Advanced Synthesis & Catalysis

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To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201801059

Link to VoR: http://dx.doi.org/10.1002/adsc.201801059

10.1002/adsc.201801059

FULL PAPER

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

C-Glycosyl styrene type compounds by Pd-catalyzed cross-coupling reactions of anhydro-aldose tosylhydrazones with benzyl bromides

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Received: ((will be filled in by the editorial staff))

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Abstract. *C*-Glycopyranosyl styrene type compounds are valuable synthetic intermediates whose syntheses are known in rather lengthy procedures. Herein palladium-catalyzed cross-couplings of *O*-peracylated 2,6-anhydro-aldose tosylhydrazones with benzyl bromides were studied under thermic conditions in the presence of LiO*t*Bu. The reactions gave the corresponding *C*-glycopyranosyl styrenes in up to 59 % yields. The transformations represent a new, short synthetic sequence to get this type of glycomimetic compounds in 4-5 steps from a free aldose.

Keywords: Alkenes; Anhydro-aldose tosylhydrazones; Carbenes; Carbohydrates; Cross-coupling; C-C coupling; *C*-Glycosides.

Introduction

C-Glycosyl compounds are present in nature, among synthetic derivatives, and active ingredients of marketed drugs, and their chemistry as well as already realized and potential applications have been comprehensively reviewed recently.[1-3]

Among many types of *C*-glycosyl derivatives *C*-glycosyl styrenes **F** (Scheme 1) are versatile starting compounds of e. g. *C*-glycosyl-aldehydes (highly appreciated intermediates for the synthesis of complex *C*-glycosyl derivatives),[4-6] *cis*- and *trans*-fused allylic and vinylic bicyclic ethers,[7, 8] (structural elements of marine toxins[9]), pyranopyran carbohydrate amino acids (building blocks of glyco- and peptidomimetic compounds),[10, 11] analogues of uridine-5'-diphosphate (UDP) sugar derivatives[12] (potential glycosyltransferase inhibitors), *C*-linked glycosyl coumarins and isocoumarins[13] (e. g. antibacterial, anticancer agents) and (parts of) natural products such as ambruticin[5] (an antifungal antibiotic) or lasonolide A[14] (anticancer activity).

The known synthetic routes to access *C*-glycopyranosyl styrenes **F** are summarized in Scheme 1. One of the applied approaches is the construction of the C-C bond between the anomeric carbon and the aglycon part of the molecules. Among these methods inter- and intramolecular variants can also be found. Thus, the intermolecular possibility is represented by the direct *C*-glycosylation of glycosyl fluoride **A** with potassium styryl trifluoroborate,[5] the irradiation of glycosylcobaloximes **B** in the presence of alkenes,[15] while in the intramolecular approaches radical-induced cyclization of the 2-phenylethynylsiloxy-glucopyranosylphenylselenide[16] **C** or 2-alkynylsiloxy-glycopyranosylphenylsulfones[17] **D** followed by desilylation gave styrenes **F**.

The most frequently applied method for the preparation of *C*-glycopyranosyl styrenes **F** is the partial reduction of the acetylene moiety in **E** by employing Lindlar catalyst[4, 7, 8, 10, 11] or zinc.[18] Arylethynyl derivatives **E** can be obtained directly from a glycopyranosyl bromide or chloride or in a two-step reaction from 1,2-anhydro aldopyranose derivatives or lactones, as detailed in the above references.

In other syntheses the construction of the C=C bond in styrenes **F** are realized in one step: dehydration reaction of *O*-perbenzylated or *O*-peracetylated 1-phenyl-2-(β-D-glucopyranosyl)ethanol **H**, prepared from free aldoses in three-step reactions[6] or the Julia olefination of the *O*-perbenzylated β-*C*-glucopyranosyl aldehyde **I** resulted in *C*-glycopyranosyl styrenes **F**.[13] Another possibility is the formation of the C=C bond in a cross-metathesis reaction between a vinyl α-*C*-D-galactopyranoside **J** with alkenes in the presence of Hoveyda-Grubbs II catalyst and CuI.[19]

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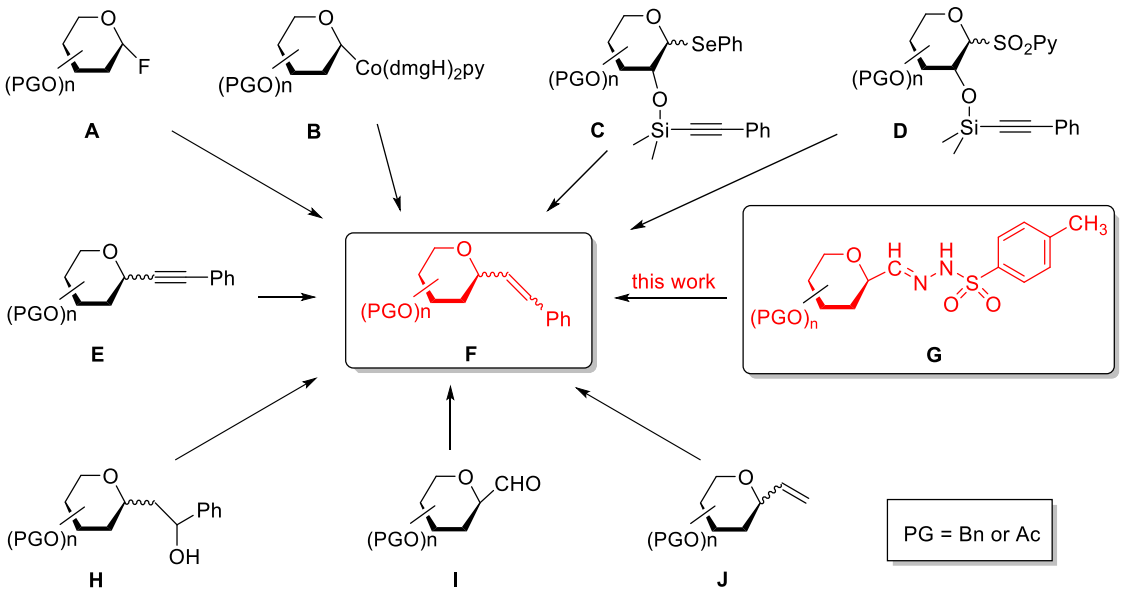

Scheme 1. Synthetic routes toward *C*-glycopyranosyl styrenes **F** (for details see text).

From a synthetic point of view, most of the above methods lack generality, need special starting materials or reagents prepared in lengthy reaction sequences, therefore, a mild catalytic methodology to prepare *C*-glycopyranosyl styrene derivatives from starting compounds easily available in any monosaccharide configuration would be desirable.

In the last decade tosylhydrazones emerged as reaction partners in various cross-coupling reactions.[20-24] In recent years we have studied the utility of anhydro-aldose tosylhydrazones **G** readily obtained from glycosyl cyanides.[25-27] Thus, metal free couplings of **G** with alcohols, phenols, carboxylic acids,[28] and thiols,[29] as well as Pd-catalyzed cross couplings with aryl bromides[30] were studied. Herein we disclose our experiences with Pd-catalyzed reactions between **G** and benzyl bromides which provide a new, alternative, and shorter reaction pathway to *C*-glycopyranosyl styrenes **F**.

Results and Discussion

At the outset, we chose *O*-perbenzoylated *C*-(β-D-glucopyranosyl)formaldehyde tosylhydrazone **1**[26, 27] and benzyl bromide as the substrates to optimize the reductive coupling reaction (Table 1). Initially, it was observed that using 5 mol% ($Pd(OAc)_2$) with (LiO*t*Bu) as the base in 1,4-dioxane at 70 °C the expected coupling product **2a** could be isolated, albeit in only very low yield (Table 1, entry 1). Other ligands such as di(1-adamantyl)-*n*-butylphosphine (CataCXium A) and 1,3-bis(diphenylphosphino)propane (DPPP) were found to be also effective (entries 3 and 5, respectively), however, the yield did not improve. On the other hand tri(2-furyl)phosphine ($P(2\text{-furyl})_3$) and 1,1'-ferrocenediyl-bis(diphenylphosphine) (DPPF) gave somewhat better results (entries 2 and 4, respectively). Performing the reaction with 2.5 mol% tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$) catalyst in the presence of $P(2\text{-furyl})_3$ and LiO*t*Bu in 1,4-dioxane at reflux temperature or in toluene at 80 °C as suggested in the literature for aromatic coupling partners[31] gave compound **2a** in very low (entry 6) or moderate yield (entry 7), respectively. Further optimization of the reaction conditions revealed that the yields could be significantly improved by raising the amount of benzyl bromide (entries 8 and 9). The optimized reaction conditions are shown in entry 9, under which the coupling product **2a** could be obtained in 48% yield. In almost every cases the formation of *exo*-glucal **3** and *N*-benzylated tosylhydrazone **4a** as by-products were observed.

With the optimized conditions in hand, the scope of the reaction was first explored with tosylhydrazone **1** and a variety of substituted benzyl bromides (Table 2). The reactions afforded the corresponding styrenes in low to medium yields. The substitution pattern of the aromatic ring with electron-donating and electron-withdrawing groups and *ortho*, *meta* or *para* position of the substituents had only a moderate effect on the yields (entries 1-10). Similarly to previous findings, the formation of *exo*-glucal **3** and *N*-benzylated tosylhydrazone **4** could never be avoided. Further by-products having no carbohydrate residue were also observed in these reactions, and in one case, from the reaction in entry 3, this compound was isolated and proved to be 3-methoxybenzyl-4-methylphenyl-sulfone **5c** clearly formed by the reaction of the toluenesulfinate anion with the corresponding benzyl bromide (see mechanistic proposal later).

A further optimization was performed with 4-cyanobenzyl bromide (Table 3) which was the reagent in one of the relatively low yielding reactions. Application of a higher ratio of the $Pd_2(dba)_3$ catalyst (10 mol%) and the $P(2\text{-furyl})_3$ ligand (40 mol%) resulted in somewhat better yields (entry 2). Nevertheless, raising the quantities in an

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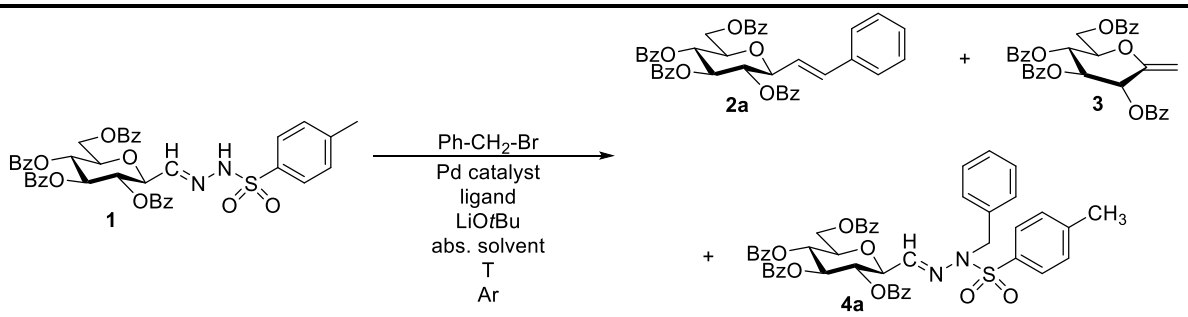
extraordinary way (50 mol% $Pd_2(dba)_3$ catalyst and 400 mol% P(2-furyl)$_3$ ligand, entry 3) doubled the yield. Application of 40 mol% P(2-furyl)$_3$ ligand with various Pd-catalysts did not affect the yields significantly (entries 4-7). Next, the effect of the ligands was also examined. The use of $Pd_2(dba)_3$ catalyst (10 mol%) with CataCXium A, DPPF and 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (XPhos) diminished the yields (entries 8, 10, 11, respectively), nevertheless, better results were achieved with DPPP and PPh_3 (entries 9, 12). Similarly to the other reactions, formation of by-products **3**, **4j** and type **5** could not be avoided.

Table 1. Optimization of reaction conditions



Entry	Pd catalyst (mol %)	Ligand (mol %)	Ph-CH_2-Br (equiv.)	LiO*t*Bu (equiv.)	Solvent	T (°C)	Yield (%)		
							2	**3**	**4**
1	$Pd(OAc)_2$ (5)	XPhos (20)	1	3	1,4-dioxane	70	3	15	4
2	$Pd(OAc)_2$ (5)	P(2-furyl)$_3$ (20)	1	3	1,4-dioxane	70	25	in traces	nd[a]
3	$Pd(OAc)_2$ (5)	CataCXium A (20)	1	3	1,4-dioxane	70	3	4	in traces
4	$Pd(OAc)_2$ (5)	DPPF (20)	1	3	1,4-dioxane	70	24	2	in traces
5	$Pd(OAc)_2$ (5)	DPPP (20)	1	3	1,4-dioxane	70	3	7	in traces
6	$Pd_2(dba)_3$ (2.5)	P(2-furyl)$_3$ (20)	1	3	1,4-dioxane	101	4	nd[a]	nd[a]
7	$Pd_2(dba)_3$ (2.5)	P(2-furyl)$_3$ (20)	1	3	toluene	80	32	2	3
8	$Pd_2(dba)_3$ (2.5)	P(2-furyl)$_3$ (20)	3	1.5	1,4-dioxane	70	22	nd[a]	nd[a]
9	**$Pd_2(dba)_3$ (2.5)**	**P(2-furyl)$_3$ (20)**	6	1.5	1,4-dioxane	70	48	11	nd[a]

[a] Not detectable

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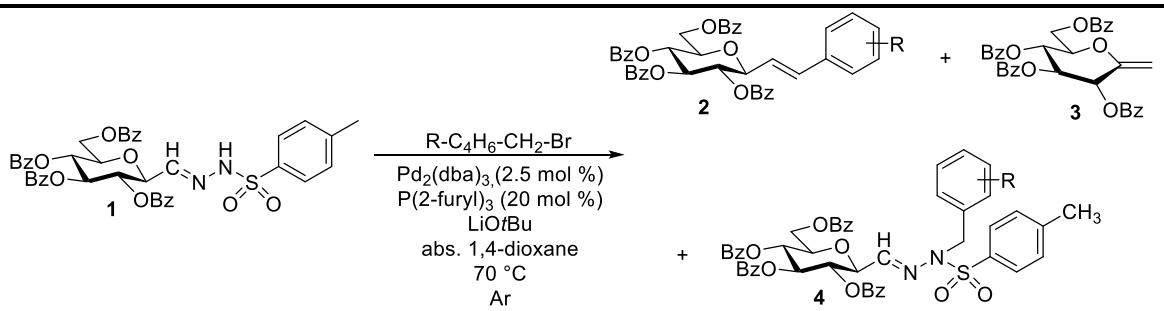
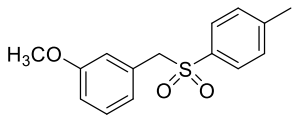
Table 2. Pd-catalyzed coupling of tosylhydrazone **1** with benzyl bromides



Entry		R	$R\text{-}C_6H_4\text{-}CH_2\text{-}Br$ (equiv.)	LiO*t*Bu (equiv.)	Yield (%)		
					2	**3**	**4**
1	**a**	H	6	1.5	48	11	nd[a]
2	**b**	4-CH_3	6	1.5	40	6	11
3[b]	**c**	3-CH_3O	6	1.5	10	nd[a]	31
4	**d**	4-Cl	6	1.5	40	5	14
5	**e**	3-Cl	6	1.5	42	6	nd[a]
6	**f**	4-Br	6	1.5	54	4	nd[a]
7	**g**	3-Br	6	1.5	32	11[c]	5
8	**h**	2-Br	6	1.5	36	20	2
9	**i**	4-NO_2	6	1.5	20[d]	in traces	16[c]
10	**j**	4-CN	6	1.5	27	16[c]	17[c]

[a] Not detectable

[b] By-product containing no carbohydrate residue isolated from the reaction:



5c

[c] Yields calculated on the basis of the ^{1}H NMR spectra of the worked-up reaction mixture.

[d] Based on the ^{1}H NMR spectrum of the crude mixture formation of an equal amount of the *Z* isomer was observed.

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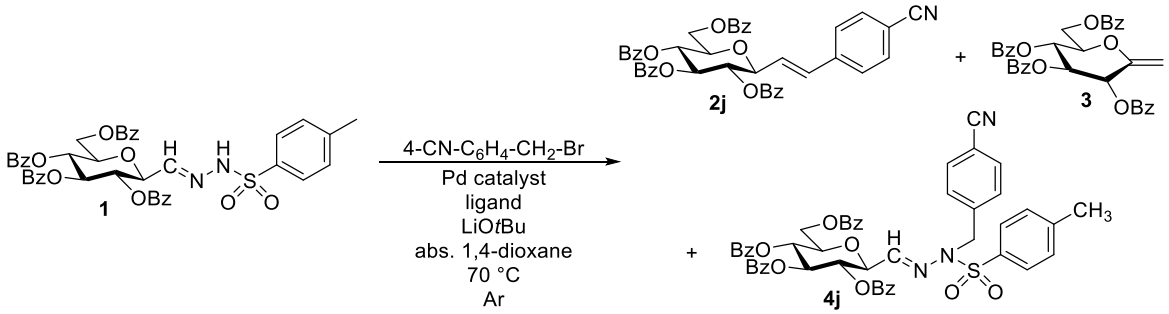
Table 3. Optimization of the reaction conditions of Pd-catalyzed coupling of tosylhydrazone **1** with 4-cyanobenzyl bromide



Entry	Pd catalyst (mol %)	Ligand (mol %)	4-CN-C_6H_4-CH_2-Br (equiv.)	LiO*t*Bu (equiv.)	Yield (%)		
					2j	**3**	**4j**
1	$Pd_2(dba)_3$ (2.5)	P(2-furyl)$_3$ (20)	6	1.5	27	16[a]	17[a]
2	$Pd_2(dba)_3$ (10)	P(2-furyl)$_3$ (40)	3	1.5	35	12	21
3	$Pd_2(dba)_3$ (50)	P(2-furyl)$_3$ (400)	6	1.5	55	5	7
4	$Pd(OAc)_2$ (19)	P(2-furyl)$_3$ (40)	6	1.5	32	10	18
5	$Pd(CH_3CN)_2Cl_2$ (10)	P(2-furyl)$_3$ (40)	6	1.5	30	4	20
6	$Pd(PPh_3)_2Cl_2$ (10)	P(2-furyl)$_3$ (40)	6	1.5	36	1	53
7	$Pd(PPh_3)_4$ (10)	P(2-furyl)$_3$ (40)	6	1.5	24	16	27
8	$Pd_2(dba)_3$ (10)	CataCXium A (40)	6	1.5	14	13	63
9	$Pd_2(dba)_3$ (10)	DPPP (40)	6	1.5	42[a]	20	29[a]
10	$Pd_2(dba)_3$ (10)	DPPF (40)	6	1.5	22[a]	in traces	28[a]
11	$Pd_2(dba)_3$ (10)	XPhos (40)	6	1.5	21	in traces	28
12	$Pd_2(dba)_3$ (10)	PPh_3 (40)	6	1.5	40	in traces	17

[a] Yields calculated on the basis of the ^{1}H NMR spectra of the worked-up reaction mixture.

The examinations were extended to the D-*galacto* configured tosylhydrazone **6** (Table 4). The corresponding styrene **7a** was isolated in good yield (entry 1). The substrates bearing both electron-donating (entries 2, 3) and electron-withdrawing (entries 4, 5) substituents on the aromatic ring could afford the corresponding products **7b-e** in low to medium yields. There was no clear correlation between the yields and the arene substitution pattern (*meta* or *para* positions, compare entries 2-3 and 4-5). The *exo*-galactal **8** and the substituted tosylhydrazone **9** by-products were isolated from the reaction mixtures in almost every case.

Some trials were conducted with allyl bromide, propargyl bromide and *n*-butyl bromide to explore the possibility of extending the reaction to aliphatic coupling partners. However, these experiments gave only very complex mixtures from which no discrete product could be isolated except for the reaction with allyl bromide which furnished the *N*-allyl tosylhydrazone **10** in a low yield (18 %).

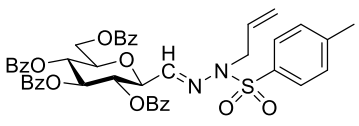


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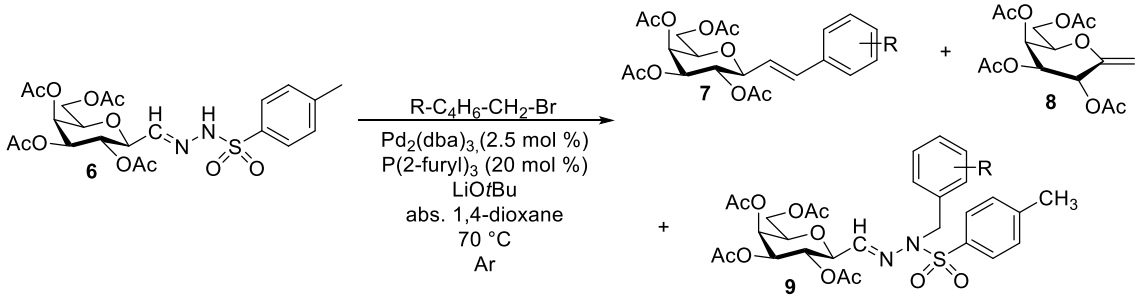
Table 4. Pd-catalyzed coupling of tosylhydrazone **6** with benzyl bromides



Entry		R	R-C_6H_4-CH_2-Br (equiv.)	LiO*t*Bu (equiv.)	Yield (%)		
					7	**8**	**9**
1	**a**	H	6	1.5	59	5	nd[a]
2	**b**	4-CH_3	3	2.2	39	7[b]	nd[a]
3	**c**	3-CH_3	6	1.5	25	3	7
4	**d**	3-Cl	6	1.5	59	3	nd[a]
5	**e**	4-Br	6	1.5	31	in traces	9

[a] Not detectable
[b] Yields calculated on the basis of the ^{1}H NMR spectra of the worked-up reaction mixture.

The configuration of the double bonds in compounds **2** and **7** was *E* as followed from the vicinal coupling constants of the olefinic protons (**2**: H-1 6.74–6.59 ppm, H-2 6.36–6.14 ppm, $J_{1,2}$ 15.9–15.8 Hz; **7**: H-1 6.66–6.60 ppm, H-2 6.12–6.06 ppm, $J_{1,2}$ 15.9–15.8 Hz). This was corroborated by a n. O. e. measurement for **2a** (Fig. 1) to show spatial vicinity of the indicated protons that is possible only in the *E* configuration of the double bond.

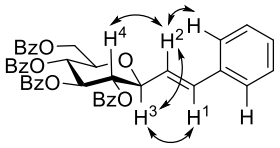


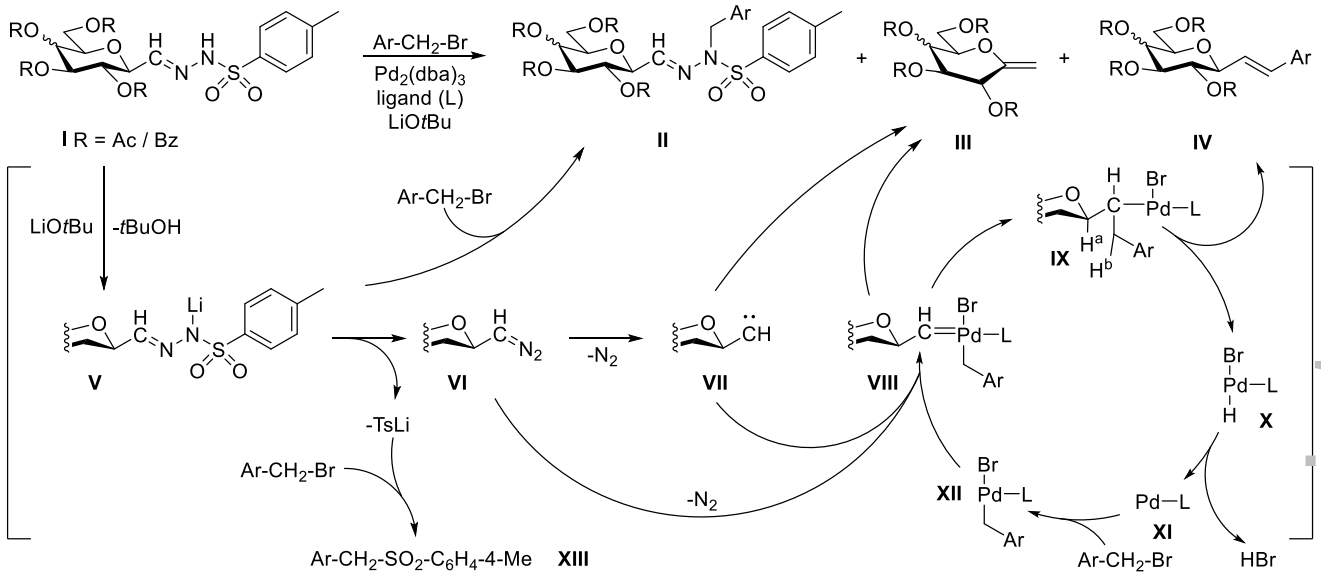
Figure 1. Characteristic nuclear Overhauser effects in *C*-glucopyranosyl styrene (*E*)-**2a**.

A mechanistic proposal to explain the formation of the desired *C*-glycosyl styrenes and the observed by-products is outlined in Scheme 2. The starting tosylhydrazone **I** is deprotonated to lithium-salt **V** which by acting as a nucleophile reacts with the benzyl bromide to give the *N*-benzylated tosylhydrazone **II**. Loss of a toluenesulfinate ion from **V** results in a diazo compound **VI**. The TsLi can react with the benzyl bromide to sulfone **XIII** observed in each reaction and isolated in one case. Diazo compound **VI** on loss of nitrogen gives carbene **VII** which can undergo an intramolecular C-H insertion to give the *exo*-glycal **III**. Alternatively, **VII** may enter the catalytic cycle by reacting with a benzylpalladium complex **XII** (formed in the usual way by oxidative addition of the benzyl bromide to a Pd(0) complex **XI**) to yield **VIII**. On the other hand, direct formation of **VIII** is also possible from **VI**. Intermediate **VIII** may also result in **III** by a H-shift, thereby providing an alternative route to the formation of the *exo*-glycal by-product **III**. Whether **III** is formed from **VII** or **VIII** cannot be proven on the basis of the present data, probably both routes may be operative. Rearrangement of **VIII** to **IX** is followed by a β-hydride elimination. From the two possibilities loss of H^b is preferred to that of H^a due to the formation of the conjugated system resulting in the target compounds **IV** and the Pd-complex **X**. Loss of HBr from **X** closes the catalytic cycle.

This complex system of reactions may account for the medium yields of the target compounds. Since the benzyl bromide reaction partner can participate in two competing transformations toward **II** and **XIII** besides **XII**, even its relatively high proportion does not lead to high conversions. On the other hand, the essential carbene intermediate **VII** is also subject of an intramolecular (to **III**) and an intermolecular (to **VIII**) reaction, and monomolecular transformations used to be faster than bimolecular ones. In the light of these competing reaction pathways the obtained yields of **IV** can be considered as satisfactory.

Taking into account that the starting anhydro-aldose tosylhydrazones of several configurations are available from a free aldose in 3-4 well established steps which generally need no chromatographic purification, except in some cases for the tosylhydrazone itself, this method gives

the target *C*-glycosyl styrene type compounds in a remarkably short reaction sequence.



Scheme 2. Mechanistic proposal for the coupling of *C*-(β-D-glycopyranosyl)formaldehyde tosylhydrazones with benzyl bromides and the formation of by-products.

Conclusion

Pd-Catalyzed cross-couplings of anhydro-aldose tosylhydrazones and benzyl bromides give *C*-glycopyranosyl styrenes as the main products with unavoidable formation of *exo*-glycals and other by-products of nucleophilic substitution. The yields of the transformations vary between 10-59 %, nevertheless, this synthetic route represents a significantly shorter sequence to the target compounds from a free aldose in comparison to the known methods.

Experimental Section

General methods

Optical rotations were determined with a Perkin–Elmer 241 polarimeter at room temperature. NMR spectra were recorded with Bruker Avance 250 II (250/63 MHz for $^{1}H/^{13}C$), Bruker Avance 300 III (300/75 MHz for $^{1}H/^{13}C$), Bruker 360 AM Avance (360/90 MHz for $^{1}H/^{13}C$) or Bruker DRX 400 (400/100 MHz for $^{1}H/^{13}C$) spectrometers. Chemical shifts are referenced to TMS as the internal reference (^{1}H), or to the residual solvent signals (^{1}H, ^{13}C). The assignments of the ^{1}H and ^{13}C NMR signals of compounds **2**, **4**, **7**, **9** were performed by their COSY (**2a**,**d**,**k**, **4b**,**d**, **7a**,**e**, **9e**), HSQC (**2a**,**d**,**k**, **4b**,**d**, **7a**,**e**, **9e**) and HMBC (**2a**,**d**,**k**, **4b**,**d**, **7a**,**e**, **9e**) spectra. Mass spectra were obtained by an Agilent GC 7890A / MS 5975C or by an Agilent HP GC / MS 5890 / 5973 instrument (EI, 70 eV) by GC inlet or by a MX-1321 and Finnigan MAT 95 XP (Thermo Electron Corp., San Jose, CA, USA) instruments (EI, 70 eV) by direct inlet or by an Agilent 1969A Time-of-Flight or a maXis II UHR ESI-QTOF MS instrument (Bruker) operated in positive ion ESI mode. TLC was performed on DCAlurolle Kieselgel 60 F254 (Merck). TLC plates were visualized under UV light, and by gentle heating. For column chromatography Kieselgel 60 (Merck, particle size (0.063–0.200 mm) or Al_2O_3 neutral (Across Organics, particle size: (0.050–0.200 mm, 60A) was applied. 1,4-Dioxane was distilled from sodium benzophenone ketyl and stored over sodium wires.

General procedure for the synthesis of ω-(*C*-2,3,4,6-tetra-*O*-acyl-β-D-glycopyranosyl)styrenes (2, 7)
A (bromomethyl)benzene (3 or 6 mmol, specified with the particular compounds), LiO*t*Bu base (2.2 or 1.5 mmol, specified with the particular compounds), P(2-furyl)$_3$ ligand (20 mol%) and $Pd_2(dba)_3$ catalyst (2.5 mol%) were added to abs. 1,4-dioxane (8 mL). The suspension was stirred and heated to 70 °C (bath temp) under an inert (Ar, N_2) atmosphere and then a solution of tosylhydrazone (**1** or **6** (1 mmol)) in abs. 1,4-dioxane (15 mL) was added dropwise in 20 min. When TLC (1:2 EtOAc–hexane or 1:2 EtOAc–heptane; 1:1 EtOAc–hexane or 1:1 EtOAc–heptane) indicated complete consumption of the starting compound (2.5 h–22 h), the mixture was cooled and the insoluble material filtered off through a pad of celite and washed thoroughly with abs. 1,4-dioxane (3 × 20 mL). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (neutral Al_2O_3) with eluents indicated for the particular compounds to give ω-(*C*-2,3,4,6-tetra-*O*-acyl-β-D-glycopyranosyl) styrenes.

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1,2-dideoxy-1-phenyl-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)styrene) (2a)
Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), (bromomethyl)benzene (6 equiv., 0.18 mL, 0.26 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (4h). Purified by column chromatography (1:8 EtOAc–heptane) to yield 85 mg (48 %) of **2a** as a white amorphous product. R_f: 0.39 (1:2 EtOAc–hexane); $[\alpha]_D$ –31 (*c* 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14–7.68 (8H, m, aromatics), 7.64–7.06 (17H, m, aromatics), 6.69 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.20 (1H, dd, $J_{2,3}$ 7.3 Hz, H-2), 5.98 (1H, pseudo t, $J_{5,6}$ 9.5 Hz, H-5), 5.76 (1H, pseudo t, $J_{6,7}$ 9.7 Hz, H-6), 5.54 (1H, pseudo t, $J_{4,5}$ 9.8 Hz, H-4), 4.67 (1H, dd, $J_{8a,8b}$ 12.3 Hz, H-8_a), 4.51 (1H, dd, H-8_b), 4.39 (1H, dd, $J_{3,4}$ 9.5 Hz, H-3), 4.21 (1H, ddd, $J_{7,8a}$ 3.1, $J_{7,8b}$ 4.8 Hz, H-7). ^{13}C NMR (100

MHz, $CDCl_3$) δ 166.4, 166.1, 165.5, 165.4 (4×CO), 135.2 (C-1), 136.7–126.1 (aromatics), 124.3 (C-2), 80.0 (C-3), 76.2 (C-7), 74.3 (C-5), 72.4 (C-4), 69.9 (C-6), 63.5 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=705.2095, found: $[M+Na]^+$=705.2096; $C_{42}H_{34}O_9$ (682.22).

2,6-Anhydro-*N*^{1}-benzyl-3,4,5,7-tetra-*O*-benzoyl-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-benzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4a)

Isolated as a by-product beside **2a** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 5 mg (3 %) of **4a** as a white amorphous product. R_f: 0.10 (1:2 EtOAc–hexane); $[\alpha]_D$ –8 (*c* 0.10, $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.13–7.69 (8H, m, aromatics), 7.67–7.12 (19H, m, aromatics), 6.93 (2H, d, *J* 8.2 Hz, aromatics), 6.82 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.87 (1H, pseudo t, $J_{4,5}$ 9.8 Hz, H-4), 5.61 (1H, pseudo t, $J_{5,6}$ 9.7 Hz, H-5), 5.33 (1H, pseudo t, $J_{3,4}$ 9.7 Hz, H-3), 4.83 (1H, d, $J_{CH2a,CH2b}$ 16.7 Hz, CH_{2a}), 4.70 (1H, d, CH_{2b}), 4.52 (1H, dd, $J_{7a,7b}$ 12.2 Hz, H-7$_a$), 4.38 (1H, dd, H-7$_b$), 4.34 (1H, dd, $J_{2,3}$ 9.7 Hz, H-2), 4.11 (1H, ddd, $J_{6,7a}$ 2.8, $J_{6,7b}$ 4.8 Hz, H-6), 2.23 (3H, s, CH_3). ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.3, 165.9, 165.4, 165.3 (4×CO), 139.8 (C-1), 144.5–125.5 (aromatics), 78.8 (C-2), 76.3 (C-6), 73.9 (C-4), 70.9 (C-3), 69.5 (C-5), 63.3 (C-7), 51.2 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=889.2402, found: $[M+Na]^+$=889.2386; $C_{49}H_{42}N_2O_{11}S$ (866.25).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1,2-dideoxy-1-(4-methylphenyl)-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-4-methylstyrene) (2b)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-4-methylbenzene (6 equiv., 0.29 g, 1.54 mmol) and Li*O*t*Bu (1.5 equiv., 0,03 g, 0.39 mmol) according to General procedure (16h). Purified by column chromatography (1:7 EtOAc–hexane) to yield 72 mg (40 %) of **2b** as a pale yellow amorphous product. R_f: 0.42 (1:2 EtOAc–hexane); $[\alpha]_D$ –20 (*c* 0.55, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–7.76 (8H, m, aromatics), 7.57–6.91 (16H, m, aromatics), 6.66 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.14 (1H, dd, $J_{2,3}$ 7.4 Hz, H-2), 5.97 (1H, pseudo t, $J_{5,6}$ 10.1 Hz, H-5), 5.75 (1H, pseudo t, $J_{6,7}$ 9.8 Hz, H-6), 5.53 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 4.66 (1H, dd, $J_{8a,8b}$ 12.2 Hz, H-8$_a$), 4.50 (1H, dd, H-8$_b$), 4.38 (1H, dd, $J_{3,4}$ 9.3 Hz, H-3), 4.21 (1H, ddd, $J_{7,8a}$ 2.9, $J_{7,8b}$ 4.8 Hz, H-7), 2.28 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 165.4 (4×CO), 135.2 (C-1), 145.3–125.1 (aromatics), 123.2 (C-2), 80.2 (C-3), 76.2 (C-7), 74.4 (C-5), 72.4 (C-4), 69.9 (C-6), 63.5 (C-8), 21.3 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=719.2252, found: $[M+Na]^+$=719.2249; $C_{43}H_{36}O_9$ (696.24).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(4-methylbenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-4-methylbenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4b)

Isolated as a by-product beside **2b** from the previous reaction mixture by column chromatography (1:7 EtOAc–hexane) to yield 25 mg (11 %) of **4b** as a white amorphous product. R_f: 0.36 (1:2 EtOAc–hexane); $[\alpha]_D$ –22 (*c* 0.60, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–7.69 (8H, m, aromatics), 7.67–7.12 (14H, m, aromatics), 7.11–6.88 (6H, m, aromatics), 6.85 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.87 (1H, pseudo t, $J_{4,5}$ 9.8 Hz, H-4), 5.61 (1H, pseudo t, $J_{5,6}$ 9.7 Hz, H-5), 5.34 (1H, pseudo t, $J_{3,4}$ 9.7 Hz, H-3), 4.78 (1H, d, $J_{CH2a,CH2b}$ 16.5 Hz, CH_{2a}), 4.66 (1H, d, CH_{2b}), 4.52 (1H, dd, $J_{7a,7b}$ 12.2 Hz, H-7$_a$), 4.39 (1H, dd, H-7$_b$), 4.34 (1H, dd, $J_{2,3}$ 10.1 Hz, H-2), 4.11 (1H, ddd, $J_{6,7a}$ 2.5, $J_{6,7b}$ 4.5 Hz, H-6), 2.27 (3H, s, CH_3), 2.23 (3H, s, CH_3-Ts). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.9, 165.4, 165.3 (4×CO), 139.7 (C-1), 144.0–126.3 (aromatics), 78.8 (C-2), 76.2 (C-6), 73.9 (C-4), 70.9 (C-3), 69.4 (C-5), 63.9 (C-7), 51.1 (CH_2), 21.8 (CH_3-Ts), 21.2 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=903.2558, found: $[M+Na]^+$=903.2566; $C_{50}H_{44}N_2O_{11}S$ (880.27).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1,2-dideoxy-1-(3-methoxyphenyl)-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-3-methoxystyrene) (2c)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-3-methoxybenzene (6 equiv., 0.22 mL, 0.31 g, 1.54 mmol) and Li*O*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (19h). Purified by column chromatography (1:8 EtOAc–hexane) to yield 19 mg (10 %) of **2c** as a yellow amorphous product. R_f: 0.31 (1:2 EtOAc–hexane); $[\alpha]_D$ –25 (*c* 0.60, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–7.78 (8H, m, aromatics), 7.62–7.23 (12H, m, aromatics), 7.18–7.11 (1H, m, aromatic), 6.99–6.72 (3H, m, aromatics), 6.66 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.18 (1H, dd, $J_{2,3}$ 7.3 Hz, H-2), 5.97 (1H, pseudo t, $J_{5,6}$ 9.8 Hz, H-5), 5.75 (1H, pseudo t, $J_{6,7}$ 9.8 Hz, H-6), 5.53 (1H, pseudo t, $J_{4,5}$ 9.5 Hz, H-4), 4.65 (1H, dd, $J_{8a,8b}$ 12.3 Hz, H-8$_a$), 4.50 (1H, dd, H-8$_b$), 4.39 (1H, dd, $J_{3,4}$ 9.2 Hz, H-3), 4.21 (1H, ddd, $J_{7,8a}$ 2.8, $J_{7,8b}$ 4.8 Hz, H-7), 3.75 (3H, s, O–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 165.4 (4×CO), 135.0 (C-1), 137.7–110.0 (aromatics), 124.6 (C-2), 80.0 (C-3), 76.2 (C-7), 74.3 (C-5), 72.4 (C-4), 69.9 (C-6), 63.5 (C-8), 55.3 (O–CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=735.2201, found: $[M+Na]^+$=735.2199; $C_{43}H_{36}O_{10}$ (712.23).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(3-methoxybenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-3-methoxybenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4c)

Isolated as a by-product beside **2c** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 72 mg (31 %) of **4c** as a yellow amorphous product. R_f: 0.23 (1:2 EtOAc–hexane); $[\alpha]_D$ –2 (*c* 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28–7.69 (8H, m, aromatics), 7.64–7.04 (16H, m, aromatics), 6.92 (2H, d, *J* 8.2 Hz, aromatics), 6.86 (1H, d, $J_{1,2}$ 6.7 Hz, H-1), 6.83–6.72 (2H, m, aromatics), 5.88 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 5.62 (1H, pseudo t, $J_{5,6}$ 10.0 Hz, H-5), 5.34 (1H, pseudo t, $J_{3,4}$ 9.7 Hz, H-3), 4.82 (1H, d, $J_{CH2a,CH2b}$ 16.6 Hz, CH_{2a}), 4.64 (1H, d, CH_{2b}), 4.53 (1H, dd, $J_{7a,7b}$ 12.3 Hz, H-7$_a$), 4.39 (1H, dd, H-7$_b$), 4.34 (1H, dd, $J_{2,3}$ 9.9 Hz, H-2), 4.12 (1H, ddd, $J_{6,7a}$ 2.4, $J_{6,7b}$ 5.2 Hz, H-6), 3.68 (3H, s, O–CH_3), 2.22 (3H, s, CH_3). ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.3, 165.9, 165.4, 165.3 (4×CO), 140.0 (C-1), 160.4–111.5 (aromatics), 78.8 (C-2), 76.3 (C-6), 73.8 (C-4), 70.9 (C-3), 69.4 (C-5), 63.4 (C-7), 55.3 (O–CH_3), 51.3 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=919.2507, found: $[M+Na]^+$=919.2508; $C_{50}H_{44}N_2O_{11}S$ (896.26).

4-Methylphenyl-3-methoxybenzyl sulfone (5c)

Isolated as a by-product beside **2c** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 40 mg (56 %) of **5c** as a yellow amorphous product. ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.53 (2H, d, *J* 8.2 Hz, Ts), 7.24 (2H, d, *J* 8.1 Hz, Ts), 7.20–7.10 (1H, m, aromatic), 6.85 (1H, d, *J* 7.3 Hz, aromatic), 6.68–6.58 (2H, m, aromatics), 4.26 (2H, s, CH_2), 3.71 (3H, s, O–CH_3), 2.41 (3H, s, CH_3). ^{13}C NMR (90 MHz, $CDCl_3$) δ 140.4–114.5 (aromatics), 63.1 (O–CH_3), 55.3 (CH_2), 21.7 (CH_3). HR-ESI-MS positive mode (m/z): calcd. for: $[M+Na]^+$=299.0712, found: $[M+Na]^+$=299.0710; $C_{15}H_{16}O_3S$ (276.08).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(4-chlorophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-4-chlorostyrene) (2d)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-4-chlorobenzene (6 equiv., 0.32 g, 1.54

mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (4.5h). Purified by column chromatography (1:8 EtOAc–hexane) to yield 74 mg (40 %) of **2d** as an orange amorphous product. R_f: 0.44 (1:2 EtOAc–hexane); $[\alpha]_D$ –17 (*c* 0.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–7.77 (8H, m, aromatics), 7.66–7.06 (16H, m, aromatics), 6.63 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.17 (1H, dd, $J_{2,3}$ 7.2 Hz, H-2), 5.98 (1H, pseudo t, $J_{5,6}$ 9.5 Hz, H-5), 5.75 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.51 (1H, pseudo t, $J_{4,5}$ 9.8 Hz, H-4), 4.67 (1H, dd, $J_{8a,8b}$ 12.3 Hz, H-8_a), 4.50 (1H, dd, H-8_b), 4.38 (1H, dd, $J_{3,4}$ 9.5 Hz, H-3), 4.21 (1H, ddd, $J_{7,8a}$ 2.9, $J_{7,8b}$ 4.8 Hz, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.1, 165.5, 165.4 (4×CO), 134.6 (C-1), 136.5–126.1 (aromatics), 125.0 (C-2), 79.9 (C-3), 76.2 (C-7), 74.2 (C-5), 72.4 (C-4), 69.8 (C-6), 63.4 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=739.1705, found: $[M+Na]^+$=739.1705; $C_{42}H_{33}ClO_9$ (716.18).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(4-chlorobenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-4-chlorobenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4d)

Isolated as a by-product beside **2d** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 33 mg (14 %) of **4d** as a yellow amorphous product. R_f: 0.30 (1:2 EtOAc–hexane); $[\alpha]_D$ –17 (*c* 0.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–7.67 (8H, m, aromatics), 7.65–7.11 (14H, m, aromatics), 7.09–6.89 (6H, m, aromatics), 6.80 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.88 (1H, pseudo t, $J_{4,5}$ 9.6 Hz, H-4), 5.62 (1H, pseudo t, $J_{5,6}$ 10.0 Hz, H-5), 5.34 (1H, pseudo t, $J_{3,4}$ 9.8 Hz, H-3), 4.75 (1H, d, $J_{CH2a,CH2b}$ 16.8 Hz, CH_{2a}), 4.68 (1H, d, CH_{2b}), 4.54 (1H, dd, $J_{7a,7b}$ 12.4 Hz, H-7_a), 4.40 (1H, dd, H-7_b), 4.34 (1H, dd, $J_{2,3}$ 9.9 Hz, H-2), 4.13 (1H, ddd, $J_{6,7a}$ 2.8, $J_{6,7b}$ 4.9 Hz, H-6), 2.23 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 165.9, 165.4, 165.3 (4×CO), 139.9 (C-1), 145.3–127.6 (aromatics), 78.7 (C-2), 76.3 (C-6), 73.7 (C-4), 70.8 (C-3), 69.4 (C-5), 63.3 (C-7), 50.5 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=923.2012, found: $[M+Na]^+$=923.2016; $C_{49}H_{41}ClN_2O_{11}S$ (900.21).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(3-chlorophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-3-chlorostyrene) (2e)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-3-chlorobenzene (6 equiv., 0.20 mL, 0.32 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (4.5h). Purified by column chromatography (1:8 EtOAc–heptane) to yield 78 mg (42 %) of **2e** as a yellow amorphous product. R_f: 0.39 (1:2 EtOAc–hexane); $[\alpha]_D$ –35 (*c* 0.70, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.12–7.74 (8H, m, aromatics), 7.63–6.92 (16H, m, aromatics), 6.60 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.18 (1H, dd, $J_{2,3}$ 7.0 Hz, H-2), 5.97 (1H, pseudo t, $J_{5,6}$ 9.8 Hz, H-5), 5.73 (1H, pseudo t, $J_{6,7}$ 9.8 Hz, H-6), 5.50 (1H, pseudo t, 1H, $J_{4,5}$ 9.5 Hz, H-4), 4.65 (1H, dd, $J_{8a,8b}$ 12.2 Hz, H-8_a), 4.48 (1H, dd, H-8_b), 4.36 (1H, dd, $J_{3,4}$ 9.2 Hz, H-3), 4.19 (1H, ddd, $J_{7,8a}$ 2.9, $J_{7,8b}$ 5.0 Hz, H-7). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.3, 166.1, 165.4, 165.3 (4×CO), 133.5 (C-1), 145.5–125.2 (aromatics), 124.9 (C-2), 79.6 (C-3), 76.2 (C-7), 74.2 (C-5), 72.4 (C-4), 69.8 (C-6), 63.4 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=739.1705, found: $[M+Na]^+$=739.1710; $C_{42}H_{33}ClO_9$ (716.18).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(4-bromophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-4-bromo-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)styrene) (2f)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-4-bromobenzene (6 equiv., 0.39 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (4h). Purified by column chromatography (1:8 EtOAc–heptane) to yield 107 mg (54 %) of **2f** as a yellow amorphous product. R_f: 0.36 (1:2 EtOAc–hexane); $[\alpha]_D$ –49 (*c* 2.10, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09–7.75 (8H, m, aromatics), 7.58–7.16 (14H, m, aromatics), 7.09 (2H, d, *J* 8.5 Hz, aromatics), 6.59 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.16 (1H, dd, $J_{2,3}$ 7.2 Hz, H-2) 5.96 (1H, pseudo t, $J_{5,6}$ 9.6 Hz, H-5), 5.73 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.49 (1H, pseudo t, $J_{4,5}$ 9.6 Hz, H-4), 4.65 (1H, dd, $J_{8a,8b}$ 12.2 Hz, H-8_a), 4.48 (1H, dd, H-8_b), 4.36 (1H, dd, $J_{3,4}$ 9.2 Hz, H-3), 4.19 (1H, ddd, $J_{7,8a}$ 2.9, $J_{7,8b}$ 4.8 Hz, H-7). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.3, 166.1, 165.5, 165.4 (4×CO), 133.7 (C-1), 135.5–122.0 (aromatics), 125.1 (C-2), 79.8 (C-3), 76.2 (C-7), 74.2 (C-5), 72.4 (C-4), 69.8 (C-6), 63.4 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=783.1200, found: $[M+Na]^+$=783.1219; $C_{42}H_{33}BrO_9$ (760.13).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(3-bromophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-3-bromo-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)styrene) (2g)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-3-bromobenzene (6 equiv., 0.39 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (20h). Purified by column chromatography (1:7 EtOAc–hexane) to yield 63 mg (32 %) of **2g** as a yellow amorphous product. R_f: 0.39 (1:2 EtOAc–hexane); $[\alpha]_D$ –20 (*c* 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–7.78 (8H, m, aromatics), 7.62–6.99 (16H, m, aromatics), 6.60 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.19 (1H, dd, $J_{2,3}$ 7.0 Hz, H-2), 5.99 (1H, pseudo t, $J_{5,6}$ 9.5 Hz, H-5), 5.76 (1H, pseudo t, $J_{6,7}$ 9.8 Hz, H-6), 5.52 (1H, pseudo t, $J_{4,5}$ 9.8 Hz, H-4), 4.67 (1H, dd, $J_{8a,8b}$ 12.3 Hz, H-8_a), 4.51 (1H, dd, H-8_b), 4.40 (1H, dd, $J_{3,4}$ 9.2 Hz, H-3), 4.23 (1H, ddd, $J_{7,8a}$ 2.3, $J_{7,8b}$ 4.7 Hz, H-7). ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.3, 166.0, 165.4, 165.3 (4×CO), 133.8 (C-1), 145.3–122.4 (aromatics), 125.3 (C-2), 79.6 (C-3), 76.2 (C-7), 74.3 (C-5), 72.4 (C-4), 69.8 (C-6), 63.4 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=783.1200, found: $[M+Na]^+$=783.1211; $C_{42}H_{33}BrO_9$ (760.13).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(3-bromobenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-3-bromobenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4g)

Isolated as a by-product beside **2g** from the previous reaction mixture by column chromatography (1:7 EtOAc–hexane) to yield 13 mg (5 %) of **4g** as a white amorphous product. R_f: 0.31 (1:2 EtOAc–hexane); $[\alpha]_D$ –7 (*c* 0.29, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–7.71 (8H, m, aromatics), 7.67–7.19 (16H, m, aromatics), 7.18–6.88 (4H, m, aromatics), 6.82 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.89 (1H, pseudo t, $J_{4,5}$ 9.9 Hz, H-4), 5.63 (1H, pseudo t, $J_{5,6}$ 9.9 Hz, H-5), 5.34 (1H, pseudo t, $J_{3,4}$ 9.6 Hz, H-3), 4.80 (1H, d, $J_{CH2a,CH2b}$ 16.8 Hz, CH_{2a}), 4.65 (1H, d, CH_{2b}), 4.54 (1H, dd, $J_{7a,7b}$ 12.3 Hz, H-7_a), 4.40 (1H, dd, H-7_b), 4.34 (1H, dd, $J_{2,3}$ 9.9 Hz, H-2), 4.13 (1H, ddd, $J_{6,7a}$ 2.8, $J_{6,7b}$ 5.1 Hz, H-6), 2.22 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.9, 165.5, 165.3 (4×CO), 133.3 (C-1), 144.5–123.1 (aromatics), 78.8 (C-2), 76.3 (C-6), 73.7 (C-4), 71.0 (C-3), 69.4 (C-5), 63.3 (C-7), 50.6 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=967.1507, found: $[M+Na]^+$=967.1519; $C_{49}H_{41}BrN_2O_{11}S$ (944.16).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(2-bromophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-2-bromo-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)styrene) (2h)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-2-bromobenzene (6 equiv., 0.39 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (21h). Purified by column chromatography (1:7 EtOAc–hexane) to yield 71 mg

(36 %) of **2h** as pale yellow amorphous product. R_f: 0.43 (1:2 EtOAc–hexane); $[\alpha]_D$ –13 (*c* 0.40, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$) δ 8.23–7.73 (8H, m, aromatics), 7.68–7.13 (15H, m, aromatics), 7.11–7.04 (1H, m, aromatic), 7.01 (1H, d, $J_{1,2}$ 15.8 Hz, H-1), 6.13 (1H, dd, $J_{2,3}$ 7.3 Hz, H-2) 5.99 (1H, pseudo t, $J_{5,6}$ 9.9 Hz, H-5), 5.75 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.53 (1H, pseudo t, $J_{4,5}$ 9.6 Hz, H-3), 4.68 (1H, dd, $J_{8a,8b}$ 12.2 Hz, H-8_a), 4.50 (1H, dd, H-8_b), 4.45 (1H, dd, $J_{3,4}$ 9.2 Hz, H-3), 4.23 (1H, ddd, $J_{7,8a}$ 2.8, $J_{7,8b}$ 4.9 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.1, 165.6, 165.4 (4×CO), 133.8 (C-1), 136.4–123.4 (aromatics), 127.3 (C-2), 79.9 (C-3), 76.2 (C-7), 74.3 (C-5), 72.3 (C-4), 69.9 (C-6), 63.4 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=783.1200, found: $[M+Na]^+$=783.1211; $C_{42}H_{33}BrO_9$ (760.13).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(2-bromobenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-2-bromobenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4h)

Isolated as a by-product beside **2h** from the previous reaction mixture by column chromatography (1:7 EtOAc–hexane) to yield 4 mg (2 %) of **4h** as a white amorphous product. R_f: 0.27 (1:2 EtOAc–hexane); $[\alpha]_D$ +3 (*c* 0.60, $CHCl_3$).^1H NMR (400 MHz, $CDCl_3$) δ 8.15–7.70 (8H, m, aromatics), 7.69–7.19 (14H, m, aromatics), 7.15–6.89 (6H, m, aromatics), 6.84 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.86 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 5.61 (1H, pseudo t, $J_{5,6}$ 9.8 Hz, H-5), 5.34 (1H, pseudo t, $J_{3,4}$ 9.7 Hz, H-3), 4.78 (1H, d, $J_{CH2a,CH2b}$ 16.5 Hz, CH_{2a}), 4.65 (1H, d, CH_{2b}), 4.52 (1H, dd, $J_{7a,7b}$ 12.3 Hz, H-7_a), 4.40 (1H, dd, H-7_b), 4.34 (1H, dd, $J_{2,3}$ 9.9 Hz, H-2), 4.11 (1H, ddd, $J_{6,7a}$ 2.8, $J_{6,7b}$ 5.0 Hz, H-6), 2.23 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.9, 165.3 (4×CO), 139.5 (C-1), 144.8–120.7 (aromatics), 78.7 (C-2), 76.3 (C-6), 73.9 (C-4), 70.8 (C-3), 69.4 (C-5), 63.3 (C-7), 51.1 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=967.1507, found: $[M+Na]^+$=967.1506; $C_{49}H_{41}BrN_2O_{11}S$ (944.16).

3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1,2-dideoxy-1-(4-nitrophenyl)-D-*glycero*-D-*gulo*-oct-1-enitol (ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-4-nitrostyrene) (2i)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 1-bromomethyl-4-nitrobenzene (6 equiv., 0.33 g, 1.54 mmol) and LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (19h). Purified by column chromatography (1:7 EtOAc–hexane) to yield 74 mg (40 %) (*E*/*Z* = 1:1) of **2i** as an orange amorphous product. R_f: 0.34 (1:2 EtOAc–hexane). *E* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.32–7.68 (8H, m, aromatics), 7.66–7.13 (16H, m, aromatics), 6.74 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.36 (1H, dd, $J_{2,3}$ 6.7 Hz, H-2), 6.00 (1H, pseudo t, $J_{5,6}$ 10.0 Hz, H-5), 5.76 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.51 (1H, pseudo t, $J_{4,5}$ 9.6 Hz, H-4), 4.69 (1H, dd, $J_{8a,8b}$ 12.4 Hz, H-8_a), 4.50 (1H, dd, H-8_b), 4.43 (1H, dd, $J_{3,4}$ 9.9 Hz, H-3), 4.22 (1H, ddd, $J_{7,8a}$ 2.7, $J_{7,8b}$ 5.0 Hz, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.0, 165.5, 165.4 (4×CO), 147.6–110.7 (C-1, C-2, aromatics), 79.3 (C-3), 76.3 (C-7), 73.9 (C-5), 72.4 (C-4), 69.7 (C-6), 63.3 (C-8). *Z* isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.32–7.68 (8H, m, aromatics), 7.66–7.13 (16H, m, aromatics), 6.81 (1H, d, $J_{1,2}$ 11.6 Hz, H-1), 6.01 (1H, dd, $J_{2,3}$ 2.5 Hz, H-2), 5.89 (1H, pseudo t, $J_{5,6}$ 9.6 Hz, H-5), 5.69 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.64 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 4.66 (1H, dd, $J_{7,8a}$ 2.5, $J_{8a,8b}$ 12.6 Hz, H-8_a), 4.56–4.45 (2H, m, H-3, H-8_b), 4.27–4.15 (1H, m, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.0, 165.4 (4×CO), 147.6–110.7 (C-1, C-2, aromatics), 76.4 (C-7), 74.5 (C-3), 74.1 (C-5), 72.5 (C-4), 69.8 (C-6), 63.7 (C-8). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=750.1946, found: $[M+Na]^+$=750.1939; $C_{42}H_{33}NO_{11}$ (727.21).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(4-nitrobenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-4-nitrobenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4i)

Isolated as a by-product beside **2i** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 39 mg (16 %) of **4i** as a yellow amorphous product. R_f: 0.23 (1:2 EtOAc–hexane); $[\alpha]_D$ –4 (*c* 0.60, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.23–7.61 (12H, m, aromatics), 7.60–7.20 (14H, m, aromatics), 6.98 (2H, d, *J* 8.3 Hz, aromatics), 6.75 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.88 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 5.63 (1H, pseudo t, $J_{5,6}$ 9.6 Hz, H-5), 5.31 (1H, pseudo t, $J_{3,4}$ 9.6 Hz, H-3), 4.85 (2H,s, CH_2), 4.56 (1H, dd, $J_{7a,7b}$ 12.4 Hz, H-7_a), 4.39 (1H, dd, H-7_b), 4.35 (1H, dd, $J_{2,3}$ 9.9 Hz, H-2), 4.13 (1H, ddd, $J_{6,7a}$ 2.6, $J_{6,7b}$ 5.3 Hz, H-6), 2.25 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 165.9, 165.5, 165.3 (4×CO), 140.4 (C-1), 147.8–123.5 (aromatics), 78.6 (C-2), 76.4 (C-6), 73.6 (C-4), 70.9 (C-3), 69.3 (C-5), 63.1 (C-7), 50.5 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=934.2252, found: $[M+Na]^+$=934.2245; $C_{49}H_{41}N_3O_{13}S$ (911.24).

(*E*)-3,7-Anhydro-4,5,6,8-tetra-*O*-benzoyl-1-(4-cyanophenyl)-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol ((*E*)-4-cyano-ω-(*C*-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)styrene) (2j)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 4-bromomethyl benzonitrile (6 equiv., 0.30 g, 1.54 mmol), LiO*t*Bu (1.5 equiv., 0.03 g, 0.39 mmol), P(2-furyl)$_3$ (4 equiv., 0.24 g, 1.02 mmol) and $Pd_2(dba)_3$ (50 mol%, 0.12 g, 0.13 mmol) according to General procedure (20.5h). Purified by column chromatography (1:8 EtOAc–hexane) to yield 100 mg (55 %) of **2j** as a pale yellow amorphous product. R_f: 0.26 (1:2 EtOAc–hexane); $[\alpha]_D$ –45 (*c* 1.75, $CHCl_3$).^1H NMR (400 MHz, $CDCl_3$) δ 8.16–7.74 (8H, m, aromatics), 7.62–7.18 (16H, m, aromatics), 6.69 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.31 (1H, dd, $J_{2,3}$ 6.8 Hz, H-2), 6.00 (1H, pseudo t, $J_{5,6}$ 9.6 Hz, H-5), 5.76 (1H, pseudo t, $J_{6,7}$ 9.9 Hz, H-6), 5.51 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 4.69 (1H, dd $J_{8a,8b}$ 12.3 Hz, H-8_a), 4.51 (1H, dd, H-8_b), 4.42 (1H, dd, $J_{3,4}$ 9.6 Hz, H-3), 4.23 (1H, ddd, $J_{7,8a}$ 2.8, $J_{7,8b}$ 4.8 Hz, H-7). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 166.0, 165.5, 165.3 (4×CO), 132.6 (C-1), 140.7–118.7 (aromatics), 128.2 (C-2), 111.6 (CN), 79.3 (C-3), 76.3 (C-7), 74.1 (C-5), 72.4 (C-4), 69.7 (C-6), 63.3 (C-8). HR-ESI-MS positive mode (*m*/*z*). calcd. for: $[M+Na]^+$=730.2048, found: $[M+Na]^+$=730.2038; $C_{43}H_{33}NO_9$ (707.22).

2,6-Anhydro-3,4,5,7-tetra-*O*-benzoyl-*N*^{1}-(4-cyanobenzyl)-D-*glycero*-D-*gulo*-heptose tosylhydrazone (*N*^{1}-4-cyanobenzyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (4j)

Isolated as a by-product beside **2j** from the previous reaction mixture by column chromatography (1:8 EtOAc–hexane) to yield 15 mg (7 %) of **4j** as a pale yellow amorphous product. R_f: 0.14 (1:2 EtOAc–hexane); $[\alpha]_D$ –9 (*c* 1.40, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.16–7.70 (8H, m, aromatics), 7.68–7.13 (18H, m, aromatics), 6.97 (2H, d, *J* 8.2 Hz, aromatics), 6.75 (1H, d, $J_{1,2}$ 6.6 Hz, H-1), 5.89 (1H, pseudo t, $J_{4,5}$ 9.5 Hz, H-4), 5.63 (1H, pseudo t, $J_{5,6}$ 10.0 Hz, H-5), 5.32 (1H, pseudo t, $J_{3,4}$ 9.8 Hz, H-3), 4.80 (2H, s, CH_2), 4.56 (1H, dd, $J_{7a,7b}$ 12.3 Hz, H-7_a), 4.39 (1H, dd, H-7_b), 4.35 (1H, dd, $J_{2,3}$ 9.8 Hz, H-2), 4.14 (1H, ddd, $J_{6,7a}$ 2.7, $J_{6,7b}$ 4.9 Hz, H-6), 2.24 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 165.8, 165.4, 165.2 (4×CO), 140.2 (C-1), 145.5–118.2 (aromatics), 111.9 (CN), 78.5 (C-2), 76.3 (C-6), 73.6 (C-4), 70.8 (C-3), 69.3 (C-5), 63.1 (C-7), 50.6 (CH_2), 21.8 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=914.2354, found: $[M+Na]^+$=914.2358; $C_{50}H_{41}N_3O_{11}S$ (891.25).

(*E*)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-1-phenyl-D-*glycero*-L-*manno*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)styrene) (7a)

10.1002/adsc.201801059

Prepared from tosylhydrazone **6** (0.20 g, 0.38 mmol), (bromomethyl)benzene (6 equiv., 0.27 mL, 0.39 g, 2.27 mmol) and LiO*t*Bu (1.5 equiv., 0.05 g, 0.57 mmol) according to General procedure (4h). Purified by column chromatography (1:2 EtOAc–heptane) to yield 98 mg (59 %) of **7a** as an orange amorphous product. R_f: 0.42 (1:1 EtOAc–hexane); $[\alpha]_D$ –3 (*c* 0.55, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.14 (5H, m, aromatics), 6.66 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.11 (1H, dd, $J_{2,3}$ 7.8 Hz, H-2), 5.48 (1H, dd, $J_{6,7}$ 0.9 Hz, H-6), 5.25 (1H, pseudo t, $J_{4,5}$ 10.2 Hz, H-4), 5.13 (1H, dd, $J_{5,6}$ 3.4 Hz, H-5), 4.17 (1H, dd, $J_{8a,8b}$ 13.5 Hz, H-8_a), 4.13 (1H, dd, H-8_b), 4.02 (1H, dd, $J_{3,4}$ 9.8 Hz, H-3), 4.00 (1H, ddd, $J_{7,8a}$ 6.6, $J_{7,8b}$ 6.6 Hz, H-7), 2.18, 2.05, 2.00, 1.95 (12H, 4s, 4×CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.4, 170.3, 169.8 (4×CO), 135.1 (C-1), 136.0–111.0 (aromatics), 124.3 (C-2), 80.3 (C-3), 74.1 (C-7), 71.8 (C-5), 68.8 (C-4), 67.8 (C-6), 61.8 (C-8), 20.8, 20.7 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=434.1469, found: $[M+Na]^+$=457.1468; $C_{22}H_{26}O_9$ (434.16). NMR spectra are identical with those reported.[6]

(*E*)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-1-(4-methylphenyl)-D-*glycero*-L-*manno*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-methylstyrene) (7b)

Prepared from tosylhydrazone **6** (0.10 g, 0.19 mmol), 1-bromomethyl-4-methylbenzene (3 equiv., 0.11 g, 0.57 mmol) and LiO*t*Bu (2.2 equiv., 0.03 g, 0.42 mmol) according to General procedure (2.5h). Purified by column chromatography (1:5 EtOAc–heptane) to yield 33 mg (39 %) of **7b** as an orange amorphous product. R_f: 0.45 (1:1 EtOAc–hexane); $[\alpha]_D$ –7 (*c* 0.70, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$) δ 7.37–6.98 (4H, m, aromatics), 6.62 (1H, d, $J_{1,2}$ 15.8 Hz, H-1), 6.06 (1H, dd, $J_{2,3}$ 7.9 Hz, H-2), 5.48 (1H, dd, $J_{6,7}$ 0.8 Hz, H-6), 5.24 (1H, pseudo t, $J_{4,5}$ 10.2 Hz, H-4), 5.11 (1H, dd, $J_{5,6}$ 3.4 Hz, H-5), 4.14 (2H, m, H-8_a, H-8_b), 4.03–3.93 (2H, m, H-3, H-7), 2.34 (3H, s, CH_3), 2.18, 2.06, 2.00, 1.95 (12H, 4s, 4×CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 170.5, 170.4, 169.9 (4×CO), 135.3 (C-1), 138.5–125.2 (aromatics), 123.4 (C-2), 80.6 (C-3), 74.3 (C-7), 71.9 (C-5), 68.9 (C-4), 67.9 (C-6), 62.0 (C-8), 21.4 (CH_3), 20.9, 20.8 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=471.1626, found: $[M+Na]^+$=471.1626; $C_{23}H_{28}O_9$ (448.17).

(*E*)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1,2-dideoxy-1-(3-methylphenyl)-D-*glycero*-L-*manno*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-methylstyrene) (7c)

Prepared from tosylhydrazone **6** (0.20 g, 0.38 mmol), 1-bromomethyl-3-methylbenzene (6 equiv., 0.31 mL, 0.42 g, 2.27 mmol) and LiO*t*Bu (1.5 equiv., 0.05 g, 0.57 mmol) according to General procedure (2.5h). Purified by column chromatography (1:4 EtOAc–heptane) to yield 43 mg (25 %) of **7c** as a white amorphous product. R_f: 0.45 (1:1 EtOAc–hexane); $[\alpha]_D$ –6 (*c* 0.35, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$) δ 7.36–6.95 (4H, m, aromatics), 6.61 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.09 (1H, dd, $J_{2,3}$ 7.8 Hz, H-2), 5.47 (1H, dd, $J_{6,7}$ 1.1 Hz, H-6), 5.24 (1H, pseudo t, $J_{4,5}$ 10.2 Hz, H-4), 5.11 (1H, dd, $J_{5,6}$ 3.4 Hz, H-5), 4.21–4.09 (2H, m, H-8_a, H-8_b), 4.06–3.93 (2H, m, H-3, H-7), 2.33 (3H, s, CH_3), 2.17, 2.04, 1.99, 1.94 (15H, 5s, 5×CH_3). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 169.8 (4×CO), 135.4 (C-1), 138.4–124.0 (aromatics), 124.2 (C-2), 80.4 (C-3), 74.2 (C-7), 71.9 (C-5), 68.9 (C-4), 67.9 (C-6), 61.9 (C-8), 21.5 (CH_3), 20.9, 20.8 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=471.1626, found: $[M+Na]^+$=471.1631; $C_{23}H_{28}O_9$ (448.17).

3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-N^1-(3-methylbenzyl)-D-*glycero*-L-*manno*-heptose tosylhydrazone (N^1-3-methylbenzyl-*C*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)formaldehyde tosylhydrazone) (9c)

Isolated as a by-product beside **7c** from the previous reaction mixture by column chromatography (1:4 EtOAc–heptane) to yield 16 mg (7 %) of **9c** as a white amorphous product. R_f: 0.36 (1:1 EtOAc–heptane); $[\alpha]_D$ –10 (*c* 0.35, $CHCl_3$).^1H NMR (250 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* 8.3 Hz, aromatics), 7.34 (2H, d, *J* 8.0 Hz, aromatics), 7.25–6.97 (4H, m, aromatics), 6.66 (1H, d, $J_{1,2}$ 6.5 Hz, H-1), 5.39 (1H, dd, $J_{5,6}$ 0.8 Hz, H-5), 5.10–5.00 (2H, strongly coupled, H-3, H-4), 4.94 (1H, d, $J_{CH2a,CH2b}$ 16.9 Hz, CH_{2a}), 4.60 (1H, d, CH_{2b}), 4.03 (1H, dd, $J_{7a,7b}$ 12.5 Hz, H-7_a), 3.98 (1H, dd, H-7_b), 3.93 (1H, strongly coupled, H-2), 3.86 (1H, ddd, $J_{6,7a}$ 6.5, $J_{6,7b}$ 6.8 Hz, H-6), 2.43 (3H, s, CH_3-Ts), 2.34 (3H, s, CH_3), 2.10, 2.02, 1.95, 1.65 (12H, 4s, 4×CH_3). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.5, 170.3, 170.1 (4×CO), 139.9 (C-1), 144.5–123.3 (aromatics), 79.0 (C-2), 74.4 (C-6), 71.3 (C-4), 67.6 (C-5), 67.0 (C-3), 61.6 (C-7), 51.1 (CH_2), 21.7 (CH_3-Ts), 21.6 (CH_3), 20.8, 20.7, 20.3 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=655.1932, found: $[M+Na]^+$=655.1948; $C_{30}H_{26}N_2O_{11}S$ (632.20).

(*E*)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-(3-chlorophenyl)-1,2-dideoxy-1-D-*glycero*-L-*manno*-oct-1-enitol ((*E*)-ω-(*C*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-chlorostyrene) (7d)

Prepared from tosylhydrazone **6** (0.20 g, 0.38 mmol), 1-bromomethyl-3-chlorobenzene (6 equiv., 0.30 mL, 0.47 g, 2.27 mmol) and LiO*t*Bu (1.5 equiv., 0.05 g, 0.57 mmol) according to General procedure (4.5h). Purified by column chromatography (1:4 EtOAc–heptane) to yield 104 mg (59 %) of **7d** as a yellow amorphous product. R_f: 0.42 (1:1 EtOAc–hexane); $[\alpha]_D$ –2 (*c* 0.80, $CHCl_3$).^1H NMR (250 MHz, $CDCl_3$) δ 7.60–7.12 (4H, m, aromatics), 6.59 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.12 (1H, dd, $J_{2,3}$ 7.5 Hz, H-2), 5.47 (1H, dd, $J_{6,7}$ 1.1 Hz, H-6), 5.23 (1H, pseudo t, $J_{4,5}$ 10.2 Hz, H-4), 5.11 (1H, dd, $J_{5,6}$ 3.3 Hz, H-5), 4.17–4.10 (2H, m, H-8_a, H-8_b), 4.05–3.93 (2H, m, H-3, H-7), 2.17, 2.04, 1.99, 1.96 (12H, 4s, 4×CH_3). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 169.8 (4×CO), 133.5 (C-1), 145.4–124.8 (aromatics), 125.0 (C-2), 79.9 (C-3), 74.3 (C-7), 71.8 (C-5), 68.8 (C-4), 67.8 (C-6), 61.9 (C-8), 20.9, 20.8 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=491.1079, found: $[M+Na]^+$=491.1077; $C_{22}H_{25}ClO_9$ (468.12).

(*E*)-4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-(4-bromophenyl)-1,2-dideoxy-D-*glycero*-L-*manno*-oct-1-enitol ((*E*)-4-bromo-ω-(*C*-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)styrene) (7e)

Prepared from tosylhydrazone **6** (0.20 g, 0.38 mmol), 1-bromomethyl-4-bromobenzene (6 equiv., 0.57 g, 2.27 mmol) and LiO*t*Bu (1.5 equiv., 0.05 g, 0.57 mmol) according to General procedure (2.5h). Purified by column chromatography (1:4 EtOAc–heptane) to yield 59 mg (31 %) of **7e** as a pale yellow amorphous product. R_f: 0.42 (1:1 EtOAc–hexane); $[\alpha]_D$ –7 (*c* 0.80, $CHCl_3$).^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* 8.4 Hz, aromatics), 7.23 (2H, d, *J* 8.4 Hz, aromatics), 6.60 (1H, d, $J_{1,2}$ 15.9 Hz, H-1), 6.11 (1H, dd, $J_{2,3}$ 7.7 Hz, H-2), 5.48 (1H, dd, $J_{6,7}$ 0.8 Hz, H-6), 5.23 (1H, pseudo t, $J_{4,5}$ 10.2 Hz, H-4), 5.12 (1H, dd, $J_{5,6}$ 3.3 Hz, H-5), 4.19–4.09 (2H, m, H-8_a, H-8_b), 4.01 (1H, dd, $J_{2,3}$ 9.7 Hz, H-3), 3.98 (1H, ddd, $J_{6,7a}$ 6.6, $J_{6,7b}$ 6.3 Hz, H-7), 2.18, 2.05, 2.00, 1.95 (12H, 4s, 4×CH_3). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 169.8 (4×CO), 133.8 (C-1), 145.4–122.8 (aromatics), 125.3 (C-2), 80.1 (C-3), 74.3 (C-7), 71.8 (C-5), 68.8 (C-4), 67.8 (C-6), 61.9 (C-9), 20.9, 20.8 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=535.0574, found: $[M+Na]^+$=535.0571; $C_{22}H_{25}BrO_9$ (512.07).

3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-N^1-(4-bromobenzyl)-D-*glycero*-L-*manno*-heptose tosylhydrazone (N^1-4-bromobenzyl-*C*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)formaldehyde tosylhydrazone) (9e)

Isolated as a by-product beside **7e** from the previous reaction mixture by column chromatography (1:4 EtOAc–heptane) to yield 24 mg (9 %) of **9e** as a yellow amorphous product. R_f: 0.36 (1:1 EtOAc–hexane); $[\alpha]_D$ –8 (*c* 0.60, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (2H, d, *J* 8.3 Hz, aromatics), 7.49 (2H, d, *J* 8.4 Hz, aromatics), 7.35 (2H, d, *J* 8.1 Hz, aromatics), 7.16 (2H, d, *J* 8.4 Hz, aromatics), 6.61 (1H, d, $J_{1,2}$ 6.5 Hz, H-1), 5.40 (1H, dd, $J_{5,6}$ 1.0 Hz, H-5), 5.04 (1H, dd, $J_{4,5}$ 4.8 Hz, H-4), 5.03 (1H, pseudo t, $J_{3,4}$ 10.2 Hz, H-3), 4.92 (1H, d, $J_{CH2a,CH2b}$ 16.9 Hz, CH_{2a}), 4.56 (1H, d, CH_{2b}), 4.03 (1H, dd, $J_{7a,7b}$ 13.4 Hz, H-7_a), 4.00 (1H, dd, H-7_b), 3.92 (1H, strongly coupled, H-2), 3.87 (1H, ddd, $J_{6,7a}$ 6.8, $J_{6,7b}$ 6.3 Hz, H-6), 2.44, (3H, s, CH_3-Ts), 2.12, 2.03, 1.96, 1.64 (12H, 4s, 4×CH_3). ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.9, 170.5, 170.2, 170.1 (4×CO), 140.2 (C-1), 144.7–121.6 (aromatics), 78.9 (C-2), 74.5 (C-6), 71.1 (C-4), 67.5 (C-5), 67.1 (C-3), 61.6 (C-7), 50.5 (CH_2), 21.7 (CH_3-Ts), 20.8, 20.7, 20.3 (4×CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=719.0881, found: $[M+Na]^+$=719.0879; $C_{29}H_{33}BrN_2O_{11}S$ (696.10).

N^1-Allyl-2,6-anhydro-3,4,5,7-tetra-*O*-benzoyl-D-*glycero*-D-*gulo*-heptose tosylhydrazone (N^1-allyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde tosylhydrazone) (10)

Prepared from tosylhydrazone **1** (0.20 g, 0.26 mmol), 3-bromoprop-1-ene (6 equiv., 0.13 mL, 0.19 g, 1.54 mmol) and Li*O*t*B*u (1.5 equiv., 0.03 g, 0.39 mmol) according to General procedure (22h). Purified by column chromatography (1:8 EtOAc–hexane) to yield 40 mg (18 %) of **10** as a yellow amorphous product. R_f: 0.33 (1:2 EtOAc–hexane); $[\alpha]_D$ +1 (*c* 0.79, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14–7.69 (8H, m, aromatics), 7.63–7.20 (14H, m, aromatics), 6.94 (1H, d, $J_{1,2}$ 6.7 Hz, H-1), 6.86 (2H, d, *J* 8.1 Hz, aromatics), 5.93 (1H, pseudo t, $J_{4,5}$ 9.7 Hz, H-4), 5.69 (1H, pseudo t, $J_{5,6}$ 10.0 Hz, H-5), 5.66–5.59 (1H, m, CH), 5.46 (1H, pseudo t, $J_{3,4}$ 9.7 Hz, H-3), 5.20–5.07 (2H, m, CH_2), 4.58 (1H, dd, $J_{7a,7b}$ 12.3 Hz, H-7_a), 4.45 (1H, dd, H-7_b), 4.39 (1H, dd, $J_{2,3}$ 9.8 Hz, H-2), 4.36–4.26 (1H, m, CH_{2a}), 4.25–4.18 (1H, m, CH_{2b}), 4.17 (1H, ddd, $J_{6,7a}$ 2.5, $J_{6,7b}$ 5.0 Hz, H-6), 2.19 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.9, 165.5, 165.3 (4×CO), 139.5 (C-1), 144.0–126.5 (aromatics, CH), 118.4 (CH_2), 78.9 (C-2), 76.3 (C-6), 73.8 (C-4), 71.0 (C-3), 69.4 (C-5), 63.3 (C-7), 49.0 (CH_2), 21.7 (CH_3). HR-ESI-MS positive mode (*m*/*z*): calcd. for: $[M+Na]^+$=839.2245, found: $[M+Na]^+$=839.2240; $C_{45}H_{40}N_2O_{11}S$ (816.24).

Acknowledgements

This work was supported by the National Research, Development and Innovation Office of Hungary (Grant K109450), by the EU co-financed by the European Regional Development Fund under the projects GINOP-2.3.2-15-2016-00008 and GINOP-2.3.3-15-2016-00004, as well as by the Alexander von Humboldt Foundation (Germany).

References

[1] É. Bokor, S. Kun, D. Goyard, M. Tóth, J.-P. Praly, S. Vidal, L. Somsák, *Chem. Rev.* **2017**, *117*, 1687-1764.

[2] Y. Yang, B. Yu, *Chem. Rev.* **2017**, *117*, 12281-12356.

[3] K. Kitamura, Y. Ando, T. Matsumoto, K. Suzuki, *Chem. Rev.* **2018**, *118*, 1495-1598.

[4] M. E. L. Sánchez, V. Michelet, I. Besnier, J.-P. Genêt, *Synlett* **1994**, 705-708.

[5] V. Michelet, K. Adiey, S. Tanier, G. Dujardin, J.-P. Genêt, *Eur. J. Org. Chem.* **2003**, 2947-2958.

[6] V. Khatri, A. Kumar, B. Singh, S. Malhotra, A. K. Prasad, *J. Org. Chem.* **2015**, *80*, 11169-11174.

[7] M. A. Leeuwenburgh, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Synlett* **1997**, 1263-1264.

[8] M. A. Leeuwenburgh, C. Kulker, H. I. Duynstee, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Tetrahedron* **1999**, *55*, 8253-8262.

[9] J. Zeng, S. Vedachalam, S. Xiang, X.-W. Liu, *Org. Lett.* **2011**, *13*, 42-45.

[10] G. M. Grotenbreg, A. W. Tuin, M. D. Witte, M. A. Leeuwenburgh, J. H. van Boom, G. A. van der Marel, H. S. Overkleeft, M. Overhand, *Synlett* **2004**, 0904-0906.

[11] M. D. P. Risseeuw, G. M. Grotenbreg, M. D. Witte, A. W. Tuin, M. A. Leeuwenburgh, G. A. Van der Marel, H. S. Overkleeft, M. Overhand, *Eur. J. Org. Chem.* **2006**, 3877-3886.

[12] B. Waldscheck, M. Streiff, W. Notz, W. Kinzy, R. R. Schmidt, *Angew. Chem., Int. Ed.* **2001**, *40*, 4007-4011.

[13] K. Sudarshan, I. S. Aidhen, *Eur. J. Org. Chem.* **2017**, 34-38.

[14] D. J. Hart, S. Patterson, J. P. Unch, *Synlett* **2003**, 1334-1338.

[15] A. Ghosez, T. Göbel, B. Giese, *Chem. Ber.* **1988**, *121*, 1807-1811.

[16] G. Stork, H. S. Suh, G. Kim, *J. Am. Chem. Soc.* **1991**, *113*, 7054-7056.

[17] D. Mazéas, T. Skrydstrup, O. Doumeix, J.-M. Beau, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1383.

[18] J. Désiré, A. Veyrières, *Carbohydr. Res.* **1995**, *268*, 177-186.

[19] I. Šnajdr, K. Parkan, F. Hessler, M. Kotora, *Beilstein J. Org. Chem.* **2015**, *11*, 1392-1397.

[20] J. Barluenga, C. Valdes, *Angew. Chem. Int. Edit.* **2011**, *50*, 7486-7500.

[21] Z. Shao, H. Zhang, *Chem. Soc. Rev.* **2012**, *41*, 560-572.

[22] Q. Xiao, Y. Zhang, J. B. Wang, *Acc. Chem. Res.* **2013**, *46*, 236-247.

[23] D. Qiu, F. Y. Mo, Y. Zhang, J. B. Wang, in *Advances in Organometallic Chemistry, Vol 67, Vol. 67* (Ed.: P. J. Perez), **2017**, pp. 151-219.

[24] Y. Xia, D. Qiu, J. B. Wang, *Chem. Rev.* **2017**, *117*, 13810-13889.

[25] M. Tóth, L. Somsák, *Tetrahedron Lett.* **2001**, *42*, 2723-2725.

[26] M. Tóth, K. E. Kövér, A. Bényei, L. Somsák, *Org. Biomol. Chem.* **2003**, *1*, 4039-4046.

[27] M. Tóth, L. Somsák, D. Goyard, in *Carbohydrate Chemistry: Proven Synthetic Methods, Vol. 1* (Ed.: P. Kováč), CRC Press, Boca Raton, **2012**, pp. 355-365.

[28] T. Kaszás, M. Tóth, S. Kun, L. Somsák, *RSC Adv.* **2017**, *7*, 10454-10462.

[29] T. Kaszás, M. Tóth, L. Somsák, *New. J. Chem.* **2017**, *41*, 13871-13880.

[30] T. Kaszás, A. Ivanov, M. Tóth, P. Ehlers, P. Langer, L. Somsák, *Carbohydr. Res.* **2018**, *466*, 30-38.

[31] Q. Xiao, J. Ma, Y. Yang, Y. Zhang, J. B. Wang, *Org. Lett.* **2009**, *11*, 4732-4735.

10.1002/adsc.201801059

FULL PAPER

C-Glycosyl styrene type compounds by Pd-catalyzed cross-coupling reactions of anhydro-aldose tosylhydrazones with benzyl bromides

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