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Synthesis and photoinitiated thiol–ene reactions of *exo*-mannals – a new route to *C*-β-D-mannosyl derivatives†

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Syntheses of acyl protected *exo*-mannal derivatives were developed starting from *O*-peracylated mannopyranoses *via* the corresponding anhydro-aldose tosylhydrazones under modified Bamford–Stevens conditions. The synthesis of analogous *O*-peralkylated (benzylated and isopropylenated) derivatives was carried out from pyranoid and furanoid mannonolactones using methylene transfer reagents. Photoinitiated thiol–ene additions of these *exo*-mannals resulted in the corresponding *C*-(mannopyranosyl/mannofuranosyl)methyl sulfides in medium to good yields with exclusive regio- and β(D) stereoselectivities.

1. Introduction

D-Mannose occurs in microbes, plants, animals in free form, but more often as a component of glycans or glycoproteins. Several articles were published in recent years about the metabolic study and biological function of mannose and mannose containing glycoconjugates demonstrating that the therapeutic applications of these derivatives receive increasing attention.[1–4] Mannose can be used as a drug in the case of specific bacterial infections, but it can be lethal or teratogenic, too.[5–7] The mannose binding lectins (MBL) of the human cells play a central role in innate immunity by the interaction with surface sugars of a wide series of microorganisms, but this specific interaction can also be used for selective delivery of anti-cancer drugs, using glycosylated (mannosylated) bioconjugates.[8–10]

The *O*-glycosidic bond in natural glycosides is characterized with low hydrolytic and/or enzymatic stability but by replacing the glycosidic oxygen with other atoms (C, N, S)[11] or groups (S–S, S–Se, SO_2–N, and N–C(=O)–N),[12] more stable molecules can be synthesized with similar biological activity. These molecules are the glycomimetics,[11] which are frequently used as leads of drug discovery.

Several routes have been published in the literature for the synthesis of *C*-glycosyl derivatives but the yield and stereoselectivity of these reactions are highly dependent on the circumstances, protecting groups and configuration of the starting compounds.[13–15] *C*-Mannosyl derivatives received special attention as summarized in a recent review.[16]

Photoinitiated thiol–ene additions, also called thio-click reactions are widely used in synthetic organic chemistry and material science for the synthesis of sulfur containing compounds.[17–20] In carbohydrate chemistry, the sugar moiety can be used both as a thiol or an alkene components, and such transformations show excellent regio- and stereoselectivities.[21] The hydrothiolation of *exo*-glycals allows the synthesis of novel, glycosylmethyl sulfide (Gly–CH_2–SR) type mimetics with very high or exclusive β-selectivity.[22–25]

Based on the above experiences we set out to study the thiol–ene additions with various *exo*-mannals with the expectation that the β-stereoselectivity observed with other *exo*-glycal configurations will be maintained here as well. This synthetic route can provide mimetics of *O*-β-D-mannosyl derivatives whose syntheses are otherwise very challenging tasks.[26]

2. Results

2.1. Synthesis of *exo*-mannal derivatives

Several methods are known in the literature for the synthesis of *exo*-glycal derivatives possessing different protecting groups.[27,28] In the case of base stable ether or acetal type protection, they can be synthesized from the corresponding aldonolactones, using well-known olefination methods with the Petasis and the Tebbe reagents[29–31] or Julia/modified Julia olefinations[32,33] under strongly basic conditions. We have developed a simple method for the preparation of *exo*-glycals with ester type protection of

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hydroxyl groups *via* anhydro-aldose tosylhydrazones starting from glycosyl cyanides.[34,35]

By using the latter method, *exo*-mannals **4a** and **4b** were synthesized in multistep reactions from commercially available 1,2,3,4,6-penta-*O*-acetyl- (**1a**) and -benzoyl-D-mannopyranose (**1b**), as summarized in Scheme 1. First, *O*-peracylated mannopyranoses **1a** or **1b** were reacted[36] with TMSCN in the presence of $BF_3 \cdot OEt_2$ to give mannosyl cyanides **2a**[37] and **2b** in 35 and 64% yields, respectively, as single anomers. Their NMR study clearly showed the $^4C_1$ conformation of the ring and the α(D) anomeric configuration which can be explained by the anchimeric effect of the 2-*O*-acyl substituent and also corresponds to the anomeric effect of the CN substituent forcing this group to occupy an axial position.[38–40]

Subsequently cyanides **2** were transformed into the tosylhydrazones **3** under reductive conditions in the presence of tosylhydrazine, which on deprotonation by K_3PO_4 [41] (instead of the less easily handled NaH[34]) and heating to reflux temperature gave *exo*-mannals **4**. The pyranoid ring of tosylhydrazones **3** and *exo*-mannals **4** had a $^5C_2$ conformation according to the ^3J coupling constants between H-2, H-3, H-4, H-5 and H-6 (Table 1).

The benzylated pyranoid *exo*-mannal 5 [31] and the isopropylenated furanoid *exo*-mannal 6 [32,42] were synthesized by literature procedures.

2.2. Thiol–ene additions of *exo*-mannal derivatives

The addition of thiols was carried out in toluene at room temperature (unless otherwise indicated) in the presence of 2,2-dimethoxy-2-phenylacetophenone (DPAP, 0.1 equiv.) as the photoinitiator with irradiation at λ_{max} 365 nm for 15 min. The progress of the reaction was monitored by TLC after this reaction period and irradiation and addition of DPAP were repeated if necessary (in most cases two irradiation cycles had to be applied for total consumption of *exo*-mannals **4–6**). The thiols were used in a 5-fold excess for **7a** and **7b** and in slightly more than equimolar amounts (1.1 equiv.) for **7c–f**.

The results of the addition of thiols **7** to *exo*-mannals **4** and **5** are summarized in Table 2. The reactions were carried out under an Ar atmosphere (except in the case of thiol **7d**) to give the expected products **8** in high yields. On addition of thiol **7d** to both *exo*-mannals **4a** and **4b** under air, beside the glycosylmethyl sulfides **8ad** and **8bd**, respectively, as the major products, sulfoxides **9ad** and **9bd** were also isolated as minor components. The structure of these side products was identified by NMR and MS measurements, and their formation could be eliminated by using an inert atmosphere.

In the case of benzenethiol **7a** no transformation was detected at room temperature, but at −78 °C [43,44] the sulfides **8aa** and **8ba** were isolated by column chromatography in 79 and 47% yields, respectively.

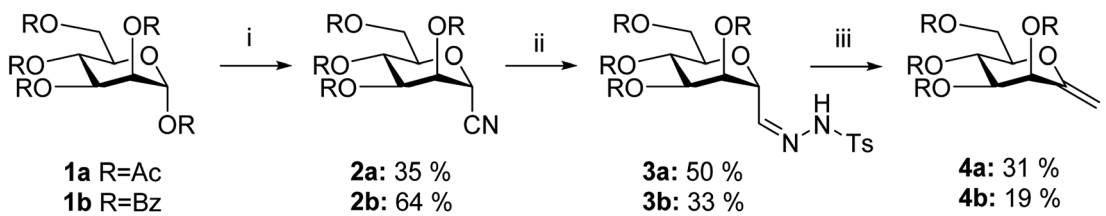
There are only a few examples in the literature for thiol–ene addition to benzylated carbohydrate derivatives, due to the low stability of this protecting group under radical conditions.[23,45] This experience was corroborated with *exo*-mannal **5**, whose reactions proceeded only with low conversion and decomposition of the starting benzylated glycal (Table 2).

The addition of thiols **7** to the furanoid *exo*-mannal **6** was carried out under the same conditions as described above (under argon atmosphere and at room temperature), and the results are summarized in Table 3. After the second irradiation total conversion of starting compound was observed, and the desired glycosylmethyl sulfides **10** were isolated in moderate to good yields (53–82%). In the case of benzenethiol **7a** the reaction at room temperature gave **10aa** in 53% yield, while at low temperature the yield raised to 70%.

The structure of the products **8** and **10** was identified by assigning each signal and connectivity in their ^{1}H NMR spectra by using COSY experiments (selected data are collected in Table 4).

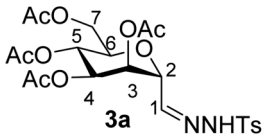
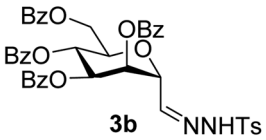
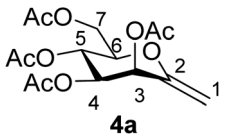
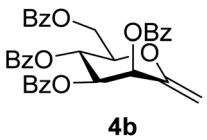
The vicinal coupling constant between H-2, H-3, H-4, H-5 and H-6 indicated the $^5C_2$ conformation of the sugar ring of **8**. The β(D)-configuration at C-2 of **8** could not be determined from the coupling constants between H-2 and H-3 but it was easily assigned from the observed NOE-s between H-2, H-4 and H-6, which also confirm the $^5C_2$ ring conformation of the products. In the case of furanoid derivatives the $^3J_{H2,H3}$ values of ∼2.9 Hz clearly indicated the β(D)-configuration at C-2 of **10**.

The exclusive regio- and stereoselectivity of these reactions can be explained by the following mechanistic considerations. The regiochemistry of the additions is determined by the different stability of the radicals that may form upon addition of the thiyl radicals to the exocyclic double bonds. The resonance stabilized *C*-glycosyl radical provides a reaction pathway with a significantly lower activation barrier than the glycosylmethyl radical (Fig. 1A). In the $^5C_2$ conformation of mannopyranosyl radicals[46] there are stabilizing overlaps between the n_O-SOMO-$\sigma^*_{C\text{-}3\text{-}O}$ orbitals due to the homo-anomeric effect. Similar considerations refer to the furanosyl radicals. The abstraction of the hydrogen by these radicals are clearly more favourable from the α-side, since both the steric shielding by the



Scheme 1 (i) 3.2 equiv. TMSCN, 2 equiv. $BF_3 \cdot OEt_2$ in CH_3NO_2, 40 °C; (ii) 1.3 equiv. $TsNHNH_2$, 8.4 equiv. NaH_2PO_2, RANEY®-Ni in pyridine–AcOH–H_2O; (iii) 5 equiv. K_3PO_4 in dry dioxane, reflux.

Table 1 Selected NMR data (δ [ppm], $^3J_{H,H}$ [Hz]) of tosylhydrazones **3** and *exo*-mannals **4**

		H-2	H-3	H-4	H-5	H-6
 **3a**	δ	4.56	5.57	5.30	5.23	3.66
	J	*3.2*, *2.6*	*3.5*, *2.6*	9.2, *3.5*	9.2	9.2, *5.3*, 2.6
 **3b**	δ	4.84	6.04	5.88	6.09	4.12
	J	*2.7*, *1.9*	*3.1*, *1.9*	9.8, *3.1*	*9.8*	9.8, *4.1*, *2.2*
 **4a**	δ	—	5.71	5.10	5.43	3.82
	J	—	*3.5*	*9.5*, *3.5*	*9.5*	*9.5*, *5.2*, *2.6*
 **4b**	δ	—	6.17	5.68	6.28	4.29
	J	—	*3.4*	*9.7*, *3.4*	*9.7*	*9.7*, *4.1*, *2.7*

O-3-substituent and the preservation of the above stabilizing overlaps act in synergy (Fig. 1B). These effects lead to a more favorable transition state (TS) with lower energy, thus determining the exclusively observed β configuration of C-2.

3. Conclusion

A synthesis of *O*-peracylated *exo*-mannals was developed from mannopyranosyl cyanides and the respective anhydro-aldose tosylhydrazones. Photoinitianed thiol–ene additions of these *O*-peracylated and also *O*-peracetalated *exo*-mannals of both pyranoid and furanoid structures were studied to result in *C*-mannosylmethyl sulfide type compounds with the R-S-CH_2 appendage in (pseudo)equatorial position as the only products. This study demonstrated that the radical-mediated thiol–ene reactions of *exo*-mannals with a wide range of thiols took place with exclusive regio- and stereoselectivities, thereby providing a new way for the construction of novel types of glycomimetic compounds of high biological relevance.

4. Materials and methods

4.1. General methods

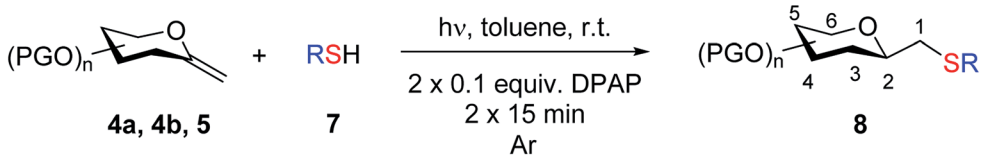
Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were measured at r.t. with a Jasco P-2000 polarimeter. TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by immersing into 5% ethanolic sulfuric acid soln. followed by heating. Column chromatography was performed on Silica gel 60 (Merck 0.063–0.200 mm). Organic solutions were dried over $MgSO_4$ and concentrated under diminished pressure. The ^{1}H (400 MHz) and ^{13}C NMR (100.28 MHz) NMR spectra were recorded with a Bruker DRX-400 spectrometer. Chemical shifts are referenced to Me_4Si (0.00 ppm for ^{1}H) and to the residual solvent signals ($CDCl_3$: 77.16 ppm for ^{13}C). The coupling constant values (J) are given in Hz. Mass spectra were recorded with MicroTOF-Q type Qq-TOF MS (Bruker Daltonik, Bremen, Germany) instruments. The photoinitiated reactions were carried out by irradiation with a Hg-lamp (maximum emission at 365 nm) in a borosilicate vessel. The benzylated pyranoid *exo*-mannal (**5**) and isopropylenated furanoid *exo*-mannal (**6**) were synthesized by literature procedures.[31,32,42]

4.1.1. Method A: general procedure for the preparation of *O*-peracylated D-mannopyranosyl cyanides. To a stirred solution of an *O*-peracylated mannopyranose (1 mmol each) in CH_3NO_2 (5 mL) TMSCN (0.4 mL; 3.2 mmol) and $BF_3{\cdot}OEt_2$ (0.25 mL; 2 mmol) were added. The mixture was stirred at 40 °C and the progress of the reaction was controlled by TLC (eluent: hexane–EtOAc = 2 : 1). When the starting material disappeared, the solvent was evaporated, and the residue was dissolved in Et_2O (50 mL). This was washed with saturated $NaHCO_3$ solution (2 × 20 mL) and brine (1 × 20 mL), dried, then concentrated and purified by column chromatography.

*4.1.1.1. 2,3,4,6-Tetra-O-acetyl-α-D-mannopyranosyl cyanide (**2a**).* Prepared from **1a** (5 g, 12.8 mmol) according to Method A to give **2a** by column chromatography (eluent: hexane–acetone = 3 : 1) as a yellow syrup (1.6 g, 35%). R_f = 0.39 (hexane–EtOAc = 1 : 1). $[\alpha]_D$ = +11.4 (c = 0.244, $CHCl_3$); lit[37] +27.8 (c 3.32, $CHCl_3$).

^{1}H-NMR of **2a** (400 MHz, $CDCl_3$) δ: 5.44 (dd, 1H, J = 3.1, 2.3 Hz, H-2), 5.38–5.28 (m, 2H, H-3, H-4), 4.92 (d, 1H, J = 2.3 Hz, H-1), 4.34 (dd, 1H, J = 12.6, 5.3 Hz, H-6_A), 4.17 (dd, 1H, J = 12.6, 2.0 Hz, H-6_B), 4.08 (ddd, 1H, J = 9.4, 5.3, 2.0 Hz, H-5), 2.19, 2.11,

Table 2 Addition of thiols **7** to *exo*-mannals **4** and **5**[a]



4a, 4b, 5 **7** **8**

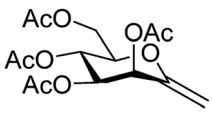
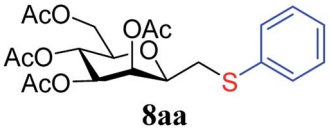
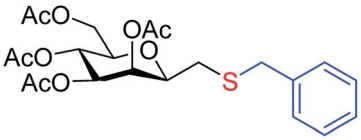
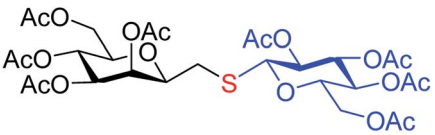
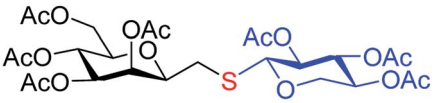
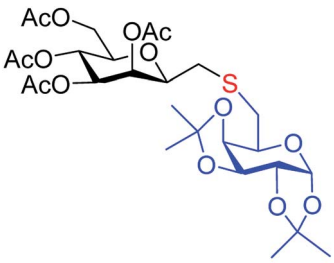
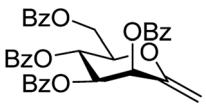
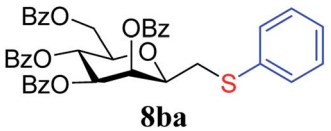
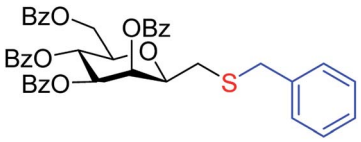
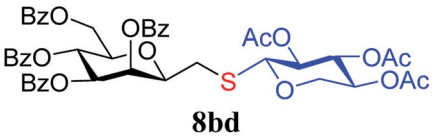
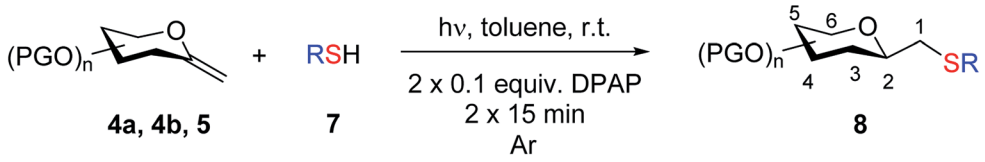
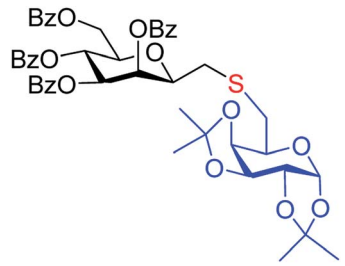
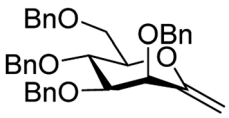
Exo-Glycal	Thiols	Yield[b] (%) of **8**	Structure of adducts **8**
 **4a**	**7a**	79[c]	 **8aa**
	7b	69	 **8ab**
	7c	78	 **8ac**
	7d	71[d]	 **8ad**
	7e	79	 **8ae**
 **4b**	**7a**	47[c]	 **8ba**
	7b	51	 **8bb**
	7d	68[d]	 **8bd**

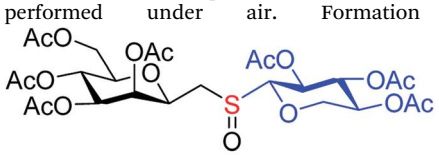
Table 2 (*Contd.*)

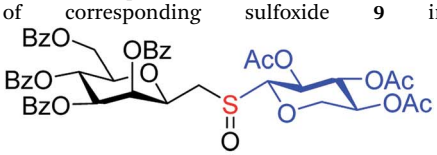


4a, 4b, 5 — 7 — 8

Exo-Glycal	Thiols	Yield[b] (%) of **8**	Structure of adducts **8**
	7e	73	 **8be**
 **5**			Low conversion and decomposition of *exo*-mannal **5** were observed with **7a**, **b**, **d**

[a] Total conversion of **4a**, **b** was detected after two irradiations of 15 min. [b] Isolated yields after purification by column chromatography. [c] The reaction was performed at −78 °C. At room temperature, no conversion of the *exo*-glycal was detected. [d] The reaction was performed under air. Formation of corresponding sulfoxide **9** in low yield was also observed:

 **9ad** (3%)

 **9bd** (12%)

2.08, 2.03 (4 × s, 4 × 3H, OAc); data correspond to lit[37] values. ^{13}C-NMR of **2a** (100 MHz, $CDCl_3$) δ: 170.5, 169.7, 169.6, 169.6 (CO), 113.5 (CN), 74.3, 69.0, 68.8, 65.7, 65.1 (C-1, C-2, C-3, C-4, C-5), 61.8 (C-6), 20.8, 20.7, 20.7, 20.6 (OAc). ESI-MS positive mode (*m*/*z*): calcd for $C_{15}H_{19}NNaO_9^+$ $[M + Na]^+ = 380.0952$. Found: $[M + Na]^+ = 380.0970$.

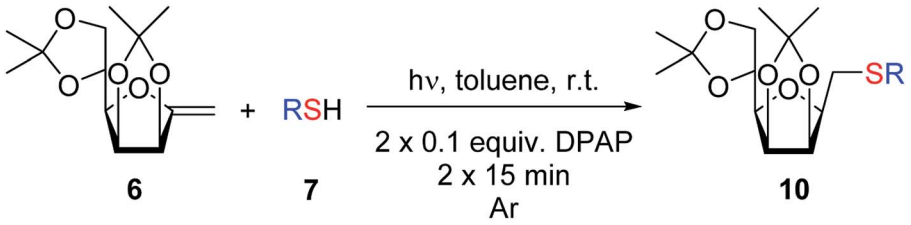
*4.1.1.2. 2,3,4,6-Tetra-O-benzoyl-α-D-mannopyranosyl cyanide (**2b**).* Prepared from **1b** (5 g, 7.1 mmol) according to Method A to give **2b** by column chromatography (eluent: hexane–acetone = 4 : 1) as a yellow syrup (2.2 g, 53%). $R_f = 0.31$ (hexane–EtOAc = 2 : 1). $[\alpha]_D = -32.9$ ($c = 0.254$, $CHCl_3$).

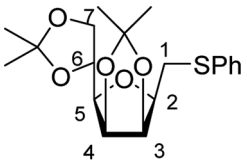
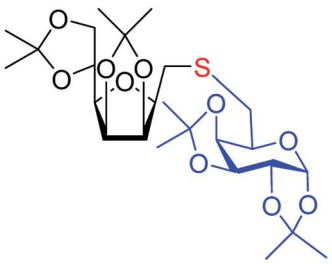
^{1}H-NMR of **2b** (400 MHz, $CDCl_3$) δ: 8.10 (dd, 2H, J = 8.1, 1.3 Hz, aromatic), 8.02 (dd, 2H, J = 8.2, 1.1 Hz, aromatic), 7.98 (dd, 2H, J = 8.2, 1.0 Hz, aromatic), 7.85 (dd, 2H, J = 8.3, 1.1 Hz, aromatic), 7.63–7.26 (m, 12H, aromatic), 6.18 (pseudo t, 1H, J = 9.8 Hz, H-4), 5.94–5.89 (m, 2H, H-2, H-3), 5.21 (d, 1H, J = 2.0 Hz, H-1), 4.77 (dd, 1H, J = 10.6, 3.2 Hz, H-6$_A$), 4.56–4.51 (m, 2H, H-5, H-6$_B$). ^{13}C-NMR of **2b** (100 MHz, $CDCl_3$) δ: 165.4, 165.2 (CO), 134.1–128.6 (aromatic), 113.8 (CN), 74.6, 70.1, 69.8, 65.9, 65.7 (C-1, C-2, C-3, C-4, C-5), 62.1 (C-6). ESI-MS positive mode (*m*/*z*): calcd for $C_{35}H_{27}NNaO_9^+$ $[M + Na]^+ = 628.1578$. Found: $[M + Na]^+ = 628.1573$.

4.1.2. Method B: general procedure for the preparation of anhydro-aldose tosylhydrazones. RANEY®-Ni (1.5 g) was added to a vigorously stirred mixture of pyridine (5.7 mL), AcOH (3.4 mL), and H_2O (3.4 mL) at room temperature. Subsequently, NaH_2PO_2 (0.74 g, 8.4 mmol), *p*-toluenesulfonyl hydrazide (0.22 g, 1.2 mmol), and the corresponding mannosyl cyanide (**2a–b**, 1 mmol each) were added to the mixture. When the reaction was complete (TLC, eluent: hexane–EtOAc = 2 : 1) the insoluble materials were filtered off with suction and washed with CH_2Cl_2 (10 mL). The organic layer of the filtrate was separated, washed sequentially with H_2O (5 mL), 10% aqueous solution of HCl (2 × 5 mL), cold, saturated $NaHCO_3$ solution (2 × 5 mL) and H_2O (5 mL), and then dried over anhydrous $MgSO_4$. The solution was concentrated under reduced pressure, and traces of pyridine were removed by repeated co-evaporations of toluene. The residue was purified by column chromatography.

*4.1.2.1. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-D-glycero-D-talo-heptose tosylhydrazone (**3a**).* Prepared from **2a** (1.6 g, 4.5 mmol)

Table 3 Addition of thiols **7** to *exo*-mannals **6**[a]



Thiols	Yield[b] (%) of **10**	Structure of adducts **10**
7a	53 (70[c])	 **10a**
7c	82	 **10c**
7e	70	 **10e**
7f	74	 **10f**

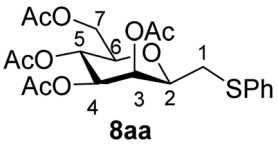
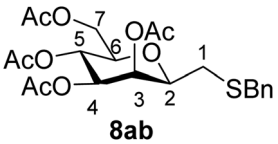
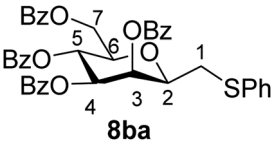
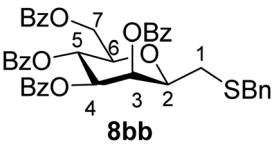
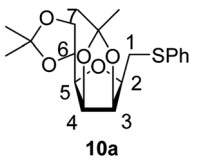
[a] Total conversion of **6** was detected after two irradiations of 15 min. [b] Isolated yields after purification by column chromatography. [c] The reaction was performed at −78 °C.

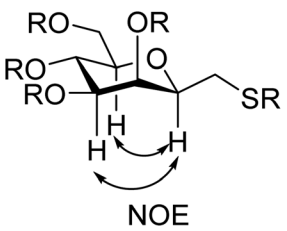
according to Method B to give **3a** by column chromatography (eluent: hexane–EtOAc = 2 : 1) as a yellow amorphous solid (1.2 g, 50%). $R_f = 0.36$ (hexane–EtOAc = 1 : 1). $[\alpha]_D = -37.7$ (c = 0.200, $CHCl_3$).

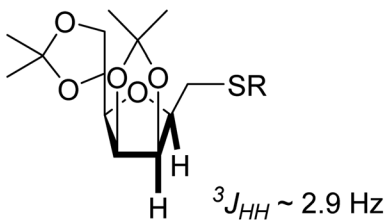
^{1}H-NMR of **3a** (400 MHz, $CDCl_3$) δ: 8.63 (s, 1H, NH), 7.92 (d, 2H, J = 8.4 Hz, aromatic), 7.34 (d, 2H, J = 8.4 Hz, aromatic), 7.17 (d, 1H, J = 3.2 Hz, H-1), 5.57 (dd, 1H, J = 3.5, 2.6 Hz, H-3), 5.30 (dd, 1H, J = 9.2, 3.5 Hz, H-4), 5.23 (pseudo t, 1H, J = 9.2 Hz, H-5), 4.56 (dd, 1H, J = 3.2, 2.6 Hz, H-2), 4.24 (dd, 1H, J = 12.3, 5.3 Hz, H-7$_A$), 4.05 (dd, 1H, J = 12.3, 2.6 Hz, H-7$_B$), 3.66 (ddd, 1H, J = 9.2, 5.3, 2.6 Hz, H-6), 2.42 (CH_3), 2.12, 2.09, 2.05, 2.03 (4 × s, 4 × 3H, OAc). ^{13}C-NMR of **3a** (100 MHz, $CDCl_3$) δ: 170.9, 170.3, 169.8, 169.8 (CO), 144.1 (C-1), 144.6–128.2 (aromatic), 74.7, 72.1, 69.3, 68.2, 66.5 (C-2, C-3, C-4, C-5, C-6), 62.3 (C-7), 21.7 (CH_3), 20.9, 20.8, 20.8, 20.7 (OAc). ESI-MS positive mode (m/z): calcd for $C_{22}H_{28}N_2NaO_{11}S^+$ $[M + Na]^+$ = 551.1306. Found: $[M + Na]^+$ = 551.1316.

*4.1.2.2. 3,4,5,7-Tetra-O-benzoyl-2,6-anhydro-D-glycero-D-talo-heptose tosylhydrazone (**3b**).* Prepared from **2b** (1.7 g, 2.8 mmol) according to Method B to give **3b** by column chromatography (eluent: hexane–EtOAc = 2 : 1) as a yellow amorphous solid

Table 4 ^{1}H-NMR data (δ [ppm], $^{3}J_{H,H}$ [Hz]) of selected thiol adducts[a]

		H-1$_A$	H-1$_B$	H-2	H-3	H-4	H-5[b]	H-6
 **8aa**	δ	3.16	2.92	3.68	5.55	5.02	5.19	3.61
	J	*13.9, 6.8*	*13.9, 7.0*	*7.0, 6.8, 1.0*	*3.4, 1.0*	*10.0, 3.4*	*10.0*	*10.0, 5.6, 2.3*
 **8ab**	δ	2.64	2.40	3.60–3.56	5.41	4.97	5.19	3.60–3.56
	J	*14.0, 7.3*	*14.0, 6.2*	*m*	*3.2*	*10.0, 3.4*	*10.0*	*m*
 **8ba**	δ	3.25	3.05	4.01	6.03	5.59	6.02	4.08
	J	*14.1, 7.1*	*14.1, 6.5*	*7.1, 6.5, 0.9*	*3.2, 0.9*	*10.0, 3.2*	*10.0*	*10.0, 4.6, 2.7*
 **8bb**	δ	2.73	2.51	3.95	5.89	5.56	6.01	4.07
	J	*14.4, 7.8*	*14.4, 5.5*	*7.8, 5.5, 0.8*	*3.2, 0.8*	*10.0, 3.2*	*10.0*	*10.0, 4.6, 2.5*
 **10a**	δ	3.24	3.22	3.67	4.79–4.73	3.49	4.38	
	J	*13.5, 6.1*	*13.5, 7.7*	*7.7, 6.1, 2.9*	*m*	*7.5, 2.9*	*7.5, 6.0, 4.7*	





[a] The NMR experiments were performed at 400 MHz in $CDCl_3$. [b] In the case of compounds **8** the signals H-5 were split into triplet.

(0.7 g, 33%). R_f = 0.44 (hexane–EtOAc = 1 : 1). $[\alpha]_D$ = +3.7 (*c* = 0.198, $CHCl_3$).

^{1}H-NMR of **3b** (400 MHz, $CDCl_3$) δ: 8.90 (s, 1H, NH), 8.10–7.26 (m, 25H, aromatic, H-1), 6.09 (pseudo t, 1H, *J* = 9.8 Hz, H-5), 6.04 (dd, 1H, *J* = 3.1, 1.9 Hz, H-3), 5.88 (dd, 1H, *J* = 9.8, 3.1 Hz, H-4), 4.84 (dd, 1H, *J* = 2.7, 1.9 Hz, H-2), 4.65 (dd, 1H, *J* = 12.2, 2.2 Hz, H-7$_A$), 4.40 (dd, 1H, *J* = 12.2, 4.1 Hz, H-7$_B$), 4.12 (ddd, 1H, *J* = 9.8, 4.1, 2.2 Hz, H-6), 2.41 (CH_3). ^{13}C-NMR of **3b** (100 MHz, $CDCl_3$) δ: 166.3, 165.6, 165.4 (CO), 144.3 (C-1), 144.8–128.5 (aromatic), 75.0, 72.4, 70.5, 69.5, 67.3 (C-2, C-3, C-4, C-5, C-6), 62.8 (C-7), 21.7 (CH_3). ESI-MS positive mode (*m*/*z*): calcd for $C_{42}H_{36}N_2NaO_{11}S^+$ $[M + Na]^+$ = 799.1932. Found: $[M + Na]^+$ = 799.1923.

4.1.3. Method C: general procedure for the synthesis of *O*-peracylated *exo*-glycals. To the stirred and refluxed suspension of K_3PO_4 (0.1 g, 5 mmol) in dry 1,4-dioxane (12 mL), a solution of an anhydro-aldose tosylhydrazone (**3a–b**, 1 mmol each) in dry 1,4-dioxane (12 mL) was added dropwise. When the reaction was complete (TLC, eluent: hexane–EtOAc = 1 : 1), the mixture was cooled and the insoluble material filtered off. The solvent was removed under reduced pressure, and the residue was purified by column chromatography.

*4.1.3.1. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-deoxy-D-manno-hept-1-enitol (**4a**).* Prepared from **3a** (1.0 g, 1.9 mmol) according to Method C to give **4a** by column chromatography (eluent: hexane–EtOAc = 2 : 1) as a yellow oil (0.2 g, 31%). R_f = 0.41 (hexane–EtOAc = 1 : 1). $[\alpha]_D$ = +34.7 (*c* = 0.126, $CHCl_3$).

^{1}H-NMR of **4a** (400 MHz, $CDCl_3$) δ: 5.71 (d, 1H, *J* = 3.5 Hz, H-3), 5.43 (pseudo t, 1H, *J* = 9.5 Hz, H-5), 5.10 (dd, 1H, *J* = 9.5, 3.5 Hz, H-4), 4.88 (d, 1H, *J* = 1.4 Hz, H-1$_A$), 4.73 (d, 1H, *J* = 1.4 Hz, H-1$_B$), 4.31 (dd, 1H, *J* = 12.4, 5.2 Hz, H-7$_A$), 4.21 (dd, 1H, *J* = 12.4, 2.6 Hz, H-7$_B$), 3.82 (ddd, 1H, *J* = 9.5, 5.2, 2.6 Hz, H-6), 2.14, 2.12, 2.07, 2.03 (4 × s, 4 × 3H, OAc). ^{13}C-NMR of **4a** (100 MHz, $CDCl_3$) δ: 170.7, 170.0, 169.9, 169.6 (CO), 152.5 (C-2), 102.0

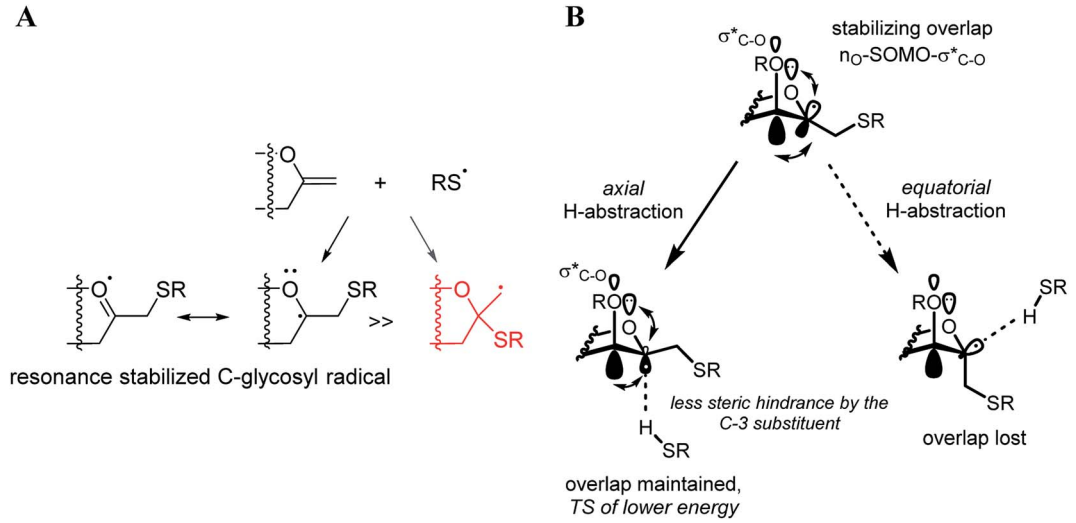


Fig. 1 Mechanistic considerations. (A) Relative stabilities of adduct radical; (B) stabilizing overlaps in mannopyranosyl radicals and transition states of H-abstraction.

(C-1), 77.1, 71.1, 69.0, 65.6 (C-3, C-4, C-5, C-6), 62.4 (C-7), 21.1, 20.8, 20.7, 20.7 (OAc). ESI-MS positive mode (*m*/*z*): calcd for $C_{15}H_{20}NaO_9^+$ $[M + Na]^+$ = 367.1000. Found: $[M + Na]^+$ = 367.0996.

*4.1.3.2. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-deoxy-D-manno-hept-1-enitol (**4b**).* Prepared from **3b** (0.2 g, 0.26 mmol) according to Method C to give **4b** by column chromatography (eluent: hexane–EtOAc = 2 : 1) as a yellow oil (64 mg, 42%). R_f = 0.43 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = +19.0 (*c* = 0.260, $CHCl_3$).

^{1}H-NMR of **4b** (400 MHz, $CDCl_3$) *δ*: 8.13–7.85 (m, 8H, aromatic), 7.60–7.26 (m, 13H, aromatic, H-1), 6.28 (pseudo t, 1H, *J* = 9.7 Hz, H-5), 6.17 (d, 1H, *J* = 3.4 Hz, H-3), 5.68 (dd, 1H, *J* = 9.7, 3.4 Hz, H-4), 5.03 (d, 1H, *J* = 1.3 Hz, H-1_A), 4.94 (d, 1H, *J* = 1.3 Hz, H-1_B), 4.78 (dd, 1H, *J* = 12.3, 2.7 Hz, H-7_A), 4.55 (dd, 1H, *J* = 12.3, 4.1 Hz, H-7_B), 4.29 (ddd, 1H, *J* = 9.7, 4.1, 2.7 Hz, H-6). ^{13}C-NMR of **4b** (100 MHz, $CDCl_3$) *δ*: 165.7, 165.6, 165.4, 165.4 (CO), 152.6 (C-2), 133.7–128.5 (aromatic), 102.8 (C-1), 77.3, 72.2, 70.1, 66.4 (C-3, C-4, C-5, C-6), 62.8 (C-7). ESI-MS positive mode (*m*/*z*): calcd for $C_{35}H_{28}NaO_9^+$ $[M + Na]^+$ = 615.1626. Found: $[M + Na]^+$ = 615.1626.

4.1.4. Method D: general procedure for the thiol–ene additions. To a solution of an *exo*-glycal (**4a**, **b**, **5**, **6** 0.5 mmol each) in dry toluene (5 mL), a thiol (2.5 mmol of **7a**, **b** and 0.55 mmol of **7c–f**) and 2,2-dimethoxy-2-phenylacetophenone (DPAP, 0.1 mmol) were added. The solution was irradiated by a mercury vapor lamp (λ_{max} 365 nm) at room temperature for 15 min. If TLC (eluent: hexane–acetone = 2 : 1) indicated incomplete transformation of the starting material another 0.1 equiv. of DPAP was added and irradiation was continued for 15 min. When the reaction was complete, the solvent was removed, then the residue was purified by column chromatography.

*4.1.4.1. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-S-phenyl-1-thio-D-glycero-D-galacto-heptitol (**8aa**).* Prepared from **4a** (35 mg, 0.11 mmol) and **7a** (56 μL, 0.55 mmol) using DPPA (3 × 2.8 mg, 0.011 mmol) in toluene (1.1 mL) at −78 °C according to Method D to give **8aa** by column chromatography (eluent: hexane–acetone = 10 : 1) as a yellow amorphous solid (31 mg, 62%). R_f = 0.41 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = +91.9 (*c* = 0.102, $CHCl_3$).

^{1}H-NMR of **8aa** (400 MHz, $CDCl_3$) *δ*: 7.39–7.22 (m, 5H, aromatic), 5.55 (dd, 1H, *J* = 3.4, 1.0 Hz, H-3), 5.23 (pseudo t, 1H, *J* = 10.0 Hz, H-5), 5.02 (dd, 1H, *J* = 10.0, 3.4 Hz, H-4), 4.27 (dd, 1H, *J* = 12.3, 5.6 Hz, H-7_A), 4.09 (dd, 1H, *J* = 12.3, 2.3 Hz, H-7_B), 3.68 (ddd, 1H, *J* = 7.0, 6.8, 1.0 Hz, H-2), 3.61 (ddd, 1H, *J* = 10.0, 5.6, 2.3 Hz, H-6), 3.16 (dd, 1H, *J* = 13.9, 6.8 Hz, H-1_A), 2.92 (dd, 1H, *J* = 13.9, 7.0 Hz, H-1_B), 2.14, 2.10, 2.03, 1.98 (4 × s, 4 × 3H, OAc). ^{13}C-NMR of **8aa** (100 MHz, $CDCl_3$) *δ*: 170.9, 170.3, 170.3, 169.8 (CO), 135.0–127.1 (aromatic), 76.5, 76.1, 72.4, 68.6, 66.1 (C-2, C-3, C-4, C-5, C-6), 62.8 (C-7), 34.3 (C-1), 20.9, 20.8, 20.7 (OAc). ESI-MS positive mode (*m*/*z*): calcd for $C_{21}H_{26}NaO_9S^+$ $[M + Na]^+$ = 477.1190. Found: $[M + Na]^+$ = 477.1189.

*4.1.4.2. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-S-benzyl-1-thio-D-glycero-D-galacto-heptitol (**8ab**).* Prepared from **4a** (100 mg, 0.29 mmol) and **7b** (170 μL, 1.45 mmol) using DPPA (3 × 7.4 mg, 0.029 mmol) in toluene (2.9 mL) according to Method D to give **8ab** by column chromatography (eluent: hexane–acetone = 10 : 1) as a yellow amorphous solid (94 mg, 69%). R_f = 0.26 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = +60.5 (*c* = 0.152, $CHCl_3$).

^{1}H-NMR of **8ab** (400 MHz, $CDCl_3$) *δ*: 7.32–7.30 (m, 5H, aromatic), 5.41 (d, 1H, *J* = 3.2 Hz, H-3), 5.19 (pseudo t, 1H, *J* = 10.0 Hz, H-5), 4.97 (dd, 1H, *J* = 10.0, 3.4 Hz, H-4), 4.24 (dd, 1H, *J* = 12.3, 5.8 Hz, H-7_A), 4.12 (dd, 1H, *J* = 12.3, 2.3 Hz, H-7_B), 3.79 (d, 1H, *J* = 13.4 Hz, CH_2Ph), 3.72 (d, 1H, *J* = 13.4 Hz, CH_2Ph), 3.60–3.56 (m, 1H, H-2, H-6), 2.64 (dd, 1H, *J* = 14.0, 7.3 Hz, H-1_A), 2.40 (dd, 1H, *J* = 14.0, 6.2 Hz, H-1_B), 2.09, 2.09, 2.04, 1.97 (4 × s, 4 × 3H, OAc). ^{13}C-NMR of **8ab** (100 MHz, $CDCl_3$) *δ*: 170.7, 170.3, 170.2, 169.8 (CO), 138.1–127.3 (aromatic), 77.7, 76.4, 72.3, 68.9, 66.1 (C-2, C-3, C-4, C-5, C-6), 62.9 (C-7), 37.1 (CH_2Ph), 31.0 (C-1), 20.9, 20.8, 20.7, 20.6 (OAc). ESI-MS positive mode (*m*/*z*): calcd for $C_{22}H_{28}NaO_9S^+$ $[M + Na]^+$ = 491.1346. Found: $[M + Na]^+$ = 491.1346.

*4.1.4.3. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-D-glycero-D-galacto-heptitol (**8ac**).* Prepared from **4a** (61 mg, 0.18 mmol) and **7c** (72 mg, 0.20 mmol) using DPPA (3 × 4.6 mg, 0.018 mmol) in toluene (1.8 mL) according to Method D to give **8ac** by column chromatography (eluent: hexane–acetone = 5 : 1) as a yellow amorphous solid (82 mg, 50%). R_f = 0.32 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = −25.10 (c = 0.1195, $CHCl_3$).

^{1}H-NMR of **8ac** (400 MHz, $CDCl_3$) δ: 5.51 (dd, 1H, J = 3.4, 1.0 Hz, H-3), 5.26–5.18 (m, 2H, H-5, H-3′), 5.12–5.05 (m, 2H, H-4, H-4′), 5.00 (pseudo t, 1H, J = 9.9 Hz, H-2′), 4.49 (d, 1H, J = 10.1 Hz, H-1′), 4.30–4.19 (m, 3H, H-7$_A$, H-6′$_A$, H-6′$_B$), 4.12 (dd, 1H, J = 12.3, 2.4 Hz, H-7$_B$), 3.87 (ddd, 1H, J = 7.2, 6.8, 1.0 Hz, H-2), 3.74–3.67 (m, 2H, H-6, H-5′), 2.87 (dd, 1H, J = 13.9, 6.8 Hz, H-1$_A$), 2.69 (dd, 1H, J = 13.9, 7.2 Hz, H-1$_B$), 2.17, 2.12, 2.11, 2.06, 2.04, 2.03, 2.01, 1.98 (8 × s, 8 × 3H, OAc). ^{13}C-NMR of **8ac** (100 MHz, $CDCl_3$) δ: 170.8, 170.7, 170.2, 170.1, 169.8, 169.5, 169.4 (CO), 83.3 (C-1′), 76.9, 76.4, 76.2, 73.8, 72.3, 69.9, 68.6, 68.2, 66.1 (C-2, C-3, C-4, C-5, C-6, C-2′, C-3′, C-4′, C-5′), 62.8 (C-7), 61.9 (C-6′), 29.6 (C-1), 20.9, 20.8, 20.7, 20.6 (OAc). Anal. calcd for $C_{27}H_{40}O_{14}S$ (620.21): C 52.24, H 6.5, S 5.16; measured C 53.07, H 6.60, S 5.03.

*4.1.4.4. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-S-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-1-thio-D-glycero-D-galacto-heptitol (**8ad**).* Prepared from **4a** (150 mg, 0.44 mmol) and **7d** (150 mg, 0.48 mmol) using DPPA (3 × 11.3 mg, 0.044 mmol) in toluene (4.4 mL) according to Method D to give **8ad** by column chromatography (eluent: hexane–acetone = 5 : 1) as a yellow amorphous solid (200 mg, 71%). R_f = 0.23 (hexane–EtOAc = 1 : 1). $[\alpha]_D$ = −22.4 (c = 0.216, $CHCl_3$).

^{1}H-NMR of **8ad** (400 MHz, $CDCl_3$) δ: 5.50 (dd, 1H, J = 3.2, 0.9 Hz, H-3), 5.22 (pseudo t, 1H, J = 10.0 Hz, H-5), 5.15 (pseudo t, 1H, J = 8.3 Hz, H-3′), 5.04 (dd, 1H, J = 10.0, 3.3 Hz, H-4), 4.96–4.91 (m, 2H, H-2′, H-4′), 4.51 (d, 1H, J = 8.4 Hz, H-1′), 4.28–4.19 (m, 2H, H-5′$_{eq.}$, H-7$_A$), 4.12 (dd, 1H, J = 12.3, 2.2 Hz, H-7$_B$), 3.79 (ddd, 1H, J = 7.2, 6.6, 0.9 Hz, H-2), 3.66 (ddd, 1H, J = 10.0, 5.4, 2.3 Hz, H-6), 3.41 (dd, 1H, J = 11.7, 9.0 Hz, H-5′$_{ax}$), 2.88 (dd, 1H, J = 13.8, 6.6 Hz, H-1$_A$), 2.69 (dd, 1H, J = 13.8, 7.2 Hz, H-1$_B$), 2.18, 2.10, 2.08, 2.05, 2.05, 2.04, 1.98, (7 × s, 7 × 3H, OAc). ^{13}C-NMR of **8ad** (100 MHz, $CDCl_3$) δ: 170.8, 170.3, 170.2, 169.9, 169.8, 169.7, 169.6 (CO), 83.4, 77.0, 76.5, 72.4, 71.9, 69.9, 68.5, 66.0, (C-2, C-3, C-4, C-5, C-6, C-1′, C-2′, C-3′, C-4′), 65.5 (C-7), 62.8 (C-5′), 29.6 (C-1), 20.9, 20.8, 20.7 (OAc). ESI-MS positive mode (m/z): calcd for $C_{26}H_{36}NaO_{16}S^+$ $[M + Na]^+$ = 659.1616. Found: $[M + Na]^+$ = 659.1615.

*4.1.4.5. 3,4,5,7-Tetra-O-acetyl-2,6-anhydro-1-S-(1,2:3,4-di-O-isopropylidene-β-D-galactopyranos-6-yl)-1-thio-D-glycero-D-galacto-heptitol (**8ae**).* Prepared from **4a** (60 mg, 0.17 mmol) and **7e** (52 mg, 0.19 mmol) using DPPA (3 × 4.4 mg, 0.017 mmol) in toluene (1.7 mL) according to Method D to give **8ae** by column chromatography (eluent: hexane–acetone = 5 : 1) as a yellow amorphous solid (102 mg, 83%). R_f = 0.28 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = −30.92 (c = 0.084, $CHCl_3$).

^{1}H-NMR of **8ae** (400 MHz, $CDCl_3$) δ: 5.54–5.52 (m, 2H, H-3, H-1′), 5.20 (pseudo t, 1H, J = 9.9 Hz, H-5), 5.10 (dd, 1H, J = 10.0, 3.4 Hz, H-4), 4.61 (dd, 1H, J = 7.8, 2.4 Hz, H-3′), 4.31 (dd, 1H, J = 5.1, 2.4 Hz, H-2′), 4.26–4.22 (m, 2H, H-7$_A$, H-4′), 4.12 (dd, 1H, J = 12.3, 2.4 Hz, H-7$_B$), 3.90 (dd, 1H, J = 7.0, 6.7, 0.8 Hz, H-2), 3.86 (ddd, 1H, J = 7.4, 6.2, 1.7 Hz, H-5′), 3.68 (ddd, 1H, J = 9.9, 5.9, 2.4 Hz, H-6), 2.82–2.76 (m, 3H, H-1$_A$, H-6′$_A$, H-6′$_B$), 2.62 (dd, 1H, J = 14.1, 6.7 Hz, H-1$_B$), 2.15, 2.10, 2.05, 1.98 (4 × s, 4 × 3H, CH_3), 1.56, 1.45, 1.34, 1.26, (4 × s, 4 × 3H, OAc). ^{13}C-NMR of **8ae** (100 MHz, $CDCl_3$) δ: 170.8, 170.3, 170.1, 169.8 (CO), 109.4, 108.8 (C_{acetal}), 96.6 (C-1′), 77.7, 76.4, 72.3, 72.0, 71.0, 70.5, 69.0, 68.3, 66.4 (C-2, C-3, C-4, C-5, C-6, C-2′, C-3′, C-4′, C-5′), 63.0 (C-7), 33.3 (C-1), 29.8 (C-6′), 26.1, 26.0, 25.0, 24.5 (CH_3), 20.9, 20.8, 20.7 (OAc). Anal. calcd for $C_{27}H_{40}O_{14}S$ (620.21): C 52.24, H 6.50, S 5.16; measured C 52.58, H 6.62, S 5.08.

*4.1.4.6. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-S-phenyl-1-thio-D-glycero-D-galacto-heptitol (**8ba**).* Prepared from **4b** (110 mg, 0.19 mmol) and **7a** (195 μL, 1.9 mmol) using DPPA (3 × 5.0 mg, 0.019 mmol) in toluene (1.9 mL) at −78 °C according to Method D to give **8ba** by column chromatography (eluent: hexane–acetone = 10 : 1) as a yellow amorphous solid (60 mg, 47%). R_f = 0.33 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = +24.3 (c = 0.180, $CHCl_3$).

^{1}H-NMR of **8ba** (400 MHz, $CDCl_3$) δ: 8.12 (dd, 2H, J = 8.3, 1.3 Hz, aromatic), 8.02 (dd, 2H, J = 8.3, 1.2 Hz, aromatic), 7.89 (dd, 2H, J = 8.4, 1.3 Hz, aromatic), 7.79 (dd, 2H, J = 8.4, 1.3 Hz, aromatic), 7.63–7.18 (m, 17H, aromatic), 6.03 (dd, 1H, J = 3.2, 0.9 Hz, H-3), 6.02 (pseudo t, 1H, J = 10.0 Hz, H-5), 5.59 (dd, 1H, J = 10.0, 3.2 Hz, H-4), 4.71 (dd, 1H, J = 12.2, 2.7 Hz, H-7$_A$), 4.46 (dd, 1H, J = 12.2, 4.6 Hz, H-7$_B$), 4.08 (ddd, 1H, J = 10.0, 4.6, 2.7 Hz, H-6), 4.01 (ddd, 1H, J = 7.1, 6.5, 0.9 Hz, H-2), 3.25 (dd, 1H, J = 14.1, 7.1 Hz, H-1$_A$), 3.05 (dd, 1H, J = 14.1, 6.5 Hz, H-1$_B$). ^{13}C-NMR of **8ba** (100 MHz, $CDCl_3$) δ: 166.3, 165.9, 165.6, 165.5 (CO), 133.6–127.0 (aromatic), 76.6, 76.5, 73.4, 69.7, 67.1 (C-2, C-3, C-4, C-5, C-6), 63.3 (C-7), 34.6 (C-1). ESI-MS positive mode (m/z): calcd for $C_{41}H_{34}NaO_9S^+$ $[M + Na]^+$ = 725.1816. Found: $[M + Na]^+$ = 725.1818.

*4.1.4.7. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-S-benzyl-1-thio-D-glycero-D-galacto-heptitol (**8bb**).* Prepared from **4b** (110 mg, 0.19 mmol) and **7b** (110 μL, 0.95 mmol) using DPPA (3 × 4.9 mg, 0.019 mmol) in toluene (1.9 mL) according to Method D to give **8bb** by column chromatography (eluent: hexane–acetone = 8 : 1) as a yellow amorphous solid (70 mg, 51%). R_f = 0.43 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = +25.2 (c = 0.110, $CHCl_3$).

^{1}H-NMR of **8bb** (400 MHz, $CDCl_3$) δ: 8.14 (dd, 2H, J = 8.2, 1.5 Hz, aromatic), 7.97 (dd, 2H, J = 8.4, 1.4 Hz, aromatic), 7.92 (dd, 2H, J = 8.4, 1.3 Hz, aromatic), 7.79 (dd, 2H, J = 8.3, 1.5 Hz, aromatic), 7.62–7.13 (m, 19H, aromatic), 6.01 (pseudo t, 1H, J = 10.0 Hz, H-5), 5.89 (dd, 1H, J = 3.2, 0.8 Hz, H-3), 5.56 (dd, 1H, J = 10.0, 3.2 Hz, H-4), 4.78 (dd, 1H, J = 12.2, 2.5 Hz, H-7$_A$), 4.46 (dd, 1H, J = 12.2, 4.6 Hz, H-7$_B$), 4.07 (ddd, 1H, J = 10.0, 4.6, 2.5 Hz, H-6), 3.95 (ddd, 1H, J = 7.8, 5.5, 0.8 Hz, H-2), 3.86 (d, 1H, J = 13.4 Hz, CH_2Ph), 3.70 (d, 1H, J = 13.4 Hz, CH_2Ph), 2.73 (dd, 1H, J = 14.4, 7.8 Hz, H-1$_A$), 2.51 (dd, 1H, J = 14.4, 5.5 Hz, H-1$_B$). ^{13}C-NMR of **8bb** (100 MHz, $CDCl_3$) δ: 166.3, 165.8, 165.6, 165.0 (CO), 138.1–127.2 (aromatic), 78.7, 76.6, 73.4, 70.1, 66.9 (C-2, C-3, C-4, C-5, C-6), 63.2 (C-7), 37.2 (CH_2Ph), 31.1 (C-1). ESI-MS positive mode (m/z): calcd for $C_{42}H_{36}NaO_9S^+$ $[M + Na]^+$ = 739.1972. Found: $[M + Na]^+$ = 739.1973.

*4.1.4.8. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-S-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-1-thio-D-glycero-D-galacto-heptitol (**8bd**).*

Prepared from **4b** (70 mg, 0.12 mmol) and **7d** (40 mg, 0.13 mmol) using DPPA (3 × 3.1 mg, 0.012 mmol) in toluene (1.2 mL) according to Method D to give **8bd** by column chromatography (eluent: hexane–acetone = 5 : 1) as a yellow amorphous solid (60 mg, 68%). $R_f = 0.33$ (hexane–EtOAc = 2 : 1). $[\alpha]_D = +0.5$ ($c = 0.162$, $CHCl_3$).

^{1}H-NMR of **8bd** (400 MHz, $CDCl_3$) δ: 8.13 (dd, 2H, $J = 8.1$, 1.1 Hz, aromatic), 8.02 (dd, 2H, $J = 8.2$, 1.2 Hz, aromatic), 7.91 (dd, 2H, $J = 8.3$, 1.4 Hz, aromatic), 7.79 (dd, 2H, $J = 8.5$, 1.3 Hz, aromatic), 7.62–7.23 (m, 12H, aromatic), 6.04 (pseudo t, 1H, $J =$ 10.1 Hz, H-5), 6.00 (dd, 1H, $J = 3.1$, 0.9 Hz, H-3), 5.62 (dd, 1H, $J =$ 10.1, 3.1 Hz, H-4), 5.14 (pseudo t, 1H, $J = 8.3$ Hz, H-2′), 4.94 (pseudo t, 1H, $J = 8.2$ Hz, H-3′), 4.92–4.87 (m, 1H, H-4′), 4.75 (dd, 1H, $J = 12.2$, 2.5 Hz, H-7_A), 4.55 (d, 1H, $J = 8.3$ Hz, H-1′), 4.45 (dd, 1H, $J = 12.2$, 4.2 Hz, H-7_B), 4.16–4.10 (m, 3H, H-2, H-6, H-$5'_{eq.}$), 3.38 (dd, 1H, $J = 11.7$, 8.9 Hz, H-$5'_{ax}$), 2.99 (dd, 1H, $J =$ 14.0, 6.6 Hz, H-1_A), 2.84 (dd, 1H, $J = 14.0$, 7.1 Hz, H-1_B), 2.04, 2.03, 2.02 (3 × s, 3 × 3H, OAc). ^{13}C-NMR of **8bd** (100 MHz, $CDCl_3$) δ: 170.1, 170.0, 169.8, 169.6, 166.3, 165.5, 165.4 (CO), 133.5–128.4 (aromatic), 83.7, 77.6, 76.5, 73.4, 72.0, 70.1, 69.5, 68.6, 66.9, (C-2, C-3, C-4, C-5, C-6, C-1′, C-2′, C-3′, C-4′), 65.4 (C-7), 63.1 (C-5′), 30.4 (C-1), 20.8 (OAc). ESI-MS positive mode (m/z): calcd for $C_{46}H_{44}NaO_{16}S^+$ $[M + Na]^+ = 907.2242$. Found: $[M + Na]^+ = 907.2238$.

*4.1.4.9. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-S-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-1-thio-D-glycero-D-galacto-heptitol-S-oxide (**9bd**).* Prepared from **4b** (70 mg, 0.12 mmol) and **7d** (40 mg, 0.13 mmol) using DPPA (3 × 3.1 mg, 0.012 mmol) in toluene (1.2 mL) according to Method D to give **9bd** by column chromatography (eluent: hexane–acetone = 5 : 1) as a yellow amorphous solid (11 mg, 12%). $R_f = 0.21$ (hexane–acetone = 1 : 2).

^{1}H-NMR of **9bd** (400 MHz, $CDCl_3$) δ: 8.13 (dd, 2H, $J = 8.2$, 1.1 Hz, aromatic), 8.05 (dd, 2H, $J = 8.2$, 1.2 Hz, aromatic), 7.92 (dd, 2H, $J = 8.2$, 1.3 Hz, aromatic), 7.78 (dd, 2H, $J = 8.4$, 1.3 Hz, aromatic), 7.65–7.22 (m, 12H, aromatic), 6.08 (pseudo t, 1H, $J =$ 10.0 Hz, H-5), 5.87 (dd, 1H, $J = 3.2$, 0.9 Hz, H-3), 5.66 (dd, 1H, $J =$ 10.1, 3.2 Hz, H-4), 5.27 (pseudo t, 1H, $J = 8.2$ Hz, H-2′), 5.21 (pseudo t, 1H, $J = 8.2$ Hz, H-3′), 4.92 (ddd, 1H, $J = 9.0$, 8.2, 5.1 Hz, H-4′), 4.74 (dd, 1H, $J = 12.2$, 2.5 Hz, H-7_A), 4.55 (ddd, 1H, $J = 10.7$, 2.3, 0.9 Hz, H-2), 4.47 (dd, 1H, $J = 12.2$, 4.5 Hz, H-7_B), 4.41 (d, 1H, $J = 8.3$ Hz, H-1′), 4.23–4.18 (m, 2H, H-6, H-$5'_{eq.}$), 3.47 (dd, 1H, $J = 11.6$, 9.0 Hz, H-$5'_{ax}$), 3.17 (dd, 1H, $J = 13.0$, 10.7 Hz, H-1_A), 3.04 (dd, 1H, $J = 13.0$, 2.3 Hz, H-1_B), 2.03, 2.02, 1.96 (3 × s, 3 × 3H, OAc). ESI-MS positive mode (m/z): calcd for $C_{46}H_{44}KO_{17}S^+$ $[M + K]^+ = 939.1936$. Found: $[M + K]^+ = 939.1934$.

*4.1.4.10. 2,6-Anhydro-3,4,5,7-tetra-O-benzoyl-1-S-(1,2:3,4-di-O-isopropylidene-β-D-galactopyranos-6-yl)-1-thio-D-glycero-D-galacto-heptitol (**8be**).* Prepared from **4b** (50 mg, 0.08 mmol) and **7e** (24 mg, 0.088 mmol) using DPPA (3 × 2.1 mg, 0.008 mmol) in toluene (0.8 mL) according to Method D to give **8be** by column chromatography (eluent: hexane–acetone = 4 : 1) as a yellow amorphous solid (51 mg, 73%). $R_f = 0.35$ (hexane–EtOAc = 2 : 1). $[\alpha]_D = -22.3$ ($c = 0.160$, $CHCl_3$).

^{1}H-NMR of **8be** (400 MHz, $CDCl_3$) δ: 8.11 (dd, 2H, $J = 8.4$, 1.4 Hz, aromatic), 8.04 (dd, 2H, $J = 8.1$, 1.0 Hz, aromatic), 7.92 (dd, 2H, $J = 8.0$, 0.9 Hz, aromatic), 7.78 (dd, 2H, $J = 8.0$, 0.9 Hz, aromatic), 7.62–7.22 (m, 12H, aromatic), 6.03 (dd, 1H, $J = 3.2$, 0.7 Hz, H-3), 6.01 (pseudo t, 1H, $J = 10.0$ Hz, H-5), 5.68 (dd, 1H, $J =$ 10.0, 3.2 Hz, H-4), 5.52 (d, 1H, $J = 5.0$ Hz, H-1′), 4.73 (dd, 1H, $J =$ 12.2, 2.7 Hz, H-7_A), 4.58 (dd, 1H, $J = 7.9$, 2.4 Hz, H-3′), 4.46 (dd, 1H, $J = 12.2$, 4.6 Hz, H-7_B), 4.28 (dd, 1H, $J = 5.0$, 2.4 Hz, H-2′), 4.24 (dd, 1H, $J = 7.9$, 1.8 Hz, H-4′), 4.23 (m, 1H, H-2), 4.15 (ddd, 1H, $J = 10.0$, 4.6, 2.7 Hz, H-6), 3.86 (ddd, 1H, $J = 7.6$, 5.8, 1.8 Hz, H-5′), 2.91 (dd, 1H, $J = 14.1$, 7.0 Hz, H-1_A), 2-86-2.74 (m, 3H, H-1_B, H-$6'_A$, H-$6'_B$), 1.46, 1.41, 1.29, 1.27 (4 × s, 4 × 3H, CH_3). ^{13}C-NMR of **8be** (100 MHz, $CDCl_3$) δ: 166.3, 165.7, 165.6 (CO), 133.5–128.4 (aromatic), 109.4, 108.7 (C_{acetal}), 96.7 (C-1′), 78.2, 76.5, 73.3, 72.0, 71.0, 70.6, 70.0, 68.3, 67.3 (C-2, C-3, C-4, C-5, C-6, C-2′, C-3′, C-4′, C-5′), 63.5 (C-7), 33.4 (C-1), 33.0 (C-6′), 26.2, 26.1, 25.0, 24.5 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{47}H_{48}NaO_{14}S^+$ $[M + Na]^+ = 891.2657$. Found: $[M + Na]^+ = 891.2659$.

*4.1.4.11. 2,5-Anhydro-3,4:6,7-di-O-isopropylidene-1-S-phenyl-1-thio-D-glycero-D-galacto-heptitol (**10a**).* Prepared from **6** (60 mg, 0.23 mmol) and **7a** (230 μL, 2.3 mmol) using DPPA (4 × 5.9 mg, 0.023 mmol) in toluene (2.3 mL) at room temperature according to Method D to give **10a** by column chromatography (eluent: hexane–acetone = 10 : 1) as a yellow amorphous solid (45 mg; 53%).

Prepared from **6** (56 mg, 0.22 mmol) and **7a** (220 μL, 2.2 mmol) using DPPA (2 × 5.6 mg, 0.022 mmol) in toluene (2.2 mL) at −78 °C according to Method D to give **10a** by column chromatography (eluent: hexane–acetone = 10 : 1) as a yellow amorphous solid (56 mg; 69%). $R_f = 0.44$ (hexane–EtOAc = 2 : 1). $[\alpha]_D = +39.9$ ($c = 0.172$, $CHCl_3$).

^{1}H-NMR of **10a** (400 MHz, $CDCl_3$) δ: 7.39 (dd, 2H, $J = 8.3$, 1.2 Hz, aromatic), 7.30–7.26 (m, 2H, aromatic), 7.21–7.17 (m, 1H, aromatic), 4.76–4.72 (m, 2H, H-3, H-4), 4.38 (ddd, 1H, $J =$ 7.5, 6.0, 4.7 Hz, H-6), 4.07 (dd, 1H, $J = 8.7$, 6.0 Hz, H-7_A), 4.03 (dd, 1H, $J = 8.7$, 4.7 Hz, H-7_B), 3.67 (ddd, 1H, $J = 7.7$, 6.1, 2.9 Hz, H-2), 3.49 (dd, 1H, $J = 7.5$, 2.9 Hz, H-5), 3.24 (dd, 1H, $J = 13.5$, 6.1 Hz, H-1_A), 3.22 (dd, 1H, $J = 13.5$, 7.7 Hz, H-1_B), 1.49, 1.43, 1.37, 1.34 (4 × s, 4 × 3H, CH_3). ^{13}C-NMR of **10a** (100 MHz, $CDCl_3$) δ: 136.0–126.3 (aromatic), 112.7, 109.2 (C_{acetal}), 81.8, 80.8, 80.6, 80.6, 73.2 (C-2, C-3, C-4, C-5, C-6), 66.9 (C-7), 31.4 (C-1), 27.1, 25.9, 25.3, 24.7 (CH_3). ESI-MS positive mode (m/z): calcd for $C_{19}H_{27}O_5S^+$ $[M + H]^+ = 367.0987$. Found: $[M + H]^+ = 367.1012$.

*4.1.4.12. 2,5-Anhydro-3,4:6,7-di-O-isopropylidene-1-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-D-glycero-D-galacto-heptitol (**10c**).* Prepared from **6** (79 mg, 0.31 mmol) and **7c** (135 mg, 0.37 mmol) using DPPA (3 × 7.9 mg, 0.031 mmol) in toluene (3.1 mL) according to Method D to give **10c** by column chromatography (eluent: hexane–acetone = 4 : 1) as a colorless syrup (168 mg; 88%). $R_f = 0.28$ (hexane–EtOAc = 2 : 1). $[\alpha]_D = -6.4$ ($c = 0.200$, $CHCl_3$).

^{1}H NMR of **10c** (400 MHz, $CDCl_3$) δ: 5.21 (pseudo t, 1H, $J =$ 9.3 Hz, H-3′), 5.08 (pseudo t, 1H, $J = 9.7$ Hz, H-4′), 5.07 (pseudo t, 1H, $J = 9.6$ Hz, H-2′), 4.79–4.73 (m, 2H, H-3, H-4), 4.61 (d, 1H, $J =$ 10.1 Hz, H-1′), 4.38 (dt, 1H, $J = 6.1$, 5.0 Hz, H-6), 4.24 (dd, 1H, $J =$ 12.4, 5.0 Hz, H-$6'_A$), 4.14 (dd, 1H, $J = 12.4$, 2.2 Hz, H-$6'_B$), 4.12–4.00 (m, 2H, H-7_A, H-7_B), 3.77 (ddd, 1H, $J = 8.5$, 5.2, 2.8 Hz, H-2), 3.70 (ddd, 1H, $J = 10.1$, 5.0, 2.2 Hz, H-5′), 3.55 (dd, 1H, $J = 7.2$,

2.8 Hz, H-5), 3.07 (dd, 1H, J = 13.8, 8.5 Hz, H-1$_A$), 2.85 (dd, 1H, J = 13.8, 5.2 Hz, H-1$_B$), 2.09 2.06, 2.03, 2.01 (4 × s, 4 × 3H, OAc), 1.47, 1.44, 1.37, 1.36 (4 × s, 4 × 3H, CH_3). ^{13}C NMR of **10c** (100 MHz, $CDCl_3$) δ:170.7, 170.4, 169.6, 169.5 (CO), 112.7, 109.1 (C_{acetal}), 84.2, 82.1, 81.8, 80.8, 80.7, 76.0, 74.0, 73.2, 70.2, 68.4 (C-2, C-3, C-4, C-5, C-6, C-1′, C-2′, C-3′, C-4′, C-5′), 66.9 (C-7), 62.2 (C-6′), 28.4 (C-1), 27.0, 25.9, 25.3, 24.9 (OAc), 20.9, 20.8, 20.7, 20.7 (CH_3). Elemental analysis: calcd for $C_{27}H_{40}O_{14}S$ (620.663): C: 52.25; H: 6.50; S: 5.17. Found: C: 50.28; H: 6.66; S: 5.12.

*4.1.4.13. 2,5-Anhydro-3,4:6,7-di-O-isopropylidene-1-S-(1,2:3,4-di-O-isopropylidene-β-D-galactopyranose-6-yl)-1-thio-D-glycero-D-galacto-heptitol (**10e**).* Prepared from **6** (111 mg, 0.40 mmol) and **7e** (100 mg, 0.36 mmol) using DPPA (3 × 10.3 mg, 0.040 mmol) in toluene (4.0 mL) according to Method D to give **10e** by column chromatography (eluent: hexane–acetone = 4 : 1) as a colorless syrup (154 mg; 81%). R_f = 0.36 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = −28.7 (c = 0.300, $CHCl_3$).

^{1}H NMR of **10e** (400 MHz, $CDCl_3$) δ: 5.53 (d, 1H, J = 5.0 Hz, H-1′), 4.77–4.70 (m, 2H, H-3, H-4), 4.62 (dd, 1H, J = 7.9, 2.2 Hz, H-3′), 4.35–4.28 (m, 2H, H-2′, H-4′), 4.38 (dd, 1H, J = 12.1, 6.1 Hz, H-6), 4.12–4.01 (m, 2H, H-7$_A$, H-7$_B$), 3.87 (pseudo t, 1H, J = 6.8 Hz, H-2), 3.71 (td, 1H, J = 6.8, 2.8 Hz, H-5′), 3.51 (dd, 1H, J = 7.6, 2.9 Hz, H-5), 2.95–2.78 (m, 4H, H-1$_A$, H-1$_B$, H-6$_A^{'}$, H-6$_B^{'}$), 1.53, 1.45, 1.44, 1.37, 1.35, 1.33 (8 × s, 8 × 3H, CH_3). ^{13}C NMR of **10e** (100 MHz, $CDCl_3$) δ: 112.5, 109.3, 109.1, 108.6 (C_{acetal}), 96.7 (C-1′), 82.1, 81.9, 80.9, 80.6, 73.1, 71.7, 71.0, 70.6, 67.6 (C-2, C-3, C-4, C-5, C-6, C-2′, C-3′, C-4′, C-5′), 67.0 (C-7′), 32.8 (C-6′) 30.4 (C-1), 27.0, 26.2, 26.1, 25.8, 25.3, 25.0, 24.7, 24.5 (CH_3). Elemental analysis: calcd for $C_{25}H_{40}O_{10}S$ (532.65): C: 56.37; H: 7.57; S: 6.02. Found: C: 58.31; H: 7.75; S: 5.94.

*4.1.4.14. 2,5-Anhydro-3,4:6,7-di-O-isopropylidene-1-S-(2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl)-1-thio-D-glycero-D-galacto-heptitol (**10f**).* Prepared from **6** (123 mg, 0.48 mmol) and **7f** (210 mg, 0.58 mmol) using DPPA (3 × 12.3 mg, 0.048 mmol) in toluene (4.8 mL) according to Method D to give **10f** by column chromatography (eluent: hexane–acetone = 4 : 1) as a colorless syrup (168 mg; 88%). R_f = 0.34 (hexane–EtOAc = 2 : 1). $[\alpha]_D$ = −15.8 (c = 0.300, $CHCl_3$).

^{1}H NMR of **10f** (400 MHz, $CDCl_3$) δ: 5.53 (d, 1H, J = 2.5 Hz, H-3), 5.25 (pseudo t, 1H, J = 10.0 Hz, H-4′), 5.04 (dd, 1H, J = 10.1, 3.4 Hz, H-2′), 4.92 (s, 1H, H-1′), 4.80–4.74 (m, 2H, H-3, H-4), 4.38 (dd, 1H, J = 11.7, 6.2 Hz, H-6), 4.26 (dd, 1H, J = 12.3, 5.9 Hz, H-6$_A^{'}$), 4.15 (dd, 1H, J = 12.3, 1.9 Hz, H-6$_B^{'}$), 4.10–3.98 (m, 2H, H-7$_A$, H-7$_B$), 3.78–3.71 (m, 1H, H-2), 3.70–3.64 (m, 1H, H-5′), 3.55 (dd, 1H, J = 6.9, 2.2 Hz, H-5), 3.04 (dd, 1H, J = 13.6, 9.1 Hz, H-1$_A$), 2.94 (dd, 1H, J = 13.6, 5.1 Hz, H-1$_B$), 2.19, 2.08, 2.05, 1.98 (4 × s, 4 × 3H, OAc), 1.47, 1.44, 1.37, 1.35 (4 × s, 4 × 3H, CH_3). ^{13}C NMR of **10f** (100 MHz, $CDCl_3$) δ: 170.7, 170.3, 170.2, 169.7 (CO), 112.7, 109.1 (C_{acetal}), 83.6, 81.9, 80.7, 80.5, 76.7, 73.2, 72.0, 70.4, 65.9 (C-2, C-3, C-4, C-5, C-6, C-1′, C-2′, C-3′, C-4′, C-5′), 66.8 (C-7), 63.0 (C-6′), 29.4 (C-1), 27.0, 25.8, 25.3, 24.8 (OAc), 20.9, 20.8, 20.8, 20.7 (CH_3). Elemental analysis: calcd for $C_{27}H_{40}O_{14}S$ (620.66): C: 52.25; H: 6.50; S: 5.17. Found: C: 52.06; H: 6.26; S: 5.21.

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Author contributions

JJ: synthesis and structure elucidation of compounds (**1a**, **b** – **4a**, **b**; every adduct except **8ac**, **8ae**, **10c**, **10a**, **10f**) wrote the manuscript; ND: synthesis and structure elucidation of compounds (**8ac**, **8ae**); ED: synthesis and structure elucidation of compounds (**10c**, **10e 10f**); AB: planned and controlled the experiments, structure elucidations (**8ac**, **8ae**, **10c**, **10a**, **10f**) and reviewed manuscript; LJ: planned and controlled the experiments, structure elucidations, wrote the manuscript; SL: conceived the research and wrote the manuscript. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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