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# Reactions of 1-C-acceptor-substituted glycals with nucleophiles under acid promoted (Ferrier-rearrangement) conditions

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ABSTRACT

The reactivity of *O*-peracetylated and *O*-perbenzoylated 1-COOMe, 1-$CONH_2$ and 1-CN-substituted glycals was studied against O-, S-, N- and C-nucleophiles in the presence of Lewis acids. Allylic substituted products with exclusive axial stereoselectivity were formed with simple alcohols, $N_3^-$, and $Cl^-$ ions, but with benzyl thiol the Ferrier rearrangement took place and thioglycosides were obtained. The use of a sugar derived thiol resulted in the formation of both the allylic substituted and the rearranged products.

## 1. Introduction

Transformations of pyranoid glycals (1,5-anhydro-hex-1-enitols) with various nucleophiles most often in the presence of an acidic catalyst to result in 2,3-unsaturated glycosidic derivatives are widely used and versatile tools in synthetic carbohydrate chemistry. The reaction, also called the Ferrier rearrangement [1–4], has been studied in a variety of conditions, and in several cases careful analysis of the reaction mixtures showed the formation of 3-substituted glycals as by-products. This diversion from the main reaction pathway is most frequent with N-, S- and C-nucleophiles [1–4].

Similar transformations with 1-substituted glycals are much less studied. In the context of the present work reactions of Neu5Ac2en and KDO/KDN derived glycals having a COOMe substituent attached to the double bond can be mentioned. Ikeda and co-workers studied the Ferrier rearrangement of the 4,5-oxazoline derivative of Neu5Ac2en with methanol using different Brønsted and Lewis acids at room temperature. They found that the corresponding rearranged 3,4-unsaturated methyl glycosides were formed in moderate to good yields with high β selectivity [5]. Similar observations were published by La Rocca and co-workers, using Montmorillonite K-10 as a promoter and different alcohols and thiols (EtOH, *n*PrOH, BuOH, EtSH, OctSH), but they also detected the formation of allylic substituted derivatives as minor products [6–8]. Watts and co-workers synthesized several 4-amino and 3,4-unsaturated *N*-glycosyl derivatives by palladium catalyzed amination of the 4,5-oxazoline derivative of Neu5Ac2en [9]. They observed that the regioselectivity of the reaction depended on the phosphine ligand, and the transformation took place at C-4 with exclusive stereo- and regioselectivity using $(Pd(\pi\text{-allyl})Cl)_2/Et_3P$ but with $Ph_3P$ the reversed regioselectivity i. e. formation of the rearranged product could be observed. Beau et al. studied the palladium catalyzed transformation of Neu5Ac2en derivatives with sodium malonate and observed the formation of 3,4-unsaturated *C*-glycosyl derivatives and C-4 allylic substituted products, too [10,11]. The regioselectivity of the transformation depended on the ligand, C-4 substituted derivatives were formed with monophosphine and 3,4-unsaturated *C*-glycosyl derivatives (C-2 substituted products) were formed with bidentate phosphine ligands. Acid catalyzed (cc. $H_2SO_4$) synthesis of 4β-acylamido derivatives of Neu5Ac2en was published by Rota and co-workers using Ritter reaction. In these experiments the allylic substituted products were isolated exclusively with high regioselectivity using different nitriles [12,13]. Rota and co-workers also studied the intermolecular nucleophilic substitution on Neu5-perfluoroacetylated glycals using different N-, O- and S-nucleophiles (including sulfonamides; primary and secondary alcohols, substituted phenols; thiols, thiophenols, and cysteine, hydride and halide ions) using $BF_3OEt_2$ as a promoter. In all cases the formation of a 4-substituted glycal was observed, apart from the reactions with cysteine and triethylsilane, where Ferrier rearrangement was observed with a shift of the double bond to give 2-substituted α glycosides [14]. Similar transformations of 2,3-didehydro-2-deoxy-Kdn (KDN2en) can be

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found in the literature to result in 4-azido [15] ($TMSN_3/TMSCl/BF_3OEt_2$), 4-acetamido [16] (Ritter reaction with nitriles and $Me_3SiOTf$ as promoter), 4-chloro [17] (with $TMSCl/BF_3OEt_2$) derivatives of KDN2en.

In this work, as a continuation of our studies on the transformations of glycals with 1-CN, 1-$CONH_2$, and 1-COOR substituents [18–21], we disclose our experiences with the reactions of these 1-C-acceptor-substituted glycals under Ferrier rearrangement conditions.

## 2. Results and discussion

The starting 1-C-substituted glycal derivatives [methyl (4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*lyxo*-hept-2-enonate (**1**); 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*lyxo*-hept-2-enonamide (**2**) and 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*lyxo*-hept-2-enononitrile (**3**)] were synthesized from the corresponding 1-C-substituted galactopyranosyl bromides using our literature methods [22–25].

First, the reaction of these glycal derivatives **1**–**3** with benzyl alcohol (**4**) were studied in dry acetonitrile at room temperature using $BF_3OEt_2$ as Lewis acid and the results are summarized in Table 1. In the case of methoxycarbonyl (**1**) and carbamoyl (**2**) substituted glycal derivatives moderate conversions were detected, but no transformation was observed in the case of nitrile **3**. Similar reactivity was also observed in the case of halogen addition [21] and thiol-ene reaction [20] of these types of compounds which is correlated with the electron density of the double bond.

The $^1H$ and $^{13}C$ NMR studies of the isolated products clearly showed that the compounds were not the desired 2,3-unsaturated glycosides (Ferrier rearranged products in Table 1) but the allylic substituted derivatives **5** and **6**. A comparison of the $^{13}C$ NMR chemical shifts of the C-2 centers in the starting compounds **1**, **2**, the products **5**, **6**, and related compounds **7**, **8** from the literature [6,21,22], respectively, indicated that the position of the double bond was not changed (Fig. 1). The configuration of the C-4 stereogenic center was determined by NOE measurements to show NOE effects between H-4/H-5 and H-4/H-3 but not between H-4/H-6.

Next, the effect of the Lewis acids was studied in the reaction of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*lyxo*-hept-2-enonamide (**2**) with benzyl alcohol (Table 2).

As the data of Table 2 show, the conversion of this transformation could be increased up to 87% by using TMSOTf, but the corrected yield was only 19% (Entry 1), and the formation of a large amount of decomposition products on the starting point of the TLC plate was observed. The decomposition of the starting compound was also preponderant with $AlCl_3$, $BCl_3$ and $BBr_3$ (Entries 2–4, respectively) while no transformation was detected with $CF_3COOH$, $ZnCl_2$, $InCl_3$, $Cu(OTf)_2$, AgOTf, $Sc(OTf)_3$, $Y(OTf)_3$, $Pd(TFA)_2$ and $Pd_2(dba)_3$/XPhos/TEA as a catalyst. In the case of $TiCl_4$, $FeCl_3$ and $I_2$ (Entries 5–7, respectively) the allylic substituted product could be isolated in a similar or slightly higher yield as with $BF_3OEt_2$ (Entry 8).

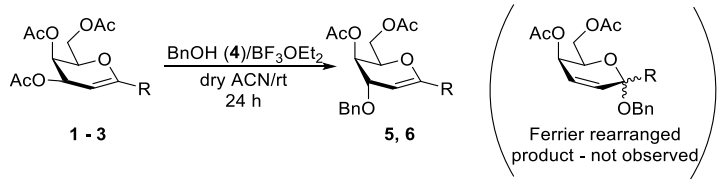
Further optimization reactions were performed using $I_2$ and $TiCl_4$ to study the effect of the temperature and the amount of benzyl alcohol as shown in Table 3.

In the case of iodine the isolated yield of **6** raised slightly with increasing of amount of benzyl alcohol from 1.0 to 2.0 equivalent, but dropped dramatically by further increasing of the amount of the nucleophile (Entries 1–3), and complex, inseparable mixture was obtained by using 10 equivalents of BnOH (Entry 4). We should also note that, the excess of iodine hampered the purification of the reaction mixtures and contaminated the product. Raising the temperature had a similar effect, yielding a complex reaction mixture (Entries 5, 6). In the case of titanium tetrachloride, no transformations were detected at lower temperatures (Entries 7, 8). Although the isolated yields of **6** were increased by the temperature (up to 50 °C), but the decomposition of the starting material was also accelerated, and the yield started to decrease at higher temperatures. (Entries 9–11).

Based on the above results and our experimental observations, we used 1 equivalent of a Lewis acid ($BF_3OEt_2$ or $TiCl_4$) and 1 equivalent of a nucleophile in dry acetonitrile at room temperature in further reactions (Table 4). The reactions of 1-methoxycarbonyl-glycal **1** with allyl alcohol (**9**) and propargyl alcohol (**10**) as O-nucleophiles gave the 4-substituted compounds **11** and **12** which were isolated in moderate yield (Entries 1, 2). On reaction of benzyl thiol (**13**) with **1** a single new spot was detected by TLC, but the $^1H$ NMR spectrum showed this to be a mixture of three compounds which could not be separated by column chromatography (Entry 3). In the case of 1-carbamoyl-glycal **2** several nucleophiles were studied (Entries 4–12). Using phenol (**14**) in the presence of $TiCl_4$ only the chlorinated **15** (Entry 4) while with $BF_3OEt_2$ the acetamido substituted **16** could be isolated from the reaction mixture in good yield (Entry 5) similar to results published earlier [12,13].

In reactions of **2** with partially protected sugar derivatives 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (**17**), 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (**18**) and methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**20**) only the decomposition of **17** and **20**, or the formation of a 1,6-anhydro-glucose type by-product **19** [26] were observed (Entries 6–9) and the starting glycal **2** could be recovered. In contrast to these experiments, by using benzyl thiol **13** as an S-nucleophile (Entry 10) the formation of the 2,3-unsaturated thioglycoside **21** was observed in moderate yield. Using sugar tiol **22** (Entry 11) the 2,3-unsaturated thioglycoside **23** and allylic substituted product **24** were isolated from the reaction mixture in moderate yields (29% and 40%, respectively). The change of the regioselectivity depending on the nucleophile is not unknown in the literature. Priebe and Zamojsky observed that the products

**Table 1**
Reaction of 1-C-acceptor substituted glycals with BnOH (**4**)[a].




| Starting compound | R | Conversion[b] (%) | Product | Corrected yield[c,d] (%) |
|---|---|---|---|---|
| **1** | COOMe | 65 | **5** | 12 |
| **2** | $CONH_2$ | 58 | **6** | 36 |
| **3** | CN | No reaction | | |

[a] Reaction conditions: Glycal (100 mg, 1 equiv.), BnOH (1 equiv.), $BF_3OEt_2$ (1 equiv.) in 2.5 mL of dry ACN under $N_2$ atmosphere at room temperature for 24 h.
[b] Unreacted starting material was collected by column chromatography.
[c] Yield was corrected with the conversion.
[d] Isolated yield.

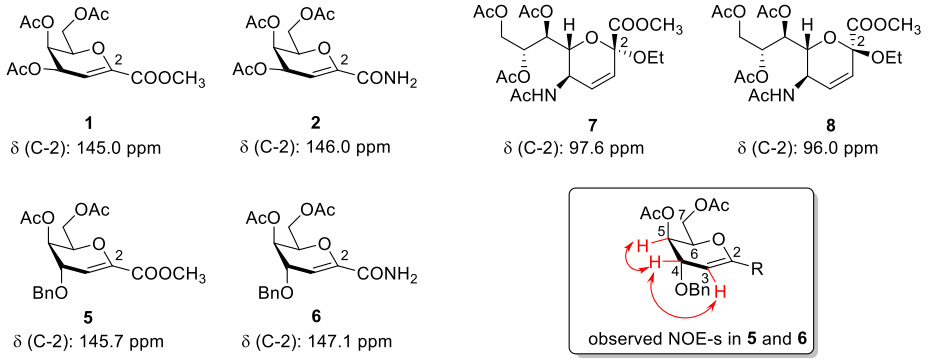
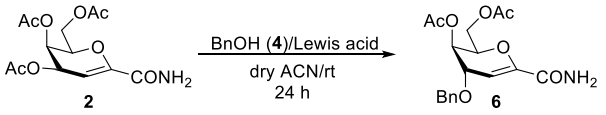



**Fig. 1.** Selected $^{13}C$ NMR data of compounds **1–2** and **5–8**.

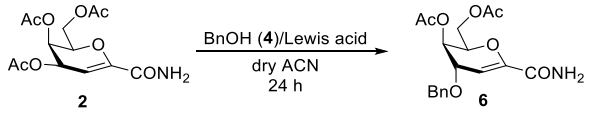
**Table 2**
Optimization of reaction circumstances I.[a]




| Entry | Lewis acid | Conversion[b] (%) | Corrected yield[c,d] (%)[a] |
|---|---|---|---|
| 1 | TMSOTf | 87 | 19 |
| 2 | $AlCl_3$ | 26 | 2 |
| 3 | $BCl_3$ | 32 | 3 |
| 4 | $BBr_3$ | 70 | 6 |
| 5 | $TiCl_4$ | 33 | 53 |
| 6 | $FeCl_3$ | 34 | 36 |
| 7 | $I_2$ | 55 | 42 |
| 8 | $BF_3OEt_2$ | 58 | 36 |

[a] Reaction conditions: Glycal (100 mg, 1 equiv.), BnOH (1 equiv.), Lewis acid (1 equiv.) in 2.5 mL of dry ACN under $N_2$ atmosphere at room temperature for 24 h.
[b] Unreacted starting material was collected by column chromatography.
[c] Yield was corrected with the conversion.
[d] Isolated yield.

**Table 3**
Optimization of reaction circumstances II.[a]




| Entry | Lewis acid | Amount of BnOH (equiv.) | T (°C) | Conversion[b] (%) | Corrected yield[c,d] (%)[a] |
|---|---|---|---|---|---|
| 1 | $I_2$ | 1 | rt | 55 | 42 |
| 2 | | 2 | rt | 73 | 34 |
| 3 | | 5 | rt | 88 | 18 |
| 4 | | 10 | rt | Complex mixture | |
| 5 | | 1 | 50 | Complex mixture | |
| 6 | | 1 | reflux | Complex mixture | |
| 7 | $TiCl_4$ | 1 | −20 | No reaction | |
| 8 | | 1 | 0 | No reaction | |
| 9 | | 1 | rt | 33 | 53 |
| 10 | | 1 | 50 | 53 | 43 |
| 11 | | 1 | reflux | 60 | 32 |

[a] Reaction conditions: Glycal (100 mg, 1 equiv.), BnOH, Lewis acid (1 equiv.) in 2.5 mL of dry ACN under $N_2$ atmosphere at the given temperature for 24 h.
[b] Unreacted starting material was collected by column chromatography.
[c] Yield was corrected with the conversion.
[d] Isolated yield.

of Lewis acid catalyzed transformations of unsubstituted glycals depended on the nature of nucleophile [27]. Hard nucleophiles (OR, OH, Cl, etc) attacked on C-1 and resulted in the Ferrier products, but soft nucleophiles ($SCH_3$, $N_3$, etc) attacked on C-3. Based on these observations and the HSAB theory it was assumed that C-1 had a hard electrophilic and C-3 had a soft electrophilic character in the carbenium ion type intermediates. Rota and co-workers studied similar transformations of Neu5Ac2en derivatives (possessing $COOCH_3$ electron withdrawing group at the formal 'glycal' C-1) and they observed opposite regioselectivity with hard/soft nucleophiles [14]. Our findings match these latter observations and may reveal a change in the hard/soft character of the acceptor substituted intermediates in comparison to the unsubstituted ones.

In the reaction of **2** with $NaN_3$ as a N-nucleophile (Entry 12) the 4-azido derivative **25** was isolated. No transformation was observed with $TMSN_3$ (Entry 13), NaCN (Entry 14) and a complex, inseparable reaction mixture was formed in the presence of TMSCN as a C-nucleophile (Entry 15).

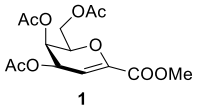
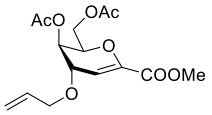
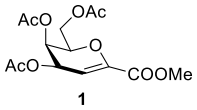
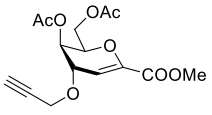
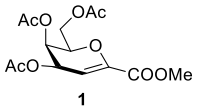
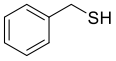
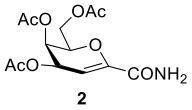
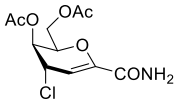
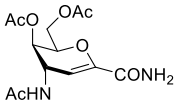
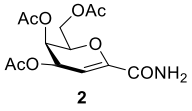
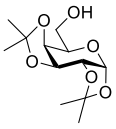
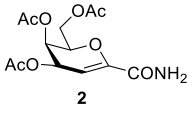
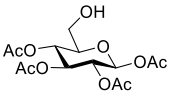
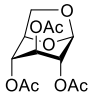
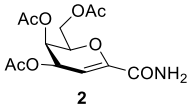
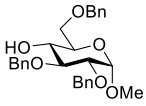
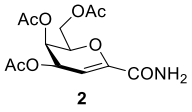
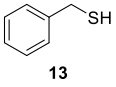
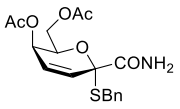
Several other glycal-nucleophile reactions were attempted under the above conditions. In the case of 1-cyano-glycal **3** (Entry 16) no reaction took place with benzyl thiol in the presence of $TiCl_4$. *O*-Perbenzoylated 1-C-substituted glycals **26-28** [23] also did not react with benzyl alcohol (**4**) using $BF_3OEt_2$ or $TiCl_4$ (Entries 17, 18 and 20, respectively), but in the reaction of **27** with benzyl thiol (**13**) using $TiCl_4$ promoter, the corresponding rearranged thioglycoside **29** was isolated in moderate yield (Entry 19). Based on these experiences one can conclude that the reactivity of these types of 1-C substituted glycals is highly dependent on the C-substituents, protecting groups and the nature of the reagents. Cyano-glycals did not react under these circumstances, but in the case of carbamoyl and methoxycarbonyl substituted acetylated galactals allylic substituted products were formed with alcohols and $NaN_3$. Using S-nucleophiles the 2,3-unsubstituted thioglycosides were formed exclusively in the reaction of D-*arabino*- and D-*lyxo* configured 1-carbamoyl glycals with benzyl thiol, but with a sugar thiol both products could be isolated.

Structural elucidation of the products was carried out by several methods. The presence of one Cl in **15** was proven by $M^+$ and $[M+2]^+$ molecular ion peaks in 3 : 1 ratio in the mass spectrum. See below further stereochemical considerations. Compound **16** gave suitable crystals, and its structure was determined by X-ray crystallography as shown in Fig. 2.

The constitution of **21, 23** and **29** was identified by NMR experiments. The chemical shift value of C-2 carbon ($\delta$ ($CDCl_3$) = 87.8 ppm for **21,** 87.9 ppm for **23** and 88.0 ppm for **29**) and the presence of two olefinic CH carbon signals ($\delta$ ($CDCl_3$) = 131.5 ppm (C-3) and 124.4 ppm (C-4) for **21**, 130.6 (C-3), 125.1 (C-4) for **23** and 129.0 ppm (C-3), 127.6 ppm (C-4) for **29**) clearly showed the formation of a rearranged thioglycoside.

The configuration of the anomeric center of **21** and **29** was determined by NOE experiments to show the vicinity of the $SCH_2$- and H-6

**Table 4**
Reactions of 1-C-acceptor substituted glycals with O-, S-, N- and C-nucleophiles[a].

| Entry | Glycal | Nucleophile | Lewis acid | Product | Conversion[b] (%) | Corrected yield[c,d] (%) |
|---|---|---|---|---|---|---|
| 1 |  **1** |  **9** | $BF_3OEt_2$ |  **11** | 71 | 24 |
| 2 |  **1** |  **10** | $BF_3OEt_2$ |  **12** | 79 | 23 |
| 3 |  **1** |  **13** | $TiCl_4$ | mixture of three products | 100 | - |
| 4 |  **2** |  **14** | $TiCl_4$ |  **15** | 46 | 71 |
| 5 | | | $BF_3OEt_2$ |  **16** | 70 | 64 |
| 6 |  **2** |  **17** | $TiCl_4$ | decomposition of **17** | | - |
| 7 |  **2** |  **18** | $TiCl_4$ |  **19** | 0[e] | 65[e] |
| 8 | | | $BF_3OEt_2$ | | 0[e] | 63[e] |
| 9 |  **2** |  **20** | $TiCl_4$ | decomposition of **20** | | - |
| 10 |  **2** |  **13** | $TiCl_4$ |  **21** | 57 | 29 |

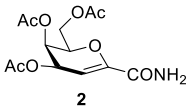
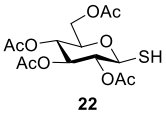
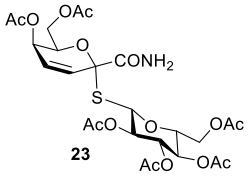
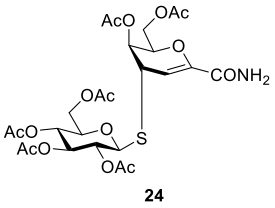
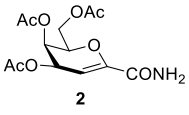
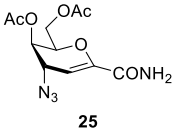
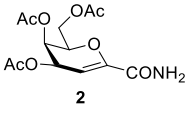
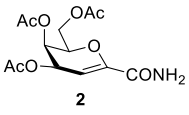
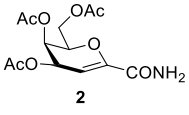
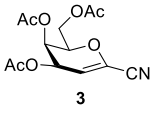
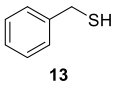
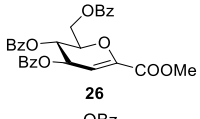
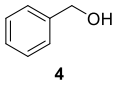
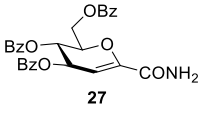
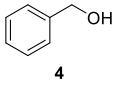
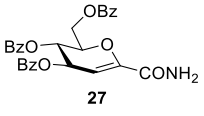
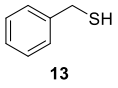
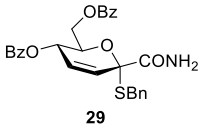
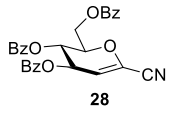
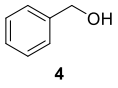
protons (Fig. 3). In the case of **23** NOESY experiment was applied, but no effect was observed between H-6 and H-1'. The α-configuration of anomeric center of **23** was proved by cross-peaks in the NOESY spectrum of **23** belonging to the H-1' - H-3 and H-1' - $CONH_2$ correlations.

The comparison of the selected $^1$H NMR data of **21**, **23** and **29** (Table 5.) demonstrated the same anomeric configuration of these compounds, because the signals of H-3, H-4 and H-6 protons appeared in a narrow range (±0.15 ppm).

The configuration of C-4 in compounds **5**, **6**, **11**, **12**, **15**, **24** and **25** was established by comparisons of NMR data. The lack of the NOE effect between H-4 and H-6 of **5** and **6** (Fig. 1, *vide supra*) made probable the axial orientation of the BnO substituent at C-4. The same configuration of C-4 in **16** was unambiguously determined by X-ray crystallography. For comparison, selected $^1$H NMR data of these compounds are summarized in Table 6. The chemical shifts of characteristic protons for compounds **5**, **6**, **11**, **12**, **24** and **25** can be found in a narrow range (H-3 6.17–6.11 ppm; H-4 4.04–3.80 ppm and H-5 5.10-4.96 ppm) proving the same configuration of C-4. Compound **15** has similar chemical shifts of H-3 and H-5, but H-4 shows ~0.4 ppm downfield shift due to the higher electronegativity of chlorine.

The formation of D-*xylo* derivatives can be explained by the pseudoaxial attack of the nucleophile on carbocation **B** (Scheme 1.) which may be formed by the anchimeric assistance of the neighboring axial AcO-5 substituent when AcO-4 is split off in **A**. This finding is consistent with the observations published by Priebe and Zamojski [27] on reactions of similar but 1-unsubstituted glycals.

In summary, the reaction of methoxycarbonyl and carbamoyl substituted glycals under conditions of the Ferrier rearrangement

| Entry | Glycal | Nucleophile | Lewis acid | Product | Conversion[b] (%) | Corrected yield[c,d] (%) |
|---|---|---|---|---|---|---|
| 11 |  **2** |  **22** | $BF_3OEt_2$ |  **23** | 70 | 29 |
| | | | |  **24** | | 40 |
| 12 |  **2** | $NaN_3$ (2.5 equiv.) | $BF_3OEt_2$ |  **25** | 63 | 45 |
| 13 |  **2** | $TMSN_3$ | $TiCl_4$ | No reaction | - | |
| 14 |  **2** | NaCN | $BF_3OEt_2$ | No reaction | | |
| 15 |  **2** | TMSCN | $TiCl_4$ | Complex mixture | - | |
| 16 |  **3** |  **13** | $TiCl_4$ | No reaction | - | |
| 17 |  **26** |  **4** | $BF_3OEt_2$ or $TiCl_4$ | No reaction | - | |
| 18 |  **27** |  **4** | $BF_3OEt_2$ or $TiCl_4$ | No reaction | - | |
| 19 |  **27** |  **13** | $TiCl_4$ |  **29** | 59 | 42 |
| 20 |  **28** |  **4** | $BF_3OEt_2$ or $TiCl_4$ | No reaction | - | |

[a]Reaction conditions: Glycal (100 mg, 1 equiv.), nucleophile (1 equiv.), Lewis acid (1 equiv.) in 2.5 mL of dry ACN under $N_2$ atmosphere. [b]Unreacted starting material was collected by column chromatography. [c]Yield was corrected with the conversion. [d]Isolated yield. [e]Yield of **19**, glycal did not react.

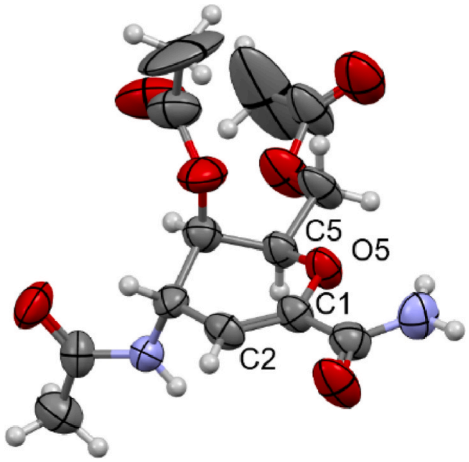



**Fig. 2.** ORTEP diagram of **16**.

showed a preference for the formation of C-4 or allylic substituted products with alcohols (benzyl, allyl, propargyl) and $NaN_3$. Reaction of the carbamoyl-substituted galactal with benzylthiol resulted only in the formation of the corresponding 3,4-unsaturated glycoside, however, in addition to this type of rearranged compound, the substitution with the sugar thiol also occurred in the allyl position. The nitrile substituted galactals and 1C- acceptor substituted *O*-perbenzoylated glucals did not react under these conditions, with exception of carbamoyl substituted *O*-perbenzoylated glucal, which gave the expected rearranged thioglycoside with benzyl thiol.

## 3. Experimental

### 3.1. General methods

Solvents were purified by distillation. Acetonitrile (ACN) was refluxed and distilled from $P_4O_{10}$ and stored over 4 Å molecular sieves. TLC was performed on DC Kieselgel 60 $F_{254}$ (Merck) plates, developed under 254 nm UV light and/or spraying with EtOH/cc. $H_2SO_4$/*p*-anisaldehyde (96 : 5: 1) and heated to 150 °C. For column chromatography

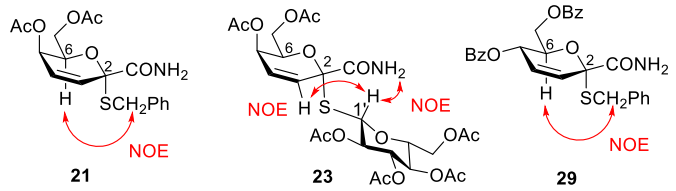



**Fig. 3.** Spectroscopic evidence for the α(D) configuration of thioglycosides **21**, **23** and **29**.

**Table 5**
Selected NMR data of Ferrier adducts **21**, **23**, and **29** ($CDCl_3$, $\delta$ [ppm], $J$ [Hz]).

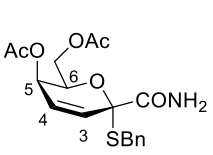
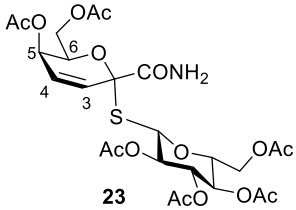
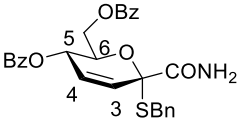
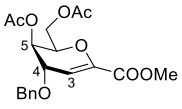
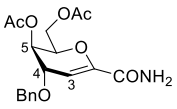
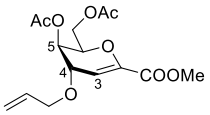
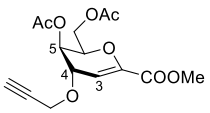
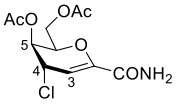
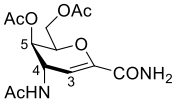
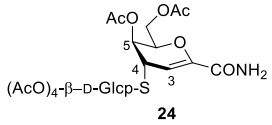
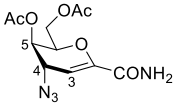
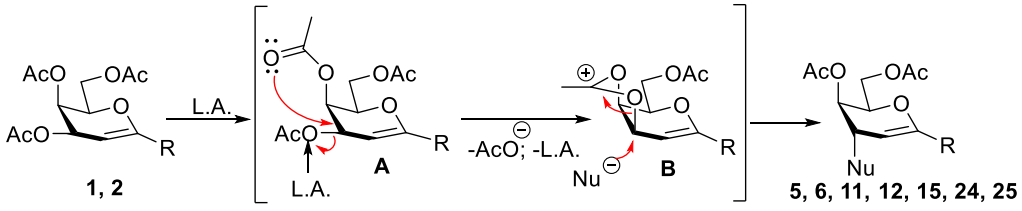
| |  **21** |  **23** |  **29** |
|---|---|---|---|
| H-3 | 6.36<br>$^3J_{3,4}$ = 10.1 | 6.36<br>$^3J_{3,4}$ = 10.0 | 6.30<br>$^3J_{3,4}$ = 10.2<br>$^4J_{3,5}$ = 1.9 |
| H-4 | 6.08<br>$^3J_{3,4}$ = 10.1<br>$^3J_{4,5}$ = 5.6 | 6.12<br>$^3J_{3,4}$ = 10.0<br>$^3J_{4,5}$ = 5.6 | 5.98<br>$^3J_{3,4}$ = 10.2<br>$^3J_{4,5}$ = 1.9 |
| H-5 | 5.13<br>$^3J_{4,5}$ = 5.6<br>$^3J_{5,6}$ = 2.6 | 5.19<br>$^3J_{4,5}$ = 5.6<br>$^3J_{5,6}$ = 2.6 | 5.78<br>$^3J_{5,6}$ = 9.4<br>$^4J_{3,5}$ = $^3J_{4,5}$ = 1.9 |
| H-6 | 4.68<br>$^3J_{6,7a}$ = 7.5<br>$^3J_{6,7b}$ = 5.1<br>$^3J_{5,6}$ = 2.6 | 4.65<br>$^3J_{6,7a}$ = 7.5<br>$^3J_{6,7b}$ = 5.6<br>$^3J_{5,6}$ = 2.6 | 4.74<br>$^3J_{5,6}$ = 9.4<br>$^3J_{6,7a}$ = 5.7<br>$^3J_{6,7b}$ = 2.6 |

**Table 6**
Characteristic $^1$H NMR data for the new compounds ($CDCl_3$, $\delta$ [ppm], $J$ [Hz]).

| |  **5** |  **6** |  **11** |  **12** |
|---|---|---|---|---|
| H-3 | 6.11<br>$^3J_{3,4}$ = 5.2<br>$^4J_{3,5}$ = 1.6 | 6.14<br>$^3J_{3,4}$ = 5.2<br>$^4J_{3,5}$ = 1.6 | 6.14<br>$^3J_{3,4}$ = 5.2<br>$^4J_{3,5}$ = 1.6 | 6.17<br>$^3J_{3,4}$ = 5.2<br>$^4J_{3,5}$ = 1.4 |
| H-4 | 3.83<br>$^3J_{4,5}$ = 2.0 | 3.85<br>$^3J_{4,5}$ = 2.1 | 3.80<br>$^3J_{4,5}$ = 2.0 | 4.00<br>$^3J_{4,5}$ = 2.0 |
| H-5 | 5.09 | 5.10 | 5.02 | 5.06 |
| |  **15** |  **16** |  **24** |  **25** |
| H-3 | 6.16<br>$^3J_{3,4}$ = 5.4<br>$^4J_{3,5}$ = 1.2 | 5.91<br>$^3J_{3,4}$ = 5.4<br>$^4J_{3,5}$ = 1.41 | 5.94<br>$^3J_{3,4}$ = 5.3<br>$^4J_{3,5}$ = 1.2 | 6.14<br>$^3J_{3,4}$ = 5.3<br>$^4J_{3,5}$ = 1.5 |
| H-4 | 4.46<br>$^3J_{4,5}$ = 2.1 | 4.24<br>$^3J_{4,5}$ = 2.6 | 3.89<br>$^3J_{4,5}$ = 1.4 | 4.04<br>$^3J_{4,5}$ = 2.3 |
| H-5 | 5.20 | 5.12 | 5.20 – 5.11 | 4.96 |




**Scheme 1.** Plausible mechanism of the formation of C-4 substituted products.

Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. Optical rotations were determined with a Jasco P-2000 Polarimeter at 25 °C. NMR spectra were recorded on a Bruker AVANCE 400 (400/100 MHz for $^1$H/$^{13}$C) spectrometer at 298 ± 0.1 K and on a Bruker Avance II (500/125 MHz for $^1$H/$^{13}$C) spectrometer at 300 ± 0.1 K. Chemical shifts are referenced to TMS or to the residual solvent peaks. Chemical shifts ($\delta$ scale) are reported in ppm, coupling constants in Hz. All compounds were characterized by one- ($^1$H and $^{13}$C) and two-dimensional (COSY, HSQC) NMR spectra. High resolution mass spectra were recorded by a Bruker maXis II UHR ESI-TOF MS or an Agilent 6200 series TOF/6500 series Q-TOF instrument in positive mode. IR spectra were recorded by Jasco FT-IR 4000. The X-ray measurement was performed on Bruker D8 VENTURE diffractometer.

### 3.2. General procedure for the reaction of 1-C substituted glycals with nucleophiles in the presence of lewis acid

Under $N_2$ atmosphere, the solution of the glycal (100 mg, 1.0 equiv.) in dry ACN (2.5 mL) was cooled down to 0 °C, then the nucleophile (1.0 equiv.) and the Lewis acid (1.0 equiv.) were added to the solution under $N_2$ atmosphere. Subsequently the reaction mixture was stirred at the appropriate temperature, and the progress of the reaction was monitored by TLC. After the given time the mixture was concentrated under reduced pressure and the crude product was purified by column chromatography.

### 3.3. Synthesis and characterization of the compounds

#### 3.3.1. Methyl 5,7-di-O-acetyl-2,6-anhydro-4-O-benzyl-3-deoxy-D-xylo-hept-2-enonate (5)

Prepared from 1-methoxycarbonyl-glycal **1** (100 mg, 0.303 mmol, 1.0 equiv.) and benzyl-alcohol (31 μl, 0.303 mmol, 1.0 equiv.) in the presence of $BF_3OEt_2$ (37 μl, 0.303 mmol, 1.0 equiv.) according to general procedure (reaction time: 1 day). Purified by column chromatography (eluent: hexane: ethyl acetate = 5:1 to 3:1 gradient) to give 9 mg (12%, conversion: 65%) **5** as a colorless oil ($R_f$ = 0.46, hexane: ethyl acetate = 1:1); $[\alpha]_D$ +90 (c 0.16, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 7.39–7.28 (5H, m, aromatics), 6.11 (1H, dd, $J$ = 5.2, 1.6 Hz, H-3), 5.09 (1H, dd, $J$ = 3.3, 1.6 Hz, H-5), 4.75 (1H, d, $J$ = 11.9 Hz $CH_{2A}$Bn), 4.71 (1H, d, $J$ = 11.9 Hz $CH_{2B}$Bn), 4.38–4.34 (2H, m, H-7, H-7'), 4.32–4.29 (1H, m, H-6), 3.84–3.81 (4H, m, H-4, $OCH_3$), 2.10 (3H, s, $CH_3CO$), 2.05 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm):

170.7, 170.2, 162.5 (C═O), 145.7 (C-2), 137.8, 128.7, 128.2, 128.0 (aromatics), 106.9 (C-3), 71.7 (C-6), 71.1 ($CH_2$), 68.1 (C-4), 66.7 (C-5), 62.2 (C-7), 52.7 ($OCH_3$), 20.9 (2 x $CH_3CO$). HRMS positive mode *m/z:* calculated $C_{19}H_{22}O_8Na^+$ $[M+Na]^+$ 401.1207, found 401.1198.

### 3.3.2. 5,7-Di-O-acetyl-2,6-anhydro-4-O-benzyl-3-deoxy-D-xylo-hept-2-enonamide (6)

Prepared from 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 equiv.) and benzyl alcohol (33 μl, 0.317 mmol, 1.0 equiv.) in the presence of in the presence of $BF_3OEt_2$ (39 μl, 0.303 mmol, 1.0 equiv.) according to general procedure (reaction time: 1 day). Purified by column chromatography (eluent: hexane: acetone = 3:1 to 2:1 gradient) to give **6** as a yellowish foam (24 mg, 36%, conversion: 58%) ($R_f$ = 0.27, hexane: acetone = 1:1); $[\alpha]_D$ +91 (c 1.21, DCM). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (ppm): 7.37–7.27 (5H, m, aromatics), 6.52 (2H, s, $CONH_2$), 6.14 (1H, dd, $J$ = 5.2 and 1.6 Hz, H-3), 5.10 (1H, dd, $J$ = 2.1, and 1.6 Hz, H-5), 4.73 (1H, d, $J$ = 12.0, $CH_{2A}$Bn); 4.69 (1H, d, $J$ = 12.0 Hz, $CH_{2B}$Bn), 4.40–4.27 (3H, m, H-6, H-7, H-7'), 3.85 (1H, dd, $J$ = 5.2, 2.1 Hz, H-4), 2.10 (3H, s, $CH_3CO$), 2.05 (3H, s, $CH_3CO$). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (ppm): 170.6, 170.1, 163.4 (C═O), 147.1 (C-2), 137.6, 128.6, 128.0, 127.9 (aromatics), 103.1 (C-3), 71.9 (C-6), 70.7 ($CH_2$), 67.8 (C-4), 66.8 (C-5), 62.5 (C-7), 20.8 (2 x $CH_3CO$). HRMS positive mode *m/z:* calculated $C_{18}H_{21}NO_7Na^+$ $[M+Na]^+$ 386.1210, found 386.1212.

### 3.3.3. Methyl 5,7-di-O-acetyl-4-O-allyl-2,6-anhydro-3-deoxy-D-xylo-hept-2-enonate (11)

Prepared from 1-methoxycarbonyl-glycal **1** (100 mg, 0.303 mmol, 1.0 equiv.) and allyl-alcohol (21 μl, 0.303 mmol, 1.0 equiv.) in the presence of $BF_3OEt_2$ (37 μl, 0.303 mmol, 1.0 equiv.) according to general procedure (reaction time: 1 day). Purified by column chromatography (eluent: hexane: ethyl acetate = 3:1) to give 27 mg (24%, conversion: 71%) **11** as a colorless oil ($R_f$ = 0.51, hexane: ethyl acetate = 1:1); $[\alpha]_D$ +86 (c 0.43, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 6.14 (1H, dd, $J$ = 5.2, 1.6 Hz, H-3), 5.91 (1H, ddt, $J$ = 17.1, 10.5, 5.6 Hz, CH-allyl), 5.32 (1H, ddd, $J$ = 17.2, 3.2, 1.7 Hz, =$CH_2$-allyl), 5.23 (1H, ddd, $J$ = 10.4, 2.7, 1.5 Hz, =$CH_2$-allyl), 5.02 (1H, dd, $J$ = 3.2, 1.6 Hz, H-5), 4.35 (2H, dd, $J$ = 6.4, 2.6 Hz, H-7, H-7'), 4.27 (1H, t, $J$ = 6.3 Hz, H-6), 4.19 (2H, tt, $J$ = 5.8, 1.4 Hz, $CH_2$-allyl), 3.83 (3H, s, $OCH_3$), 3.80 (1H, dd, $J$ = 5.2, 2.0 Hz, H-4), 2.10 (3H, s, $CH_3CO$), 2.06 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.6, 170.2, 162.5 (C═O), 145.6 (C-2), 134.2 (=**C**H-allyl), 118.0 (=**C**$H_2$-allyl), 106.8 (C-3), 71.6 (C-6), 70.1 (**C**$H_2$-allyl), 68.0 (C-4), 66.7 (C-5), 62.2 (C-7), 52.6 ($OCH_3$), 20.9 (2 x $CH_3CO$). HRMS positive mode *m/z:* calculated $C_{15}H_{20}O_8Na^+$ $[M+Na]^+$ 351.1050, found 351.1052.

### 3.3.4. Methyl 5,7-di-O-acetyl-2,6-anhydro-3-deoxy-4-O-propargyl-D-xylo-hept-2-enonate (12)

Prepared from 1-methoxycarbonyl-glycal **1** (100 mg, 0.303 mmol, 1.0 equiv.) and propargyl-alcohol (17 μl, 0.303 mmol, 1.0 equiv.) in the presence of $BF_3OEt_2$ (37 μl, 0.303 mmol, 1.0 equiv.) according to general procedure (reaction time: 1 day). Purified by column chromatography (eluent: hexane: ethyl acetate = 3:1) to give 29 mg (23%, conversion: 79%) **12** as a colorless oil ($R_f$ = 0.53, hexane:ethyl acetate = 1:1); $[\alpha]_D$ +111 (c 0.41, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 6.17 (1H, dd, $J$ = 5.2, 1.4 Hz, H-3), 5.06 (1H, dd, $J$ = 3.4, 1.6 Hz, H-5), 4.33 (4H, m, H-7, H-7', $CH_2$-propargyl), 4.25 (1H, t, $J$ = 6.3 Hz, H-6), 4.00 (1H, dd, $J$ = 5.2, 2.0 Hz, H-4), 3.84 (3H, s, $OCH_3$), 2.50 (1H, t, $J$ = 2.4 Hz, C≡CH), 2.10 (3H, s, $CH_3CO$), 2.08 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.6, 170.1, 162.3 (C═O), 146.0 (C-2), 106.1 (C-3), 79.2 ($CH_2$–**C**≡CH), 75.4 ($CH_2$–C≡**C**H), 71.7 (C-6), 67.9 (C-4), 66.4 (C-5), 62.1 (C-7), 56.3 (**C**$H_2$–C≡CH), 52.7 ($OCH_3$), 20.9 (2x $CH_3CO$). HRMS positive mode *m/z:* calculated $C_{15}H_{18}O_8Na^+$ $[M+Na]^+$ 349.0894, found 349.0891.

### 3.3.5. 5,7-Di-O-acetyl-2,6-anhydro-4-chloro-3,4-dideoxy-D-xylo-hept-2-enonamide (15)

It was isolated from the reaction of 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 equiv.) with phenol (30 mg, 0.317 mmol, 1.0 equiv.) in the presence of $TiCl_4$ (35 μl, 0.317 mmol, 1.0 equiv.) according to the general procedure (reaction time: 4 days). Purified by column chromatography (eluent: hexane: acetone = 3:1 to 1:1 gradient) to give 30 mg (71%, conversion: 46%) **15** as a yellowish foam ($R_f$ = 0.34, hexane: acetone = 1:1); $[\alpha]_D$ +196 (c 0.53, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 6.46 (1H, s, $CONH_2$), 6.16 (1H, d, $J$ = 5.4 Hz, H-3), 6.11 (1H, s, $CONH_2$), 5.20 (1H, brs, H-5), 4.60 (1H, t, $J$ = 6.2 Hz, H-6), 4.46 (1H, dd, $J$ = 5.4, 2.1 Hz, H-4), 4.38 (1H, dd, $J$ = 11.7, 7.0 Hz, H-7), 4.30 (1H, dd, $J$ = 11.7, 5.4 Hz, H-7'), 2.13 (3H, s, $CH_3CO$), 2.11 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.6, 169.8, 162.7 (C═O), 146.8 (C-2), 103.9 (C-3), 71.0 (C-6), 68.6 (C-5), 62.2 (C-7), 48.6 (C-4), 20.9, 20.8 ($CH_3CO$). HRMS positive mode *m/z:* calculated $C_{11}H_{14}NO_6ClNa^+$ $[M+Na]^+$ 314.0402, found 314.0402.

### 3.3.6. 4-Acetamido-5,7-di-O-acetyl-2,6-anhydro-3,4-dideoxy-D-xylo-hept-2-enonamide (16)

It was isolated from the reaction of 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 equiv.) with phenol (30 mg, 0.317 mmol, 1.0 equiv.) in the presence of $BF_3OEt_2$ (39 μl, 0.317 mmol, 1.0 equiv.) according to general procedure (reaction time: 7 days). Purified by column chromatography (eluent: hexane: acetone = 3:1 to 1:3 gradient) to give 45 mg (64%, conversion: 70%) **16** as a white foam ($R_f$ = 0.20, hexane: acetone = 1:3); $[\alpha]_D$ +132 (c 0.32, DCM). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (ppm): 7.02 (1H, d, $J$ = 7.7 Hz, CONH), 6.68 (1H, s, $CONH_2$), 6.54 (1H, s, $CONH_2$), 5.91 (1H, d, $J$ = 5.2 Hz, H-3), 5.12 (1H, brs, H-5), 4.46 (1H, ddd, $J$ = 7.87 Hz, 5.23 Hz, 2,53 Hz H-6), 4.27 (2H, brs, H-7, H-7'), 4.24 (1H, brs, H4). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (ppm): 171.0, 169.8, 169.7, 163.6 (C═O), 146.7 (C-2), 103.7 (C-3), 72.3 (C-6), 67.1 (C-5), 62.7 (C-7), 43.9 (C-4), 23.1 ($CH_3CONH$), 20.9 (2 x $CH_3CO$). HRMS positive mode *m/z:* calculated $C_{13}H_{18}N_2O_7Na^+$ $[M+Na]^+$ 337.1012, found 337.1015.

### 3.3.7. (Benzyl 5,7-di-O-acetyl-3,4-dideoxy-2-thio-α-D-threo-hept-3-en-2-ulopyranoside)onamide (21)

Prepared from 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 equiv.) and benzyl thiol (37 μl, 0.317 mmol, 1.0 equiv.) in the presence of $TiCl_4$ (35 μl, 0.317 mmol, 1.0 equiv.) according to general procedure (reaction time: 2 days). Purified by column chromatography (eluent: hexane: acetone = 6:1 to 2:1 gradient) to give 20 mg (29%, conversion: 57%) **21** as a yellowish foam ($R_f$ = 0.40, hexane: acetone = 1:1); $[\alpha]_D$ −157 (c 0.28, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 7.33–7.22 (5H, m, aromatics), 6.72 (1H, s, $CONH_2$), 6.36 (1H, d, $J$ = 10.1 Hz, H-3), 6.09 (1H, s, $CONH_2$), 6.08 (1H, dd, $J$ = 10.1, 5.6 Hz, H-4), 5.13 (1H, dd, $J$ = 5.6, 2.6 Hz, H-5), 4.68 (1H, ddd, $J$ = 7.5, 5.1, 2.6 Hz, H-6), 4.25–4.18 (2H, m, H-7, H-7'), 3.85 (2H, dd, $J$ = 19.3, 12.1 Hz, $CH_2$), 2.09 (3H, s, $CH_3CO$), 2.08 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.7, 170.3, 170.1 (C═O), 136.6 (aromatics), 131.5 (C-3), 129.2, 128.7, 127.5 (aromatics), 124.4 (C-4), 87.8 (C-2), 69.5 (C-6), 62.8 (C-5), 62.4 (C-7), 34.5 ($CH_2$), 21.0, 20.9 ($CH_3CO$). HRMS positive mode *m/z:* calculated $C_{18}H_{21}NO_6SNa^+$ $[M+Na]^+$ 402.0982, found 402.0981.

### 3.3.8. [(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl) 5,7-di-O-acetyl-3,4-dideoxy-2-thio-α-D-threo-hept-3-en-2-ulopyranoside]onamide (23) and 4-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5,7-di-O-acetyl-2,6-anhydro-3-deoxy-4-thio-D-xylo-hept-2-enonamide (24)

Prepared from 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 equiv.) and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**22**) (115 mg, 0,317 mmol, 1.0 equiv.) in the presence of $BF_3OEt_2$ (39 μl, 0.317 mmol, 1.0 equiv.) in dry acetonitrile (2.5 mL), according to general procedure (reaction time: 3 days). Purified by column chromatography (eluent: hexane: acetone = 2:1) to give 29 mg **23** and 40 mg **24** (conversion: 70%, yields: 21% and 40%) as a yellowish foam ($R_f$ = 0.44 for **23** and 0.28 for **24**, hexane: acetone = 1:1). $[\alpha]_D$ −31,08 (c 0.166, DCM)

of **23**. $[\alpha]_D$ +15.33 (c 0.17, DCM) of **24**.

$^1$H NMR data of **23** (500 MHz, $CDCl_3$) $\delta$ (ppm): 6.71 (1H, d, $J$ = 3.1 Hz, $CONH_2$), 6.36 (1H, d, $J$ = 10.0 Hz, H-3), 6.12 (1H, dd, $J$ = 10.0, 5.6 Hz, H-4), 5.63 (1H, d, $J$ = 3.1 Hz, $CONH_2$), 5.22 (1H, t, $J$ = 9.4 Hz, H-3′), 5.19 (1H, dd, $J$ = 5.6, 2.6 Hz, H-5), 5.04 (1H, t, $J$ = 9.8 Hz, H-4′), 4.98 (1H, dd, $J$ = 10.2, 9.4 Hz, H-2′), 4.74 (1H, d, $J$ = 10.2 Hz, H-1′), 4.65 (1H, ddd, $J$ = 7.5, 5.6, 2.6 Hz, H-6), 4.38 (1H, dd, $J$ = 11.0, 7.5 Hz, H-7a), 4.23–4.15 (3H, m, H-7b, H-6′a, H-6′b), 3.71 (1H, ddd, $J$ = 10.0, 4.2, 2.9 Hz, H-5′), 2.09 (3H, s, $CH_3CO$), 2.07 (9H, s, 3x $CH_3CO$), 2.02 (3H, s, $CH_3CO$), 2.00 (3H, s, $CH_3CO$). $^{13}$C NMR data of **23** (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.6 (2x), 170.2 (2x), 169.9, 169.5, 168.8 (C═O), 130.6 (C-3), 125.1 (C-4), 87.9 (C-2), 82.8 (C-1′), 76.3 (C-5′), 73.8 (C-3′), 69.9 (C-2′), 69.3 (C-6), 68.4 (C-4′), 62.5 (C-6′), 62.1 (C-5), 61.3 (C-7), 20.9 (2x), 20.8 (2x), 20.7 (2x) ($CH_3CO$). HRMS positive mode *m/z:* calculated $C_{25}H_{33}NO_{15}SNa^+$ $[M+Na]^+$ 642.1463, found 642.1465.

$^1$H NMR data of **24** (500 MHz, $CDCl_3$) $\delta$ (ppm): 6.39 (1H, s, $CONH_2$), 5.94 (1H, dd, $J$ = 5.3, 1.2 Hz, H-3), 5.81 (1H, s, $CONH_2$), 5.26 (1H, t, $J$ = 9.3 Hz, H-3′), 5.15 (1H, d, $J$ = 9.9 Hz; H-4′), 5.13 (1 H, d, $J$ = 9.9 Hz; H-2′), 5.11 (m, H-5), 4.74 (1H, d, $J$ = 10.0 Hz, H-1′), 4.51–4.45 (1H, m, H-6), 4.38 (1H, dd, $J$ = 11.7, 7.2 Hz, H-7a), 4.31 (1H, dd, $J$ = 11.7, 4.8 Hz, H-7b), 4.26 (1H, dd, $J$ = 12.4, 4.7 Hz, H-6′a), 4.15 (1H, dd, $J$ = 12.4, 2.1 Hz, H-6′b), 3.89 (1H, d, $J$ = 5.2 Hz, H-4), 3.75 (1H, ddd, $J$ = 9.8, 4.7, 2.1 Hz, H-5′), 2.10 (3H, s, $CH_3CO$), 2.08 (3H, s, $CH_3CO$), 2.05 (3H, s, $CH_3CO$), 2.04 (3H, s, $CH_3CO$), 2.02 (3H, s, $CH_3CO$), 2.01 (3H, s, $CH_3CO$). $^{13}$C NMR data of **24** (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.7 (2x), 170.3 (2x), 169.5 (2x), 162.8 (C═O), 146.8 (C-2), 102.3 (C-3), 82.3 (C-1′), 76.5 (C-5′), 73.8 (C-3′), 71.0 (C-6), 69.6 (C-5), 69.2 (C-2′), 68.2 (C-4′), 63.1 (C-7), 62.0 (C-6′), 37.6 (C-4), 21.0, 20.9, 20.8, 20.7 (3x) ($CH_3CO$). HRMS positive mode *m/z:* calculated $C_{25}H_{33}NO_{15}SNa^+$ $[M+Na]^+$ 642.1463, found 642.1467.

### *3.3.9. 5,7-Di-O-acetyl-2,6-anhydro-4-azido-3,4-dideoxy-D-xylo-hept-2-enonamide (25)*

Prepared from 1-carbamoyl-glycal **2** (100 mg, 0.317 mmol, 1.0 eqiuv.) and sodium azide (52 mg, 0.793 mmol, 2.5 equiv.) in the presence of $BF_3OEt_2$ (39 μl, 0.317 mmol, 1.0 equiv.) according to general procedure (reaction time: 4 days). Purified by column chromatography (eluent: hexane: acetone = 3:1 to 2:1 gradient) to give 27 mg (45%, conversion: 63%) **25** as a yellowish foam ($R_f$ = 0.36, hexane: acetone = 1:1); $[\alpha]_D$ +257 (c 0.37, DCM). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (ppm): 6.49 (1H, s, $CONH_2$), 6.15 (1H, s, $CONH_2$), 6.14 (1H, dd, $J$ = 5.3, 1.5 Hz, H-3), 4.96 (1H, brs, H-5), 4.37 (1H, dd, $J$ = 11.4, 6.9 Hz, H-7), 4.31–4.24 (2H, m, H-6, H-7'), 4.04 (1H, dd, $J$ = 5.3, 2.3 Hz, H-4), 2.13 (3H, s, $CH_3CO$), 2.10 (3H, s, $CH_3CO$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.6, 169.9, 162.6 (C═O), 147.9 (C-2), 100.1 (C-3), 71.9 (C-6), 66.7 (C-5), 62.2 (C-7), 53.3 (C-4), 20.9, 20.8 ($CH_3CO$). IR (KBr, $cm^{-1}$): 2103 ($N_3$). HRMS positive mode *m/z:* calculated $C_{11}H_{14}N_4O_6Na^+$ $[M+Na]^+$ 321.0806, found 321.0807.

### *3.3.10. (Benzyl 5,7-di-O-benzoyl-3,4-dideoxy-2-thio-α-D-erythro-hept-3-en-2-ulopyranoside)onamide (29)*

Prepared from 1-carbamoyl-glycal **27** (100 mg, 0.199 mmol, 1.0 equiv.) and benzyl thiol (24 μl, 0.199 mmol, 1.0 equiv.) in the presence of $TiCl_4$ (22 μl, 0.199 mmol, 1.0 equiv.) according to general procedure (reaction time: 4 days). Purified by column chromatography (eluent: hexane: acetone = 5:1 to 2:1 gradient) to give 25 mg (42%, conversion: 59%) **29** as a yellowish foam ($R_f$ = 0.50, hexane: acetone = 1:1); $[\alpha]_D$ +125 (c 0.52, DCM). $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ (ppm): 8.10–8.00 (4H, m, aromatics), 7.59 (1H, t, $J$ = 7.4 Hz, aromatics), 7.54 (1H, t, $J$ = 7.4 Hz, aromatics), 7.45 (2H, t, $J$ = 7.8 Hz, aromatics), 7.39 (2H, t, $J$ = 7.8 Hz, aromatics), 7.26–7.21 (5H, m, aromatics), 6.82 (1H, d, $J$ = 3.8 Hz, $CONH_2$), 6.30 (1H, dd, $J$ = 10.2, 1.9 Hz, H-3), 6.24 (1H, d, $J$ = 3.8 Hz, $CONH_2$), 5.98 (1H, dd, $J$ = 10.2, 1.9 Hz, H-4), 5.78 (1H, dt, $J$ = 9.4, 1.9 Hz, H-5), 4.74 (1H, ddd, $J$ = 9.4, 5.7, 2.6 Hz, H-6), 4.53 (1H, dd, $J$ = 12.2, 5.7 Hz, H-7), 4.44 (1H, dd, $J$ = 12.2, 2.6 Hz, H-7'), 3.86 (1H, d, $J$ = 12.3 Hz, $CH_2$), 3.78 (1H, d, $J$ = 12.3 Hz, $CH_2$). $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ (ppm): 170.5, 166.6, 165.9 (C═O), 136.6, 133.7, 133.5, 130.0, 129.8, 129.7, 129.3, 129.2 (aromatics), 129.0 (C-3), 128.7 (aromatics), 127.6 (C-4), 127.4 (aromatics), 88.0 (C-2), 70.2 (C-6), 65.3 (C-5), 63.3 (C-7), 35.1 ($CH_2$). HRMS positive mode *m/z:* calculated $C_{28}H_{25}NO_6SNa^+$ $[M+Na]^+$ 526.1295, found 526.1294.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carres.2022.108582.

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