 (dd, J = 3.0, 2.3 Hz, 1H, H-2), 5.13 (d, J = 2.3 Hz, 1H, H-1), 4.63 (dd, J = 8.4, 0.8 Hz, 1H, H-5), 3.69 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3) ppm.

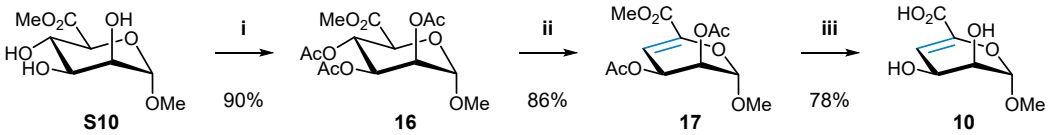
Methyl (methyl 2,3-di-O-benzoyl-4-deoxy-α-L-threo-hex-4-enopyranosid)uronate (9)

According to general procedure 2.1.3., **15** (500 mg, 0.93 mmol) and DBU (0.28 mL, 1.87 mmol) in CH_2Cl_2 (5 mL) were reacted for 2 h. Flash chromatography using hexane/EtOAc (70:30) afforded **9** (324 mg, 84%) as a yellow solid. $\mathbf{R_f}$ (**9**) = 0.45 (hexane/EtOAc 75:25).



***9*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 8.4, 1.6 Hz, 2H, 2CH), 7.91 (dd, J = 8.4, 1.6 Hz, 2H, 2CH), 7.60-7.55 (m, 1H, 1CH), 7.53-7.48 (m, 1H, CH), 7.44-7.40 (m, 2H, 2CH), 7.36-7.32 (m, 2H, 2CH), 6.24 (dd, J = 2.8, 1.6 Hz, 1H, H-4), 6.03 (ddd, J = 4.4, 2.8, 0.4 Hz, 1H, H-3), 5.64 (ddd, J = 4.4, 2.8, 1.6 Hz, 1H, H-2), 5.32 (dd, J = 2.8, 0.4 Hz, 1H, H-1), 3.87 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 165.7 (COO), 165.6 (COPh), 162.3 (COPh), 141.8 (C-5), 133.6 (CH), 133.4 (CH), 130.1 (CH), 129.9 (CH), 129.5 (C), 129.4 (C), 129.2 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 125.4 (CH), 109.0 (C-4), 99.5 (C-1), 65.0 (C-2), 64.4 (C-3), 56.9 (OCH_3), 52.7 (OCH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{22}H_{24}NO_8$ $[M+NH_4]^+$: 430.1496; found: 430.1499.

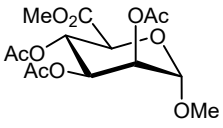
Synthesis of methyl 4-deoxy-α-L-threo-hex-4-enopyranosiduronic acid (10)



Scheme S5. Synthesis of **10** from **S10**. Reaction conditions: (i) Ac_2O, pyridine, rt, 2 h; (ii) DBU, CH_2Cl_2, 0 ºC to rt, 2h; (iii) NaOH, EtOH/H_2O (1:1), rt, 6h.

Methyl (methyl 2,3,4-tri-O-acetyl-α-D-mannopyranosid)uronate (16)

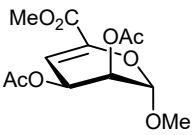
To a solution of methyl (methyl α-D-mannopyranosid)uronate[12] (**S10**, 500 mg, 2.25 mmol) in pyridine (6 mL) was added dropwise Ac_2O (3 mL), and the reaction mixture was stirred at room temperature for 2 h. Then, the solvent was removed *in vacuo*, and the residue was purified by silica gel flash column chromatography using hexane/EtOAc (80:20), affording **16**[13] (705 mg, 90%) as a white solid. $\mathbf{R_f}$ (**16**) = 0.50 (hexane/EtOAc 60:40).



***16*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.43-5.37 (m, 2H, H-3 and H-4), 5.24 (dd, J = 2.8, 2.0 Hz, 1H, H-2), 4.83 (d, J = 2.0 Hz, 1H, H-1), 4.31 (dd, J = 9.0 Hz, 1H, H-5), 3.78 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 2.15 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO) ppm.

Methyl (methyl 2,3-di-O-acetyl-4-deoxy-α-L-threo-hex-4-enopyranosid)uronate (17)

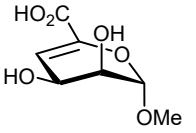
According to general procedure 2.1.3., **16** (705 mg, 2.02 mmol) and DBU (0.60 mL, 4.05 mmol) in CH_2Cl_2 (6 mL) were reacted for 2 h. Flash chromatography using hexane/EtOAc (50:50) afforded **17** (502 mg, 86%) as a white solid. $\mathbf{R_f}$ (**17**) = 0.50 (hexane/EtOAc 50:50).



***17*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.01 (dd, J = 2.8, 1.6 Hz, 1H, H-4), 5.68 (dd, J = 4.8, 2.8 Hz, 1H, H-3), 5.25 (ddd, J = 4.8, 3.2, 1.6 Hz, 1H, H-2), 5.10 (dd, J = 3.2 Hz, 1H, H-1), 3.84 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 2.09 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.2 (CO), 170.1 (CO), 162.2 (COO), 141.7 (C-5), 108.8 (C-4), 99.3 (C-1), 64.4 (C-2), 63.6 (C-3), 56.8 (OCH_3), 52.7 (OCH_3), 20.92 (CH_3), 20.90 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{12}H_{20}NO_8$ $[M+NH_4]^+$: 306.1183; found: 306.1182.

Methyl 4-deoxy-α-L-threo-hex-4-enopyranosiduronic acid (10)

To a solution of **17** (233 mg, 0.81 mmol) in EtOH/H_2O (1:1, 4 mL) was added NaOH (161.7 mg, 4.04 mmol), and the reaction mixture was stirred at room temperature for 6 h. Then, Amberlite resin (H^+ form) was added to adjust the pH to ~2. The resin was removed by filtration, the filtrate concentrated *in vacuo* and residual water was removed by lyophilisation, affording **10** (120 mg, 78%) as a yellow solid. $\mathbf{R_f}$ (**10**) = 0.40 (CH_2Cl_2/MeOH/H_2O 10:5:1).

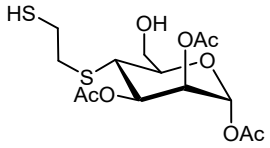


***10*: ^{1}H NMR** (400 MHz, D_2O) δ 6.10 (dd, J = 3.2, 1.2 Hz, 1H, H-4), 5.06 (d, J = 4.4 Hz, 1H, H-1), 4.46 (dd, J = 4.4, 3.2 Hz, 1H, H-3), 3.91 (td, J = 4.4, 1.2 Hz, 1H, H-2), 3.54 (s, 3H, OCH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, D_2O) δ 165.4 (COO), 140.3 (C-5), 112.5 (C-4), 101.3 (C-1), 65.5 (C-2), 62.1 (C-3), 56.6 (OCH_3) ppm. **HRMS** (ESI^-) *m/z* calcd. for $C_7H_9O_6^-$ $[M]^-$: 189.0405; found: 189.0401.

2.2.5. Thiol-ene reactions on 4,5-glycals 7-10

1,2,3-tri-O-acetyl-4-S-(2-mercaptoethyl)-4-thio-α-D-mannopyranose (18)

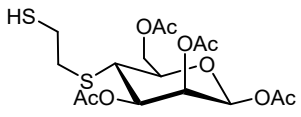
According to general procedure 2.1.1., 1,2,3-tri-*O*-acetyl-4-deoxy-*β*-L-*erythro*-hex-4-enopyranose (**7**, 95.1 mg, 0.33 mmol), **4a** (0.08 mL, 0.98 mmol), DPAP (8.5 mg, 0.03 mmol) and MAP (5 mg, 0.03 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **18** (61.8 mg, 49%) as a colourless syrup. $\mathbf{R_f}$ (**18**) = 0.24 (hexane/acetone 70:30).



***18*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.06 (d, J = 2.2 Hz, 1H, H-1), 5.21 (dd, J = 11.6, 3.2 Hz, 1H, H-3), 5.16 (dd, J = 3.2, 2.2 Hz, 1H, H-2), 4.03 (dd, J = 12.4, 3.2 Hz, 1H, H-6a), 3.92 (dd, J = 12.4, 2.4 Hz, 1H, H-6b), 3.79-3.74 (m, 1H, H-5), 3.13 (t, J = 11.6 Hz, 1H, H-4), 2.89-2.83 (m, 2H, SCH_2), 2.76-2.69 (m, 2H, $C\underline{H}_2SH$), 2.15 (s, 3H, CH_3CO), 2.14 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 1.72 (t, J = 8.1 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.9 (CO), 169.8 (CO), 168.7 (CO), 91.0 (C-1), 74.9 (C-5), 69.2 (C-3), 67.7 (C-2), 62.3 (C-6), 42.3 (C-4), 36.7 (SCH_2), 25.0 (CH_2SH), 21.0 (CH_3), 20.96 (CH_3), 20.92 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{14}H_{22}NaO_8S_2$ $[M+Na]^+$: 405.0654; found: 405.0648.

1,2,3,6-tetra-O-acetyl-4-S-(2-mercaptoethyl)-4-thio-β-D-mannopyranose (19)

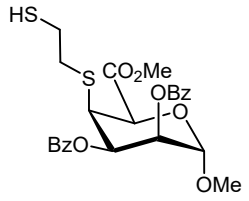
According to general procedure 2.1.1., 1,2,3,6-tetra-*O*-acetyl-4-deoxy-*α*-L-*erythro*-hex-4-enopyranose (**8**, 57.4 mg, 0.17 mmol), **4a** (0.04 mL, 0.52 mmol), DPAP (4.4 mg, 0.017 mmol) and MAP (2.6 mg, 0.017 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **19** (27.3 mg, 37%) as a colourless syrup. $\mathbf{R_f}$ (**19**) = 0.26 (hexane/acetone 70:30).



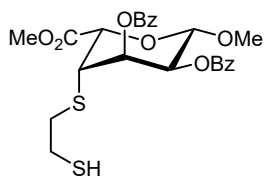
***19*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.77 (d, J = 1.2 Hz, 1H, H-1), 5.41 (dd, J = 3.2, 1.2 Hz, 1H, H-2), 5.02 (dd, J = 11.2, 3.2 Hz, 1H, H-3), 4.62 (dd, J = 12.0, 2.0 Hz, 1H, H-6b), 4.43 (dd, J = 12.0, 5.2 Hz, 1H, H-6a), 3.75 (ddd, J = 11.2, 5.2, 2.0 Hz, 1H, H-5), 2.92 (t, J = 11.2 Hz, 1H, H-4), 2.85-2.74 (m, 2H, SCH_2), 2.71-2.64 (m, 2H, $C\underline{H}_2SH$), 2.20 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.08 (s, 6H, $2CH_3CO$), 1.70 (t, J = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.7 (CO), 170.2 (CO), 169.6 (CO), 168.5 (CO), 90.5 (C-1), 75.1 (C-5), 71.3 (C-3), 68.0 (C-2), 64.0 (C-6), 42.5 (C-4), 35.9 (SCH_2), 24.8 (CH_2SH), 21.0 (CH_3), 20.9 (CH_3), 20.88 (CH_3), 20.84 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{16}H_{24}NaO_9S_2$ $[M+Na]^+$: 447.0759; found: 447.0759.

Methyl 2,3-di-O-benzoyl-4-S-(2-mercaptoethyl)-6-O-methyl-4-thio-α-D-talopyranosiduronate (20a) and methyl 2,3-di-O-benzoyl-4-S-(2-mercaptoethyl)-6-O-methyl-4-thio-β-L-gulopyranosiduronate (20b)

According to general procedure 2.1.1., methyl 2,3-di-*O*-benzoyl-4-deoxy-6-*O*-methyl-*β*-L-*erythro*-hex-4-enopyranosiduronate (**9**, 75 mg, 0.18 mmol), **4a** (46 µL, 0.55 mmol), DPAP (4.7 mg, 0.018 mmol) and MAP (2.7 mg, 0.018 mmol) were reacted for 1 h. Flash chromatography using hexane/acetone (90:10) afforded **20a** (25.8 mg, 28%) as an off-white solid and **20b** (54.3 mg, 59%) as an off-white solid. Combined isolated yield: 80.1 mg, 87%, **20a**/**20b** = 32:68. $\mathbf{R_f}$ (**20a**/**20b**) = 0.18 / 0.14 (hexane/acetone 80:20).



***20a*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29-8.24 (m, 2H, 2CH), 7.99-7.94 (m, 2H, 2CH), 7.62-7.57 (m, 1H, CH), 7.56-7.51 (m, 1H, CH), 7.49-7.44 (m, 2H, 2CH), 7.40-7.34 (m, 2H, 2CH), 5.71 (dd, *J* = 5.2, 3.6 Hz, 1H, H-3), 5.44 (ddd, *J* = 3.6, 1.6, 0.8 Hz, 1H, H-2), 5.04 (d, *J* = 1.6 Hz, 1H, H-1), 4.94 (d, *J* = 2.6 Hz, 1H, H-5), 3.89 (s, 3H, OCH_3), 3.77 (dd, *J* = 5.2, 2.6 Hz, 1H, H-4), 3.49 (s, 3H, OCH_3), 2.73-2.62 (m, 2H, SCH_2), 2.54-2.43 (m, 2H, $C\underline{H}_2SH$), 1.49 (t, *J* = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 168.8 (COO), 166.0 (COPh), 165.6 (COPh), 133.7 (CH), 133.6 (CH), 130.7 (CH), 130.0 (CH), 129.37 (C), 129.33 (C), 128.7 (CH), 128.5 (CH), 100.0 (C-1), 70.6 (C-5), 68.3 (C-2), 67.7 (C-3), 56.1 (OCH_3), 52.7 (OCH_3), 46.9 (C-4), 39.0 (SCH_2), 24.9 (CH_2SH) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{24}H_{26}NaO_8S_2$ $[M+Na]^+$: 529.0967; found: 529.0962.

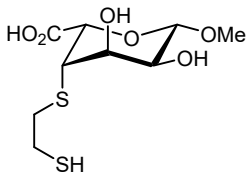


***20b*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06-8.02 (m, 2H, 2CH), 7.95-7.92 (m, 2H, 2CH), 7.66-7.61 (m, 1H, CH), 7.54-7.48 (m, 3H, 3CH), 7.38-7.34 (m, 2H, 2CH), 5.79 (t, *J* = 3.6 Hz, 1H, H-3), 5.63 (dd, *J* = 8.0, 3.6 Hz, 1H, H-2), 4.98 (d, *J* = 8.0 Hz, 1H, H-1), 4.87 (d, *J* = 2.8 Hz, 1H, H-5), 3.85 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3), 3.47 (dd, *J* = 3.6, 2.8 Hz, 1H, H-4), 2.97-2.91 (m, 2H, SCH_2), 2.84-2.77 (m, 2H, $C\underline{H}_2SH$), 1.76 (t, *J* = 8.0 Hz, 1H, SH) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 168.6 (COO), 165.4 (COPh), 165.2 (COPh), 133.9 (CH), 133.4 (CH), 129.9 (CH), 129.8 (CH), 129.6 (C), 129.4 (C), 128.9 (CH), 128.5 (CH), 100.7 (C-1), 73.3 (C-5), 72.7 (C-2), 68.4 (C-3), 57.1 (OCH_3), 52.8 (OCH_3), 47.4 (C-4), 37.6 (SCH_2), 24.8 (CH_2SH) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{24}H_{26}NaO_8S_2$ $[M+Na]^+$: 529.0967; found: 529.0959.

Methyl 4-S-(2-mercaptoethyl)-4-thio-β-L-gulopyranosiduronic acid (21)

According to general procedure 2.1.1., methyl 4-deoxy-*β*-L-*erythro*-hex-4-enopyranosiduronic acid (**10**, 50 mg, 0.26 mmol), **4a** (66 µL, 0.79 mmol), DPAP (6.7 mg, 0.026 mmol) and MAP (3.9 mg, 0.026 mmol) were reacted for 1 h. For solubility reasons, MeOH (0.1 mL) was added. Flash

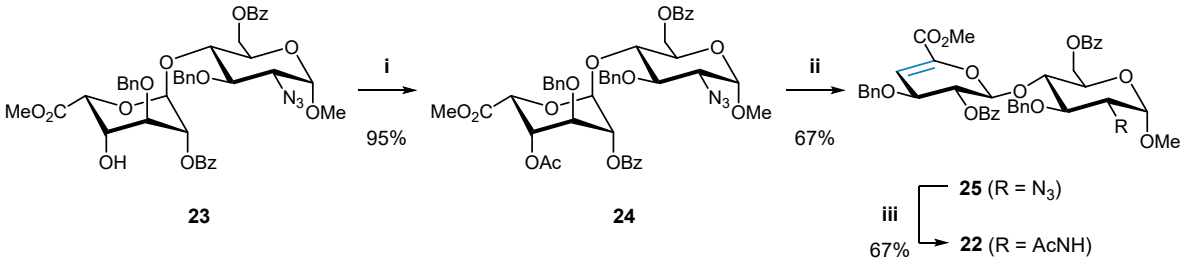
chromatography using Et_2O/EtOAc/MeOH/AcOH (30:30:1:0.25) afforded **21** (33.6 mg, 45%) as an off-white solid. $\mathbf{R_f}$ (**21**) = 0.30 (Et_2O/EtOAc/MeOH/AcOH 3:3:0.25:0.25).



***21*: ^{1}H NMR** (400 MHz, CD_3OD) δ 4.69 (d, J = 2.4 Hz, 1H, H-5), 4.50 (d, J = 8.0 Hz, 1H, H-1), 4.13 (t, J = 3.6 Hz, 1H, H-3), 3.60 (dd, J = 8.0, 3.6 Hz, 1H, H-2), 3.53 (s, 3H, OCH_3), 3.16 (t, J = 3.6, 2.4 Hz, 1H, H-4), 2.87-2.77 (m, 2H, SCH_2), 2.74-2.67 (m, 2H, $C\underline{H}_2SH$) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_3OD) δ 103.7 (C-1), 74.0 (C-3), 73.7 (C-5), 69.4 (C-2), 57.4 (OCH_3), 51.9 (C-4), 38.6 (SCH_2), 25.4 (CH_2SH) ppm, COOH not observed. **HRMS** (ESI^-) *m/z* calcd. for $C_9H_{15}O_6S_2$ $[M-H]^-$: 283.0310; found: 283.0318.

2.2.6. Synthesis of disaccharide 22 and thiol-ene reaction

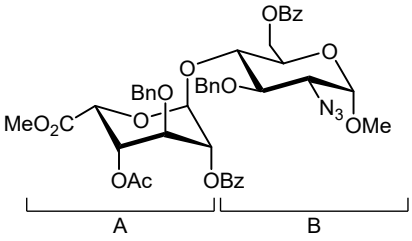
Synthesis of methyl (methyl 2-O-benzoyl-3-O-benzyl-4-deoxy-α-L-threo-hex-4-enopyranosyl) uronate-(1→4)-2-acetamido-6-O-benzoyl-3-O-benzyl-2-deoxy-α-D-glucopyranoside (22)



Scheme S5. Synthesis of **22** from**23**. Reaction conditions: (i) Ac_2O, pyridine, rt, 2 h; (ii) DBU, CH_2Cl_2, 0 ºC to rt, 2h; (iii) thioacetic acid, 2,6-lutidine, $CHCl_3$, 60 ºC, 36h.

Methyl (methyl 4-O-acetyl-2-O-benzoyl-3-O-benzyl-α-L-idopyranosyl)uronate-(1→4)-2-azido-6-O-benzoyl-3-O-benzyl-2-deoxy-α-D-glucopyranoside (24)

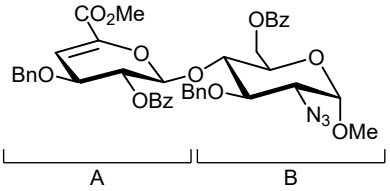
To a solution of the commercial disaccharide methyl (methyl 2-*O*-benzoyl-3-*O*-benzyl-*α*-L-idopyranosyl)uronate-(1→4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-*α*-D-glucopyranoside (**23**, 500 mg, 0.63 mmol) in pyridine (1.5 mL) was added dropwise Ac_2O (1 mL), and the reaction mixture was stirred at room temperature for 2 h. Then, the solvent was removed *in vacuo*, and the residue was purified by silica gel flash column chromatography using hexane/EtOAc (75:25), affording **24** (500 mg, 95%) as a white solid. $\mathbf{R_f}$ (**24**) = 0.68 (hexane/EtOAc 70:30).



***24*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2H, 2CH), 8.02-7.98 (m, 2H, 2CH), 7.57-7.51 (m, 2H, 2CH), 7.44-7.35 (m, 6H, 6CH), 7.35-7.26 (m, 8H, 8CH), 5.43 (d, J = 2.8 Hz, 1H, H-1 A), 5.22-5.16 (m, 2H, H-2 A and H-4 A), 4.99 (d, J = 3.2 Hz, 1H, H-5 A), 4.82 (dd, J = 11.2, 1.6 Hz, 2H, ½CH_2Ph A and ½CH_2Ph B), 4.79 (d, J = 3.6 Hz, 1H, H-1 B), 4.76-4.69 (m, 3H, H-6b B, ½CH_2Ph A and ½CH_2Ph B), 4.49 (dd, J = 12.0, 4.4 Hz, 1H, H-6a B), 4.08 (dd, J = 10.0, 8.8 Hz, 1H, H-4 B), 3.98 (ddd, J = 10.0, 4.4, 2.4 Hz, 1H, H-5 B), 3.94 (t, J = 3.6 Hz, 1H, H-3 A), 3.88 (dd, J = 10.0, 8.8 Hz, 1H, H-3 B), 3.47 (dd, J = 10.0, 3.6 Hz, 1H, H-2 B), 3.43 (s, 3H, OCH_3 A), 3.42 (s, 3H, OCH_3 B), 1.92 (s, 3H, CH_3CO A) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.9 (COO A), 168.8 (CO), 166.2 (COPh B), 165.3 (COPh A), 149.8 (CH), 137.8 (C), 137.4 (C), 133.7 (CH), 133.2 (CH), 130.0 (CH), 129.9 (C), 129.3 (C), 128.59 (CH), 128.55 (CH), 128.5 (CH), 128.4 (CH), 128.23 (CH), 128.18 (CH), 127.9 (CH), 127.6 (CH), 123.9 (CH), 98.6 (C-1 B), 98.0 (C-1 A), 78.8 (C-3 B), 75.6 (C-4 B), 75.1 (CH_2Ph B), 73.4 (C-3 A), 73.1 (CH_2Ph A), 69.4 (C-5 B), 68.6 (C-4 A), 68.3 (C-2 A), 67.6 (C-5 A), 63.9 (C-2 B), 62.8 (C-6 B), 55.6 (OCH_3), 52.1 (OCH_3), 20.8 (CH_3) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{44}H_{49}N_4O_{14}$ $[M+NH_4]^+$: 857.3240; found: 857.3229.

Methyl (methyl 2-O-benzoyl-3-O-benzyl-4-deoxy-α-L-threo-hex-4-eno pyranosyl)uronate-(1→4)-2-azido-6-O-benzoyl-3-O-benzyl-2-deoxy-α-D-glucopyranoside (25)

According to general procedure 2.1.3., disaccharide **24** (500 mg, 0.60 mmol) and DBU (0.18 mL, 1.19 mmol) in CH_2Cl_2 (7 mL) were reacted for 2 h. Flash chromatography using PhMe/EtOAc (90:10) afforded **25** (311 mg, 67%) as a white solid. $\mathbf{R_f}$ (**25**) = 0.70 (PhMe/EtOAc 85:15).

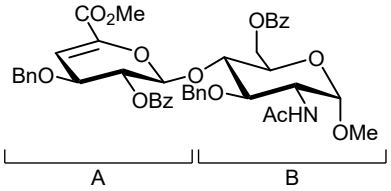


***25*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04-8.00 (m, 2H, 2CH), 7.95-7.91 (m, 2H, 2CH), 7.57-7.50 (m, 2H, 2CH), 7.45-7.34 (m, 8H, 8CH), 7.32-7.23 (m, 6H, 6CH), 6.23 (dd, J = 4.4, 1.2 Hz, 1H, H-4 A), 5.63 (dd, J = 3.2, 1.2 Hz, 1H, H-1 A), 5.48 (ddd, J = 3.2, 2.8, 1.2 Hz, 1H, H-2 A), 5.19 (d, J = 10.8 Hz, 1H, ½CH_2Ph B), 4.80-4.76 (m, 3H, H-1 B, ½CH_2Ph B and ½CH_2Ph A), 4.74 (d, J = 12.0 Hz, 1H, ½CH_2Ph A), 4.68 (dd, J = 12.4, 2.0 Hz, 1H, H-6b B), 4.50 (dd, J = 12.4, 4.4 Hz, 1H, H6a B), 4.10 (ddd, J = 4.4, 2.8, 1.2 Hz, 1H, H-3 A), 4.04 (dd, J = 10.0, 8.4 Hz, 1H, H-4 B), 3.99 (d, J = 8.4 Hz, 1H, H-3 B), 3.96 (ddd, J = 10.0, 4.4, 2.0 Hz, 1H, H-5 B), 3.62 (s, 3H, OCH_3 A), 3.43-3.39 (m, 4H, H-2 B and OCH_3 B) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 166.2 (COPh B), 165.2 (COPh A), 162.3 (COO A), 142.1 (C-5 A), 138.4 (C), 137.6 (C), 133.7 (CH), 133.3 (CH), 130.3 (CH), 130.0 (CH), 129.9 (C), 129.1 (CH), 128.63 (CH), 128.60 (CH), 128.56 (CH and C), 128.3 (CH), 128.06 (CH), 128.04 (CH), 127.6 (CH), 108.9 (C-4 A), 98.7 (C-1 B), 97.4 (C-1 A), 78.7 (C-3 B), 77.4 (C-4 B), 75.3 (CH_2Ph B), 71.3 (CH_2Ph A), 69.7 (C-3

A), 69.1 (C-2 A), 68.8 (C-5 B), 64.0 (C-2 B), 62.8 (C-6 B), 55.5 (OCH_3 A) 52.5 (OCH_3 B) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{42}H_{45}N_4O_{12}$ $[M+NH_4]^+$: 797.3028; found: 797.3041.

Methyl (methyl 2-O-benzoyl-3-O-benzyl-4-deoxy-α-L-threo-hex-4-enopyranosyl)uronate-(1→4)-2-acetamido-6-O-benzoyl-3-O-benzyl-2-deoxy-α-D-glucopyranoside (22)

According to a previously described method,[14] to a solution of 4,5-glycal disaccharide **25** (100 mg, 0.13 mmol) in $CHCl_3$ (ca. 0.3M, 0.4 mL) was added, under an inert atmosphere, 2,6-lutidine (39 μL, 0.33 mmol) and thioacetic acid (24 μL, 0.33 mmol), and the mixture was stirred at 60 ºC for 36 h. Then, the solvent was removed *in vacuo* and the residue was purified by silica gel flash column chromatography using hexane/acetone (70:30), affording **22** (68.3 mg, 67%) as a yellowish syrup. $\mathbf{R_f}$ (**22**) = 0.16 (hexane/acetone 70:30).



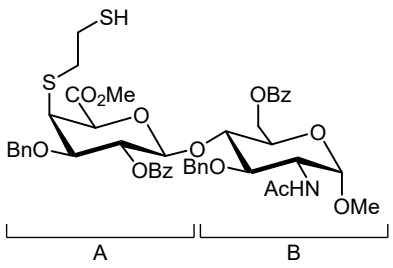
***22*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04-8.01 (m, 2H, 2CH), 7.96-7.93 (m, 2H, 2CH), 7.57-7.50 (m, 2H, 2CH), 7.45-7.35 (m, 6H, 6CH), 7.31-7.27 (m, 8H, 8CH), 6.25 (dd, *J* = 4.4, 1.2 Hz, 1H, H-4 A), 5.57 (dd, *J* = 3.6, 1.2 Hz, 1H, H-1 A), 5.50 (ddd, *J* = 3.6, 3.2, 1.2 Hz, 1H, H-2 A), 5.22 (d, *J* = 9.2 Hz, 1H, NH B), 5.00 (d, *J* = 11.6 Hz, 1H, ½CH_2Ph B), 4.78 (d, *J* = 12.0 Hz, 1H, ½CH_2Ph A), 4.73 (d, *J* = 12.0 Hz, 1H, ½CH_2Ph A), 4.65 (dd, *J* = 12.0, 2.4 Hz, 1H, H-6b B), 4.64 (d, *J* = 3.2 Hz, 1H, H-1 B), 4.60 (d, *J* = 11.6 Hz, 1H, ½CH_2Ph B), 4.50 (dd, *J* = 12.0, 4.4 Hz, 1H, H-6a B), 4.23 (td, *J* = 9.6, 3.2 Hz, 1H, H-2 B), 4.12 (ddd, *J* = 4.4, 3.2, 1.2 Hz, 1H, H-3 A), 4.08 (dd, *J* = 9.6, 8.4 Hz, 1H, H-4 B), 3.92 (ddd, *J* = 9.6, 4.4, 2.4 Hz, 1H, H-5 B), 3.74-3.68 (m, 4H, H-3 B and OCH_3 A), 3.31 (s, 3H, OCH_3 B), 1.76 (s, 3H, CH_3CO B) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.9 (CONH B), 166.2 (COPh B), 165.2 (COPh A), 162.4 (COO A), 142.1 (C-5 A), 138.8 (C), 137.7 (C), 133.6 (CH), 133.2 (CH), 130.0 (CH), 129.85 (CH), 129.83 (C), 129.0 (C), 128.53 (CH), 128.50 (CH), 128.1 (CH), 128.0 (CH), 127.7 (CH), 108.9 (C-4 A), 98.4 (C-1 B), 97.6 (C-1 A), 78.1 (C-3 B), 77.7 (C-4 B), 75.0 (CH_2Ph B), 71.2 (CH_2Ph A), 70.0 (C-3 A), 69.2 (C-2 A), 69.0 (C-5 B), 62.9 (C-6 B), 55.2 (OCH_3 A), 52.6 (C-2 B), 52.5 (OCH_3 B), 23.5 (CH_3 B) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{44}H_{45}NNaO_{13}$ $[M+Na]^+$: 818.2789; found: 818.2785.

Thiol-ene reaction on disaccharide 22

Methyl (methyl 2-O-benzoyl-3-O-benzyl-4-S-(2-mercaptoetyl)-4-thio-β-D-galactopyranosyl)uronate-(1→4)-2-acetamido-6-O-benzoyl-3-O-benzyl-2-deoxy-α-D-glucopyranoside (26)

According to general procedure 2.1.1., 4,5-glycal disaccharide **22** (159 mg, 0.20 mmol), **4a** (50 μL, 0.60 mmol), DPAP (5.1 mg, 0.02 mmol) and MAP (3 mg, 0.02 mmol) were reacted for 2 h. Flash

chromatography using hexane/acetone (60:40) afforded **26** (71.1 mg, 40%) as a yellowish syrup. $\mathbf{R_f}$ (**26**) = 0.20 (hexane/acetone 60:40).



***26*: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06-8.01 (m, 2H, 2CH), 7.91-7.85 (m, 2H, 2CH), 7.58-7.53 (m, 1H, CH), 7.44-7.32 (m, 9H, 9CH), 7.29-7.27 (m, 1H, CH), 7.21-7.09 (m, 5H, 5CH), 5.62 (dd, *J* = 10.0, 7.6 Hz, 1H. H-2 A), 5.21 (d, *J* = 12.4 Hz, 1H, ½CH_2Ph A), 5.14 (d, *J* = 8.8 Hz, 1H, NH B), 4.68-4.58 (m, 4H, ½CH_2Ph A, H-1 A, H-1 B and ½CH_2Ph B), 4.45 (d, *J* = 12.0 Hz, 1H, ½CH_2Ph B), 4.40 (dd, *J* = 12.0, 4.0 Hz, 1H, H-6a B), 4.32 (dd, *J* = 12.0, 2.0 Hz, 1H, H-6b B), 4.18 (ddd, *J* = 10.4, 8.8, 3.6 Hz, 1H, H-2 B), 4.08 (d, *J* = 2.0 Hz, 1H, H-5 A), 3.90 (dd, *J* = 10.0, 8.4 Hz, 1H, H-4 B), 3.80 (dd, *J* = 10.0, 4.0 Hz, 1H, H-3 A), 3.74 (ddd, *J* = 10.0, 4.0, 2.0 Hz, 1H, H-5 B), 3.68 (dd, *J* = 10.4, 8.4 Hz, 1H, H-3 B), 3.62 (s, 3H, OCH_3 A), 3.48 (dd, *J* = 4.0, 2.0 Hz, 1H, H-4 A), 3.23 (s, 3H, OCH_3 B), 2.87 (dt, *J* = 13.6, 7.6 Hz, 1H, ½SCH_2 A), 2.79 (dt, *J* = 13.6, 7.6 Hz, 1H, ½SCH_2 A), 2.61 (app q, *J* = 7.6 Hz, 2H, C$\underline{H}_2$SH A), 1.75 (s, 3H, CH_3CO B), 1.62 (t, *J* = 8.0 Hz, 1H, SH A) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.0 (CONH B), 168.2 (COO A), 166.2 (COPh B), 165.2 (COPh A), 139.7 (C), 137.0 (C), 133.4 (CH), 133.3 (CH), 130.0 (CH), 129.79 (C), 129.75 (CH), 129.2 (C), 128.65 (CH), 128.64 (CH), 128.53 (CH), 128.51 (CH), 128.2 (CH), 128.03 (CH), 128.01 (CH), 127.5 (CH), 101.9 (C-1 A), 98.3 (C-1 B), 79.0 (C-4 B), 78.7 (C-3 A), 78.4 (C-3 B), 75.1 (CH_2Ph B), 74.5 (C-5 A), 72.6 (CH_2Ph A), 72.5 (C-2 A), 68.7 (C-5 B), 62.8 (C-6 B), 55.2 (OCH_3 B), 52.7 (OCH_3 A), 52.5 (C-2 B), 48.7 (C-4 A), 37.6 (SCH_2 A), 24.6 (CH_2SH A), 23.5 (CH_3 B) ppm. **HRMS** (ESI^+) *m/z* calcd. for $C_{46}H_{51}NNaO_{13}S_2$ $[M+Na]^+$: 912.2700; found: 912.2689.

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