Unprecedented β-*manno* type thiodisaccharides with a *C*-glycosylic function by photoinitiated hydrothiolation of 1-C-substituted glycals

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Abstract

Free-radical hydrothiolation of *O*-peracylated 1-C-(carbamoyl-, methoxycarbonyl- and cyano) substituted glycals with a range of sugar derived thiols gave the corresponding β-*manno* type 3-deoxy-S-disaccharides with full regio- and stereoselectivity. The configuration of the glycals (*arabino vs lyxo*) and the size of the protecting groups had no significant effect on the outcome of the transformations. Formation of by-products was tracked down by LCMS studies and correlated with the electron density of the double bonds to show that the reactions were synthetically useful with a COOMe and especially with a $CONH_2$ group as the 1-C-substituent.

Keywords

Carbohydrates; *C*-glycosyl compounds; radical reactions; thiol-ene additions; thiodisaccharides.

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Introduction

Although radical-mediated addition of thiols to alkenes has been known for a long time[1] this transformation has its renaissance with the advent of click chemistries[2] in various fields such as drug discovery,[3] material science,[4] bioconjugation,[5, 6] and polymer functionalization,[7] just to mention a few. The use of various thiyl radical additions to alkenes and alkynes in carbohydrate chemistry to obtain thiosugars, glycoconjugates, and glycodendrimers has also been reviewed recently.[8] In these reactions the sugar unit may play the role of both the thiol and the unsaturated component.

An especially favourable case of radical additions to alkenes occurs with the so-called capto-dative olefins,[9] i. e. double bonds substituted geminally by an electron withdrawing and an electron releasing substituent. Due to the highly radicophilic nature of the resulting adduct radicals[10] dimerization is facilitated and the final double adducts can be obtained in synthetically useful yields. This was demonstrated with thiyl additions to 2-alkylsulfanyl acrylonitriles and 2-methoxy-acrylic acid methyl ester.[11]

In recent years we and others have studied the photoinitiated thiol-ene additions with sugar derived alkenes with the double bond in endo-[12-14] or exocyclic[14-19] positions. These reactions exhibited very high or even exclusive regio- and stereoselectivities in most cases and offer thereby possibilities to design glycomimetic compounds with hydrolytically stable C-S linkages between the sugar and the attached moiety. Herein we disclose our comparative studies on additions of various thiyl radicals to capto-datively substituted sugar alkenes, i. e. 1-C-acceptor ($CONH_2$, COOMe, and CN) substituted glycals (2,6-anhydro-hept-2-enonic acid

derivatives[*]). The aim of these investigations has been to reveal the reactivity of the above substrates to select the most promising starting compounds towards the synthesis of novel, complex carbohydrate structures.

Results and discussion

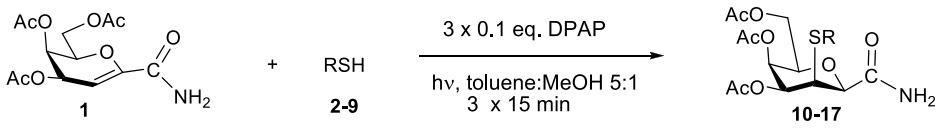
The hydrothiolation reactions of 1-C-substituted glycals were carried out in a mixture of toluene and MeOH (5:1) at ambient temperature with a 2:1 thiol:alkene molar ratio by irradiation at λ_{max} 365 nm for 3 x 15 min in the presence of the cleavable photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DPAP, 3 x 0.1 equiv).

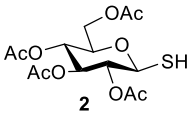
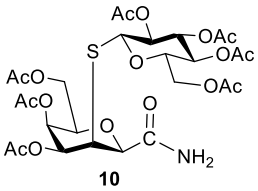
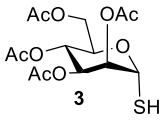
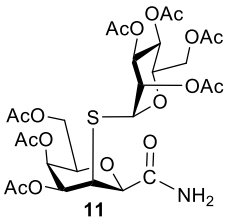
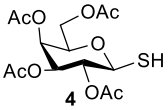
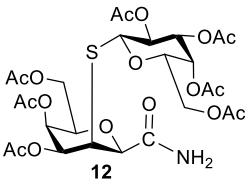
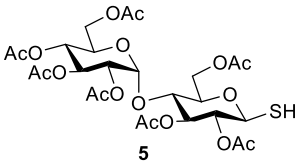
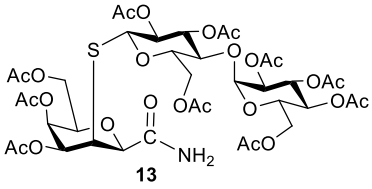
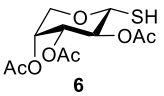
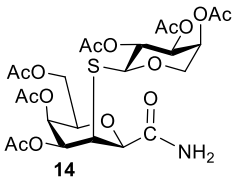
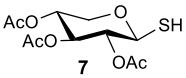
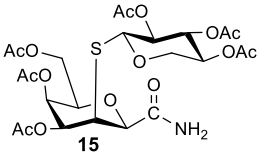
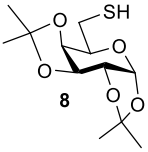
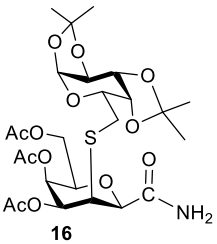
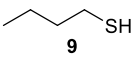
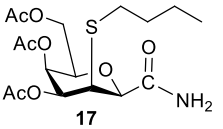
We were pleased to find that free radical addition of thiols **2-9** to amide-substituted galactal **1**[20] took place with full regio- and stereoselectivity affording the corresponding 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-substituted-3-thio-D-*glycero*-L-*altro*-heptonamides **10-17**, respectively (Table 1). The position of the S-linkage (regioselectivity) could easily be determined by the low chemical shift obtained for C-3 (43.5 ppm for compound **10**). The complete assignment of the ^{1}H and ^{13}C NMR spectra of **10** was performed by using COSY and HSQC measurements. The configuration of the new stereogenic centers (C-2 and C-3) was evidenced by crosspeaks between H-3 and both H-2 and H-4 hydrogens that appeared in the ROESY spectrum of compound **10** (see supporting information). For compounds **11-17** the analogous structure was deduced from the similarities of their ^{1}H and ^{13}C NMR spectra to those of **10**. The formation of the 3-*S*-substituted-D-*glycero*-L-*altro*-heptonamides (**10-17**) with axial 3-S-linkages as the sole isolable products can be explained by the preferred β-side attack on the less substituted ene-carbon in the thiyl radical addition step and the more favourable α-side attack on the C-2 radical in the hydrogen abstraction step.[15, 21-23]

[*] According to the carbohydrate nomenclature this is the systematic name of the starting materials, and also the addition products are named and numbered following these rules.

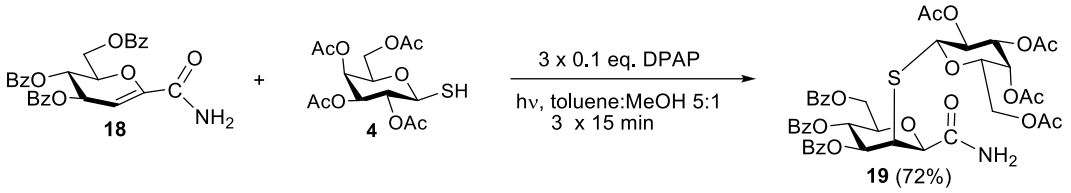
In all of the above addition reactions incomplete conversion of the starting galactal **1** was indicated by TLC. Our attempts to promote the progress of the reaction by applying higher excess of thiol (3 equiv), increasing the amount of DPAP (1 equiv), and prolongation of the irradiation time (5 x 15 min) were unsuccessful. The resulting yields ranged between 16 and 64 %. We observed earlier that electron-donating substituents on the thiol partner reduced its reactivity in the reversible thioladdition reaction.[14, 18] Thus, the low yields obtained for compounds **16** and **17** (16% and 19% respectively) are assumedly due to the electron-releasing substituents of the thiols **8** and **9**, respectively.

Table 1. Addition of thiols **2-9** to amide-substituted galactal **1**.



Thiol (2 eq.)	Product	Yield (%)
 **2**	 **10**	64
 **3**	 **11**	63
 **4**	 **12**	62
 **5**	 **13**	41
 **6**	 **14**	41
 **7**	 **15**	43
 **8**	 **16**	16
 **9**	 **17**	19

Next, the *O*-perbenzoylated amide-substituted glucal **18**[24] was subjected to coupling with 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4**, Scheme 1). The reaction conditions were the same as those used in the case of the hydrothiolation of amide-substituted galactal **1**. Pleasingly, selective addition occurred with the thiyl radical adding from the β-side to C-3 of the substrate and the subsequent hydrogen abstraction by the C-2 radical took place from the α-side, thus resulting in the 3-deoxy-3-thiodisaccharide **19**. Reactions of galactal **1** and glucal **18** with the thiol **4** revealed that neither the orientation nor the nature of the 5-*O*-substituent affected the stereochemical outcome of the hydrothiolation. It is known that the overall reaction rate of the thiol-ene reaction is directly related to the electron density of the ene partner for a given thiol, electron-rich enes react much more rapidly than electron-poor ones.[25, 26] Compound **18**, possessing a more electron-rich double bond than **1** owing to the *O*-benzoyl groups, was expected to show higher conversions with the thiol **4**. Accordingly, in this case a significantly enhanced yield (72%) could be reached in comparison to that obtained for **1** (62%).

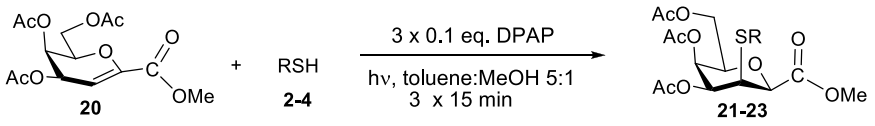


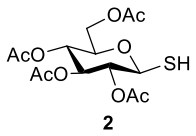
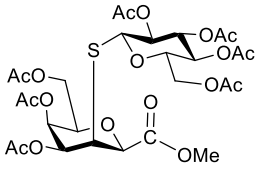
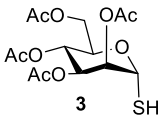
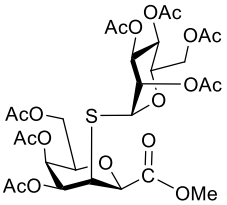
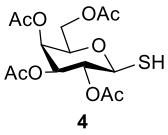
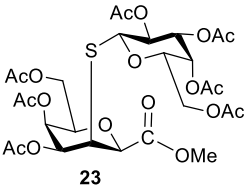
Scheme 1. Addition of thiol **4** to amide-substituted glucal **18**.

Reactions of the methoxycarbonyl-substituted galactal **20**[27] with thiols **2-4** under the above mentioned conditions gave exclusively the corresponding methyl 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-substituted-3-thio-D-*glycero*-L-*altro*-heptonates (**21-23**, Table 2).

Nevertheless, notable decrease of the isolated yields (19-28%) was observed in comparison to those of the adducts derived from the amide-substituted galactal **1** (62-64%).

Table 2. Addition of thiols **2-4** to methoxycarbonyl-substituted galactal (**20**).



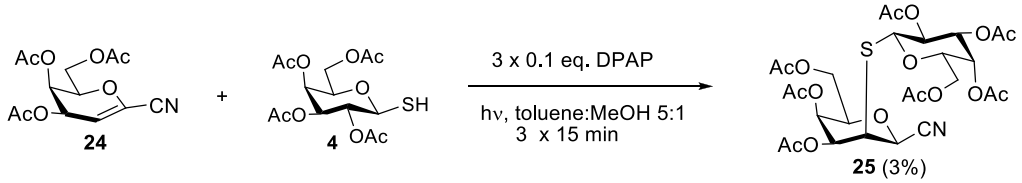
Thiol (2 eq.)	Product	Yield (%)
 **2**	 **21**	28
 **3**	 **22**	19
 **4**	 **23**	26

Like in the case of the amide-substituted galactal **1**, the conversion of the starting material **20** was incomplete, and applying a higher excess of the thiol, increasing the amount of DPAP, or prolongation of the irradiation time did not promote the reaction further. Therefore, the reaction of **20** with thiol **4** was studied under different conditions in order to facilitate the progress of the transformation (Table 3). Unfortunately the efforts to improve the yield by applying a range of photoinitiators/sensitizers (Entries 4-8) and other solvents (Entries 3, 7 and 8) did not give rise to a noticeable increase of the conversion. We could only obtain a slightly better yield in comparison to the original reaction conditions (Entry 1) when the thiol **4** was added in four portions (Entry 2).

Table 3. Additions of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4**) to the methoxycarbonyl-substituted galactal **20** under varied reaction conditions.

Entry	Radical initiator / photosensitizer	Thiol (**4**)	Reaction time	UV light	Solvent	Temperature (°C)	Yield (%, for **23**)
1	DPAP (3 x 0.2 eq.)	2 eq.	3 x 15 min	yes	Toluene : MeOH (5 : 1)	rt	26
2	DPAP (4 x 0.2 eq.)	4 x 0.5 eq.	4 x 15 min	yes	Toluene : MeOH (5 : 1)	rt	33
3	DPAP (3 x 0.2 eq.)	2 eq.	3 x 15 min	yes	2-propanol	rt	28
4	Benzophenone (1 eq. + 2 x 0.5 eq.)	2 eq.	3 x 15 min	yes	Toluene : MeOH (5 : 1)	rt	16
5	Benzil (1 eq. + 2 x 0.5 eq.)	2 eq.	3 x 15 min	yes	Toluene : MeOH (5 : 1)	rt	24
6	AIBN (3 x 0.1 eq.)	2 eq.	48 h	yes	Toluene : MeOH (5 : 1)	65	27
7	BEt_3	2 eq.	30 h	no	CH_2Cl_2	rt	6
8	Benzoyl-peroxide	2 eq.	30 h	no	Toluene	70	13

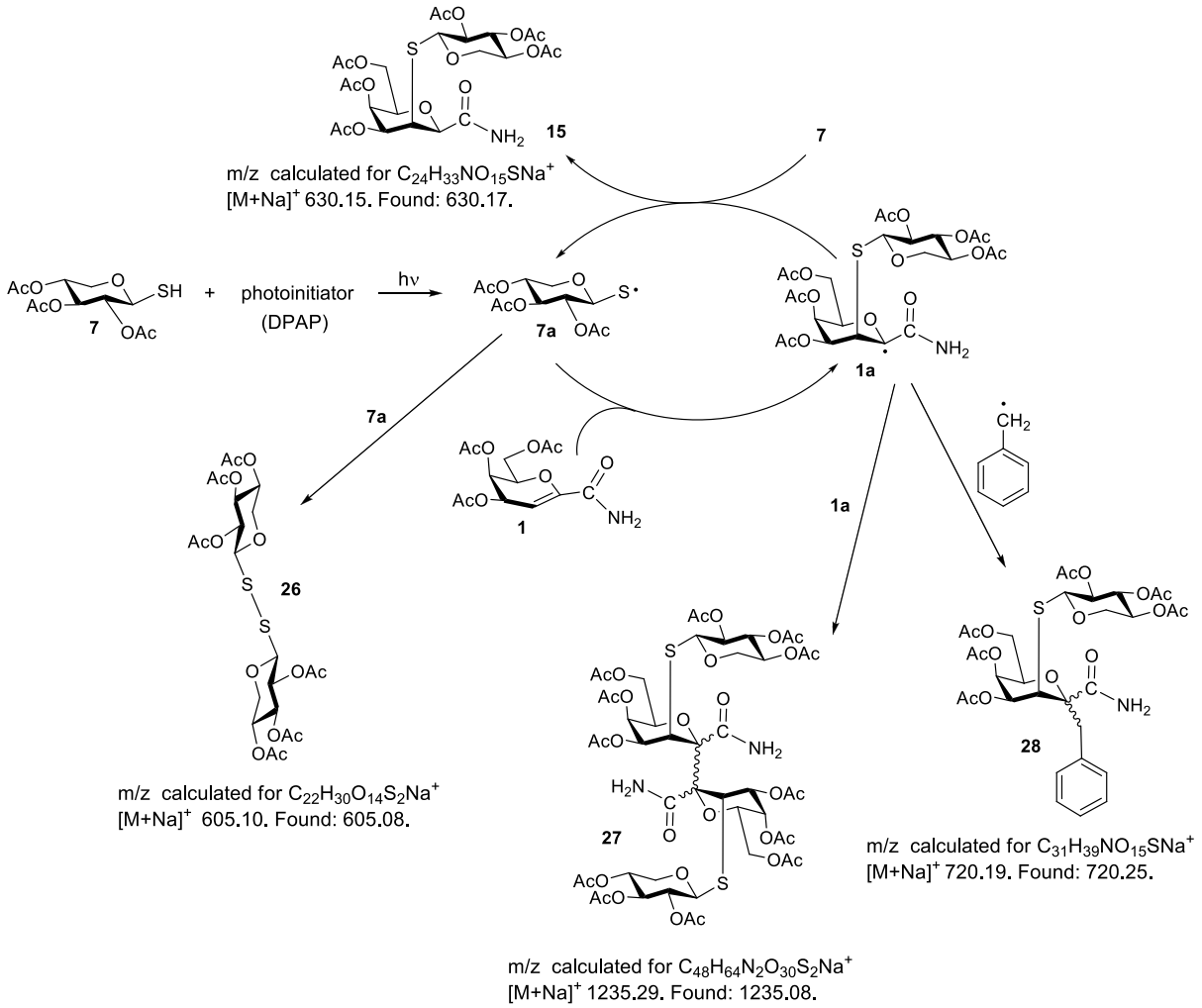
Thereafter, the reaction of the cyano-substituted galactal **24**[28] with thiol **4** was studied under the original reaction conditions (Scheme 2). In this case, the formation of a complex reaction mixture was observed, which made the isolation of the desired product very difficult. From the several components of the mixture detected by TLC the expected thiol-ene addition product could be isolated in very low yield (3%). 2D NMR data revealed that the reaction took place with the same regio- and stereochemical outcome as seen before, affording 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptononitrile (**25**).



Scheme 2. Addition of thiol **4** to cyano-substituted galactal **24**.

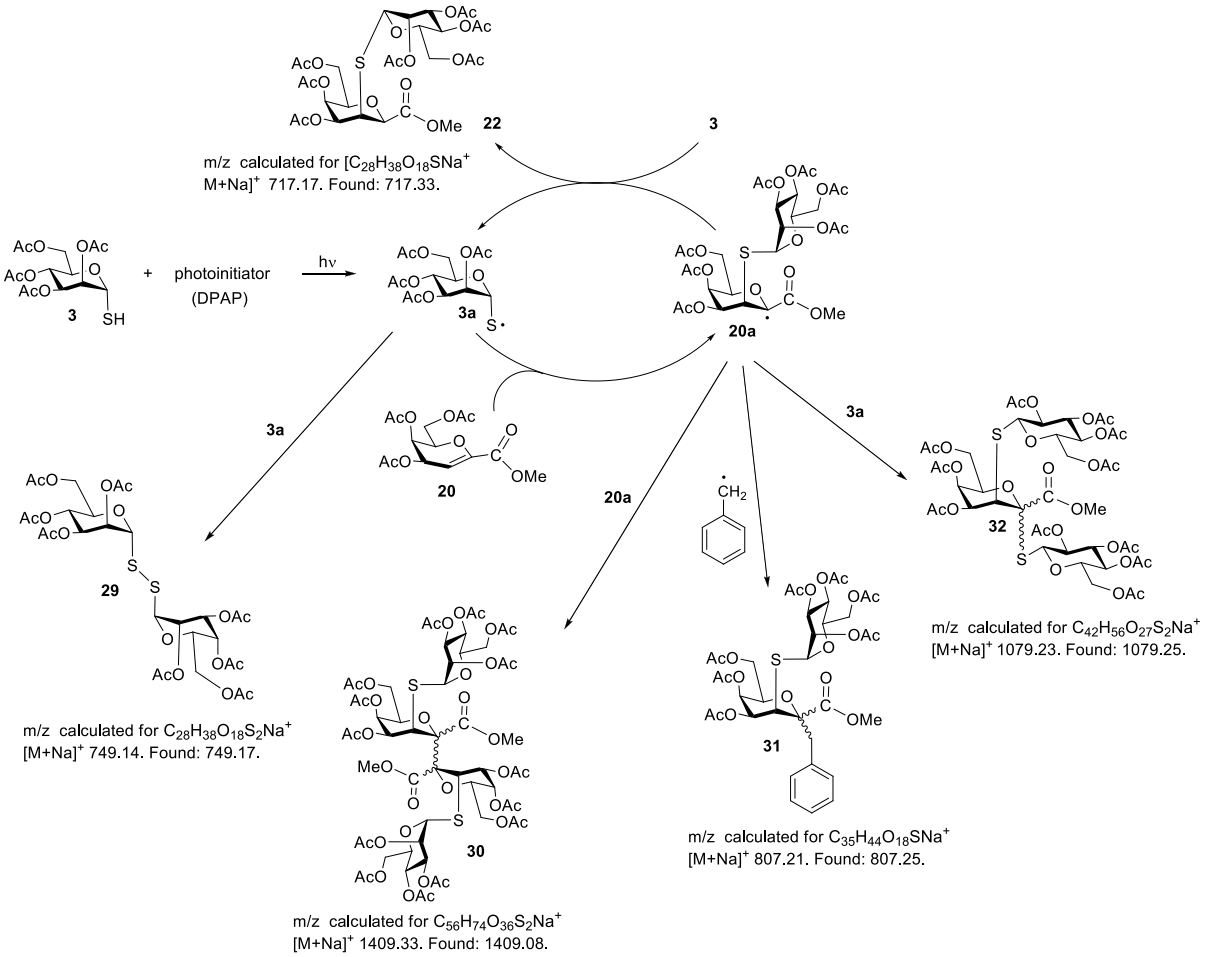
In general, the isolated yields in all hydrothiolation reactions of the 1-C-substituted glycals (**1**, **18**, **20** and **24**) were affected to some extent by the formation of side products, which could be detected by LC–MS measurements. The main by-product in all addition reactions was the corresponding disulfide, which formed from the applied thiol. In addition, practically each possible dimerization or combination product of the radicals present in the mixtures could be observed.

In the reaction of thiol **7** with galactal **1** the addition of thiyl-radical **7a** to compound **1** resulted in the formation of the C-2 radical **1a** (Scheme 3), which was transformed into the aimed addition product **15** by abstraction of a hydrogen from the thiol **7**. The dimerization of radical **7a** afforded the disulfide **26**. Dimerization of the radicophilic capto-dative C-2 radical **1a** to **27** could also be observed. The side product **28** could be formed by free radical combination of radical **1a** and benzyl radical presumedly present in the mixture as the result of a hydrogen abstraction from the solvent toluene.



Scheme 3. Side products **26-28** detected in the addition reaction of 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranose (**7**) to the amide-substituted galactal **1**.

Analogously, the reaction between thiol **3** and the methoxycarbonyl-substituted galactal **20** furnished not only the aimed addition product **22** but the side products **29**, **30** and **31** could also be detected by LC-MS as depicted in Scheme 4. Moreover, the formation of a further side product **32** was also observed, which could be produced by the combination of radicals **3a** and **20a**.



Scheme 4. Side products (**29-32**) detected in the addition reaction of 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranose (**3**) to the methoxycarbonyl-substituted galactal (**20**).

The comparison of the free radical addition of thiol **4** to amide-, methoxycarbonyl- and cyano-substituted galactals (**1**, **20** and **24** respectively) evidenced that the overall conversion in these reactions was greatly influenced by the nature of the 1-C-substituent. In addition, the appearance and the amount of the by-products, especially that of the disulfides, showed a similar correlation. As previously mentioned, in thiol-ene reactions electron-rich enes react much more rapidly than electron-poor ones. The Hammett σ substituent constants[29] (Table 4) reflect the electron-withdrawing effect of the 1-C-substituents of glycals **1**, **20** and **24** ($CONH_2$, COOMe and CN groups, respectively: the higher the positive value the more electron-withdrawing the substituent). The influence of the substituents on the electronic nature of the double bond of these glycal derivatives was also characterized by cyclic

voltammetry and the HOMO energy levels were calculated by semiempirical methods (Table 4).[30] Thus, the low reactivity observed in the hydrothiolation of glycals **20** and **24** (especially in the latter case), could be a result of the lower electron density/lower HOMO energy of the endocyclic double bond, which favours rather the backward than the forward reaction in the reversible thiyl addition step.[31]

Table 4. Data for the characterization of the electronic properties of the double bond in 1-C-substituted glycals

Glycal	1-C-Substituent	σ_m[a]	σ_p[a]	E_{ox}[b] (V)	HOMO energy[c] (eV)
1	$CONH_2$	0.28	0.36	1.96	-9.80
20	COOMe	0.37	0.45	>2.2	-10.03
24	CN	0.56	0.66	>2.2	-10.41

[a]Hammett constans obtained from the ionization of organic acids in solution.[29]
[b]Oxidation potentials vs ferrocene obtained from cyclic voltammograms.[30]
[c]Computed by the semiempirical PM3 method implemented in MOPAC from Sybyl 8.0.[30]

Conclusion

Photoinitiated, radical-mediated hydrothiolation of *O*-peracylated amide-, methoxycarbonyl- and cyano-substituted glycals with a range of thiols was studied. In all cases, the thiol-ene coupling reactions took place with full regio- and stereoselectivities, whereby the thiyl radical added from the β-side to C-3 of the glycal and the subsequent hydrogen abstraction step took place from the α-side of the C-2 radical. Neither the orientation (*galacto vs gluco*) nor the size (Ac *vs* Bz) of the 5-*O*-substituent affected the stereochemical outcome of the hydrothiolation. The conversions of the starting materials and the isolated yields of the products were highly variable and could not be improved by applying a range of photoinitiators/sensitizers and solvents. This was attributed to the different electron-withdrawing capabilities of the 1-C substituents (CN > COOMe > $CONH_2$) affecting the electron density of the double bonds. *O*-Perbenzoylated derivatives gave higher yields of the products than *O*-peracetylated ones, and this can also be explained by the electron density of the double bonds. Based on these results,

preparation of β-D-configured *talo*- or *manno* thiodisaccharides became feasible. The best results were achieved with the 1-carbamoyl-substituted glycals in which the $CONH_2$ substituent offers further possibilities for conjugation and other transformations (e. g. cross coupling via the NH_2 moiety or conversion to CN and CO_2Me and several further carboxylic acid as well as heterocyclic derivatives). Such compounds may give access to not readily available glycomimetics with hydrolytically stable C-S and C-C bonds. Extension of the approach to other 1-C-substituted glycals, transformations of the 1-C-substituents, as well as the study of these reactions by computational methods are in progress in our laboratory.

Experimental section

General Information

Optical rotations were measured at room temperature with a Perkin-Elmer 241 automatic polarimeter. TLC was performed on Kieselgel 60 F254 (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 in vacuum. The ^1H (360, 400 and 500 MHz) and ^{13}C NMR (90.54, 100.28 and 125.76 MHz) NMR spectra were recorded with Bruker DRX-360, Bruker DRX-400 and Bruker Avance II 500 spectrometers. Chemical shifts are referenced to Me_4Si (0.00 ppm for ^1H) and to the residual solvent signals ($CDCl_3$: 77.16 ppm for ^{13}C). The coupling constant values (*J*) are given in Hz. To aid spectral assignment and measure spatial connectivities new, zero quantum filtered ^1H-ROESY experiments[32] were applied at 500 MHz. Mass spectra were recorded with a Thermo LTQ XL mass spectrometer (Thermo Electron Corp., San Jose, CA, USA) operated in a full scan positive ion ESI mode. Elemental analyses (C, H, N, S) were performed using an Elementar Vario Micro Cube instrument. The

photocatalytic reactions were carried out at room temperature by irradiation with a Hg-lamp with a borosilicate vessel giving maximum emission at 365 nm.

General method A for the photoinitiated addition of thiols to 1-C-Substituted galactal derivatives

To a solution of the starting 1-C-substituted galactal (158 mg, 0.50 mmol) in a mixture of dry toluene : dry MeOH (5:1, 6 mL) thiol (2 equiv, 1.00 mmol) and 2,2-dimethoxy-2-phenylacetophenone (DPAP, 13 mg, 0.05 mmol) were added. The solution was deoxygenated and irradiated at room temperature for 15 min. Addition of DPAP and irradiation were repeated twice more. Then the solution was concentrated and the residue was purified by column chromatography.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (10)

Compound **1** (158 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**2**,[33] 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **10** (216 mg, 64%) as a white foam. $[\alpha]_D^{25}$ −56.7 (*c* 0.15 in $CHCl_3$); R_f 0.30 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 47.8; H, 5.5; N, 2.1; S, 4.75. Calc. for $C_{27}H_{37}NO_{17}S$: C, 47.7; H, 5.5; N, 2.1; S, 4.7%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si): δ (ppm) 1.93, 1.94, 1.98, 2.00, 2.01, 2.07 (21 H, 5 x s,7 x C*H*$_3$), 3.62−3.64 (1 H, m, 5'-H), 3.83 (1 H, br s, 3-H), 3.89−3.95 (2 H, m, 6$_B$'-H, 6-H), 4.00 (1 H, dd, $J_{7A,7B}$ 11.1, $J_{7B,6}$ 5.9, 7$_B$-H), 4.18 (1 H, dd, $J_{7A,7B}$ 10.8, $J_{7A,6}$ 6.3, 7$_A$-H), 4.25 (1 H, dd, $J_{6A',6B'}$ 8.4, $J_{6A',5'}$ 3.9, 6$_A$'-H), 4.31 (1 H, s, 2-H), 4.66 (1 H, d, $J_{1',2'}$ 10.2, 1'-H), 4.83 (1 H, t, *J* 9.6, 2'-H), 4.98 (1 H, t, *J* 9.6, 4'-H), 5.05−5.10 (2 H, m, 3'-H, 4-H), 5.21 (1 H,

br s, 5-H), 6.66 (1 H, d, $J_{NH2A,NH2B}$ 2.6, NH_{2B}), 6.77 (1 H, br s, NH_{2A}); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.5, 20.5, 20.6, 20.7, 20.9 (7C, 7 x *C*H_3), 43.5 (C-3), 61.7, 61.9 (C-6', C-7), 65.8 (C-5), 67.9 (C-4'), 69.2 (C-4), 70.5 (C-2'), 73.8 (C-3'), 75.6 (C-6), 75.8 (C-5'), 78.8 (C-2), 85.3 (C-1'), 169.4, 169.4, 169.7, 169.8, 170.2, 170.3, 170.4, 170.6 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 702.17. Found: 702.50.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (11)

Compound **1** (158 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranose (**3**,[34] 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **11** (214 mg, 63%) as a white foam. $[\alpha]_D^{25}$ +40.7 (*c* 0.31 in $CHCl_3$); R_f 0.32 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 47.6; H, 5.45; N, 2.05; S, 4.65. Calc. for $C_{27}H_{37}NO_{17}S$: C, 47.7; H, 5.5; N, 2.1; S, 4.7%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 2.01, 2.03, 2.06, 2.07, 2.11, 2.16, 2.18 (21 H, 7 x s, 7 x C*H*$_3$), 3.72 (1 H, br s), 3.97 (1 H, t, *J* 5.8), 4.08−4.30 (5 H, m), 4.42 (1 H, dd, *J* 12.6, 3.3), 5.18 (1 H, dd, *J* 10.1, 3.3), 5.26−5.28 (2 H, m), 5.34−5.39 (2 H, m), 5.42 (1 H, s), 5.96 (1 H, s), 6.58 (1 H, d, *J* 2.4); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.5, 20.7, 20.8, 20.8, 20.9, 21.0 (7C, 7 x *C*H_3), 43.9 (C-3), 61.9, 62.1 (C-6', C-7), 65.8, 69.4, 69.4, 70.4, 71.5, 76.1, 79.1 (8C, skeleton carbons), 83.4 (C-1'), 169.5, 169.7, 169.9, 170.0, 170.2, 170.4, 170.6, 170.9 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 702.17. Found: 702.50.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (12)

Compound **1** (158 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4**,[35] 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **12** (210 mg, 62%) as a white foam. $[\alpha]_D^{25}$ −33.7 (*c* 0.19 in $CHCl_3$); R_f 0.32 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 47.5; H, 5.4; N, 2.05; S, 4.6. Calc. for $C_{27}H_{37}NO_{17}S$: C, 47.7; H, 5.5; N, 2.1; S, 4.7%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.97, 2.05, 2.07, 2.16, 2.17 (21 H, 5 x s, 7 x C*H*$_3$), 3.88 (1 H, d, *J* 4.1), 3.95 (2 H, t, *J* 6.1), 4.02−4.15 (3 H, m), 4.24 (1 H, dd, *J* 11.3, 6.9), 4.36 (1 H, s), 4.69−4.74 (1 H, m), 5.07−5.08 (2 H, m), 5.18−5.20 (1 H, m), 5.27 (1 H, s), 5.38 (1 H, s), 6.55 (1 H, d, *J* 2.3), 6.67 (1 H, br s); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.5, 20.6, 20.7, 20.7, 20.8, 20.9, 21.0 (7C, 7 x *C*H$_3$), 43.8 (C-3), 61.4, 61.8 (C-6', C-7), 65.9, 67.6, 67.8, 69.2, 71.6, 74.1, 75.9, 78.9 (8C, skeleton carbons), 86.0 (C-1'), 169.6, 169.8, 169.9, 170.1, 170.2, 170.5, 170.6 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 702.17. Found: 702.50.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,2',3,3',4',6,6'-hepta-*O*-acetyl-β-D-maltopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (13)

Compound **1** (158 mg, 0.50 mmol) and 2,2',3,3',4',6,6'-hepta-*O*-acetyl-1-thio-β-D-maltopyranose (**5**,[36] 653 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **13** (197 mg, 41%) as white crystals. Mp 113−115 °C; $[\alpha]_D^{25}$ +13.2 (*c* 0.28 in $CHCl_3$); R_f 0.23 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 48.2; H, 5.45; N, 1.45; S, 3.3. Calc. for $C_{39}H_{53}NO_{25}S$: C, 48.4; H, 5.5; N, 1.45; S, 3.3%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 2.00, 2.02, 2.03, 2.05, 2.06, 2.10, 2.13, 2.15 (30 H, 8 x s, 10 x C*H*$_3$), 3.66−3.68 (1 H, m), 3.88−3.96 (4 H, m), 4.01−4.08 (2 H, m), 4.21−4.36 (5 H, m), 4.72−4.81 (2 H, m), 4.85 (1 H,

dd, *J* 10.4, 3.9), 5.05 (1 H, t, *J* 9.8), 5.14−5.16 (1 H, m), 5.22 (1 H, t, *J* 8.6), 5.26 (1 H, br s), 5.30−5.36 (2 H, m), 6.32 (1 H, d, *J* 2.1), 6.67 (1 H, d, *J* 2.7); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.7, 20.7, 20.7, 20.8, 20.8, 20.9, 21.0, 21.0 (10C, 10 x *C*H_3), 43.5 (C-3), 61.6, 61.8, 63.3 (C-6', C-6", C-7), 65.9, 68.0, 68.6, 69.3, 69.4, 70.1, 71.3, 73.2, 76.0, 76.5, 79.0 (12C, skeleton carbons), 84.8 (C-1'), 95.8 (C-1"), 169.6, 169.6, 169.7, 169.9, 170.1, 170.2, 170.6, 170.6, 170.6 (11C, 11 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 990.25. Found: 990.67.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4-tri-*O*-acetyl-α-D-arabinopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (14)

Compound **1** (158 mg, 0.50 mmol) and 2,3,4-tri-*O*-acetyl-1-thio-α-D-arabinopyranose (**6**,[37] 292 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **14** (126 mg, 41%) as a white foam. $[\alpha]_D^{25}$ −114.1 (*c* 0.17 in $CHCl_3$); R_f 0.29 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 47.5; H, 5.45; N, 2.3; S, 5.3. Calc. for $C_{24}H_{33}NO_{15}S$: C, 47.4; H, 5.5; N, 2.3; S, 5.3%; ^{1}H NMR (360 MHz, $CDCl_3$, Me_4Si) δ (ppm) 2.03, 2.05, 2.07, 2.11, 2.13, 2.20 (18 H, 6 x s, 6 x C*H*$_3$), 3.64 (1 H, dd, *J* 12.8, 2.8), 3.67−3.71 (1 H, m), 3.93−3.97 (1 H, m), 4.11 (1 H, dd, *J* 11.5, 5.5), 4.26−4.31 (2 H, m), 4.40 (1 H, d, *J* 12.7), 5.18 (1 H, dd, *J* 10.2, 3.4), 5.23 (1 H, dd, *J* 5.0, 3.0), 5.26−5.31 (3 H, m), 5.63 (1 H, d, *J* 5.1), 6.23 (1 H, d, *J* 3.1), 6.59 (1 H, d, *J* 3.3); ^{13}C NMR (91 MHz, $CDCl_3$) δ (ppm) 20.8, 20.9, 20.9 (6C, 6 x *C*H_3), 43.1 (C-3), 60.9, 62.0 (C-5', C-7), 66.0, 67.5, 68.3, 68.6, 69.8, 75.9, 79.5 (7C, skeleton carbons), 84.3 (C-1'), 169.7, 169.8, 170.1 (7C, 7 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 630.15. Found: 630.50.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonamide (15)

Compound **1** (158 mg, 0.50 mmol) and 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranose (**7**,[36] 292 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **15** (130 mg, 43%) as white crystals. Mp 94−98 °C; $[\alpha]_D^{25}$ −77.8 (*c* 0.18 in $CHCl_3$); R_f 0.24 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 47.32; H, 5.4; N, 2.3; S, 5.2. Calc. for $C_{24}H_{33}NO_{15}S$: C, 47.4; H, 5.5; N, 2.3; S, 5.3%; ^{1}H NMR (360 MHz, $CDCl_3$, Me_4Si) δ (ppm) 2.03, 2.04, 2.07, 2.16 (18 H, 4 x s, 6 x C*H*$_3$), 3.34 (1 H, dd, *J* 11.3, 9.2), 3.80 (1 H, d, *J* 3.3), 3.93 (1 H, t, *J* 6.0), 4.06−4.17 (2 H, m), 4.22−4.35 (2 H, m), 4.68 (1 H, d, *J* 8.6), 4.85 (1 H, t, *J* 8.4), 4.88−4.94 (1 H, m), 5.10−5.16 (2 H, m), 5.28 (1 H, s), 6.35 (1 H, s), 6.62 (1 H, s); ^{13}C NMR (91 MHz, $CDCl_3$) δ (ppm) 20.7, 20.9 (6C, 6 x *C*H$_3$), 44.4 (C-3), 61.9, 64.9 (C-5', C-7), 65.9, 68.8, 69.5, 70.3, 72.1, 76.0, 79.1 (7C, skeleton carbons), 85.8 (C-1'), 169.5, 169.8, 169.9, 169.9, 170.1, 170.1, 170.6 (7C, 7 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 630.15. Found: 630.17.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(1,2:3,4-di-*O*-isopropylidene-6-deoxy-α-D-glucopyranos-6-yl)-3-thio-D-*glycero*-L-*altro*-heptonamide (16)

Compound **1** (158 mg, 0.50 mmol) and 1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose (**8**,[38] 276 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **16** (48 mg, 16%) as a colourless syrup. $[\alpha]_D^{25}$ −5.0 (*c* 0.06 in $CHCl_3$); R_f 0.40 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 50.8 H, 6.25; N, 2.4; S, 5.45. Calc. for $C_{25}H_{37}NO_{13}S$: C, 50.75; H, 6.3; N, 2.4; S, 5.4%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.32 (6 H, 2 x s, 2 x C*H*$_3$), 1.45 (6 H, 2 x s, 2 x C*H*$_3$), 2.06, 2.10, 2.16 (9 H, 3 x s, 3 x COC*H*$_3$), 2.71 (1 H, dd, *J* 13.8, 9.0), 2.85 (1 H, dd, *J* 13.8, 5.8), 3.46−3.49 (1 H, m), 3.78 (1 H, dd, *J* 8.1, 6.4), 3.90 (1 H,

t, *J* 6.3), 4.07−4.10 (1 H, m), 4.24−4.29 (3 H, m), 4.51 (1 H, dd, *J* 7.9, 1.5), 4.59 (1 H, dd, *J* 7.9, 2.2), 5.16 (1 H, dd, *J* 4.8, 3.0), 5.28 (1 H, s), 5.48 (1 H, d, *J* 4.9), 5.74 (1 H, s), 6.57 (1 H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.8, 20.9, 21.0 (3C, 3 x CO*C*H_3), 24.6, 25.0, 26.1, 26.2 (4C, 4 x *C*H_3), 34.7 (C-6'), 47.0 (C-3), 62.2 (C-7), 66.1, 67.6, 70.2, 70.7, 71.0, 71.1, 75.7, 79.9 (8C, skeleton carbons), 96.8 (C-1'), 108.5, 109.3 (2C, 2 x Cq), 169.9, 170.3, 170.5, 171.3 (4C, 4 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 614.19. Found: 614.58.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-butyl-3-thio-D-*glycero*-L-*altro*-heptonamide (17)

Compound **1** (158 mg, 0.50 mmol) and 1-butanethiol (**9,** 107 μL, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:8 CH_2Cl_2−EtOAc) to give **17** (38 mg, 19%) as white crystals. Mp 138−139 °C; $[\alpha]_D^{25}$ −34.6 (*c* 0.11 in $CHCl_3$); R_f 0.43 (2:8 CH_2Cl_2−EtOAc); Elemental analysis: found: C, 50.3; H, 6.6; N, 3.4; S, 7.8. Calc. for $C_{17}H_{27}NO_8S$: C, 50.4; H, 6.7; N, 3.45; S, 7.9%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 0.89 (3 H, t, *J* 7.2, C*H*$_3$), 1.32−1.53 (4 H, m), 2.06, 2.08, 2.16 (9 H, 3 x s, 3 x COC*H*$_3$), 2.44−2.51 (1 H, m), 2.56−2.62 (1 H, m), 3.50 (1 H, dd, *J* 4.9, 1.8), 3.89−3.92 (1 H, m), 4.11 (1 H, dd, *J* 11.5, 5.6), 4.23−4.28 (2 H, m), 5.14 (1 H, dd, *J* 5.1, 3.1), 5.26−5.31 (1 H, m), 5.91 (1 H, d, *J* 2.2), 6.60 (1 H, d, *J* 2.4); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 13.8 (*C*H_3), 20.8, 20.9 (3C, 3 x CO*C*H_3), 21.8, 32.0, 35.1 (3C, 3 x *C*H_2), 45.8 (C-3), 62.1 (C-7), 66.1, 70.3, 75.9, 79.7 (4C, skeleton carbons), 170.2, 170.3, 170.6 (4C, 4 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 428.13. Found: 428.42.

4,5,7-Tri-*O*-benzoyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-thio-D-*glycero*-D-*galacto*-heptonamide (19)

Compound **18** (251 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4,** 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (97:3 CH_2Cl_2−MeOH) to give **19** (310 mg, 72%) as white crystals. Mp 136−140 °C; $[\alpha]_D^{25}$ −24.3 (*c* 0.14 in $CHCl_3$); R_f 0.35 (96:4 CH_2Cl_2−MeOH); Elemental analysis: found: C, 58.15; H, 5.0; N, 1.6; S, 3.65. Calc. for $C_{42}H_{43}NO_{17}S$: C, 58.3; H, 5.0; N, 1.6; S, 3.7%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.92, 1.92, 1.95, 1.96 (12 H, 4 x s, 4 x C*H*$_3$), 3.17 (1 H, dd, $J_{6A',6B'}$ 11.2, $J_{6B',5'}$ 6.4, H-6'b), 3.28 (1 H, dd, $J_{6A',6B'}$ 11.2, $J_{6A',5'}$ 7.3, H-6$_A$'), 3.73 (1 H, t, *J* 6.7, 5'-H), 3.97−4.08 (1 H, m, 6-H), 4.21 (1 H, d, *J* 4.1, 3-H), 4.41 (1 H, dd, $J_{7A,7B}$ 12.3, $J_{6,7B}$ 4.2, 7$_B$-H), 4.53 (1 H, s, 2-H), 4.68 (2 H, d, *J* 10.1, H-1', H-7$_A$), 4.93 (1 H, dd, $J_{2',3'}$ 10.0, $J_{3',4'}$ 3.3, 3'-H), 5.10 (1 H, t, *J* 10.0, 2'-H), 5.19 (1 H, d, $J_{3',4'}$ 3.0, 4'-H), 5.58 (1 H, dd, $J_{4,5}$ 10.1, $J_{3,4}$ 4.4, 4-H), 5.68 (1 H, t, *J* 9.9, 5-H), 5.73 (1 H, d, *J* 3.2, N*H*$_{2B}$), 6.63 (1 H, d, $J_{NH2A,NH2B}$ 3.2, 1H, N*H*$_{2A}$), 7.34−7.40 (4 H, m, arom), 7.48−7.51 (4 H, m, arom), 7.60 (1 H, t, *J* 7.3, arom), 7.94 (2 H, d, *J* 7.4, arom), 8.06−8.08 (4 H, m, arom); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.6, 20.6, 20.7, 20.7 (4C, 4 x *C*H$_3$), 47.7 (C-3), 60.7 (C-6'), 62.6 (C-7), 67.0 (C-5), 67.1 (C-4'), 68.1 (C-2'), 71.7 (C-3'), 73.1 (C-4), 74.0 (C-5'), 76.8 (C-6), 78.3 (C-2), 85.5 (C-1'), 128.4, 128.6, 128.7, 128.9, 129.4, 129.6, 129.9, 129.9, 130.4, 133.3, 133.5, 133.6 (18C, arom), 165.2, 165.8, 166.6, 169.6, 169.6, 170.0, 170.1, 170.2 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 888.21. Found: 888.58.

Methyl 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonate (21)

Compound **20** (165 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**2,** 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:3 *n*-hexane−EtOAc) to give **21** (97 mg, 28%) as white crystals. Mp 75−78 °C; $[\alpha]_D^{25}$ −85.3 (*c* 0.32 in $CHCl_3$); R_f 0.24 (2:3 *n*-hexane−EtOAc); Elemental analysis: found: C, 48.5; H, 5.5; S, 4.55. Calc. for $C_{28}H_{38}O_{18}S$: C, 48.4; H, 5.5; S, 4.6%; ^{1}H NMR (500 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.99, 2.01, 2.04, 2.05, 2.06, 2.09, 2.15 (21 H, 7 x s, 7 x C*H*$_3$), 3.60−3.63 (1 H, m, 5'-H), 3.78 (1 H, dd, $J_{3,4}$ 5.3, $J_{2,3}$ 2.1, 3-H), 3.83−3.89 (4 H, m, 6-H, OC*H*$_3$), 4.03 (1 H, dd, $J_{6A',6B'}$ 12.5, $J_{6B',5'}$ 1.8, 6$_B$-H), 4.16−4.19 (2 H, m, 7$_{A,B}$-H), 4.32 (1 H, dd, $J_{6A',6B'}$ 12.5, $J_{6A',5'}$ 4.6, H-6a'), 4.40 (1 H, d, $J_{1',2'}$ 10.3, H-1'), 4.48 (1 H, d, $J_{2,3}$ 2.2, 2-H), 4.92 (1 H, dd, $J_{1',2'}$ 10.1, $J_{2',3'}$ 9.2, 2'-H), 5.06 (1 H, t, *J* 9.7, 4'-H), 5.10−5.15 (2 H, m, 3'-H, 4-H), 5.26 (1 H, d, *J* 2.6, 5-H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 20.6, 20.7, 20.8, 20.8, 20.8 (7C, 7 x *C*H$_3$), 45.3 (C-3), 52.5 (O*C*H$_3$), 61.9 (2C, C-6', C-7), 65.5 (C-5), 67.9 (C-4'), 69.1 (C-4), 70.2 (C-2'), 74.9 (C-3'), 75.6 (C-6), 76.1 (C-5'), 78.4 (C-2), 86.4 (C-1'), 167.6, 169.3, 169.5, 170.0, 170.0, 170.3, 170.5, 170.7 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 717.17. Found: 717.50.

Methyl 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonate (22)

Compound **20** (165 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranose (**3,** 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:3 *n*-hexane−EtOAc) to give **22** (66 mg, 19%) as a colourless syrup. $[\alpha]_D^{25}$ +30.7 (*c* 0.45 in $CHCl_3$); R_f 0.27 (2:3 *n*-hexane−EtOAc); Elemental analysis: found: C, 48.3; H, 5.55; S, 4.6. Calc. for $C_{28}H_{38}O_{18}S$: C, 48.4; H, 5.5; S, 4.6%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 2.00, 2.05, 2.05, 2.06, 2.12, 2.16, 2.19 (21 H, 7 x s, 7 x C*H*$_3$), 3.68 (1 H, dd, *J* 4.1, 1.9), 3.84−3.88 (4 H, m), 3.92 (1 H, t, *J* 6.5), 4.07−4.24 (4 H,

m), 4.32 (1 H, dd, *J* 12.6, 4.0), 4.47 (1 H, d, *J* 2.2), 5.18 (1 H, dd, *J* 10.1, 3.3), 5.25−5.27 (2 H, m), 5.31 (1 H, dd, *J* 3.1, 1.5), 5.34 (1 H, br s); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.5, 20.7, 20.8, 20.8, 20.8, 21.0 (7C, 7 x *C*H_3), 46.8 (C-3), 52.8 (O*C*H_3), 61.8, 61.9 (C-6', C-7), 65.4, 65.6, 69.2, 70.0, 70.2, 71.8, 75.7, 78.7 (8C, skeleton carbons), 84.9 (C-1'), 167.7, 169.6, 169.8, 170.0, 170.1, 170.4, 170.5, 170.7 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 717.17. Found: 717.33.

Methyl 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptonate (23)

Compound **20** (165 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4,** 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (2:3 *n*-hexane−EtOAc) to give **23** (90 mg, 26%) as a white foam. $[\alpha]_D^{25}$ −24.3 (*c* 0.14 in $CHCl_3$); R_f 0.25 (2:3 *n*-hexane−EtOAc); Elemental analysis: found: C, 48.4; H, 5.4; S, 4.5. Calc. for $C_{28}H_{38}O_{18}S$: C, 48.4; H, 5.5; S, 4.6%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.97, 2.04, 2.08, 2.16, 2.17 (21 H, 5 x s, 7 x C*H*$_3$), 3.74−3.76 (1 H, m), 3.83−3.89 (4 H, m), 4.02−4.21 (5 H, m), 4.37 (1 H, d, *J* 10.1), 4.48 (1 H, d, *J* 2.0), 4.95 (1 H, dd, *J* 10.0, 3.4), 5.07−5.14 (2 H, m), 5.26 (1 H, d, *J* 2.3), 5.40 (1 H, d, *J* 3.0); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.5, 20.6, 20.7, 20.9, 20.9 (7C, 7 x *C*H_3), 45.6 (C-3), 52.3 (O*C*H_3), 61.4, 61.8 (C-6', C-7), 65.5, 67.3, 67.4, 69.1, 71.9, 74.6, 75.6, 78.4 (8C, skeleton carbons), 87.0 (C-1'), 167.5, 169.4, 169.7, 169.9, 170.0, 170.2, 170.4, 170.6 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 717.17. Found: 717.50.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-3-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-thio-D-*glycero*-L-*altro*-heptononitrile (25)

Compound **24** (149 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**4,** 364 mg, 1.00 mmol) were reacted according to general method **A**. The crude product was purified by column chromatography (first in 9:1 CH_2Cl_2−acetone, and then in 6:4 *n*-hexane−acetone) to give **25** (22 mg, 3%) as a white foam. $[\alpha]_D^{25}$ −24.6 (*c* 0.11 in $CHCl_3$); R_f 0.30 (6:4 *n*-hexane−acetone); Elemental analysis: found: C, 48.9; H, 5.3; N, 2.1; S, 4.8. Calc. for $C_{27}H_{35}NO_{16}S$: C, 49.0; H, 5.3; N, 2.1; S, 4.85%; ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ (ppm) 1.98, 2.06, 2.08, 2.09, 2.13, 2.17, 2.19 (21 H, 7 x s, 7 x C*H*$_3$), 3.61 (1 H, dd, $J_{3,4}$ 4.8, $J_{2,3}$ 2.1, 3-H), 3.89−3.92 (2 H, m, 5'-H, 6-H), 4.02−4.19 (4 H, m, $6_{A,B'}$-H, $7_{A,B}$-H), 4.58 (1 H, d, $J_{1',2'}$ 9.9, 1'-H), 4.72 (1 H, d, $J_{2,3}$ 2.2, 2-H), 5.04−5.07 (2 H, m, 3'-H, 4-H), 5.18 (1 H, t, *J* 9.9, 2'-H), 5.25 (1 H, s, 5-H), 5.43 (1 H, d, $J_{3',4'}$ 3.0, 4'-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.7, 20.8, 20.8, 20.9, 21.0 (7C, 7 x *C*H_3), 44.6 (C-3), 61.6, 61.7 (C-6', C-7), 65.4 (C-5), 67.3 (C-4'), 67.5 (C-2'), 68.3 (C-4), 69.3 (C-2), 71.8 (C-3'), 74.7 (C-5'), 76.4 (C-6), 85.7 (C-1'), 114.8, 169.7, 169.8, 170.0, 170.2, 170.3, 170.5, 170.7 (8C, 8 x *C*O); MS: *m/z* calc. for $[M+Na]^+$: 684.16. Found: 684.50.

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