Carbohydrate Research 504 (2021) 108292

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Halogen addition to some 1-C-substituted pyranoid glycals

Levente Homolya, László Juhász, László Somsák *

Department of Organic Chemistry, University of Debrecen, POB 400, H-4002, Debrecen, Hungary

ARTICLE INFO

Keywords:
1-C-Substituted glycal
Halogen addition
Glycosyl halide
Glycosylation

ABSTRACT

Addition of bromine and chlorine to *O*-peracylated 1-CN-, COOMe- and $CONH_2$-substituted glycals was studied under ionic and radical conditions. The main or exclusive products were the corresponding 2,3-*trans*-diaxial (3-bromo-3-deoxy-α-D-heptopyranosylbromide)onic acid derivatives. Bromination of the *O*-peracetylated D-*lyxo*-hept-2-enopyranosononitrile and all chlorinations proved selective towards the 2-axial-3-equatorial (3-halogeno-3-deoxy-α-D-heptopyranosylhalide)onic acid derivatives. Silver triflate promoted glycosylation of methanol was successful with each 2,3-*trans*-diaxial (3-bromo-3-deoxy-α-D-heptopyranosylbromide)onic acid derivative, however, several attempted nucleophilic substitution and elimination reactions gave the parent glycal only.

1. Introduction

Glycals, the 1,2-unsaturated cyclic monosaccharide derivatives, are versatile and widely used starting materials in carbohydrate and natural product syntheses [1,2]. 1-C-Substituted glycals having a carbon substituent attached to the C-1 centre of glycals are much less frequent and explored [3]. We have a long standing interest in glycals with 1-CN, 1-$CONH_2$, and 1-COOR substitution which can be considered as special anhydro-aldonic acid derivatives [4]. These substituents of electron withdrawing nature alter the properties of the glycal double bond and together with the ring oxygen atom make the C-1 centre capto-datively substituted thereby rendering such compounds to be sensitive to radical reactions [5]. As a part of a program to explore the reactivity of these compounds we have reported their transformations with malonyl [6,7] and thiyl [8] radicals. On the other hand, ionic reactions of these 1-C-substituted glycals have not yet been investigated except keto-deoxy-octulosonic acid (KDO) and *N*-acetyl-neuraminic acid (Neu5Ac) derived variants, therefore, we have embarked to systematically study such reactions.

Electrophilic addition of halogens to C–C double bonds are among the basic transformations of olefins in general [9] and also of glycals in particular [10]. The reaction of Neu5Ac2en and F_2 was reported to give a *syn* addition product with 2-axial and 3-equatorial fluorines ($^2C_5$ conformation) [11,12], and XeF_2 in the presence of $BF_3{\cdot}OEt_2$ gave the same difluoro compound [12,13]. Addition of bromine was investigated with Neu5Acyl2en derivatives [13–18] and KDO glycal [19]. These reactions gave excellent yields of the 2,3-dibromo *anti* addition products with both bromines in axial positions ($^2C_5$ conformation). In several cases AgOTf promoted glycosylations were also carried out to demonstrate the differential reactivity of the two bromine atoms [14,16,18,20].

Herein we report our observations in reactions of *O*-peracylated 1-CN, 1-$CONH_2$, and 1-COOMe substituted glycals with bromine and chlorine as well as some ensuing reactions of the halogen addition products.

2. Results and discussion

The starting compounds e. i. the D-*arabino* configured 1-cyano- **1** [4], 1-methoxycarbonyl- **2** [4], 1-carbamoyl-glycal **3** [4], and the D-*lyxo* configured 1-cyano- **4** [21] and 1-carbamoyl-glycal **6** [22] were obtained by the published procedures. 1-Methoxycarbonyl-glycal **5** was prepared from methyl (3,4,5,7-tetra-*O*-acetyl-α-D-*galacto*-hept-2-ulopyranosylbromide)onate [23] by Zn/*N*-methylimidazole mediated reductive elimination [4,21,24] to give the target glycal identical to that obtained by different methods in the literature [7,25].

The halogen addition reactions are collected in Table 1. Brominations were studied first in CH_2Cl_2 at room temperature in the presence of 1.1 equiv. of Br_2 to show that *O*-perbenzoylated glycals **1** and **2** with a 1-cyano and a 1-methoxycarbonyl substituent gave the corresponding 2,3-*trans*-diaxial dibromo derivatives **7a** and **8a**, respectively, as sole products, while the 1-carbamoyl-glycal **3** furnished an inseparable mixture of the 2,3-*trans*-diaxial **9a** and the 2-axial-3-equatorial **9b** dibromo compounds in a ratio of 87 : 13. Under these conditions the *O*-peracetylated glycals **5** and **6** led to product mixtures **12a** + **12b** (ratio 96 : 4) and **14a** + **14b** (ratio 71 : 29), respectively. Cyano-glycal **4** gave a mixture of three products **10a** + **10b** + **16** in a ratio of 22 : 60 : 18. The formation of

* Corresponding author.
E-mail address: somsak.laszlo@science.unideb.hu (L. Somsák).

https://doi.org/10.1016/j.carres.2021.108292
Received 10 February 2021; Received in revised form 11 March 2021; Accepted 12 March 2021
Available online 19 March 2021

16 may be understood by a HBr elimination from **10b** where the *trans*-diaxial arrangement of H-3 and Br-2 meets the stereoelectronic conditions of the *anti* β-elimination. This may also suggest that the primary bromine addition reaction is more selective towards **10b**. Thus, under ionic conditions the 2,3-*trans*-diaxial dibromo (**a** type) stereoisomers proved the only or highly preponderant products. A single exception was the case of 1-cyano-glycal **4** whose reaction resulted in a different stereoselectivity.

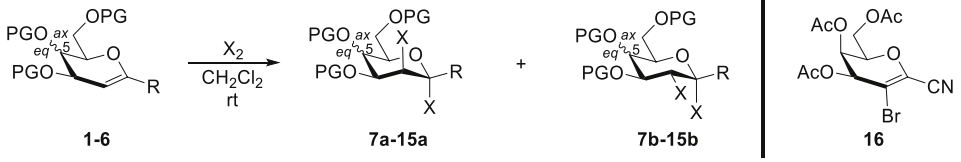
In general, the *O*-benzoyl protected **1**–**3** reacted slower than the *O*-peracetylated **4**–**6** which we tend to explain by the steric bulk of the protecting groups. The reaction times in both series (slowest CN < COOMe < $CONH_2$ fastest) correlate very well with the electron density of the double bonds influenced by the electron withdrawing power of the 1-C-substituent (CN > COOMe > $CONH_2$) as it follows from the corresponding Hammett σ values of the respective groups [8] and HOMO energies [7] of the double bonds.

Irradiation of the reaction mixtures significantly accelerated the transformations by a factor of 4–8 (Table 1). The reaction rates had the same trend as in the dark reactions with respect to both the protecting groups and the 1-C-substituents. Therefore, the same factors (steric hindrance and HOMO energy levels, respectively) must be considered to understand the differences. The irradiation left the stereoselectivity of the reactions essentially unchanged, though in cases of glycals **1**–**4** the measure of the selectivity increased.

Chlorine addition was performed with glycals **4**–**6** whereby the solvent CH_2Cl_2 was saturated with gaseous Cl_2 at r. t. These reactions gave the corresponding mixtures **11a** + **11b** (ratio 44 : 56), **13a** + **13b** (ratio 7 : 93) and **15a** + **15b** (ratio 5 : 95), respectively, to show a slight (CN substituent) or almost exclusive preference (COOMe and $CONH_2$ substituents) for the formation of the 2-axial-3-equatorial dichloro (**b** type) products.

The structural elucidation of the dihalogeno adducts was based on MS and NMR measurements. Mass spectra clearly showed the expected molecular ion clusters to indicate the presence of two halogen atoms in the products (see spectra in the supporting material). Structural peculiarities of the dihalogeno compounds were established by an analysis of their ^{1}H NMR spectra and comparisons with data of related compounds known in the literature. The most relevant data are presented in Table 2. Thus, the $^5C_2$(D) conformation of the sugar rings followed from the vicinal coupling constants that requires no further comments. The configuration of the C-3 centre was deduced from the $^3J_{H\text{-}3,H\text{-}4}$ coupling constants which were either in the range of 3–4 Hz or 10–11 Hz indicating the corresponding D-*manno/talo* or D-*gluco/galacto* configurations for the products, respectively (see columns C and D in Table 2). In the absence of NMR methods providing direct evidence, the anomeric configuration of the dihalogeno products was concluded from comparisons with chemical shift changes observed in pairs of 2,6-anhydro-hept-topyranosonic acid (Table 2, column A) and (α-D-hept-2-ulopyranosylhalide)onic acid derivatives (column B) known from the literature. Thus, replacement of H-2 of the 2,6-anhydro-heptonic acid derivatives by bromine resulted in downfield shifts of the H-4 and H-6 protons by 0.2–0.3 and 0.5–0.6 ppm, respectively (comparisons of data in entries 1–4, 6, and 8 for compounds in columns A and B). The only example for a similar chlorine replacement (entry 5) showed ~0.3 ppm downfield shift. The observation of similar downfield chemical shift changes for the brominated compounds (entries 1–4, 6, and 8) in the pairs A-C (H-4: 0.1–0.7 ppm, H-6: 0.4–0.7 ppm) and A-D (H-4: 0.1–0.3 ppm, H-6: 0.6–0.7 ppm) and the chlorinated ones (entries 5, 7, and 9) for the pairs A-C (H-4: ~0.6 ppm, H-6: 0.2–0.3 ppm) and A-D (H-4: 0.6–0.7 ppm, H-6: 0.6–0.7 ppm) allow to establish the α(D) anomeric configuration of the compounds in columns C and D. In addition, the downfield shifts of H-5 (0.4–0.6 ppm) for compounds **7a-9a** (entries 1–3) in comparison with the respective compounds in columns A and B corroborate the axial position of Br-3. For the bromo-glycal derivative

Table 1
Addition of halogens to 1-C-acceptor-substituted glycals.

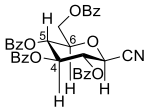
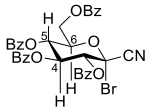
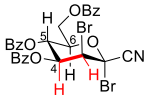
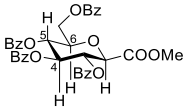
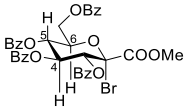
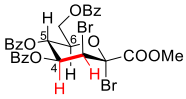
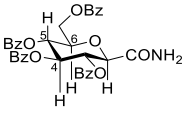
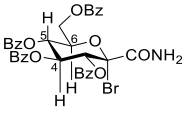
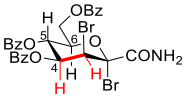
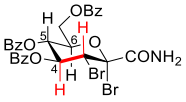
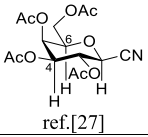
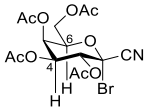
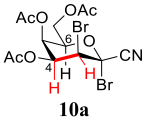
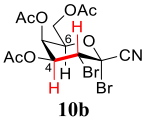
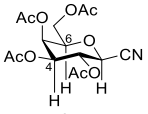
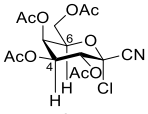
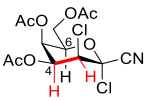
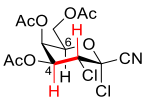


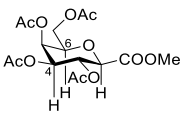
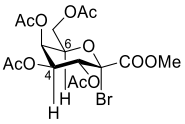
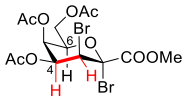
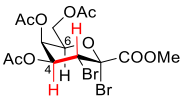
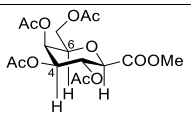
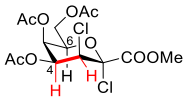
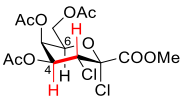
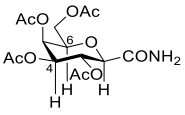
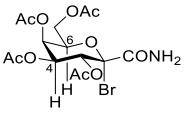
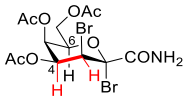
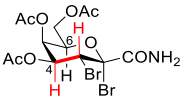
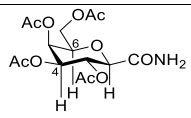
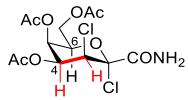
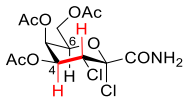
1-6 **7a-15a** **7b-15b** **16**

Starting compd.	R	PG	Orientation of PGO-5	X	Reaction time [h] (Other cond.)	Product (Yield [%])	Product ratio[a]
1	CN	Bz	*equatorial*	Br	24	**7a** (64)[b]	
					3 (hν)	**7a** (97)[c]	
2	COOMe			Br	12	**8a** (79)[b]	
					1.5 (hν)	**8a** (98)[c]	
3	$CONH_2$			Br	4	**9a** + **9b** (89)[b,d]	**9a** : **9b** = 87 : 13
					0.5 (hν)	**9a** (97)[c]	
4	CN	Ac	*axial*	Br	16	**10a** + **10b** + **16** (68)[b,d]	**10a**: **10b**: **16** = 22 : 60: 18
					2 (hν)	**10b** (95)[c]	
				Cl	36	**11a** + **11b** (66)[b,d]	**11a**: **11b** = 44 : 56
5	COOMe			Br	3	**12a** + **12b** (88)[b,d]	**12a**: **12b** = 96 : 4
					0.5 (hν)	**12a** + **12b** (98)[c,d]	**12a**: **12b** = 93 : 7
				Cl	2	**13a** + **13b** (71)[b,d]	**13a**: **13b** = 7 : 93
6	$CONH_2$			Br	1	**14a** + **14b** (77)[b,d]	**14a**: **14b** = 71 : 29
					0.25 (hν)	**14a** + **14b** (99)[c,d]	**14a**: **14b** = 80 : 20
				Cl	0.5	**15a** + **15b** (66)[b,d]	**15a**: **15b** = 5 : 95

[a] Based on the ^{1}H NMR spectrum of the product mixture.
[b] Isolated yield.
[c] Crude product.
[d] Inseparable mixture.

Table 2
Characteristic ^{1}H NMR data ($CDCl_3$, δ [ppm], J [Hz]) [23,26–30].

		A	B	C	D
Entry		2,6-anhydro-heptopyranosonic acid derivative	(α-D-*gluco*/*galacto*-hept-2-ulopyranosylhalide)onic acid derivative	(2-halogeno-2-deoxy-α-D-*manno*/*talo*-hept-2-ulopyranosylhalide)onic acid derivative	(2-halogeno-2-deoxy-α-D-*gluco*/*galacto*-hept-2-ulopyranosylhalide)onic acid derivative
1.		 ref.[26]	 ref.[26]	 **7a**	
	H-4	5.90-5.67	6.11	5.96 $^{3}J_{3,4} = 3.7$	
	H-5	5.90-5.67	5.84	6.23	
	H-6	4.20	4.72	4.61	
2.		 ref.[23]	 ref.[23]	 **8a**	
	H-4	5.96	6.17	6.08 $^{3}J_{3,4} = 3.6$	
	H-5	5.69	5.85	6.28	
	H-6	4.18	4.77	4.69	
3.		 ref.[26]	 ref.[26]	 **9a**	 **9b**
	H-4	5.96	6.14	6.13 $^{3}J_{3,4} = 3.5$	6.06 $^{3}J_{3,4} = 10.8$
	H-5	5.80-5.60	5.81	6.30	6.06
	H-6	4.20	4.72	4.64	4.78
4.		 ref.[27]		 **10a**	 **10b**
	H-4	5.01	5.33 (acetone-d6) [28] 5.28	5.60 $^{3}J_{3,4} = 4.0$	5.32 $^{3}J_{3,4} = 11.0$
	H-6	3.95	4.73 (acetone-d6) [28] 4.47	4.56	4.52
5.		 ref.[27]	 ref.[29]	 **11a**	 **11b**
	H-4	5.01	5.30	5.63 $^{3}J_{3,4} = 3.9$	5.30 $^{3}J_{3,4} = 10.8$
	H-6	3.95	4.54	4.59	4.59

6.		 ref.[23]	 ref.[23]	 **12a**	 **12b**
	H-4	5.11	5.34	5.73 $^3J_{3,4} = 4.0$	5.41 $^3J_{3,4} = 11.1$
	H-6	3.95	4.53	4.62	4.62
7.		 ref.[23]		 **13a**	 **13b**
	H-4	5.11		5.73 $^3J_{3,4} = 3.9$	5.36 $^3J_{3,4} = 11.0$
	H-6	3.95		4.53	4.63
8.		 ref.[30]	 ref.[22]	 **14a**	 **14b**
	H-4	5.08	5.31	5.76 $^3J_{3,4} = 4.0$	5.39 $^3J_{3,4} = 11.2$
	H-6	3.99	4.53	4.65	4.59
9.		 ref.[30]		 **15a**	 **15b**
	H-4	5.08		5.75 $^3J_{3,4} = 3.7$	5.35 $^3J_{3,4} = 11.1$
	H-6	3.99		4.67	4.60

16 the mass spectrum showed the presence of one Br. Small vicinal couplings of the ring protons ($^3J_{4,5} = 4.7$ Hz) in the ^{1}H NMR as well as quaternary carbon signals (130.9 ppm (C-2), 111.0 ppm (C-3)) in the ^{13}C NMR spectra indicated the presence of a fully substituted double bond to result in a half chair type ring to correspond to the depicted structure of **16**.

Mechanistic considerations to explain the observed stereoselectivities may not only rely on the gross electron withdrawing nature of the investigated substituents, since these groups may also exert stabilizing effects on the carbocations formed as intermediates. In addition, the specific configurational and conformational properties of the sugar rings as well as the protecting groups may also contribute to the final stereochemical outcome of the reactions. Effects of acceptor substituents on carbocationic centres have long been considered [31], and more recently a thorough study by high level quantum chemical calculations has shed light on the stability and structure of carbocations bearing electron-withdrawing groups [32]. Based on this latter work, one can count on two types of effects of such substituents on the positively charged carbon, namely resonance stabilization and bridging (see Fig. 1, **II** and **III**, as well as **IV**-**VI**, respectively, illustrating these intermediates adapted to sugar derivatives). Numerical representation of these effects (Table 3) show that acyl and carbamoyl substituted cations may benefit from both stabilization modes and the effects are comparable to the stabilization of secondary carbocations. The effect of a methoxycarbonyl substituent appearing in our work can most probably be placed between those of the acyl and carbamoyl groups. On the other hand, the cyano substituent, lacking the bridging possibility, is a neat destabilizing group (Fig. 1, **VIII**, **IX**, Table 3). These effects are complemented in the sugar derivatives by the resonance stabilization of the ring oxygen as depicted in Fig. 1, **I** and **VII**.

These considerations can be applied to the cations that may form during the halogen additions to glycals **1**–**6** (Scheme 1). Formula **A** shows the possibilities of the electrophilic attack by the halogen on the more stable $^5H_6$ conformation [4,33,34] of the glycals. Attack from the α-side may result in cations **B** and **C**, while the β-side attack may form **D** and **E**. The α-side attack may be preponderant especially with an axial PGO-5 substituent. This is corroborated by the fact that products of type **c** and **d**, that might be formed via **D** and **E**, were not observed in the product mixtures. However, cation **E** may, at least theoretically, contribute to the formation of type **a** products. This possibility may receive some support by reactions of iodide ions and glycals under oxidative conditions that show very high β-side selectivity with the assumed intermediacy of iodonium ions [10].

To estimate the relative stabilities of cations **B** and **C** resulting from the α-side attack, various electronic effects need to be considered. If R = CN (glycals **1** and **4**), **B** must be more stable than **C** due to i) the destabilization effect of CN in **C** and ii) the stabilizing anomeric effect of the axial X in **B**. The product can be formed by a β- *vs.* α-side attack of the nucleophile X^- on **B/B'**. The β-side attack may be more probable if the PGO-5 substituent is equatorial and this attack is also favoured by a possible stabilization of the positive charge on C-3 by the lone pair of X (especially Br) [9]. Thus, glycal **1** gave only **7a**. On the contrary, the bromination of **4** resulted in the formation of **10b** as the major product, that may be explained by the axial position of PGO-5 shielding the β-side of the sugar ring. Chlorination of **4** gave **11a** and **11b** in a ratio close to 1 : 1 which might be attributed to the smaller size of Cl relative to Br to result in less bridging by Cl in **B/B'** [9] and to allow both β- and α-side attacks.

If R = COOMe (glycals **2** and **5**), **B** may be more stable than **C**, and the above considerations can be applied to understand the sole formation of brominated **8a** from **2**, and the high prevalence of **12a** over **12b** (96 : 4)

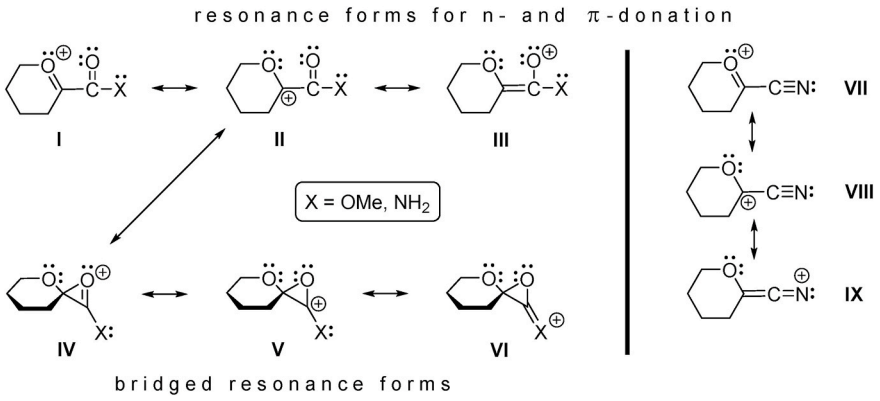


Fig. 1. Possibilities for the stabilization of 1-C-acceptor substituted glycosylium ions.

in the reaction of **5.** On the other hand, the chlorination of **5** gave an opposite product ratio **13a** : **13b** = 7 : 93 which may also raise the participation of **C** to open a parallel reaction pathway. In this case the relative stability of **C** may be closer to that of **B** due to the lesser anomeric stabilization of **B** by the axial Cl in comparison to Br. Attack of a Cl^- nucleophile on **C** must be more favourable from the axial direction due to a kinetic anomeric effect, thereby contributing to the dominant formation of the **b** type product.

If R = $CONH_2$ (glycals **3** and **6**), the stabilities of **B** and **C** may be even closer, thus, **C** may better contribute to the product formation as it is reflected by the higher proportion of the **b** type brominated compounds (**9a** : **9b** = 87 : 13; **14a** : **14b** = 71 : 29). It is of note that very recently an investigation of cations **C′** and **E'** (R = H, PG = Ac for both) in superacidic medium revealed their $^4H_5$ and $_3H^4$ conformations, respectively [35]. If the preferred conformation for cations **C** and **E** (R = COOMe, $CONH_2$) would be a similar half chair, the stereoelectronically preferred direction of attack of an X^- nucleophile would result in the **b** and **a** type products, respectively. Chlorination of **6** gave a similar product ratio (**15a** : **15b** = 5 : 95) to that of **5** (R = COOMe), therefore, the above explanation can be applied.

Table 3
Selected carbocation stabilization enthalpies (CSE, [kcal/mol]) from Ref. [32].

Carbocation	Experimental/ calculated value	Calculated value	
		Bridged form	Resonance stabilized form
$H_3C^{\oplus}$	0	–	–
$H_2C^{\oplus}-CH_3$ CH_3	67.5/58.2	–	–
$H_2C^{\oplus}-CH_2-CH_3$ CH_3	67.5/63.5	–	–
$H_2C^{\oplus}-C\equiv N$	–	–	−5.7
$H_2C^{\oplus}-C(=O)-CH_3$	–	42.1	5.3
$H_2C^{\oplus}-C(=O)-NMe_2$	–	66.1	20.1

Brominations under irradiation resulted in an increased formation of those stereoisomers which were the main products (**7a-9a**, **10b**, **12a**, **14a**) in the dark reactions. Radical attack on the least substituted carbon of a double bond is expected to follow the Bürgi-Dunitz trajectory (Scheme 2, **F**). In the present case this leads to capto-dative radicals **G** or **H** which, most probably similar to their fully *O*-peracetylated counterparts (PG = Ac, X = OAc), exist in the depicted $_{3,6}B$ and $^5C_2$ conformations, respectively [36]. Subsequent bromine abstraction from the α-side, characteristic of glycosyl radicals [36], gives the final products. The preference for the α- or β-side attack of $Br^{\bullet}$ radicals on **F** to give **G** or **H**, respectively, may be influenced by the steric shielding of the ring by the substituents. Thus, the addition of the bromine radical from the α-side could be expected, especially with the substrates having an axial PGO-5. However, only one of the products (**10b**) was formed via **G**, while all the others must have been formed via **H**. Though radical attacks on glycals from both sides of the sugar ring are known [10] and are also exemplified within glycals **1**–**6** [6–8], such a differential behaviour in the same type of reaction of very similar substrates is unusual. Nevertheless, in these reactions the β-side attack of $Br^{\bullet}$ radicals seems to be the rule rather than the exception. This may resemble similar β-side selectivity in reactions of 1-unsubstituted glycals with iodide ion under oxidative conditions where the intermediacy of $I^{\bullet}$ radicals cannot be excluded [10].

Next we have investigated some transformations of the dibromides **7**–**9**. First, glycosylation of methanol was carried out in the presence of AgOTf as a promoter (Table 4). The reactions gave good yield of the corresponding glycosides **17a** and **18a**. When the mixture **9a** + **9b** was reacted, the formation of **19a** + **19b** was observed in the same ratio as that of the starting materials. The reactions gave the α-glycosides in each case that may be attributed to the operation of a kinetic anomeric effect. This observation corresponds to literature experiences with Neu5Ac and

KDO derived dibromides [14,16,18,20].

The α(D) configuration of glycosides **17**–**19** followed from measurements of nuclear Overhauser effects showing proximity of the OMe group with the H-4 and H-6 protons of the sugar ring (Table 5).

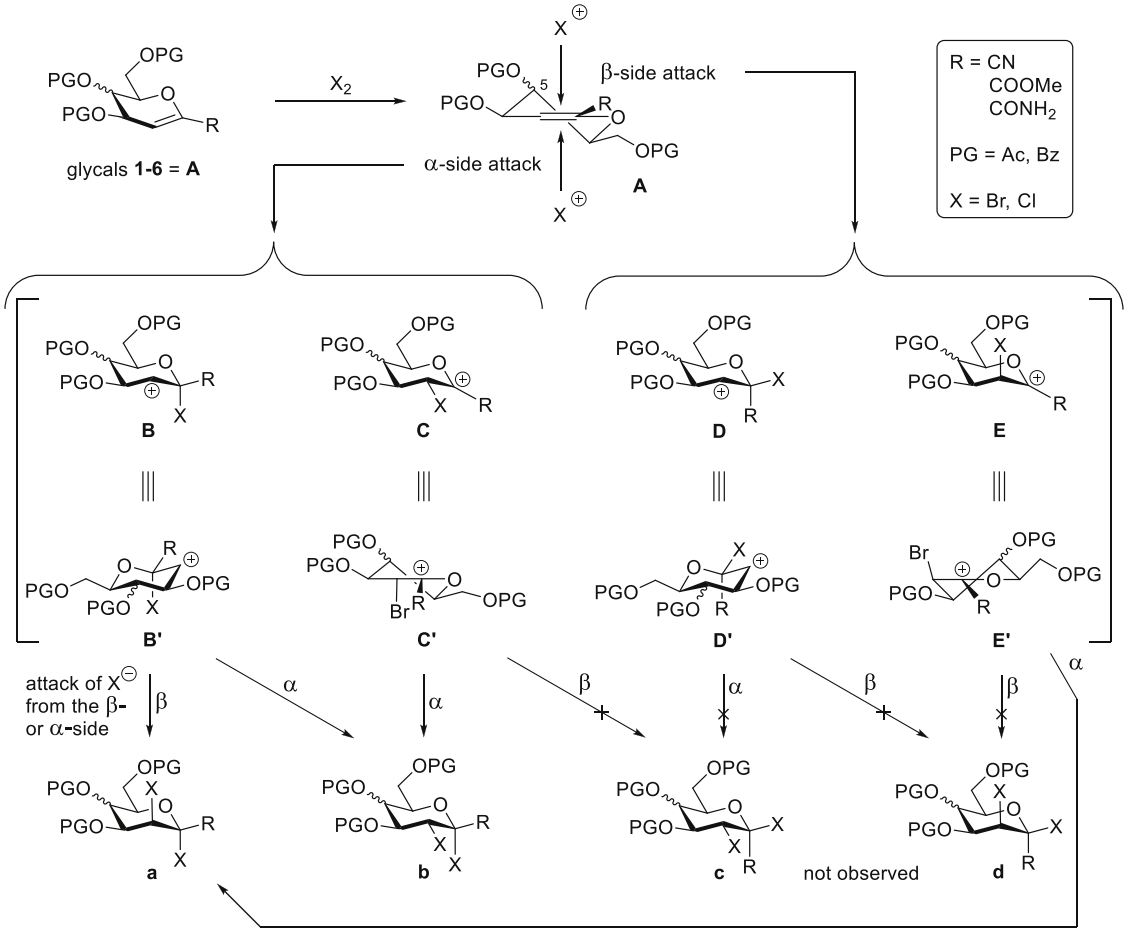
Several other substitution and elimination reactions of **8a** were also tried (NaI/acetone/rt, NaN_3/DMSO/rt, KSCN/acetone/18-crown-6, thiourea/acetone/reflux, KSAc/DMF-CH_2Cl_2/rt, AgF/dry CH_3CN/rt; DBU/dry CH_2Cl_2/-70 °C to rt, K_2CO_3/acetone/reflux, *t*BuOK/Et_2O/-15 °C to rt), nevertheless, these attempts resulted solely in the formation of glycal **2**. The reaction of a similar dibromo ester with Bu_3SnH in boiling benzene also gave the corresponding glycal [37]. There are some traces in the literature showing that reductive elimination may take place under otherwise differently designed substitution and elimination conditions [38]. These observations may reveal why transformations of Neu5Ac and KDO derived dibromides other than Ag-salt mediated glycosylations are missing in the literature.

In summary, a study on addition of bromine under ionic and radical conditions to several 1-C-acceptor substituted glycal (hept-2-enopyranosonic acid) derivatives showed a preference for the formation of the 2,3-*trans*-diaxial dibromo products with the exception of an *O*-peracetylated 1-cyano-galactal which gave the 2-axial-3-equatorial dibromide as the major product. Irradiation of the bromination reaction mixtures led to enhanced formation of the main products observed in dark reactions. Chlorination resulted in stereoselective formation of the 2-axial-3-equatorial dichlorides. AgOTf promoted glycosylation proved feasible with the 2,3-*trans*-diaxial dibromides, however, only the formation of the parent glycal could be observed in many attempted substitution and elimination reactions.

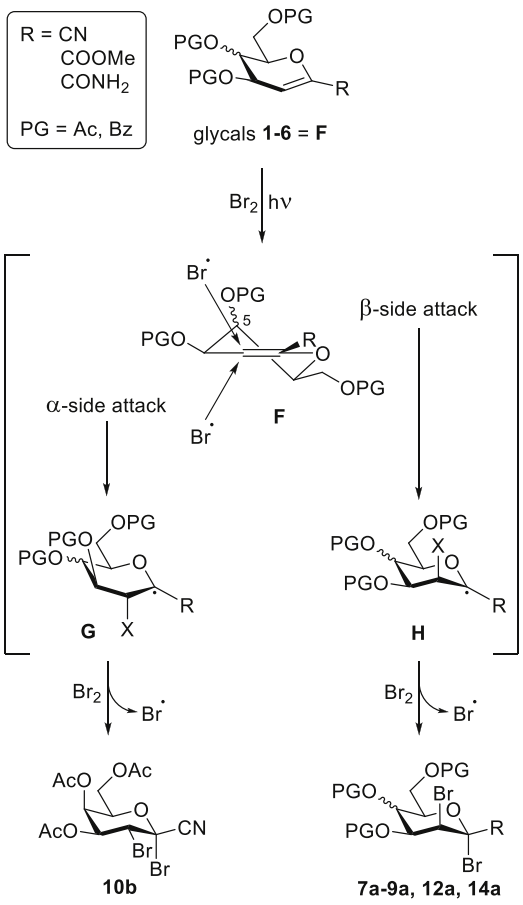
3. Experimental

3.1. General methods

Solvents were purified by distillation. Dichloromethane (DCM) and ethyl acetate were refluxed and distilled from P_4O_{10} and stored over 4 Å molecular sieves. Methanol was refluxed with magnesium turnings and iodine for a couple of hours and was distilled. Diethyl ether was stored over sodium wires. 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. Bromine containing compounds were visualized by heating the TLC to 150 °C after spraying with EtOH/fluorescein and glacial acetic acid/H_2O_2 (1:1). For column chromatography Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. Optical rotations were determined with a Jasco P-2000



Scheme 1. Possible mechanistic pathways for the ionic halogenations of glycals **1**–**6**.



Scheme 2. Mechanistic considerations for radical-mediated addition of bromine to glycals **1**–**6**.

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 are reported in ppm. All the compounds were characterized by their one- (^{1}H and ^{13}C) and two-dimensional (COSY, HSQC, HMBC) NMR spectra. Mass spectra were obtained by a Thermo Accela 600 HPLC + LTQ XL MS instrument using APCI ionization in positive mode. High resolution mass spectra were recorded by a Bruker maXis II UHR ESI-TOF MS instrument in positive mode. The reactions under irradiation were carried out in a home-made photoreactor containing 16 commercially available UV light sources (6 W each, maximum emissions at 254 and 366 nm for 8-8 tubes) in a circular arrangement with a mirror surface behind them to ensure an approx 10 cm distance between the light source and the reaction vessel (see photograph in the supporting information). The reaction mixtures were put into a borosilicate vessel placed in the middle of the above apparatus and both types of lamps were operating.

3.2. General procedure I for the synthesis of the dibromo derivatives

To a solution of the corresponding glycal derivative **1**–**6** (100 mg, 1.0 eq.) in dry dichloromethane (3 mL), a solution of bromine (1.1 eq.) in dry dichloromethane (3 mL) was added dropwise and the mixture was stirred at room temperature. After completion of the reaction monitored by TLC, saturated sodium sulfite solution (5 mL) was added and the mixture was stirred vigorously. The phases were separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with water (5 mL) and dried over $MgSO_4$, filtered and the solvent was removed by reduced pressure. The crude product was purified by column chromatography.

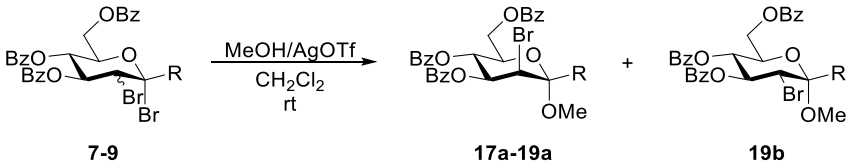
3.3. General procedure II for the synthesis of the dibromo derivatives under irradiation

Bromine (1.1 eq.) was dissolved in dry dichloromethane (2 mL) and was irradiated with UV light (254 and 366 nm) for 15 min. After that, the solution of the corresponding glycal derivative **1**–**6** (100 mg, 1.0 eq.) in dry dichloromethane (2 mL) was added and the mixture was irradiated continuously. After completion of the reaction monitored by TLC, saturated sodium sulfite solution (5 mL) was added and the mixture was stirred vigorously. The phases were separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with water (5 mL) and dried over $MgSO_4$, filtered and the solvent was removed by reduced pressure. The crude product was used without further purification.

3.4. General procedure III for the synthesis of the dichloro derivatives

To a solution of the corresponding glycal derivative **4**–**6** (100 mg, 1.0 eq.) in dry dichloromethane (3 mL), a saturated solution of chlorine (chlorine was obtained in the reaction of $KMnO_4$ with cc. HCl, and bulbed trough two traps filled with water and cc. H_2SO_4) in dry dichloromethane (3 mL, saturated at 0 °C) was added dropwise and the mixture was stirred at room temperature. After completion of the reaction monitored by TLC, the excess of chlorine was removed by reduced pressure. Saturated sodium sulfite solution (5 mL) was added to the remaining solution and the mixture was stirred vigorously. The phases were separated, and the aqueous layer was extracted with

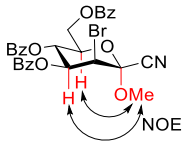
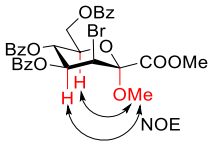
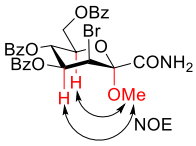
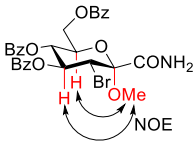
Table 4
Glycosylation of methanol with some dibromo adducts.



Starting compound	R	Product (Yield [%])
7a (Br-3 axial)	CN	**17a** (75)
8a (Br-3 axial)	COOMe	**18a** (76)
9a + **9b** (87 : 13/Br-3 ax:eq)	$CONH_2$	**19a** + **19b** (84, ratio 87 : 13[a])[b]

[a] Based on the ^{1}H NMR spectrum of the product mixture.
[b] Not fully separable mixture. Pure **19b** could be obtained in 8% yield.

Table 5
Characteristic ^{1}H NMR data of compounds **17**–**19** (δ [ppm], J [Hz]).

				
	17a	18a	19a	19b
H-4	5.69 $^3J_{3,4} = 3.8$	5.80 $^3J_{3,4} = 3.9$	5.89 $^3J_{3,4} = 3.7$	6.08 $^3J_{3,4} = 10.7$
H-6	4.29	4.34	4.34	4.34
CH_3O-2	3.72	3.41	3.45	3.50

dichloromethane (3 × 10 mL). The combined organic layers were washed with brine (5 mL) and dried over $MgSO_4$, filtered and the solvent was removed by reduced pressure. The crude product was purified by column chromatography.

3.5. General procedure IV for the glycosylation reactions

To a solution of the corresponding 1,2-dibromo derivative **7**–**9** (1 eq.) in dry dichloromethane (5 mL), dry methanol (20 eq.) was added, and the solution was cooled down to 0 °C. Under an argon atmosphere, AgOTf (1.2 eq.) was added in the dark and the mixture was stirred and let warm up to room temperature. After completion of the reaction monitored by TLC, it was quenched with 5 drops of pyridine and filtered through a Celite pad. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography.

3.6. Synthesis and characterisation of the compounds

Methyl 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*lyxo*-hept-2-enonate (5)

Activated zinc dust (3.5 g, 53.3 mmol, 10 eq.) was suspended in dry EtOAc (25 mL) and *N*-methylimidazole (2.2 mL, 27.2 mmol, 5.1 eq.) was added. This mixture was vigorously stirred and refluxed, and a solution of methyl (3,4,5,7-tetra-*O*-acetyl-α-D-*galacto*-hept-2-ulopyranosyl-bromide)onate [23] (2.5 g, 5.33 mmol, 1 eq.) in dry EtOAc (80 mL) was added dropwise so that the temperature of the solution remained over boiling temperature. After completion of the reaction monitored by TLC, the mixture was filtered warmly trough a Celite pad. The filtrate was extracted with 2 M HCl solution (40 mL), saturated $NaHCO_3$ solution (40 mL) and water (40 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (eluent: hexane : ethyl acetate = 3 : 1) to give 0.95 g (54%) of **5** as a white foam ($R_f = 0.40$, hexane : ethyl acetate = 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.92 (1H, s, H-3 or H-4 or H-5), 5.69 (1H, s, H-3 or H-4 or H-5), 5.46 (1H, dd, $J = 4.6$, 1.4 Hz, H-3 or H-4 or H-5), 4.42 (1H, td, $J = 6.6$, 1.4 Hz, H-6), 4.37–4.24 (2H, m, H-7, H-7'), 3.83 (3H, s, OCH_3), 2.12 (3H, s, CH_3CO), 2.09 (3H, s, CH_3CO), 2.05 (3H, s, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.5, 170.2, 170.1, 161.8 (C═O), 145.0 (C-2), 107.5 (C-3), 74.1, 64.6, 62.5 (C-4, C-5, C-6), 61.5 (C-7), 52.7 (OCH_3), 20.8, 20.7, 20.7 (CH_3CO). The spectral data correspond to those reported in the literature [7,25].

Zinc was activated by the following method: zinc dust was washed 2x with 2 M HCl solution, 2x with distilled water, 2x with acetone, 2x with diethyl ether and lastly 1x with dry diethyl ether and dried before use.

(4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulo-pyranosylbromide)ononitrile (7a)

Prepared from 1-cyano-glycal **1** (100 mg, 0.207 mmol, 1.0 eq.) and bromine (12 μL, 0.228 mmol, 1.1 eq.) according to general procedure I (reaction time 24 h). Purified by column chromatography (eluent: DCM : hexane = 3 : 2) to give 85 mg (64%) of **7a** as a white foam ($R_f = 0.62$, DCM : hexane = 5 : 1); $[\alpha]_D$ +71 (c 0.27, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.15–8.06 (2H, m, aromatics), 7.96–8.00 (4H, m, aromatics), 7.65–7.50 (3H, m, aromatics), 7.49–7.35 (6H, m, aromatics), 6.23 (1H, t, $J = 9.8$ Hz, H-5), 5.96 (1H, dd, $J = 9.8$, 3.7 Hz, H-4), 5.21 (1H, d, $J = 3.7$ Hz, H-3), 4.69–4.50 (3H, m, H-6, H-7, H-7'). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.9, 165.4, 165.0 (C═O), 134.2, 134.1, 133.6, 130.2, 130.1, 130.0, 129.3, 128.8, 128.7, 128.7, 128.3, 128.2 (aromatics), 113.8 (CN), 79.0 (C-2), 76.0 (C-6), 69.3 (C-4), 64.9 (C-5), 61.4 (C-7), 53.2 (C-3). APCI-MS positive mode *m/z*: calculated $C_{28}H_{22}Br_2NO_7^+$ $[M+H]^+$ 642.0, found 641.8. HRMS positive mode *m/z:* calculated $C_{28}H_{21}Br_2NO_7Na^+$ $[M+Na]^+$ 663.9577, found 663.9580.

Also prepared from 1-cyano-glycal **1** (100 mg, 0.207 mmol, 1.0 eq.) and bromine (12 μL, 0.228 mmol, 1.1 eq.) according to general procedure II (reaction time 3 h) to give 130 mg (97%) of **7a** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product only **7a** was obtained in the reaction.

Methyl (4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulopyranosylbromide)onate (8a)

Prepared from 1-methoxycarbonyl-glycal **2** (100 mg, 0.194 mmol, 1.0 eq.) and bromine (11 μL, 0.213 mmol, 1.1 eq.) according to general procedure I (reaction time 12 h). Purified by column chromatography (eluent: hexane : ethyl acetate = 4 : 1 to 3 : 1 gradient) to give 104 mg (79%) of **8a** as a white foam ($R_f = 0.45$, hexane : ethyl acetate = 2 : 1); $[\alpha]_D$ +70 (c 0.24, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.08 (2H, d, $J = 7.2$ Hz, aromatics), 8.00 (2H, d, $J = 7.3$ Hz, aromatics), 7.97 (2H, d, $J = 7.5$ Hz, aromatics), 7.60–7.49 (3H, m, aromatics), 7.43–7.36 (6H, m, aromatics), 6.28 (1H, t, $J = 9.9$ Hz, H-5), 6.08 (1H, dd, $J = 9.9$, 3.6 Hz, H-4), 5.39 (1H, d, $J = 3.6$ Hz, H-3), 4.69 (2H, m, H-6, H-7 or H-7′), 4.59 (1H, dd, $J = 12.3$, 3.6 Hz, H-7 or H-7'), 3.93 (3H, s, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.1, 165.5, 165.2, 164.2 (C═O), 133.9, 133.8, 133.3, 130.1, 130.0, 130.0, 129.6, 128.7, 128.7, 128.5 (aromatics), 91.0 (C-2), 75.6 (C-6), 70.4 (C-4), 65.8 (C-5), 62.0 (C-7), 54.1 (OCH_3), 53.1 (C-3). APCI-MS positive mode *m/z*: calculated $C_{29}H_{25}Br_2O_9^+$ $[M+H]^+$ 675.0, found 674.9. HRMS positive mode *m/z:* calculated $C_{29}H_{24}Br_2O_9Na^+$ $[M+Na]^+$ 696.9679, found 696.9682.

Also prepared from 1-methoxycarbonyl-glycal **2** (100 mg, 0.194 mmol, 1.0 eq.) and bromine (11 μL, 0.213 mmol, 1.1 eq.) according to general procedure II (reaction time 1.5 h) to give 129 mg (98%) of **8a** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product only **8a** was obtained in the reaction.

(4,5,7-Tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulo-pyranosylbromide)onamide (9a) and (4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*gluco*-hept-2-ulopyranosylbromide)onamide (9b)

Prepared from 1-carbamoyl-glycal **3** (100 mg, 0.199 mmol, 1.0 eq.) and bromine (11 μL, 0.219 mmol, 1.1 eq.) according to general procedure I (reaction time 4 h). Purified by column chromatography (eluent: hexane : acetone = 5 : 1 to 2 : 1 gradient) to give 117 mg (89%) of **9a** and **9b** as a white foam (**9a** : **9b** = 87 : 13) ($R_f = 0.65$, hexane : acetone = 1 : 1).

9a: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.12 (2H, d, $J = 7.2$ Hz, aromatics), 8.02 (2H, d, $J = 7.2$ Hz, aromatics), 7.99 (2H, d, $J = 7.3$ Hz, aromatics), 7.62–7.34 (9H, m, aromatics), 6.77 (1H, s, $CONH_2$), 6.30 (1H, t, $J = 9.9$ Hz, H-5), 6.13 (1H, dd, $J = 9.9$, 3.5 Hz, H-4), 5.93 (1H, s, $CONH_2$), 5.36 (1H, d, $J = 3.5$ Hz, H-3), 4.95 (1H, dd, $J = 12.7$, 2.2 Hz, H-7 or H-7′), 4.70–4.57 (1H, m, H-6), 4.44 (1H, dd, $J = 12.7$, 3.4 Hz, H-7 or H-7′). ^{1}H NMR (C_6D_6) δ (ppm): 8.32 (2H, dd, $J = 7.9$, 1.8 Hz, aromatics), 8.05 (2H, d, $J = 7.0$ Hz, aromatics), 7.99 (2H, d, $J = 7.1$ Hz, aromatics), 7.09–6.88 (7H, m, aromatics), 6.84 (2H, t, $J = 7.5$ Hz, aromatics), 6.65 (1H, t, $J = 9.9$ Hz, H-5), 6.47 (1H, dd, $J = 9.9$, 3.5 Hz, H-4), 6.23 (1H, s, $CONH_2$), 5.49 (1H, d, $J = 3.5$ Hz, H-3), 4.96 (1H, s, $CONH_2$), 4.66 (1H, dd, $J = 12.9$, 2.2 Hz, H-7), 4.35 (1H, dt, $J = 9.9$, 2.5 Hz, H-6), 3.88 (1H, dd, $J = 12.9$, 2.7 Hz, H-7'). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.8, 166.6, 165.4, 165.3 (C═O), 134.0, 133.8, 133.7, 130.1, 130.1, 130.0, 129.4, 128.7, 128.7 (aromatics), 92.1 (C-2), 76.5 (C-5), 70.3 (C-4), 65.7 (C-5), 61.2 (C-6), 52.6 (C-3).

9b characteristic ^{1}H NMR data: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.09 (1H, dd, $J = 10.8$, 9.8 Hz, H-4), 5.71 (1H, t, $J = 9.8$ Hz, H-5), 4.78 (1H, ddd, $J = 10.0$, 4.7, 2.7 Hz, H-6), 4.71 (1H, dd, $J = 12.6$, 2.7 Hz, H-7), 4.67 (1H, overlap with **9a** H-6, H-3), 4.54 (1H, dd, $J = 12.6$, 4.7 Hz, H-7′). ^{1}H NMR (C_6D_6) δ (ppm): 8.17 (2H, dd, $J = 8.2$, 1.4 Hz, aromatics), 6.39 (1H, dd, $J = 10.8$, 9.6 Hz, H-4), 5.95 (1H, s, $CONH_2$), 5.76 (1H, dd, $J = 10.2$, 9.6 Hz, H-5), 4.99 (1H, s, $CONH_2$), 4.58 (1H, d, $J = 10.8$ Hz, H-3), 4.56 (1H, ddd, $J = 10.2$, 4.3, 2.8 Hz, H-6), 4.44 (1H, dd, $J = 12.7$, 2.8 Hz, H-7), 4.23 (1H, dd, $J = 12.7$, 4.3 Hz, H-7').

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{28}H_{24}Br_2NO_8^+$ $[M+H]^+$ 660.0, found 659.9.

Also prepared from 1-carbamoyl-glycal **3** (100 mg, 0.199 mmol, 1.0 eq.) and bromine (11 μL, 0.219 mmol, 1.1 eq.) according to general procedure II (reaction time 30 min) to give 128 mg (97%) of **9a** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product only **9a** was obtained in the reaction.

(4,5,7-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*talo*-hept-2-ulopyranosylbromide)ononitrile (10a) and (4,5,7-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylbromide)ononitrile (10b) and 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-bromo-3-deoxy-D-*lyxo*-hept-2-enononitrile (16)

Prepared from 1-cyano-glycal **4** (100 mg, 0.336 mmol, 1.0 eq.) and bromine (19 μl, 0.370 mmol, 1.1 eq.) according to general procedure I (reaction time 16 h). Purified by column chromatography (eluent: hexane : ethyl acetate = 4 : 1) to give 105 mg (68%) of **10a**, **10b** and **16** as a white foam (**10a** : **10b** : **16** = 22 : 60 : 18), (R_f = 0.25, 0.26 and 0.28, hexane : ethyl acetate = 2 : 1).

10a: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.60 (1H, pt, $J = 4.1$, 3.9 Hz, H-4), 5.47 (1H, ddd, $J = 3.8$, 2.0, 0.9 Hz, H-5), 4.73 (1H, d, $J = 4.2$ Hz, H-3), 4.56 (1H, overlap with **10b** and **16** H-6, H-6), 4.30 (1H, dd, $J = 11.7$, 5.8 Hz, H-7), 4.23 (1H, overlap with **10b** H-7′, H-7'), 2.17 (3H, s, CH_3CO), 2.16 (3H, s, CH_3CO), 2.08 (3H, s, CH_3CO). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.3, 169.8, 169.4 (C═O), 113.8 (CN), 80.8 (C-2), 75.4, 64.4, 63.8, 60.9, 47.6 (C-3), 20.7, 20.6, 20.4 (CH_3CO).

10b: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.44 (1H, dd, $J = 3.2$, 1.4 Hz, H-5). 5.32 (1H, dd, $J = 11.0$, 3.2 Hz, H-4), 4.56 (1H, td, $J = 6.5$, 1.4 Hz, H-6), 4.39 (1H, d, $J = 11.0$ Hz, H-3), 4.23 (1H, dd, $J = 11.7$, 6.1 Hz, H-7), 4.14 (1H, dd, $J = 11.7$, 6.8 Hz, H-7'), 2.19 (3H, s, CH_3CO), 2.07 (3H, s, CH_3CO), 2.07 (3H, s, CH_3CO). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.2, 169.5, 169.1 (C═O), 114.0 (CN), 84.5 (C-2), 74.0 (C-6), 69.7 (C-4), 66.7 (C-5), 60.4 (C-7), 49.3 (C-3), 20.6, 20.5, 20.4 (CH_3CO).

16: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.78 (1H, dd, $J = 4.7$, 1.2 Hz, H-5), 5.51 (1H, dd, $J = 4.7$, 1.5 Hz, H-4), 4.52 (1H, overlap with **10a** and **10b** H-6, H-6), 4.23 (2H, overlap with **10a** H-7′, and **10b** H-7, H-7, H-7'), 2.10 (3H, s, CH_3CO), 2.10 (3H, s, CH_3CO), 2.10 (3H, s, CH_3CO). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.3, 169.7, 169.3 (C═O), 130.9 (C-2), 112.2 (CN), 111.0 (C-3), 74.9 (C-6), 65.8 (C-5), 63.5 (C-4), 60.7 (C-7), 20.7, 20.6, 20.5 (CH_3CO).

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: for **10a** and **10b** calculated $C_{13}H_{16}Br_2NO_7^+$ $[M+H]^+$ 455.9, found 456.0, and for **16** calculated $C_{11}H_{11}BrNO_5^+$ $[M - AcO]^+$ 316.0, found 315.9.

Compound **10b** was also prepared from 1-cyano-glycal **4** (100 mg, 0.336 mmol, 1.0 eq.) and bromine (19 μL, 0.370 mmol, 1.1 eq.) according to general procedure II (reaction time 2 h) to give 146 mg (95%) of **10b** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product only **10b** was obtained in the reaction.

(4,5,7-Tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*talo*-hept-2-ulopyranosylchloride)ononitrile (11a) and (4,5,7-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylchloride)ononitrile (11b)

Prepared from 1-cyano-glycal **4** (100 mg, 0.336 mmol, 1.0 eq.) and chlorine according to general procedure III (reaction time 2 days). Purified by column chromatography (eluent: hexane : ethyl acetate = 4 : 1) to give 82 mg (66%) of **11a** and **11b** as a white foam (**11a** : **11b** = 44 : 56) (R_f = 0.28 and 0.33, hexane : ethyl acetate = 2 : 1).

11a: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.63 (1H, t, $J = 3.9$ Hz, H-4), 5.43 (1H, dd, $J = 3.9$, 1.1 Hz, H-5), 4.60 (1H, overlap with H-6 of the **11b**, H-6), 4.54 (1H, d, $J = 3.9$ Hz, overlap with H-3 of the **11b,** H-3), 4.28 (1H, dd, $J = 11.7$, 5.8 Hz, H-7), 4.23 (1H, dd, $J = 11.7$, 2.5 Hz, H-7'), 2.16 (3H, s, CH_3CO), 2.11 (3H, s, CH_3CO), 2.08 (3H, s, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.3, 169.9, 169.4 (C═O), 113.0 (CN), 89.9 (C-2), 72.8 (C-6), 64.2 (C-4), 64.0 (C-5), 60.8 (C-7), 57.7 (C-3), 20.7, 20.5, 20.4 (CH_3CO).

11b: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.48 (1H, dd, $J = 3.2$, 1.3 Hz, H-5), 5.30 (1H, dd, $J = 10.8$, 3.2 Hz, H-4), 4.59 (1H, td, $J = 6.5$, 1.3 Hz, H-6), 4.53 (1H, d, $J = 10.8$ Hz, H-3), 4.22 (1H, dd, $J = 11.6$, 6.1 Hz, H-7), 4.14 (1H, dd, $J = 11.6$, 6.8 Hz, H-7'), 2.19 (3H, s, CH_3CO), 2.07 (6H, s, 2x CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.2, 169.6, 169.3 (C═O), 113.3 (CN), 91.3 (C-2), 72.3 (C-6), 68.9 (C-4), 66.6 (C-5), 60.4 (C-7), 58.1 (C-3), 20.7, 20.5, 20.4 (CH_3CO).

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{13}H_{15}ClNO_7^+$ $[M - Cl]^+$ 332.1, found 332.1.

Methyl (4,5,7-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*talo*-hept-2-ulopyranosylbromide)onate (12a) and methyl (4,5,7-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylbromide)onate (12b)

Prepared from 1-methoxycarbonyl-glycal **5** (100 mg, 0.303 mmol, 1.0 eq.) and bromine (17 μL, 0.333 mmol, 1.1 eq.) according to general procedure I (reaction time 3 h). Purified by column chromatography (eluent: hexane : ethyl acetate = 3 : 1) to give 130 mg (88%) of **12a** and **12b** as a white foam (**12a** : **12b** = 96 : 4). (R_f = 0.45, hexane : ethyl acetate = 1 : 1).

12a: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.73 (1H, t, $J = 4.0$ Hz, H-4), 5.49 (1H, ddd, $J = 3.6$, 1.9, 0.9 Hz, H-5), 4.89 (1H, dd, $J = 4.0$, 1.0 Hz, H-3), 4.62 (1H, td, $J = 6.6$, 1.9 Hz, H-6), 4.39 (1H, dd, $J = 11.4$, 6.6 Hz, H-7), 4.29 (1H, dd, $J = 11.4$, 6.6 Hz, H-7'), 3.94 (3H, s, OCH_3), 2.14 (3H, s, CH_3CO), 2.10 (3H, s, CH_3CO), 2.07 (3H, s, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.4, 170.0, 169.5, 164.4 (C═O), 92.5 (C-2), 74.7 (C-6), 65.6 (C-4), 64.0 (C-5), 60.8 (C-7), 53.9 (OCH_3), 47.9 (C-3), 20.8, 20.7, 20.7 (CH_3CO).

12b characteristic ^{1}H NMR data: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.45 (1H, dd, $J = 3.2$, 1.4 Hz, H-5), 5.41 (1H, dd, $J = 11.1$, 3.2 Hz, H-4), 4.58 (1H, d, $J = 11.1$ Hz, H-3), 4.22 (1H, dd, $J = 11.4$, 6.9 Hz, H-7 or H-7').

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{14}H_{19}Br_2O_9^+$ $[M+H]^+$ 488.9, found 488.7.

Also prepared from 1-methoxycarbonyl-glycal **5** (100 mg, 0.303 mmol, 1.0 eq.) and bromine (17 μL, 0.333 mmol, 1.1 eq.) according to general procedure II (reaction time 30 min) to give 146 mg (98%) of **12a** and **12b** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product **12a** and **12b** (**12a** : **12b** = 93 : 7) was obtained in the reaction.

Methyl (4,5,7-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*talo*-hept-2-

ulopyranosylchloride)onate (13a) and methyl (4,5,7-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylchloride)onate (13b)

Prepared from 1-methoxycarbonyl-glycal **5** (100 mg, 0.303 mmol, 1.0 eq.) and chlorine according to general procedure III (reaction time 3 h). Purified by column chromatography (eluent: hexane : ethyl acetate = 4 : 1) to give 86 mg (71%) of **13a** and **13b** as a white foam. ($R_f = 0.63$, hexane : ethyl acetate = 1 : 1).

13a: characteristic ^{1}H NMR data: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.32 (1H, ddd, $J = 3.6$, 2.2, 0.9 Hz, H-5), 5.18 (1H, t, $J = 3.7$ Hz, H-4), 4.87 (1H, d, $J = 3.7$, 0.9 Hz, H-3), 4.47 (1H, m, H-6), 4.34 (1H, dd, $J = 11.6$, 6.7 Hz, H-7), 4.27 (1H, dd, $J = 11.6$, 6.3 Hz, H-7'). **13b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.49 (1H, dd, $J = 3.3$, 1.3 Hz, H-5), 5.36 (1H, dd, $J = 11.0$, 3.3 Hz, H-4), 4.73 (1H, d, $J = 11.0$ Hz, H-3), 4.63 (1H, td, $J = 6.6$, 1.3 Hz, H-6), 4.21 (1H, dd, $J = 11.4$, 6.6 Hz, H-7), 4.12 (1H, dd, $J = 11.4$, 6.6 Hz, H-7'), 3.94 (3H, s, OCH_3), 2.17 (3H, s, CH_3CO), 2.06 (3H, s, CH_3CO), 2.05 (3H, s, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.3, 169.8, 169.5, 163.8 (C═O), 101.6 (C-2), 71.9 (C-6), 70.1 (C-4), 67.0 (C-5), 60.7 (C-7), 57.0 (C-3), 54.5 (OCH_3), 20.7, 20.6, 20.5 (CH_3CO).

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{14}H_{19}Cl_2O_9^+$ $[M+H]^+$ 401.0, found 400.9.

(4,5,7-Tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*talo*-hept-2-ulopyranosylbromide)onamide (14a) and (4,5,7-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylbromide)onamide (14b)

Prepared from 1-carbamoyl-glycal **6** (100 mg, 0.317 mmol, 1.0 eq.) and bromine (18 μL, 0.349 mmol, 1.1 eq.) according to general procedure I (reaction time 1 h). Purified by column chromatography (eluent: hexane : acetone = 3 : 1 to 2 : 1 gradient) to give 116 mg (77%) of **14a** and **14b** as a white foam (**14a**: **14b** = 71 : 29), ($R_f = 0.55$, hexane : acetone = 1 : 1).

14a: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.66 (1H, s, $CONH_2$), 6.21 (1H, s, $CONH_2$), 5.76 (1H, t, $J = 4.0$ Hz, H-4), 5.52 (1H, ddd, $J = 3.5$, 2.1, 1.0 Hz, H-5), 4.94 (1H, dd, $J = 4.0$, 1.0 Hz, H-3), 4.65 (1H, ddd, $J = 7.2$, 5.0, 2.1 Hz, H-6), 4.47 (1H, dd, $J = 11.7$, 7.2 Hz, H-7), 4.24 (1H, dd, $J = 11.7$, 5.0 Hz, H-7'), 2.16 (3H, s, CH_3CO), 2.10 (6H, s, 2x CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.7, 170.0, 169.5, 166.9 (C═O), 94.0 (C-2), 76.0 (C-6), 65.9 (C-4), 64.3 (C-5), 61.3 (C-7), 47.0 (C-3), 20.8, 20.8, 20.7 (CH_3CO).

14b: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.73 (1H, s, $CONH_2$), 6.28 (1H, s, $CONH_2$), 5.46 (1H, dd, $J = 3.2$, 1.4 Hz, H-5), 5.39 (1H, dd, $J = 11.2$, 3.2 Hz, H-4), 4.60 (1H, td, $J = 6.4$, 1.4 Hz, H-6), 4.58 (1H, d, $J = 11.2$ Hz, H-3), 4.45 (2H, d, $J = 6.4$ Hz, H-7, H-7'), 2.17 (3H, s, CH_3CO), 2.07 (6H, s, 2x CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.5, 169.9, 169.6, 165.8 (C═O), 101.2 (C-2), 74.1 (C-6), 71.2 (C-4), 67.1 (C-5), 60.9 (C-7), 48.2 (C-3), 20.8, 20.7, 20.6 (CH_3CO).

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{13}H_{18}Br_2NO_8^+$ $[M+H]^+$ 473.9, found 473.9.

Also prepared from 1-carbamoyl-glycal **6** (100 mg, 0.317 mmol, 1.0 eq.) and bromine (18 μL, 0.349 mmol, 1.1 eq.) according to general procedure II (reaction time 15 min) to give 150 mg (99%) of **14a** and **14b** as a white foam. Based on the ^{1}H and ^{13}C NMR spectra of the crude product **14a** and **14b** (**14a** : **14b** = 80 : 20) was obtained in the reaction.

(4,5,7-Tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*talo*-hept-2-ulopyranosylchloride)onamide (15a) and (4,5,7-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-*galacto*-hept-2-ulopyranosylchloride)onamide (15b)

Prepared from 1-carbamoyl-glycal **6** (100 mg, 0.317 mmol, 1.0 eq.) and chlorine according to general procedure III (reaction time 30 min). Purified by column chromatography (eluent: hexane : acetone = 2 : 1) to give 80 mg (66%) of **15a** and **15b** as a white foam (**15a** : **15b** = 5 : 95) ($R_f = 0.53$, hexane : acetone = 1 : 1).

15a characteristic ^{1}H NMR data: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.71 (1H, s, $CONH_2$), 6.61 (1H, s, $CONH_2$), 5.75 (1H, t, $J = 3.8$ Hz, H-4), 5.71 (1H, d, $J = 3.8$ Hz, H-3), 4.96 (1H, dd, $J = 3.7$, 1.1 Hz, H-5), 4.67 (1H, ddd, $J = 7.2$, 5.0, 2.0 Hz, H-6), 4.50 (1H, dd, $J = 11.5$, 7.8 Hz, H-7), 4.46 (1H, dd, $J = 11.7$, 7.3, H-7'), 2.16 (3H, s, CH_3CO), 2.10 (6H, s, 2x CH_3CO).

15b: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.77 (1H, s, $CONH_2$), 6.49 (1H, s, $CONH_2$), 5.50 (1H, dd, $J = 3.2$, 1.2 Hz, H-5), 5.35 (1H, dd, $J = 11.1$, 3.2 Hz, H-4), 4.78 (1H, d, $J = 11.1$ Hz, H-3), 4.60 (1H, td, $J = 6.5$, 1.2 Hz, H-6), 4.19 (2H, dd, $J = 6.5$, 1.3 Hz, H-7, H-7'), 2.18 (3H, s, CH_3CO), 2.07 (6H s, 2x CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.5, 170.0, 169.7, 165.6 (C═O), 102.9 (C-2), 72.3 (C-6), 70.4 (C-4), 67.0 (C-5), 60.9 (C-7), 56.3 (C-3), 20.7, 20.7, 20.6 (CH_3CO).

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{13}H_{18}Cl_2NO_8^+$ $[M+H]^+$ 386.0, found 386.1.

(Methyl 4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulopyranoside)ononitrile (17a)

Prepared from **7a** (123 mg, 0.191 mmol, 1.0 eq.) with methanol (155 μl, 3.82 mmol, 20 eq.) in the presence of AgOTf (59 mg, 0.229 mmol, 1.2 eq.) according to general procedure IV. Purified by column chromatography (eluent: hexane : ethyl acetate = 5 : 1) to give 86 mg (75%) of **17a** as a white foam ($R_f = 0.24$, hexane : ethyl acetate = 3 : 1); $[\alpha]_D$ +15 (c 0.35, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.05 (2H, d, $J = 7.6$ Hz, aromatics), 7.98 (2H, d, $J = 7.6$ Hz, aromatics), 7.94 (2H, d, $J = 7.6$ Hz, aromatics), 7.60–7.49 (3H, m, aromatics), 7.46–7.34 (6H, m, aromatics), 6.05 (1H, t, $J = 9.9$ Hz, H-5), 5.69 (1H, dd, $J = 9.9$, 3.8 Hz, H-4), 4.82 (1H, d, $J = 3.8$ Hz, H-3), 4.62 (1H, dd, $J = 12.4$, 2.8 Hz, H-7), 4.49 (1H, dd, $J = 12.4$, 5.1 Hz, H-7'), 4.29 (1H, ddd, $J = 9.9$, 5.1, 2.8 Hz, 1H), 3.72 (3H, s, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.1, 165.4, 165.2 (C═O), 133.9, 133.8, 133.5, 130.1, 130.0, 129.9, 129.5, 128.7, 128.6 (aromatics), 113.3 (CN), 98.4 (C-2), 71.3 (C-6), 69.3 (C-4), 66.0 (C-5), 62.6 (C-7), 54.3 (OCH_3), 50.7 (C-3). APCI-MS positive mode *m/z*: calculated $C_{29}H_{25}BrNO_8^+$ $[M+H]^+$ 594.1, found 593.9. HRMS positive mode *m/z:* calculated $C_{29}H_{24}BrNO_8Na^+$ $[M+Na]^+$ 616.0577, found 616.0582.

Methyl (methyl 4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulopyranoside)onate (18a)

Prepared from **8a** (123 mg, 0.182 mmol, 1.0 eq.) with methanol (148 μl, 3.64 mmol, 20 eq.) in the presence of AgOTf (56 mg, 0.218 mmol, 1.2 eq.) according to general procedure IV. Purified by column chromatography (eluent: hexane : ethyl acetate = 4 : 1) to give 87 mg (76%) of **18a** as a white foam ($R_f = 0.26$, hexane : ethyl acetate = 2 : 1); $[\alpha]_D$ −4 (c 0.67, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04–7.93 (6H, m, aromatics), 7.55–7.48 (3H, m, aromatics), 7.41–7.32 (6H, m, aromatics), 6.04 (1H, pt, $J = 9.9$, 9.8 Hz, H-5), 5.80 (1H, dd, $J = 9.8$, 3.9 Hz, H-4), 4.93 (1H, d, $J = 3.9$ Hz, H-3), 4.66 (1H, dd, $J = 12.2$, 3.2 Hz, H-7), 4.58 (1H, dd, $J = 12.2$, 5.2 Hz, H-7'), 4.34 (1H, ddd, $J = 9.9$, 5.2, 3.2 Hz, H-6), 3.87 (3H, s, OCH_3), 3.41 (3H, s, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.3, 165.6, 165.4, 165.4 (C═O), 133.7, 133.6, 133.2, 130.1, 130.0, 129.8, 129.8, 128.9, 128.6, 128.6, 128.5 (aromatics), 100.6 (C-2), 70.5 (C-6), 70.0 (C-4), 67.0 (C-5), 63.3 (C-7), 53.2 (OCH_3), 52.6 (OCH_3), 51.3 (C-2). APCI-MS positive mode *m/z*: calculated $C_{30}H_{28}BrO_{10}^+$ $[M+H]^+$ 627.1, found 626.8. HRMS positive mode *m/z:* calculated $C_{30}H_{27}BrO_{10}Na^+$ $[M+Na]^+$ 649.0680, found 649.0687.

(Methyl 4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*manno*-hept-2-ulopyranoside)onamide (19a) and (Methyl 4,5,7-tri-*O*-benzoyl-2-bromo-2-deoxy-α-D-*gluco*-hept-2-ulopyranoside)onamide (19b)

Prepared from **9** (137 mg, 0.207 mmol, 1.0 eq.) with methanol (168 μl, 4.14 mmol, 20 eq.) in the presence of AgOTf (64 mg, 0.249 mmol, 1.2 eq.) according to general procedure IV. Purified by column chromatography (eluent: hexane : acetone = 3 : 1 to 3 : 2 gradient) to give 107 mg (84%) of **19a** and **19b** as a white foam (**19a** : **19b** = 87 : 13), (R_f = 0.42 and 0.49, hexane : acetone = 1 : 1). Pure **19b** yield: 9 mg (8%).

19a: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.13 (2H, d, $J = 7.0$ Hz, aromatics), 8.01 (4H, d, $J = 7.1$ Hz, aromatics), 7.66–7.35 (9H, m, aromatics), 6.87 (1H, d, $J = 2.5$ Hz, $CONH_2$), 6.14 (1H, t, $J = 9.8$ Hz, H-5), 6.05 (1H, d, $J = 2.5$ Hz, $CONH_2$), 5.89 (1H, dd, $J = 9.8$, 3.7 Hz, H-4), 4.92 (1H, d, $J = 3.7$ Hz, H-3), 4.86 (1H, dd, $J = 12.3$, 2.5 Hz, H-7), 4.50

(1H, dd, $J = 12.3$, 4.4 Hz, H-7'), 4.34 (1H, ddd, $J = 9.9$, 4.4, 2.5 Hz, H-6), 3.45 (3H, s, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.7, 166.8, 165.5, 165.3 (C═O), 133.7, 133.6, 133.5, 130.1, 130.0, 129.9, 129.6, 129.0, 128.9, 128.7, 128.6, 128.6 (aromatics), 100.5 (C-2), 71.6 (C-6), 69.8 (C-4), 66.7 (C-5), 62.3 (C-7), 52.4 (OCH_3), 50.8 (C-3).

19b: ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.97 (2H, d, $J = 6.9$ Hz, aromatics), 7.91 (2H, d, $J = 6.9$ Hz, aromatics), 7.82 (2H, d, $J = 6.9$ Hz, aromatics), 7.70–7.57 (3H, m, aromatics), 7.55–7.42 (6H, m, aromatics), 6.57 (1H, dd, $J = 10.4$, 9.7 Hz, H-4), 5.61 (1H, t, $J = 9.7$ Hz, H-5), 4.94 (1H, d, $J = 10.4$ Hz, H-3), 4.85 (1H, dt, $J = 9.9$, 3.3 Hz, H-6), 4.47 (1H, dd, $J = 12.5$, 2.8 Hz, H-7), 4.37 (1H, dd, $J = 12.5$, 3.7 Hz, H-7').

Mass spectrum was obtained from the mixture. APCI-MS positive mode *m/z*: calculated $C_{29}H_{27}BrNO_9^+$ $[M+H]^+$ 612.1, found 611.9.

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.

Acknowledgement

This work was financially supported by the Hungarian National Research, Development and Innovation Office (Grant: FK 128766) and by the EU and co-financed by the European Regional Development Fund under the project GINOP-2.3.2-15-2016-00008. Levente Homolya thanks the Gedeon Richter Talentum Foundation for supporting his PhD studies. The authors thank Attila Kiss-Szikszai for the APCI-MS measurements, and István Timári for the help in the NMR measurements.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carres.2021.108292.

References

[1] W. Priebe, G. Grynkiewicz, Formation and Reactions of Glycal Derivatives, in: B. Fraser-Reid, K. Tatsuta, J. Thiem (Eds.), Glycoscience: Chemistry and Chemical Biology, Springer, Berlin, Heidelberg, 2001, pp. 749–784.
[2] L. Somsák, Carbanionic reactivity of the anomeric center in carbohydrates, Chem. Rev. 101 (2001) 81–135.
[3] A.N. Gómez, J. Cristóbal López, Recent Strategies for the Preparation of C-1 Glycals in: Carbohydr. Chem, The Royal Society of Chemistry, 2009, pp. 289–309.
[4] S. Kun, S. Deák, K. Czifrák, L. Juhász, L. Somsák, O. Apelt, Preparation of 2,6-Anhydro-Hept-2-Enonic Acid Derivatives and Their 3-deoxy Counterparts, in: C. Vogel, P.V. Murphy (Eds.), Carbohydrate Chemistry: Proven Synthetic Methods, CRC Press, Boca Raton, 2017, pp. 79–90.
[5] H.G. Viehe, Z. Janousek, R. Merényi, The captodative effect, Acc. Chem. Res. 18 (1985) 148–154.
[6] V. Gyóllai, D. Schanzenbach, L. Somsák, T. Linker, Addition of malonyl radicals to glycals with C-1 acceptor groups: remarkable influence of the substituents on the product distribution, Chem. Commun. (2002) 1294–1295.
[7] T. Linker, D. Schanzenbach, T. Sommermann, W. Fudickar, V. Gyóllai, L. Somsák, W. Demuth, M. Schmittel, The remarkable oxidation stability of glycals – excellent substrates for cerium(IV)-Mediated radical reactions, J. Am. Chem. Soc. 130 (2008) 16003–16010.
[8] L. Lázár, L. Juhász, G. Batta, A. Borbás, L. Somsák, Unprecedented β-manno type thiodisaccharides with a *C*-glycosylic function by photoinitiated hydrothiolation of 1-C-substituted glycals, New J. Chem. 41 (2017) 1284–1292.
[9] J. Bock, S. Guria, V. Wedek, U. Hennecke, Enantioselective dihalogenation of alkenes, Chem. Eur J. 27 (2021) 4517–4530.
[10] T. Linker, Addition of heteroatom radicals to endo-glycals, Chemistry 2 (2020) 80–92.
[11] T. Nakajima, H. Hori, H. Orui, H. Meguro, T. Ido, Synthesis of *N*-acetyl-3-fluoroneuraminic acids, Agric. Biol. Chem. 52 (1988) 1209–1215.
[12] K. Ikeda, S. Kitani, K. Sato, T. Suzuki, C. Hosokawa, Y. Suzuki, K. Tanaka, M. Sato, 2β,3β-Difluorosialic acid derivatives structurally modified at the C-4 position: synthesis and biological evaluation as inhibitors of human parainfluenza virus type 1, Carbohydr. Res. 339 (2004) 1367–1372.
[13] C.R. Petrie III, M. Sharma, O.D. Simmons, W. Korytnyk, Synthesis of analogs of *N*-acetylneuraminic acid and their effect on CMP-sialate synthase, Carbohydr. Res. 186 (1989) 326–334.
[14] K. Okamoto, T. Kondo, T. Goto, Synthetic studies on gangliosides. 1. A stereospecific synthesis of β-glycosides of *N*-acetylneuraminic acid and secondary alcohols, Chem. Lett. (1986) 1449–1452.
[15] K. Okamoto, T. Kondo, T. Goto, Synthetic studies on gangliosides. 2. Functionalization of 2-deoxy-2,3-dehydro-*N*-acetylneuraminic acid methyl ester, Bull. Chem. Soc. Jpn. 60 (1987) 631–636.
[16] K. Okamoto, T. Kondo, T. Goto, Synthetic studies on gangliosides. 6. A stereospecific β-glycosylation of 2β,3α-dibromo-*N*-acetylneuraminic acid, Tetrahedron 43 (1987) 5909–5918.
[17] M. Pascolutti, P.D. Madge, R.J. Thomson, M. von Itzstein, Access to 3-*O*-functionalized *N*-acetylneuraminic acid scaffolds, J. Org. Chem. 80 (2015) 7746–7751.
[18] P. Rota, F. Cirillo, M. Piccoli, A. Gregorio, G. Tettamanti, P. Allevi, L. Anastasia, Synthesis and biological evaluation of several dephosphonated analogues of CMP-neu5Ac as inhibitors of GM3-synthase, Chem. Eur J. 21 (2015) 14614–14629.
[19] K. Ikeda, S. Akamatsu, K. Achiwa, A new synthesis of α-glycosidically-linked disaccharides using 2α-chloro-3β-phenylthio KDO derivatives, Chem. Pharm. Bull. 38 (1990) 279–281.
[20] Y. Hatanaka, M. Hashimoto, K.I.P.J. Hidari, Y. Sanai, Y. Nagai, Y. Kanaoka, Synthesis of a carbon-linked CMP-NANA analog and its inhibitory effects on GM3 and GD3 synthases, Heterocycles 43 (1996) 531–534.
[21] L. Somsák, I. Bajza, G. Batta, Preparation of 2,6-Anhydro-3-deoxyhept-(or hex)2-enononitriles (1-cyanoglycals) from 1-Bromo-D-glycosyl cyanides with zinc under aprotic conditions, Liebigs Ann. Chem. (1990) 1265–1268.
[22] L. Kiss, L. Somsák, Evaluation of β-D-galactosyl and 2-Deoxy-D-*lyxo*-hex-1-enopyranosyl (D-Galactal) type *C*-glycosides as inhibitors of β-D-galactosidase from *E. coli*, Carbohydr. Res. 291 (1996) 43–52.
[23] K. Czifrák, P. Szilágyi, L. Somsák, Anomeric α-azido acid (2-azido-2-deoxy-hept-2-ulopyranosonic acid) derivatives en route to peptides incorporating sugar amino acids, Tetrahedron: Asymmetry 16 (2005) 127–141.
[24] L. Somsák, I. Németh, A simple method for the synthesis of acylated pyranoid glycals under aprotic conditions, J. Carbohydr. Chem. 12 (1993) 679–684.
[25] A. Banaszek, The first synthesis of 3-Deoxy-D-*lyxo*-2-heptulosaric acid (DHA) derivatives, Tetrahedron 51 (1995) 4231–4238.
[26] L. Somsák, V. Nagy, A new, scalable preparation of a glucopyranosylidene-spiro-thiohydantoin: one of the best inhibitors of glycogen phosphorylases, Tetrahedron: Asymmetry 11 (2000) 1719–1727. Corrigendum 2247.
[27] R.W. Myers, Y.C. Lee, Synthesis and characterization of some anomeric pairs of per-*O*-acetylated aldohexopyranosyl cyanides (per-*O*-acetylated 2,6-anhydrohep-tononitriles). On the reaction of per-*O*-acetylaldohexopyranosyl bromides with mercuric cyanide in nitromethane, Carbohydr. Res. 132 (1984) 61–82.
[28] L. Somsák, G. Batta, I. Farkas, *C*-Nucleosides VI. Preparation of acetylated *C*-(1-Bromo-D-glycosyl)heterocycles and 1-Bromo-D-glycosyl cyanides, Carbohydr. Res. 124 (1983) 43–51.
[29] L. Somsák, E. Sós, Z. Györgydeák, J.-P. Praly, G. Descotes, Synthesis and some transformations of 1-Cyano-glycopyranosyl azides " precursors of anomeric α-amino acids, Tetrahedron 52 (1996) 9121–9136.
[30] R.W. Myers, Y.C. Lee, Synthesis of diazomethyl β-D-galactopyranosyl and β-D-glucopyranosyl ketones. Potential affinity-labeling reagents for carbohydrate-binding proteins, Carbohydr. Res. 152 (1986) 143–158.
[31] X. Creary, Electronegatively substituted carbocations, Chem. Rev. 91 (1991) 1625–1678.
[32] S. Gronert, J.R. Keeffe, Calculated stabilities and structures for carbocations and singlet carbenes bearing electron-withdrawing groups, J. Phys. Org. Chem. 26 (2013) 1023–1031.
[33] I. Farkas, G. Snatzke, L. Somsák, CD of 1-cyano derivatives of pyranoses, Liebigs Ann. Chem. (1989) 599–600.
[34] S.H. Mahmoud, L. Somsák, I. Farkas, *C*-Nucleosides VII. Preparation of *C*-(2'-Deoxy-hex/pent-1'-enopyranosyl)-heterocycles, Carbohydr. Res. 254 (1994) 91–104.
[35] L. Lebedel, A. Arda, A. Martin, J. Desire, A. Mingot, M. Aufiero, N. Aiguabella Font, R. Gilmour, J. Jimenez-Barbero, Y. Bleriot, S. Thibaudeau, Structural and computational analysis of 2-halogeno-glycosyl cations in the presence of a superacid: an expansive platform, Angew. Chem. Int. Ed. 58 (2019) 13758–13762.
[36] J.-P. Praly, Structure of anomeric glycosyl radicals and their transformations under reductive conditions, Adv. Carbohydr. Chem. Biochem. 56 (2001) 65–151.
[37] A. Lubineau, Y. Queneau, A concise synthesis of (±)-ketodeoxyheptulosonic acid derivatives via aqueous hetero Diels Alder reaction and NBS mediated dibromination, J. Carbohydr. Chem. 14 (1995) 1295–1306.
[38] J.F. King, R.G. Pews, Reaction mechanism. II. Reductive elimination of 1,2-dihalides with lithium aluminum hydride, Can. J. Chem. 42 (1964) 1294–1314.